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Spatial and regional aspects of health

Special Issue edited by **Anna-Theresa Renner**, **Rita Santos**, **Benedetta Pongiglione** and **Roman Hoffmann**

Table of Contents

continued on next page ...

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continued from previous page ...

This special issue on “”Spatial and regional aspects of health” is edited by Anna-Theresa Renner (Vienna Technical University, Vienna, Austria and Harvard University, Cambridge, USA), Rita Santos (University of York, York, United Kingdom), Benedetta Pongiglione (Bocconi University, Milan, Italy) and Roman Hoffmann (Austrian Academy of Sciences, Vienna, Austria and International Institute for Applied Systems Analysis, Laxenburg, Austria). With the exception of the editorial, all contributions to this special issue have already been published in earlier issues of REGION, for the sake of immediate exposure of the content.

- *The determinants of Covid-19 mortality rates across Europe: Assessing the role of demographic and socioeconomic factors during the first wave of the pandemic* by Yannis Psycharis, Cleon Tsimbos, Georgia Verropoulou and Leonidas Doukissas was originally published in vol. 8, nr. 1, 199–219.
- *Spatial analysis of the COVID-19 pandemic in Hungary: Changing epidemic waves in time and space* by Annamária Uzzoli, Sándor Zsolt Kovács, Attila Fábián, Balázs Páger and Tamás Szabó was originally published in vol. 8, nr. 2, 147–165.
- *Flatten the Curve! Modeling SARS-CoV-2/COVID-19 growth in Germany at the county level* by Thomas Wieland was originally published in vol. 7, nr. 2, 43–83.
- *The Pandemic Economy: Exploring the change in new business license activity in Chicago, USA from March – September, 2020* by Kevin Credit and Emma van Lieshout was originally published in vol. 8, nr. 2, 29–56.
- *Territorial cohesion, the COVID-19 crisis and the urban paradox: Future challenges in urbanization and economic agglomeration* by Panagiotis Artelaris and George Mavrommatis was originally published in vol. 9, nr. 1, 135–146.
- *The promise of endogenous potential in times of crisis – Analysis of the effects of the COVID pandemic on the socio-economic embeddedness in local economies* by Anna Herzog and Marieke Vomberg was originally published in vol. 8, nr. 2, 99–120.
- *Urban tourism and Covid-19 in Poland* by Karolina Józefowicz was originally published in vol. 8, nr. 2, 187–199.
- *Approximating the impact of COVID–19 on regional production in countries with scarce subnational data: A proposal and application for Argentina during the first wave* by Andrés Niembro and Carla Daniela Calá was originally published in vol. 8, nr. 2, 167–186.
- *Isolation and well-being in the time of lockdown* by Lise Bourdeau Lepage and Balázs Kotosz was originally published in vol. 8, nr. 2, 83–97.
- *Regional innovation systems of medical technology: A knowledge production function of cardiovascular research and funding in Europe* by Rucha Vadia and Katharina E. Blankart was originally published in vol. 8, nr. 2, 57–81.

- *EU funds as a catalyst of change for the Slovak healthcare system?* by Jan Fidrmuc, Kristína Gardoňová, Martin Hulényi, Lukáš Sekelský and Veronika Zlaczká was originally published in vol. 9, nr. 1, 29–49

- *Antibiotic self-medication and antibiotic resistance: Multilevel regression analysis of repeat cross-sectional survey data in Europe* by Alistair Anderson was originally published in vol. 8, nr. 2, 121–145.

- *Spatial health inequality and regional disparities: Historical evidence from Italy* by Marco Percoco was originally published in vol. 8, nr. 1, 53–73.

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Editorials

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Editorial for the Special Issue "Spatial and regional aspects of health"

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Abstract. The health crisis caused by the COVID-19 pandemic highlights, more than ever, the necessity of scientific research to inform policy action. During such a crisis it is vital that any measure taken by policy makers mitigates the consequences on health without causing long-lasting social and economic harm. Spatial aspects play an important role here: knowledge about the spread of a disease through space and social networks, the effectiveness of different policy responses, and the economic and social implications for the population are of particular relevance. As any policy action is embedded in its institutional and social environment, not every measure is effective in all contexts. Moreover, infectious diseases can spread at different speed in different places, requiring tailored interventions. Careful evaluation and comparison of different settings, including the organization of the healthcare systems and the geographic and demographic characteristics of a region or country, are therefore essential. The COVID-19 pandemic has made manifest the importance of the spatial and geographical dimension of health, however, the relevance of this interlinkage is not limited to the spread of contagious diseases. Differences in accessibility of services between urban and rural regions, the varying costs of access to healthcare for different (socioeconomic) groups of the population, the impact of these on healthcare utilization, and environmental shocks on population health are just a few examples illustrating the close link between space, socioeconomic factors and health.

This special issue of REGION is presented in two parts. In the first part, papers explore the spread and impact of the COVID-19 pandemic on the health and economy. In the second part, papers investigate regional and spatial aspects of the healthcare sector with a focus on health disparities.

1 Introduction

Health and space are highly associated. This is reflected in the plethora of research that studies spatial aspects of health in different ways, for example, as spatial patterns of diseases and mortality (e.g. Marshall 1991, Lawson 2018, Kulldorff, Nagarwalla 1995, Santos et al. 2020, Nowakowska et al. 2021), geographical distribution of healthcare services and their utilization (e.g. Santana et al. 2009, Gravelle et al. 2014, 2019, Longo et al. 2017, Okoli et al. 2020, Shinjo, Aramaki 2012, Pongiglione et al. 2020, Renner 2020), or environmental shocks on population health (Gemmell et al. 2000, Analitis et al. 2008, Almendra et al. 2017).

There is ample evidence that regional disparities in mortality and life-expectancy exist (Taulbut et al. 2013, Dwyer-Lindgren et al. 2017), and that they are persistent or even increasing in many European countries – with the notable exception of Germany (van Raalte et al. 2020). Often these differences in health are associated with differences in economic indicators such as wealth, income levels, or unemployment. This association has been proven to be causal at the individual level, as monetary and non-monetary resources increase the ability to improve health (e.g. Pickett, Wilkinson 2015), either through healthcare utilization or through behavioural changes in life-style (e.g. Ploubidis et al. 2019, Mackenbach et al. 2019). On the other hand, a reversed causal pathway is also conceivable: health as part of the human capital has been shown to positively affect regional economies (Gumbau Albert 2021).

Regional health inequalities are of interest to researchers not only because of their economic implications, but also because they constitute a form of inadmissible unfairness if they are merely due to the (rather arbitrary) place of residence (Fleurbaey, Schokkaert 2009). Policy makers oriented towards social welfare, therefore, try to attenuate regional inequities – at least within their own country. To inform respective actions, GIS-based methods, developed and established in the fields of regional science and geography, are increasingly used to generate policy-relevant evidence on the association between space and health. Additionally, the explicit modelling of spatial dependencies and spillovers between geographic regions has been shown to be of importance in quantitative health(care) research (e.g. Tosetti et al. 2018, Baltagi et al. 2018, Moscone et al. 2007, Atella et al. 2014).

Another relevant field of study where health and space meet, is the analysis and planning of the geographic distribution of healthcare providers. A fair and efficient distribution of healthcare resources, such as hospitals, outpatient doctors, pharmacies etc., is a necessary condition for needs-based utilization to eventually reduce regional health inequalities (Chandra, Skinner 2003, Santos et al. 2020, Moscone et al. 2019).

The public health crisis caused by the COVID-19 pandemic highlighted, more than ever, the necessity of scientific research to inform policy action and the role played by space in our understanding of health disparities (Bourdin et al. 2021, Jeanne et al. 2022). For example, Ji et al. (2020) show that early on in the pandemic, mortality rates differed considerably among different Chinese provinces. The authors hypothesise that those disparities can be at least partly attributed to differences in healthcare resources availability. Rodrigueze-Pose, Burlina (2021) studied excess mortality during the first wave of the Covid-19 pandemic in 206 European regions across 23 countries. They found that in addition to health system endowment, regional factors such as pollution, climate, as well as institutional and government capacities were drivers of increased death rates. Important mediators/moderators of this relationship are pre-existing, mostly chronic comorbidities and population age structure (Dowd et al. 2020). In an extensive systematic review of the literature, it has been shown that the extent to which these affect disease severity and mortality differ substantially between geographic regions (Thakur et al. 2021).

2 Contents of this Special Issue

This special issue addresses the various links between space and health with a particular focus on the COVID-19 pandemic. In the first part, we showcase studies that examine the spread of the disease and its determinants (Psycharis et al. 2021, Uzzoli et al. 2021, Wieland 2020), illustrate the impact of COVID-19 on the economy (Credit, van Lieshout 2021, Artelaris, Mavrommatis 2022, Herzog, Vomberg 2021, Józefowicz 2021, Niembro, Calá 2021) as well as on mental health (Bourdeau-LePage, Kotosz 2021).

Psycharis et al. (2021) investigate the role of demographic and socio-economic differences in explaining Covid-19 mortality rates across Europe during the first wave in spring 2020 using a Bayesian approach. Their findings suggest that differences in mortality across 29 European countries are best explained by the degree of urbanization, the level of economic development and number of available hospital beds. The spatial patterns of the pandemic within one country, Hungary, has been explored by Uzzoli et al. (2021). They examined how the disease spread during the first, second and third wave and found that while the first wave was characterised by hotspots, the latter two were due to community-based epidemic spreading. Whether and how nonpharmaceutical interventions were able to mitigate the spread of the coronavirus during the first pandemic wave in Germany, was investigated by Wieland (2020). The county-level analysis shows that the epidemic curve already flattened before hard lockdowns and curfews were implemented.

In their paper, Credit, van Lieshout (2021) explore the consequences of the first Covid-19 wave on economic activity in Chicago, USA, from March to September 2020. They find that new business license activity dropped by a third compared to previous years, and that ZIP codes with the largest declines have less dense, diverse, and walkable built neighborhoods. This is closely linked to the study by Artelaris, Mavrommatis (2022) on how city centers and inner-city areas with high population density emerged as the prime victims of the pandemic. They reflect on the urban paradox and how new policy perspectives on territorial cohesion and regional policy might need to take into account the strengthen and merits of urban agglomeration while counteracting its negative aspects.

An explorative qualitative approach was used by Herzog, Vomberg (2021) to investigate the effects of the pandemic on local economies. Their results from interviews and focus groups in deprived neighbourhoods in the Middle Lower Rhine region of Germany show that while the level of uncertainty is generally high, locally embedded organisations benefit from a positive push in the areas of digitization and new life and working environments (home-based work), as well as from a strengthening of local solidarity and cohesion. Józefowicz (2021) used a survey to research the reaction of Polish tourists to the pandemic. The study shows that tourists mostly targeted cities during the pandemic since those are the main tourist destination for Poles. Polish tourists, who took part in the survey, were not afraid of coronavirus infection during their trips but they were mainly young adults who would likely have less adverse health consequences of a coronavirus infection. This suggests that Polish young adults planned their tourist destinations as before the pandemic. In many countries, data limitations represent a major issue in assessing the consequences of health crises and the impacts of policy measures. In their contribution, Niembro, Calá (2021) propose a novel approach to measuring economic impacts of the pandemic in contexts with scarce subnational data. They illustrate the applicability of their newly developed index measure for the case of Argentina which represents a context with scarce and outdated public data and find highly heterogeneous impacts of the pandemic within and across regions. They validated the index using public data sources and discuss its potential to expand the geographic and temporal scope of official statistics.

Finally, Bourdeau-LePage, Kotosz (2021) study the impact of the French government's social-distancing measures (including lockdown) in response to the coronavirus pandemic, on population well-being. The authors report the regional variation of French residents' vulnerability to social-distancing measures and their implication on well-being. They find that the accentuated decrease of well-being in the southern regions changed the French well-being geography considerably.

The second part of the special issue includes four papers that discuss regional and spatial aspects of the healthcare sector more broadly. Two of them investigate the impact of public investments (Vadia, Blankart 2021, Fidrmuc et al. 2022), one analyses antibiotic self-medication (Anderson 2021) and one the effects of Malaria on the height distribution in Italy (Percoco 2021).

Vadia, Blankart (2021) investigate the role of public funding in cardiovascular device innovation. Studying 31 European countries, they find that, indeed, innovatory efforts in the form of public research investments can effectively promote innovation in the medical device industry at the regional level. The paper by Fidrmuc et al. (2022) assesses whether the European Structural and Investment Funds 2007-2013 improved healthcare quality in Slovakia. Results indicate that the injection of EU funds is associated with a significant but small decrease in the readmission rate in the following year, but not with a change in mortality.

Anderson (2021) considers drivers and consequences of antibiotic self-medication in Europe using extensive survey data from the Eurobarometer. The author explores the individual-level and national-contextual determinants of self-medication among antibiotic consumers in European countries. He shows that antibiotic consumption is higher in countries with higher levels of inequality, burdens of out-of-pocket expenditure, and corruption.

In the final paper of this issue, Percoco (2021) investigates the effect of malaria as a proxy for "bad geography" on the height distribution in Italy using historical evidence. He finds that malaria mortality rates can predict regional differences in height of conscripts between 1889 and 1900. Further, results from an instrumental variable approach suggest that average height increased after the eradication of malaria around 1950.

The papers presented in this special issue are heterogeneous in their content and methodologies, but they all highlight the importance and implications of regional and spatial aspects in health research. This is shown in the first part of the special issue by research analysing the spread of the COVID-19 pandemic and its consequences on the economy. That these aspects are not only relevant when studying a global pandemic, but in broader health research, is underlined by the second part of the special issue that includes papers reporting on the geography of public investment in health, medication and diseases.

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Articles

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The determinants of Covid-19 mortality rates across Europe: Assessing the role of demographic and socio-economic factors during the first wave of the pandemic

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Abstract. The aim of this paper is to examine empirically the impact of the demographic structure and socio-economic environment on the Covid-19 mortality rate across 29 European countries. The analysis is based on empirical data recorded cumulatively from 15th February 2020 until 26th May 2020, thus covering 'the first wave of the pandemic'. Results indicate that, although countries with a higher degree of population ageing are anticipated to be more vulnerable to Covid-19, this study provides evidence that population ageing contributes only marginally to Covid-19 death rates across Europe. The degree of urbanization, the level of economic development, and the state of health care systems, seem to better explain patterns of interstate mortality rates. The analysis provides important policy implications since it underlines the importance of urbanization and socio-economic conditions in the accelerating incidence of casualties, and it signifies the importance of health care systems for the protection of people and places from the pandemic.

Key words: Covid-19, mortality rates, Europe, population ageing, urbanization, ANOVA, Bayesian BYM spatial model

1 Introduction

Over the past few months, the scientific community's interest has been focused largely on the Covid-19 pandemic, which is spreading rapidly in almost all parts of the world. Researchers from different scientific fields have approached the issue from various angles, but in all instances there is a common goal, to understand the behaviour of the virus, to formulate methods and policies to control its spread and to find the right treatment.

However, the pandemic of Covid-19 is a very recent phenomenon, which is still in progress. Thus, scientific knowledge about the disease is imperfect and the statistical documentation limited. The numbers of documented events (deaths, cases) vary widely across and within countries. So far, estimations of the eventual impact on the population and on the spread of the disease rely largely on mathematical and statistical models which are formulated on an assortment of assumptions (Fauci et al. 2020, Georgiou 2020). Empirical research has led to some sound findings, revealing that people suffering from certain underlying conditions such as cardiovascular and respiratory diseases, neoplasms and diabetes face an elevated risk of an adverse outcome (Chen et al. 2020, Guan et al.

2020, Halvatsiotis et al. 2020). It is also pointed out that the elderly comprise the most vulnerable group of the population as they often have a less favourable clinical picture than younger people, and once infected they usually have lower chances of survival (Ioannidis et al. 2020). Statistical observations deriving from a wide range of countries demonstrate that deaths from Covid-19 are concentrated mostly among older people (Dowd et al. 2020). The implication of this finding is that demographic ageing may result in structural changes in the demo-pathology of the population that should be taken into account by the health and socioeconomic policy makers. Most European populations already exhibit an age-structure with a large number of older people, while national population projections indicate that demographic ageing will continue; therefore, in the short and medium term, the demographic aspects of the pandemic must not be ignored.

The actual number of cases and deaths due to the virus is not known; however, it can be argued that Covid-19 mortality data may be a more reliable means of analyzing the impact of the disease than statistics on confirmed Covid-19 cases. Of course, mortality reflects the incidence of the disease, the adequacy of the health system as well as practices of reporting, but mortality data, although potentially undercounted, may serve as a more tangible approach for assessing the effects of the disease.

Given that older people are more vulnerable to Covid-19, the demographic structure and ageing of the population could be considered as significant determinants of the mortality rates from Covid-19. However, the fact that the Covid-19 mortality rate disproportionally affects older people does not necessarily imply that the higher the degree of population ageing the higher are the risks for the society as a whole. In order to capture the incidence of the disease and the outcomes on mortality rates, additional factors such as urbanization and the socio-economic environment should be taken into consideration.

Socio-economic determinants are important contributing factors to the incidence and fatalities from the pandemic. Poverty, deprivation and job insecurity are important issues in poorer countries and more deprived populations within countries, cities and regions. Environmental degradation and pollution, poor education, employment insecurity, conditions of built environment, and access to care are factors unequally distributed across regions, that influence the population health in Europe (Marmot et al. 2012, Santana et al. 2017, Mitsakou et al. 2019). The health consequences of the economic crisis induced by Covid-19 are likely to be similarly, unequally distributed, exacerbating heath inequalities. Health inequalities will probably increase during the pandemic (Bambra et al. 2020).

In this context, the aim of this study is twofold; first, to explore the demographic dimension of the pandemic with respect to age structure effects; more specifically we aim to examine whether populations experiencing a high degree of ageing tend to exhibit higher mortality rates due to Covid-19 and vice versa. Second, we further explore the demographic structure along with socio-economic determinants in order to test how they affect the mortality rates of the disease. To address our research questions, we employ recent statistical information from 29 European countries and we apply well established demographic, econometric and statistical techniques.

The analysis refers to the first wave of the pandemic and has some important merits. First, it provides an initial accounting of the mortality rates and the determinants of the pandemic across Europe. Second, this provides the baseline data which allow us to follow the evolution of the disease and to provide comparisons with subsequent waves. Third it serves as a basis for policy measures for better responses and preventive policies in response to future pandemics. Fourth, this analysis provides useful insights concerning Covid-19 which could enrich interdisciplinary dialogue across fields such as demography, economics, epidemiological studies, and health policy. Finally, it could be utilized for scientific discussion regarding the spread of disease that goes beyond the Covid-19 pandemic.

The paper is structured as follows. Following the introduction, section 2 provides a concise literature review regarding the demographic and socio-economic determinants of the pandemic. Section 3 presents data sources and methods of analysis for the estimation of the significance of the age structure on Covid-19 mortality rates. Section 4 presents and discusses the empirical results. Section 5 provides a Bayesian model for analysing Covid-19 mortality rates. Section 6 summarizes the findings, codifies policy proposals and sketches the framework for the expansion/extension of this work.

2 Literature review

The issue of the spread of the pandemic has attracted the attention of scientists, international organizations, citizens and governments across the globe. Epidemiological episodes and the spread of epidemiological diseases is not at all a new issue. Historically, on numerous occasions, humankind has faced similar outbreaks of diseases and a fair number of analyses have been the subject of scientific investigation (Carillo, Jappelli 2020, Jordà et al. 2020, Percoco 2016). However, under the current circumstances of economic globalization, the high degree of concentration of people and economic activities in large cities and urban agglomerations, the soaring income inequalities as well as the highly developed means of transportation and communication have made this disease unique in world health history. This disease could undermine: fundamental aspects of the organization of economic activity; social interaction and participation in the social processes; social activities and possibly personal life, and psychological health. Today, a vaccine has been used for the protection against Covid-19. However, during the first wave of the pandemic the absence of a medication or a vaccine to limit the spread, to protect against and eventually to cure Covid-19 make this disease a distinct case in world history. The shock was exogenous and global (Faggian 2020). However, it had an asymmetrical impact across countries, social groups and individuals. Demography and spatial statistical analysis and spatial epidemiology constitute scientific disciplines that have explicitly contributed to the analysis of diseases. Demography has provided some important insights regarding the spread and the consequences of Covid-19. Demographic ageing has been quite an important issue for Europe in recent decades. The ageing of the population exerts pressures on the pension systems and on the health-care systems, and it requires actions to support the everyday life of elderly people. Covid-19 brings an additional risk to elderly people and to societies. The lives of elderly people are at high risk: the mortality rate is higher among this category and the incidence of Covid-19 peaks in areas where elderly people are concentrated such as old-age homes. The higher vulnerability of older people to Covid-19 is a well-documented statistical fact. As a result, the age structure of a society and the vulnerability of populations, along with other socio-economic conditions that prevail in a society, should be examined in scientific research (ECDC 2020).

The level of urbanization is also an important determinant for the incidence and spread of the pandemic. Empirical analyses have demonstrated that the impacts of the current Covid-19 crisis alone will be vast, as well as spatially uneven. Given the high concentration of both population and economic activities in cities, these are often hotspots of Covid-19 infections (Sharifi, Khavarian-Garmsir 2020). Other factors being equal, for the first wave of the pandemic the incidence of Covid-19 is higher in urban areas compared to the semi-urban and rural areas of countries. Indeed, there are some who advocate a rediscovery of rurality as a reaction to the pandemic (Cotella, Vitale Brovarone 2020).

The social mix of the population is another important factor. The most deprived parts of the population tend to be more vulnerable to the disease. The UK Office of National Statistics (ONS) released the March–April 2020 data for England and Wales which revealed that Covid-19-related death rates in the most deprived areas are more than double those in the less deprived (Dodds et al. 2020, p. 289). Income inequality reflects different mortality rates in the USA. Mortality rate of the less well-off Black and Latino people, is twice that of White people (Wade 2020).

The level of economic development of an area is also factor that serves as an important determinant for explaining the incidence and spread of the disease. Spatial analysis for Italy provides statistical evidence that the level of economic development of regions is positively correlated with the incidence of Covid-19 (Ghose, Cartone 2020). The highest positive spatial correlation in the Northern provinces stresses the link between economic development and Covid-19. LISA indicators confirm that the most economically developed areas in the country are more likely to be affected by Covid-19. Ascani et al. (2020) corroborate these findings providing further statistical evidence that the striking spatial unevenness of Covid-19 suggests that the infection hits core economic locations harder.

Furthermore, empirical analysis for Germany highlights spatial patterns of the disease.

First, there was a regional outbreak in Western Germany centred around the Heinsberg district. Second, tourists returned to their home regions carrying the infection. Third, the spread of the disease took place through specific events (Kuebart, Stabler 2020).

Burlina, Rodríguez-Pose (2020) have shown that highly connected regions, in colder and dryer climates, with high air pollution levels, and relatively poorly endowed health systems witnessed the highest incidence of excess mortality.

These unprecedented conditions have made state intervention even more urgent. The intensity of state intervention has become obvious across the globe. National health systems have played an important role in the health care policy. European countries and others, including the United States, are now choosing to inject large sums of money in order to kick-start economics, resume business, and maintain good polling for the ruling parties. The EU recovery plan constitutes an initiative in this line of action (European Council 2020). The OECD has so far produced comprehensive briefings on policy responses including the topics of cities (OECD 2020a), rural development (OECD 2020b), as well as the territorial and multilevel governance (OECD 2020c).

This paper focuses on European countries. This aggregate level of analysis provides an initial approach to the European space which is characterised by a high degree of integration and interaction, and where geography and the socioeconomic environment are significant diversification factors.

3 Examining demographic factors: Data sources and methods of analysis

3.1 Data and data sources

Data that have been utilised for this analysis can be grouped into two main categories. The first category focuses on the data of deaths from Covid-19, while the second includes demographic and socio-economic variables. The statistical data regarding deaths from Covid-19 have been collected from various official sources (see Table A.1 in the Appendix).

For the purposes of the study, we used numbers of deaths recorded cumulatively until May 26, 2020. The comprehensive databases we used include 32 European populations (EU members, EEA countries as well as Switzerland and UK). Three countries (Iceland, Liechtenstein, and Malta) exhibit very small numbers of deaths (<15) and high relative standard errors (>25%); thus, they are excluded from our study as in such instances the results derived are unreliable (NCHS 1999, Klein et al. 2002). Hence, the present analysis focuses on 29 national populations. For 18 of these countries, the available statistical material refers to the total number of deaths (all ages, both sexes combined). Classification of deaths by age is available only for eleven European countries: Austria; Denmark; France; Germany; Greece; Italy; Netherlands; Norway; Spain; Switzerland; and Portugal. This provides a valuable piece of information which allows application of demographic age-standardisation techniques (see below).

The first Covid-19 death in Europe was reported on February 15, 2020 in France. By February 21, nine countries had reported cases: Belgium (1); Finland (1); France (12); Germany (16); Italy (3); Russia (2); Spain (2); Sweden (1); and the UK (9) (Spiteri et al. 2020). In the EU/EEA and the UK, 121 cases and three deaths had been reported as of February 23. The rate of infection and deaths rapidly expanded across Europe. In Greece for example, the first case was diagnosed on February the 26 and only a month later, on March the 23 there were 695 confirmed cases and 17 deaths. Nation-wide restrictions on the freedom of movement were imposed at that time.

Furthermore, the dataset includes demographic and socio-economic data. Information on the population by age (January 1, 2020), as well as on selected socioeconomic indicators used in the analysis, was obtained from Eurostat official site (see Table A.1). These data include Population, Gross Domestic Product per capita (ppp-adjusted), Number of Hospital Beds per 100,000 population, Life Expectancy at Birth and percent of Urban Population. The variables used in this analysis are presented in the Appendix Table A.2.

3.2 Variables and methods of analysis

Combining the basic statistical information (total numbers of deaths and cases due to Covid-19) with the relevant population data, we calculated three broad (crude) measures:

Death Rate (DR) defined as number of deaths per 100,000 population;

Incidence Rate (IR) referring to number of cases per 100,000 population;

Fatality Rate (FR) expressing number of deaths per 1,000 cases.

It is well known, however, that crude demographic rates are affected by the age-structure of the study populations; hence, for comparative purposes we computed standardised indices to eliminate age affects (Siegel, Swanson 2004). Two types of standardisation procedures are employed:

First, for the eleven European countries for which statistics on deaths from Covid-19 by age are available, we computed standardised death rates (DSDR) directly, choosing the average age composition of the eleven populations under consideration as the more appropriate reference age structure rather than the average European standard age-distribution, which encompasses populations excluded from the present analysis.

Second, for the 29 populations under investigation we calculated Standardised Mortality Ratios (SMR) using the age-specific death rates (of Covid-19) of the Italian population as the reference mortality schedule. The SMRs are expressed per 100 and compare the national figures of the study populations to the mortality levels of Italy. Multiplying the SMRs (per unit) by the observed death rate of the standard population (Italy) we obtain the corresponding indirectly standardised death rates (ISDR).

To explore the potential association between death rates and demographic and socioeconomic factors, we applied a linear correlation analysis as well as a one-way analysis of variance (ANOVA). The factors of interest considered include the proportions of the elderly population (ages 65+, 70+, 80+), the percentage of the urban population, the per capita Gross Domestic Product (ppp-adjusted) and the number of hospital beds per 100,000 population. The statistical analysis was performed using SPSS version 24.

4 Results: ageing and Covid-19 death incidence

Table 1 presents the data used in the analysis considering up-to-date outcomes due to Covid-19 reported cumulatively until May 26. Cases and, particularly, deaths show large variations across European countries. Numbers of deaths range from 17 (Cyprus) to 36914 (UK) exhibiting a relative dispersion of 193%. Numbers of cases range from 937 (Cyprus) to 261184 (UK); the relative dispersion is 164%. The average death rate (DR) is about 18 deaths per 100,000 people, the average incidence rate (IR) 210 cases per 100,000 population while the average fatality rate (FT) is 71 deaths per 1000 cases.

Empirical research indicates that mortality risk due to Covid-19 is greatly concentrated in the older age ranges, mainly at the ages of 70, 80 and older. This finding often leads to the assumption that countries exhibiting higher proportions of older persons in the population are expected to experience higher death rates from the disease. To test this hypothesis, we apply four different approaches.

First, we computed correlation coefficients between ageing indicators (the percentages of the population aged 65, 70 and 80 years or more) and the Covid-19 rates. We also calculated the correlation coefficients between these indicators and the general economic conditions of the countries, based on the per capita gross product, the availability of hospital infrastructure (hospital beds per 100,000 inhabitants) and the percentage of the urban population as it reflects, to some extent, the concentration and density of the population. The correlation matrix is presented in Table 2. The correlation coefficients between incident rates and the ageing measures are inconsistent; for death and fatality rates they are very low and trivial, though they point in the expected direction for persons aged 70+ and 80+. Nevertheless, there is a palpable and noteworthy association between death and incidence rates and the proportions of the urban population while it seems that good hospital infrastructure plays a favourable role. It may be interesting to note that the associations and the impact of the proportion of the urban population, GDP

Table 1: Data used in the analysis and basic descriptive statistics (26/5/2020) and indirectly standardised death rates

Country	cases	deaths	death rate	incidence rate	fatality rate	Pop 65+ (%)	Pop 70+ (%)	Pop 80+ (%)	e(o)	GDP	Urban (%)	Beds	ISDR
Austria	16459	641	7.20	185	39	19.0	13.9	5.3	81.8	128	57	737	9.1
Belgium	57342	9312	81.06	499	162	19.2	13.8	5.7	81.7	118	98	566	100.3
Bulgaria	2433	130	1.87	35	53	21.6	15.0	4.9	75.0	51	76	745	2.4
Croatia	2244	100	2.47	55	45	21.1	14.5	5.5	78.2	63	58	554	3.1
Cyprus	937	17	1.92	106	18	16.3	11.2	3.7	82.9	90	67	340	3.1
Czechia	9004	317	2.97	84	35	20.0	13.6	4.1	79.1	91	74	663	4.1
Denmark	11387	563	9.64	195	49	19.8	14.3	4.7	81.0	129	88	261	12.7
Estonia	1824	65	4.90	137	36	20.1	14.3	5.9	78.5	82	68	469	6
Finland	6599	308	5.57	119	47	22.3	15.8	5.7	81.8	112	86	328	6.4
France	145279	28432	42.31	216	196	20.4	14.6	6.1	82.9	104	82	598	49.1
Germany	179002	8302	9.98	215	46	21.8	15.9	6.8	81.0	123	76	800	10.8
Greece	2882	172	1.61	27	60	22.3	16.6	7.2	81.9	69	85	421	1.7
Hungary	3771	499	5.12	39	132	19.9	13.3	4.5	76.2	71	72	702	7
Ireland	24698	1606	32.49	500	65	14.4	9.9	3.4	82.3	191	63	296	57.8
Italy	230158	32877	54.58	382	143	23.2	17.4	7.4	83.4	97	69	318	54.6
Latvia	1049	22	1.15	55	21	20.6	14.8	5.8	75.1	69	69	557	1.4
Lithuania	1635	63	2.28	59	39	20.1	14.5	5.9	76.0	81	71	656	2.7
Luxembourg	3993	110	17.58	638	28	14.6	10.2	4.1	82.3	263	88	466	28.8
Netherlands	45445	5830	33.62	262	128	19.6	13.8	4.7	81.9	130	92	332	44.4
Norway	8352	235	4.38	156	28	17.5	12.4	4.3	82.8	153	70	360	6.3
Poland	21631	1007	2.65	57	47	18.2	11.8	4.4	77.7	71	60	662	3.8
Portugal	30788	1330	12.96	300	43	22.2	16.1	6.6	81.5	77	66	339	14.2
Romania	18283	1197	6.21	95	65	19.0	12.7	4.8	75.3	66	55	689	8.5

Continued on the next page ...

Table 1: Data used in the analysis and basic descriptive statistics (26/5/2020) and indirectly standardised death rates (*continued*)

Country	cases	deaths	death rate	incidence rate	fatality rate	Pop 65+ (%)	Pop 70+ (%)	Pop 80+ (%)	e(o)	GDP	Urban (%)	Beds	ISDR
Slovakia	1511	28	0.51	28	19	16.6	10.5	3.3	77.4	74	54	582	0.9
Slovenia	1469	106	5.09	71	72	20.4	13.9	5.5	81.5	88	55	450	6.3
Spain	235400	26834	57.03	500	114	19.7	14.5	6.1	83.5	91	80	297	66.8
Sweden	33843	4029	38.93	327	119	19.9	14.7	5.2	82.6	121	88	222	49.0
Switzerland	30601	1645	19.11	356	54	18.7	13.7	5.3	83.8	156	78	453	24.4
UK	261184	36914	55.02	389	141	18.5	13.5	5.0	81.3	106	88	254	72.8

Statistics	cases	deaths	death rate	incidence rate	fatality rate	Pop 65+ (%)	Pop 70+ (%)	Pop 80+ (%)	e(o)	GDP	Urban (%)	Beds	ISDR
min	937	17	0.5	27.0	18.1	14.4	9.9	3.3	75.0	51.0	54.0	222	0.9
max	261184	36914	81.1	638.2	195.7	23.2	17.4	7.4	83.8	263.0	98.0	800	100.3
range	260247	36897	80.6	611.2	177.6	8.7	7.4	4.0	8.8	212.0	44.0	578	99.4
mean	47904	5610	17.9	209.9	70.5	19.6	13.8	5.2	80.4	105.7	73.6	487	22.7
std. dev.	78753	10817	21.8	173.2	48.6	2.1	1.8	1.0	2.8	44.2	12.4	173	26.9
CV (%)	164	193	121	83	69	11	13	20	3	42	17	35	119

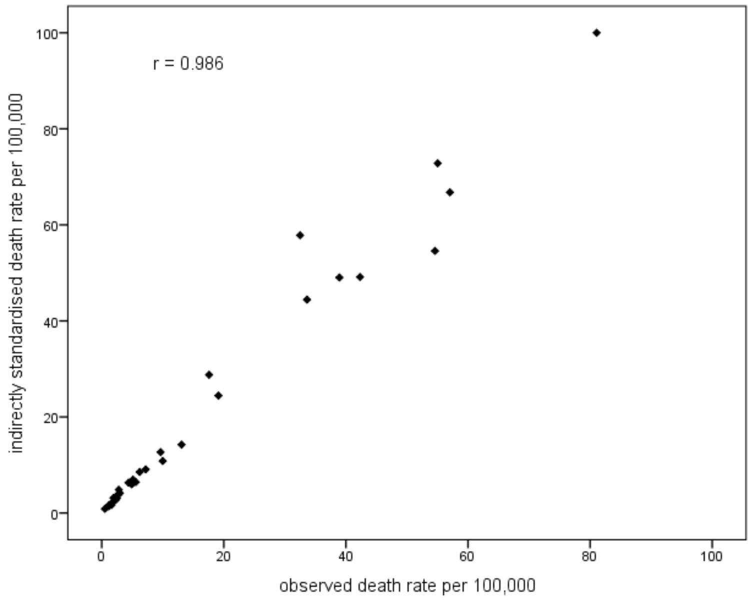

Figure 1: Association between observed death rate and standardised death rate using the indirect method of standardisation: data 26-5-2020

per capita and hospital infrastructure are clearer with respect to incidence rates. One explanation might be that countries with relatively higher levels of economic development are usually characterized by higher trade openness, interactions and connections with the international community. It seems that the spread of Covid-19 puts into question openness, internationalization and globalization. Covid-19 is following the paths of international connections and integration.

Second, in order to eliminate age structure effects and to increase the validity of our results, we calculated indirectly standardized death rates and we examined the association between observed and indirectly standardised death rates. Table 1 presents the computational results. Compared to Italy (standard population), Belgium, Spain and the UK exhibit higher mortality, however the overall association between observed and adjusted death rates is positive and very strong implying that ageing effects do not seem to be present (Figure 1).

Third, a direct comparison of the observed death rates with demographic ageing indicators across countries at different stages of the disease progression that have adopted different policies of social distancing and have different health systems and capabilities may be naive. To overcome to some extent these incompatibilities, it may be more appropriate to compare countries with roughly similar levels of mortality. Hence, we divided our sample into three sub-groups reflecting low, medium and high mortality rates (<5, 6-19 and 20+ deaths per 100000 population, respectively) and we applied one-way ANOVA to examine if the differences in mean population ageing indicators between the three groups differ considerably. The results of the statistical analysis are presented in Table 3 and confirm that the mean proportions of populations aged 65, 70 or 80 or more do not in fact differ across mortality levels (p-values 0.863, 0.936 and 0.661, respectively).

Fourth, we applied direct standardisation for countries where the relevant information was available, as this demographic technique perhaps more accurately clarifies the potential connection between observed death rates and population ageing. The results of our computations are presented in Figure 2. The pattern of the observed and standardised rates across countries is consistent; the association between observed and directly standardised death rates is very high (r = 0.986) implying that the age differentials do not seem to have an effect on the mortality rates.

Table 2: Correlation matrix of variables of interest (2-tailed p-values in parenthesis): data 26/5/2020

	Death rate	Incidence rate	Fatality rate	Pop 65+ (%)	Pop 70+ (%)	Pop 80+ (%)	e0	GDP	Urban % (%)	Beds
Death rate	1									
Incidence rate	0.762** (0.000)	1								
Fatality rate	0.807** (0.000)	0.387* (0.038)	1							
Pop 65+ (%)	-0.019 (0.923)	-0.349 (0.064)	0.216 (0.260)	1						
Pop 70+ (%)	0.118 (0.541)	-0.160 (0.407)	0.262 (0.169)	0.962** (0.000)	1					
Pop 80+ (%)	0.238 (0.214)	0.030 (0.877)	0.295 (0.120)	0.815** (0.000)	0.894** (0.000)	1				
e0	0.513** (0.004)	0.632** (0.000)	0.304 (0.109)	-0.117 (0.545)	0.069 (0.721)	0.170 (0.378)	1			
GDP	0.252 (0.187)	0.724** (0.000)	-0.025 (0.897)	-0.594** (0.001)	-0.436* (0.018)	-0.300 (0.114)	0.566** (0.001)	1		
Urban (%)	0.545** (0.002)	0.475** (0.009)	0.476** (0.009)	0.120 (0.536)	0.250 (0.190)	0.191 (0.321)	0.396* (0.034)	0.354 (0.060)	1	
Beds	-0.391* (0.036)	-0.464* (0.011)	-0.177 (0.357)	0.116 (0.549)	-0.025 (0.896)	0.004 (0.985)	-0.633** (0.000)	-0.310 (0.101)	-0.360 (0.055)	1

** Significant at the 0.01 level (2-tailed)
* Significant at the 0.05 level (2-tailed)

Table 3: One-Way Analysis of Variance examining differences in mean ageing indicators by low, medium and high levels of death rates due to Covid-19: 26-5-2020

(A) Descriptive statistics

		N	Mean	Std. Dev.	Std. Error
Pop 65+ (%)	death rate 0 - 5	14	19.8	1.9	0.5
	death rate 6 - 19	7	19.3	2.5	0.9
	death rate 20 +	8	19.4	2.4	0.9
	Total	29	19.6	2.1	0.4
Pop 70+ (%)	death rate 0 - 5	14	13.7	1.7	0.5
	death rate 6 - 19	7	13.9	2.0	0.8
	death rate 20 +	8	14.0	2.0	0.7
	Total	29	13.8	1.8	0.3
Pop 80+ (%)	death rate 0 - 5	14	5.0	1.0	0.3
	death rate 6 - 19	7	5.4	1.0	0.4
	death rate 20 +	8	5.5	1.2	0.4
	Total	29	5.2	1.0	0.2

(B) ANOVA: F-test

		Sum of Squares	df	Mean Square	F	Sig.
Pop 65+ (%)	Between Groups	1.447	2	0.723	0.148	0.863
	Within Groups	127.125	26	4.889		
	Total	128.572	28			
Pop 70+ (%)	Between Groups	0.470	2	0.235	0.066	0.936
	Within Groups	92.568	26	3.560		
	Total	93.039	28			
Pop 80+ (%)	Between Groups	0.964	2	0.482	0.421	0.661
	Within Groups	29.738	26	1.144		
	Total	30.702	28			

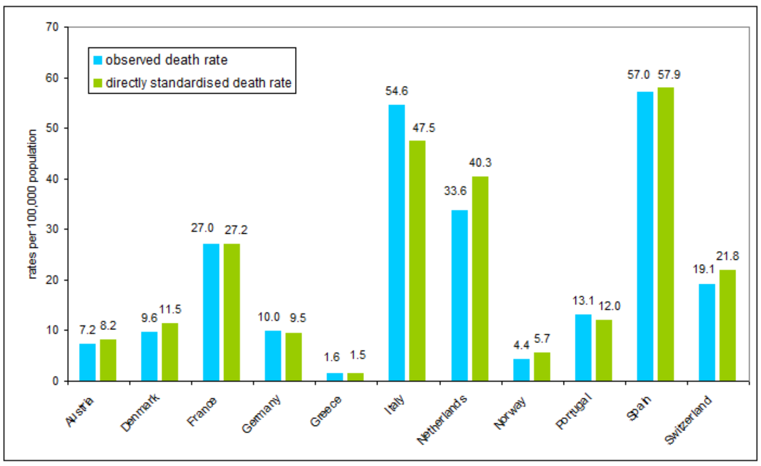

Figure 2: Observed and directly standardised death rates on the basis on the average population age-structure of the countries under investigation: data 26-5-2020

5 Modeling Covid-19 mortality rates: a Bayesian BYM spatial model

5.1 Presentation of the Model

In recent years, epidemiology has used Bayesian models widely (Greenland 2006). Quite frequently, the spatial and/or the temporal framework of the epidemiological data upgrades the Bayesian approach into a very efficient strategy for a plethora of epidemiological studies (Diggle, Ribeiro 2007, Jewell et al. 2009, Blangiardo et al. 2013).

In order to further analyse the risk of Covid-19 mortality rate, we employ a spatial econometric epidemiological model that explains the mortality rates integrating a number of covariates. Therefore, in the following section we have a dual goal: on the one hand to smooth the Standardized Mortality Ratios (SMRs) with the Hierarchical Bayesian method; and on the other hand to fit the Besag-York Mollie (BYM) spatial model with a view of estimating relative risk while quantifying the effect of a set of covariates (Mollié 1996, Morris et al. 2019).

The BYM model incorporates two types of effects: spatial and non-spatial: a spatially structured effect and an unstructured random effect. Rigorously, we assume that the observed counts, O_i, are conditionally independently Poisson distributed (Moraga 2019):

Model based approaches enable us to incorporate covariates and borrow information from neighbouring countries to improve local estimates, resulting in the smoothing of extreme values based on small sample size. We take the following equation:

$$O_i \sim \text{Poisson}(E_i\theta_i) \qquad i = 1, \dots, n \tag{1}$$

where E_i is the expected count and θ_i is the relative risk in area i. The logarithm of θ_i is expressed as:

$$\log(\theta_i) = \boldsymbol{d_i}\boldsymbol{\beta} + u_i + v_i \tag{2}$$

$\boldsymbol{d_i} = (1, d_{i1}, \dots, d_{ip})$ is the vector of the intercept and p covariates corresponding to area i, and $\boldsymbol{\beta} = (\beta_0, \beta_1, \dots, \beta_p)$ denotes the coefficient vector.

The error term u_i is modeled with a CAR distribution $u_i|u_{-i} \sim N(\bar{u}_{\delta_i}, \frac{\sigma_u^2}{n_{\delta_i}})$ where $\bar{u}_{\delta_i} = \frac{\sum_{j\in\delta_i} u_j}{n_{\delta_i}}$, δ_i, and n_{δ_i} represent the set of neighbors and the number of neighbors of area i respectively. v_i is modeled as identically distributed normal variables with zero mean and variance σ_v^2, namely, $v_i \sim N(0, \sigma_v^2)$.

For the analysis, R statistical software was used. Inferences for Bayesian Hierarchical models were approximated by Integrated Nested Laplace approximation (INLA) with R-INLA package (Rue et al. 2018).

5.2 Empirical application

We employ a spatial epidemiology model in order to estimate the disease risk due to Covid-19 in 29 European countries during the first wave of the pandemic. Following equation 1 as the dependent variable, we use observed deaths per country (O_i) which are conditionally independently Poisson distributed with expected deaths (E_i) and θ_i the relative risk for each country. Equation 2 allows us to include a set of covariates in our model in order to quantify the effect and incorporate this information into relative risk estimates. Five variables are examined as covariates in our spatial econometric model, Gross Domestic Product (GDP), ageing indicators (the percentages of the population aged 70 and 80 years or more), the availability of hospital infrastructure (hospital beds per 100,000 inhabitants) and the percentage of population living in an urban context. Our analysis comprises the mean posterior, the standard deviation and the 95% credible intervals of the relative risks which represent the 2.5 and 97.5 percentiles respectively. Additionally, with the purpose of interpreting the relative risk in our model, we construct an additional column where we calculate the factor increase, $\exp(\beta_j)$, keeping all other covariates constant. Finally, in order to compare the different Bayesian models we use the Watanabe Akaike information Criterion (WAIC) (Watanabe 2010).

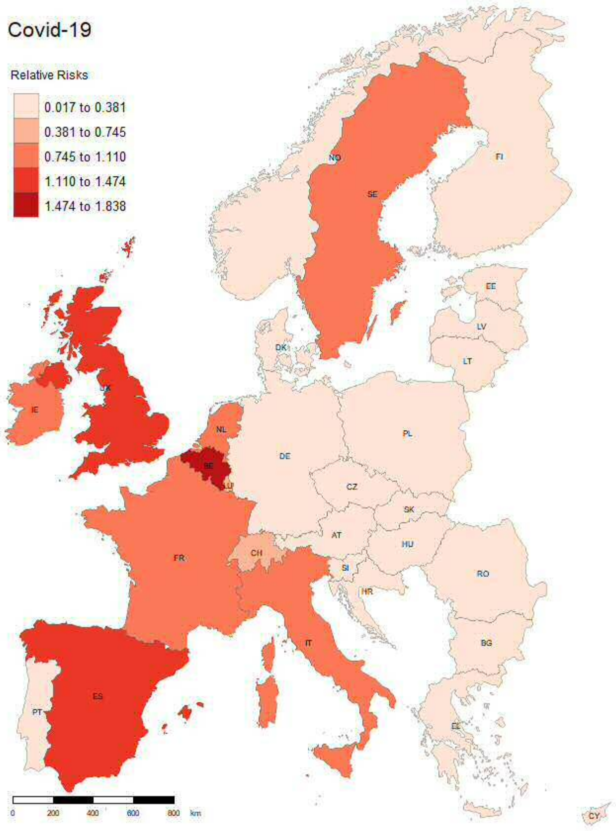

Figure 3: Mapping Covid-19 relative risk across European countries

5.3 Mapping the evidence

Figures 3 and 4 illustrate the output of the BYM model regarding the relative mortality risk, considering Italy as a baseline. As Italy exhibits the highest mortality rate, the probability of death is estimated based on Italy=1: higher values denote higher mortality rates and vice versa.

Figures 3 and 4 indicate that there is a geographical pattern in mortality rates. Countries on the left part of the map show higher probability rates than countries on the right. Belgium, Spain, UK and Ireland show the greatest values above the baseline. France, Slovenia and the Netherlands are a little below the baseline. Conversely, a large number of countries including Germany and Denmark from the North, Greece and Portugal from the South and a large number of former Eastern European countries exhibit rates below that of Italy and well below the baseline. This demonstrates the spatial heterogeneity of mortality rates across Europe.

5.4 The results

The application of the spatial epidemiology model provides some interesting results which are presented in Table 4. These could be summarized as follows:

First, in all models the coefficient of the variable URBAN is positive, indicating that urbanization is an important explanatory factor for the probability of the mortality rate and overall increases Covid-19 risk.

Second, in all models, the variable BEDS is negatively associated with the probability of mortality indicating an inverse relationship between hospital beds and Covid-19 risk. This is achieved taking into account the observed deaths from Covid-19, the expected number of deaths but also a set of covariates. The greater the bed availability per 100,000 population, the lower the Covid-19 mortality risk. This signifies the importance of sound health care systems to efficiently tackle the negative impacts of the pandemic.

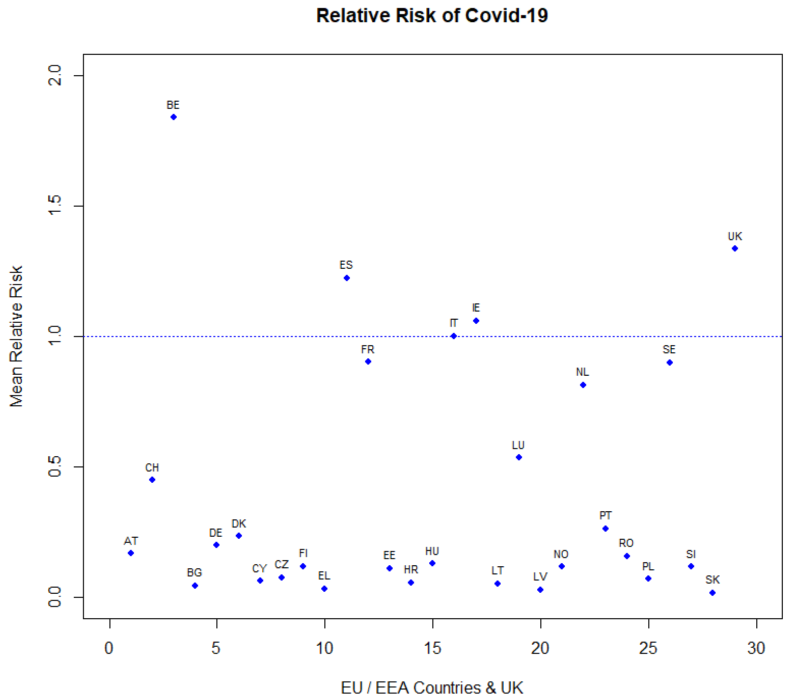

Figure 4: Covid-19 relative risk across European countries

Third, where the explanatory factor of GDP is taken into account, its coefficient was positive, suggesting that countries with greater GDP tend to have greater Covid-19 risk. The higher the market size and the level of development, the higher the risks. This finding corroborates the literature that the most advanced and open economies are more vulnerable to Covid-19 (Sorci et al. 2020). Developed economies are expected to be more affected in 2020 than developing economies, at -5.8 per cent and -2.1 per cent, respectively (United Nations 2020, p. 13). Since GDP and urbanization show a high level of correlation in the data, they are inserted separately in the analysis.

Fourth, the coefficient of variable P80 is positive, indicating that there is a higher risk of mortality for people above 80 years of age.

Finally, in line with WAIC criterion, the best model is model 3 which has the lowest value and therefore the highest explanatory power of those that are presented (Table 4).

Figure 4 presents all the posterior distributions of covariates P70, GDP, Urban and Beds. On the one hand, covariates GDP and Urban display positive distribution of values for the coefficients indicating an increase in Covid-19 risk. On the other hand, the posterior distribution of the coefficient of Beds is mainly negative, demonstrating this inverse relationship between Beds and Covid-19 risk.

6 Conclusions and discussion

The Covid-19 pandemic is a new phenomenon that has been ongoing for one year. Empirical studies from various countries reveal that older people are at a higher risk of developing the disease than younger people. Furthermore, not only are the majority of cases concentrated in older ages but elderly people have a much higher risk of a fatal outcome. These findings often lead to the assumption that countries with high proportions of aged population would tend to exhibit higher death rates from Covid-19.

However, our results based on recent cross-sectional data from 29 European countries, referring to what now is termed ‘the first wave of the pandemic’, do not agree with the standpoint expressed in the literature, that the population age structure may explain notable variations in fatality or death rates across countries (Dowd et al. 2020). Although a correlation is apparent between death rates and proportions of persons aged 70 or more,

Table 4: Besag-York-Mollié model using Bayesian Hierarchical smoothing on SMRs

Covariates	Mean	S.d.	2.5%	97.5%	Exp(Mean)
		Model 1:			
P70+	-0.059	0.122	-0.301	0.183	0.943
Urban	0.047	0.019	0.009	0.085	1.048
Beds	-0.002	0.054	-0.005	0.000	0.998
Constant	-3.179	2.156	-7.450	1.076	
Marginal log-likelihood	-271.02				
WAIC	292.64				
		Model 2:			
P80+	0.084	0.211	-0.332	0.500	1.088
Urban	0.043	0.019	0.005	0.081	1.044
Beds	-0.002	0.001	-0.005	0.000	0.998
Constant	-4.101	1.896	-7.854	-0.359	
Marginal log-likelihood	-270.52				
WAIC	292.58				
		Model 3:			
P70+	0.111	0.141	-0.169	0.391	1.117
GDP	0.013	0.006	0.001	0.025	1.013
Urban	0.028	0.020	-0.013	0.068	1.028
Beds	-0.002	0.001	-0.004	0.001	0.998
Constant	-5.711	2.372	-10.411	-1.031	
Marginal log-likelihood	-277.38				
WAIC	292.47				
		Model 4:			
P80+	0.282	0.210	-0.134	0.698	1.326
GDP	0.013	0.005	0.002	0.023	1.013
Urban	0.027	0.019	-0.010	0.064	1.027
Beds	-0.002	0.001	-0.004	0.001	0.998
Constant	-5.576	1.847	-9.235	-5.571	
Marginal log-likelihood	-276.34				
WAIC	292.48				

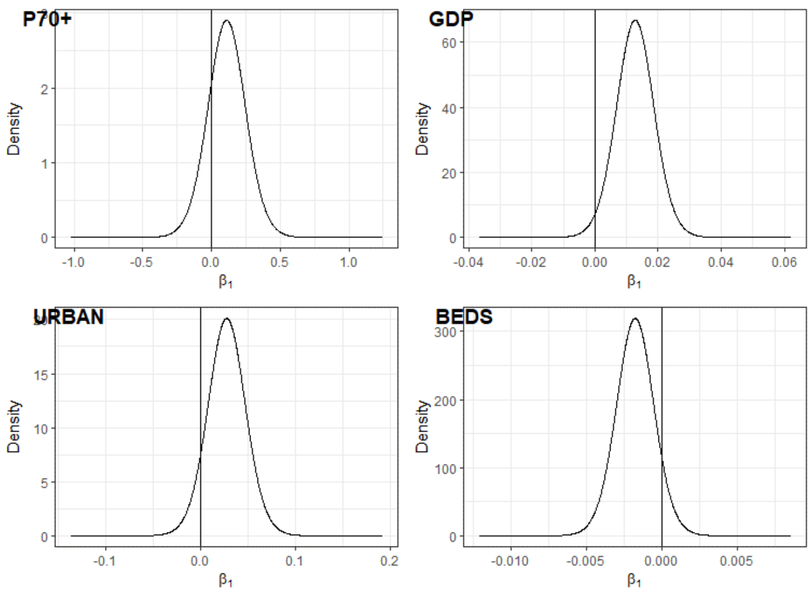

Figure 5: Posterior Distribution of the coefficient of covariatest

and, especially, 80 or more, the associations are small in magnitude. Several factors contribute to this discrepancy. First, the degree of ageing does not differ substantially between European countries; hence, the standardization methodology used in this study did not result in sizeable differences. Second, it may be still too early to confirm the effects and the interrelationships of the disease with the structural characteristics of the population. As the Covid-19 pandemic is still under way additional deaths are recorded every day and more statistical material is collected globally. Comparisons may be inconsistent because different countries are at different stages of the epidemic while additionally, they employ different social and health policies to protect their citizens. Third, differential reporting of Covid-19 deaths (and of cases) adds to the confusion. There is evidence that, at present, there is a significant under-reporting of deaths from Covid-19, particularly in developing countries, while different definitions and practices are employed by different countries (for instance, in the UK, only deaths occurring in hospitals are registered; in Sweden deaths occurring in nursing homes are not recorded). Furthermore, even accurate identification of Covid-19 deaths is a difficult task. Additionally, in many instances, it is mainly some cities or regions that have been disproportionally affected by the virus compared with the rest of the country (e.g. in Sweden Stockholm, in Greece mostly Athens, etc.).

Analysis has shown that explanations on high fatality rates of Covid-19 for elderly people don't necessarily imply high fatality rates for aging societies. Moving from the individual determinants of fatality to societal fatality rates, the determinants are changing significantly. It is not only age that matters. It is the socio economic environment and the broader conditions that affect vulnerability to Covid-19.

Furthermore, our analysis has unveiled the issue that socio-economic variables exert a significant impact on the incidence of and fatalities from Covid-19. Testing for socio-economic and demographic factors, the Bayesian Besag-York Mollie (BYM) spatial model provides some interesting results which we present below.

First, the level of urbanization of a country is a significant determinant of death rates from Covid-19. The level of urbanization proxies the market size along with the level of interaction and interconnections. The higher the level of interactions, the higher the risk of the disease. This risk is caused by the large number of those affected vis-a-vis the limits of the health system. As a result this observation signifies the role of health systems and corroborates previous findings in the literature of epidemiological studies (Neiderud 2015). At the same time the more deprived populations within urban areas are more vulnerable to fatality rates (Wade 2020).

Second, the level of economic development emerges as a significant factor for the spread of the disease. The level of economic development proxies the openness and the international connectedness of the economy. The higher the connections through trade and transport, the higher the risks from the disease. According to Sorci et al. (2020), GDP per capita was positively associated with the levels of fatality rates in Europe. Similarly, Hamidi et al. (2020) identified connectivity as a risk factor for COVID-19 in the US, while Burlina, Rodríguez-Pose (2020) show that highly connected regions witnessed the highest incidence of excess mortality.

The 'first wave of the pandemic' made evident that Covid-19 challenges the two fundamental trends/issues of the contemporary global economic system: globalization and urbanization. This could mean that factors which were clear advantages for the economic development in the past (such as agglomeration and interactions) might operate differently in the context and aftermath of Covid-19 (Bailey et al. 2020).

Third, the number of beds, which proxies the quality of health system, plays a significant role in protection from the disease. The higher the standards of the health system, the greater the protection of people from the disease. This finding corroborates with the results of Sorci et al. (2020) who demonstrated that fatality rates in the EU countries were negatively associated with the number of hospital beds per 1000 inhabitants.

The present pandemic is raising fundamental questions about what makes a community, a population and a nation resilient and sustainable to external shocks (Psycharis et al. 2014). As a result, this analysis highlights some interesting challenges and policy implications for the future.

First, this disease questions the pace of urbanization and the functioning of urban systems. The international trend towards urbanization witnessed in recent years is anticipated to be affected or even halted by the recent spread of the pandemic. In addition, the organization of everyday life and the economic activities within cities has changed drastically. It is very early to predict the long term consequences. However, it is certain that these trends introduce another factor that should be taken into consideration in urban development and urban policy in the future.

Second, the Covid-9 pandemic questions the pace of globalisation. The world appears to be becoming less globalized as the pandemic persists (United Nations 2020).

Third, these trends place into question: the specialization of the economy; the organization of production; and location choices. More remote and rural areas may provide safer and healthier types of economic activity and choices for residence. Although it is still early, the location choices of people and enterprises may be affected by the spread of the disease. Will people move to peripheral areas? It is very early and would be premature to make such a prediction. However, the balance between centrifugal or centripetal forces that operate and determine the location choices of people and enterprises will probably change and the underlying forces will be reshuffled in the post-Covid-19 period.

Fourth, the pandemic threatens the inclusiveness of societies. Historically, pandemics have hit minorities and people at the bottom of the socioeconomic ladder disproportionately (Wade 2020). During the pandemic the most vulnerable populations have been hit the hardest (United Nations 2020, p. 111). Inequality, one of the major issues in contemporary societies, will probably deteriorate further.

Fifth, the spread of the pandemic requires the improvement of public health care systems. An unequal distribution of resources or the uneven delivery of healthcare could incur harmful effects on people across and within regions. The structure of health systems is a vital condition for the wellbeing of people and the proper functioning of the economy. Thus, a more active role of states in upgrading the health systems is a fundamental factor in modern public policy.

Finally, the European Union has launched the Recovery Fund for the support of the economy and society. It seems that the disease is leading to a reconstruction of the priorities and the means of cohesion policy. This may transform the cohesion policy and the functioning of public policy as we knew it in the pre-Covid-19 era.

This study also opens some new directions for future work.

We believe that a robust age-specific analysis of the mortality from Covid-19 cannot be performed at this time. Such studies will be much more reliable and fruitful later on, when governments relax the restrictive measures already taken. There may also be more recurrent waves of the disease. No clear conclusions can be drawn yet with respect to the correlation between demographic dimensions and the levels of mortality due to the virus. It is however a fact that the Covid-19 pandemic has already led most countries into a major economic recession. The adverse effects of this crisis could impact public health care service capabilities and efficiency, adding a further future complication to the estimation of the association of demographic factors with Covid-19 mortality.

Nevertheless, one of the interesting outcomes of the present analysis is that higher rates of the disease are associated with higher levels of economic development and urbanization. These factors could offer a partial explanation of the patterns and the spread of disease. The most developed countries are usually those with greater trade openness and frequent interactions on a global scale.. Furthermore, empirical studies have shown that in urban areas, certain population groups tend to advance the transmission of pathogens and provide suitable conditions for the manifestation of infectious disease (Neiderud 2015). At the same time Covid-19 places an unequal burden on more deprived populations (Wade 2020). Therefore, Covid-19 requires a place-specific and people-centered implementation of public policy (Bag et al. 2020). This constitutes an important challenge for public policy in the current circumstances. A closer analysis of the association of urbanization with the spread of and fatalities from the disease, the impact of income level and spatial segregation on the spread of the disease, as well as analyses on smaller geographical scales constitute fruitful avenues for future research.

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A Appendix:

Table A.1: Data sources

Country and material	Source of data
Deaths and cases of Covid-19	
Deaths by age	
Austria, Denmark, France, Germany, The Netherlands, Norway, Spain, Portugal	Institut National D' Etudes Démographiques (IDED) https://dc-covid.site.ined.fr/en/
Greece	Greek National Public Health Organisation (EODY) https://eody.gov.gr/en/covid-19/
Italy	Instituto Superiori di Sanita (epicentre) https://www.epicentro.iss.it/coronavirus/sars-cov-2-sorveglianza-dati
Switzerland	Switzerland's Federal Office of Public Health https://www.bag.admin.ch/bag/en/home/krankheiten/ausbrueche-epidemien-pandemien/aktuelle-ausbrueche-epidemien/novel-cov/situation-schweiz-und-international.html#1867597016
Total deaths and cases (all ages)	
EU countries, EEA (European Economic Area) countries U.K.	European Center for Disease Prevention & Control (ECDC) for the EU / EEA https://www.ecdc.europa.eu/en/cases-2019-ncov-eueea
Socio-economic and demographic data and indices	
Population size and structure (1.1.2020); Life expectancy at birth (both sexes, last available year); Percent urban population (2017); Hospital beds per 100,000 population (2017); Gross Domestic Product per capita in 2018 (ppp-adjusted)	https://ec.europa.eu/eurostat/data/database

Table A.2: Variable definition and variable name

Variable	Definition
(death rate):	deaths of covid-19 per 100000 population
(incidence rate):	cases of covid-19 per 100000 population
(fatality rate):	deaths of covid-19 per 1000cases
Pop (65+) %:	percentage of population aged 65 or higher
Pop (70+) %:	percentage of population aged 70 or higher
Pop (80+) %:	percentage of population aged 80 or higher
e(o):	life expectancy at birth (latest data)
GDP:	Gross Domestic Product per capita ppp adjusted (2018)
Urban (%):	percentage of urban population (latest data)
Beds:	Hospital beds per 100,000 inhabitants
ISDR:	Indirectly Standardised Death Rates per 100000 population

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Spatial Analysis of the COVID-19 Pandemic in Hungary: Changing Epidemic Waves in Time and Space

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Abstract. This paper examines the spatial dynamics and regional distribution of the novel coronavirus epidemic in Hungary in an effort to obtain a deeper understanding of the connection between space and health. The paper also presents comprehensive epidemiologic data on the spatiotemporal spread of the COVID-19 pandemic in terms of the epidemic waves. Following a comparison of the growth rates of infection numbers, the current study explores the geographical dimension of the three pandemic waves. The partial transformation of spatial characteristics during the three epidemic waves is among the most important results found. While geographical hotspots influenced the first wave, newly confirmed coronavirus cases in the second and third waves were due to community-based epidemic spreading. Furthermore, the western-eastern spatial relation and the core-periphery model also affected the regional distribution of new cases and deaths in the initial two waves. However, a new spatial pattern – realised by the northern-southern spatial orientation – appeared during the third wave. The outputs of this paper offer feasible suggestions for evidence-based policymaking in pandemic prevention, mitigation, and preparedness.

1 Introduction

The link between human health and environment is not only strong but also multidimensional. Environmental factors affect health in extremely varied and complex ways, both in terms of socio-economic consequences and in terms of spatial significance (Remoundou, Koundouri 2009). The novel coronavirus pandemic has given us a clear understanding of the relationship between space and health. The effects the COVID-19 pandemic have had on society and the economy interconnect in varying ways at every spatial level. Spatial locations, human environments and geographical regions have differing effects on the actual epidemic situation, because social interactions among people have particular relevance in the number of people infected (Wang 2020).

The outbreak of a novel coronavirus pandemic based on the SARS-CoV-2 virus and its disease (COVID-19) occurred at the end of 2019. It spread rapidly and impacted the entire world by the end of February 2020. Combating the COVID-19 was the primary task facing all countries in the past year-and-a-half or more. The spatial scope, spatiotemporal distribution of the epidemic spread, the turning point time, and infection severity all provide policymakers with the essential information needed to create efficient epidemic prevention plans for future pandemics (Amdaoud et al. 2021). The COVID-19 pandemic triggered health and economic crisis the world over. Current challenges are long-term, and their societal and economic impacts remain unpredictable. The creation of effective solutions requires new approaches that integrate a community-based management strategy.

Pressing issues associated with monitoring and prevention concern everyone, and long-term issues related to the spread of this infection are naturally related to the spatial dimensions of human social interaction (Appiah-Otoo, Kursah 2021). The pandemic continues to surge all around us, which, in turn, requires the constant intervention of the public authorities. In the face of this significant health crisis, governments are multiplying containment measures, including border closures and travel bans, in an effort to decelerate the rapid spatial diffusion of the virus (Bavli et al. 2020).

Many Central and Eastern European (CEE) countries imposed tight restrictions at the very beginning of the first wave of the novel coronavirus in the spring of 2020. As a result, these countries experienced low infection rates and low death rates as the virus ravaged Western European countries (Röst et al. 2020). When the second wave of the virus hit the CEE region, it became apparent that Central and Eastern Europe would not avert the full brunt of the pandemic the second time around. The CEE countries also faced much larger outbreaks over the late summer and early autumn than in the spring of 2020. They managed the first wave of COVID-19 in the first half of 2020 very rapidly, but the governments of CEE countries have been struggling since. Reintroducing restrictions has been politically challenging, particularly after many months of eased restrictions. The third epidemic wave hit all European countries in the spring of 2021, with the CEE countries experiencing the most severe epidemiological situation. The second and the third pandemic waves in Europe had a more severe effect on CEE countries, which had been less affected by the first wave, indicating a change in the spatiality of the pandemic (Kovalcsik et al. 2021).

Unfortunately, Hungary is also part of the ongoing worldwide pandemic. Compared to Western European and the other CEE countries, the first pandemic wave was mild in Hungary, resulting in relatively low numbers of new coronavirus cases (Gombos et al. 2020). During the first wave, Hungary conducted a cross-sectional nationwide survey called H-UNCOVER. The survey revealed a low active infection rate (2.9 out of 10,000 people) and a low prevalence of prior SARS-CoV-2 exposure (68/10,000) (Merkely et al. 2020). However, Hungary experienced its highest number of cases and deaths during the third wave in the spring of 2021. Hungary is also a member of the Visegrad Group, where the spatial heterogeneity in the spread of the COVID-19 pandemic was similar during previous epidemic waves. One key piece of scientific evidence is that the pandemic hit countries and regions differently. The health crisis varied sharply across countries and within regions in the same country (Urbanovics et al. 2021), which is the main reason this paper focuses on the spatial distribution in the spread of the COVID-19 pandemic within Hungary.

2 Aims and Methods

The paper reviews spatial features of the three pandemic waves between 4 March 2020 and 11 June 2021 to discover how restrictions and mitigation interventions influenced the spatial distribution of infection in Hungary. This article concentrates solely on the spatial distribution of the pandemic and does not address economic challenges. Moreover, the present study is based on an investigation of Hungarian epidemiological data and does not aim to provide a European or a Central European overview of the pandemic.

The primary aim of this paper is to analyse the spatial features of the 2020 and 2021 COVID-19 pandemic in Hungary. Two main objectives focusing on the empirical analysis of health geography determine the framework of the study:

- Objective 1 is to produce statistical evidence on the spatial characteristics of the epidemic waves. The objective contains a spatial analysis of the new coronavirus cases during the first, the second, and the third waves of the epidemic. It also presents the main spatial characteristics of the three pandemic waves based on their comparison.

- Objective 2 is a regional assessment of policy responses implemented to mitigate social interactions during the three waves of the novel coronavirus pandemic. The analysis contains national, regional, and local measures targeting pandemic containment and the countering of spatial effects.

The secondary scope of the study is to develop a mixed methodology based on both quantitative and qualitative techniques to make a regional assessment of mitigation measures by targeting their spatial relevance.

The emphasis of our analysis is on evaluating the regional distribution of the incidence and prevalence of the COVID-19 disease. The other focus is on analysing the territorial adequacy of policy interventions and the capacity of these interventions to tackle territorially differentiated implications. The crucial questions are the following:

- What part of Hungary has been most affected by the pandemic?
- What is the typical spatial pattern of the pandemic?
- How did the spatial pattern of the pandemic change during the three relevant waves?
- How did territorial or spatial adequacy appear in policy interventions during the three waves of this pandemic?

Methodologically, our examination is a multidimensional approach integrating both quantitative and qualitative techniques.

The quantitative part of the examination is built on secondary, databased statistical analysis. The analysed data are taken from official sources (e.g. Hungarian Central Statistical Office, koronavirus.gov.hu).

Statistical data analysis covers the period between 4 March 2020 and 11 June 2021. The first two confirmed coronavirus cases were announced in Hungary on 4 March 2020, which denotes the start date of the Hungarian epidemic as well as our analysis. Over the more than 16 months of the COVID-19 epidemic in Hungary, the most relevant epidemiological data were announced daily. However, the daily data announcements were officially cancelled on 11 June 2021 and were shifted to include only weekdays.

The majority of epidemiological data was published only at the national level, but some regional level data was also reported. To calculate the proportion of crude epidemiological data per 100,000 inhabitants, we utilized officially published population data from the Hungarian Central Statistical Office (www.ksh.hu).

Our spatial analysis used some quantitative variables based on epidemiological data. These epidemiological variables have spatial relevance, but they are available at different geographical scales, which means the variables are not synchronised with each other according to spatial examination level. Here is a classification based on their official availability:

Variables available at the national level (whole country): these are only available at the national level to describe the total or the daily number of confirmed cases and deaths, e.g. the total number of confirmed cases, the total number of active cases[1], new daily confirmed cases, the total number of deaths, the total number of recovered cases etc. These variables are only suitable for describing national tendencies and changes in time.

Variables available at the county level (NUTS 3): only two are available at the county level and suitable for analysing the regional distribution of the total number of confirmed cases and new daily confirmed cases.

Variables available at the micro-regional level (LAU 1): these two variables are available at the local level to evaluate the spatial pattern of epidemic waves, e.g. the total number of confirmed cases and the total number of deaths.

[1] It is based on the total number of confirmed cases without the number of recovered cases and deaths.

Missing detailed spatial data does not allow an in-depth spatial analysis, because officially present epidemiological data such as total confirmed cases are published only at the county level. Available spatial data allow only a certain type of analysis that focuses on reviewing changes in regional patterns regarding the waves, especially at the county level. Two variables, such as the total confirmed cases and the total number of deaths, were announced only once at the micro-regional level at the beginning of June 2021. The examination period of these variables was not officially synchronised: the total number of confirmed cases covers the period between 4 March 2020 and 14 February 2021, while the total number of deaths included the period between 4 March 2020 and 4 March 2021. This explains why we could examine the first two epidemic waves at the micro-regional level, whereas we could only examine the spatial pattern of the third wave at the county level.

Official epidemiological data are analysed according to the three pandemic waves. The beginning and end dates of each wave are based on the changing number of active cases. We decided to use these as key indicators because the variable shows the number of people currently infected within the country. Thus, the long-term changes of this indicator also provide comprehensive information about the increasing or decreasing tendency of the given epidemic wave, while its highest number indicates the peak of the wave.

Our descriptive analysis compares the growth rates of active numbers among the three pandemic waves. It also studies the spatial dimension of the pandemic. There were significant differences among the waves due to the number of active cases – especially between the first wave and the subsequent two waves. Therefore, we chose separated figures to visualise each epidemic wave, which explains why the y-axis of each figure is shown on a different scale. Nevertheless, using separated figures to analyse each wave despite summarising each in only one figure helped us to harmonise the aim of the analysis with the research question, thereby providing a complete picture of the common and spatial characteristics of the COVID-19 pandemic in Hungary.

The present study considers the role of geographical distribution of infections and deaths and assigns a greater role to the territorial divisions of the sub-national levels as units of analysis within the spatial limitations of the study. Therefore, besides descriptive data, we also apply spatial analysis to record the results. Firstly, we examined the relationship between epidemiological data and different socioeconomic indicators using Pearson's correlation coefficient. Secondly, we examined the spatial concentrations of the epidemiological data using Location Quotient (LQ), which indicates the relative distributions or relative concentrations of a subarea to the area as a whole (Pandey et al. 2021). Thirdly, we conducted a cluster analysis of the micro-regions (LAU 1) involving the rate of deaths within COVID-19 infected persons and three socio-economic indicators (annual income per taxpayer, unemployment rate and life expectancy at birth). For clustering micro-regions, we used hierarchical cluster analysis and applied Ward's method, which is based on the size of an error sum-of-squares criterion. To choose the number of clusters, we applied Calinski–Harabasz's and Duda–Hart's criteria (Everitt et al. 2011). Finally, we decided to create eight groups from the micro-regions.

Calculations were prepared in Microsoft Excel and Stata, while maps were created with QGIS 3.12 software.

The content analysis within the qualitative part focuses on reviewing the restrictions ordered by the Hungarian government during the COVID-19 pandemic. The objective is to evaluate the spatial relevance of specific measures. All official documents, such as government decrees, circulars, regulations and other policy documents announced under the state of epidemiological emergencies, are examined. These documents are taken from the following three governmental sources:

Hungarian Official Gazette (http://www.magyarkozlony.hu/): this source provides the official text of any newly issued piece or amendment to Hungarian legislation. The website is operated by the Central Office for Administrative and Electronic Public Services and is only available in Hungarian.

Official Governmental Website in English (https://abouthungary.hu/): this source offers news in brief about Hungary, but also contains official speeches and remarks written in English.

Official Governmental Website on the pandemic (koronavirus.gov.hu): this is the official information website on the pandemic written only in Hungarian, covering news, epidemiological data, brochures, legislation etc., regarding the Hungarian novel coronavirus epidemic.

The contextual framework of our content analysis is constructed on the following relevant questions, which are the specific focus for studying the Official Hungarian Policy Documents on the pandemic:

- How does the given governmental regulation integrate spatial adequacy regarding the epidemic? Does the policy intervention contain territorially or spatially sensitive measures at all?
- Which is the relevant spatial scale in restrictions and measures? Is there a balance between nationally and locally introduced measures?
- How can local competency appear in the restrictive and mitigating measures? Do municipalities have a role in policy responses to the challenges of the pandemic in Hungary?

In response to the fundamental questions of our content analysis, the results are suitable to compare spatial consequences of the restrictions; thus, it is also appropriate to discover the connection between measures and the growth of epidemic waves.

Based on applied quantitative and qualitative methods, the logical structure of our research is as follows:

1. The first step comprises the processing of epidemiological data related to the coronavirus epidemic and investigating territorial patterns of infections in Hungary.
2. The second step covers a comparison of the spatial effects of the first and the second waves of the pandemic.
3. The third step constitutes the evaluation of the policy measures and interventions introduced in the first and the second waves of the pandemic from the perspective of efficiency in providing adequate solutions and integrating spatial aspects.
4. The fourth step encompasses an overview of the connection between the spatial distribution of the pandemic and the spatial adequacy of policy interventions.

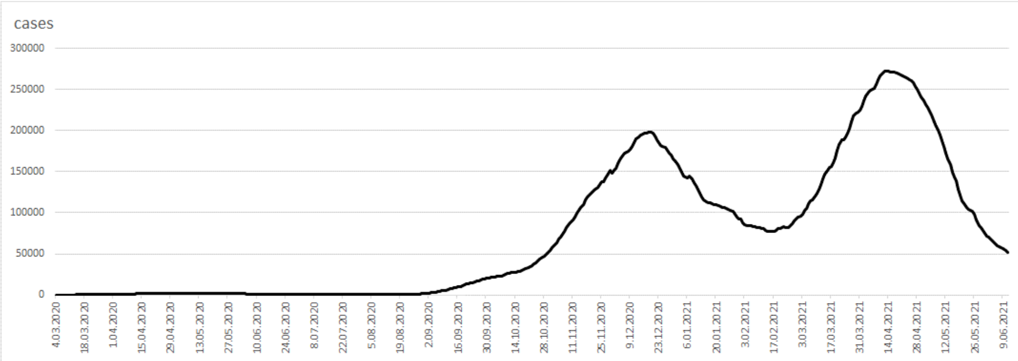
The results and experiences of this research can contribute to successful preparation for and prevention of further pandemic waves as well as inform the mitigation of adverse spatial impacts.

3 Results

The structure of this chapter is as follows: Firstly, via a statistical analysis focusing on epidemiological data of the pandemic, we present a comprehensive comparison of the epidemic waves in Hungary. Secondly, we provide a description of our statistical analysis regarding the spatiality of the epidemic waves. Thirdly, we summarise our experiences in analysing the spatial adequacy of the Hungarian restrictions.

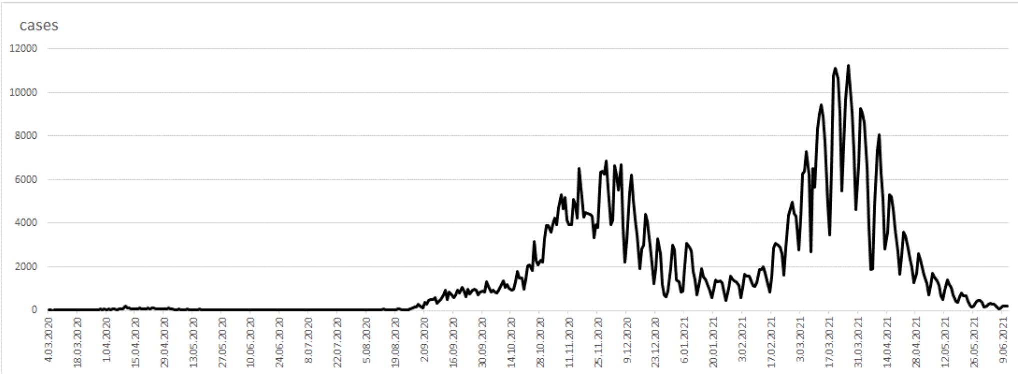
3.1 The Most Important Characteristics of the Epidemic Waves of the COVID-19 Pandemic in Hungary – 'Flatten the Curve' Versus 'Over the Top'

The first two confirmed coronavirus cases were announced in Hungary on 4 March 2020. These two known cases were foreign students studying in Hungary. According to the government's official website (koronavirus.gov.hu), the first coronavirus-related death happened on 15 March 2020. The first recovered patient left the hospital on 12 March 2020. On 11 March 2020, the Hungarian government declared a state of epidemic emergency



Data source: koronavirus.gov.hu

Figure 1: Total number of active COVID-19 cases in Hungary (4 March 2020 – 11 June 2020)



Data source: koronavirus.gov.hu

Figure 2: Daily new confirmed COVID-19 cases in Hungary (4 March 2020 – 11 June 2021)

lasting until 18 June 2020, and the state of emergency was reinstated on 11 November 2020. The second announced state of emergency was extended several times and was valid until the 18 December 2021.

When examining the daily evolution of COVID-19 confirmed active cases, the three waves based on the pace of the spread of the epidemic in Hungary become apparent (Figure 1, Figure 2).

The first epidemic wave (4 March 2020 – 17 July 2020): this period followed the public health strategy of 'flatten the curve'. The number of active cases was below 2,100, and the number of daily new cases only reached 210. This first wave lasted longer than four months and integrated different phases of the incidences. At the beginning of this period, in the phase of isolated cases, the daily number of new cases exhibited a steady increase. In the phase of group incidences, a partial acceleration of epidemic spread was witnessed after 21 March 2020. The rising number of active cases reached its peak on 4 May 2020 (2055 people). The phase of a continuous decline in the number of active cases started on 5 May 2020, and the daily number of confirmed cases of infections dropped below 50. A steady declining trend generally implied a low number of infected patients per day. The lowest number of active cases was reported on 17 July 2020 (478 people). The new daily cases generally remained below 10 throughout the middle of summer, which was similar to the initial phase of the first wave. A slight increase in the daily number of new cases linked to regional or institutional hotspots was detected from the end of July. These new cases were easy to isolate.

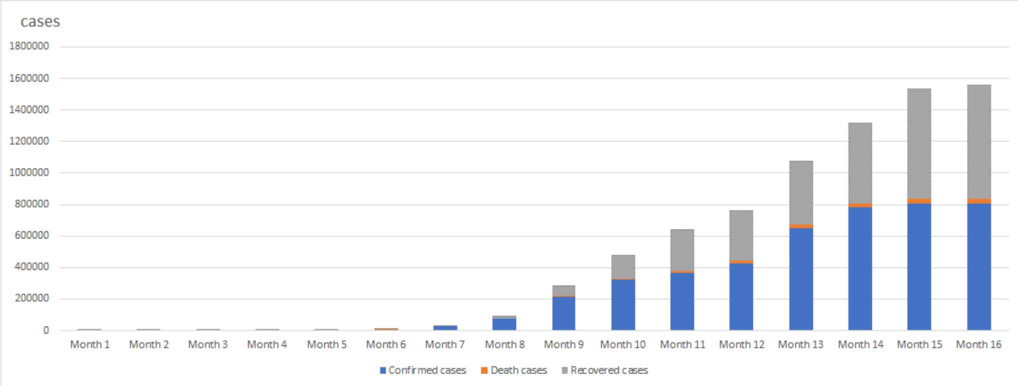
The second epidemic wave (18 July 2020 – 16 February 2021): this period could be described by the term 'over the top', meaning that the number of daily new cases and active cases as well as deaths were significantly higher than in the first wave of the Hungarian COVID-19 epidemic. A phase of stagnating numbers of active and daily new cases began in the middle of June, while a slight increase began at the end of July, which is why we detect it as the boundary between the first and the second waves of the epidemic. Furthermore, a breakout in the number of daily new cases, which tripled from the previous day, occurred on 26 August 2020. Moreover, the number of weekly new cases displayed a nearly five-time difference during this period. The highest number of daily new cases occurred on 29 November 2020. That day saw 6,868 daily new cases, which was 33 times greater than the highest number of daily new first wave cases (210) reached on 10 April 2020. The sharply rising number of active cases from the beginning of September peaked on 17 December 2020 with 86,954 cases. Following this day, a continuous, slightly decreasing tendency started in the second epidemic wave. This second wave lasted longer than six months, but it could not reach the lows in the number of active or daily cases recorded in the first wave. The main reason behind this lack of bottoming is the beginning of the third epidemic wave, which erupted on 17 February 2021.

The third epidemic wave (17 February 2021 – 16 May 2021): during this period, the term 'over the top' refers to the number of daily new cases and active cases as well as deaths, which were the highest ever in the Hungarian COVID-19 epidemic thus far. All the examined epidemiological data peaks were tilted, and the three-month period of this epidemic wave proved the most challenging. Over 90% of all confirmed cases in Hungary during the third epidemic wave were caused by the Alpha variant of the SARS-CoV-2 virus.

The highest number of active confirmed cases, 272,066, was recorded on 14 April 2021, marking the peak of the third wave. The phase of intensive increase in this phase lasted from 17 February 2021 to 18 April 2021. The highest number of daily new cases during this period, 11,265, occurred on 26 March 2021. The moderate decreasing phase of the third wave started on 19 April 2021. The wave persisted well into June as the number of active cases remained over 50,000. The number of daily new confirmed cases fell below 1,000 in the middle of May. By the middle of June, daily new cases averaged 150-200. Though the third wave extended beyond three months, the Government Special Operational Body announced the measures in place at the beginning of June.

The relatively quick exit from the third wave compared to the other two waves has been attributed to the progressive vaccination program in Hungary. The government published its vaccination strategy at the end of 2020 and based its national plan on a detailed list that prioritised citizens according to vulnerability (based on age, occupation, or chronic illnesses). Healthcare worker vaccinations started at the end of 2020, while older people began receiving vaccines at the end of February 2021. Mass vaccination started at the beginning of April 2021. By 22 April 2021, 3.5 million Hungarians had received the first dose of the Covid vaccine. A month later, on 23 May 2021, 5 million had been registered as having received the first shot.

Besides vaccination, the other significant difference between the epidemic waves is in the number of PCR tests. The number of PCR tests has changed over time, which can significantly affect the number of cases detected. Test numbers remained low during the first wave due to the lack of testing capacity, which resulted in a very low number of daily new confirmed cases. The official coronavirus figures seemed reliable regarding a high number of tests during the second wave because there was a 30-40 times larger difference in new daily cases between the first two epidemic waves. There were on average 3,000-7,000 PCR tests per day during the spring of 2020. During the autumn of 2020, the number of tests rose to 10,000-12,000 on average. By the peak of the second wave, it was more than 20,000. The rate of positive tests varied between 8% and 24%. However, at the peak of the third wave, over 30,000 PCR tests were administered per day. Of these, at least 30 % were positive. The number of PCR tests declined in unison with the decreasing phase of the third wave, flattening out at 1,000-2,000 tests per day with a 1-2% positive test result ratio. On 11 June 2021, the total confirmed number of people infected with SARS-CoV-2 in Hungary stood at 806,790, and active COVID-19 cases amounted to 52,272. There were 5,567 people in compulsory home quarantine. The total number of



Data source: koronavirus.gov.hu

Figure 3: Total number of confirmed COVID-19 cases, deaths and recovered patients in Hungary per month (4 March 2020 – 11 June 2021)

recovered patients was 724,614, while deaths numbered 29,904. Hungary ranked among European countries with the highest ratio of COVID-19 deaths per million inhabitants. The mortality rate for the novel coronavirus reached 3.7 % of the total infection rate by the middle of June 2021, which was higher than the European average. More than 80% of deaths occurred in people over 65. Eight per cent of all inhabitants in Hungary were registered as confirmed COVID-19 cases.

According to the official government website, 25% of daily new confirmed cases at the beginning of September 2020 were in the 20-29 age group (koronavirus.gov.hu). By contrast, at the beginning of November, the average age of those who contracted the virus was 45. Out of every 100,000 residents, 1,540 Covid-19 patients were in the 20-29 age group, 1,331 in the 30-39 age group, 1,632 in the 40-49 age group, and 1,473 in the 50-59 age group. 1,589 patients were aged 60-79, and 1,408 were older than 80 (koronavirus.gov.hu). Unfortunately, there was no further information on the mean age of daily new confirmed cases after the September 2020 announcement; data are not available yet.

The total number of confirmed cases significantly increased from the beginning of the second wave (Figure 3). In the first half of October 2020, the number of daily deaths was less than 50, and daily new confirmed cases already exceeded 1,000 at this time. The continuous increasing tendency in the number of deaths began from the beginning of November. Daily deaths hovered around the hundred mark. During the second wave, the number of deaths per day remained below 200, but peaked at 311 deaths in the third wave. On the other hand, the total number of recovered patients slowly followed the number of new daily cases, implying an increase in complicated cases requiring hospitalisation or longer recovery periods. The number of hospitalised patients on ventilators continuously increased from the middle of the second wave and peaked during the third wave. The highest number of hospitalised patients was 12,553 on 30 March 2021, while the greatest number of patients on ventilators hit 1,529 on the same day. Healthcare capacity became overloaded during the second wave, while Hungary's healthcare system reached the point of exhaustion in the middle of the third wave.

In sum, the most relevant differences among the three pandemic waves in Hungary are realised in the following features. Firstly, the number of daily new cases and active confirmed cases in the second and third waves were generally 30-50 times higher than in the first wave. Secondly, the typical figure of the epidemic curve was flattened in the first wave; steep in the second wave, and a wide plateau in the third wave. Thirdly, the epidemic curve reached a bottom at the end of the first wave, but not in the second wave because the third wave, based on the spatial spreading of the Alpha variant of the SARS-CoV-2 virus, erupted quickly. Fourthly, at the beginning of the second wave, social interactions among the younger generation exacerbated the epidemic wave, giving rise to an ascending phase. This resulted in a mean age of confirmed cases that was significantly lower at the beginning of the second wave. Still, it steadily increased in parallel with the spatial spreading of the epidemic curve. Finally, hospitalised patients needing ventilators reached a peak during the third wave, resulting in an overloaded healthcare system.

3.2 Spatial Distribution of the Epidemic Waves of the COVID-19 Pandemic in Hungary – Local Hotspots versus National Chain of Infections

The spatial distribution of the COVID-19 pandemic partially transformed during the three epidemic waves in Hungary. On the one hand, the geographical centres of the infections were Budapest and Pest County, with the highest numbers of total confirmed and daily new cases in the waves. Home to 31% of the Hungarian population, the dense population of the capital city (Budapest) and its surroundings (Pest County) played a decisive role in case numbers. On the other hand, there were significant spatial inequalities among different parts of the country according to the number of confirmed cases per 100,000 inhabitants.

According to regular official spatial data published at the county level in Hungary (NUTS 3 level), the spatial pattern differed in the waves.

The county-level distribution of new confirmed COVID-19 cases in Hungary revealed a spatial concentration in the capital city (Budapest) and its surroundings (Pest county) in the first wave and pointed to a western-eastern division of the country (Figure 4). According to the total number of confirmed cases per 100,000 inhabitants, the eastern half of Hungary (with the exception of Csongrád-Csanád County) was less affected, based on the lower number of infections. From the final days of April 2020, an increasing number of new confirmed cases were detected predominantly in the western counties – Fejér, Komárom-Esztergom, Veszprém, and Zala counties – where infections affected larger institutions (hospitals, nursing homes). Institutional hotspots – e.g., those based on the increasing number of infections in nursing homes or hospitals – significantly influenced the geographical concentration of new cases per week. This growing tendency for new and active cases led to a peak at the beginning of May, resulting in a typical spatial pattern of COVID-19 diseases within the country based on a western-eastern division. From the beginning of July, the daily number of new infections increased in the eastern part of the country, specifically in Borsod-Abaúj-Zemplén, Csongrád-Csanád, and Hajdú-Bihar counties. The spatial conclusions of the first wave reveal that the north-western part of the country was severely affected in contrast to the southern and eastern parts of Hungary. This north-western part is more economically developed than the rest of the country (with the exception of Budapest and its immediate surroundings).

The spatial distribution of new confirmed coronavirus cases during the second wave demonstrated the changing spatial distribution of the epidemic within the country, based on spatial chains of the infection (Figure 5). Firstly, the capital city (Budapest) and its surroundings (Pest County) were also the most affected by the infectious disease, but at a slowly declining rate from the end of October 2020. Secondly, a high number of new confirmed cases affected all counties from the beginning of the second wave. Thirdly, the spatial pattern of new confirmed cases did not indicate a western-eastern division, because the number of new cases was high everywhere in the country during the second wave. Fourthly, the ranking position of counties based on new confirmed cases per 100,000 inhabitants was completely different week per week during the second wave. Fifthly, the continuous increasing tendency was experienced in new confirmed cases in all counties until the week of the peak during the second wave. Still, there were significant differences among counties in growth rates week after week.

The landing phase of the second wave did not bottom like the first wave did in the summer of 2020, because the third epidemic wave occurred unexpectedly at the end of February 2021. The taking off phase of the third wave resulted in the highest number of confirmed cases experienced in the Hungarian COVID-19 epidemic (Figure 6). During this taking off phase, Nógrád County, in the northern part of the country, was the most affected. On the other hand, it became obvious from the initial phase of the third wave that Budapest and Pest County were not the most infected areas according to the number of confirmed cases per 100,000. Another general observation was that the northern part of the country – especially Nógrád County – along the Slovakian border was the

(a) A week in the taking off phase (23 March 2020 – 29 March 2020)

(b) The week of the peak (04 May 2020 – 10 May 2020)

(c) A week in the landing phase (22 June 2020 – 28 June 2020)

Data source: koronavirus.gov.hu
Note: Budapest – the capital city; Pest – the name of a county

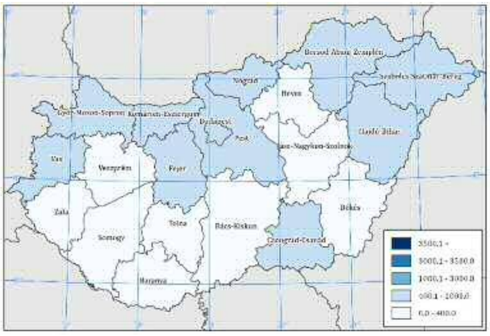
Figure 4: Total number of confirmed COVID-19 cases per 100,000 inhabitants in Hungarian counties (NUTS 3) during the different phases of the first wave, based on weeks

most affected area from the beginning of the third wave. The spatial distribution of the confirmed cases showed a very high number in all counties during the entire wave. At the same time, its spatial pattern also represented a combined western-eastern and northern-southern relation. Chains of infections influenced the spatial distribution of the third wave and resulted in a mass outbreak based on the spatial spreading of the Alpha variant of the new coronavirus. The landing phase of the third wave lasted more than one month, but the typical spatial distribution of confirmed cases based on western-eastern and northern-southern spatial pattern did not change at all.

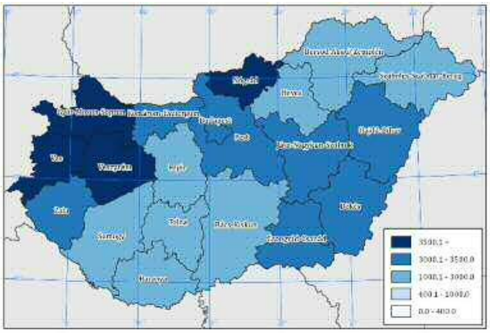
According to official epidemical data at the micro-regional level in Hungary (LAU 1 level), the spatial pattern is more sophisticated than could be seen at the county level.

There were 387,462 confirmed COVID-19 cases in Hungary between 4 March 2020 and 14 February 2021, while the number of deaths was 13,706. Among the 3,230 Hungarian settlements, only 71 averted infections during this period, while 1,197 settlements recorded no deaths from the infection.

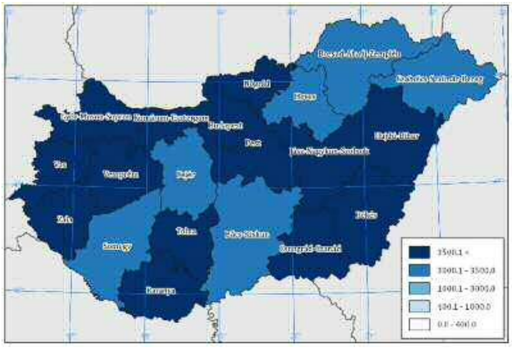
The spatial distribution of the total number of confirmed patients per 100,000 inhabitants shows a pattern with increasing occurrence from the north and the north-western parts of the country to the south and the north-eastern areas (Figure 7). Developed and urbanised regions of the country were being affected by the pandemic, especially during the first two epidemic waves. However, another pattern appears in the spatial distribution of the total number of deaths per 100,000 inhabitants in Hungary (Figure 8). The deaths were primarily recorded in the less developed areas of the country, e.g. the north-eastern part or the southern borderline. A similar pattern can be observed in the rate of deaths among confirmed cases (Figure 9). On the one hand, the number of confirmed cases is higher in more developed parts of the country, but on the other hand, the



(a) A week in the taking off phase (12 October 2020 – 18 October 2020)



(b) The week of the peak (14 December 2020 – 20 December 2020)



(c) A week in the landing phase (25 January 2021 – 31 January 2021)

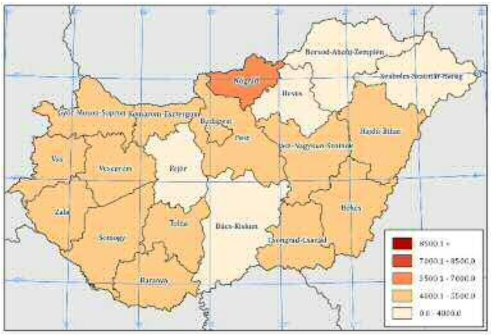
Data source: koronavirus.gov.hu
Notes: Budapest – the capital city; Pest – the name of a county

Figure 5: Total number of confirmed COVID-19 cases per 100,000 inhabitants in Hungarian counties (NUTS 3) during the different phases of the third wave, based on weeks

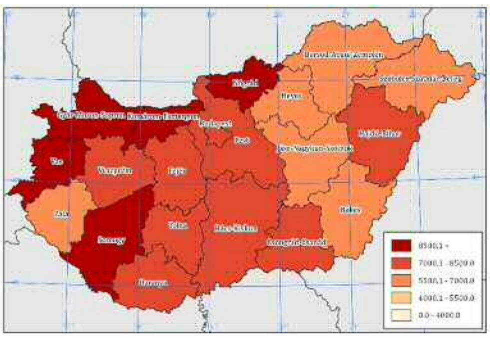
survival rate is better than the rate in less developed areas in Hungary. Namely, a higher number and rate of deaths caused by COVID-19 was experienced in the socioeconomically disadvantaged parts of the country, e.g., inner peripheries, southern border, north-eastern regions etc. Poor health, lower life expectancy and a higher rate of cardiovascular diseases are also prevalent in these areas (Uzzoli et al. 2020).

Pearson's correlation coefficient values show a moderate connection between examined epidemiological data and different socioeconomic indicators in Hungary. Among them, income and unemployment rate as economic indicators, and life expectancy as a health indicator, are in a middle strong relationship with the variable of COVID-19 cases. This indicates that higher income and life expectancy, as well as lower unemployment, go together with a higher number of registered coronavirus cases. However, these economic indicators play a weaker role in the occurrence of deaths caused by COVID-19. The connection between health indicators and the number of deaths is stronger than the connection with economic indicators. In other words, health plays a larger role in COVID-19 deaths than financial status does.

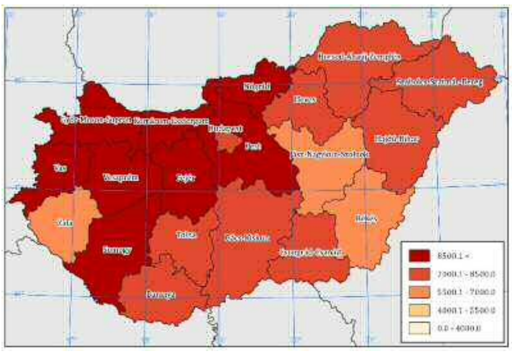
The LQ analysis showed the micro-regional concentration of deaths and COVID-19-infected people compared to the national average. Using the LQ values of the micro-regions, we created three categories for each indicator. Those micro-regions, where the value of LQ exceeded 1.1 (at least 10% higher than the national average), represent a "high" level of concentration, while micro-regions, where the LQ value remained below 0.9 (at least 10% lower than the national average), suggest a "low" level of concentration. As we labelled the micro-regions by the concentration level of each indicator, nine different combinations of categories have been created (Figure 10). The results illustrate that the less developed micro-regions displayed a high concentration of COVID-19 deaths, even though the



(a) A week in the taking off phase (22 February 2021 – 28 February 2021)



(b) The week of the peak (12 April 2021 – 18 April 2021)



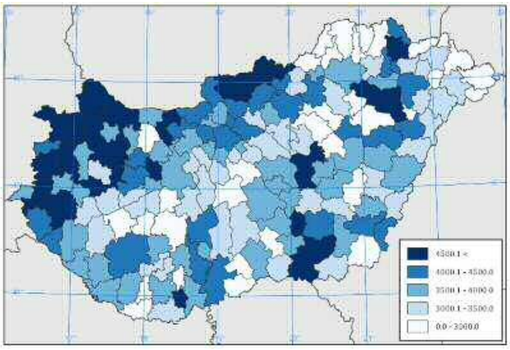
(c) A week in the landing phase (24 May 2021 – 30 May 2021)

Source: koronavirus.gov.hu
Notes: Budapest – the capital city; Pest – the name of a county

Figure 6: Total number of confirmed COVID-19 cases per 100,000 inhabitants in Hungarian counties (NUTS 3) during the different phases of the third wave, based on weeks

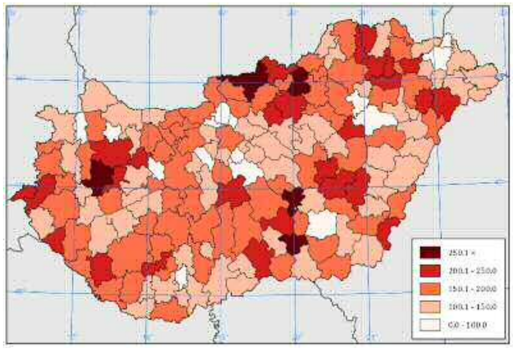
concentration of infected people was at moderate or low levels. However, there are some less developed regions (mostly in the southern and eastern parts of Hungary) in which the concentration levels of deaths and infected people were relatively low. This can be explained by the lower risk of serious infection due to social distancing. The concentration levels in the county seats and Budapest varied between moderate and low. The results of the cluster analysis provide a more detailed picture about the role of socioeconomic conditions (Figure 11). Clusters that had a relatively low death rate (Cluster 1 to 4) were indicative of a relatively high level of income per taxpayer, a high life expectancy at birth and a low unemployment rate. These groups include primarily urbanized and developed regions. In clusters (Cluster 5 to 8) where the income per taxpayer and life expectancy at birth was relatively low, the COVID-19 death rate was higher. Although these data provide only a snapshot of the possible relationship of socioeconomic conditions and the COVID-19 death rate in micro-regions, the results suggest that these conditions might influence the concentration of deaths and infected people.

Summarising the spatial relevance of the Hungarian epidemic waves highlights the following observations. Spatial diffusion of newly confirmed coronavirus cases was influenced by the community-based epidemic in the first wave, while the chain of infections affected the second and the third waves. Budapest and Pest County were the permanent population-based geographical centres of new infections during the waves, but the hotspots existed only in the first wave. In addition to Budapest and Pest County, some periodic spatial concentrations resulted in county-based hotspots in the country. This indicates that the spatial concentration of infections by county was permanently changing week after week. In the spring of 2021, COVID-19 infected more than 97% of Hungarian settlements, with 63% of these settlements recording at least one death from the virus.



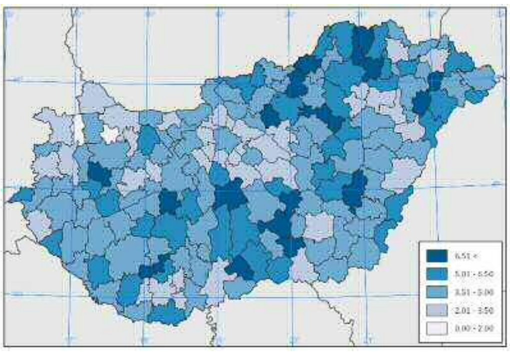
Data Source: K-Monitor

Figure 7: Total number of confirmed COVID-19 cases per 100,000 inhabitants at the micro-regional level of Hungary (LAU 1) between 4 March 2020 and 14 February 2021



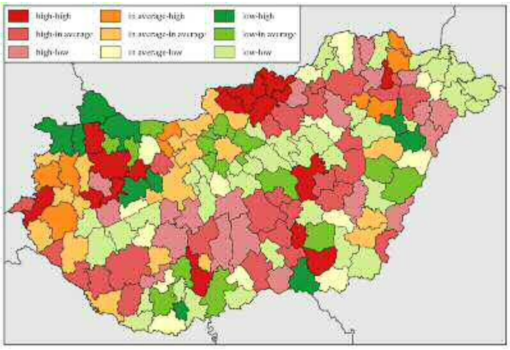
Data source: K-Monitor

Figure 8: Total number of deaths caused by COVID-19 per 100,000 inhabitants at the micro-regional level of Hungary (LAU 1) between 4 March 2020 and 4 March 2021



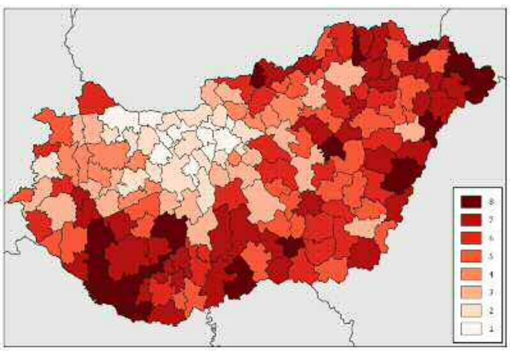
Data source: K-Monitor

Figure 9: Rate of deaths among confirmed COVID-19 cases (%) at the micro-regional level of Hungary (LAU 1) between 4 March 2020 and 14 February 2021



Data source: K-Monitor
Notes: The red-coloured areas reported a high level (LQ >1.1), orange-coloured micro-regions had a moderate level (0.9 <LQ <1.1), while green-coloured areas showed a low level of concentration (LQ <0.9) of deaths. The darker coloured areas reported a high level, while lighter coloured micro-regions had a low level of concentration of infected people.

Figure 10: The spatial concentration of deaths (first term) and infected (second term) people at the micro-regional level in Hungary (LAU 1) between 4 March 2020 and 14 February 2021



Data source: K-Monitor
Notes: The darker, red-coloured areas reported a higher rate of death, while the lighter red-coloured micro-regions showed a lower rate of death.

Figure 11: Clustering of the micro-regions based on the death rate within COVID-19 infected people and various socio-economic indicators

At the county level, the typical spatial pattern of the epidemic waves was mainly based on a western-eastern division completed by a northern-southern spatial relation during the third wave. At the micro-regional level, centre-periphery relation was the dominant spatial pattern in the occurrence of the newly registered cases and deaths. The highest number of reported cases occurred in the most developed and urbanised micro-regions at the LAU 1 level. On the other hand, poor health conditions had a more substantial role in the number and rate of deaths with the most disadvantaged micro-regions experiencing the highest death rates. In other words, centres are significantly influenced by COVID-19 cases, while peripheries are primarily affected by COVID-19 deaths.

3.3 Spatial Relevance of Covid-19 Restrictions to the Pandemic in Hungary – Based on Continuous Tightening and Easing

In response to the emerging COVID-19 pandemic, the Hungarian government declared a state of emergency twice in 2020: initially, between 11 March and 18 June 2020, during the first epidemic wave, and again on 11 November 2020, during the second wave. The latter state of emergency has been continuously extended and is scheduled to end on 18 December 2021. Governments must design new, innovative instruments to counter the health and socio-economic impacts of the pandemic and induced crisis. The restrictions under the state of epidemiological emergencies had similarities and differences during the three examined epidemic waves in Hungary according to the primary objectives of prevention. These policy responses were specially introduced at the national level. Still, due to the diverse spatial impacts of the epidemic, there is some degree of uncertainty about whether territorially sensitive measures should be among policy responses, and to what extent spatial aspects should be incorporated into these interventions.

During the first wave, the state of emergency restrictions required people to quarantine themselves, employees to engage in home office, and students to participate in online education. These restrictive measures affected the entire country, but municipalities were given the discretion to close various parts of their respective settlements in the intensive increasing phase of the epidemic. Various spatially sensitive protection measures were implemented in the territorial hotspots of the epidemic (e.g. the masks required to be worn on public transport and in stores in the capital city). The restrictions were lifted gradually from 4 May 2020, through the so-called sliding mode control displaying a marked spatial approach. It implied an easing of restrictions in less infected areas outside of the capital city and its neighbouring Pest County. In contrast, partial restrictions remained in force in Budapest and Pest County for two additional weeks, and preventive measures were strongly encouraged across the country. On 18 June 2020, the Hungarian government lifted the state of emergency and the lockdown imposed in spring to combat the COVID-19 pandemic. This allowed Hungarian employers to prepare for a return to business as usual.

Overall, the restrictive and mitigating measures designed to tackle the COVID-19 emergency had diverse spatial implications during the first wave of the epidemic in Hungary in the first half of 2020. In addition to granting settlements more room to manoeuvre concerning containment efforts, the location of territorial focal points was also taken into account (in a capital city-countryside context), and the role of geographical isolation was emphasised in preventing group infections. When the relaxation of restrictions produced a growing number of social interactions and, thus, a higher number of infections, it led to the enforcement of tighter restrictions nationally and regionally (e.g. specific counties). This foreshadowed the sustained presence of tightening and easing policies along with their cyclical nature and spatially heterogeneous distribution in the country over the year 2020. In the first wave of the fight against the pandemic, Hungary managed to avoid mass infections, but due to the permanent imminence of the pandemic threat, the state of epidemiological preparedness remained in force in the country over the second half of 2020 as well.

The anti-epidemic approach of epidemiological preparedness during the three epidemic waves was based on mainly national measures (e.g. masks required to be worn on public transport and in stores for the whole country) (Figure 12). In comparison to the beginning of the three waves, a significant gap emerged. At the beginning of the first wave, the nationally introduced general lockdown was combined with the state of emergency. The second wave saw only restrictions in two phases, which were ended in the third wave. The first phase of introduced restrictions during the second wave started on 1 September when the Hungarian borders were closed and some mask rules were tightened. In parallel with these national regulations, local and institutional competencies of restrictions against the COVID-19 pandemic were strengthened. For instance, employers could decide about ordering home office, or schools could choose between online and personal education or some mix of both (such as "hybrid education"), based on the number of infected students and teachers. Besides these new national rules and local opportunities in decision-making, anti-epidemic measures strongly highlighted the role of individual protection based on mask wearing, social distancing, and disinfecting. The second phase of newly introduced restrictions during the second wave was fittingly connected to the published emergency degree on 11 November. These new restrictions against COVID-19 were organised to be the strictest pandemic measures Hungary had taken: e.g. nightly curfew between 20.00-05.00; mask rules tightened; sports facilities closed to the public; a general events ban with very few exceptions; restaurants operating with take-out and delivery only; shops closed at 19.00; high schools and universities switched to remote learning, etc.

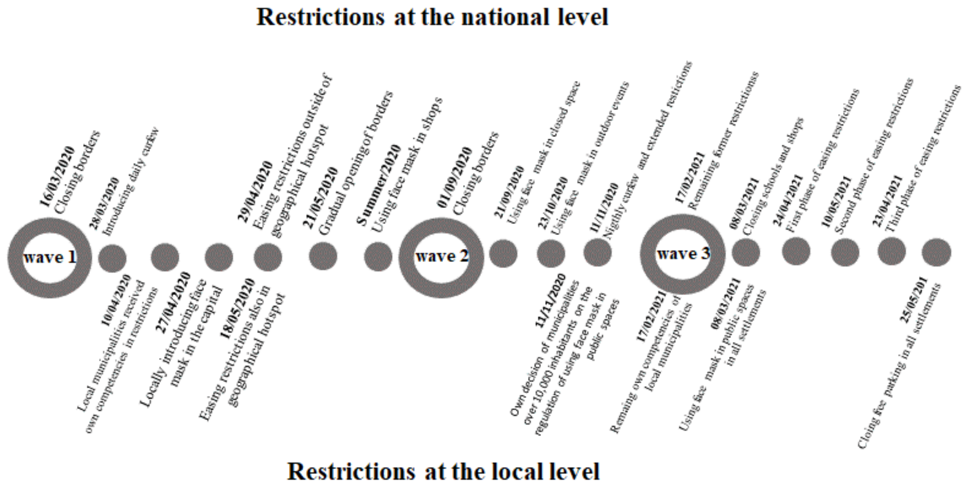


Figure 12: Restrictions regarding the COVID-19 epidemic waves in Hungary and their spatial relevance (04 March 2020 – 11 June 2021)

Masks were mandatory in all public spaces after 11 November. Still, municipalities also received the decree to make detailed local rules for public mask mandate in settlements with populations over 10,000.

This multi-stage regulation of anti-epidemic measures of the second wave was extended and completed during the third wave. New elements of restrictions, which had been in effect since November 2020, were introduced on 8 March 2021. During this lockdown, kindergartens, primary schools, and shops (except for hypermarkets, post offices, drugstores, and pharmacies) closed. Other measures (e.g. nightly curfew, public mask mandates, online education in secondary schools, etc.) remained unchanged. On the other hand, during the third wave, a new element of protection measures appeared in the form of vaccination. A new basis for organising Hungarian anti-epidemic measures emerged. The easing of multi-stage regulations was directly connected to the number of vaccinated inhabitants. The first phase of easing was triggered on 24 April 2021 when the goal of 3.5 million vaccinated people was reached; e.g. one of the eased measures was the reopening of restaurants. The second phase of multi-stage regulation of easing on 10 May was implemented after the 4 million mark was reached – e.g. school opening and the phasing out of home office. The third phase of easing on 22 May occurred after the 5 million threshold was reached, which represents roughly half of Hungary's population. This third phase brought the greatest easing measures: e.g. lifting the curfew, dropping the mask mandate, permitting the organisation of private events with up to 50 people, etc. As part of the vaccination drive, people who received their first vaccine doses were issued government immunity certificates. On 24 June 2021, Hungary reopened the Schengen borders. Local authorities received some powers to introduce additional restrictions, e.g. closing the settlements to visitors on weekends.

Summarising our knowledge on the spatial relevance of restrictions resulting from the new coronavirus pandemic in Hungary, the most essential features are nationally-introduced regulations supplemented by local competencies. In addition to introduced restrictions, other tools could be deployed. For instance, targeted measures to reduce infection numbers could be taken in severely affected geographical locations.

The most important highlight is that national level mitigation measures play the primary role in the anti-epidemic approach in Hungary. The municipalities' competencies in setting restrictions appeared in the very beginning of the Hungarian epidemic, but their function remained of secondary importance. The municipalities at the local level differed in taking measures because only settlements over 10,000 inhabitants could make their own decisions concerning face masks in public spaces. These decisions were not related to the number of newly infected cases because there were no detailed epidemiological data at the local level (e.g. settlements). For example, there were no data about the number of PCR tests in the counties either. National-level restrictions implemented by policymakers were connected to the dynamics of the disease. These restrictions were based on multi-stage regulations related to the actual number of new daily confirmed cases from the second epidemic wave.

The government will have to use a greater number of tools based on spatially sensitive measures in potential epidemic waves. The number of possible scenarios is relatively high, depending on the actual epidemiological situation, based on the spatial spreading of the Delta variant during the summer of 2021.

4 Conclusion

The COVID-19 pandemic has severely affected European countries and their healthcare systems. Many healthcare services in severely affected countries are undergoing decentralisation and fragmentation (Boccia et al. 2020).

According to their temporal appearance, the healthcare systems of developed countries have to face different health consequences of the COVID-19 pandemic. The short-term health consequences were manifest in a growing demand for the hospitalisation of confirmed patients. Massification risks overburden the health care system and may produce capacity shortages. In the medium to long term, a rise of non-communicable diseases can also be anticipated because non-coronavirus infected patients had many access barriers to healthcare services on various grounds during the epidemic waves (e.g. suspension of screening and the treatment of chronic patients), triggering a deterioration of health and avoidable deaths (Kovács, Uzzoli 2020). Among other things, social distancing during the epidemic may cause a deterioration in mental health (Grünhut, Bodor 2020, WHO 2020). The new coronavirus pandemic will also affect the spatial distribution of health inequalities in the future, leading to their intensification and the emergence of new types of inequalities (Bambra et al. 2020, Kovács et al. 2020). In addition, Hungary belongs to the middle-ground countries of the world according to the general state of health of the population (Uzzoli 2016). Poor Hungarian health indicators can lead to a further intensification of the COVID-19 pandemic with increased serious health consequences among confirmed cases.

Our study gives a concise summary in light of the findings regarding the study objective.

Firstly, significant differentiation can be detected among the parts of Hungary most affected by the pandemic. The most developed north-western region and the central part with the capital city and its surroundings exhibited the highest total number of confirmed infection cases. From a geographical point of view, the spatial diffusion of the virus referred to the number of social interactions, which increase from the bottom to the top of the settlement hierarchy, resulting in a higher number of infections in the most developed and urbanised geographical locations (Gu et al. 2020, Sigler et al. 2020).

Secondly, some parts of the country are affected most by higher numbers of COVID-19 deaths. These parts of the country differ completely from those which experienced higher numbers of new COVID-19 cases. Poor health and lower quality of life in the most disadvantaged parts of the country (e.g. inner peripheries, south-eastern border, north-eastern counties) go together with a shorter life expectancy. Poor health is one of the major risk factors of death caused by COVID-19 (Kovács, Uzzoli 2020, Uzzoli et al. 2021). Thirdly, the geographical location of infections and the spreading of the pandemic have spatially changed during the three examined epidemic waves in Hungary. The spatial pattern of the first epidemic wave was mainly affected by infections in institutional hotspots (hospitals, nursing homes) (Kemenesi et al. 2020). Still, the role of geographical hotspots came from the hierarchical spatial spreading of the pandemic (Lennert 2020). The community-based epidemic spreading of the first wave has transformed to the chain of infections within the country in the second and the third wave. At the county level, the typical spatial pattern of the epidemic waves was mainly based on a western-eastern division completed by a northern-southern spatial relation during the third wave. At the micro-regional level, centre-periphery relation was the dominant spatial pattern in the occurrence of the newly registered cases as well as deaths.

Fourthly, our analysis on the micro-regional level suggests that the socioeconomic conditions of the micro-regions might also influence the spatial inequalities among the districts in terms of death rates and COVID-19 infections. Although the infection rate of urbanised areas implied they were infection hubs, the death rate was lower in these micro-regions than in the less developed ones. This result might also refer to the spatial differences of healthcare, which may have a central role in a pandemic situation.

Finally, the most important finding in the examination of the policy interventions is that the mitigation measures taken at the national level are primary in Hungary's anti-epidemic approach. The competencies of municipalities in restrictions were apparent at the very beginning of the Hungarian epidemic, but their role remained of secondary importance.

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Flatten the Curve! Modeling SARS-CoV-2/COVID-19 Growth in Germany at the County Level

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Abstract. Since the emerging of the "novel coronavirus" SARS-CoV-2 and the corresponding respiratory disease COVID-19, the virus has spread all over the world. Being one of the most affected countries in Europe, in March 2020, Germany established several nonpharmaceutical interventions to contain the virus spread, including the closure of schools and child day care facilities (March 16-18, 2020) as well as a full "lockdown" with forced social distancing and closures of "nonessential" services (March 23, 2020). The present study attempts to analyze whether these governmental interventions had an impact on the declared aim of "flattening the curve", referring to the epidemic curve of new infections. This analysis is conducted from a regional perspective. On the level of the 412 German counties, logistic growth models were estimated based on daily infections (estimated from reported cases), aiming at determining the regional growth rate of infections and the point of inflection where infection rates begin to decrease and the curve flattens. All German counties exceeded the peak of new infections between the beginning of March and the middle of April. In a large majority of German counties, the epidemic curve has flattened before the "lockdown" was established. In a minority of counties, the peak was already exceeded before school closures. The growth rates of infections vary spatially depending on the time the virus emerged. Counties belonging to states which established an additional curfew show no significant improvement with respect to growth rates and mortality. Furthermore, mortality varies strongly across German counties, which can be attributed to infections of people belonging to the "risk group", especially residents of retirement homes. The decline of infections in absence of the "lockdown" measures could be explained by 1) earlier governmental interventions (e.g., cancellation of mass events, domestic quarantine), 2) voluntary behavior changes (e.g., physical distancing and hygiene), 3) seasonality of the virus, and 4) a rising but undiscovered level of immunity within the population. The results raise the question whether formal contact bans and curfews really contribute to curve flattening within a pandemic.

1 Background

The "novel coronavirus" SARS-CoV-2 ("Severe Acute Respiratory Syndrome Coronavirus 2") and the corresponding respiratory disease COVID-19 ("Coronavirus Disease 2019") caused by the virus initially appeared in December 2019 in Wuhan, Province Hubei, China. Since its emergence, the virus has spread over nearly all countries across the world. On March 12, 2020, the World Health Organization (WHO) declared the SARS-CoV-2/COVID-19 outbreak a global pandemic (Lai et al. 2020, World Health Organization 2020b). As of May 10, 2020, 3,986,119 cases and 278,814 deaths had been reported worldwide. In Europe, the most affected countries are Spain, Italy, United Kingdom and Germany (European Centre for Disease Prevention and Control 2020).

The virus is transmitted between humans via droplets or through direct contact (Lai et al. 2020). In a very influential simulation study from March 2020, the Imperial College COVID-19 Response Team (Ferguson et al. 2020) suggested a series of public health measures aimed at slowing or stopping the transmission of the virus in absence of a vaccine or a successful therapy. These so-called *nonpharmaceutical interventions* (NPI) aim at reducing contact rates in the population, including social distancing and closures of schools and universities as well as the quarantine of infected persons. The Chinese government had imposed containment measures in the Provice Hubei already at the end of January 2020. This "lockdown" included a quarantine of the most affected city Wuhan and movement restrictions for the population as well as school closures (CNN 2020). In March 2020, nearly all European countries have introduced measures against the spread of Coronavirus. These measures range from appeals to voluntary behaviour changes in Sweden to strict curfews, e.g. in France and Spain (Deutsche Welle 2020a). The public health strategy to contain the virus spread is commonly known as "flatten the curve", which refers to the epidemic curve of the number of infections: "Flattening the curve involves reducing the number of new COVID-19 cases from one day to the next. This helps prevent healthcare systems from becoming overwhelmed. When a country has fewer new COVID-19 cases emerging today than it did on a previous day, that's a sign that the country is flattening the curve" (Johns Hopkins University 2020).

In Germany, due to the federal political system, measures to "flatten the curve" were introduced on the national as well as the state level. As the German "lockdown" has no single date, we distinguish here between four phases of NPIs, of which the main interventions were the closures of schools, child day care centers and most retail shops etc. in calendar week 12 (phase 2), and the nationwide establishment of a contact ban (attributed to phase 3), including forced social distancing and a ban of gatherings of all types, on March 23, 2020. The German states Bavaria, Saarland, and Saxony established additional curfews (see Table 1). Occasionally, these governmental interventions were criticized because of the social, psychological and economic impacts of a "lockdown" and/or the lack of its necessity (Capital 2020, Süddeutsche Zeitung 2020a, Tagesspiegel 2020a, Welt online 2020a). Apart from the economic impacts emerging from a worldwide recession (The Guardian 2020), the psychosocial consequences of movement restrictions and social isolation (resulting from NPIs) have also become apparent now in terms of an increase of several mental health illnesses (Carvalho Aguiar Melo, de Sousa Soares 2020, Mucci et al. 2020, Williams et al. 2020). The effects of (forced) isolation as well as school and child day care closures are also visible through a worldwide increase in domestic abuse (New York Times 2020), reported in Germany as well (Stuttgarter Zeitung 2020, Süddeutsche Zeitung 2020b).

It is therefore all the more important to know whether these restrictions really contributed to the flattening of the epidemic curve of Coronavirus in Germany (RKI 2020a). This question should be addressed from a regional perspective for two reasons.

1. In May 2020, the competences for the measures in Germany have shifted from the national to the state and regional (county) level. In the future, counties with more than 50 new infections per 100,000 in one week are expected to implement regional measures (see Table 1).

2. A spatial perspective allows the impact of the German measures of March 2020 to be identified.

In his statistical study, the mathematician Ben-Israel (2020) compares the epidemic curves of Israel, the USA and several European countries. These curves demonstrate a decline of new infections, regardless of the national measures to contain the virus spread. Furthermore, the study reveals the trend that the peak of infections is typically reached in the sixth week after the first reported case, while a decline of the curve starts in week eight. This occurs in all assessed countries on the national level, no matter whether a "lockdown" was established (e.g. Italy) or not (e.g. Sweden).

Table 1: Main governmental nonpharmaceutical interventions with respect to COVID-19 pandemic in Germany

Phase	Measure	Entry into force	Competence /level
1	First quarantines of infected persons and suspected cases	February 2020	nationwide
up to CW	Minister of health Spahn recommends cancellation of large events ($\geq$ 1,000 participants)	(March 8, 2020)	
10/11	Bundesliga games behind closed doors ("ghost games")	March 11, 2020	nationwide
	Speeches of chancellor Merkel and president Steinmeier, recommondation to avoid social contacts and large events	(March 12, 2020)	
2	Closure of schools, child day care centers and universities	March 16-18, 2020	states
CW 12	Closure of retail facilities (except for basic supply), bars and leisure facilities	March 17-19, 2020	states
	Travel restrictions	March 17, 2020	nationwide
3	Curfew in Bavaria, Saarland and Saxony	March 21-23, 2020	states
CW 12/13 ("Lock-down")	Contact ban: ban of gatherings > 2 people (including political and religious gatherings), forced social distancing (distance $\geq$ 1.5 m), closure of "nonessential" services (e.g., gastronomy, hairdressers)	March 23, 2020	nationwide
4	Reopening of several retail facilities and services	April 20, 2020	states
CW	Mandatory face masks in public transport and shops	April 22-29, 2020	states
17	Further liberalizations; implementation of an "emergency brake": lockdowns on the county level on condition of 50 new infections per 100,000 in one week	May 6, 2020	nationwide

Source: own compilation based on an der Heiden, Hamouda (2020), Deutsche Welle (2020a,b), Tagesschau.de (2020a,b).

The focus of the present study is on the main nonpharmaceutical interventions with respect to the SARS-CoV-2/COVID-19 pandemic in Germany. This means the concrete "lockdown" measures affecting the social and economic life of the whole society (distinguishing from measures taken in most cases of infectious dieseases, such as quarantine of affected persons). In the terminology of the present study, these are the phase 2 and 3 measures, denoted in Table 1. Building upon the discrepancy outlined by Ben-Israel (2020), the present study addresses the following research questions:

- Pandemic or epidemic growth has a regional component due to regional infection hotspots or other behavioral or spatial factors. Thus, growth rates of infections may differ between regions in the same country (Chowell et al. 2014). In Germany, the prevalence of SARS-CoV-2/COVID-19 differs among the 16 German states and 412 counties, clearly showing "hotspots" in South German counties belonging to Baden-Wuerttemberg and Bavaria (RKI 2020a). Thus, the first question to be answered is: *How does the growth rate of SARS-CoV-2/COVID-19 vary across the 412 German counties?*

- The German measures to contain the pandemic entered into force nearly at the same time, especially in terms of closures of schools, childcare infrastructure and retailing (starting March 16/17, 2020) as well as the nationwide contact ban (starting March 23, 2020). Ben-Israel (2020) found a decline of new infection cases on the national level regardless of the Corona measures. To examine the effect of the German measures, we need to estimate the time of the peak and the declining of the curves of infection cases, respectively: *At which date(s) did the epidemic curves of SARS-CoV-2/COVID-19 flatten in the 412 German counties?*

- Regional prevalence and growth, as well as the mortality of SARS-CoV-2/COVID-19, are attributed within media discussions to several spatial factors, including population density or demographic structure of the regions (Welt online 2020b). Furthermore, the German measures differ on the state level, as three states – Bavaria, Saarland and Saxony – established additional curfews supplementing the other interventions (see Table 1). Focusing on growth rate and mortality, and addressing these regional differences, the third research question is: *Which indicators explain the regional differences of SARS-CoV-2/COVID-19 growth rate and mortality on the level of the 412 German counties?*

2 Methodology

2.1 Logistic growth model

According to Li (2018), in simple terms, an infectious disease spread (pandemic or epidemic) can be summarized as follows: At the beginning, one or more infectious individuals are introduced into a population of *susceptibles* (non-infected/healthy individuals). As the pathogen (e.g., virus) is transmitted from one individual to another, the number of *infected* individuals increases over time. Depending on the regarded pathogen/disease, infected individuals *recover* due to medical interventions and/or reactions of the individuals' immune system and, in many cases, gain partial or full immunity against the pathogen (e.g., through the development of antibodies against a virus). In other cases, infected people may also die from the disease. In all aforementioned cases and on condition of a stationary population, the number of susceptibles decreases and, thus, the number of new infections decreases as well. As a consequence, the pandemic/epidemic slows down and ends. The disease spread may also be contained by vaccination and/or other control and preventive measures. Note that, technically, one must distinguish between an *infection* and the *disease* which is (or may be) caused by the pathogen: "Disease is not the same as infection. Infection is said to have occurred when an organism successfully avoids innate defense mechanisms and stably colonizes a niche in the body. To establish an infection, the invader must first penetrate the anatomic and physiological barriers that guard the skin and mucosal surfaces of the host. Secondly, the organism must be able to survive in the host cellular milieu long enough to reproduce. This replication may or may not cause visible, clinical damage to the host tissues, symptoms that we call 'disease"' (Mak, Saunders 2006).

Analyzing the transmission and spreading process of infectious diseases involves the utilization of mathematical models. Pandemic growth can be modeled by deterministic models such as the SIR (susceptible-infected-recovered) model and its extensions, or by stochastic, phenomenological models such as the exponential or the logistic growth model. The former type of model does not depend on large empirical data on disease cases but requires additional information about the disease and the transmission process. The latter type of model is based on linear or nonlinear regression. Only empirical data of infections and/or confirmed cases of disease (or death) is required to estimate such models (Batista 2020a,b, Chowell et al. 2014, 2015, Li 2018, Ma 2020, Pell et al. 2018). Recently, there have already been several attempts to model the SARS-CoV-2 pandemic on the country (or even world) level, by using either the original or extended SIR model (Batista 2020b), the logistic growth model (Batista 2020a, Vasconcelos et al. 2020, Wu et al. 2020), or both (Zhou et al. 2020).

In this paper, we regard the spread of the Coronavirus primarily as an empirical phenomenon over space and time and ignore its epidemiological characteristics. We focus on 1) the regional growth speed of the pandemic and 2) the time when exponential growth ends and the infection rate decreases again. Apart from that, only infection cases and some further information are available, but not additional epidemiological information. Thus, the method of choice is a phenomenological regression model. In an early phase of an epidemic, when the number of infected individuals growths exponentially, an exponential function could be utilized for the phenomenological analysis (Ma 2020). However, officially reported SARS-CoV-2 infections in Germany (measured by the time of onset of symptoms) declined from mid-March. The corresponding reproduction number was estimated at $R = 0.71$ based on the case reports as of May 6, 2020 (RKI 2020a). This indicates that the phase of exponential growth was exceeded at this time. Thus, a logistic growth model is used for the analysis of SARS-CoV-2 growth in the German counties.

The following representations of the logistic growth model are adopted from Batista

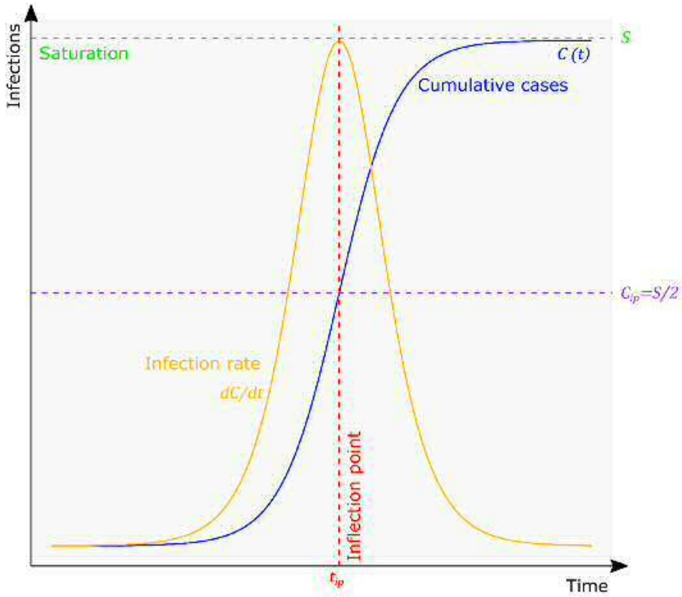


Figure 1: Logistic growth of an epidemic

(2020a), Chowell et al. (2014) and Tsoularis (2002). Unlike exponential growth, logistic growth includes two stages, allowing for a saturation effect. The first stage is characterized by an exponential growth of infections due to an unregulated spreading of the disease. As more infections accumulate, the number of at-risk susceptible persons decreases because of immunization, death, or behavioral changes as well as public health interventions. After the inflection point of the infection curve, when the infection rate is at its maximum, the growth decreases and the cumulative number of infections approximate its theoretical maximum, which is the saturation value (see Figure 1).

In the logistic growth model, the cumulative number of infected or diseased persons at time t, $C(t)$ is a function of time:

$$C(t) = \frac{C_0 S}{C_0 + (S - C_0)\exp(-rSt)} \tag{1}$$

where C_0 is the initial value of C at time 0, r is the intrinsic growth rate, and S is the saturation value.

The infection rate is the first derivative:

$$\frac{dC}{dt} = rC\left(1 - \frac{C}{S}\right) \tag{2}$$

The inflection point of the logistic curve indicates the maximal infection rate before the growth declines, which means a flattening of the cumulative infection curve. The inflection point, ip, is equal to:

$$ip = \frac{S}{2} \tag{3}$$

at time

$$t_{ip} = \frac{c}{rS} \tag{4}$$

where:

$$c = \ln \frac{C_0}{C - C_0} \tag{5}$$

When empirical data (here: time series of cumulative infections) is available, the three model parameters r, S and C_0 can be estimated empirically.

We fit the models in a three-step estimation procedure including both OLS (Ordinary Least Squares) and NLS (Nonlinear Least Squares) estimation. The former is used for generating initial values for the iterative NLS estimation, making use of the linearization and stepwise parametrization of the logistic function. Following Engel (2010), the nonlinear logistic model (Equ. 1) can be transformed into a linear model (on condition that the saturation value is known) by taking the reciprocal on both sides, taking natural logarithms and rearranging the function:

$$\ln(\frac{1}{C(t)} - \frac{1}{S}) = \ln(\frac{S - C_0}{SC_0}) - rSt \tag{6}$$

The transformed dependent variable, y_i^*, can be expressed by a linear relationship with two parameters, the intercept ($\hat{b}$) and slope ($\hat{m}$):

$$y_i^* = \ln(\frac{1}{C(t)} - \frac{1}{S}) \tag{7}$$

$$\hat{y}^* = \hat{b} + \hat{m}t \tag{8}$$

In step 1, an approximation of the saturation value is estimated, which is necessary for the linear transformation of the model. Transforming the empirical values $C(t)$ according to Equ. (7), we have a linear regression model (Equ. 8). By utilizing bisection (Kaw et al. 2011), the best value for S is searched minimizing the sum of squared residuals. The bisection procedure consists of 10 iterations, while the start values are set around the current maximal value of $C(t)$ (Interval: $[\max(C(t)) + 1;\ \max(C(t)) * 1.2]$).

The resulting preliminary start value for the saturation parameter, $\hat{S}_{\text{start}}$, is used in step 2. We transform the observed $C(t)$ using Equ. (7) with the preliminary value of $\hat{S}$ from step 1, $\hat{S}_{\text{start}}$. Another OLS model is estimated (Equ. 8). The estimated coefficients are used for calculating the start values of $\hat{r}$ and $\hat{C}_0$ for the nonlinear estimation (Engel 2010):

$$\hat{r}_{\text{start}} = -\frac{\hat{m}}{\hat{S}_{\text{start}}} \tag{9}$$

and

$$\hat{C}_{0_{\text{start}}} = \frac{\hat{S}_{\text{start}}}{1 + \hat{S}_{\text{start}} \exp{(\hat{b})}} \tag{10}$$

In step 3, the final model fitting is done using Nonlinear Least Squares (NLS), while inserting the values from steps 1 and 2, $\hat{S}_{\text{start}}$, $\hat{C}_{0_{\text{start}}}$ and $\hat{r}_{\text{start}}$, as start values for the iterative process. The NLS fitting uses the default Gauss-Newton algorithm (Ritz, Streibig 2008) with a maximum of 500 iterations.

Using the estimated parameters $\hat{r}$, $\hat{C}_0$ and $\hat{S}$, the inflection point of each curve is calculated via equations (3) to (5). The inflection point t_{ip} is of unit time (here: days) and assigned to the respective date $t_{ip_{\text{date}}}$ (YYYY-MM-DD). Based on this date, the following day $t_{ip_{\text{date}+1}}$ is the first day after the inflection point at which time the infection rate has decreased again. For graphical visualization, the infection rate is also computed using Equ. (2).

2.2 *Estimating the dates of infection*

In the present study, we use the daily updated data on confirmed SARS-CoV-2/COVID-19 cases, provided by federal authorities, the German Robert Koch Institute (RKI) (RKI 2020b). This dataset includes all persons who have been tested positive on the SARS-CoV-2 virus using a PCR (*polymerase chain reaction*) test and reported from local health authorities to the RKI. However, one must consider that neither the volume of tests nor the criteria for conducting a test are constant over time: Up to and including May 2020, almost exclusively people with acute respiratory symptoms were tested for SARS-CoV-2, as, with few exceptions, the presence of relevant symptoms is an exclusion criterion for testing in the RKI guidelines for medical doctors (IBBS 2020). In other words, this testing policy is targeted at the *disease* (COVID-19), not the *virus* (SARS-CoV-2). Thus, most of the cases in the present data are COVID-19 sufferers, whilst asymptomatic infected people and individuals with milder course are underrepresented. In the vast majority of cases, the date of onset of symptoms is reported in the dataset as well (an der Heiden, Hamouda 2020). The test volume was increased heavily from calendar week 11 (127,457 tests) to 12 (348,619 tests) but remains in the same order of magnitude until calendar week 18 (300,000-400,000 tests per week) (RKI 2020c).

The dataset used here is from May 5, 2020 and includes 163,798 cases. This data includes information about age group, sex, the related place of residence (county) and the date of report (Variable *Meldedatum*). The reference date in the dataset (Variable *Refdatum*) is either the day the disease started, which means the onset of symptoms, or the date of report (an der Heiden, Hamouda 2020). The date of onset of symptons is reported in the majority of cases (108,875 and 66.47%, respectively).

The date of infection, which is of interest here, is either unknown or not included in the official dataset. Thus, it is necessary to estimate the approximate date of infection dependent on two time periods: the time between the infection and the onset of symptons (incubation period) and the delay between onset of symptoms and official report (reporting delay). From the 108,875 cases where the onset of the symptoms is known, we can calculate the mean reporting delay as 6.84 days. Additionally, we assume an incubation period of five days. This is a rather conservative assumption (which means a relatively short time period) referring to the current epidemiological estimates (see Table 2). In their model-based scenario analysis towards the total number of diseases and deaths, the RKI also assumes an average incubation period of five days (an der Heiden, Buchholz 2020). Taking into account incubation period and reporting delay, there is an average all-over delay between infection and reporting of about 12 days (see Figure 2).

But this is just one side of the coin. As an inspection of the case data reveals, the delay differs by case characteristics (age group, sex) and counties. In their current prognosis, the RKI estimates the dates of onset of symptoms by Bayesian nowcasting based on the reporting date, but not taking into account the incubation time. The RKI nowcasting model incorporates delays of reporting depending on age group and sex, but not including spatial (county-specific) effects (an der Heiden, Hamouda 2020). Exploring the dataset used here, we see obvious differences in the reporting delay with respect to age groups and sex. There seems to be a tendency of lower reporting delays for young children and older infected individuals (see Table 3). Taking a look at the delays between onset of symptoms and reporting date on the level of the 412 counties (not shown in table), the values range between 2.39 days (Würzburg city) and 17.0 days (Würzburg county).

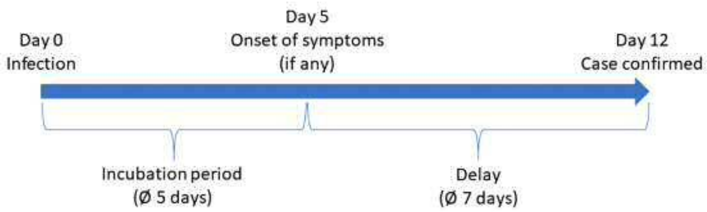


Figure 2: Time between infection and reporting of case

Table 2: Studys estimating the incubation period of SARS-CoV-2/COVID-19

Study	n	Distribution	Mean (CI95)	SD (CI95)	Median (CI95)	Min.	Max.
Backer et al. (2020)	88	Weibull	NA	2.3 (1.7, 3.7)	6.4 (5.6, 7.7)	NA	NA
Lauer et al. (2020)	181	Lognormal	5.5	1.52 (1.3, 1.7)	5.1 (4.5, 5.8)	NA	NA
Leung (2020)	175 (a)	Weibull	1.8 (1.0, 2.7)	NA	NA	NA	NA
	175 (b)	Weibull	7.2 (6.1, 8.4)	NA	NA	NA	NA
Li et al. (2020)	10	Lognormal	5.2 (4.1, 7.0)	NA	NA	NA	NA
Linton et al. (2020)	158	Lognormal	5.6 (5.0, 6.3)	2.8 (2.2, 3.6)	5.0 (4.4, 5.6)	2	14
Sun et al. (2020)	33	NA	4.5	NA	NA	NA	NA
Xia et al. (2020)	124	Weibull	4.9 (4.4, 5.4)	NA	NA	NA	NA

Notes: (a) = Travelers to Hubei, (b) = Non-Travelers. *Source*: own compilation.

Table 3: Delay between onset of symptoms and official report by age group and sex

Age group	Sex	Delay between onset of symptoms and reporting date [days] Mean	SD
A00-A04	female	5.82	5.68
A05-A14	female	6.09	5.34
A15-A34	female	6.82	5.59
A35-A59	female	7.00	5.98
A60-A79	female	7.08	6.22
A80+	female	5.10	5.83
unknown	female	8.71	9.79
A00-A04	male	5.93	5.98
A05-A14	male	6.04	5.12
A15-A34	male	6.78	5.52
A35-A59	male	7.18	5.90
A60-A79	male	7.20	6.14
A80+	male	5.70	5.84
unknown	male	9.86	8.42
A00-A04	unknown/diverse	3.50	2.39
A05-A14	unknown/diverse	4.00	5.20
A15-A34	unknown/diverse	6.44	4.87
A35-A59	unknown/diverse	6.95	5.51
A60-A79	unknown/diverse	7.36	5.87
A80+	unknown/diverse	6.50	11.40
unknown	unknown/diverse	9.60	3.58
all-over		6.84	5.90

Source: own calculation based on data from RKI (2020b). *Note*: The date of onset of symptoms is known for 108,875 (66.47%) of 163,798 cases in the dataset.

For the estimation of the dates of infection, it is necessary to distinguish between the cases where the date of symptom onset is known or not. In the former case, no assumption must be made towards the delay between onset of symptoms and date report. The calculation is simply:

$$\hat{di}_i = do_i - incp \tag{11}$$

where $\hat{di}_i$ is the estimated date of infection of case i, do_i is the date of onset of symptoms reported in the RKI dataset and $incp$ is the average incubation period equal to five (days).

For the 54,923 cases without information about onset of symptoms, we estimate this delay based on the 108,875 cases with known delays. As the reporting delay differs between age group, sex and county, the following dummy variable regression model is estimated (stochastic disturbance term is not shown):

$$\hat{ds}_{asc} = \alpha + \sum_{a}^{A-1} \beta_a D_{\text{agegroup}_a} + \sum_{s}^{S-1} \gamma_s D_{\text{sex}_s} + \sum_{c}^{C-1} \delta_c D_{\text{county}_c} \tag{12}$$

where $\hat{ds}_{asc}$ is the estimated delay between onset of symptoms and report depending on age group a, sex s and county c, D_{agegroup_a} is a dummy variable indicating age group a, D_{sex_s} is a dummy variable indicating sex s, D_{county_c} is a dummy variable indicating county c, A is the number of age groups, S is the number of sex classifications, C is the number of counties and α, β, γ and δ are the regression coefficients to be estimated.

Taking into account the delay estimation, if the onset of symptoms is unknown, the date of infection of case i is estimated via:

$$\hat{di}_i = dr_i - \hat{ds}_{asc} - incp \tag{13}$$

where dr_i is the date of report in the RKI dataset.

2.3 Models of regional growth rate and mortality

To test which variables predict the intrinsic growth rate and the regional mortality of SARS-CoV-2/COVID-19, respectively, two regression models were estimated. In the first model with the intrinsic growth rate r as dependent variable, we include the following predictors:

- In the media coverage about regional differences with respect to COVID-19 cases in Germany, several experts argue that a lower population density and a higher share of older population reduce the spread of the virus, with the latter effect being due to a lower average mobility (Welt online 2020b). It is well known that human mobility potentially increases the spread of an infectious disease. Also work-related commuting and tourism are considered as drivers of virus transmission (Charaudeau et al. 2014, Dalziel et al. 2014, Findlater, Bogoch 2018). To test these effects, four variables are included into the model: 1) The population density ($POPDENS$), 2) the share of population of at least 65 years ($POPS65$), 3) an indicator for the intensity of commuting (CMI) formulated by Guth et al. (2010), and 4) the number of annual tourist arrivals per capita ($TOUR$) for each county. All variables were calculated based on official statistics for the most recent year (2018/2019) (Destatis 2020a,b,c).

- In the media coverage, the lower prevalence in East Germany is also explained by 1) a different vaccination policy in the former German Democratic Republic and 2) a lower affinity towards carnival events as well as 3) less travelling to ski resorts due to lower incomes (Welt online 2020b). Thus, a dummy variable (1/0) for East Germany is included in the model ($EAST$).

- We test for the influence of different governmental interventions by including dummy variables for the states ("Länder") Bavaria (BV), Saarland (SL), Saxony (SX) and North Rhine Westphalia (NRW), as well as Baden-Wuerttemberg (BW). Unlike the other 13 German states, the first three states established a curfew additional to the other measures at the time of phase 3, as is identified in the present study. Like Bavaria, North Rhine Westphalia and Baden-Wuerttemberg belong to the "hotspots" in Germany, with the latter state having a prevalence similar to Bavaria. Saxony has a prevalence below the national average (RKI 2020a).

- Apart from any interventions, when a disease spreads over time, also the susceptible population *must* decrease over time. As more and more individuals get infected (maybe causing temporal or lifelong immunization or, in other cases, death), there are continually fewer healthy people to get infected (Li 2018) (see also Section 2.1). Consequently, regional growth *must* decrease with increasing regional prevalence and over time (and vice versa). In the specific case of SARSCoV-2/COVID-19, the outbreak differs between German counties (starting with "hotspots" like Heinsberg or Tirschenreuth county). Differences in growth may be due to different periods of time the virus is present and differences in the corresponding prevalence. Thus, two control variables are included in the model, the county-specific prevalence (PRV) and the number of days since the first (estimated) infection ($DAYS$).

In the second model for the explanation of regional mortality (MRT), five more independent variables have to be incorporated:

- From the epidemiological point of view, the "risk group" of COVID-19 for severe courses (and even deaths) is defined as people of 60 years and older. The arithmetic mean of deceased attributed to COVID-19 is equal to 81 years (median: 82 years). Out of 6,831 reported deaths on May 5 2020, 6,524 were of age 60 or older (95.51%). This is, inter alia, because of outbreaks in residential homes for the elderly (RKI 2020a). Thus, the raw data from the RKI (RKI 2020b) was used to calculate the share of confirmed infected individuals of age 60 or older in all infected persons for each county ($INFS60$), which is included into the regression model for regional mortality.

- Several health-specific variables are found to influence the mortality risk (as well as the risk of severe course) of COVID-19. These individual-specific risk factors include, inter alia, diabetes, obesity, other respiratory diseases, or smoking (Engina et al. 2020, Selvan 2020). There are several possible health indicators which are unfortunately not available for German counties. Thus, the average health situation is captured by incorporating the average regional life expectancy into the model (*LEXP*), which is made available by the German Federal Institute for Research on Building, Urban Affairs and Spatial Development (BBSR 2020).

- On the regional level, air pollution was found to be a contributing factor to COVID-19 fatality (Ogen 2020, Wu et al. 2020). According to Wu et al. (2020), the regional air pollution with respect to particulate matter (annual mean of daily PM_{10} values, unit: $\mu g/m^3$) is included into the model (*PM10*). Since Ogen (2020) shows a correlation between nitrogen dioxide concentration and COVID-19 fatality, this type of air pollution (annual mean of daily NO_2 values, unit: $\mu g/m^3$) is incorporated into the model as well (*NO2*). Both air quality indicators are made available by the German Environment Agency (UBA 2020a) on the level of single monitoring stations. These stations are available geocoded (UBA 2020b) and have been assigned to the German counties via a nearest neighbor join. Thus, the county-level values of both indicators equal the values of the nearest monitoring station.

- The intrinsic growth rate of each county is incorporated into the model as well. Considering the chronology of an infectious disease spread, there must be a reciprocal relationship between growth speed and mortality: The more individuals die in the context of the regarded disease, the fewer susceptibles are left to be infected, resulting in a deceleration of the pandemic spread (Li 2018) (see also Section 2.1). Thus, there *must* be a negative correlation between mortality and growth rate, all other things being equal. Consequently, the county-specific intrinsic growth rate (r) is included as control variable.

See Table 4 for all variables included into the models. All continuous variables, including the dependent variables (r and *MRT*, respectively), were transformed via natural logarithm in the regression analysis. This leads to an interpretation of the regression coefficients in terms of elasticities and semi-elasticities (Greene 2012). Two variants were estimated for the growth rate model (with and without dummy variables) and three for the mortality model (with and without growth rate as well as a third model including both growth rate and dummy variables). The minimum significance level was set to $p \leq 0.1$. In the first step, the regression models were estimated using an Ordinary Least Squares (OLS) approach and tested with respect to multicollinearity using variance inflation factors (*VIF*) with a critical value equal to five (Greene 2012).

However, SARS-CoV-2/COVID-19 cases are obviously not evenly distributed across all German counties as the disease spread started in a few "hotspots" in Bavaria, Baden-Wuerttemberg and North Rhine Westphalia (RKI 2020a, Tagesspiegel 2020b). Of course, an infectious disease can be transmitted across county borders, in particular, by contact between residents of one region and a nearby region. As a consequence, it is to be expected that indicators of disease spread – such as the regarded variables growth rate and mortality – are similar between nearby regions. Thus, further model-based analyses require considering possible spatial autocorrelation in the dependent variables (Griffith 2009). Consequently, both dependent variables were tested for spatial autocorrelation using Moran's I-statistic and the model estimation was repeated using a spatial lag model. In this type of regression model, spatial autocorrelation is modeled by a linear relationship between the dependent variable and the associated spatially lagged variable, which is a spatially weighted average value of the nearby objects. The influence of spatial autocorrelation is captured by adding a further parameter, ρ, to the regression equation, which is also tested for significance. Spatial linear regression models are not fitted by OLS but by Maximum Likelihood (ML) estimation. Both Moran's I and the spatial lag model require a weighting matrix to define the proximity of the regarded spatial object to nearby objects (Chi, Zhu 2008, Rusche 2008). Here, the weighting matrix for the spatial object (county i) was defined as all adjacent counties.

Table 4: Variables in the regression models for growth rate and mortality

Variable		Calculation/unit	Data source
r	Intrinsic growth rate	see Section 2.1	own calculation based on RKI (2020b)
MRT	Mortality cumulative (Porta 2008)	$\frac{D_i}{pop_i} * 100000$	own calculation based on RKI (2020b), Destatis (2020b)
PRV	Prevalence cumulative (Porta 2008)	$\frac{C_i}{pop_i} * 100000$	own calculation based on RKI (2020b), Destatis (2020b)
$DAYS$	Time since first infection	days (discrete)	own calculation based on RKI (2020b)
$POPDENS$	Population density	$\frac{pop_i}{A_i}$	own calculation based on Destatis (2020b)
$POPS65$	Share of population age 65 or older	$\frac{pop_{65+_i}}{pop_i} * 100$	own calculation based on Destatis (2020b)
CMI	Intensity of commuting (Guth et al. 2010)	$\frac{CM_{out_i}+CM_{in_i}}{L_{res_i}+L_{work_i}}$	own calculation based on Destatis (2020c)
$TOUR$	Tourist density	$\frac{T_i}{pop_i} * 1000$	own calculation based on Destatis (2020a,b)
$INFS60$	Share of infected age 60 or older in all infected persons	$\frac{C_{60+_i}}{C_i} * 100$	own calculation based on RKI (2020b)
$LEXP$	Life expectancy	years (mean)	BBSR (2020)
$PM10$	Air pollution PM_{10}	$\mu g/m^3$ (annual mean)	UBA (2020a,b)
$NO2$	Air pollution NO_2	$\mu g/m^3$ (annual mean)	UBA (2020a,b)
$EAST$	Dummy for East Germany	1=East Germany, else 0	
BV	Dummy for Bavaria	1=Bavaria, else 0	
SL	Dummy for Saarland	1=Saarland, else 0	
SX	Dummy for Saxony	1=Saxony, else 0	
NRW	Dummy for North Rhine Westphalia	1=North Rine Westphalia, else 0	
BW	Dummy for Baden-Wuerttemberg	1=Baden-Wuerttemberg, else 0	

Note: C_i is the cumulative number of reported SARS-CoV-2/COVID-19 cases in county i, D_i is the cumulative number of reported deaths attributed to COVID-19 in county i, C_{60+_i} is the cumulative number of reported infected persons of age 60 or older in county i, emphpop$_i$ is the population of county i, A_i is the area of county i, emphpop$_{65+_i}$ is the number of inhabitants of county i of age 65 or older, emphCM$_{\text{emphout}_i}$ and CM_{in_i} is the number of commuters from and to county i, respectively, L_{emphres_i} and L_{emphwork_i} is the number of employees whose place of residence is county i and whose place of work is county i, respectively.

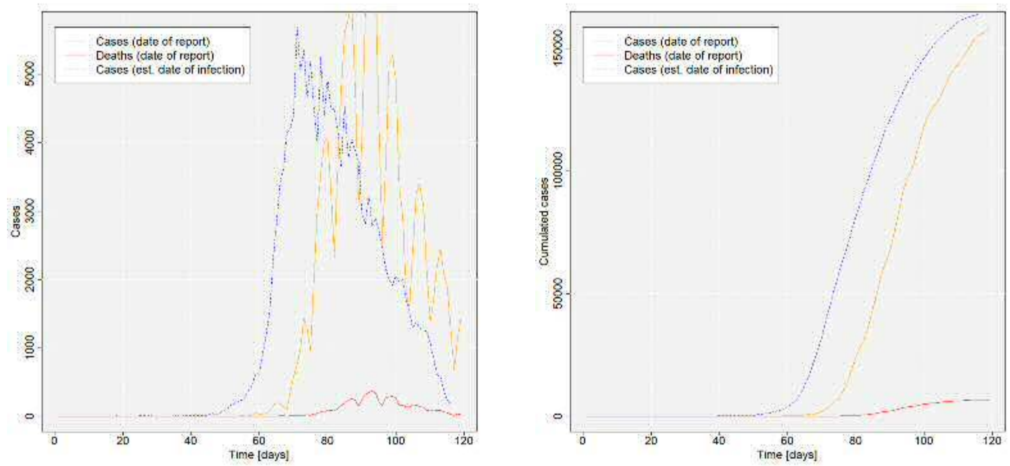
2.4 Software

The analysis in this study was executed in `R` (R Core Team 2019), version 3.6.2. The parametrization of logistic growth models was done using own functions for the OLS estimation based on the description in Engel (2010) and the `nls()` function for the final NLS estimation. For the steps of the regression analyses and presentation of results, the packages `car` (Fox, Weisberg 2019), `REAT` (Wieland 2019), `spdep` (Bivand et al. 2013), and `stargazer` (Hlavac 2018) were used. For creating maps, `QGIS` (QGIS Development Team 2019), version 3.8, was used, including the plugin `NNJoin` (Tveite 2019) for one further analysis.

3 Results

3.1 Estimation of infection dates and national inflection point

Figure 3 shows the estimated dates of infection and dates of report of confirmed cases and deaths for Germany. The curves are not shifted exactly by the average delay period



(a) Daily cases (b) Cumulative cases

Figure 3: Reported SARS-CoV-2 infections in Germany over time (dates of report vs. estimated dates of infection)

Source: own illustration.
Data source: own calculations based on RKI (2020b)

Table 5: Date of inflection point depending on assumed incubation period

Study	Median of incubation time (CI-95)	Date of inflection point Lower	Median	Upper
Linton et al. (2020)	5.0 (4.4, 5.6)	2020-03-20	2020-03-20	2020-03-19
Backer et al. (2020)	6.4 (5.6, 7.7)	2020-03-20	2020-03-19	2020-03-17

Source: own calculation based on data from RKI (2020b).

because of the different delay times with respect to case characteristics and county. The average time interval between estimated infection and case reporting is $\bar{x} = 11.92$ [days] ($SD = 5.21$). When applying the logistic growth model to the estimated dates of infection in Germany, the inflection point for Germany as a whole is on March 20, 2020.

Before switching to the regional level, we take into account the statistical uncertainty resulting from the estimation of the infection dates. About one third of the delay values for the time between onset of symptoms and case reporting was estimated by a stochastic model. Furthermore, the estimates of SARS-CoV-2/COVID-19 incubation period differ from study to study. This is why in the present case a conservative – which means a small – value of five days was assumed. Thus, we compare the results when including 1) the 95% confidence intervals of the response from the model in Equ. (12), and 2) the 95% confidence intervals of the incubation period as estimated by Linton et al. (2020). Figure 4 shows three different modeling scenarios, the mean estimation and the lower and upper bound of incubation period and delay time, respectively. The lower bound variant incorporates the lower bound of both incubation period and delay time, resulting in smaller delay between infection and case reporting and, thus, a later inflection point. The upper bound shows the counterpart. On the basis of the upper bound, the inflection point is already on March 19. Using the higher values of incubation period estimated by Backer et al. (2020), the upper bound results in an inflection point on March 17, while the lower bound variant leads to the turn on March 20. Considering confidence intervals of incubation period and delay time, the inflection point for the whole of Germany can be estimated between March 17 and March 20, 2020 (see Table 5).

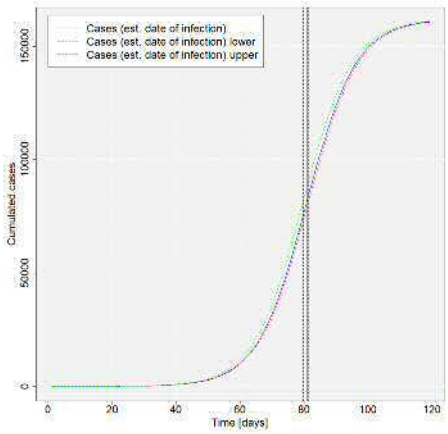


Figure 4: Estimated logistic growth model (including inflection point) for cumulative SARS-CoV-2 infections in Germany (based on estimated dates of infection) incorporating upper and lower bounds (95%-CI)
Source: own illustration. Data source: own calculations based on RKI (2020b)

3.2 Estimation of growth rates and inflection points on the county level

Figure 5 shows the estimated intrinsic growth rates (r) for the 412 counties. Figure 6 provides six examples of the logistic growth curves with respect to four counties identified as "hotspots" (Tirschenreuth, Heinsberg, Greiz and Rosenheim) and two counties with a low prevalence (Flensburg and Uckermark). There are obvious differences in the growth rates, following a spatial trend: The highest growth rates can be found in counties in North Germany (especially Lower Saxony and Schleswig-Holstein) and East Germany (especially Mecklenburg-Western Pomerania, Thuringia and Saxony). To the contrary, the growth rates in Baden-Wuerttemberg and North Rine Westphalia appear to be quite low. Taking a look at the time since the first estimated infection date in the German counties (see Figure 7a), the growth rates tend be much smaller the longer since the disease appeared in the county.

The regional inflection points indicate the day with the local maximum of infection rate. From this day forth, the exponential disease growth turns into degressive growth. In Figure 7b, the dates of the first day after the regional inflection point are displayed. The dates are categorized according to the coming into force of relevant nonpharmaceutical interventions (see Table 1). Table 6 summarizes the number of counties and the corresponding population shares by these categories. Figure 8 shows the intrinsic growth rate (y axis) and the day after the inflection point (colored points) against time (x axis). Figure 9 shows the same information against regional prevalence (x axis).

In 255 of 412 counties (61.89%) with 54.58 million inhabitants (65.66% of the national population), the SARS-CoV-2/COVID-19 infections had already decreased before phase 3 of measures came into force on March 23, 2020. In a minority of counties (51, 12.38%),

Table 6: German counties by first day after inflection point

First day after inflection point	Counties [no.]	Counties [%]	Population [Mill.]	Population [%]
Before March 13	6	1.46	0.98	1.17
March 13 to March 16	45	10.92	8.27	9.95
March 17 to March 20	138	33.50	31.03	37.33
March 21 to March 22	66	16.02	14.30	17.20
March 23 to April 19	157	38.11	28.54	34.34
Sum	412	100	83.13	100

Source: own illustration. Data source: own calculations based on RKI (2020b)

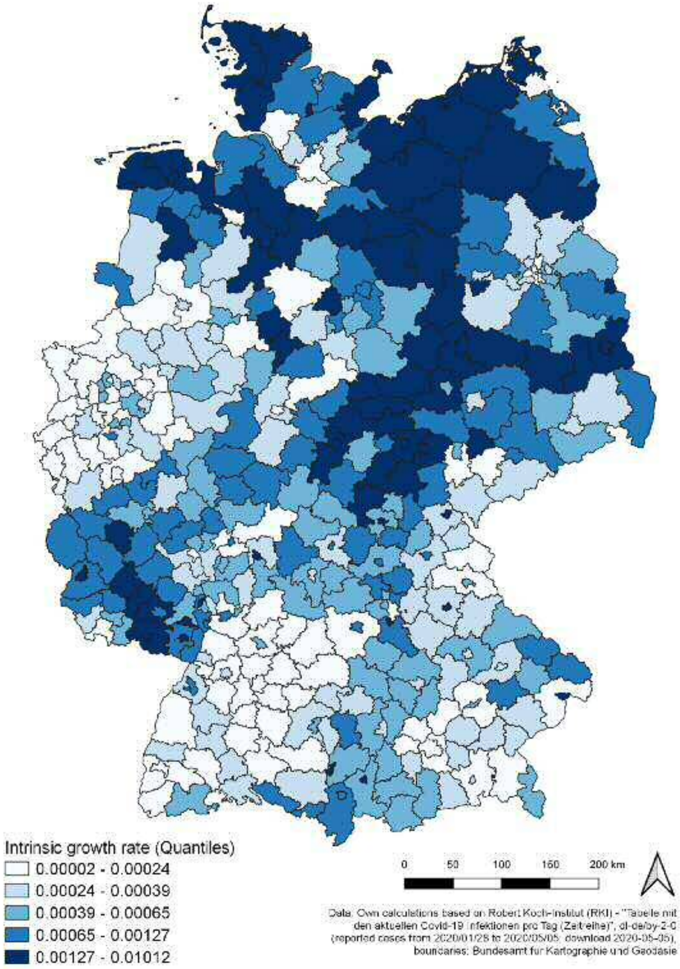


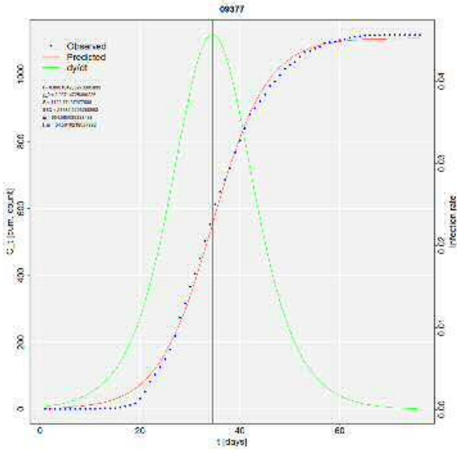
Figure 5: Intrinsic growth rate by county

the curve already flattened before the closing of schools and child day care centers (March 16-18, 2020). Six of them exceeded the peak of new infections even before March 13. This category refers to the appeals of chancellor Merkel and president Steinmeier on March 12. In 157 counties (38.11%) with a population of 28.54 million people (34.34% of the national population), the decrease of infections took place within the period of strict regulations towards social distancing and ban of gatherings.

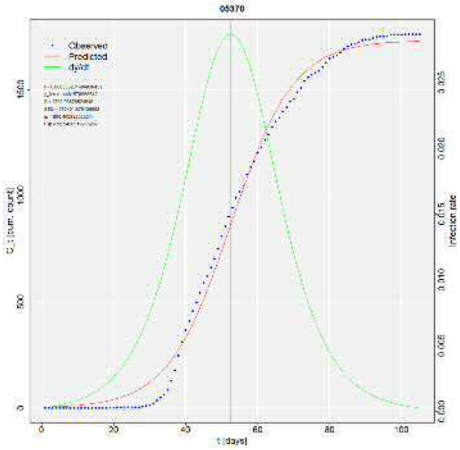
The average time interval between the first estimated infection and the respective inflection point of the county is $\bar{x} = 30.32$ [days]. However, the time until inflection point is characterized by a large variance ($SD = 11.92$), but this may be explained partially by the (de facto unknown) variance in the incubation period and the variance in the delay between onset of symptoms and reporting date.

In all counties, the inflection points lie between March 6 and April 18, 2020, which means a time period of 43 days between the first and the last flattening of a county's epidemic curve. The first regional decrease can be found in Heinsberg county (North Rhine Westphalia; 254,322 inhabitants), which was one of the first Corona "hotspots" in Germany. The estimated inflection point here took place at March 6, 2020, leading to a date of the first day after the inflection point of March 7. The latest estimated inflection point (April 18, 2020) took place in Steinburg county (Schleswig-Holstein; 131,347 inhabitants).

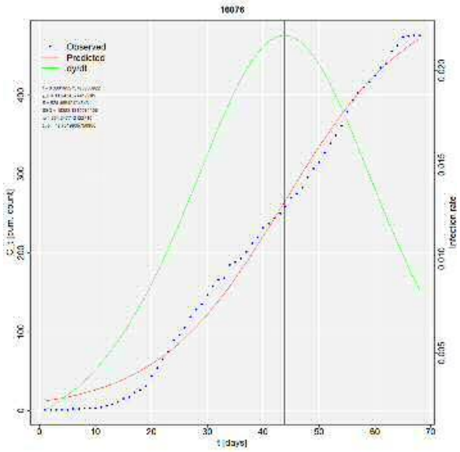
As Figure 8 shows, the intrinsic growth rates, which indicate an average growth level over time, and inflection points of the logistic models are linked. Growth speed declines



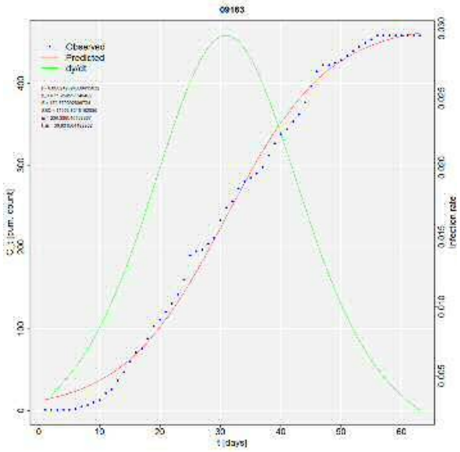
(a) Tirschenreuth county (Bavaria)



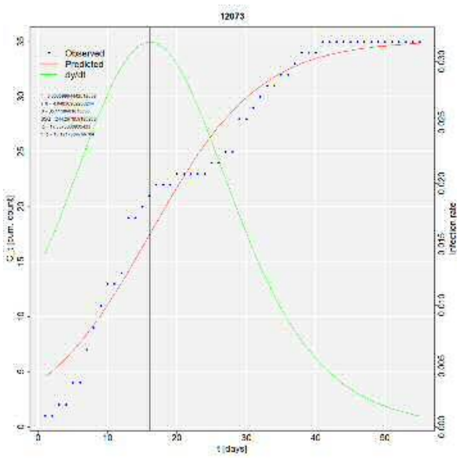
(b) Heinsberg county (North Rhine Westphalia)



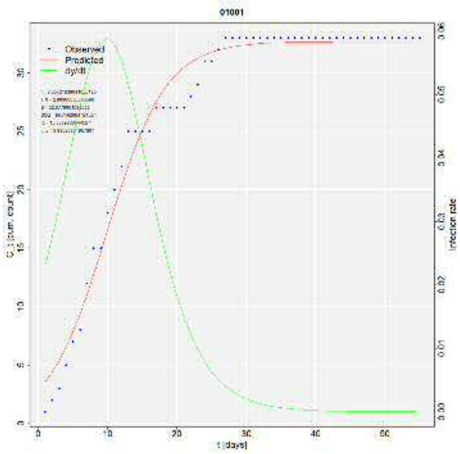
(c) Greiz county (Thuringia)



(d) Rosenheim county (Bavaria)



(e) Uckermark county (Brandenburg)



(f) Flensburg (Schleswig-Holstein)

Figure 6: Cumulative SARS-CoV-2 infections (based on estimated dates of infection) and estimated logistic growth models (including infection rate and inflection point) in six German counties

Source: own illustration. Data source: own calculations based on RKI (2020b)

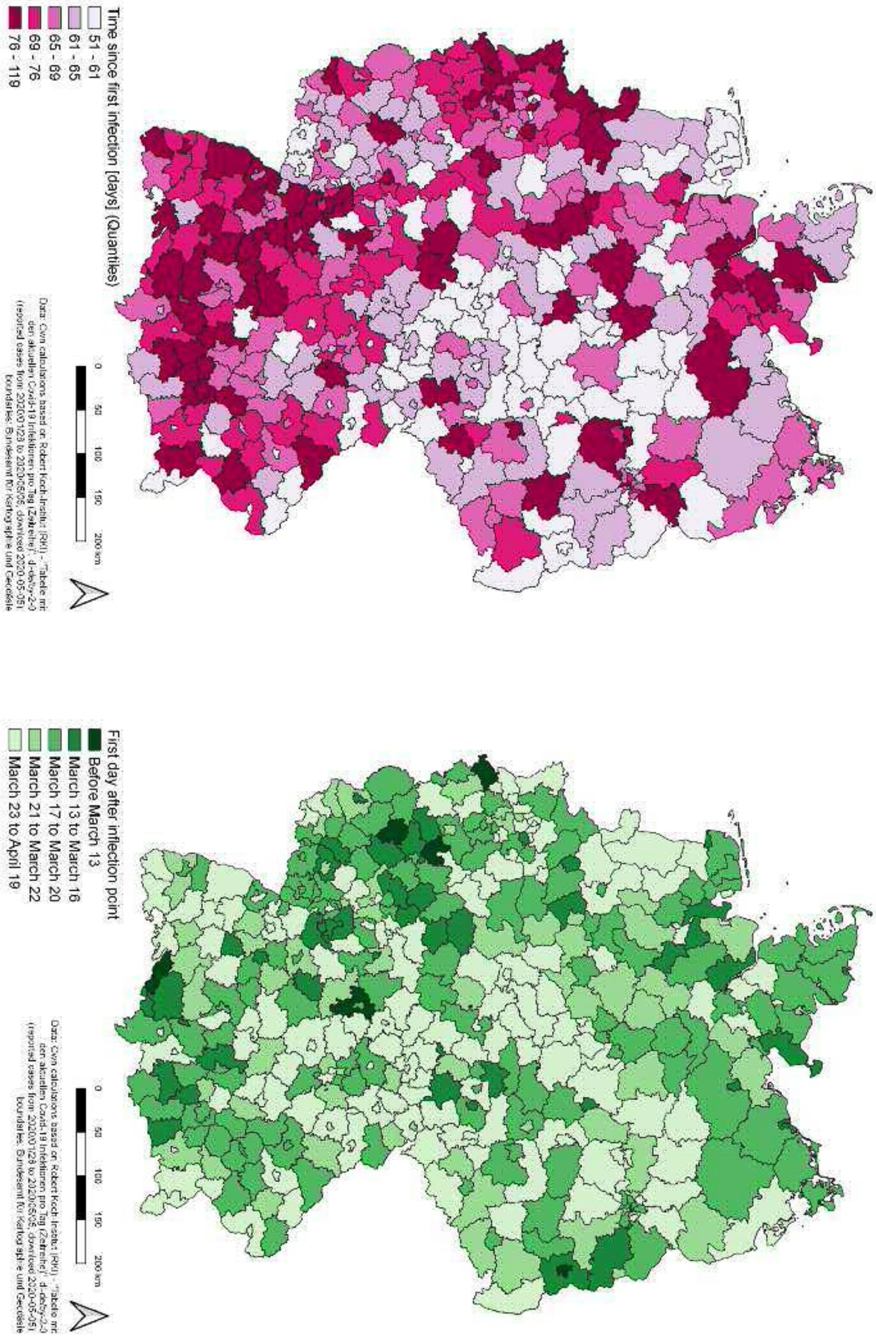


Figure 7: Time since first infection by county (left) and First day after inflection point by county (right)

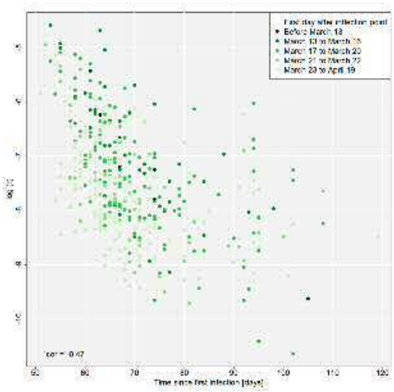


Figure 8: Growth rate and first day after inflection point vs. time
Source: own illustration. Data source: own calculations based on RKI (2020b)

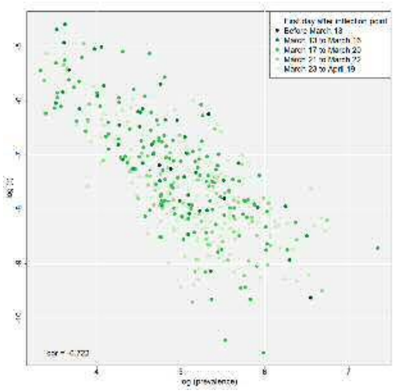


Figure 9: Growth rate and first day after inflection point vs. prevalence
Source: own illustration. Data source: own calculations based on RKI (2020b)

over time (see also Figures 5 and 8), more precisely, it declines in line with the time the disease is present in the regarded county (Pearson correlation coefficient of -0.47, $p < 0.001$). The longer the time between inflection point and now, the lower the growth speed, and vice versa. This process takes place over all German counties with a time delay depending on the first occurrence of the disease. As shown in Figure 9, there is also a negative correlation between regional prevalence and growth rate (Pearson correlation coefficient of -0.722, $p < 0.001$). These relationships, which are closely linked to the chronology of an infectious disease spread and the characteristics of the logistic growth model, respectively, are included into the regression models as control variables.

3.3 Regression models for intrinsic growth rates and mortality

The variables of most interest used within the models are mapped in Figures 10a (prevalence, *PRV*), 10b (mortality, *MRT*) and 11a (share of infected individuals of age ≥ 60, *POPS65*). Additionally, Figure 11b shows the current case fatality rate on the county level. Tables 7 and 8 show the estimation results for the OLS regression models explaining the intrinsic growth rates and the mortality, respectively, both transformed via natural logarithm. Table 9 displays the Moran's I-statistic for the dependent variables of the two models. Tables 10 and 11 show the estimation results for the spatial lag models.

In all of the OLS models, no variable exceeded the critical value of $VIF \geq 5$. For the prediction of the intrinsic growth rate, two model variants were estimated without and with the state dummy variables (Table 7). From the aspect of explained variance, the second OLS model provides a better fit ($R^2 = 0.731$ and Adj.$R^2 = 0.723$, respectively)

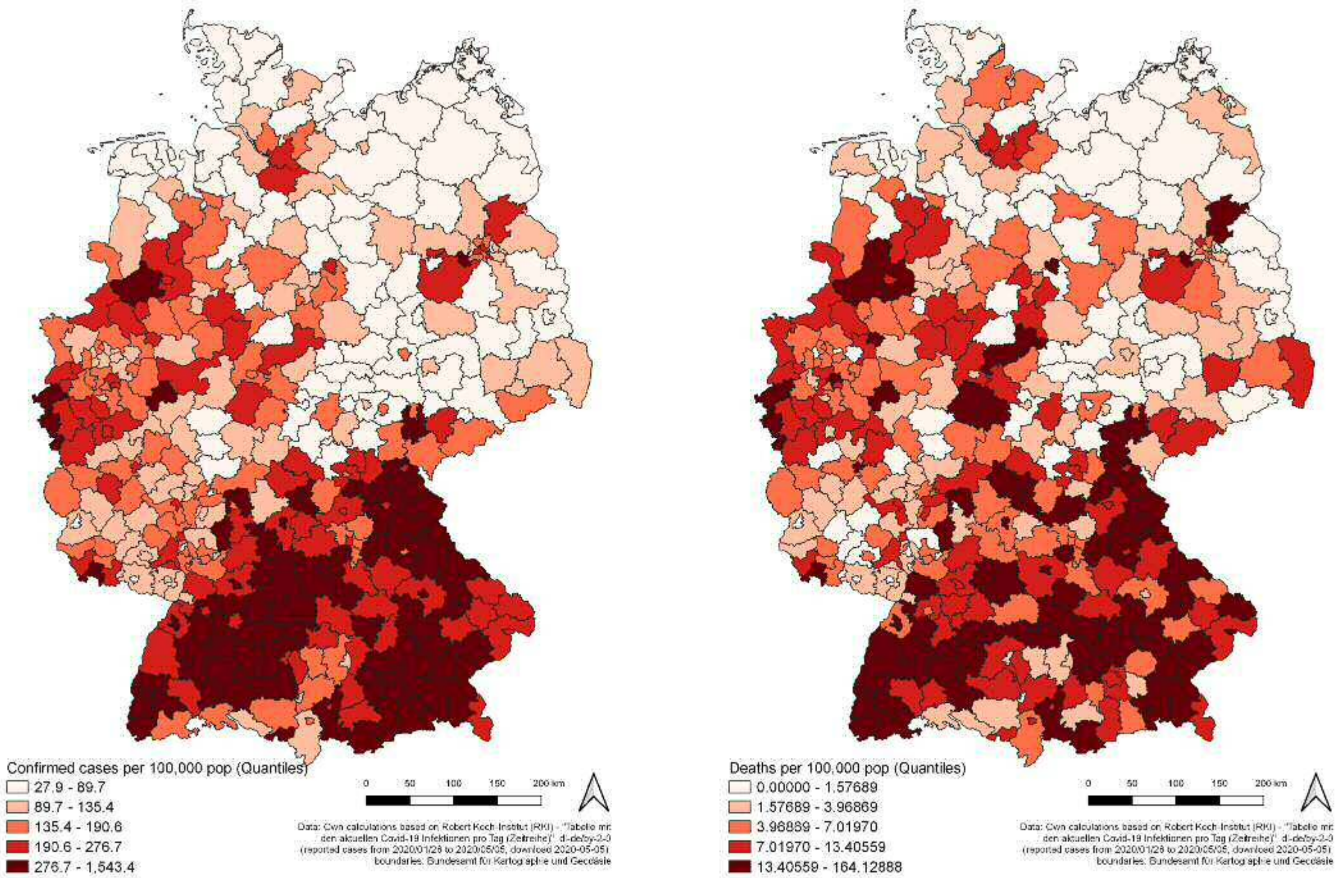


Figure 10: Prevalence by county (left) and Mortality by county (right)

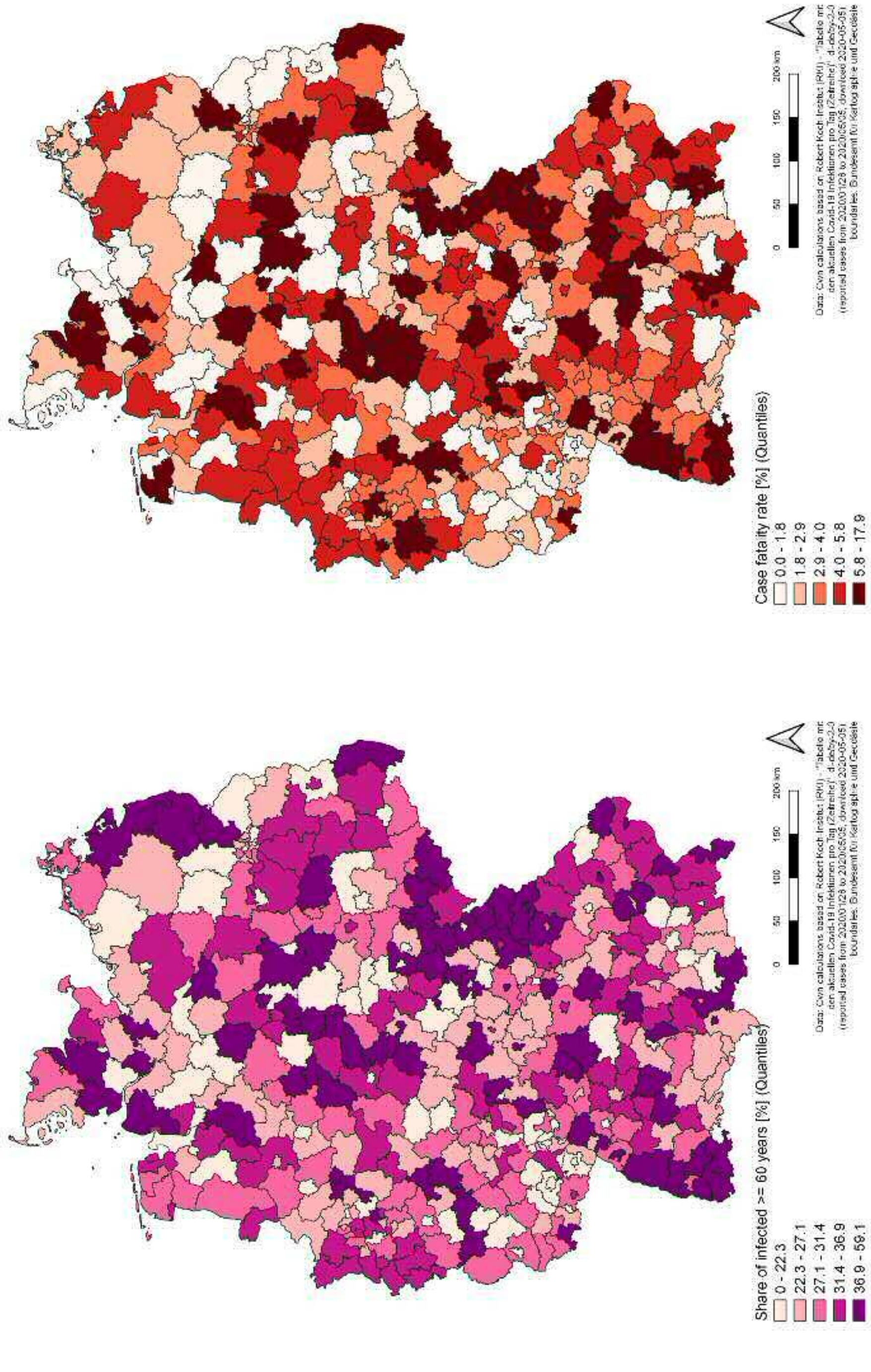


Figure 11: Share of reported infected individuals of age 60 and older by county (left) and CFR by county (right)

Table 7: Estimation results for the growth rate model (OLS)

	Dependent variable: ln(r)	
	(1)	(2)
ln (POPDENS)	−0.177***	−0.102***
	(0.028)	(0.027)
ln (POPS65)	0.830***	1.165***
	(0.284)	(0.269)
ln (CMI)	0.607***	0.420***
	(0.091)	(0.087)
ln (TOUR)	0.146***	0.035
	(0.042)	(0.041)
EAST	−0.087	−0.045
	(0.091)	(0.089)
BV		0.473***
		(0.091)
SL		0.118
		(0.231)
SX		−0.580***
		(0.168)
NRW		−0.428***
		(0.097)
BW		0.011
		(0.108)
ln (PRV)	−0.911***	−1.039***
	(0.049)	(0.056)
DAYS	−0.019***	−0.014***
	(0.003)	(0.003)
Constant	−3.660***	−4.214***
	(1.144)	(1.079)
Observations	412	412
R^2	0.678	0.731
Adjusted R^2	0.672	0.723
Residual Std. Error	0.587	0.540
Degrees of Freedom	404	399
F Statistic	121.278***	90.307***
Degrees of Freedom	7; 404	12; 399

Note: *p<0.1; **p<0.05; ***p<0.01

compared to the first ($R^2 = 0.678$ and Adj.$R^2 = 0.672$, respectively), thus, the second model is to be preferred for interpretation. Different than expected, population density (*POPDENS*) does not affect growth rate positively. A 1% increase of population density decreases the growth rate by 0.1%. Also the demographic indicator (*POPS65*) is correlated with growth contrary to expectations: An increase of 1% in the share of inhabitants of age ≥ 65 increases the growth rate by 1.2%. As expected, the intensity of commuting (*CMI*) has a significant positive effect on the intrinsic growth rate: An increase of commuting intensity by 1% increases the growth rate by 0.4%. Tourist density (*TOUR*) is only significant in the first model. On average, the intrinsic growth rate is significantly higher in Bavarian counties (dummy variable *BV*), and significantly lower in Saxony and North Rhine-Westphalian counties (*SL* and *SX*, respectively). The coefficients for Baden-Wuerttemberg (*BW*) and Saarland (*SL*) are not significant, which means that no significant deviation from the average growth rate is found for counties in these German states. The *EAST* dummy is insignificant in both models. Considering the necessary control variables, the current prevalence (*PRV*) and time (*DAYS*) decelerate the growth of infections significantly. The former has a nearly proportional impact: An increase of prevalence equal to 1% decreases the intrinsic growth rate by 1.04%. For each day

SARS-CoV-2/COVID-19 is present in the county, the growth speed declines on average by 1.4%. Here, one has to keep in mind that these relationships are reciprocal and represent the mandatory decline of susceptible individuals over time.

For the prediction of mortality (*MRT*), the growth rate (r) and the state dummy variables (*BV*, *SL*, *SX* and *NRW*) are entered into the model analyis successively, resulting in the three models shown in Table 8. When comparing models 1 and 2, adding the growth rate as independent variable increases the explained variance substantially (Adj.$R^2 = 0.219$ and 0.367, respectively). The third model provides the best fit, adjusted for the number of explanatory variables (Adj.$R^2 = 0.383$). No significant influence can be found for the spatial (*POPDENS*), demographic (*POPS65*), mobility (*PI* and *TOUR*), and air pollution variables (*PM10* and *NO2*). Life expectancy (*LEXP*) and the dummy for East German counties (*EAST*) are only significant in the first model. However, the share of infected people of age ≥ 60 (*INFS60*) significantly increases the regional mortality: An increase in the share of people of the "risk group" in all infected by 1% increases the mortality by approx. 0.5%. The only significant state-specific effect is found for Bavaria: The mortality in Bavarian counties is higher than in the counties of other states. Furthermore, a two-sample t-test reveals that Bavarian counties have a significantly higher share of infected belonging to the risk group ($\bar{x} = 31.11\%$) compared to the remaining states ($\bar{x} = 29.28\%$), with a difference of 1.83 percentage points ($p = 0.054$). The reciprocal relationship between mortality and growth rate is also significant.

As expected, spatial autocorrelation can be detected among the dependent variables. The Moran's I-statistic for both regional growth rate and mortality (0.49 and 0.16, respectively) is significant (see Table 9). Consequently, the OLS estimations are expected to be biased. Therefore, we apply a spatial lag model in the next step.

With respect to the spatial lag model for regional growth rates (Table 10), the ρ-parameter in both model variants is significant ($\rho = 0.158$ and $\rho = 0.095$, respectively), which indicates a significant spatial lag effect. However, when comparing the second spatial lag model (with $AIC = 674.96$, which is superior to model 1 with $AIC = 733.37$) to the second OLS model (see Table 7), there are only negligible differences in the parameter estimates and significance levels: The same independent variables are found to be significantly correlated with growth rates. They also have the same sign, which indicates the same direction of influence. Intrinsic growth rates on the county level are predicted by population density (approx. -0.9), population share of 65 and older (approx. 1.1), commuting intensity (approx. 0.4), and state-specific dummy variables (Bavaria: approx. 0.5, Saxony: approx. -0.5, North Rhine Westphalia: approx. -0.4) as well as the control variables (Prevalence: approx. -1.0 and time since first infection: approx. -0.01).

The same conclusion can be drawn with respect to the spatial lag models for mortality (Table 11), when comparing them to the OLS models (Table 8). The spatial lag effect is only significant in the first model ($\rho = 0.165$) but not in models 2 ($\rho = 0.042$) and 3 ($\rho = -0.044$). Regional mortality is significantly influenced by the share of infected people of age ≥ 60 (approx. 0.5) and the dummy variable for Bavarian counties (approx. 1.2) as well as correlated with regional growth rates (approx. -1.6). As spatial autocorrelation was also detected for the regional growth rate, which is an independent variable in the mortality models, a further robustness check of the estimations is necessary: Table 12 shows the results for the second and third mortality model in a spatial Durbin model, which incorporates a spatial lag effect for both the dependent variable (ρ) and the regional growth rate (*lag ln (r)*). The lag effect of $\ln(r)$ is statistically significant, but the other results remain qualitatively the same (share of infected people of age ≥ 60: approx. 0.5; dummy variable for Bavarian counties: approx. 1).

With respect to the regression models for regional growth and mortality, the results of the OLS estimations were confirmed by those from the models allowing for spatial autocorrelation. Although there is obvious spatial autocorrelation (which can be explained plausibly by interregional transmission of the infectious disease), both OLS and spatial regression models show nearly the same results with respect to strength and direction of correlations. From the spatial statistic point of view, this can be explained with the incorporated independent variables as regional differences in both growth rate and mortality are predicted entirely by the interregional variation in causal factors.

Table 8: Estimation results for the mortality model (OLS)

	Dependent variable: ln (MRT+0.0001) (1)	(2)	(3)
ln (POPDENS)	−0.060	−0.268**	−0.148
	(0.132)	(0.121)	(0.124)
ln (POPS65)	−0.738	0.883	1.730
	(1.316)	(1.196)	(1.230)
ln (CMI)	−0.627	0.397	0.025
	(0.412)	(0.385)	(0.396)
ln (TOUR)	−0.265	0.066	−0.081
	(0.188)	(0.173)	(0.178)
ln (LEXP)	54.205***	11.409	12.349
	(12.259)	(11.877)	(12.556)
ln (PM10)	0.053	−0.226	−0.200
	(0.716)	(0.645)	(0.653)
ln (NO2)	0.428	0.178	0.213
	(0.287)	(0.259)	(0.259)
ln (INFS60+0.0001)	0.618***	0.459***	0.462***
	(0.104)	(0.095)	(0.094)
EAST	−0.980**	−0.496	−0.148
	(0.395)	(0.359)	(0.385)
BV			1.110***
			(0.334)
SL			0.800
			(0.983)
SX			−0.909
			(0.738)
NRW			−0.144
			(0.433)
BW			0.193
			(0.465)
DAYS	0.017	−0.014	−0.011
	(0.013)	(0.012)	(0.012)
ln (r)		−1.570***	−1.535***
		(0.161)	(0.171)
Constant	−237.384***	−62.529	−69.684
	(55.406)	(53.006)	(55.923)
Observations	412	412	412
R^2	0.238	0.384	0.407
Adjusted R^2	0.219	0.367	0.383
Residual Std. Error	2.596	2.336	2.308
Degrees of Freedom	401	400	395
F Statistic	12.525***	22.679***	16.916***
Degrees of Freedom	10; 401	11; 400	16; 395

Note: *p<0.1; **p<0.05; ***p<0.01

Table 9: Moran's I-statistic for intrinsic growth rates and mortality (Weighting matrix: all adjacent counties)

Indicator	Moran's I	Expectation	Variance	Standard deviate
ln (r)	0.4856***	-0.0024	0.0011	14.738
ln (MRT+0.0001)	0.1635***	-0.0024	0.0011	5.0555

Note: *p<0.1; **p<0.05; ***p<0.01
Source: own calculation.

Table 10: Estimation results for the growth rate model (spatial lag model)

	Dependent variable: ln(r)	
	(1)	(2)
ln (POPDENS)	-0.151^{***}	-0.089^{***}
	(0.027)	(0.027)
ln (POPS65)	0.755^{***}	1.119^{***}
	(0.279)	(0.265)
ln (CMI)	0.561^{***}	0.402^{***}
	(0.092)	(0.087)
ln (TOUR)	0.121^{***}	0.024
	(0.041)	(0.041)
EAST	-0.148^{*}	-0.076
	(0.089)	(0.089)
BV		0.498^{***}
		(0.090)
SL		0.096
		(0.226)
SX		-0.538^{***}
		(0.166)
NRW		-0.368^{***}
		(0.100)
BW		0.073
		(0.110)
ln (PRV)	-0.827^{***}	-1.002^{***}
	(0.058)	(0.060)
DAYS	-0.018^{***}	-0.014^{***}
	(0.003)	(0.003)
Constant	-2.677^{**}	-3.562^{***}
	(1.159)	(1.110)
ρ	0.158^{***}	0.095^{*}
	(0.049)	(0.050)
Observations	412	412
Log Likelihood	-356.682	-322.481
σ^2	0.329	0.280
Akaike Inf. Crit.	733.365	674.962
LR Test (df = 1)	9.283^{***}	3.193^{*}
Wald Test (df = 1)	10.325^{***}	3.608^{*}

Note: *p<0.1; **p<0.05; ***p<0.01 *Source*: own calculation.

Table 11: Estimation results for the mortality model (spatial lag model)

	Dependent variable: ln (MRT+0.0001)		
	(1)	(2)	(3)
ln (POPDENS)	−0.085	−0.272**	−0.138
	(0.129)	(0.119)	(0.121)
ln (POPS65)	−0.500	0.921	1.731
	(1.289)	(1.178)	(1.204)
ln (CMI)	−0.586	0.394	0.013
	(0.403)	(0.379)	(0.387)
ln (TOUR)	−0.250	0.066	−0.086
	(0.184)	(0.170)	(0.175)
ln (LEXP)	51.311***	11.262	12.321
	(12.101)	(11.713)	(12.288)
ln (PM10)	0.197	−0.186	−0.224
	(0.700)	(0.637)	(0.639)
ln (NO2)	0.397	0.174	0.215
	(0.280)	(0.255)	(0.254)
ln (INFS60+0.0001)	0.614***	0.460***	0.461***
	(0.102)	(0.094)	(0.092)
EAST	−0.764*	−0.448	−0.180
	(0.399)	(0.365)	(0.382)
BV			1.185***
			(0.349)
SL			0.800
			(0.962)
SX			−0.914
			(0.722)
NRW			−0.119
			(0.426)
BW			0.245
			(0.466)
DAYS	0.017	−0.013	−0.011
	(0.012)	(0.012)	(0.012)
ln (r)		−1.549***	−1.550***
		(0.162)	(0.168)
Constant	−225.876***	−62.008	−69.584
	(54.613)	(52.268)	(54.731)
ρ	0.165**	0.042	-0.044
	(0.064)	(0.062)	(0.065)
Observations	412	412	412
Log Likelihood	−969.231	−927.965	−920.308
σ^2	6.435	5.293	5.100
Akaike Inf. Crit.	1,964.461	1,883.930	1,878.615
Wald Test (df = 1)	6.714***	0.449	0.454
LR Test (df = 1)	5.551**	0.378	0.365

Note: *p<0.1; **p<0.05; ***p<0.01 *Source*: own calculation.

Table 12: Estimation results for the mortality model (spatial Durbin model)

	Dependent variable: ln (MRT+0.0001)	
	(1)	(2)
ln (POPDENS)	−0.328***	−0.202
	(0.121)	(0.124)
ln (POPS65)	0.984	1.816
	(1.173)	(1.195)
ln(CMI)	0.476	0.092
	(0.379)	(0.386)
ln (TOUR)	0.146	−0.012
	(0.172)	(0.176)
ln (LEXP)	6.216	7.535
	(11.834)	(12.352)
ln (PM10)	−0.189	−0.358
	(0.633)	(0.636)
ln (NO2)	0.160	0.238
	(0.254)	(0.252)
ln (INFS60+0.0001)	0.467***	0.465***
	(0.093)	(0.092)
EAST	−0.236	0.022
	(0.373)	(0.388)
BV		0.980***
		(0.357)
SL		0.829
		(0.955)
SX		−1.131
		(0.722)
NRW		−0.474
		(0.450)
BW		−0.139
		(0.489)
DAYS	−0.013	−0.009
	(0.012)	(0.011)
$\ln(r)$	−1.422***	−1.456***
	(0.172)	(0.172)
lag $\ln(r)$	−0.555**	−0.634**
	(0.254)	(0.278)
Constant	−43.482	−52.706
	(52.507)	(54.744)
ρ	-0.033	-0.116
	(0.070)	(0.072)
Observations	412	412
Log Likelihood	−925.583	−917.677
σ^2	5.233	5.025
Akaike Inf. Crit.	1,881.167	1,875.355
Wald Test (df = 1)	0.223	2.607
LR Test (df = 1)	0.190	2.145

Note: *p<0.1; **p<0.05; ***p<0.01 *Source*: own calculation.

4 Discussion

4.1 Curve flattening in the context of nonpharmaceutical interventions

Taking a look at the national level, the flattening of the epidemic curve in Germany occurred between three to six days before phase 3 of measures (as defined in this study) came into force. Due to this temporal mismatch, the decline of infections cannot be causally linked to the nationwide formal "lockdown" (including forced social distancing and ban of gatherings) of March 23. Note that the results for whole Germany, estimating the inflection point between March 17 and March 20, are rather conservative when compared with the RKI estimations. In the RKI nowcasting study, the peak of onset of symptoms (not infection time, which is not considered in the mentioned study) is found at March 18 and a stabilization of the reproduction number equal to $R = 1$ at March 22 (an der Heiden, Hamouda 2020). Subtracting an average incubation period of five days from these dates, the peak of infections occured around March 13 and the reproduction number stabilizes approximately at March 17. An earlier RKI study (an der Heiden, Buchholz 2020) estimated the peaks between June and July, depending on the parameters of the scenarios.

The main focus of this analysis is on the regional level, which reveals a more differentiated picture. In all German counties the curves of infections clearly flattened within a time period of about six weeks from the first to the last county. On average, it took one month from the first infection to the inflection point of the epidemic curve. However, the regional trend change in infections is not in line with the governmental nonpharmaceutical interventions to contain the virus spread. In nearly two thirds of the German counties which account for two thirds of the German population, the flattening of the infection curve occured before the "lockdown" (measures of phase 3) came into force (March 23). One in eight counties experienced a decline of infections even before the closures of schools, child day care facilities and retail facilities, which is attributed to phase 2 of interventions in this study. Consequently, in a majority of counties, the regional decline of infections cannot be attributed to the formal "lockdown". In a minority of counties, also closures of educational and retail facilities (measures of phase 2) cannot have caused the decline. Keeping in mind that SARS-CoV-2 emerged at different times across the counties, it is at least questionable whether these measures primarily caused the flattening of the infection curve in the other counties. Furthermore, in a minority of counties, the regional trend change occurred several weeks (up to about four weeks) after the nonpharmaceutical interventions came into force. One might argue that there could be a time lag between the date of official enforcement of the regulations and the time they became effective in practice. However, this could only be conceivable for the contact ban but not for the closures of schools and other services as these infrastructures are either closed or not and, thus, can be potential places of virus transmission or not. Moreover, it seems unlikely that an intervention like a contact ban becomes effective only after several weeks and regionally differentiated.

Bringing together these aspects, regional curve flattening seems to have occurred independently from the governmental measures of phase 2 and 3. Instead, regional pandemic growth appears as a function of time, reaching the peak of infection rates with a time lag depending on the date the virus emerged.

The results presented here tend to support the findings in the study by Ben-Israel (2020) that curve flattening in the SARS-CoV-2/COVID-19 pandemic occurs with or without a strict "lockdown". However, neither this study nor the study by Ben-Israel (2020) provides explicit epidemiological, virological or other kinds of clarifications for this phenomenon. The further interpretation must be limited to a collection of explanation attempts, which are non-mutually exclusive. Some reasons for the decline of infections relate to other types of interventions both voluntary and mandatory are:

- First of all, it must be pointed out that the focus of this study is on regional pandemic growth in the context of the nonpharmaceutical interventions of phase 2 and 3 starting in mid March 2020, especially the "lockdown" from March 23. One has to keep in mind that some interventions against virus spread were already established in the first half of March (phase 1), e.g. the cancellation of large events or "ghost games" in soccer (see Table 1). These early measures could have contributed substantially to curve flattening, as the cancellation of events might have prevented people from being infected in the context of so-called *super-spreading events*, which play an enormous role during infectious disease spreads (Al-Tawfiq, Rodriguez-Morales 2020, Stein 2011). Many infections and death cases attributed to COVID-19 in the early phase of the pandemic in Germany can be traced back to super-spreading events in February and early March 2020, such as in Heinsberg or Tirschenreuth county (Tagesspiegel 2020b). Also, the domestic quarantine of infected persons (which is the default procedure in the case of infectious diseases) might have reduced new infections. In Heinsberg county, about 1,000 people were in domestic quarantine at the end of February 2020 (Tagesschau.de 2020c), which could explain the early curve flattening in this Corona "hotspot".

- Also media reports from China or Italy as well as appeals and recommendations from the government could have influenced people's behavior on a *voluntary* basis already in the first half of March 2020 (or even earlier), e.g. with respect to physical distancing, thorough and frequent hand washing, coughing and sneezing in the arm fold, or reducing mobility in general. Unfortunately, there is no explicit indicator of changes in the individual behavior. However, some other findings give a hint towards voluntary behavorial changes: Several surveys show a high degree of public awareness in Germany (and other countries) towards the SARS-CoV-2/COVID-19 threat already in February and the first half of March 2020 (Ipsos 2020, YouGov 2020). This increasing awareness might be reflected by more caution in daily life: The RKI has documented an "abrupt" decline of *other* infectious respiratory diseases with shorter incubation periods (such as influenza) in Germany since the 10th calendar week (March 2 to 8, 2020). This decline is regarded as "extremely unusual" (Buchholz et al. 2020). This reduction might be attributed to voluntary cautious behavior in the context of the public discussion towards SARS-CoV-2, as this decrease started before any public health intervention came into force (except for the quarantines of SARS-CoV-2-infected persons, see Table 1). Furthermore, the analysis of mobility patterns shows a decline of mobility in Germany, starting already in the first half of March 2020. Additionally, a strong correlation between (aggregated) mobility and the acceptance of social restrictions (obtained by surveys) was found: The higher the agreement with the statement "I think the current measures are too strict", the higher the increase in mobility (Covid-19 Mobility Project 2020a,b). All these phenomenons suggest voluntary behavior changes within the (German) population, which reduce the transmission of infectious diseases and preceded the "lockdown" by several weeks. Another indicator for an increased awareness in the (German) population – although not intended or desired – is the enormous tendency of hoarding groceries, which started in the second half of February 2020 (Rheinische Post online 2020).

- Additionally, one has to keep in mind the seasonal cycle of respiratory viral diseases: Influenza viruses and most cold viruses (including those from the family of Coronaviridae) mainly occur during the winter months due to changes in environmental parameters (e.g., temperature and humidity) and human behavior (more or fewer activities outside, whilst the risk of infection is, all other things being equal, lower outside) (Moriyama et al. 2020). Several virologists expressed cautious optimism towards the sensitivity of the SARS-CoV-2 virus to increasing temperature and ultraviolet radiation (Focus 2020). Model-based analyses from biogeography show that temperate warm and cold climates facilitate the virus spread, while arid and tropical climates are less favorable (Araujo, Naimi 2020). By consequence, there might have also been a decline of SARS-CoV-2 infections due to weather changes in early spring (mid-March).

Furthermore, there is another possible reason for curve flattening with or without a "lockdown", which is of epidemiological nature and related to the transmission process of SARS-CoV-2/COVID-19 in the context of immunization. Note that "immunity" may have different causes (e.g., antibodies due to previous infections, vaccination, immunological memory) and does not necessarily prevent individuals from being infected (in terms of an invasion of an individual's body) but leads to an effective response of the immune system and prevents the emergence of (severe) symptoms (Mak, Saunders 2006). At the beginning of the pandemic, two assumptions towards the role of immunization were stated: 1) Nobody is immune, which means that all individuals of the population belong to the group of susceptibles, 2) Without any interventions (e.g., vaccine, nonpharmaceutical interventions), *herd immunity* – a share of a population is immune, which provides protection to those who are not immune, causing the pandemic to slow down and stop – is achieved when about 70% of the population was infected (D'Souza, Dowdy 2020). This percentage share is commonly known as *herd immunity threshold* (*HIT*) and is, in its basic form, calculated based on the infection's basic reproduction number, R_0: $HIT = 1 - 1/R_0$ (Fine et al. 2011). Early modeling studies focusing on the effect of nonpharmaceutical interventions are based on these (or similar) assumptions (an der Heiden, Buchholz 2020, Ferguson et al. 2020). However, there are some issues regarding the *HIT* for SARS-CoV-2/COVID-19 which need to be considered:

- In epidemiology, it is well known that disease transmission is mostly concentrated on a minor part of individuals causing a large majority of secondary infections: "In what became known as the 20/80 rule, a concept documented by observational and modeling studies and having profound implications for infection control, 20% of the individuals within any given population are thought to contribute at least 80% to the transmission potential of a pathogen, and many host-pathogen interactions were found to follow this empirical rule" (Stein 2011). Gomes et al. (2020) incorporate inter-individual variation in susceptibility and exposure to a SARS-CoV-2 infection into an epidemiological model (SEIR [susceptible-exposed-infectious-recovered] model). Depending on the assumptions on this *overdispersion*, the *HIT* of SARS-CoV-2 reduces to 10-20%. Thus, the achievement of herd immunity would require a considerably lower number of SARS-CoV-2 infections.

- Although the SARS-CoV-2 virus is highly infective, the "Heinsberg study" by Streeck et al. (2020) found a relatively low secondary infection risk (*secondary attack rate*, SAR). Infected persons did not even infect other household members in the majority of cases. The authors conjecture that this could be due to a present immunity (T helper cell immunity) not detected as positive in the test procedure. This kind of immunity is not to be confused with (temporal or everlasting) immunity due to antibodies against a specific virus but may be regarded as a functional immune memory. In a current virological study by Braun et al. (2020), 34% of test persons who have never been infected with SARS-CoV-2 had relevant T helper cells because of earlier infections with other harmless Coronaviruses causing common colds. In a study by Grifoni et al. (2020), SARS-CoV-2-reactive T cells were detected in even 40%–60% of unexposed individuals. If this explanation proves correct, the absolute number of susceptible individuals would have been substantially lower already at the beginning of the pandemy. Other Coronaviruses are responsible for about 10-15% of seasonal "common colds" (Padberg, Bauer 2006). Cross protection due to related virus strains has also been determined e.g. with respect to influenza viruses (Broberg et al. 2011).

- Considering the aforementioned aspects, we have to keep in mind that all data related to infections used here underestimate the real number of infected individuals in Germany as well as in nearly all countries where the Coronavirus emerged. Typically, at the beginning of the pandemic, only suspected cases with COVID-19 symptoms were tested, leading to a heavy underestimation of infected people without symptoms (see Section 2.2). Several recent studies have tried to estimate the real prevalence of the virus and/or the infection fatality rate (IFR), including all infected cases rather than the confirmed (see Table 13). Estimated rates of unreported cases (estimate PRV/reported PRV) lie between 5 (Gangelt, Germany) and 50-85 (Santa Clara County, USA). Obviously, when estimated CFR values exceed the estimated IFR values by ten times or more, there must be a large number of unreported cases and the total number of infected individuals must be

> considerably higher than reported, respectively. The logical consequence is that there is a hidden decrease of the absolute number of susceptible individuals because of many infected persons without symptoms not knowing that they have been infected (and probably immunized) in the past. These individuals were not tested for the *pathogen* (SARS-CoV-2 virus) because they did not suffer from the *disease* (COVID-19). Quantifying the "dark figure" of SARS-CoV-2 infections by using representative sample-based tests on current infection as well as seroprevalence will be a challenge in the near future.

Of course, the present empirical results cannot prove or disprove the presence or absence of (herd) immunity. However, the number of infected individuals is obviously higher than reported (see Table 13), whilst the number of susceptibles could have been considerably smaller than expected already at the beginning of the pandemic. If a SARS-CoV-2 infection leads to (lifelong or temporal) immunity (which is not yet clarified), the current level of immunity must be higher as well. Similar results were found in the UK: Stedman et al. (2020) also find decreasing infection rates (R_{ADIR}) related to (reported and unreported) prevalence on the regional level (Upper Tier Local Authority areas) and conclude that "the only factor that could be related to the R_{ADIR} in this analysis was the historic number of confirmed number infection/,000 population suggesting that some of the reduction in reported cases is due to the build-up of immunity due to larger numbers of historic cases in the population".

However, we have to keep in mind that even if herd immunity was achieved, this does not mean that *no* new infections occur. Furthermore, herd immunity implies a closed population, where there are too many immunized individuals to infect the remaining susceptibles. In reality, there are migratory and mobility flows between regions and nations (e.g., work-related commuting, tourism) and, thus, new infections may occur due to transmissions driven by spatial interactions. More precisely, a susceptible individual living in a given region with herd immunity might get infected when traveling to another region. Finally, there is a difference between *infection* and *disease*, whilst the infectiousness of asymptomatically infected individuals is not yet clarified, although they are regarded as much less likely to transmit the virus than infected with symptoms (World Health Organization 2020a).

4.2 Determinants of regional growth and mortality

Two regression models were estimated, with intrinsic growth rates (indicating the speed of pandemic growth) and mortality (indicating the severity of the disease) as dependent variables. For both variables, spatial autocorrelation was detected, which can be explained comprehensively by virus transmission across borders of nearby counties. However, both the OLS and the spatial regression models give qualitatively the same results.

With respect to the determinants of growth speed, two explanatory variables have a significant effect opposite to the expected: A slower disease spread is not due to lower population density. In contrast, intrinsic growth rates decrease with higher density values on the level of German counties. This could be explained with the validity of this indicator as it is questionable whether population density is a sufficient proxy for the amount and intensity of physical contacts between individuals. There is no empirical evidence that inhabitants living in larger and densely populated municipalities (such as large cities) have more social interactions than in people in rural areas (Mitterer 2013, Petermann 2001). There is also no dampening effect of virus spread by an older population on the county level. Instead, growth rates increase with the share of inhabitants of 65 years and older, although this age category covers the retired population. This result might be due to a bias in testing for SARS-CoV-2 infections: Most tests in the past were conducted on people with COVID-19 symptoms. As older people are more likely to have a severe course of the disease, these age groups are obviously overrepresented in the tested and confirmed cases (RKI 2020a). Differing from the expectations, no isolated effect of East German counties was found.

However, regional growth rates of infections are increased by inter-regional mobility, especially with respect to work-related commuting. This result is quite plausible and

Table 13: Studys on unreported cases and/or IFR of SARS-CoV-2/COVID-19

Study	Study area	n	Time of data collection	Est. PRV [%] (CI95)	Est.asymp-tomatic cases [%]	Est.PRV/ reported PRV	Est. IFR [%] (CI95)
Bendavid et al. (2020)	Santa Clara county (USA)	3,324	04/2020	2.8 (2.2, 3.4)	NA	50-85	NA
Bennett, Steyvers (2020) - re-analysis of Bendavid et al. (2020)	Santa Clara county (USA)	3,324	04/2020	0.27-3.21	NA	5-65	NA
Gudbjartsson et al. (2020)	Iceland						
Targeted testing 1		177	01-03/2020	9.2	13.6	NA	NA
Population screening 1		10,797	03/2020	0.8	41.4	NA	NA
Targeted testing 2		7,275	03/2020	14.4	5.7	NA	NA
Population screening 2 (Random sample)		2,283	04/2020	0.6	53.8	NA	NA
LAPH (2020)	Los Angeles county (USA)		04/2020	4.1 (2.8, 5.6)	NA	28-55	NA
Lavezzo et al. (2020)[1]	Vo						
First survey	(Italy)	2,812	02/2020	2.6[2] (2.1, 3.3)	41.1	NA	NA
Second survey		2,343	03/2020	1.2[2] (0.8, 11.8)	44.8	NA	NA
Nishiura et al. (2020)[1]	Wuhan (China)[3]	565	02/2020	1.4	62.5	5-20	0.3-0.6
Russell et al. (2020)[1]	Diamond Princess cruise ship	3,711	02/2020	17	51.4	NA	1.3 (0.38, 3.6)
Shakiba et al. (2020)	Guilan province (Iran)	551	04/2020	33[4] (28, 39)	18	NA	0.08-0.12
Streeck et al. (2020)	Gangelt (Germany)	919	03/2020	15.5 (12.3, 19)	22.2	5	0.36 (0.29, 0.45)

Source: own compilation. *Notes*: [1]full survey or nearly full survey, [2]only active infections (not including seroprevalence), [3]Japanese citizens evacuated from Wuhan (China), [4]adjusted for test performance.

supports previous findings in the literature on empirical and model-based approaches towards infectious disease spreads in the past (Charaudeau et al. 2014, Dalziel et al. 2014, Findlater, Bogoch 2018).

Taking a look at state-specific effects, the results show a significantly higher average growth rate in Bavarian counties and lower growth rates in Saxony and North Rhine Westphalia, while Saarland and Baden-Wuerttemberg counties did not deviate from the national average. Thus, no dampening effect on pandemic growth can be confirmed for German states with additional curfews for the containment of the virus spread (Bavaria, Saarland, Saxony). The growth rate in Bavaria is even considerably above the average, although the time since the virus emerged and the current prevalence were included into the models as control variables.

With respect to the determinants of mortality, few clear statements can be made. SARS-CoV-2/COVID-19 mortality on the county level is not significantly influenced by demographic, spatial or mobility factors. However, these variables explain the regional growth rate, which was added to the mortality model as a control variable (and is significant, as expected). There is no specific "East Germany effect" as well.

Considering previous studies on the influence of air pollution on COVID-19 severity (Ogen 2020, Wu et al. 2020), it was expected that particulate matter and NO_2 concentration would have an influence on mortality. Although it is plausible to assume that air pollution increases fatality rates of respiratory diseases, this hypothesis was not confirmed in the present study, which may result from an obvious data problem: The annual mean values of daily pollution was obtained on the level of monitoring stations, which are not evenly distributed across the counties and measure the air pollutant level at a specific point (e.g. traffic crossroad). It is unlikely that these obtained values are representative for the whole county. Thus, the validity of this indicator is questionable. Unfortunately, county-based data towards air pollution is not available nationwide.

Obviously, the variance of regional mortality reflects the regional variance of infected individuals belonging to the "risk group", defined as people of 60 years and above. Although no regional data is available for cases and deaths in retirement homes, a large share should be attributed to these facilities. Nationwide, people accommodated in facilities for the care of elderly make up at least 2,473 of 6,831 deaths (36.20%) as of May 5, 2020 (RKI 2020a). The share of residents of retirement homes in all COVID-19-related deaths is equal to 51% in France and 33% in Denmark, ranging internationally from 11% in Singapore to 62% in Canada (Comas-Herrera et al. 2020). The relevance of retirement homes in Germany can be underlined with examples based on information available in local media which depicts the regional situation:

- In the city of Wolfsburg (Lower Saxony), the current mortality (MRT) is equal to 41.08 deaths per 100,000 inhabitants, while the current case fatality rate (CFR) is the highest in all German counties (17.89%). Both values are calculated from the data used here (of date May 5, 2020). As of May 11, there have been 51 deaths attributed to COVID-19 in Wolfsburg, with 44 of these deaths (86.27%) stemming from residents of one retirement home (Wolfsburger Nachrichten 2020).
- In the Hessian Odenwaldkreis with MRT = 54.75 and CFR = 14.60%, 29 people who tested positive to SARS-CoV-2/COVID-19 died until April 14, 2020, 21 of them (72.41%) were living in retirements homes in this county (Echo online 2020).
- In the city of Würzburg (Bavaria) with MRT = 38.32 and CFR = 10.75%, there have been 44 COVID-19 positive deceased in two retirement homes until April 24, 2020, leading to investigations by the public prosecution authorities (BR24 2020). Up to April 23, 2020, in the whole administrative district Unterfranken, 64% of all people who died from or with Corona were residents of retirement homes for elderly people (Mainpost 2020).

With respect to state-specific effects, there is a clear significant impact regarding Bavaria: Although the measures in Bavaria, based on the Austrian model, were probably the strictest of all German states, both regional growth rates and mortality are significantly *higher* than in the other states. This effect is isolated, as other effects (time, population density etc.) were controlled. In addition, the share of individuals belonging to the "risk group" is slightly higher in Bavaria. In the other states with curfews, Saarland and Saxony, no significant impact of this additional intervention was found, especially with respect to mortality which does not differ significantly from other states.

5 Conclusions and limitations

In the present study, regional SARS-CoV-2/COVID-19 growth was analyzed as an empirical phenomenon from a spatiotemporal perspective. Using infection dates estimated from reported cases, logistic growth models were estimated for the disease spread at the level of German counties as well as at the national level. The resulting intrinsic growth rates vary across the 412 German counties. The inflection points of the epidemic curves were contrasted to the dates where nonpharmaceutical interventions against the disease spread came into force. As a result, Germany as a whole as well as the majority of German counties have experienced a decline of the infection rate – which means a flattening of the infection curve – before the main social-related measures (contact ban, ban of gatherings and closure of "nonessential" services) were established. In a minority of counties, curve flattening even occured before schools and child day care facilities were closed. In contrast, some regional trend changes took place several weeks after the measures came into force. *Due to this temporal mismatch, we have to conclude that the decline of infections cannot*

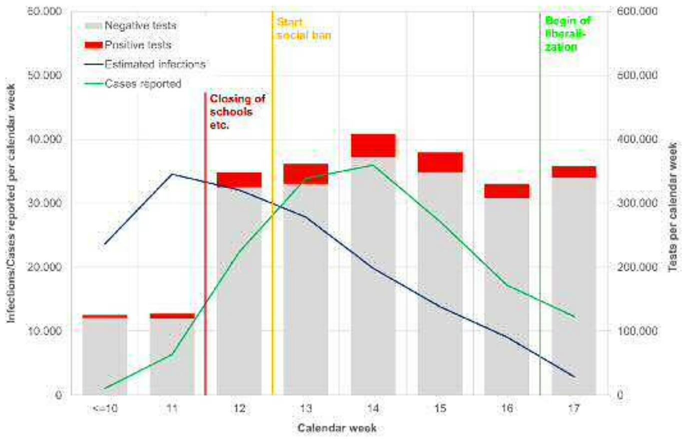


Figure 12: Estimated infections, reported cases and conducted tests by calendar week
Source: own illustration. Data source: own calculations based on RKI (2020b,c)

be causally linked to the "lockdown" of March 23. Moreover, also the impact of school and child care infrastructure closures on the pandemic spread remains questionable.

However, this does not mean that the disease spread slows down automatically. Four possible reasons have been identified for curve flattening independent from school closures and the "lockdown", with the first two relating to other types of (state-run and voluntary) measures which could reduce the transmission of an infectious disease: 1) Positive effects of *previous governmental nonpharmaceutical interventions* (especially the cancellation of large-scale events), 2) *voluntary behavior changes* (e.g., with respect to physical distancing and hygiene), 3) *seasonality* of the virus, and 4) a rising but undiscovered level of *immunity* within the population. However, whether these determinants may have contributed to the decline of infections, is outside the scope of the model-based analysis.

The determinants of regional intrinsic growth rates (as an indicator for the speed of pandemic spread) and mortality (as an indicator of the disease's severity) were explored using regression models. Among other things, regional pandemic growth is found to be driven by inter-regional mobility. Mortality on the county level obviously depends on the share of infected individuals belonging to the "risk group" (people of age 60 or older). This share is considerably influenced by SARS-CoV-2/COVID-19 outbreaks in retirement homes for the eldery, which have occurred in many German counties. Obviously, neither strict measures in Germany nor other countries were able to prevent these location-specific outbreaks. *By consequence, it must be concluded that the severity of SARS-CoV-2/COVID-19 depends on the local/regional ability to protect the "risk group", especially older people in care facilities. This is the more important as virus transmission in care homes is nearly independent from the nonpharmaceutical interventions concerning e.g. schools, commercial services, and private residences.* Three German states (Bavaria, Saarland, Saxony) established curfews additional to the nationwide interventions. *We must conclude that these state-specific curfews did not contribute to a more positive outcome with respect to growth speed and mortality.*

On the one hand, these findings pose the question as to whether contact bans and curfews are appropriate measures for containing the virus spread, especially when weighing the effects against the social and economic consequences as well as the curtailment of civil rights. On the other hand, when looking at regional mortality and case fatality rate, the protection of "risk groups", especially older people in retirement homes, is obviously of moderate success.

From the methodological point of view, two further conclusions must be stated: Nonpharmaceutical interventions aim at the reduction of new infections, thus, their impact must be assessed regarding temporal coincidences with new infections. *Regardless of the modeling approach used for the analysis of pandemic spread, any analysis concerning the effectiveness of nonpharmaceutical interventions must be based on realistic infection* *dates rather than reporting dates of infected persons. An over- or underestimation of the time between infection and report – in particular, the reporting delay – might lead to senseless conclusions towards the influence of specific measures.* Estimating the true infection dates from reported cases in official statistics is the biggest methodological challenge in this context. Moreover, the present study reveals the importance of a spatial perspective on pandemic spread: *Spatially varying growth rates and severity measures show that the spread of an infectious disease is to be regarded as a spatiotemporal phenomenon. Thus, further studies should address regional differences of epidemiological variables with respect to transmission.*

However, despite these conclusions, the study is faced with two important limitations:

- One has to keep in mind that previous model-based simulation studies which prove the effectiveness of nonpharmaceutical interventions already make *a priori* assumptions about the impact of these measures: In particular, the *input* parameters of the epidemiological models (such as the intensity of physical contacts between individuals) are set in a way that interventions (such as school closures or social distancing) reduce the transmission of the virus in any case and, thus, the simulation *output* shows a decline of infections subsequent to these interventions (an der Heiden, Buchholz 2020, Ferguson et al. 2020). This type of modeling approach (and the corresponding results) might be regarded either as a "causal model" or a tautology. In contrast, the modeling approach used here is of purely empirical nature, only incorporating time series of infections. By consequence, the results are not causal but correlative with respect to the presence or absence of temporal coincidences. It can be shown that curve flattening does not coincide with the focused interventions but occurred after previous interventions and might be due to several other causes. However, the actual reasons *why* the infections declined cannot be deduced from modeling results but must be explored based on interpretations of several empirical hints. Furthermore, as the focus is on inflection points and trend changes, respectively, the present empirical analysis cannot rule out *additional* impacts of the German "lockdown", e.g., in terms of a stabilization effect.

- Finally, it is necessary to take a look at the quality of the data on reported cases of SARS-CoV-2/COVID-19 used here. While several statistical uncertainties have been addressed by estimating the dates of infection in the present study, the method of data collection also raises concerns. The confirmed cases of infections reported by regional health departments to the RKI result from SARS-CoV-2 tests conducted in the case of specific symptoms. When aggregating the reported cases to time series and analyzing their temporal evolvement, it is implictly assumed that the testing strategy remains the same over time. However, the number of tests was increased enormously during the pandemic – which is to be welcomed from the point of view of public health. From a statistic perspective, it might cause a bias because an increase in testing *must* result in an increase of reported infections, as a larger share of infections is revealed, all other things being equal. In his statistical study, Kuhbandner (2020) argues that the detected SARS-CoV-2 pandemic growth is mainly due to increased testing, leading to the conclusion that "the scenario of a pandemic spread of the Coronavirus in based on a statistical fallacy". To confirm or deny this conclusion is not subject of the present study. However, taking a look at the conducted tests per calendar week (see Figure 12) reveals weekly differences. From calendar week 11 to 12, there has been an increase of conducted tests from 127,457 (5.9% positive) to 348,619 (6.8% positive), which means a raise by factor 2.7. The maximum of tests was conducted in CW 14 (408,348 with 9.0% positive results), decreasing beyond that time, rising again in CW 17. The absolute number of positive tests is reflected plausibly in the number of reported cases (green line), as the confirmed cases result from the tests. The most estimated infections occurred in CW 11 and 12, showing again the delay between infection and case confirmation. Apart from the fact that excessive testing is probably the best strategy to control the spread of a virus, the resulting statistical data may suffer from underestimation and overestimation, dependent on which time period is regarded.

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The Pandemic Economy: Exploring the change in new business license activity in Chicago, USA from March – September, 2020

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Abstract. Since its emergence in 2019, the worldwide spread of the novel coronavirus SARS-CoV-2 (COVID-19) has created a vast economic crisis as government lockdowns place considerable strain on businesses of all kinds – particularly those that rely on face-to-face contact, such as retail restaurants, and personal services. Given the importance of these businesses to local economic development and urban vitality, this paper makes use of the point-level Chicago Business License dataset to examine the impact of the COVID-19 pandemic on new business activity in the City of Chicago. The results indicate that on average, from March to September 2020, total monthly new business starts have declined by 33.4% compared to the monthly average of new starts in the City from 2016 to 2019. Food service and retail businesses have been hardest hit during this period, while chains of all types have seen larger average declines in new startup activity than independent businesses. These patterns also demonstrate interesting intra-urban spatial heterogeneity; ZIP codes with the largest resilience to pandemic-related drops in new business activity tend to have more dense, diverse, and walkable built environments, lower levels of social vulnerability, lower percentages of young residents, and higher percentages of Black and Asian (non-Hispanic) residents. These findings provide some useful evidence in support of the "15-minute city" and ethnic enclave resilience hypotheses. Interestingly, observed COVID-19 case rates also appear to have a positive relationship with new business resilience for new chain and food service establishments. This is likely due to the fact that neighborhoods with relatively high levels of new food service business activity also have relatively higher proportions of food service employees, who are more at risk for contracting COVID-19 as "essential" workers.

1 Introduction and Background

Since the emergence of the novel SARS-CoV-2 (COVID-19) virus in late 2019, its global spread has led to a variety of negative economic consequences, from restrictions on business operations and government lockdowns to reduced consumer confidence, discretionary mobility, and stock market fluctuations (McKinsey & Company 2020). According to some estimates, real global Gross Domestic Product (GDP) dropped by 10% between 2019Q4 and 2020Q2 (McKinsey & Company 2020), while US GDP experienced its largest quarterly drop in history (9.1% in Quarter 2 of 2020), far outstripping the impact of any previous recessions (measured since data collection began in 1947) (Bauer et al. 2020,

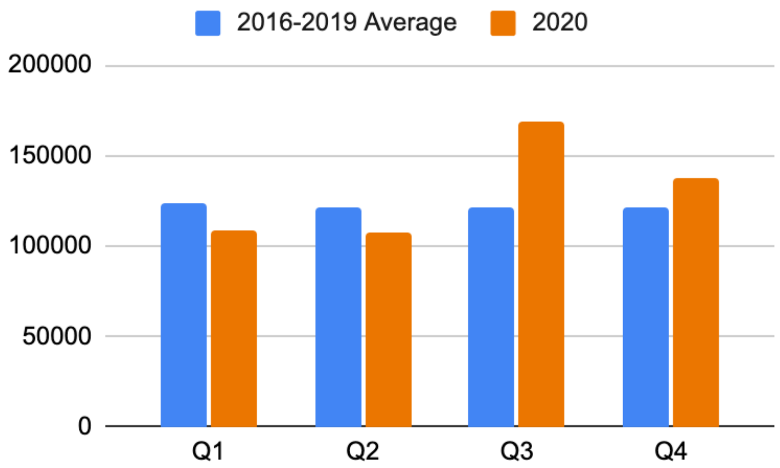


Figure 1: Applications for new businesses with planned wages, 2016 - 2019 average and 2020 (US Census Bureau 2020)

Routley 2020). Concurrently, the US unemployment rate reached its highest-ever recorded value in April 2020 at 14.7% (FRED 2020), while the S&P 500 lost 33% of its value in just one month (Capelle-Blancard, Desroziers 2020).

Accordingly, US national data show that small business revenues across all industrial sectors dropped by 40% in April and had not yet recovered to pre-pandemic (January 2020) levels by August, remaining at a 20% deficit; revenue in “leisure and hospitality” small businesses, which includes the arts, entertainment, recreation, accommodation, and food service sectors, have fared even worse, bottoming out at a roughly 70% deficit and only recovering to around 40% of pre-pandemic levels (Chetty et al. 2020, Bauer et al. 2020). At the same time, as Figure 1 shows, applications for new businesses “with planned wages” dropped significantly in 2020Q1 and 2020Q2 compared to recent years, before significantly rebounding in 2020Q3 and 202Q4 (US Census Bureau 2020). While this amounts to a higher net number of applications in the first four quarters of 2020 compared to the 2016-2019 average, it is not yet clear whether this is due primarily to an administrative backlog created by the pandemic, the entrepreneurial activity of the newly unemployed, or re-adjustments in the market due to increased demand for particular kinds of goods and services (Bauer et al. 2020).

Further understanding the specific effects of the pandemic on entrepreneurial activity is particularly important because new business creation is the primary engine for diversity, economic growth, and innovation in the economy as a whole (Frenken et al. 2007, Neumark et al. 2006, Wennekers, Thurik 1999), and declines in startup activity can have substantial negative long-term economic consequences (Sedláček 2020, Guorio et al. 2016). There is also significant spatial heterogeneity in startup activity that plays an important role in cluster formation, regional economic development, and even the development trajectory of individual neighbourhoods within regions (Mack, Credit 2016, Malmberg, Maskell 2002, Florida 2002, Klepper 2009a,b, Porter 2000, Rutten, Boekema 2007). Understanding the fine-grained spatial and industrial effects of the pandemic on new businesses in more detail can help researchers and local governments to understand how to develop more economically resilient regions, which can provide insulation from future economic shocks.

Data on new business applications are available on a weekly basis at the state level from the US Census Bureau’s Business Formation Statistics (2020). However, other datasets used to evaluate new business activity at finer spatial scales are not updated quickly enough to allow researchers to examine the fine-grained spatial and industrial/sectoral effects of the pandemic on new business activity. These include public datasets like the ZIP Code Business Patterns, as well as private datasets such as InfoUSA or the National Establishment Time Series (NETS).

To overcome this problem, this paper utilizes a novel large dataset of business establishments (at the point level) derived from the open source Chicago Business License dataset, which is updated weekly and contains a comprehensive set of information on all new business license applications in the City of Chicago (2020) to assess two primary questions: first, to what extent has there been a decline in new business establishment[1] starts during the pandemic (March to September, 2020) when compared to recent pre-pandemic trends (averages from 2016 to 2019)? Specifically, we are interested in whether there are distinct temporal trends by business sector or type (e.g., retail, food service, personal care and fitness, etc.) or between multi-establishment (or "chain") (≥ 4 establishment) businesses and "independent" (< 4 establishment) businesses.

Second, given the temporal analysis, what is the spatial expression of these trends? Are there particular areas of the city that are more resilient to declines in new business startups, and, if so, what are the characteristics of these areas? To analyse this formally, we aggregate changes in pandemic-related (i.e., March to September 2020) business activity to the ZIP code level in order to explore the relationship between pandemic-related decline and characteristics of social vulnerability, the built environment, demographics, and cumulative COVID-19 activity.

The results of the analysis indicate that 1) on average, from March to September 2020 (through which complete data was available at the time of writing), total monthly new business starts have declined by 33.4% compared to the monthly average of new starts in the City from January 2016 to December 2019. 2) In general, food service and retail businesses have been hardest hit during this period (although all categories have experienced declines), while chains of all types have seen larger average declines in new startup activity (an average monthly drop of 61.9% from March to September compared to pre-pandemic averages) than independent businesses (a 29.2% drop). 3) These patterns demonstrate interesting intra-urban spatial heterogeneity; overall, a regression analysis suggests that the ZIP codes with the smallest pandemic-related declines in new business activity (i.e., those most resilient to the effects of the pandemic) tend to have more dense, diverse, and walkable built environments (defined in more detail below), lower levels of social vulnerability, lower percentages of young (age 18-39) residents, and higher percentages of Black and Asian (non-Hispanic) residents. Interestingly, observed COVID-19 case rates appear to have a positive relationship with new business resilience (after controlling for a variety of covariates), particularly for new chain and food service establishments. This could be a case of reverse causality, where areas with relatively high levels of new food service business activity also have relatively higher proportions of food service employees, who are more at risk for contracting COVID-19 as "essential" workers.

2 Theoretical Framework

2.1 Economic Benefits of New Business Creation

New business creation provides a number of benefits to both local and macro-level economies that make it particularly important in the contemporary era of "flexible specialization" (Harvey 1989, Piore, Sabel 1984). The theoretical pathways from new business creation to economic benefits are diagrammed in Figure 2. Most directly, new (generally small) businesses create jobs that contribute to local economic growth (Birch 1987, Kirchhoff, Phillips 1988, Neumark et al. 2006). While on net these jobs may not always exceed the number of jobs lost from the older businesses they replace (Mack, Credit 2017), this process of business "churn" increases the probability of creating high-growth firms (so-called "gazelles") that tend to produce the majority of new jobs (Henrekson, Johansson 2010, Nightingale, Coad 2014) and also provides for the "creative destruction" that fosters evolution and innovation in the economy[2] by replacing jobs and businesses in

[1] In this case, a new establishment is considered to be a new unique physical location of a given business; this is determined by coordinating the address and business name information for individual business licenses in the Chicago Business License dataset.

[2] In addition to generating 1) productivity gains, 2) new knowledge that fosters new business creation, and 3) specialized clusters and entrepreneurial ecosystems, sustained innovation over time leads to technological change. This is particularly important for economic growth at two scales: locally, individual

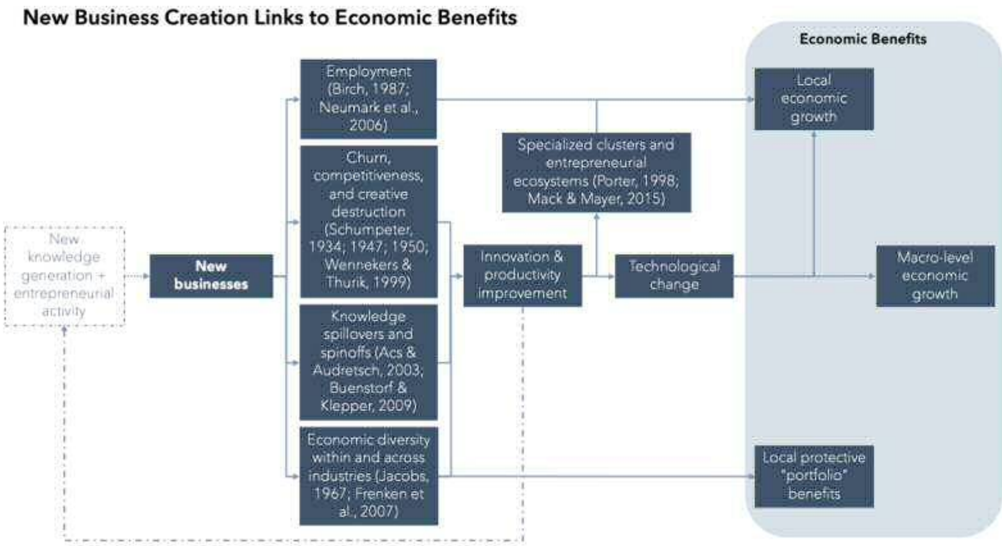


Figure 2: Diagram showing the theoretical connections between new business creation and economic benefits at both the local and macro levels

older declining industries with new jobs in more innovative industries (Schumpeter 1934, 1947, 1950, Brown et al. 2006, Fogel et al. 2008).

Another way that entrepreneurship fosters innovation and productivity improvement is through the creation of a more competitive economic environment that produces a selection process through which only the most viable and/or innovative businesses survive (Wennekers, Thurik 1999, Carree, Thurik 2003). Interestingly, this more competitive environment can drive a positive feedback loop through which increased competitiveness drives demand for better products, which creates incentives for additional innovation and new business creation (Teece 2007, Asheim 1996, Florida 1995, Porter 2000, Rutten, Boekema 2007, Malmberg, Maskell 2002). Fully fledged clusters, such as Silicon Valley, can develop a unique entrepreneurial culture of "competition and community" (Saxenian 1994) and attract additional educational, political, and financial investments that foster a holistic "entrepreneurial ecosystem" (Mack, Mayer 2015, Stam 2015) that captures the indigenous benefits of innovation, leading to economic success for individual businesses and associated local economic benefits, as well as providing a more supportive environment for further new business creation (Delgado et al. 2010). New businesses also contribute to innovation because they are often created as a direct result of knowledge spillovers, i.e., a new business is formed specifically to take advantage of some newly generated knowledge or idea (Acs, Audretsch 2003, Acs et al. 2009). These are often in the form of spinoffs from large existing companies, which some argue constitute the bulk of cluster forming activity (Buenstorf, Klepper 2009, Klepper, Sleeper 2005, Klepper 2009a,b).

Finally, new businesses directly contribute to economic diversity. Increased diversity within related industries (i.e., "related variety") provides another engine for innovation as the pool of new ideas and possible interactions and exchanges increases with the diversity of firms (Jacobs 1967, Boschma, Lambooy 1999, Boschma, Frenken 2006, Saviotti, Pyka

high technology businesses are often significant contributors to economic growth because they drive competitiveness and attract highly skilled and highly compensated workers (Malecki 1984, 1991, DeVol, Wong 1999, Chapple et al. 2004), and there are substantial local productivity benefits for regions that develop transformative technologies rather than lagging behind technological change and being forced to adapt to new structures and activities (Boschma, Lambooy 1999, Boschma, Frenken 2006, Jacobs 1967, Saviotti, Pyka 2004, Frenken et al. 2007). But perhaps more importantly, at the macro-economic level new technology restructures the basic functions, markets, products, and demands of the economy as a whole (Schumpeter 1934, 1947, 1950, Breschi et al. 2000, Wennekers, Thurik 1999), which (if these gains are distributed throughout the economy) has the potential to significantly improve overall human development outcomes and standards of living.

2004, Frenken et al. 2007). On the other hand, diversity through "unrelated variety" provides important portfolio benefits to local economies by distributing economic risk across a variety of different industries, making the economic system more resilient to unexpected shocks that may occur, no matter what sector they are concentrated in (Montgomery 1994, Frenken et al. 2007).

In this paper, we are particularly interested in new business creation for small, independently owned businesses in customer-facing sectors such as retail and food service, for several reasons. These businesses are significant contributors to land use diversity, street life, and overall urban vitality (Jacobs 1961, Gehl 2010). At the same time, small retail shops help to contribute to a unique "sense of place" in a given locality that is the direct product of local creative efforts and sensibilities (Jacobs 1961, Relph 1976, Robertson 1999, Kunstler 1994, Walljasper 2007, Alexander 1977, Montgomery 1998). The owners of these kinds of businesses themselves are also often more connected to the specific dynamics, demands, and politics of the local community, and tend to contribute to local import substitution (increasing the local multiplier effect) by spending profits to purchase requisite subsidiary goods and services locally, rather than exporting profits to another region, as is the case with larger chain businesses (Jacobs 1967, Talen, Jeong 2019a,b).

2.2 Fostering Economic Resilience

Given this paper's interest in exploring features of economic resilience at the neighbourhood level, it is useful to lay out the theoretical justifications for a number of possible hypotheses about the characteristics that might foster increased protection to the pandemic-related shock on new business activity. First, the literature on disaster resilience has identified a range of basic sociodemographic vulnerabilities to natural and man-made disasters, as codified in measures such as the Centers for Disease Control's (CDC) "Social Vulnerability Index" (SVI) (Flanagan et al. 2011, 2018, Cutter et al. 2003, Bolin 2006, Morrow 1999, Juntunen 2005, Gay et al. 2016, Tate 2012, Rufat et al. 2019, Cimellaro et al. 2016, Kotzee, Reyers 2016, Ramirez, Lee 2020). Importantly, these include not only the standard features of socioeconomic status such as educational attainment and income, but also demographic features such as age, disability status, and race/ethnicity, as well as housing and transportation characteristics[3] (e.g., vehicle access and crowded housing) that make it more difficult to avoid or recover from a disaster. In this case, given previous research on the impact of COVID-19 deaths on new business applications at the state level (Sedláček, Sterk 2020), we are specifically interested in the role of COVID-19 vulnerability on economic resilience, and have included observed COVID-19 case and testing rates by neighbourhood to account for this potential relationship.

In addition to sociodemographic vulnerability, scholars and practitioners in urban planning have long posited that the fundamental form of the built environment plays an important role in economic resilience. A variety of literature argues that walkable, high density, mixed use districts with short blocks and high accessibility to a range of destinations tend to foster urban vitality and economic resilience by providing the physical "habitat" for the economic engine of new business activity described above (Jacobs 1961, 1967, Talen 2006, Desouza, Flanery 2013, Talen, Jeong 2019a,b, Abstante et al. 2020).

Finally, we have included racial and ethnic neighbourhood composition variables in the analysis to account for the beneficial role that "ethnic enclaves" can play in fostering protected markets for particular racial/ethnic demographic groups located in specific neighbourhoods (Cummings 1999, Li 1998, Liu 2009, Waldinger et al. 1990). These enclaves develop initially to serve the segregated residential neighbourhoods of particular immigrant or migrant communities – in the US, often Black, Asian, or Hispanic – and provide a supportive environment for new business creation, acting as incubators in part

[3] In this paper's analysis (as described below), some of the race/ethnicity, age, housing, and transportation characteristics have been broken out of the composite social vulnerability indicator due to specific interest in these individual relationships with new pandemic-related change in new business activity. Additional adjustments were made to the social vulnerability indicators used in this paper due to our focus on economic resilience specifically, rather than a generalized resilience to all kinds of natural and man-made disasters.

because of the pervasive shared knowledge in these areas. In addition to providing all of the benefits of community involvement, profit re-circulation, and local responsiveness provided by small, independently owned businesses in general (described above), as ethnically oriented businesses grow, they are often able to orient themselves outside of the enclave to serve larger (non-ethnic) markets, improving business performance (Waldinger et al. 1990, Li 1998).

3 Data and Methods

3.1 Chicago Business License Data

To use the Chicago Business License dataset to analyse recent spatial and temporal trends in new business activity, the data had to first be prepared and transformed rather extensively to capture the presence of individual business establishments – and estimates of their industrial sector or type – from the license data. In raw form, the dataset contains entries for individual business license filings, organized with each observation or row representing one filing (either for original issuance or renewal) of a single business license with its own license ID. Account numbers identify unique owners/applicants; thus one account number can be associated with multiple individual business establishment locations (i.e., businesses with unique addresses), and each individual establishment can have more than one license associated with it if it fulfils functions that fall under more than one of the city's license types (e.g., a restaurant may have both a "Consumption on Premises" liquor license and a "Retail Food" license)[4]. In addition to the license type, an establishment may also be associated with additional "business activities," of which there can be several or none listed for each license (these are somewhat subjectively chosen by the individual applying for a business license in their online portal). See Figure 3 for a sample of the data structure.

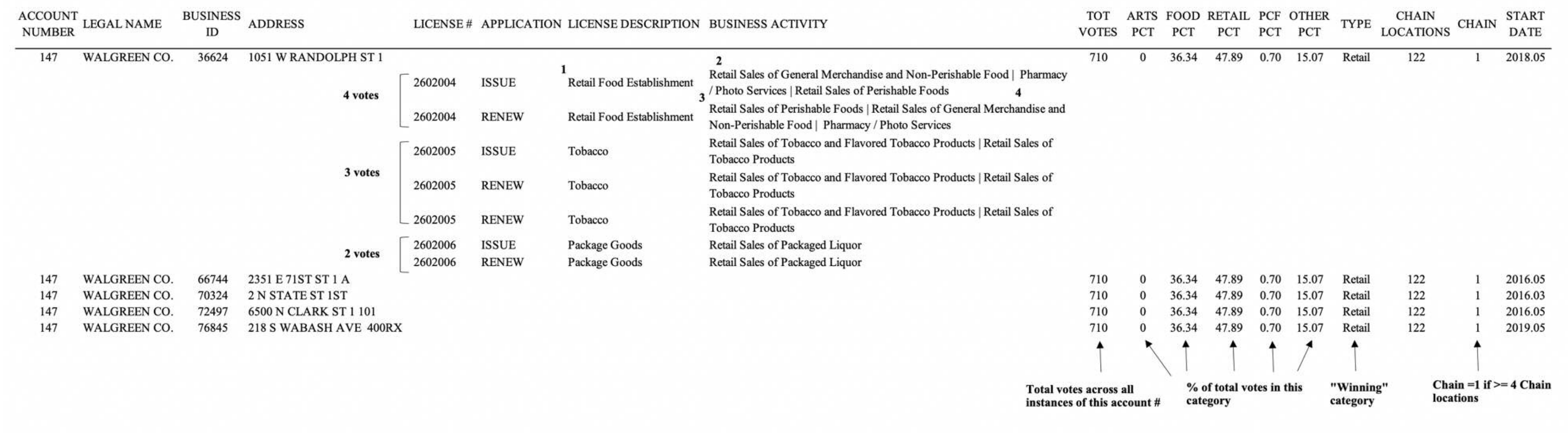
Because the City of Chicago employs a multitude of descriptors for business activity and license description that vary in their specificity and usage, an original categorization scheme was developed for the purposes of this investigation. Each "business activity" or "license description" that exists in the data is sorted into one of five super-categories that focus on distinguishing the effect of the pandemic on neighbourhood-level goods and services: Food, Retail, Personal Care and Fitness, Arts, and Other[5]. A shortened sample of the classification scheme is shown in Table 1; the full version is available by request from the authors. Though many of the labels for each business activity or license description fell intuitively into these categories, some were more ambiguous or commonly caused conflict with other categories[6]. To ensure these categorizations were internally consistent, an analysis was conducted in which business activities were compared against the license descriptions they most often appeared with in the data. Those combinations that shared the same categorization confirmed the validity of the final categorization scheme, and in the few cases where there were discrepancies, classifications of those labels were adjusted to resolve them. Finally, licenses or activity descriptions not relevant to the research objective, such as home occupations, mobile food vendors, vending machines, and parking garages, were removed from the dataset.

To begin assigning the devised categories to individual business establishments, the

[4]For a comprehensive list of all of Chicago's business license types, see: https://www.chicago.gov/-city/en/depts/bacp/sbc/business_licensing.html.

[5]Due to the ambiguous nature of the widely used "Limited Business License" and "Regulated Business License" types and the lack of comprehensive entry for the business activities associated with these license types, a larger "catch-all" category of "Other" was created. While it is possible that finer distinctions could be made between, e.g., manufacturing/production, office/consulting, and accommodation businesses within this category, given the focus of this paper on neighbourhood-level goods and services, these distinctions were not made for the purposes of this analysis.

[6]Food-related services, which are of special interest to a pandemic-related analysis due to the unique set of restrictions placed on these establishments, were not easily sorted. While it was the original intent of the researchers to split restaurants from retail food operations like grocery stores, the "retail food" license does not adequately distinguish between these two types of activities, and no clarification of the meaning of the various "business activity" labels is provided to those who apply for business licenses on the city's website, which likely leads to their inconsistent appearances in the data. Therefore all food-related services are grouped together for the purposes of this analysis.



ACCOUNT NUMBER	LEGAL NAME	BUSINESS ID	ADDRESS		LICENSE #	APPLICATION	LICENSE DESCRIPTION	BUSINESS ACTIVITY	TOT VOTES	ARTS PCT	FOOD PCT	RETAIL PCT	PCF PCT	OTHER PCT	TYPE	CHAIN LOCATIONS	CHAIN	START DATE
147	WALGREEN CO.	36624	1051 W RANDOLPH ST 1						710	0	36.34	47.89	0.70	15.07	Retail	122	1	2018.05
				4 votes	2602004	ISSUE	Retail Food Establishment	Retail Sales of General Merchandise and Non-Perishable Food | Pharmacy / Photo Services | Retail Sales of Perishable Foods										
					2602004	RENEW	Retail Food Establishment	Retail Sales of Perishable Foods | Retail Sales of General Merchandise and Non-Perishable Food | Pharmacy / Photo Services										
				3 votes	2602005	ISSUE	Tobacco	Retail Sales of Tobacco and Flavored Tobacco Products | Retail Sales of Tobacco Products										
					2602005	RENEW	Tobacco	Retail Sales of Tobacco and Flavored Tobacco Products | Retail Sales of Tobacco Products										
					2602005	RENEW	Tobacco	Retail Sales of Tobacco and Flavored Tobacco Products | Retail Sales of Tobacco Products										
				2 votes	2602006	ISSUE	Package Goods	Retail Sales of Packaged Liquor										
					2602006	RENEW	Package Goods	Retail Sales of Packaged Liquor										
147	WALGREEN CO.	66744	2351 E 71ST ST 1 A						710	0	36.34	47.89	0.70	15.07	Retail	122	1	2016.05
147	WALGREEN CO.	70324	2 N STATE ST 1ST						710	0	36.34	47.89	0.70	15.07	Retail	122	1	2016.03
147	WALGREEN CO.	72497	6500 N CLARK ST 1 101						710	0	36.34	47.89	0.70	15.07	Retail	122	1	2016.05
147	WALGREEN CO.	76845	218 S WABASH AVE 400RX						710	0	36.34	47.89	0.70	15.07	Retail	122	1	2019.05

Figure 3: Data sample showing how licenses aggregate to business establishments, and categories are assigned by voting across all rows of a given account number

Table 1: Sample of classification scheme for assigning license types and business activities to business super-categories

Category: *Retail*

License Type

Electronic Equipment Repair; Package Goods; Pawnbroker; Public Place of Amusement-TCC; Retail Computing Center; Secondhand Dealer; Secondhand Dealer - Children's Products; Secondhand Dealer (No Valuable Objects); Sports Facilities Authority License

Business Activity

Retail Sales of Animal Treats and Animal Food; Retail Sales of Carpet and/or Furniture; Retail Sales of New Electronics and Accessories; Retail Sales of Outdoor Equipment and Supplies; Retail Sales of Used Electronics; Sale of Furniture; Retail Sales of General Merchandise; Retail Sales of Clothing / Accessories / Shoes; Retail Sales of Jewelry and Jewelry Repair; Retail Sales of Appliances; Buying and Reselling of Used Cell Phones; Retail Sale of Musical Instruments; Retail Sale of Tobacco; Retail Sales of Laundry Cleaning Products; Retail Sales of Tobacco Products; Retail Sales of Tobacco Accessories; Retail Sales of Tobacco and Flavored Tobacco Products; Retail Sales of Packaged Liquor; Retail Sales of Flowers; Pharmacy / Photo Services; Shipping / Printing Services; Sales / Rental / Lease of Motorized Vehicles

Category: *Food*

License Type

Caterer's Liquor License; Caterer's Registration (Liquor); Consumption on Premises - Incidental Activity; Outdoor Patio; Produce Merchant; Retail Food Establishment; Special Event Food; Special Event Liquor; Tavern; Wholesale Food Establishment

Business Activity

Wholesale Food Sales; Retail Sale of Food for Offsite Consumption; Retail Sales of Fresh Fruits and Vegetables; Retail Sales of Perishable Foods; Retail and Wholesale of Perishable Foods; Retail Sales of General Merchandise and Non-Perishable Food; Deli, Butcher or Bakery; Sale of Food Prepared Onsite With Dining Area; Preparation and Sale of Coffee and/or Drinks; Consumption of Liquor on Premises; Preparation of Food and Dining on Premise With Seating

Category: *Other*

License Type

Affiliation; Animal Care Facility; Animal Care License; Animal Exhibition; Assisted Living/Shared Housing Establishment; Automatic Amusement Device Operator; Bed-And-Breakfast Establishment; Bicycle Messenger Service; Board-Up Work; Children's Services Facility License; Commercial Passenger Vessel; Explosives; Filling Station; Grooming Facility; Guard Dog Service; Hazardous Materials; Home Repair; Hospital; Hotel; Laboratories; Late Hour; Laundry, Late Hour; License Manager; Long-Term Care Facility; Manufacturing Establishments; Motor Vehicle Repair: Engine Only (Class II); Motor Vehicle Repair: Specialty(Class I); Motor Vehicle Repair: Engine/Body(Class III); Motor Vehicle Services License; Night Care Privilege; Pet Shop; Public Place of Amusement; Veterinary Hospital

Business Activity

Administrative Commercial Office; Commercial Landscaping Services; Commissioned Staffing of Professional, Secretarial and Clerical Work; Advertising / Marketing / Sales Office; Computer Design/Development Consulting; Cable or Satellite Installation - Commercial Properties; Computer and Electronic Products Manufacturing; Drug, Chemical, Paint Factory; Food Manufacturing; Machinery Manufacturing; Plastics, Foams, Construction Materials, Glass, Rubber; Printing Activities, Metal Processing; Production; Textile Mills, Leather, Paper Products, Rubber, Petroleum, Coal; Toy, Furniture, Household Goods Factory; Miscellaneous Manufacturing; Machine Shop, Foundry, Roof / Paving Materials; Business and Management Consulting; Business Consulting; Financial and Accounting Services; Hotel - 7 or More Sleeping Rooms; Provides Onsite Amusement or Entertainment; Provides Onsite Entertainment or Rentals; Self Storage Facility; Smoking of Tobacco on Premises; Clothing Alterations; Dry Cleaning - Drop Off Location; Laundromat - Self Service; Laundry Service; Commercial Construction; Demolition / Wrecking; Home Repair Services; Residential Construction number of rows associated with each license number is reduced to one, to eliminate the effect of differential renewal frequencies for different types of licenses. Then, after removing those rows with duplicate information, the amount of activity information (either business activities or license types) falling into each of the five categories is counted and aggregated to each account number ("TOT VOTES"). This enables a calculation of the proportion of associated rows that falls into each of the five categories and ensures that different business establishments with the same account number (i.e., chain locations) retain the same classification as other chain locations. The "winning" category is determined by the category (across account numbers) that demonstrates the highest percentage; if tied, a random selection among tied categories is made. The start date is determined by the earliest license term start date associated with a given business ID.

Finally, a "chain" label is assigned to any business whose account number is associated with four or more unique locations in the data. Though four locations is not a rigid cut-off at which all businesses should be considered chains[7], the limit is not arbitrary, but rather a balance between conceptual matching (i.e., a large enough number of establishments per account to constitute a truly non-independent business) and sample size (i.e., a small enough number of establishments per account to produce a useful sample size for regression analysis). As Figure A.1 in the Appendix shows, the density of account numbers with different numbers of associated establishments decreases systematically as the number of establishments increases. While the largest difference is between accounts with 1 and 2 associated establishments (a drop of 85.8%), and the second largest difference is between accounts with 2 and 3 associated establishments (a drop of 76.3%), we feel that accounts with these numbers of establishments are fundamentally too small to embody the concept of non-independent chains. At the same time, using 5 or more as the cut-off reduces the sample size of chain establishments significantly. Fortunately, sensitivity analyses of the regression results (shown in Tables A.2, A.3, and A.4 in the Appendix) do not show large differences in the results when using alternate numbers of establishments to define chains. Additionally, studying random samples of business names at or above the 4 establishment cut-off suggests that the majority could plausibly be considered chain businesses. The end result of this categorization scheme is shown in Figure 3.

3.2 Exploratory Covariates

In addition to the individual business points by category and start date, this paper also utilizes data from the American Community Survey (ACS) to explore the neighbourhood characteristics that are associated with resilience to the pandemic-related shock to new business activity. Two indices are created to capture effects related to the built environment and social vulnerability. The built environment index ($JACOBS$) is based primarily on Jacobs' (1961) principles of vibrant, diverse neighborhoods, which have been generalized and expanded on over time to include various "D" variables: density, diversity, design, and distance to transit (Cervero, Kockelman 1997, Ewing, Cervero 2010). To compute the JACOBS index for this paper, data from the 2014-2018 ACS on the average Census block perimeter, housing unit density, building age diversity[8], and

[7] "Chainness" as a concept for customer-facing businesses exists across multiple dimensions, including national orientation/distribution, corporate ownership, standardized design/place qualities, and the existence of multiple establishments under one unified brand. Of course, these features are not so straightforward to categorize – for example, despite having unified branding, McDonald's restaurants operate through a franchise system, so individual McDonald's establishments are independently owned (although some franchisees own multiple, regional groupings of McDonald's, which complicates the matter even further, creating a kind of "chain-within-a-chain"). But by the conceptual definition we are interested in here vis-a-vis small, independently owned businesses, McDonald's restaurants should certainly constitute a "chain." Unfortunately, in large open source datasets such as the one that we employ in this analysis, information on most of the complicated dimensions of chainness is limited. Generally the only available information is the number of occurrences/establishments under one account name or number, which can be counted, as is the case in this paper. Thus we follow an empirical approach in operationalizing the "chain" concept by selecting a cut-off of establishments under one corporate account based on the distribution of the data – in this case, 4 was chosen; similar analyses have used other cut-offs based on their specific research questions, e.g., a recent analysis of chain restaurants in the US used 5 establishments as the cut-off for classification as a "chain" (Liang, Andris 2021).

[8] Computed by calculating a Herfindahl Index using the share of units built in the following decade ranges: 2010-current, 2000-2010, 1990-2000, 1980-1990, 1970-1980, 1960-1970, 1950-1960, 1940-1950, and

percent of workers 25 and older commuting to work by public transit at the ZIP Code Tabulation Area (ZCTA) are used. To create the index, we add (+) together the z-scored variables that positively contribute to built environment diversity, i.e., density and transit commuting, and subtract (-) the variables that negatively contribute to built environment diversity, i.e., block length (because shorter blocks are seen as encouraging more activity) and building age diversity (because the Herfindahl Index used to create the building age diversity measures ranges from 0 to 1, with larger values indicating lower diversity).

An index of social vulnerability (*SOLCVULN*), based generally on the CDC's SVI index, is calculated in a similar way using z-scores for a range of 2014-2018 ACS variables that capture increased vulnerability to environmental and economic shocks (Flanagan et al. 2018): median household income (-), percent population that are not citizens (+), percent families with public assistance income (+), percent population 25 years and older with a Bachelor's degree or higher (-), percent of the civilian noninstitutionalized population without health insurance coverage (+), and percent of the population 65 years or older (+).

Beyond the *JACOBS* and *SOLCVULN* indices, 2014-2018 ACS data on the percent of Black non-Hispanic population (*BLACKPER*), Hispanic population (*HISPER*), and Asian non-Hispanic population (*ASNPER*) – as an operationalization of the presence of ethnic enclaves – and the percent of the population aged 18-39 (P1339) – as an indicator of neighbourhood "hipness" and pre-pandemic demand for customer-facing businesses such as bars and restaurants – by ZCTA are also collected for use in the regression models. In addition, the cumulative number of confirmed COVID-19 cases and tests[9] by ZIP code as of November 10, 2020, are obtained from the website of the Illinois Department of Public Health (IDPH 2020) and divided by ZCTA population to create a COVID-19 case rate (*COVIDR*) and test rate (*TESTR*).

3.3 Analysis Methods

To visually assess temporal trends during the pandemic timeframe for the entire city, the number of monthly new starts by category from January 2016 to September 2020 is plotted on a line graph; graphs of the % difference in new starts (by category) for each month in 2020 compared to the monthly average from January 2016 to December 2019 for both chains and independent businesses are also created.

For visual analysis of spatial trends, Kernel Density Estimate (KDE) maps for all new business starts for each business type for the period March to September for each year from 2016 to 2020 are created using the same set of specifications in the "kernelUD" function in R[10] (Yin 2020). Then, using the raster calculator, a KDE showing the average density of new starts from 2016 to 2019 (*KDEAVE*) is calculated for each business type (t), as shown in Equation (1):

$$KDEAVE_t = \frac{KDE2016_t + KDE2017_t + KDE2018_t + KDE2019_t}{4} \tag{1}$$

This provides a 4-year average of the fine-grained spatial pattern of new starts for each business type and allows us to subtract these values from the 2020 KDE to find the pandemic-related difference in new starts ($KDEDIF_t$) in order to observe the areas in which the density of 2020 pandemic-era (March to September) new starts significantly under- or over-perform the previous 4-year average, according to Equation (2):

$$KDEDIF_t = KDE2020_t - KDEAVE_t \tag{2}$$

While the use of KDE allows for a finer-grained examination of the spatial pattern of the individual business points that is not obscured by the specific boundaries of the

pre-1940.

[9] To control for the fact that there were structural heterogeneities in testing rates by racial/ethnic neighbourhood type in the city (in particular, lower testing in Hispanic neighbourhoods), testing rate is included as a variable in the analysis (Credit 2021).

[10] The kernel function ("bivnorm"), bandwidth (h = .005), and cell size (grid = 5000) are maintained for each SpatialPointsDataFrame (sp) for a given business type/year. No projection is used – spatial points are instantiated directly from latitude and longitude coordinates provided in the Chicago Business License dataset.

ZIP codes (or other areal zones), aggregating the individual counts of new starts in each period to ZIP code boundaries allows us to bring additional sociodemographic and built environment covariates into the analysis. To control for the size of the average baseline new business activity in a given ZIP code from 2016 - 2019 (March to September), we calculate the percent difference ($PERDIF_t$) in the number of new business starts (N) by type (t) between 2020 and the 2016-2019 average ($N_{(2016-2019)}$) for each ZIP code, as shown in Equation (3):

$$PERDIF_t = \frac{N_{2020} - N_{2016-2019}}{N_{2016-2019}} \tag{3}$$

Finally, a set of regression models are estimated at the ZIP code level according to the specification shown in Equation (4):

$$\begin{aligned} PERDIF_t \quad = \quad & \beta_1 JACOBS + \beta_2 SOLCVULN + \beta_3 P1839 + \beta_4 COVIDR + \beta_5 TESTR + \\ & \beta_6 HISPER + \beta_7 ASNPER + \beta_8 BLACKPER + \epsilon \end{aligned} \tag{4}$$

The covariates (described in the section above) are included to explore the features of neighbourhoods that are associated with pandemic-related declines in new business activity. All models are estimated using Ordinary Least Squares (OLS) in R v.4.0.4. Robust Lagrange multiplier (LM) tests for spatial dependence were conducted for the pooled model; while the Robust LM Lag test was significant for the pooled model at $p < .05$, this was matched only in the Independent and Other subset models, so to maintain consistency, standard OLS model specifications were used throughout[11]. The studentized Breusch-Pagan test of heteroskedasticity and the adjusted Jarque-Bara test for normality were also applied to the pooled model, but were both non-significant at $p < .05$, so the unadjusted standard error estimates were also used throughout.

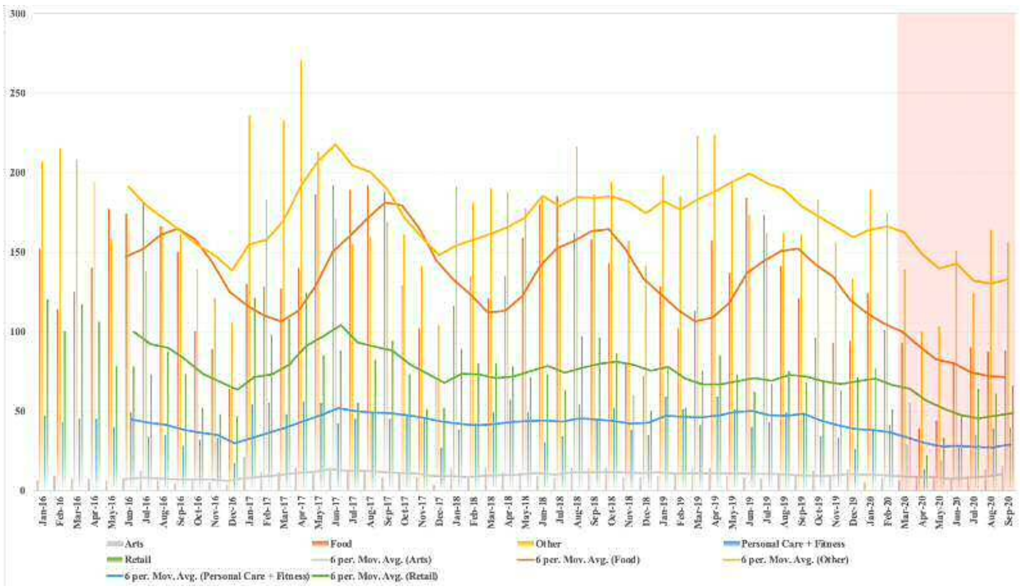
4 Results and Discussion

Figure 4 shows the monthly trend in new starts by business type from January 2016 to September 2020. The lines on the bar graph display a 6-month rolling average to smooth the month-to-month (and seasonal) oscillations, and the pandemic era is marked in red. This graph shows the relative size of each category (with Other, Food, and Retail as the largest categories in terms of number of new starts), as well as the fact that each of the five categories has clearly declined in the pandemic era compared to its recent trend (with the exception of Arts, whose trend is generally very flat).

To see these trends in more detail, and to compare chains and independent businesses, Figures 5 and 6 show the percent difference in new starts between each month in 2020 and the average number of monthly new starts for each category from January 2016 to December 2019 for independent and chain establishments, respectively. This clarifies the general patterns observed in Figure 4: all categories decline significantly in April and May, with some recovery towards recent averages in July, although all categories for both chains and independents demonstrated declines relative to recent averages in nearly every month since the pandemic began. However, it does appear that new business starts in particular industries, such as chain Retail and Personal Care and Fitness, as well as independent Arts, have come close to matching or exceeding pre-pandemic levels by September. This finding is supported by the national data showing a significant rebound in new businesses "with planned wages" in 2020Q3 and Q4 shown in Figure 1 and perhaps reflects business planning in anticipation of an easing of lockdown restrictions sometime in 2021.

Overall, chain new starts declined on average 61.9% per month from March to September 2020 (compared to 2016-2019 averages), while independents declined only 29.2%. In some ways this may reflect the difference in the average number of new starts in each category. From January 2016 to December 2019, the city averaged around 58 new

[11] As shown in Table A.5 in the Appendix, coefficient signs and significances were robust to the choice of spatial or non-spatial specification in each case, so the use of a non-spatial specification is empirically justified.



Notes: Red shading denotes pandemic time period

Figure 4: Monthly new starts by business type from January 2016 – September 2020

chain and 387 new independent establishments per month; from March to September 2020, the city averaged only 22 new chain and 274 new independent establishments per month, so a relatively smaller drop in the number of chains generates a much sharper drop in terms of percentage due to the smaller denominator. The issue of small denominators may also help to explain the fact that some of the smaller categories, e.g., chain Personal Care and Fitness and independent Arts, show relatively “spiky” temporal patterns.

However, Figure 7 shows that these aggregate declines are not homogenous across space. For independent establishments, the biggest declines are in gentrifying north- and northwest-side neighbourhoods like Albany Park, Bucktown, Roscoe Village, Lakeview, and the West Loop – high growth areas with active commercial districts. The biggest increases are in River North and Lincoln Park, long-gentrified neighbourhood centres that attract a large amount of export retail, dining, and entertainment activity. Interestingly, the spatial pattern for chain establishments is somewhat different. Roscoe Village, Albany Park, and Lakeview all show up as hotspots of pandemic-related decline for chains, along with the rapidly growing, younger-population neighbourhoods of Pilsen and South Loop. On the other hand, Bucktown, Hyde Park, and the West Loop join River North and Lincoln Park as neighbourhoods with relatively high levels of pandemic-era chain business activity.

When new business points are aggregated to ZIP codes and the percent change between pandemic and pre-pandemic trends ($PERDIF_t$) are calculated, we can see (in Figure 8) that these patterns intersect in interesting ways with the spatial patterns of the paper's primary covariates of interest. The aggregate pattern of new business change shows significant declines across the majority of the city, with pockets of resilience in the near north (Lakeview/Lincoln Park) and south sides, including the Hyde Park, Beverly/Mount Greenwood, and South Shore neighbourhoods[12]. There is some overlap here with the spatial pattern of the city's Black population, which is primarily focused on the south and southwest sides of the city. However, there is less visible overlap with the city's Hispanic population, which tends to be concentrated in the west and northwest sides, or Asian population, which is most concentrated in the near south side, around the Chinatown neighbourhood. On the other hand, there appears to be some spatial association between

[12]It is worth noting that the two positive outliers on the map – Hyde Park and Beverly/Mount Greenwood – have very small denominators for the percent change calculation (average new business counts of 3.12 and 1.42, respectively, per year between March-September 2016-2019), so it only takes a small increase in 2020 to create a positive percent change.

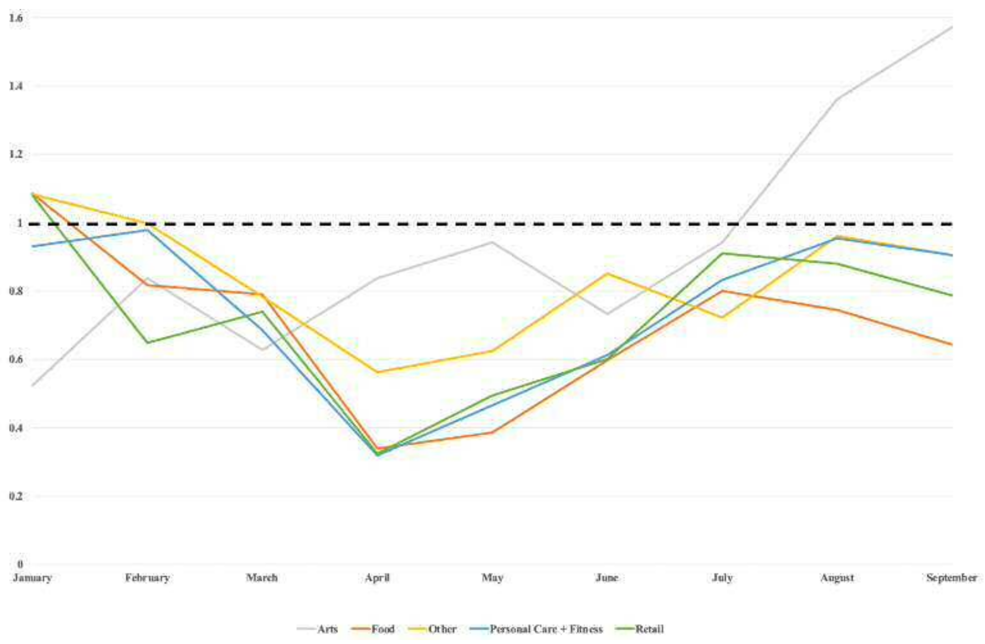


Figure 5: Percent difference in new starts between each month in 2020 and the average number of monthly new starts from January 2016 - December 2019 for independent establishments

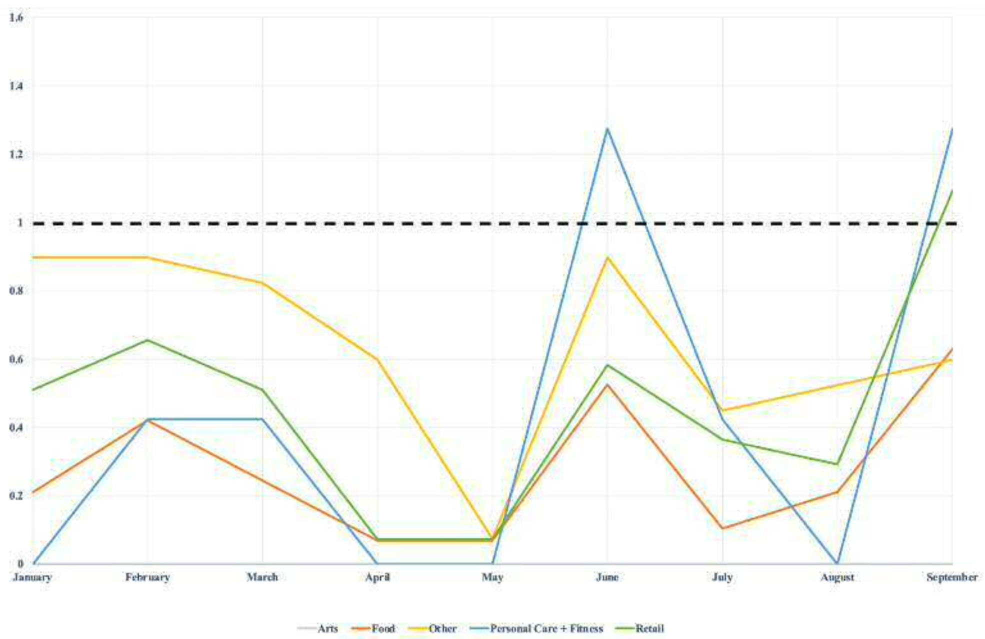


Figure 6: Percent difference in new starts between each month in 2020 and the average number of monthly new starts from January 2016 - December 2019 for chain establishments

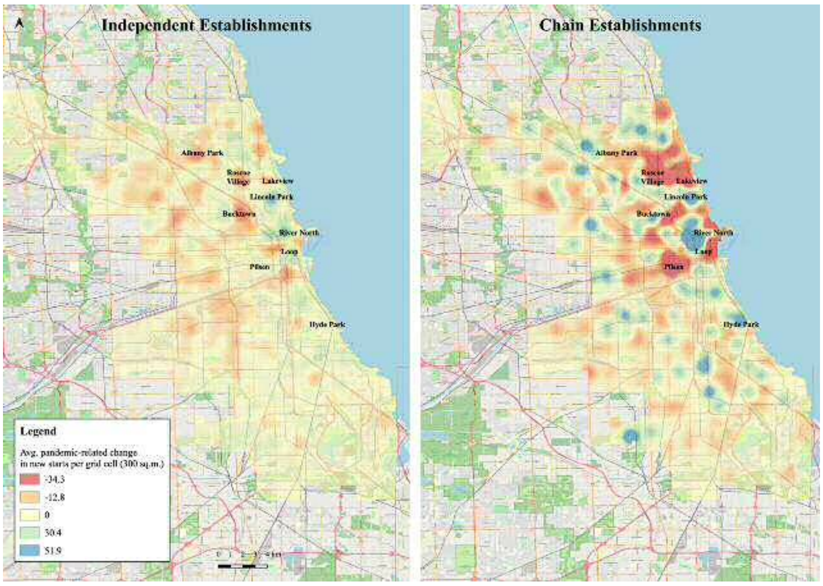


Figure 7: Difference in new start density between 2020 (March - Sept.) and average new start density from 2016 - 2019 (March - Sept.) for independent and chain establishments

ZIP codes with relatively high levels of resilience and high JACOBS index values, which are most concentrated on the historic, high density north and northwest sides. Interestingly, the patterns of the *SOLCVULN* index and COVID-19 case rates reflect a nearly inverse image, demonstrating significant overlaps with the pattern of Hispanic population[13] (in particular) (Credit 2021). Finally, we see the highest concentration of young population in the rapidly gentrifying, "hip" West Loop, Lincoln Park, and Bucktown neighbourhoods, many of which have been particularly hard hit by the pandemic-related decline in new business activity.

In order to statistically characterize these spatial patterns in pandemic-related resilience in new business starts, a number of regression models (one for each business type) at the ZIP code level are run to associate these changes with various measures of the built environment, social vulnerability, age, and the existing baseline new start activity (2016-2019 average). Results of the regression analysis are shown in Table 2[14]. Several interesting findings stand out. First, in the pooled model for all businesses, the JACOBS built environment index is significantly positively related to pandemic-related change in new business density, while the social vulnerability index, *SOLCVULN*, is significantly negatively related to the dependent variable. This suggests that the *JACOBS* factors are associated with some resiliency to the economic effects of the pandemic, even after controlling for the other covariates of interest. The percent of population aged 18-39 is also negatively related to resilience in new business activity, which suggests that some of the economically hardest-hit neighbourhoods are those that had a high level of pre-pandemic investment, particularly in the Retail and Personal Care and Fitness categories. We also see some evidence of enclave effects in Black and Asian neighbourhoods, which both display significant positive relationships with the dependent variable. Finally, we see a surprising significant positive relationship between pandemic-related change in new business starts and observed COVID-19 rates (after controlling for the full suite of other covariates). There are a couple of possible explanations for this result: 1) reverse causality (assessed in Table A.1 in the Appendix) in that neighbourhoods with high levels of new business resilience (particularly in the Food category, which, based on the individual

[13]The significant spatial overlaps between Hispanic population, COVID-19 rates, social vulnerability index values, and some of the constituent factors in the *JACOBS* index may provide another explanation for the somewhat surprising positive significance of the *COVIDR* variable in the final regression model.

[14]Table A.1 in the Appendix presents the regression results without the COVID-19 case and testing rate variables, and shows the robustness of the primary findings of the analysis.

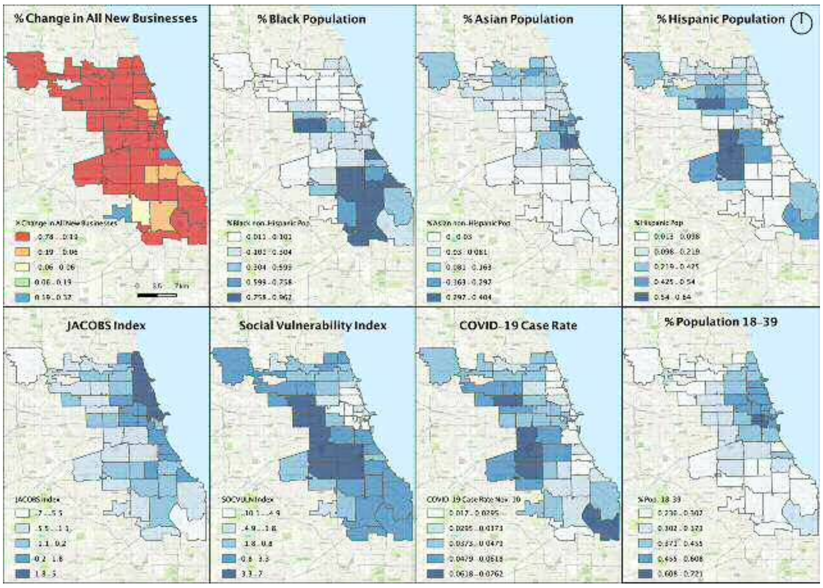


Figure 8: Panel map showing spatial distribution of the primary dependent variable and covariates used in the regression analysis

regression results, appears to be driving the relationship) also have high proportions of essential workers who are more at risk for contracting COVID-19; 2) collinearity and spatial overlap in the pattern of Hispanic population, $SOLCVULN$, and COVID-19 rates (e.g., the raw relationship between $PERDIF_t$ and $COVIDR$ is negative). However, the inclusion of each of these covariates is central to this paper's exploratory research objective and cannot be omitted without changing the nature of the results and risking omitted variable bias. We are interested in the partial effect of each variable on the dependent variable while controlling for the presence of the other covariates, so it is essential to control for baseline social vulnerability before assessing the relationship between the other factors and economic resilience.

These relationships generally also hold for the individual regressions of various subsets of the business data, with some interesting differences. Asian enclave effects are particularly pronounced for chain, Other, and Personal Care and Fitness businesses, while Black enclave effects are significant for independent and Other businesses. Food businesses demonstrate negative enclave effects for the Hispanic and Asian groups, which perhaps is a result of the fact that pre-pandemic activity in these neighbourhoods was particularly strong. Given the fact that our measure of resilience is a percent change from average pre-pandemic new start activity, this penalizes neighbourhoods with particularly strong pre-pandemic levels of activity as much as it rewards neighbourhoods with particularly strong pandemic-related levels of new start activity.

5 Conclusion

Given the widespread national and international economic impacts of the COVID-19 pandemic, the purpose of this paper is to assess the fine-grained spatial and temporal impacts of the pandemic on new business starts. This is accomplished using a novel dataset on all business establishments in the city compiled from the frequently updated City of Chicago Business License dataset. The results of the temporal analysis for the City of Chicago through the end of September 2020 closely mirror the national data on small business revenue, with significant declines in April that have somewhat (although not fully) recovered through September, with food service and retail businesses hardest hit. In April, the total number of food service and retail new starts had dropped 71.6% and 72% compared to the 2016-2019 monthly average, respectively; in September, they were still 35.9% and 16% below monthly averages, respectively. While the national data

Table 2: OLS regression results for dependent variable $PERDIF_t$ – Percent Change in New Establishments: 2020 (March to September) vs. Average 2016-2019 (March to September) by ZIP Code

	All (Pooled)	All Chains	All Independents	Other	Food	Retail	Personal Care and Fitness	Arts
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
JACOBS	0.040***	0.056**	0.034**	0.081***	0.013	0.061	0.046	-0.132
	(0.014)	(0.027)	(0.015)	(0.030)	(0.021)	(0.038)	(0.041)	(0.196)
SOLCVULN	-0.057***	-0.019	-0.064***	-0.107***	0.030	-0.102**	-0.052	0.178
	(0.017)	(0.031)	(0.018)	(0.034)	(0.024)	(0.044)	(0.041)	(0.206)
%Aged 18-39	-1.727***	-1.550*	-1.657***	-2.926***	0.183	-3.248**	-1.585	4.550
	(0.462)	(0.878)	(0.494)	(0.955)	(0.680)	(1.225)	(1.124)	(5.388)
COVID-19 Case Rate	5.137	11.228*	3.193	6.826	10.125**	4.136	-2.235	-5.751
(Nov. 10)	(3.092)	(5.881)	(3.306)	(6.397)	(4.554)	(8.208)	(7.493)	(32.373)
COVID-19 Testing Rate	0.238	-0.208	0.298	0.434	-0.017	-0.896*	0.406	2.110
(Nov. 10)	(0.186)	(0.354)	(0.199)	(0.385)	(0.274)	(0.494)	(0.438)	(1.967)
% Hispanic Population	0.132	-0.394	0.236	0.601	-1.184**	-0.190	0.781	-1.126
	(0.303)	(0.577)	(0.324)	(0.628)	(0.447)	(0.805)	(0.716)	(3.734)
% Black Population	0.429***	0.261	0.476***	0.886***	-0.302	0.036	0.130	0.284
	(0.149)	(0.284)	(0.160)	(0.309)	(0.220)	(0.396)	(0.369)	(1.911)
% Asian Population	0.741*	2.297***	0.539	1.633*	-1.053*	0.752	0.969	-4.622
	(0.415)	(0.790)	(0.444)	(0.859)	(0.611)	(1.102)	(0.993)	(4.857)
Constant	-0.257	-0.544*	-0.209	-0.181	-0.552**	1.317***	-0.208	-2.174
	(0.168)	(0.319)	(0.179)	(0.347)	(0.247)	(0.446)	(0.395)	(1.741)
Observations	59	59	59	59	59	59	57	53
R^2	0.452	0.288	0.459	0.355	0.229	0.32	0.113	0.134
F Statistic	5.161***	2.530**	5.300***	3.441***	1.852*	2.941***	0.762	0.853
	(df=8; 50)	(df=8; 50)	(df=8; 50)	(df=8; 50)	(df=8; 50)	(df=8; 50)	(df=8; 48)	(df=8; 44)

Notes: *$p < 0.1$; **$p < 0.05$; ***$p < 0.01$

on applications for new businesses with planned wages show a significant uptick in 2020Q3 and 2020Q4 (Figure 1) that is not reflected in the Chicago data, given the significant heterogeneity in the progression of the pandemic and various government restrictions across the country, it remains to be seen whether Chicago is a unique case in this regard among large urban areas (US Census Bureau 2020).

It is also unclear whether this paper's finding that chain establishments have experienced larger pandemic-era drops in new starts (on a percentage basis) than independent establishments is representative of the larger national trend or unique to Chicago (or unique to the empirical definition used in this paper, i.e., individual business accounts with 4 or more associated establishments). It is possible that, given larger financial resources and planning capabilities, multi-establishment firms are better able to defer new establishment openings in this pandemic period to avoid immediate losses, while smaller firms must go ahead with planned openings despite low-revenue conditions. Smaller firms may also be more flexible and able to adapt their business concept to access new market opportunities generated by the pandemic (e.g., a restaurant modifying its operations to become a take-out grocery-style service).

Given these temporal trends, this paper also provides useful insight on the fine-grained spatial patterns of pandemic-related changes in new business density using kernel density estimates and OLS regression at the ZIP code scale. In general, the results confirm the hypothesis that areas of the city with a higher proportion of goods and services provided at the neighbourhood scale, in more diverse, walkable built environments have been more resilient to the effects of the pandemic on new starts across all business types. However, younger (population) neighbourhoods, including gentrifying residential neighbourhoods like Albany Park, Roscoe Village, Bucktown, and the West Loop appear to be hardest hit in terms of new independent business creation in the pandemic era. At the same time, the results support the hypothesis that ethnic enclaves – in particular, Asian and Black neighbourhoods – provide additional resilience from the economic shock of the pandemic. Interestingly, COVID-19 infection rates appear to play a significant role in predicting positive change in new business activity in the pandemic era, particularly for food service businesses, which could be a result of the fact that employees in these businesses were classified as "essential" workers and thus places at higher risk of COVID-19 infection.

While additional research is needed to confirm whether these patterns hold as the pandemic progresses – and whether there are long term economic consequences for particular neighbourhoods that have seen decreased new business activity as a result of the pandemic – these results provide some useful information to city planners and researchers looking to foster economic resilience for this (or future) large-scale economic shocks that significantly restrict mobility. Another pandemic of this magnitude may or may not arise in the near- or medium-term future, but reducing the volume of travel – and providing services closer to residents – remains a fundamental goal for sustainable urban planning practice. This paper's results provide some evidence that the built environment conditions commonly thought to enhance economic vitality at the fine-grained neighbourhood scale, do, in fact, work.

This is particularly important to consider as regions plan for changes in urban development and mobility patterns in the wake of the pandemic. Suburban, auto-oriented areas enjoy some advantages in the strict lockdown conditions of the pandemic (e.g., larger homes with interior and exterior private space, widespread design for enclosed private automobiles, etc.) (Florida 2020). Increased rates (and acceptance) of remote working may also reduce some of the of the intense agglomeration benefits that large, expensive cities currently enjoy, as well as demand for the full range of diverse amenities and business types currently provided in those cities (Wolff-Mann 2020, Lister 2020, Florida et al. 2021).

However, this paper's results provide evidence in favour of the view that more suburban environments may not, in fact, be as economically resilient to large-scale shocks as those with an inherently urban, diverse, and walkable character. Thus, it would seem to be a mistake, from an economic perspective, to abandon dense, diverse urban environments in post-pandemic regional planning processes, even if the pandemic conditions have temporarily made dense, urban living less appealing to some residents. Similarly, the demonstrated resilience of specific ethnic enclaves supports continued investment in these neighbourhoods and the adoption of more explicit economic development strategies that focus on upgrading these enclaves and connecting them to the larger economic networks of the city and globe.

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A Appendix

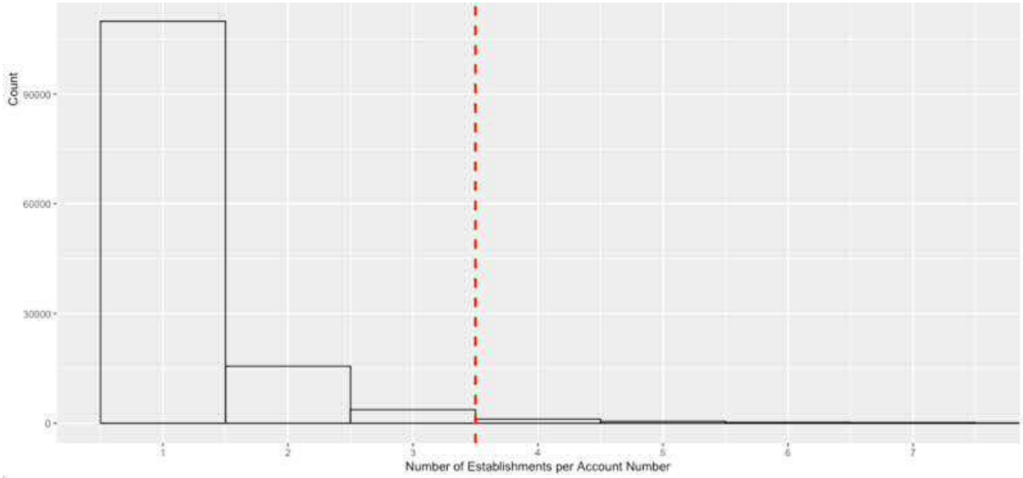

Figure A.1: Histogram showing the distribution of the number of establishments associated with a unique account number. 97.9% of establishments in the dataset are in accounts with fewer than 4 associated establishments

Table A.1: Regression results without the COVID-19 case and testing rate variables (to avoid possible reverse causality) – Percent Change in New Establishments: 2020 (March to September) vs. Average 2016-2019 (March to September) by ZIP Code

	All (Pooled)	All Chains	All Independents	Other	Food	Retail	Personal Care and Fitness	Arts
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
JACOBS	0.025*	0.037	0.021	0.058**	-0.007	0.071**	0.042	-0.183
	(0.013)	(0.025)	(0.014)	(0.027)	(0.020)	(0.035)	(0.034)	(0.172)
SOLCVULN	-0.057***	-0.020	-0.064***	-0.107***	0.030	-0.103**	-0.052	0.206
	(0.017)	(0.032)	(0.018)	(0.035)	(0.025)	(0.044)	(0.040)	(0.203)
%Aged 18-39	-1.489***	-1.603*	-1.391***	-2.518***	0.268	-3.913***	-1.295	6.627
	(0.457)	(0.849)	(0.481)	(0.921)	(0.668)	(1.181)	(1.050)	(4.968)
% Hispanic Population	0.294	0.168	0.293	0.782	-0.726*	0.253	0.570	-2.452
	(0.266)	(0.496)	(0.280)	(0.538)	(0.390)	(0.689)	(0.630)	(3.245)
% Black Population	0.419***	0.319	0.453***	0.860***	-0.268	0.148	0.090	-0.144
	(0.153)	(0.284)	(0.161)	(0.308)	(0.224)	(0.396)	(0.363)	(1.851)
% Asian Population	0.618	2.235***	0.421	1.437	-1.157*	0.961	0.884	-5.661
	(0.428)	(0.795)	(0.450)	(0.863)	(0.625)	(1.106)	(0.965)	(4.698)
Constant	-0.008	-0.316	0.011	0.201	-0.272	1.044***	-0.095	-1.386
	(0.139)	(0.259)	(0.147)	(0.281)	(0.204)	(0.360)	(0.304)	(1.328)
Observations	59	59	59	59	59	59	57	53
R^2	0.386	0.236	0.412	0.312	0.147	0.275	0.097	0.112
F Statistic	5.437***	2.681**	6.067***	3.925***	1.492	3.291***	0.891	0.963
	(df=6; 52)	(df=6; 52)	(df=6; 52)	(df=6; 52)	(df=6; 52)	(df=6; 52)	(df=6; 50)	(df=6; 46)

Notes: $^{*}p < 0.1$; $^{**}p < 0.05$; $^{***}p < 0.01$

Table A.2: Regression results for account numbers with 2 establishments – Percent Change in New Establishments: 2020 (March to September) vs. Average 2016-2019 (March to September) by ZIP Code

	All (Pooled) (1)	All Chains (2)	All Independents (3)	Other (4)	Food (5)	Retail (6)	Personal Care and Fitness (7)	Arts (8)
JACOBS	0.040***	0.069***	0.034**	0.081***	0.013	0.061	0.046	-0.132
	(0.014)	(0.021)	(0.015)	(0.030)	(0.021)	(0.038)	(0.041)	(0.196)
SOLCVULN	-0.057***	-0.037	-0.064***	-0.107***	0.030	-0.102**	-0.052	0.178
	(0.017)	(0.024)	(0.018)	(0.034)	(0.024)	(0.044)	(0.041)	(0.206)
%Aged 18-39	-1.727***	-1.420**	-1.657***	-2.926***	0.183	-3.248**	-1.585	4.550
	(0.462)	(0.681)	(0.494)	(0.955)	(0.680)	(1.225)	(1.124)	(5.388)
COVID-19 Case Rate	5.137	13.299***	3.193	6.826	10.125**	4.136	-2.235	-5.751
(Nov. 10)	(3.092)	(4.561)	(3.306)	(6.397)	(4.554)	(8.208)	(7.493)	(32.373)
COVID-19 Testing Rate	0.238	-0.227	0.298	0.434	-0.017	-0.896*	0.406	2.110
(Nov. 10)	(0.186)	(0.274)	(0.199)	(0.385)	(0.274)	(0.494)	(0.438)	(1.967)
% Hispanic Population	0.132	-0.377	0.236	0.601	-1.184**	-0.190	0.781	-1.126
	(0.303)	(0.448)	(0.324)	(0.628)	(0.447)	(0.805)	(0.716)	(3.734)
% Black Population	0.429***	0.222	0.476***	0.886***	-0.302	0.036	0.130	0.284
	(0.149)	(0.220)	(0.160)	(0.309)	(0.220)	(0.396)	(0.369)	(1.911)
% Asian Population	0.741*	1.098*	0.539	1.633*	-1.053*	0.752	0.969	-4.622
	(0.415)	(0.612)	(0.444)	(0.859)	(0.611)	(1.102)	(0.993)	(4.857)
Constant	-0.257	-0.488*	-0.209	-0.181	-0.552**	1.317***	-0.208	-2.174
	(0.168)	(0.248)	(0.179)	(0.347)	(0.247)	(0.446)	(0.395)	(1.741)
Observations	59	59	59	59	59	59	57	53
R^2	0.452	0.294	0.459	0.355	0.229	0.32	0.113	0.134
F Statistic	5.161***	2.608**	5.300***	3.441***	1.852*	2.941***	0.762	0.853
	(df=8; 50)	(df=8; 50)	(df=8; 50)	(df=8; 50)	(df=8; 50)	(df=8; 50)	(df=8; 48)	(df=8; 44)

Notes: $^{*}p < 0.1$; $^{**}p < 0.05$; $^{***}p < 0.01$

Table A.3: Regression results for account numbers with 3 establishments – Percent Change in New Establishments: 2020 (March to September) vs. Average 2016-2019 (March to September) by ZIP Code

	All (Pooled)	All Chains	All Independents	Other	Food	Retail	Personal Care and Fitness	Arts
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
JACOBS	0.040***	0.062***	0.034**	0.081***	0.013	0.061	0.046	-0.132
	(0.014)	(0.024)	(0.015)	(0.030)	(0.021)	(0.038)	(0.041)	(0.196)
SOLCVULN	-0.057***	-0.0558	-0.064***	-0.107***	0.030	-0.102**	-0.052	0.178
	(0.017)	(0.028)	(0.018)	(0.034)	(0.024)	(0.044)	(0.041)	(0.206)
%Aged 18-39	-1.727***	-1.795**	-1.657***	-2.926***	0.183	-3.248**	-1.585	4.550
	(0.462)	(0.773)	(0.494)	(0.955)	(0.680)	(1.225)	(1.124)	(5.388)
COVID-19 Case Rate	5.137	10.511**	3.193	6.826	10.125**	4.136	-2.235	-5.751
(Nov. 10)	(3.092)	(5.179)	(3.306)	(6.397)	(4.554)	(8.208)	(7.493)	(32.373)
COVID-19 Testing Rate	0.238	-0.055	0.298	0.434	-0.017	-0.896*	0.406	2.110
(Nov. 10)	(0.186)	(0.312)	(0.199)	(0.385)	(0.274)	(0.494)	(0.438)	(1.967)
% Hispanic Population	0.132	0.087	0.236	0.601	-1.184**	-0.190	0.781	-1.126
	(0.303)	(0.508)	(0.324)	(0.628)	(0.447)	(0.805)	(0.716)	(3.734)
% Black Population	0.429***	0.504**	0.476***	0.886***	-0.302	0.036	0.130	0.284
	(0.149)	(0.250)	(0.160)	(0.309)	(0.220)	(0.396)	(0.369)	(1.911)
% Asian Population	0.741*	2.121***	0.539	1.633*	-1.053*	0.752	0.969	-4.622
	(0.415)	(0.695)	(0.444)	(0.859)	(0.611)	(1.102)	(0.993)	(4.857)
Constant	-0.257	-0.654**	-0.209	-0.181	-0.552**	1.317***	-0.208	-2.174
	(0.168)	(0.281)	(0.179)	(0.347)	(0.247)	(0.446)	(0.395)	(1.741)
Observations	59	59	59	59	59	59	57	53
R^2	0.452	0.279	0.459	0.355	0.229	0.32	0.113	0.134
F Statistic	5.161***	2.414**	5.300***	3.441***	1.852*	2.941***	0.762	0.853
	(df=8; 50)	(df=8; 50)	(df=8; 50)	(df=8; 50)	(df=8; 50)	(df=8; 50)	(df=8; 48)	(df=8; 44)

Notes: $^{*}p < 0.1$; $^{**}p < 0.05$; $^{***}p < 0.01$

Table A.4: Regression results for account numbers with 5 or more establishments – Percent Change in New Establishments: 2020 (March to September) vs. Average 2016-2019 (March to September) by ZIP Code

	All (Pooled) (1)	All Chains (2)	All Independents (3)	Other (4)	Food (5)	Retail (6)	Personal Care and Fitness (7)	Arts (8)
JACOBS	0.040***	0.050	0.034**	0.081***	0.013	0.061	0.046	-0.132
	(0.014)	(0.031)	(0.015)	(0.030)	(0.021)	(0.038)	(0.041)	(0.196)
SOLCVULN	-0.057***	-0.044	-0.064***	-0.107***	0.030	-0.102**	-0.052	0.178
	(0.017)	(0.036)	(0.018)	(0.034)	(0.024)	(0.044)	(0.041)	(0.206)
%Aged 18-39	-1.727***	-2.009**	-1.657***	-2.926***	0.183	-3.248**	-1.585	4.550
	(0.462)	(0.996)	(0.494)	(0.955)	(0.680)	(1.225)	(1.124)	(5.388)
COVID-19 Case Rate	5.137	8.579	3.193	6.826	10.125**	4.136	-2.235	-5.751
(Nov. 10)	(3.092)	(6.673)	(3.306)	(6.397)	(4.554)	(8.208)	(7.493)	(32.373)
COVID-19 Testing Rate	0.238	-0.305	0.298	0.434	-0.017	-0.896*	0.406	2.110
(Nov. 10)	(0.186)	(0.401)	(0.199)	(0.385)	(0.274)	(0.494)	(0.438)	(1.967)
% Hispanic Population	0.132	-0.003	0.236	0.601	-1.184**	-0.190	0.781	-1.126
	(0.303)	(0.655)	(0.324)	(0.628)	(0.447)	(0.805)	(0.716)	(3.734)
% Black Population	0.429***	0.309	0.476***	0.886***	-0.302	0.036	0.130	0.284
	(0.149)	(0.322)	(0.160)	(0.309)	(0.220)	(0.396)	(0.369)	(1.911)
% Asian Population	0.741*	2.556***	0.539	1.633*	-1.053*	0.752	0.969	-4.622
	(0.415)	(0.896)	(0.444)	(0.859)	(0.611)	(1.102)	(0.993)	(4.857)
Constant	-0.257	-0.362	-0.209	-0.181	-0.552**	1.317***	-0.208	-2.174
	(0.168)	(0.362)	(0.179)	(0.347)	(0.247)	(0.446)	(0.395)	(1.741)
Observations	59	59	59	59	59	59	57	53
R^2	0.452	0.222	0.459	0.355	0.229	0.32	0.113	0.134
F Statistic	5.161***	1.788	5.300***	3.441***	1.852*	2.941***	0.762	0.853
	(df=8; 50)	(df=8; 50)	(df=8; 50)	(df=8; 50)	(df=8; 50)	(df=8; 50)	(df=8; 48)	(df=8; 44)

Notes: $^{*}p < 0.1$; $^{**}p < 0.05$; $^{***}p < 0.01$

Table A.5: Regression results for the spatial lag specification, estimated using a first-order queen spatial weights matrix – Percent Change in New Establishments: 2020 (March to September) vs. Average 2016-2019 (March to September) by ZIP Code

	All (Pooled)	All Chains	All Independents	Other	Food	Retail	Personal Care and Fitness	Arts
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
JACOBS	0.040***	0.056**	0.034**	0.077***	0.012	0.061*	0.041	-0.146
	(0.013)	(0.025)	(0.014)	(0.027)	(0.019)	(0.035)	(0.036)	(0.160)
SOLCVULN	-0.052***	-0.017	-0.058***	-0.098***	0.031	-0.102**	-0.042	0.182
	(0.015)	(0.029)	(0.016)	(0.031)	(0.022)	(0.040)	(0.037)	(0.169)
%Aged 18-39	-1.635***	-1.510*	-1.578***	-2.779***	0.194	-3.235***	-1.498	5.713
	(0.411)	(0.808)	(0.446)	(0.865)	(0.622)	(1.135)	(1.003)	(4.413)
COVID-19 Case Rate	5.913**	10.884**	3.706	7.337	9.783**	4.164	-2.202	-10.157
(Nov. 10)	(2.728)	(5.390)	(2.974)	(5.769)	(4.172)	(7.556)	(6.690)	(26.469)
COVID-19 Testing Rate	0.218	-0.153	0.290	0.391	-0.032	-0.901**	0.369	1.932
(Nov. 10)	(0.164)	(0.325)	(0.179)	(0.347)	(0.251)	(0.455)	(0.391)	(1.609)
% Hispanic Population	0.083	-0.382	0.192	0.479	-1.213***	-0.189	0.581	-0.304
	(0.268)	(0.529)	(0.292)	(0.567)	(0.410)	(0.745)	(0.640)	(3.053)
% Black Population	0.353***	0.279	0.411***	0.740***	-0.306	0.036	-0.041	1.234
	(0.135)	(0.261)	(0.148)	(0.285)	(0.201)	(0.369)	(0.332)	(1.571)
% Asian Population	0.658*	2.303***	0.448	1.393*	-1.152**	0.741	0.944	-3.288
	(0.368)	(0.728)	(0.400)	(0.778)	(0.563)	(1.016)	(0.886)	(3.970)
Constant	-0.164	-0.666**	-0.153	-0.084	-0.585**	1.319***	-0.244	-2.844**
	(0.153)	(0.313)	(0.166)	(0.316)	(0.235)	(0.412)	(0.357)	(1.425)
Observations	59	59	59	59	59	59	57	53

Notes: $^{*}p < 0.1$; $^{**}p < 0.05$; $^{***}p < 0.01$

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Territorial cohesion, the COVID-19 crisis and the urban paradox: Future challenges in urbanization and economic agglomeration

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Abstract. The recent COVID-19 pandemic and the subsequent economic downturn due to the lockdown of economic activities have spurred a lively debate concerning their effects across locations in the EU and the resulting challenges to territorial cohesion policy. The COVID-19 emergency not only has provoked EU cohesion policy responses but also may change some of the basic principles on which these policies have been built. This paper briefly casts light on some present and future implications of the COVID-19 pandemic for two fundamental aspects of territorial cohesion policy, namely urbanization and economic agglomeration. Both aspects are linked to territorial cohesion's significant dimension of polycentricity (as balanced and harmonious development), and together they constitute a challenge to established norms of urban agglomeration. Finally, the paper discusses some policy ideas that have recently (re)appeared on the European policy landscape. Such policy options bring together urban development and regional policy agendas with the aim of promoting territorial cohesion by attempting to solve the 'urban paradox' – the coexisting positive and negative effects of urban agglomeration and its established geography.

Key words: territorial cohesion, COVID-19, urbanization, economic agglomeration, urban paradox, regional policy

1 Introduction

The recent COVID-19 pandemic and the subsequent economic downturn due to the lockdown of economic activities have greatly affected the economic well-being of Europeans, putting the European Union (EU) member states under severe stress. The recession had not only economic but also social effects, as relative indicators reveal (Grasso et al. 2021). Furthermore, the effects of the crisis appear anything but spatially uniform, affecting different EU locations in very different ways (Bailey et al. 2020, Kapitsinis 2020). These new developments have triggered a growing and heated debate concerning the uneven impact of the pandemic on different locations in the EU and the resulting challenges to territorial cohesion and territorial cohesion policy (Capello, Caragliu 2021).

Territorial cohesion is a shared competence distributed between the European Commission and the various EU member states/governments. It is an ambiguous and multifaceted concept with many interpretations. It has been the subject of numerous efforts to (re)construct its character and meaning (Artelaris, Mavrommatis 2020). Among other interpretations, Mirwaldt et al. (2008) have argued that territorial cohesion is comprised of the following dimensions: 1) a form of polycentricity that can promote economic competitiveness and innovation; 2) balanced development that reduces socioeconomic disparities; 3) access to services, facilities and knowledge irrespective of where one lives; 4) networking and the creation of physical and interactive connections between centres and other areas. For Medeiros (2019), the most characteristic dimension of territorial cohesion is polycentricity as it promotes balanced and harmonious development.

The emergence of the European policy discourse on territorial cohesion has also led to the re-conceptualization of regional policy by supplementing it with the notion of spatial justice (Davoudi 2005). This notion considers justice as a matter of geography (Heynen et al. 2018) associated with 'both processes (income distribution mechanisms) and outcomes (level of imbalances) prevailing in different territories' (Petrakos et al. 2021, p. 2). Great strides have been made in academia during recent years toward the application of the concept of spatial justice in relation to EU cohesion policy concerns (Kearns et al. 2014, Jones et al. 2020), and some European policymakers have explored whether the concept of spatial justice can be used as an effective alternative to territorial cohesion (Jones et al. 2019, p. 99).

This paper sheds light on the possible effects of the COVID-19 pandemic on a few critical aspects of EU territorial cohesion and territorial cohesion policy. It can be argued that the COVID-19 emergency has provoked EU cohesion policy responses by possibly increasing territorial inequality and necessitating recovery across EU territories. It can also be suggested that the COVID-19 emergency might lead to changes in some of the basic foundations on which territorial cohesion policies have been built. More to the point, the paper envisages some present and future implications of the COVID-19 pandemic for two fundamental aspects of territorial cohesion, namely urbanization and economic agglomeration (which, in combination, are called urban agglomeration). Although territorial cohesion policy has many dimensions, extending from social cohesion to environmental sustainability and from physical and digital networking to regions that are lagging behind, this paper's emphasis on urbanization (urban agglomeration) stems from the following two considerations. Firstly, although urbanization is a highly differentiated process across EU space, almost 75% of EU residents are based in cities and towns, with that share estimated to reach almost 85% by 2050 (Bachtler et al. 2020). In other words, the EU is clearly an urbanized and urbanizing space. Secondly, territorial cohesion has a clearly marked urban dimension (Medeiros 2019) as it is related to polycentricity, which promotes harmonious and balanced development across regions; cities are the centres of economic growth and have the potential to lead regions toward economic development. Accordingly, as we shall see, urban development and regional policy agendas can be interconnected and interrelated.

2 Territorial cohesion, spatial inequalities and the COVID-19 pandemic

During the last two decades, the EU has experienced rising levels of territorial inequality as a result of important socioeconomic and political changes (Artelaris, Tsirbas 2018, Iammarino et al. 2019, Bailey et al. 2020, Dijkstra et al. 2020). The increase in, and need to limit, spatial inequalities among EU localities have lately been highlighted in several official EU documents, such as the Territorial Agenda 2030 (Ministers 2020). Furthermore, it has been argued that spatial disparities might not only endanger what is perceived as the European Model of Society and EU economic, social and territorial cohesion (Faludi 2007a,b, Zaucha, Böhme 2020) but also hamper European integration and even threaten democracy.

Territorial cohesion is the opposite of territorial inequality; when the aims and goals of territorial cohesion are met, spatial inequalities and disparities between and within places gradually diminish. However, the COVID-19 pandemic encountered an environment of increased territorial inequality across EU space. Only a few years after the end of the 2008 crisis, the COVID-19 crisis once again poses great challenges for several EU countries and the EU as a whole; this is probably the most serious test of the EU in terms of crisis management since the end of World War II (Russack, Blockmans 2020), calling many past certainties into question. Beyond its effects on health, COVID-19 has triggered an economic and social crisis. However, the 'footprint' of the crisis is expected to be spatially uneven rather than homogeneous. Although the literature on geographies of crisis is scarce and underdeveloped, and rigorous explanations for the respective responses of different regions to shocks are lacking (Eraydin 2016, Martin et al. 2016, Artelaris 2017),[1] a clear message from studies of the 2008 economic crisis in the EU was that some regions were more affected than others (Committee of the Regions 2010, Martin 2010, Kitson et al. 2011, Brakman et al. 2015, Capello et al. 2015).

Although more and better data is needed to understand and evaluate the economic and social effects of COVID-19 at the spatial level, a few recent studies, mainly focusing on GDP per capita, reveal that the pandemic crisis has left an uneven spatial footprint and show evidence of increasing levels of territorial inequality (OECD 2020). For instance, Capello, Caragliu (2021), using the latest generation of the Macroeconomic, Sectoral, Social, Territorial (MASST4) model, show evidence of increasing regional inequality in the EU, mainly arising from the heterogeneous effects of the crisis at the country level. In a similar vein, Brada et al. (2021) also offer evidence of growing regional inequalities in their examination of 199 NUTS-3 regions in Central and Eastern Europe (CEE). In short, the COVID-19 crisis appears to have reinforced and even deepened spatial disparities, posing new challenges to EU territorial cohesion.

From a policy point of view, the existing (preliminary) empirical evidence encourages the implementation of a sound territorial policy and the adoption of spatially selective interventions to ameliorate the effects of the pandemic crisis on the areas most affected. Moreover, (past) experience suggests that there is a need for appropriate and focused policy efforts to actively protect social outcomes rather than trying to recover losses in the aftermath of crises, as economic recoveries do not necessarily and inevitably lead to recoveries for human and social indicators; very often, the damage is permanent or highly persistent because some of these losses are simply not recoverable (Martin 2010, Mohseni-Cheraghlou 2016, Artelaris 2017). As stated in the Territorial Agenda 2030:

> While revising the Territorial Agenda, the COVID-19 pandemic has changed policy making and future development outlooks. As implications and policy responses vary across territories due to different conditions, the pandemic shows that territories matter and are highly interdependent. Territorial cohesion should play an important role in the recovery process. (Ministers 2020, p. 2)

3 European Union Policy Responses to the COVID-19 Pandemic

In this challenging environment, some questions naturally arise in terms of EU policy: What were the immediate EU policy responses to the pandemic? What changes did the COVID-19 pandemic bring to EU cohesion policies and territorial cohesion policy in particular? To start with, the EU adjusted its budget to cope with the negative socioeconomic consequences of the pandemic. In July 2020, the Special European Council decided on a massive European Recovery Plan increasing the budget of the post-2020 period. The main aim was to support a 'sustainable and resilient recovery' while promoting the already-intended green and digital transitions (Bachtler et al. 2020). The most significant measures were the launching of the 'Next Generation EU' initiative (2021-2024) and a new, revamped budget for the current programming period (2021-2027) exceeding one billion euros. Other significant measures included the creation of a financial

[1] It is worth noting that the literature focusing on this issue has two main strands. The first strand relates the spatial concentration of economic activities to cycles, suggesting that regional disparities exhibit a pro-cyclical behavior, increasing in periods of expansion and decreasing in periods of recession (Berry 1988). The second strand, known as regional resilience and triggered by the 2008 crisis, refers to the manner in which spatial entities or systems react to and recover from adverse disruptions, such as recessionary downturns and economic shocks (Martin 2012, Martin et al. 2016, Sensier et al. 2016). Although there is no consensus, potential critical determinants of the crisis have been considered to include geography, economic structures, policies, the openness of trade and instability of exports of goods, infrastructure and regional innovation systems (Artelaris 2017).

instrument providing (temporary) support to mitigate unemployment risks in a crisis-ridden environment (SURE), amendments to the EU budget to address urgent issues, redirection of EU funds to help the member states most in need and support to the sectors most affected[2]. Apart from these emergency measures, the main priorities remained the facilitation of a transition to a 'smarter' and 'greener' Europe. For the European Commission, the advent of the pandemic was not only a challenge but also an opportunity to bring closer the much-needed digital and green revolutions. As stated by the European Commission: 'Our generational challenges – the green and digital revolutions – are even more important now than before the [COVID-19] crisis started. Through the recovery, we will press fast-forward on the twin green and digital revolutions' (EC 2020b).

Cohesion policy has proven to be an effective and efficient policy tool in mitigating economic crises, such as the 2008 economic crisis and the 2014-15 refugee crisis. The current pandemic is no exception as cohesion policy has been one of the cornerstones of the European response to the COVID-19 crisis. For example, a new initiative, REACT-EU, was established to increase the 2014-2020 budget for cohesion policies by 55 billion euros. The REACT-EU initiative stands for Recovery Assistance for Cohesion and Territories of Europe. The extra funding was distributed between the European Regional Development Fund (ERDF), the European Social Fund (ESF) and the European Fund for Aid to the Most Deprived (EC 2020a). The new instrument was launched in 2020 and continues in 2021-2022 through funds from the 'Next Generation EU' initiative. It aims to provide financial support for the recovery of significant sectors of the economy while decisions for the allocation of funds take place at the national level. All these initiatives offer great help in all EU countries, but those hit hardest benefit the most (Sapir 2020).

4 Looking into the future: Changes in urbanization?

All across Europe, economic development concentrates in cities and their adjacent metropolitan (functional) areas. These are the places where the bulk of innovation, digitization and rapid economic growth are concentrated; these are the hotspots of our established economic system. The concentration of people, activity and resources in a small number of big cities advances economic growth and innovation and even drags surrounding regions into development through a number of positive externalities (Annez, Buckley 2009). European societies are based on the concentration of population and human activity in cities and thus are highly urbanized in nature. Apart from being significant economic growth machines, cities are also the social, cultural and political pinnacles of our urban civilization. In short, urbanization and city life constitute the mainstream of our way of life (Quigley 2009). However, this state of affairs is not without problems. For instance, the concentration of people and wealth in a few urban areas creates traffic congestion, pollution, inflated housing prices and spatial inequality not only within cities but also between developed cities and other, less developed areas. This is the 'urban paradox' that characterizes established forms of urbanization in the EU and beyond (Eurostat 2016, p. 34).

As far as the COVID-19 crisis is concerned, it is widely accepted that the spread of the pandemic has been positively correlated with levels of urbanization and population density (Connolly et al. 2020). For instance, city centres and inner-city areas with high population density have proved to be the prime victims of the pandemic, leading, in several cases (such as New York), to the collapse of their healthcare systems. In this context, demand has greatly increased, at least during the early stage of the pandemic, for housing away from neighbourhoods with high population density; the main cause of this trend is related to the decreased need to live near jobs (Liu, Su 2021). Furthermore, the pandemic appears to have intensified socio-spatial inequalities as infection rates were much higher in deprived neighbourhoods and among ethnic minorities (Biglieri et al. 2020).

The positive relation between urbanization and levels of infection raises questions about the future of our crowded cities. The current pandemic has changed city life

[2]For a thorough presentation, see https://www.consilium.europa.eu/en/policies/coronavirus/covid-19-economy.

and, even more importantly, the ways we think about urban density. During successive lockdowns and acute restrictions on mobility, cities and city centres lost much of their liveliness and economic activity (Lee, Huang 2022). Gradually, a small but growing literature has begun to emerge documenting the ways that cities have coped and are still coping with the evolving pandemic crisis. An uncertainty about the future of cities has come to the fore (Gill et al. 2020).

More to the point, the COVID-19 crisis and its urban effects have created dual scenarios for the future of cities. One line of thought (for instance, Graziano 2021) envisions de-urbanization and a 'back to the villages, towns and rural areas' movement. In this scenario, technology is deemed to play a paramount role in facilitating forms of remote work and providing other technology-driven services. Closely related to this notion of de-urbanization is the concept of the 'distanced city' (Gill et al. 2020), where people work from home, engage in electronic shopping and adopt various measures of physical detachment to protect themselves from the crowdedness of city life. For instance, Lee, Huang (2022) showed the existence of strong support for 'urban' flight within metropolitan areas in the United States during the pandemic. In sharp contrast to this, the second scenario envisions the emergence of the city of 'proximity' (Cerasoli et al. 2022). According to this scenario, COVID-19-related mobility restrictions have made proximity extremely important. Some other writers have even argued for the need to create 'an economy of proximity' (Tricarico, De Vidovich 2021); all these ideas bring to the fore the notion of a new 'hyper-local' urbanism. According to such narratives, there is a need to reconfigure the role of proximity in city life by eradicating travel time and thus creating more compact and coherent neighbourhoods where residents can work, shop, be entertained and receive health-related services close to their homes. Many cities around the world, from Seoul to Paris, appear to have adopted this philosophy by working towards the creation of the 10- or 15-minute city. On this model, travel on foot or by cycling should be sufficient to meet all one's needs. To cut a long story short, the COVID-19 pandemic appears to have produced dual future urban scenarios, based either on de-urbanization and distanced living or on urban living characterized by proximity, neighbourhood self-sufficiency and 'hyper-localism'.

Furthermore, the post-pandemic city has been envisaged as greener and sustainable (Ferrini, Gori 2020). A new urban planning philosophy and even architectural paradigm have been deemed necessary (Sharifi, Kharavian-Garmsir 2020). Through the prism of the 'distanced city', it has been argued that a dominance of suburbs over city centres might characterize post-pandemic times. E-commerce and remote work might become permanent features of our lives and lead to the decentralization of activities and forms of dwelling (Pisano 2020). As a result, urban centres might lose a large part of their vitality and even experience a gradual economic and cultural decline. However, we should not forget that since Louis Mumford's 'Culture of Cities' (Mumford 1970), cities and urban centres have been regarded as manifesting life in its highest form. Jane Jacobs (1961) and Richard Sennett (1970) perceived face-to-face interaction and urban encounters as the very essence of city life. Economic geography contributed a perception of spatial clustering as responsible for producing innovation and economic growth. Richard Florida spoke of the creativity of cities (Florida 2002). All these ideas are, in one way or another, close to the notion of 'proximity'. One is left wondering whether the pandemic might bring some of these aspects of city life close to an end, changing our urban lives and the ways we think about cities and city centres.

For some authors, the expected effect of the pandemic on cities depends on its duration. If the pandemic lasts for years, they believe, cities will change to a significant extent; if its duration is shorter, changes to cities might not be of great concern (Florida et al. 2021). Currently, we are in the midst of an economic recovery, compromised by rising inflation, near the end of a pandemic and facing the risk that COVID-19 might become endemic. Consumption has increased, and many city centres are open to customers and workers alike. Several reports anticipate that cities and urban centres will prosper as people are eager for face-to-face contact (Giorgi et al. 2022). However, some cities are still empty as people continue to work from home. For Mumford (1970), as long as people desire face-to-face contact, cities and city centres will exist in one form or another. Again, only the passage of time will make clear whether the pandemic eventually changes urbanization or cities continue as they have been.

5 Looking into the future: A more dispersed economic agglomeration?

The COVID-19 pandemic has the potential not only to transform cities and urbanization but also, more importantly, to challenge the territorial logic on which our economic system is based. As argued above, polycentric development is one of the most important aspects of territorial cohesion. The idea of polycentricity is close to the notions of economic competitiveness, smart growth and digital connectivity (Artelaris, Mavrommatis 2020). For territorial cohesion policy, the concentration of people, activity and prosperity in a few specific urban areas both increases costs (land values, quality of life, commuting time, etc.) and creates obstacles to spatial justice (concentration of economic opportunity, facilities, infrastructure, etc.). These are the negative aspects of the urban paradox. Nevertheless, territorial cohesion policy accepts the positive side of the urban paradox, namely that cities are the main engines of economic growth and innovation. In a way, one of the goals of territorial cohesion policy is to take advantage of the positive side (urban growth) while counteracting the negative aspects of the urban paradox. The aim of territorial cohesion can further be described as facilitating harmonious and balanced development through the creation of a polycentric urban system able to produce significant economic growth and development. The creation of such a system can increase the economic competitiveness of different regions and break the monopolistic conditions attendant on the European global city model.

Leaving aside for a moment the idea of the polycentric system, the reality is that cohesion policies in general and territorial cohesion policy in particular are based on the notion of economic agglomeration. Since the 1990s, the agglomeration of economic activity has been the model on which cohesion policies were built. To put it differently, cohesion and territorial cohesion policies have followed, or simply accepted, an agglomeration-centric approach by adopting neoliberal economic principles: the free economy boosts economic growth while finding, in parallel, ways for it to trickle down (Davoudi 2020). In short, the agglomeration model has been the economic cornerstone of cohesion policy (Cotella, Vitale Brovarone 2021). Agglomeration is even the basis for the idea of creating a polycentric European urban system, albeit a more dispersed one with more cities (polycentric development) creating growth, advancing economic development and bringing along surrounding regions.

However, the COVID-19 pandemic appears to create barriers to the efficiency of the economic agglomeration or urban agglomeration model. As the pandemic has spread widely in cities, those are the places under the greatest threat (Connolly et al. 2020). In this sense, the vulnerability of (crowded) cities to the pandemic calls into question the future viability of the agglomeration-centric approach according to which economic activity and human skills concentrate in urban densely populated areas. Accordingly, in the light of the COVID-19 pandemic, some pertinent (although theoretical) questions arise: What is the future of economic agglomeration or urban agglomeration? What alternative types of spatial models could emerge to create economic growth in a post-pandemic world that takes seriously the possibility of new pandemic outbreaks? Could these new spatial models be closer to the aims of territorial cohesion?

The reality is that the European economic model cannot really abandon its urban agglomeration logic; practically, it cannot leave cities behind and extensively relocate economic activities to the countryside and beyond. This is not feasible under current circumstances as the economic system is clearly urban in nature. Nevertheless, for some scholars, massive investment could render rural areas more livable and functional as a complement to the urban dimension (Cotella, Vitale Brovarone 2021). In such a scenario, agglomeration would spread from cities to the surrounding rural areas, creating more opportunities for people and economic activities. However, the 'new' rural would not substitute for the urban; instead, the rural and the urban would work together to create a new, more 'spread-out' form of the agglomeration model (Cotella, Vitale Brovarone 2021). This is probably similar to Lefebvre's (2003) idea of the creation of an urban capitalist economic system that is found not only in cities but also in areas that lie between them – a more dispersed agglomeration that encompasses both urban and rural spaces. Will the pandemic bring Lefebvre's urban 'capitalist revolution' closer to reality than before? This is debatable. However, it is time to shift our focus to some policy ideas and options that have recently appeared on the European policy landscape.

6 Policy options: From the urban paradox to territorial cohesion policy for post-pandemic recovery

By situating the idea of the urban paradox within the context of this paper, we seek to put forward some policy thinking and options that, while not new, have lately experienced a boost. In very simple terms, the urban paradox can be summarized as follows: the growth of cities and urban areas promotes economic development and innovation. However, such urban growth also creates problems, including inequality within urban centres and disparities between them and less developed areas. Paradoxes are logical contradictions, which are not exactly meant to be solved. A paradox is inherently unsolvable; solving it would prove it was not a true paradox. From Zeno of Elea to Bertrand Russell, paradoxes have been central to philosophical thinking by challenging us and provoking fresh thought. According to the Cambridge Dictionary, a paradox is 'a situation or statement that seems impossible or difficult to understand because it contains two opposite facts or characteristics'. A paradox presents a contradiction and shows the limitations of reason.

Bringing these ideas closer to the subject of this paper, we could argue that the urban paradox can be rephrased by saying that urban agglomeration is 'good' and urban agglomeration is 'bad' (for the aforementioned reasons). These contradictory statements both characterize our European urban system and its geographical economic logic. Nevertheless, the COVID-19 crisis poses a test for the present and future of our crowded cities, for the established economic system as well as its territorial logic; the pandemic constitutes a challenge to the regime of urban agglomeration in the EU (and elsewhere). Consequently, its effects seem to influence the salience of the urban paradox. As argued, de-urbanization and the creation of a 'distanced city' have the potential to change cities and urban areas. At the same time, the possibility of a more spread-out regime of economic agglomeration might influence the territoriality of our economic system. These developments render the future existence of the urban paradox less certain, partly jeopardizing the 'truth' of the two contradictory statements it contains. Time will tell.

The existence of the urban paradox is a significant reason for the creation of territorial cohesion policy as that policy attempts to ameliorate the negative effects of urban agglomeration without compromising its positive ones. How does it do that? By promoting polycentricity within the European urban system, and through that, a harmonious and balanced development across EU space. In more concrete policy terms, the urban paradox can be seen as the relationship between regional policy, urbanization and economic agglomeration (Ferry, den Hoed 2020). Bringing regional policy to the forefront, the urban paradox can be recast as following: urban agglomeration is 'good' for regional economic growth but 'bad' in terms of regional inequality (at the national level). Regional policy deserves foregrounding here because the harmonious, balanced development that is its very essence makes it part and parcel of territorial cohesion policy.

In this context, the key question is what regional policy can do in relation to the urban paradox, specifically how it can take advantage of the positive while ameliorating the negative effects. It should be highlighted that, in general terms, regional and urban policy are distinct and autonomous fields at the national policy level. Nevertheless, regional policy attempts to promote and facilitate urban growth and development as it accepts that regional growth is (mostly) dependent on the economic performance of urban centres that economically strengthen surrounding areas through spillover effects and positive externalities. At the same time, it attempts to ameliorate the negative effects of urban agglomeration on the equity of inter-regional growth. How can this be done? By bringing urban development and regional policy agendas closer together. As a matter of fact, during the pandemic in the last two years, regional policies in a number of EU member states have addressed urban issues; there has been an ongoing effort to combine urban and regional agendas by acknowledging the contribution of urban areas to regional development. This has taken place mostly through policy governance measures and strategic frameworks that integrate urban and regional concerns (Ferry, den Hoed 2020).

One such approach is the promotion of urban-rural linkages that acknowledge the complex dependencies between urban and rural areas. As Cotella, Vitale Brovarone (2020) argue, the COVID-19 pandemic is 'a specific moment in time where contextual conditions allow to push forward conditions that would not take root in normal times as for instance those insisting on the valorization of inner areas [inner rural areas in Italy] and the potential synergies that could be established with denser urban regions' (Cotella, Vitale Brovarone 2020, p. 115). Furthermore, the role of medium-sized cities increases in prominence as a means of promoting regional development and moving towards the always sought-after, yet never attained, goal of regional equity. In close relevance to this, Medeiros, Rauhut (2020), within the context of territorial cohesion policy, have highlighted the importance of strengthening medium-sized towns through targeted public and private investment as a way of achieving territorial cohesion within countries and across EU space. Their rationale is based on the hypothesis that the growth of medium-sized cities, or 'Territorial Cohesion cities', will lead to the growth of undeveloped areas and thus contribute to territorial cohesion or regional equity. It is interesting and deserving of further research how the effects of the COVID-19 pandemic may transform these policy ideas (rural-urban relationships and the role of medium-sized cities) in relation to the urban paradox.

7 Conclusions

The recent pandemic, probably resulting in the most dramatic economic crisis in the history of the EU, constitutes a major challenge for the EU's economic, social and territorial cohesion. Although more and better data is needed, there is reason to think that the effects of this multifaceted crisis are not geographically homogeneous across Europe; instead, new forms and increasing levels of inequality have emerged across and within EU countries, regions and localities, undermining the European objectives of economic, social and territorial cohesion. From this perspective, European territorial cohesion policy might be a sound and effective policy tool for bringing about a post-pandemic economic, social and territorial revival. There is also reason to think that the COVID-19 emergency might lead to changes in some of the basic foundations on which territorial cohesion policies have been built.

This paper has shed some light on the possible effects of the COVID-19 crisis on two fundamental aspects of territorial cohesion, namely urbanization and economic agglomeration (urban agglomeration). As city centers and inner-city areas with high population density emerged as the prime victims of the pandemic, the positive relation between urbanization and levels of infection raised questions about the future of our crowded cities. The current pandemic has both transformed city life and, even more significantly, brought changes to the ways we think about urbanization and urban density. As a result, an ambiguity about the future of cities has come to the fore as cities face the choice between a distanced model and a model that prioritizes proximity. Partly as a result of this ambiguity, the pandemic has the potential not only to change cities and urbanization patterns but also, more importantly, to challenge the territorial logic on which our economic system is based. The COVID-19 crisis creates barriers to the efficiency of the economic agglomeration or urban agglomeration model. The vulnerability of (crowded) cities exposed by the pandemic calls into question the future viability of the urban-agglomeration-centric approach. In consequence, we are left to wonder not only about the future of our cities but also about the prospects of the established urban agglomeration model.

In most circumstances, regional and urban policies are distinct and autonomous fields. However, during the last two years, the regional policies of many EU member states have attempted to address urban issues; there have been significant efforts to integrate urban and regional agendas. One such effort works through the promotion of urban-rural linkages. Additionally, a more prominent role is emerging for medium-sized cities as means of promoting regional development and regional equity. For the urban paradox to be addressed, European territorial cohesion and regional policy should work together to strengthen the merits of urban agglomeration and counteract its negative aspects. However, we do not expect the urban paradox to be solved; if it were solvable, it would not be a true paradox. As a matter of fact, in philosophy, logic and mathematics, paradoxes are not there to be solved; instead, they urge us to think afresh and change our perspective. In the light of the COVID-19 pandemic and the changes it has brought to the established regime of urban agglomeration in and across the EU, our policy perspectives on territorial cohesion and regional policy might well be in need of some novelty and fresh thinking.

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The promise of endogenous potential in times of crisis – Analysis of the effects of the COVID pandemic on the socio-economic embeddedness in local economies

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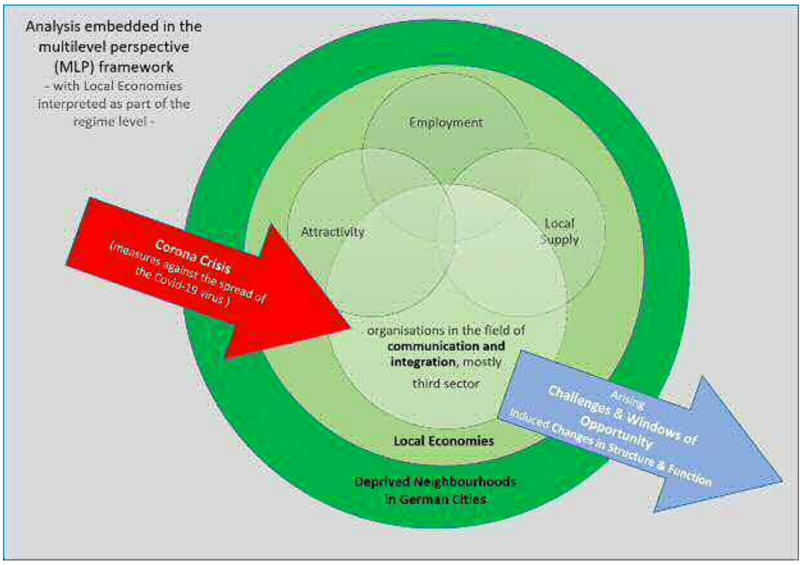
Abstract. The measures against the spread of the COVID virus have massive effects on local economies. By means of an exploratory qualitative case study in deprived inner-city neighbourhoods in the cities of Mönchengladbach and Krefeld in Germany, this paper explicitly aims at examining the COVID pandemic's impact on their endogenous potential. In this context, the focus lies on organisations which contribute to the local economy's function of integration and communication. The analysis is based on theoretical concepts of the local economy, but it also refers to crisis as well as transition management research, especially the multilevel perspective framework. By means of desktop research, a focus group with multipliers involved in local economic contexts as well as thirteen guideline-based interviews with the heads of local organisations, the subsequent analysis reveals the partially counteracting effects of the COVID pandemic on the organisations' socio-economic embeddedness. On the one hand, they are threatened by economic bottlenecks, by pending social consequences of a longer period with restrictive regulations as well as by fear of contagion and exhaustion. While the organisations' perceived level of urgency varies greatly, their level of uncertainty is generally high. On the other hand, organisations of the local economy benefit from a positive push in the areas of digitization and new life and working environments (home-based work), as well as from a strengthening of local solidarity and cohesion.

1 Introduction

The measures against the spread of the Covid virus accelerate and intensify the structural change processes and its associated problems in local economies, especially in already deprived neighbourhoods. Faced with such challenges, one can observe an increased focus either on acquiring external support for local economic actors or on the recollection of neighbourhoods' endogenous potential in hope of mitigation.

To the best of the authors' knowledge, research regarding the effects of the COVID pandemic on the local economy is still strongly limited. To narrow this research gap, this analysis is based on research regarding local economies, a field of research characterised by its evidence-based development without clear theory-based references (Henn, Behling 2019). Therefore, the confrontation with theoretical considerations might help improve the understanding of local economic contexts. To this end, the authors adopt reflections from crisis research as well as the multi-level-perspective (MLP) framework from transition management research.



Source: own representation

Figure 1: Visualization of the research question

The aim is to analyse the impact and potential outcomes of the COVID pandemic, as a major crisis, on local economies in deprived neighbourhoods in the medium-sized cities of Mönchengladbach and Krefeld in the Middle Lower Rhine region in Northrhine-Westfalia, Germany. A special focus is placed on organisations committed to the function of communication and integration, as illustrated in Figure 1.

The overarching research question is operationalised as follows:

- What are the major challenges of organisations committed to communication and integration in the local economy? To what extent do those challenges reflect the typical characteristics of a crisis?
- What windows of opportunity do organisations committed to communication and integration perceive in the local economy? How lasting and thus transforming are the applied measures, especially in relation to the MLP framework?
- How do change processes induced by those potential windows of opportunity reflect in the discussion on the preservation or collapse of structure versus function?

The analysis is built on the assumption that a major function of the local economy is to strengthen communication and integration in the neighbourhood and thereby the mobilisation of endogenous potential, which in turn can help improve the overall development of the neighbourhood.

The case study is based on a comprehensive literature review, a focus group interview and thirteen guideline-based interviews. The interviews have been conducted with heads of locally embedded, community-oriented organisations in deprived neighbourhoods in the cities of Mönchengladbach and Krefeld in the Middle Lower Rhine region in Germany. Due to the functional focus on communication and integration, most of the selected organisations belong to the so-called third sector (see Section 2.1).

The analysis reveals the partially counteracting effects of the COVID pandemic on the endogenous potential in local economies. On the one hand, locally embedded organisations are threatened by economic bottlenecks, the pending social consequences of a longer period without or with minimized range of services and products offered as well as fear of contagion and exhaustion. While the organisations' perceived level of urgency varies greatly, their level of uncertainty is generally high. On the other hand, locally embedded organisations benefit from a positive push in the areas of digitization and new life and working environments (home-based work), as well as from a strengthening of local solidarity and cohesion.

Table 1: Concepts and terms relevant to the case study, own representation

Concepts and terms from local economy research	Concepts and terms from crisis research	Concepts and terms from transition management research
• local economy (sector classification and functions, especially communication and integration) • (socio-)economic embeddedness • deprived neighbourhood • endogenous potential • solidarity and cohesion	• crisis characteristics: (existential) threat, urgency and uncertainty • conceptualization of crises in different research streams • productive functions of crisis • typology of change processes in relation to the preservation or collapse of structure versus function	• specific features and relevance of the local level • concept of proximity • MLP framework with a focus on the development and diffusion of innovations
concept of “windows of opportunity” appears in all three research streams (connecting link)		

The introduction (Section 1) is followed by explanations of the theoretical background considerations (Section 2). Subsequently, the applied methodology is presented (Section 3), including the reason regarding the selection of the interviewees. This section is followed by the analysis (Section 4). It includes both, the challenges and opportunities of local organisations in dealing with the COVID pandemic and an assessment of structural versus functional adaptation processes. The findings are discussed in Section 5, including policy recommendations. Section 6 presents a conclusion and further research questions.

2 Theoretical Background

The conceptual framework is inspired by three different research streams: local economy, crisis and transition management research. The following table illustrates the concepts and terms relevant to the case study (see Table 1). The idea of “windows of opportunity” is voiced in all three research streams and represents a connecting link between them.

2.1 The Promise of Endogenous Potential in a Local Economy

There is no universal definition for “local economy” (Henn, Behling 2019). In the context of this research, it can be broadly understood as comprising all economic activities referring to the development of a spatial unit, preferably a neighbourhood (Birkhölzer 2000). Although the primary focus of this concept is on economic activities, it is an integrative approach including social and ecological perspectives aiming at the enablement of sustained economic activities.

The original classification of Birkhölzer (2000) divides the local economy into three sectors: the first (private) sector, the second (public) sector and the third sector, which is constituted like the private sector, but primarily addresses social concerns. However, it should be taken into account that this classification is not clear-cut, and there are many overlaps between the sectors.

Typically, a local economy is oriented towards four functions: local supply (retail sector), employment (creation of jobs and training positions close to home), upgrading (supply diversification, combating vacancies, reducing population loss) as well as communication and integration (strengthening local economic cycles, mobilization of endogenous potential) (Henn et al. 2019).

As many of the organisations committed to the function of communication and integration can be found in the so-called third sector, the authors assume that this sector is highly relevant for the local economy and the mobilisation of endogenous potential. The literature offers various definitions for the third sector. In the context of this paper, the authors base their reflections on the definition of the third sector proposed by the third or social-economy (TSE) concept (Salamon, Sokolowski 2018)[1]. This definition covers the German non-profit associations as well as the church- or university related welfare organisations which were interviewed in this case study. According to the TSE concept, the role of these organisations is to address social concerns and to mobilize volunteer activity (Salamon, Sokolowski 2018). This is necessary whenever it is not economically attractive for the private sector to get involved, and in cases where the beneficiaries are dependent on state assistance but the public sector cannot provide the required type and nature of the services and assistance, especially if those are highly individual (Schubert, Klein 2018).

A much discussed characteristic of local economies is “local embeddedness” (Läpple, Walter 2003). It refers to the embeddedness of a neighbourhood’s economy in broader contexts, such as the regional or global economy. But – as is the case in this contribution – it also refers to the embeddedness in local actor structures, also referred to as socio-economic embeddedness (Granovetter 1985) or “social embedding / anchoring” (Henn, Behling 2019, p. 6).

The concept of socio-economic embeddedness was prominently addressed by Granovetter (1985). He argues that “the behaviour and institutions to be analysed are so constrained by ongoing social relations that to construe them as independent is a grievous misunderstanding” (Granovetter 1985, p. 482). The embeddedness argument highlights the importance of personal relations for building trust and preventing misconduct. The local level has a greater role to play in this argument, as the spatial proximity it provides increases the chances of getting to know your counterpart personally. But spatial proximity is not a compulsory requirement in times of digitization. In his work, Granovetter (1985) emphasises the general applicability of the concept, and indeed, its application to the local economic context can be traced in existing literature (e.g. Boschma 2005, Wittmayer, Loorbach 2016).

According to Läpple, Walter (2003), the local embeddedness mainly results from four aspects. First, the customers of the business mostly come from the neighbourhood or via cooperation partners working together with the locally based business in the production or marketing of goods or services. Second, the employees live in the neighbourhood where they work. Third, the business owners live in the building, where their (work)shop is located or in the immediate vicinity. Forth, the local context has the function of a business contact or information exchange platform and provides information regarding potential employment and cooperation opportunities or the initiation of new business relationships. The last argument is especially closely related to the function of communication and integration. With regard to the residents but also people from other parts of the city, gastronomic businesses fulfil a particularly important task as a meeting place for information exchange (Jakubowski, Koch 2009, p. 242).

Locally embedded businesses have a close interrelationship with their neighbourhood, which is expressed in a twofold way. On the one hand, they have a decisive influence on the quality of work of the employees and the quality of life of the residents in the neighbourhood; on the other hand, they are dependent on various location factors and possible synergy effects, which can entail both, development opportunities and obstacles (Läpple 2013, p. 135). The underlying assumption is, that a strengthened socio-economic embeddedness favours an overall positive neighbourhood development, as local economic actors are more concerned with their neighbourhood’s development.

[1] According to this concept, to be considered as part of the third sector, entities must exhibit the following five features: organisations (in terms of “some institutional reality”), private (in terms of “not being controlled by government”), self-governed (in terms of bearing “full responsibility for economic risks or rewards”), noncompulsory (in terms of “participation with the organisation must be free of compulsion or coercion”) and totally or significantly limited from distributing any surplus they earn to investors, members or other stakeholder (Salamon, Sokolowski 2018).

In the context of this paper, the term "deprived neighbourhoods" refers to the definition used in the German urban development programme "Soziale Stadt" (Deutsches Institut für Urbanistik 2003). It relates to "highly densified and densely populated neighbourhoods in urban areas that show considerable deficits with regard to their social structure, the building stock, the range of jobs, the level of education, the provision of social and neighbourhood cultural infrastructure, the quality of the housing, the residential environment as well as the overall environment" (Deutsches Institut für Urbanistik 2003, p. 298; author's translation). These deficits are often caused and exacerbated by socio-spatial segregation. They mostly concern inner-city or near the inner-city (industrial) neighbourhoods as well as large housing estates on the outskirts (Krummacher et al. 2003).

In search of development options for deprived neighbourhoods, the local economy is often discussed in connection with endogenous potential. A comprehensive overview regarding the varying operationalisations of this term in theoretical concepts is given by Antonescu (2015). However, within the scope of this contribution, endogenous potential is understood along the lines of Rommelspacher (1997). He defines endogenous potential as the opportunities arising from existing sector structures and their interconnections, historically and culturally co-determining factors as well as people and institutions, that can be involved in local-economic development strategies either because of their mission (e.g. welfare associations, church communities, local associations) or because of specific, local interests. This understanding of endogenous potential stresses that a sole focus on private sector actors is not enough to deal with the challenges faced by deprived neighbourhoods. Following this line of thought, the mobilization of all actors, including non-economic actors and non-market-mediated forms of welfare production, seems necessary (Rommelspacher 1997). In this regard, Birkhölzer (2000) emphasises that a positive development of deprived neighbourhoods from endogenous potential is only possible, when a community or at least parts thereof act with an economic mind-set. Brandt, Gärtner (2016, p. 6) also argue that "the entire economic activity in a neighbourhood should be taken into account and that the exchange processes and networks between private/commercial, public/communal, the creative sector, the pioneers and do-gooders as well as the informal/non-governmental sector should be examined and promoted or initiated" (author's translation). Läpple, Walter (2003) specify that the main ingredients for the development of endogenous potential by groups of civil society actors are local embeddedness, trust and acceptance in a community. In addition, Birkhölzer (2000) argues that places are unique, and that their richness derives from the specific combination of individual factors, i.e. in the synergies resulting from endogenous potentials.

The described concept of endogenous potential is closely connected to the willingness to take responsibility for other community members, not just for one's own interests. Accordingly, solidarity is described by Bude (2020, p. 26) as "practices of responsibility for others" (authors' translation). This understanding of solidarity is closely related to Durkheim's 'mechanical solidarity' referring to a shared "collective conscience, a common body of beliefs and sentiments that give individuals a feeling of belonging to the group" (Giuffre 2013, p. 31). Alternatively, a rather network-based understanding of solidarity relates to 'cohesion' in terms of "the degree to which members of a community are actually tied to each other, either directly through personal contact or indirectly through joint group membership" (Giuffre 2013, pp. 31-32).

Birkhölzer (2000, p. 13) discusses the role of "windows of opportunity" fuelled by endogenous potential as follows (authors' translation): "In crisis regions (...), the local level of action and thus the community plays a key role, whereby the disintegration associated with the crisis – possibly previously regarded as irrefutable or overpowering – from interdependencies (...) can also be seen as an opportunity for a new beginning, an independently defined development (or independent regional development)". This positive notion can also be found in literature on crisis research.

2.2 *Crisis as an Opportunity*

Crises are conceptualized differently in a variety of disciplines. In the context of disaster research, Boin, 't Hart (2007) refer to a crisis as the gap between an actual and a desired state, which simultaneously fulfils the following three characteristics: (existential) threat, urgency and uncertainty. The existential threat relates to major societal assets. In the case of the COVID pandemic, those include, amongst others, public health, economic interests and behavioural patterns of social interactions. The characteristic of urgency points to the need for action, despite high levels of uncertainty. Inactivity would aggravate the situation, e.g. cause the uncontrollable spread of the COVID virus. The willingness to become active and to cooperate is further strengthened by the perception of external threat (Stöhr 1992). The final characteristic of uncertainty is the lack of knowledge of what will happen in the future and how individual options for action will impact the overall situation (Brinks, Ibert 2020).

In contrast to the above mentioned idea of fast intervention due to high urgency, Birkhölzer (2000) argues that organized economic self-help (the mobilization of endogenous potential) is rather delayed in communities hit by a crisis in the context of structural change processes caused by deindustrialisation and globalisation. According to him, the process of organized economic self-help in communities only commences after a phase of prolonged waiting and vain hope for relief as a result of external remedies from above (the state) or from outside (investors). Perhaps the reason for this is that the onset of this type of crisis is less immediate and is therefore perceived as less urgent.

Unlike a catastrophe, the term crisis leaves room for manoeuvre to improve the situation. Or, in other words, a positive course of events is still possible, depending on agents' individual or collective will and power to create it (Kornberger et al. 2019). These considerations emphasize the importance of human agency, defined as "the ability of people to act, usually regarded as emerging from consciously held intentions, and as resulting in observable effects in the human world" (Gregory 2009, p. 347). These reflections also lead to the questions of what (windows of) opportunities are perceived, and how they are exploited during a crisis.

As mentioned above, the connection to the terminologies of crises and (windows of) opportunity rests also in the considerations of local economy research. It is expressed in the assumption that a crisis can act as an opportunity for reset, a new starting point for a more independent local economic development (Birkhölzer 1993). However, it should be borne in mind that Birkhölzer's remarks refer to structural change-induced, spatially limited economic and employment crises, i.e. situations in which the activation of endogenous potentials can be verifiably helpful (Stöhr 1992). As Stöhr (1992, p. 8) argues, in the case of restructuring processes in old industrial core areas of Europe, "the magnitude of crisis symptoms surpassed central government capacity" and triggered strong local initiatives. However, the COVID crisis has a different background and global impact. Although local economies and their actors are certainly among those affected, it is not an economic crisis at its core, and the medium- to long-term consequences for local economies are still unclear. This is particularly important when considering that the study period for this paper was shortly after the so-called first wave of the COVID crisis in Germany.

Within transition management research, a crisis is conceptualised as an event or chain of events, which has the power to lead to systemic changes in terms of transitions towards sustainability. It is yet unknown whether the COVID crisis will fall into that category.

Nevertheless, specifically referring to the COVID crisis, Schneidewind et al. (2020) predict three main areas (proximity, publicity, agility) for windows of opportunity towards a more sustainable development on the local or rather urban level. Amongst others those include a greater cohesion within and between neighbourhoods and municipalities as well as the expansion of local economic cycles. According to Schneidewind et al. (2020), the crisis highlights the meaning of local solidarity.

Contrary to the generally rather negative connotation of the concept of crisis, Newig (2013) elaborates on four productive functions for sustainable development that are inherent in crises, and underlines the importance of agency. These functions include learning from failed attempts, triggering adjustments in existing systems towards sustain-

Table 2: Typology of change processes in relation to the preservation or collapse of structure and function

Intensity of the dimensions	Structure Preservation	Structure Collapse / complete reorientation
Function Preservation	Type 0: Stable System	Type 1: System-Transformation / Adaptation
Function Collapse / complete reorientation	Type 2: Path-depended reorientation	Type 3: System Collapse / completely new creation

Source: own representation based on Newig (2013, p. 142)

ability, the targeted use of destabilization of non-sustainable structures as an instrument for creating space for the development and implementation of more sustainable structures, and the targeted management of decay processes to achieve a new desirable state. Newig's explanations are based inter alia on considerations of Luhmann (2018) regarding social systems and the ecology-oriented panarchy approach developed by Gunderson, Holling (2002). In both schools of thought, crises are assigned a productive and renewing function. Following this logic, systems are dependent on constant disintegration, as ongoing disintegration creates space and demand for successor elements. Disintegration is thus a necessary contributory cause of reproduction. Accordingly, a crisis serves to ensure the incessant renewal of the system elements and not, as in classical equilibrium theories, to return to a stable state of rest after absorption of disturbances. In this context, Newig (2013, p. 137) also refers to "dynamic stability". Brinks, Ibert (2020) are not so clear in this respect. They offer a description of a typical course of a crisis in phases, which ends with the "(re)turn to [a] (new) normality" (Brinks, Ibert 2020, p. 4). Overall, these considerations suggest that the local economy and its reactions to the COVID crisis are best analysed from a process perspective.

Referring to the productive functions inherent in a crisis, it seems obvious that a destabilization alone does not lead to more sustainable structures. The central question is therefore: under what conditions and to what extent do destruction and destabilization actually lead to innovation[2] and a positive system transformation (Newig 2013). This consideration is also applicable to the context of local economy and the COVID pandemic. A useful tool for structuring possible scenarios is the typology of change processes in relation to the preservation or collapse of structure[3] versus function developed by Newig (2013). As illustrated in Table 2, a stable system (type 0) is characterized by the preservation of structure and function. System-transformation or rather adaptation (type 1) occurs when the function is preserved while the structure collapses and needs to be reorganized. In contrast, a path-dependent reorientation (type 2) is characterized by the preservation of structure while the according function collapses. The last type (type 3) of complete system collapse is marked by structural as well as functional collapse. However, in practice, the change processes during a crisis are highly dynamic, overlapping and are therefore hard to delimit. It is less about complete collapse, but rather about tendencies in the context-related interaction of structure and function.

2.3 From Crisis to Sustainable Transition

Relating above considerations to urban sustainability transition management research, it is important to highlight the role of neighbourhoods as basic building blocks of cities, which simultaneously combine the core problems of sustainability as well as all the elements for their solution (Brocchi 2018). There is a considerable overlap between

[2] An innovation is defined as "an idea, practice, or object that is perceived as new to an individual or another unit of adoption" (Rogers 2003, p. 1).

[3] Newig (2013) suggests ten social structural categories relevant to sustainability, which mostly are applicable to the local economy: states and societies, organisations, social-ecological systems / utilization systems, socio-technical systems, built environment: urbanization, built structures, culture and social cohesion, social capital, civil society, education, values and norms, networks, regulation / governance: laws and process forms, communication systems (Luhmann) and public opinion and awareness.

the prerequisites for successfully releasing endogenous potential at the local level and the local level's relevance for comprehensive, overarching transformation processes toward sustainability. In this regard, Vázquez Barquero (2002) outlines the connection between the theory of proximity and the development of endogenous potentials in urban contexts. The smaller spatial unit promotes personal proximity[4] and hence does justice to "the human measure" (Brocchi 2019, p. 250). It enables an emotional identification with the neighbourhood, facilitates social interaction and has a positive effect on relationships of trust. This shapes the sense of community, enables collective action (synergies) and promotes the experience of self-reliance and self-efficacy (Brocchi 2019).

A well-established concept in the transition management literature is the multilevel perspective (MLP) framework. The framework consists of three levels. The niche level describes protected spaces, where innovations can flourish (Geels 2011). The regime level comprises technologies, institutions and actors (Holtz et al. 2008). The subordinate landscape level encompasses norms and values or rather "a set of deep structural trends" (Geels 2002, p. 1260). According to Geels (2002), radical innovations are usually generated in niches, while incremental innovations are created on the regime level. Changes on the landscape level are even harder to realize and are slower. But once achieved, they can generate new opportunities for niches and put pressure on the regime level for change (Smith et al. 2010).

One of the framework's ideas is that all three levels need to convene in order to promote change or rather a transition. First, innovations need to be developed and wait to be exploited on the niche level (bottom-up pressure). Second, values, norms, etc. on the superordinate landscape level need to have evolved demanding changes on the regime level (top-down pressure). Third, a crisis or shock needs to destabilize the status quo of the regime level providing new scope for action or rather a so-called "window of opportunity" (Grin et al. 2010, p. 88). From a multilevel perspective, the authors argue that the COVID pandemic can be interpreted as an external shock to the system resulting in a destabilization of the regime (local economy) and thus creating many challenges as well as windows of opportunity for change. The latter include opportunities for the diffusion of innovations from the niches on the regime level in order to adapt to the new circumstances, changing the regime but also the landscape. In this regard, it is important to consider that the diffusion process is not the starting point of an innovation but "that relevant activities and decisions usually occurred long before the diffusion process began" (Rogers 2003, pp. 136-137), typically on the niche level.

3 Methodology

The exploratory single case study was realized in the medium-sized cities of Mönchengladbach and Krefeld in the Middle Lower Rhine region in Northrhine-Westfalia, Germany (see Figure 2).

The locations were selected because they qualify as "deprived neighbourhoods" in a twofold way[5]. The above mentioned challenges of deprived neighbourhoods are often found in cities that underwent massive structural change processes in the course of globalisation or rather de-industrialisation. This is also true in the case of the crisis in the textile and clothing industry in Mönchengladbach and Krefeld. The migration of the textile and clothing production since the 1960s transformed both cities into typical examples of old industrial towns showing the classic symptoms of deprived neighbourhoods. In addition, the omnipresent crisis in the retail trade in Germany did not leave Mönchengladbach and Krefeld unaffected either. The rise of online trading, declining customer frequencies and struggling local retail reinforce functional change processes in both inner-city areas. The situation is further aggravated by the COVID crisis (Bunzel, Kühl 2020).

[4] Personal proximity refers to "cities as living environments in which people have personal, emotional, and social stakes, including socially embedded relations and a level of trust" (Wittmayer, Loorbach 2016, p. 15). The different notions of proximity are further elaborated in the work of Boschma (2005).

[5] Both inner-cities participate to date in urban development programs applying the definition of deprived neighbourhoods presented in Section 2.1 (Bundesministerium des Innern, für Bau und Heimat 2021).

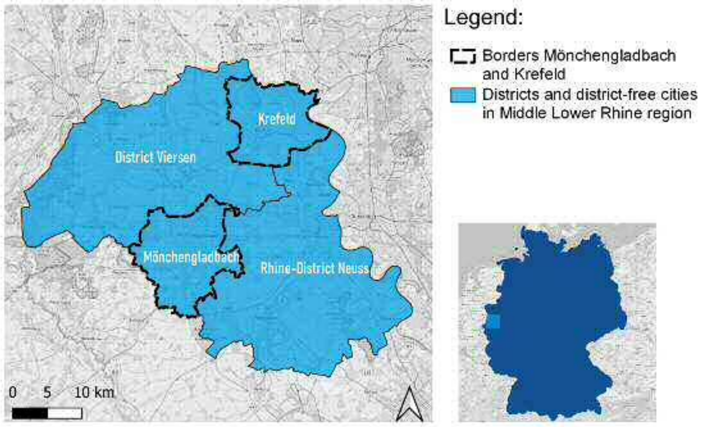


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Figure 2: Map of the Middle Lower Rhine region in Germany

Most of the interviewees are from organisations located in or in close proximity to the inner cities. Their services and products are primarily aimed at the neighbourhoods' residents, but are also available to the entire city (or even regional) audience. In both cases, the residents of the inner-city neighbourhoods can be characterised as younger, poorer and more culturally diverse with higher shares of unemployment and more individuals receiving transfer payments compared to the citywide average (Hamm et al. 2017, Stadt Krefeld 2020, Stadt Mönchengladbach 2019). Although both (inner-)cities have individual characteristics, they are understood as largely homogeneous in the face of the challenges described above and therefore considered as one unit in the context of this case study[6].

The research questions were initially addressed by means of a focus group discussion (on the 13th of July 2020) with six multipliers working in several fields related to local economy development[7]. Subsequently, thirteen exploratory guideline-based interviews were conducted between the 17th of August 2020 and the 14th of October 2020, or rather some months after the end of the first lockdown (22nd of March until the 30th of April 2020 (Mitteldeutscher Rundfunk 2020)) and two weeks before the announcement of the more stringent measures for November 2020 (second light lockdown in Germany).

Regarding the choice of interviewees, three selection criteria were applied. First, the organisation's affiliation to the local economy as discussed in Section 2.1. This includes entrepreneurial activity in the broadest sense as well as its embeddedness in the local economy (see criteria in Section 2.1). Second, with reference to the four functions of the local economy, all the selected organisations provide services that are closely linked to integration and communication. With exception of a gastronomy business (private sector) and a cultural office (public sector), all interviewed organisations belong to the TSE sector (see definition in Section 2.1). As illustrated in Table 3, the selected organisations are involved in areas of community development, art and culture, integration, youth, adult and family education, sustainability-oriented initiatives and gastronomy – activities that inherently promote communication and integration. More than half of the organisations work closely with volunteers, thereby contributing to the mobilization of endogenous potential; bringing people together is even part of their official mission. Third, the interviews were conducted with the heads of the corresponding organisations to ensure a comprehensive perspective on the organisations' problems and windows of opportunity related to the COVID pandemic.

Table 3 indicates the organisations' names, fields of activity, forms of organisation, locations (city) and sectors.

[6] A location-based comparison of the interview results was carried out, but did not yield any relevant differences, which is why it will be dispensed within the context of this contribution.

[7] A complete overview of the focus group participants can be provided on request.

Table 3: Overview of organisations included in the case study

Organisation	Field of activity	Form of organisation	City	Sector
Krefelder Kunstverein e.V.	art and culture (organisation of exhibitions and the like)	non-profit-making association	Krefeld	TSE
Bürgerinitiative Rund um St. Josef e.V. (Jugendfreizeitstätte, Jugendkunstschule, Familien- und Weiterbil- dungsstätte)	youth work, youth and family education, art and culture	non-profit-making association	Krefeld	TSE
Kulturfabrik Krefeld e.V.	art and culture (organisation of exhibitions, concerts and the like)	non-profit-making association	Krefeld	TSE
Kulturbüro Krefeld	art and culture (organisation of exhibitions, concerts, theatre performances and the like)	part of the city administration	Krefeld	second (public) sector
Repair Café Krefeld	repair Work	volunteer initiative at LAKUM, the catholic university center (Facility of the Diocese of Aachen)	Krefeld	TSE
Katholisches Forum	adult and family education	non-profit-making association	Krefeld	TSE
Nachbarschaft Samtweberei gGmbH	co-Working spaces	non-profit private limited company	Krefeld	TSE
Repair Café Mönchengladbach	repair Work	volunteer initiative at non-profit-making association "Deutscher Paritätischer Wohlfahrtsverband Landesverband Nordrhein-Westfalen e.V."	Mönchengladbach	TSE
Mönchengladbach im Wandel e.V.	operation of community gardens, environmental protection and education	non-profit-making association	Mönchengladbach	TSE
Kulturküche e.V.	integration and rehabilitation of addicts, Café business, art and culture (event location)	Employment and socio-cultural project of the non-profit Intres gGmbH	Mönchengladbach	TSE
Kulturlöwe Niederrhein e.V.	art and culture, cultural participation, families and cultural encounters	non-profit-making association	Mönchengladbach	TSE
Verein Wohlfahrt e.V.	support and reintegration of homeless	non-profit-making association	Mönchengladbach	TSE
Club der Wirte	representation of interests for gastronomes in Mönchengladbach	informal representation of interests	Mönchengladbach	first (private) sector

Source: own representation

Note: TSE . . . Third or social economy

The standardized interview guide included questions about the interviewee's own function and general information on the represented organisation (year of foundation, form of organisation, number of employees and type of employment, mission, local reference, field of activity, funding, etc.). It also addressed the challenges caused by the COVID pandemic, implemented and planned (counter)measures and innovations as well as an assessment of the future development of their organisation and the local economy in the next months.

The conducted interviews were examined via qualitative content analysis according to Mayring (1994). First, relevant items were derived from the interview material. Second, these items were structured in categories[8]. Third, the categorised items were analysed

[8]Following this approach, it turned out that the mentioned challenges could easily be sorted according

in a cross-tabulation across all interviews. The resulting overview allowed for a clear identification of the frequency of the mentions of each category, providing indications regarding its relevance.

With regard to limitations, it should be kept in mind that the findings presented in the analysis and discussion sections are the result of a limited number of interviews held in a very specific context. Applying the findings and recommendations to other (locational) settings should be done with care, as the preconditions there might be quite different.

4 Analysis

In relation to the first so-called "lockdown" in Germany (22nd of March until the 30th of April 2020) and the following weeks, the participating organisations can be divided into three groups:

- those which stopped all activities (mostly due to legal requirements),
- those which were not allowed to offer their typical services and products but used the time otherwise and
- those which could operate and adapted their services to fit the new circumstances.

To the authors' knowledge, none of the organisations remained completely unaffected, but while some had to stop all activities, others could almost pursue business as usual. This variance is already a first indication of the diversity of the impact of the COVID pandemic on the local economy.

4.1 Challenges along the key characteristics of crisis

The analytical findings regarding the challenges for the local economy during the first wave of the COVID crisis will be presented in the following section alongside the three main dimensions of a crisis – (existential) threat, urgency and uncertainty –, as outlined in Section 2.2.

4.1.1 (Existential) Threat

According to the analysis, the threat concerns three main dimensions: first – the threat to social livelihood due to cancelled or minimized range of services and products offered; second – the threat to economic livelihood; and third – the threat to individual health from the virus itself.

Threat to social livelihood: The perception and impact of this threat varies greatly depending on the services and products offered and the concerned target group. While the services of a volunteer art association targeting better off pensioners from the educated middle-class seem dispensable for a few months, the clientele of meal centres for the homeless will have a hard time without them. In this regard, the dependency of local public welfare services concerns especially the already disadvantaged or marginalized social groups. Other examples from the interviews concern children and youth from low-income families or the elderly, who are confronted with loneliness and isolation by breaking away from socially engaging offers. As their accessibility to services could already be a challenge before the COVID pandemic, it became even more difficult. Nonetheless, all social groups feel the impact of the measures against the spread of the COVID virus to a certain extent in their daily lives. In this sense, the threat consists of the hardly accessible social consequences of a longer crisis period.

Threat to economic livelihood: The negative economic effects are omnipresent. They affect amongst others the traditional retail trade and chain store business, but also gastronomy and the culture and event industry (Clemens et al. 2020). The latter two suffer from underutilization of their premises due to social distance regulations or complete closure.

to the three main characteristics of a crisis.

The change in the legal regulation in Germany, which restricted non-profit associations to building up financial reserves only to a very limited extent (§55 Abs.1 Nr.5 AO, 2013, BGBl. I p. 556), was especially significant to most of the interviewees. As a result of this change non-profit associations are left ill-equipped to operate for several months without or with reduced income in the event of a crisis. This is especially true if they do not have any kind of third-party basic funding, e.g. from the municipality.

Almost all interviewees confirmed the financial survival of their organisations until the end of the year 2020. The only exception was the representative of the gastronomy business, who predicted that half of the gastronomic facilities in his city would close by the end of the year (interview 9). For the rest, the spectrum of economic threat is very wide, ranging from concerns about survival beyond 2020 to the relaxed certainty that basic funding will continue unaffected by the crisis. But the mood among organisations without or with little external subsidies was very critical. Since the end of the pandemic was not in sight at the time, the interviewees expressed their concerns regarding developments over the next one to three years.

Threat to individual health: This threat translates into potential customers' fear of contagion, a frequently mentioned aspect in the interviews. For parts of the population, it leads to reluctance to participate in events, restaurant visits, etc. and thus limits the utilization of the said events. This can lead to events or establishments, with an already reduced number of seats due to social distance regulations, being not fully utilized. Thus, the economic efficiency of the corresponding organisations is affected in a twofold way.

The fear of contagion, however, does not only affect the profitability of several organisations, but also their core activities or rather their mission. This is especially true for the function of integration and communication: embedding people in their neighbourhoods and promoting social interaction and cohesion (see social livelihood). But also, other missions such as promoting sustainability (e.g. with services in repair cafés), can be hampered.

The interviews also hint at a further aspect related to individual health: the double burden of people who are not just privately affected by the COVID pandemic, but also professionally. The interviews show that the COVID pandemic has led to additional workload for organisations which kept working throughout the time of lockdown: observing and implementing new regulations, elaboration and realization of hygiene practices, developing alternative products and services. This extra work required resources in terms of working hours, creativity as well as emotional and social competencies. The consequent threat of exhaustion refers to a range of interview statements including, amongst others, the emotional state of employees, the challenge to handle childcare and work simultaneously, or the readiness for holiday after the lockdown.

4.1.2 Urgency

It might be argued that in deprived neighbourhoods with a long history of economic decline, the sense of urgency regarding economic developments is diminished and may even be replaced by a feeling of resignation. Nevertheless, the COVID pandemic and the severity of the sudden lockdown have given rise to urgency, even in the neighbourhoods in supposedly long-term crisis mode.

The interviews reveal that the urgency to adapt to the new situation varies among the actors. Apparently, one major aspect influencing the degree of active adaptation and willingness to innovate is the financial compensation for the work. On the one hand, unpaid voluntary work tends to be at a standstill or shows only a reluctant implementation of the most necessary means to continue the previous activity (such as a hygiene concept). On the other hand, paid employees are much more willing to find creative solutions and reorganize their services. The interviews hint at the following explanations:

First, the most essential local welfare services are in public hands (second sector) or at least supported with basic funding. Thus, they are secured with paid work, while unpaid volunteer work can be suspended temporarily.

Second, regardless of their willingness to work, volunteers do not have access to the premises typically used for their activities, as those are provided by third parties, which are responsible for decisions regarding the opening and closing of facilities.

Third, volunteers do not feel the economic (financial) pressure to be entrepreneurially active in terms of fast adaptation while paid workers must – to a certain extent – provide proof of performance, whether to their employer or third-party funding agencies. In this sense, standstill is not an option, since it would lead to job loss.

Fourth, the general problem of obsolescence in associations has a double impact during the COVID pandemic. On the one hand, many volunteers are part of the risk group, which explains and justifies their reluctance. On the other hand, they often lack the necessary know-how to develop and use potential solutions in the field of digitization, which will be discussed further as a window of opportunity in Section 4.2.

In addition to these higher-level observations regarding the remuneration of work, the analysis also shows that the individual perception of urgency and the corresponding level of engagement of actors varies greatly. Individual actors with above-average commitment, who acted as forerunners, could be found both in unpaid and paid positions. Illustrative examples include the founder of the "Support Your Local Heroes" initiative (König 2020, MitGedacht.-Block 2020)[9] as well as the head of an open meeting place for the homeless, who decided to keep the premises open during the weeks of lockdown while all similar organisations in neighbouring cities were closed (interview 13). This observation supports the importance of individual agency discussed in Section 2.2.

4.1.3 Uncertainty

Regarding the question of the future development of the individual organisations and the local economy in times of COVID, the analysis illustrates the high level of uncertainty that unites all interviewees. The uncertainty is usually expressed in statements regarding non-plannability or a very short-term planning horizon and the constant expectation that the course of events will render all plans invalid. Notwithstanding the above, the interviewees have quite different levels of optimism or pessimism when it comes to predicting the development of their own organisations and the local economy. The spectrum varies from pure optimism to despair. In this sense, uncertainty does not necessarily lead to a negative view on future developments.

4.2 Windows of Opportunity, Incremental Innovations and Landscape Changes

In terms of windows of opportunity, the analysis reveals several aspects which can be sorted according to their temporal consistency as well as to their potential regime or landscape changing impact. Table 4 gives an overview of the short-term as well as potential medium- to long-term adjustments, which were revealed by the analysis.

4.2.1 Short-term adjustments

Except for those who have not completely stopped their activities because of the lockdown, most interviewees came up with means and services, which were feasible during the lockdown and under COVID related regulations. Some of these means – although justified in the acute crisis – will prove to be obsolete when the COVID related restrictions no longer apply. Thus, those means provide short-term solutions, but probably do not bring about any long-term adjustments in terms of changes on the regime or landscape levels. These short-term adjustments include the following:

First, tidying up, sorting, repairing, renovation and beautifying work – during the weeks of the lockdown.

[9] The initiative was started by an engaged citizen. Supporters can buy a T-Shirt worth 20 Euro. The revenue less costs of production are donated to local companies.

Table 4: Windows of Opportunity according to their temporal consistency and level (MLP)

Short-term adjustments without lasting impact	Medium- to long-term adjustments (incremental changes on regime level)	Medium- to long-term adjustments (changes on landscape level)
• Tidying, sorting and renovation work; • Alternative products and services; • Elaboration and implementation of hygiene concepts • Increased use of outside areas; • Cooperation for the use of larger or alternative premises	• Digitization (cashless payment, online booking systems, digitization of course offers, streaming of cultural events) • Introduction and expansion of home-based work (new life and working environments)	• Solidarity and cohesion between local actors

Source: own representation

Second, particularly the organisations which continued working throughout the lockdown focused on the elaboration and implementation of alternative products and services in order to continue to serve their target groups and stay in touch. Examples include, amongst others, online streaming of cultural events, the compilation of bags with toys, painting and handicrafts for children from low-income families, letter writing, "read aloud" phone calls, shopping support and cultural walks.

Third, adaptation measures related primarily to the development and implementation of hygiene concepts were mentioned in all, but two interviews. According to the interviews, the event industry has very few opportunities to switch to other services. Discotheques and providers of large premises for concerts and major events are affected by high fix costs in terms of rent or rental fees for the premises. Rather than on own innovations, hopes are pinned on subsidies and new hygiene concepts inspired by new scientific findings on the spread of diseases at major events (Universitätsklinikum Halle (Saale), Medizinische Fakultät der Martin-Luther-Universität Halle-Wittenberg 2020).

Fourth, the increased use of outside areas in order to avoid gatherings in closed rooms was mentioned several times, especially by interviewees with gastronomic offers but also as a way to provide seating and conversation opportunities.

Fifth, cooperation for the use of larger or alternative premises for group events appeared in several interviews. Those, who actively sought larger premises in order to realize their meetings under the new safety requirements, always found solutions. New collaborations were started in order to fill newly unused spaces with events that were formerly held in smaller rooms.

4.2.2 Medium- to long-term adjustments (incremental changes on regime level)

Furthermore, the interviews revealed some windows of opportunity with the potential to contribute to lasting changes on the regime level. These include the following:

First, digitization: At least four interviewees mentioned the implementation or expansion of digital products and services (introduction of online booking system, digitization of course offers, online streaming, increased use of cashless payment). In addition, all interviewees described the new or expanded use of digital communication solutions in their work processes.

Second, home-based work and team communication: More than half of the interviewees reported the introduction or expansion of home-based work. They indicated that they believe it will become a permanent fixture in terms of new life and work environments. Most interviewees state that – so far – the overall communication within the organisations did not suffer from alternatives to classic face-to-face communication, including telephone calls, video conferencing and chats. However, the interviews also suggest that home-based work and the associated use of digital communication solutions reinforces pre-existing trends in terms of group communication, both positive and negative. Besides, the authors assume that the effects also depend on the duration of the sole use of digital communication solutions, since informal, yet important intermediate talks are largely absent if no conscious countermeasures are taken.

4.2.3 Medium- to long-term adjustments (changes on landscape level)

The interviews reveal changes in behavioural patterns of interaction, which can be assembled under solidarity and cohesion. As explained below, the authors assign these changes in behavioural patterns of interaction to the landscape level, as they are rooted in a changed prioritisation of values and norms.

According to the interviews, humility, gratitude for local infrastructure as well as the support to local companies are more present since the beginning of the COVID pandemic. They are expressed verbally by customers, but also in their behaviour (norms). Apparently, the shortage of offers due to the lockdown and the following restrictions have increased the customer's awareness of their benefits and made some of them humbler towards their overall living situation.

The analysis suggests that this emotional realignment translates into a strengthened sense of solidarity and cohesion among the actors in the local economy. Examples from the interviews include, amongst others:

- increased cooperative attitude of actors in the local economy, e.g. the public order authorities and customers
- strengthened awareness for consumption of local services and products
- successful crowd funding initiative
- strengthened willingness to donate and support local businesses
- increased awareness for hygiene and the avoidance of infection
- new offers to increase the sense of community

Another important aspect in the discussion of strengthened solidarity in the local context refers to cohesion. The analysis indicates an increase in networking activities, on the one hand in existing networks and on the other hand through the creation of new networks. This is illustrated by these statements: "In my opinion, all the networks that were already – latently – present, work better now. The longing for cooperation is greater." (author's translation, interview 12). In this context, the hopes also relate to the sustainability of this new quality in cooperation, ideally beyond the time of crisis: "Even after Corona, no one will be able to take this network and this togetherness away from us. No matter what anyone needs or what is going on, we will cooperate, and we will create shortcuts in a dimension, that has never existed before." (author's translation, interview 12).

The most prominent examples of newly formed networks mentioned in the interviews include the initiatives "Corinna e.V." (CORINNA e.V. 2020)[10] and "Support Your Local Heroes" (see Section 4.1). However, in both cases, the new networks were formed based

[10] The association of cultural actors in the city of Mönchengladbach was initiated within the first two weeks of the lockdown by an entrepreneur and cultural worker in the entertainment industry, who contacted his professional network via email demanding common action to maneuver together through the coming crisis.

on existing informal networks. They were not created in a vacuum, but through the expansion and reconnection of pre-existing relationships.

Nevertheless, the analysis also shows opposing trends. For example, one interview and a statement from a focus group participant confirm that local networking events were postponed for several months due to the COVID pandemic. According to the interviewees, postponing resulted from the fact that the actors concerned were busy maintaining or adapting their own business activities to the new circumstances with no time left for community-oriented tasks. Another explanation refers to the lack of experience with digital meeting formats, especially of older actors, which prohibited a quick adaptation. One further example for the ambivalent relationship towards solidarity is the rather cynically formulated statement regarding the "opportunity of market cleansing" (and thus decrease in competition) thanks to the COVID pandemic.

5 Discussion

Overall, the analysis shows an ambivalent picture regarding the extent to which the COVID pandemic has been affecting the local economy in deprived neighbourhoods in the cities of Mönchengladbach and Krefeld. The interviews do not illustrate a mere downward spiral, but rather opposing effects in a complex process. On the one hand, the individual economic actors are heavily weakened by the measures against the spread of the COVID pandemic. On the other hand, a strengthening of solidarity-oriented behaviour among the actors can be observed. In addition, existing trends towards new life and working environments (home-based work) and digitization are propelled. The different and in part opposite processes weaken and strengthen the socio-economic embeddedness of the local organisations simultaneously. The authors assume that the negative effects will come to a halt as soon as the measures against the spread of the COVID virus are revoked. In contrast, the positive effects in terms of digitization, new work environment and local solidarity are expected to have a lasting effect, changing the regime and landscape levels. In this case, the COVID pandemic would strengthen the socio-economic embeddedness of local actors in the long run.

With reference to the research question regarding the major challenges and their reflection in the typical characteristics of a crisis, the analysis confirms that the findings fit well in the three main dimensions of a crisis; namely (existential) threat, urgency and uncertainty. The findings related to the perceived urgency and the role of remuneration illustrate how important it is not to leave essential local welfare services entirely to voluntary work, but to anchor them institutionally or at least to secure them with basic funding, whenever the target group of services should not remain unattended for a longer period. If those services are covered by paid work, faster rates of adaptation in times of crisis can be expected. The question of which services are most essential cannot be discussed conclusively in this paper. Furthermore, the analysis suggests that a short-term suspension of volunteer activities may not have a major impact. But a medium to longer-term standstill is likely to have worrying consequences in terms of integration and communication, especially in already deprived neighbourhoods relying on their endogenous potential. Therefore, the development of volunteer activities should be given special attention, and supporting measures should be envisaged.

Overall, the search for potential windows of opportunity in the local economy illustrates that it is a matter of standstill or selective incremental adjustments, rather than ground-breaking innovations. Especially organisations committed to the function of integration and communication suffer greatly from the limitation of spatial proximity and the resulting negative effects on personal proximity. Nonetheless, the research question regarding perceived windows of opportunity revealed the two medium- to long-term adjustments – digitization and home-based work. Both trends already existed before the COVID pandemic, but the crisis acts as a catalyst, accelerating the diffusion process and the incremental changes on the regime level (see Section 2.3). In accordance with the considerations within the MLP framework, the analysis shows that the technical prerequisites, e.g. digital communication solutions, were successfully developed on the niche level before the crisis and were therefore promptly available. The COVID pandemic provides the necessary pressure to disseminate them on the regime level and to ensure that they transform the life and work environment. Nevertheless, the analysis also shows partly opposing trends. None of the potential windows of opportunity at regime or landscape levels is free of contradictions. The "pre- COVID" quality of team communication and networks is also amplified during the crisis, for better or worse. The finding that new networks were built through the expansion and reconnection of pre-existing relationships further suggests that neighbourhoods with well-established network structures are at an advantage in mobilizing endogenous potential and can increase their speed of reaction in times of crisis. Referring to digitization, the analysis reveals that while it can help facilitate some tasks and opens additional communication channels, it is not suitable for all products and services. Offers targeting the function of "integration and communication" especially often depend on spatial and personal proximities. Organisations in this field often deal with social groups with limited or no access to digital services (e.g. children from low-income households, homeless people or elderly people). In this regard, the analysis uncovers problems related to digital inequality. Therefore it will be decisive how digital innovations are designed to increase or decrease socio-economic inequality (Rogers 2003). Besides, organisations wanting to digitalise their offers first need to make significant financial investments in hardware, software and training to translate their products and services into digital formats. This can also be a barrier.

Despite these somewhat contradictory statements, the authors assume that the comparatively acute onset of the crisis, especially in form of the lockdown, and the fact that everyone was affected, greatly emphasized the sense of urgency and togetherness. In contrast to a crisis with a prolonged phase of powerlessness and inactivity, these two aspects led to a rather prompt implementation of support initiatives and solidarity attitudes. This finding relativises the idea of a "delayed response to crisis" by Birkhölzer (see Section 2.2).

The research question of how change processes induced by potential windows of opportunity reflect in the interplay between structure and function is discussed below Referring to Newig's typology (see Section 2.2), the organisations in the local economy tend to move towards the area of "system transformation / adaptation" (type 1: preservation of function and structural collapse or complete reorientation). This makes sense, as the individual organisations do not directly reinvent their field of activity, but (initially) strive to continue to fulfil their key function or rather core business despite the crisis. The interviews show that efforts are being made to continue the work, even if it is to a lesser extent or under unprofitable conditions. From an overarching perspective (and in connection with structural changes in the retail sector in general), an increased focus on the quality of stay in neighbourhoods is an essential element of future reorientation (Bunzel, Kühl 2020). This aspect was also discussed in the focus group and mentioned in several interviews. This debate is linked to a reorientation of the mix of uses in local economies and its four core functions. Those trends are accelerated by the COVID crisis. Thus, in the medium to long term, it can be assumed that functional changes will occur. As a result, the local economy will develop towards path-dependent reorientation (type 2: functional collapse or complete reorientation while maintaining structures). The extreme version of a system collapse or complete re-creation (type 3: functional and structural collapse) is a rather theoretical consideration and highly unlikely, as development processes are very dynamic and it cannot be assumed that all structures (especially the institutionalized ones) and functions will break down simultaneously, even if several organisations should be forced to give up.

Despite the limitations explained in Section 3, the analysis suggests three general conditions that can help to perceive and explore potential windows of opportunity in a crisis. First, the simultaneous and comprehensive involvement of all actors. This results in the sense of urgency and involvement triggering understanding, common action and solidarity. Second, well-established and diverse network structures allowing a fast adaptation and exploitation of potential windows of opportunity. Third, the duration of the crisis. If the crisis lasts only shortly, no profound changes might be needed nor occur. By contrast, if it lasts too long, too many actors might fall victim to the related challenges to a point of no return, where recovery is no longer possible.

Referring to the room for manoeuvre inherent in a crisis (Kornberger et al. 2019), the authors suggest the following recommendations based on the context of the presented case study:

- Organisations with essential local public welfare services should be institutionalized or financially secured. Aiming at securing these services, procedures for different crisis scenarios should also be defined.
- A special focus should be on the prompt resumption of volunteer activities, if the incidence of infection allows it.
- There should be a focus on marginalized groups and how to support them best in times of the COVID pandemic. Alternative ways to strengthen integration and communication in the local context should be sought and applied. A focus should be on creative means that help to promote social proximity while overcoming the barrier of spatial distancing.
- The aspect of digital inequality should be handled with care, with a focus on facilitating the access to digital devices and supporting digital participation processes, which allow marginalized groups to be involved.
- Regarding the aspect of solidarity, efforts should be made to support social cohesion and to counteract symptoms of exhaustion. As stated in Section 2.2, an opportunity lies in recognising decay processes and actively controlling or rather shaping them as far as possible. In this sense, promoting a vision building process regarding a desirable post-COVID future (in local economies) might be a suitable tool.
- Continuous efforts should be made to initiate and support local networking processes, as diverse, strong and even informal networks are important assets in times of crises.

6 Conclusion

The study realized in deprived inner-city neighbourhoods in Mönchengladbach and Krefeld illustrates that the mobilization of endogenous potential in the local economies is strongly affected by the measures to restrict the spread of the COVID virus. While the mobilization of endogenous potential seems to depend to a great extent on spatial and personal proximities, the restriction of the virus depends on the prevention of the latter.

The study shows how the main characteristics of a crisis reflect in the context of the local economy. The interviews reveal that the (existential) threat consists of economic considerations, the hardly accessible social consequences of a longer period without or with only a minimized range of products and services offered, the (clients') fear of contagion, and exhaustion. The three characteristics of a crisis are also interdependent, for instance the perceived threat is also fed by the omnipresent uncertainty regarding future developments. Concerning the perceived urgency, the spectrum of activity is very wide, from total standstill to above normal engagement and workload. The degree of activism seems to depend on the legal requirements, the (non)remuneration of work, the age of the personnel or volunteers, as well as individual aspects. In total, the activities of the interviewed local organisations committed to communication and integration seem to be at a standstill, or they are continued on a reduced scale. In this sense, the impact of a prolonged crisis on the local economy is worrying.

Regarding windows of opportunity, the analysis indicates several short-term adjustments. Although those are often creative and helpful in the specific situation, they are not expected to have a lasting impact. Furthermore, the study reveals digitization and home-based work as major trends which are propelled by the crisis and therefore lead to (incremental) changes on the regime level. In addition, a shift in values towards local solidarity and cohesion is identified as a potential window of opportunity affecting the landscape level. Of course, the windows of opportunity are subject to reservations. Future developments will show whether the adjustments will sustain and become part of a "new normal".

Referring to Newig's typology of change processes in relation to the preservation or collapse of structure and function, the analysis shows that a "system transformation/adaptation" (type 1) is likely to occur in the short term, as organisations focus on the fulfilment of their functions (core business) while adapting their structures in order to do so. In the medium to long term, however, overarching trends might lead to a reorientation of functions in local economies, resulting in a path-dependent reorientation (type 2).

Altogether, the analysis does provide important insight for further research questions:

- The effects of the COVID pandemic on volunteer work raises many issues,: To what extent does the composition of volunteers change as a result of the crisis (e.g. in terms of age structure and educational level)? Is there is a shift in the fields of activity? With what adjustments will voluntary activities be continued?
- Another research gap refers to novel approaches in overcoming the barrier of spatial distancing while supporting personal proximity. What innovative solutions can be established? How can the challenge of digital inequality in participation processes be overcome?
- This also raises the question of what medium- to long-term effects the trends towards digital communication and home-based work (reduced presence at the workplace) will have on the functions of communication and integration in local economies.
- The analysis supports findings regarding the importance of individual and collective agency as key drivers in realizing windows of opportunity and promoting change (Grillitsch, Sotarauta 2019, Kristof 2010). What is the role of promoters in the local economy? How can they be activated and supported?

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Urban tourism and Covid-19 in Poland

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Abstract. World Tourism Organisation estimates an 80% drop in tourist arrivals by the end of 2020. The Polish tourism industry is also dramatically affected by the ongoing pandemic, with a 30% drop in the number of tourists in July 2020 compared to July 2019. The global lockdown has limited the functioning of the tourism sector, therefore domestic tourism, including urban tourism, may rise in importance. Domestic urban tourism can become a useful response to the growing resilience of the tourism industry, for example in the context of reducing dependence between the tourism industry and mobility which favours the spread of coronavirus. The potential of urban tourism in Poland is clearly visible (in 2019, it was three times higher than rural tourism in terms of overnight stays provided). However, the COVID-19 pandemic is not conducive to urban tourism in Poland, for instance, because infections are much more frequent in cities than in rural areas. The aim of the research, in addition to checking destinations of Poles in the context of urban tourism in the era of the pandemic, was to learn about the behaviour of tourists during their holiday trips. To achieve the aim of the paper, the study was conducted from 16 to 31 August 2020, using CAWI survey method, among people who visited Polish cities starting from May 2020 through the end of August 2020 (following the partial lifting of restrictions). The research indicated, despite the threat, the popularity of the largest tourist destinations in Poland. It also indicated that the behaviour and decisions of tourists were not different from those before the pandemic.

1 Introduction

The ongoing COVID-19 pandemic is causing great havoc to the world economy. A broad range of consequences of the pandemic is also experienced by the tourism sector, which according to Fletcher et al. (2020) is considered to be the world's largest industry, generating 10% of global GDP (is closely linked to socio-economic progress) (Anand, Kim 2021, Kyrylov et al. 2020). For the European Union, tourism is the fourth largest export category, and for countries such as France, Spain and Italy it is one of the main economic segments (Komisja Europejska 2020). According to the World Tourism Organization (2020), the global tourist blockade may cause the estimated number of international tourist arrivals at the end of 2020 to be nearly 60-80% lower than last year. In the research carried out by Richards, Morrill (2020), almost all of the analyzed companies from the tourism industry have already experienced a decline in demand and expect this trend to last another year, which is tantamount to a deterioration of their business prospects[1].

[1]The study was conducted in the period from 3-9 March 2020, among the respondents who are representatives of the tourism industry and who have connections with WYSE Travel. The surveys were conducted in 73 countries and 421 questionnaires were retained for analysis (Richards, Morrill 2020,

Current statistics show that in Poland, in May 2020, the number of tourists decreased by nearly 90% compared to May 2019, in June 2020 by more than 60% compared to the previous year, and in July 2020, compared to the same month last year, by more than 30%, while the number of foreign tourists was lower by nearly 70% (Główny Urząd Statystyczny 2020b,c).

The COVID-19 pandemic is not the first crisis of the tourism sector (SARS epidemic in early 2000, economic downturn in 2009, terrorist attack of 11 September 2001, MERS in 2012), but the first of such a wide scale that the industry is experiencing (Richards, Morrill 2020, Jamal, Budke 2020, Gössling et al. 2020, Richards 2020). The SARS outbreak caused tourists to avoid areas considered to be at risk (Napierała et al. 2020), and the same is true for geopolitical situations that result in a reduction in available tourism infrastructure (Więckowski, Saarinen 2019).

Global changes, such as increase in population and its mobility, population concentration, urbanisation trends or the development of global transport networks are the causes of the growing threat of a pandemic and the spread of infectious diseases (tourism also indirectly contributes to the development of pandemic) (Labonte et al. 2011). In order to reduce the number of infections, restrictions were introduced that directly affected tourism: suspension of domestic and international flights, cancellation of events (Napierała et al. 2020) or limiting the number of hotel stays or closing them completely for a certain period of time. According to Orîndaru et al. (2021), hygiene and health conditions at the destination have become important for tourists' travel decisions. This has forced hotel companies to change their operating strategies (Rodríguez-Anton, del Mar Alonso-Almeida 2020).

The COVID-19 crisis, according to Gössling et al. (2020), provides an opportunity to take a slightly more critical look at the tourism industry and, at the same time, to search for bigger benefits, focusing on sustainable development issues, among other things, which means rejecting the classical "growth" which is based on bringing profits only to the selective sectors (e.g. airlines, hotels; more extensively on this topic Polukhina et al. 2021, Lerario, Di Turi 2018, Grah et al. 2020). Covid-19 also prompted discussion of sustainable tourism (Lama, Rai 2021, Vărzaru et al. 2021, Purcell et al. 2021) defined as minimizing the negative and maximizing the positive social, economic, and environmental impacts of tourism (Więckowski 2021).

The coronavirus has transformed part of social and economic life, reducing transport and making videoconferences more popular. Both provide a good solution both in education and office work because they allow avoiding unnecessary travel, thus reducing mobility. The observed changes can represent the beginning of the tourism system transformation and thus the process of building resilience, which is currently at a marginal level. The current changes are a sort of precursor for the modifications that will take place in the future. The motivation for their consolidation and development should be based on the fact that in the era of globalization and ongoing transformations, even assuming that the COVID-19 pandemic will end (or return to normality will be allowed), it should be noted that this will not be the last infectious disease threatening society and the entire economy.

2 Tourism of a place against the pandemic

Cities have always been tourist destinations, from those of a cognitive (cultural-historical) (Lerario, Di Turi 2018, Barrera-Fernandez et al. 2016) nature to more modern forms of individual tourism, such as business tourism (e.g. conferences, exhibitions)[2]. As a result of the transformations in the area of creating new forms of tourism, a new concept appeared, i.e. urban tourism, which has become an element of the socio-economic development of the city (Żabińska 2013) and one of the fastest-growing forms of tourism in the world (Królikowska-Tomczak, Machnik 2019). Urban tourism is one of the key factors in the development of European cities (Popescu, Corbos 2010).

WYSE Travel Confederation 2020).

[2]This study focuses on cognitive tourism trips, or leisure tourism.

The majority of foreign tourists coming to Poland, but also the domestic tourist trips of Poles, are aimed at cities (Sala 2012). In 2019, the number of nights spent by tourists in cities was three times higher than the number of nights spent in the countryside (Główny Urząd Statystyczny 2020a). Urban agglomerations are the leading destination for urban tourism. Moreover, among the most visited cities in the world there are examples where, per year, the number of tourists exceeds the number of inhabitants (e.g. Venice) (Królikowska-Tomczak, Machnik 2019). The COVID-19 pandemic, therefore, affects urban tourism in a special way because most cases of infections (Roman et al. 2020) and deaths are accumulated in cities[3], which negatively affects the city's attractiveness score (Szołtysek, Otręba 2020).

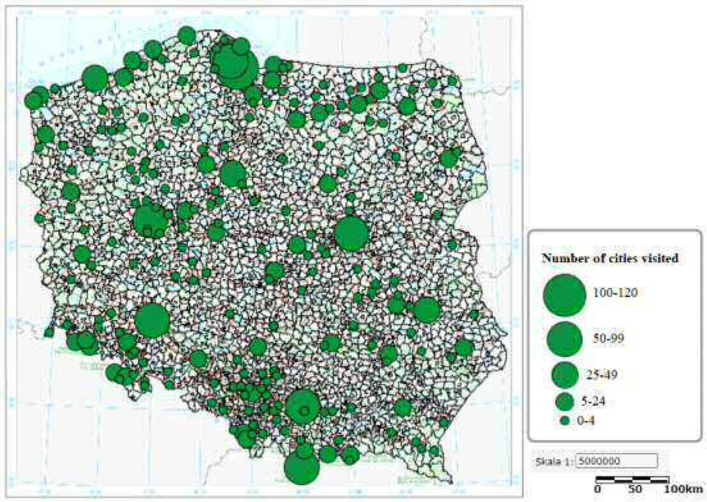
However, due to the restrictions introduced, but also due to people's fear of foreign trips, in the short term, domestic trips will prevail (Komisja Europejska 2020). Therefore, domestic tourism is particularly relevant and an opportunity to revive the tourism industry in the era of pandemic. It can also be said that the situation has stimulated a creative approach to tourism by taking advantage of the diversity, culture and nature offered by the home country. According to a survey commissioned by the Polish Tourist Organisation (2020) in June 2020 on Poles' holiday plans, 64% of the respondents indicated that the pandemic affected their travel plans. Moreover, among the respondents who declared that they are not planning any vacations in 2020, for nearly 80% the reason is the COVID-19 pandemic. Among those who intended to go on vacation in summer 2020, 82% of Poles plan to take advantage of domestic tourism.

The ongoing pandemic gives a possibility to analyze tourist's behaviour during the epidemic, thus finding opportunities to maintain the future sustainability of the tourism industry (Wachyuni, Kusumaningrum 2020). Before the pandemic, the choice of holiday destination was determined by specific features including age, marital status, income, and education. An additional group of factors were the features that can be attributed to the place of departure (tourist attractions, services, facilities) (Wachyuni, Kusumaningrum 2020), i.e. tourist resources that the place offers. That group of factors should also include determinants related to the availability of a given area, transport connections, or factors including, among others, security or political stability issues. It can therefore be concluded, as Keller (2020) rightly points out that tourism is a "good weather sector". A certain breakdown in cross-sectoral characteristics, especially in the areas related to epidemics or political issues, disturbs the tourism industry causing crises. As a result, the factors related to the destination's tourist resources are somewhat secondary in nature. The pandemic has tourists face a limited choice, combined with their own concerns about safety during the rest time. Therefore, tourists aware of the limitations are looking for holiday attractions that are within their reach.There are many benefits of such solutions, from support of the national tourism industry to more indirect ones, connected with education, discovering local attractions or culture, normally lost to foreign vacations.

3 Polish tourist voucher as support for the weakened tourism industry

One of the possibilities to support the reviving tourism industry is to subsidize tourism consumption (Yang et al. 2020). Such a solution was applied, among others, in China after the global economic crisis. In Poland, the collapse of the tourism industry, confirmed by the statistics and forecasts conducted in the country, has led to the government to introduce a tool that will indirectly support the Polish tourism sector, weakened by the COVID-19 pandemic. This tool is the Polish Tourist Voucher, which was introduced on 1 August 2020. It is a form of support that can be used by Polish families with children to pay for a stay in a hotel, an agritourism farm, a sports camp or a colony, as well as to finance a tourist event organized by a tourist entrepreneur or public benefit organization in the country[4]. This kind of element of subsidizing tourism consumption in Poland, although mainly supposed to benefit the tourism industry, also indirectly supports Polish families during the crisis caused by the pandemic. As an incentive for domestic tourism, it can also contribute to the popularization of urban tourism.

[3] According to estimates, 90% of the reported COVID-19 cases concern cities (UN Habitat 2020).
[4] https://www.gov.pl/web/rozwoj/bonturystyczny (Date of access: 14.09.2020).



Source: Own study based on surveys, $n = 543$.

Figure 1: Number of tourists surveyed by urban destination in Poland

4 Material and test methods

In the Holiday Plans of Poles report, half of Polish tourists declared that they will realize their holiday trips in the second half of July and the first half of August (Polish Tourist Organisation 2020). Taking into account the information contained in the report, CAWI surveys were conducted in the period from mid to late August. The survey was addressed to Polish tourists who, after the lockdown and the restart of the tourist industry[5], chose Polish cities as their holiday destination.

The questionnaire was supposed to reveal the behaviour of tourists during the pandemic, showing, among other things, whether urban tourism was an alternative to cancelled trips abroad, or whether it allowed seeing the advantages of domestic tourism.

The specification of the survey, due to the pandemic and the group of respondents to whom the questionnaire was addressed, did not make it easier to obtain a satisfactory number of questionnaires. As a result of the research, conducted between the 16th and 31st of August[6], 2020, 559 questionnaires were collected, with 456 taken into account for the final analysis of the results[7].

5 Urban tourism in the era of pandemic in Poland

In the period from May to August, 2020, as a part of the urban tourism, the respondents visited a total of 232 cities[8] (Figure 1), i.e. almost 25% of urban centres in Poland (these cities comprised more than 60 percent of the country's urban population.). Additionally, more than 70% of respondents indicated that they are planning further tourist trips to Polish cities by the end of 2020.

Taking into consideration the number of tourists visiting, large cities (over 100 thousand residents) were the most popular destination. Most respondents chose Gdańsk (112

[5]In Poland, the period of the so called "defrosting of the economy" began on May 4, 2020, when hotels and other accommodation, as well as some tourist attractions were reopened. Since June 13, border traffic within the internal borders of the European Union has been restored.

[6]Due to the ongoing pandemic, the survey was conducted remotely using a google questionnaire sheet. The prepared form has been made available on facebook social network, more precisely on a private account, groups dedicated to tourism and the Linkedin website.

[7]In the analysis of the results (except for the elements from Figure 1 and Table 1) 103 surveys were not included, due to the fact that respondents in their questionnaire forms, apart from cities, also indicated villages as tourist destinations, which was contrary to the test assumptions.

[8]When presenting the results involving cities indicated and visited by the respondents, it was decided to include also those questionnaires in which the participants pointed several cities and villages they visited. In those cases, only the cities were taken into account from their answers. As a result, the analyze of 543 questionnaires was presented.

Table 1: Cities visited as part of urban tourism according to the size of the city center

Cities / Number of tourists	Number of cities	0-4	5-24	25-49	50-99	100-120
Large cities (<100 thousand residents)	34	11	15	2	5	1
Medium cities (20–100 thousand residents)	79	61	15	1	2	0
Small towns (>20 thousand residents)	119	101	18	0	0	0
Total	232	173	48	3	7	1

Source: Own study based on surveys, $n = 543$.

respondents), Kraków, Wrocław and Poznań (more than 80 respondents) as their holiday destinations (Table 1). The smallest number of people decided to opt for urban tourism in small towns (cities with population below 20 thousand) residents) – 71 small towns in Poland were visited by one respondent.

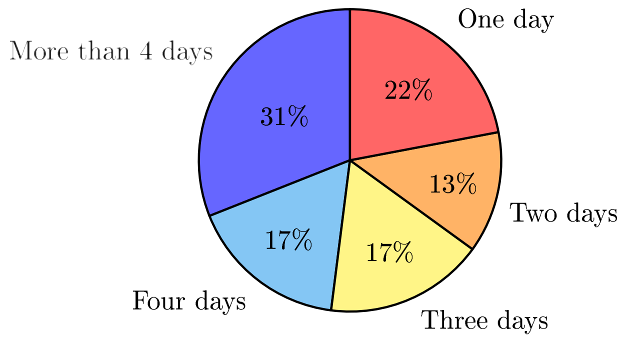
Although the largest urban centres in Poland were more attractive to the respondents, small and medium-sized centres dominated in the general structure of cities indicated by the respondents. This is due to the fact that a significant part of small towns is located in areas with high environmental values (in the vicinity of seas, mountains, forests, lakes), which strengthens their interest among tourists. On the other hand, small and medium-sized cities, located in the vicinity of bigger ones could complement tourist trips to the largest cities (as can be seen in the case of the city of Poznań, which belongs to large urban centres, and small towns located in its surroundings) (see Figure 1).

The respondents differed significantly when it comes to the list of indicated cities and later, when that number was summed up. As a result, it was observed that nearly 40% of the respondents visited only one city, while less than half of that visited two cities. Their choices included the largest urban centres (among others Warszawa, Kraków, Wrocław, Poznań). Tourists who visited more than three cities opted for the directions of urban tourism destinations concentrated in the area of a certain region (primarily located in the northern Poland, coastal cities: Gdańsk, Gdynia, Sopot, Hel, Łeba, Kołobrzeg, Ustroń, Ustka, Mielno). Among the respondents some people declared that during the pandemic they visited seven or even more cities (2 people indicated that they visited 10 cities, 1 person – 11 cities, 1 person – 13 cities). In this group, there were no certain choices among the cities given by tourists which would indicate one specific tourist region. This may result from the adopted form of recreation, focusing on touring urban tourism in previously selected Polish cities.

Urban tourism trips during the pandemic were associated with longer periods. Nearly half of the trips lasted 4 days and more (Figure 2). At that time, the respondents most often pointed to numerous seaside towns and much less frequently to urban centres located in the southern part of Poland. Before the pandemic, tourists used an average of 2.5 nights in cities in 2019. It can be concluded that the trend of those surveyed during the pandemic was close to similar to the nationwide statistics before Covid-19 (Główny Urząd Statystyczny 2020a).

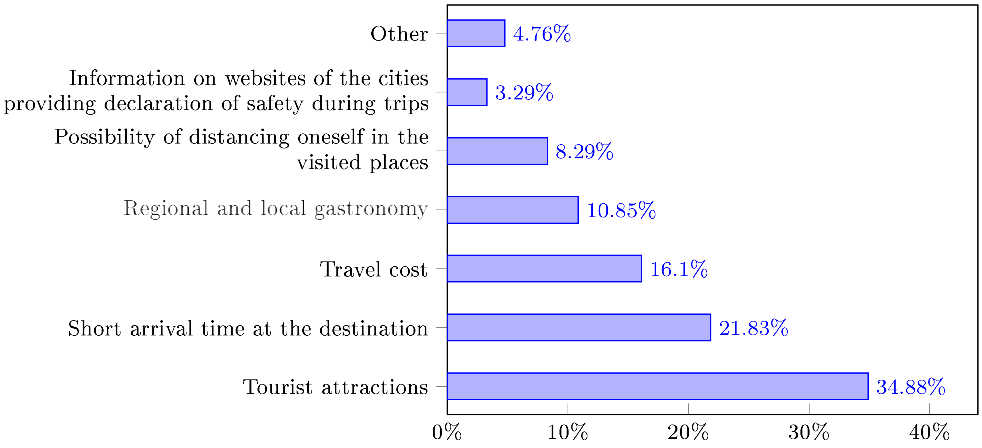
In the case of one-day trips, the choice of cities was clearly linked to the place of residence. The respondents decided to opt for urban tourism in the area of the same or neighbouring province (see Table A.1). Decisions on the length of trips are justified, among others, by the indicated factors of the place (Figure 3) which determined the direction of the tourist destination. Nearly 22% of the respondents indicated that the short arrival time to the destination was an important factor in choosing the direction of the trip.

However, it is tourist attractions that have become the most relevant decision factor for the largest number of respondents. Issues related to the pandemic, namely the possibility to distance oneself in cities (10,85%), or the information placed on websites



Source: Own study based on surveys, $n = 456$.

Figure 2: Length of the holiday trips as a part of urban tourism



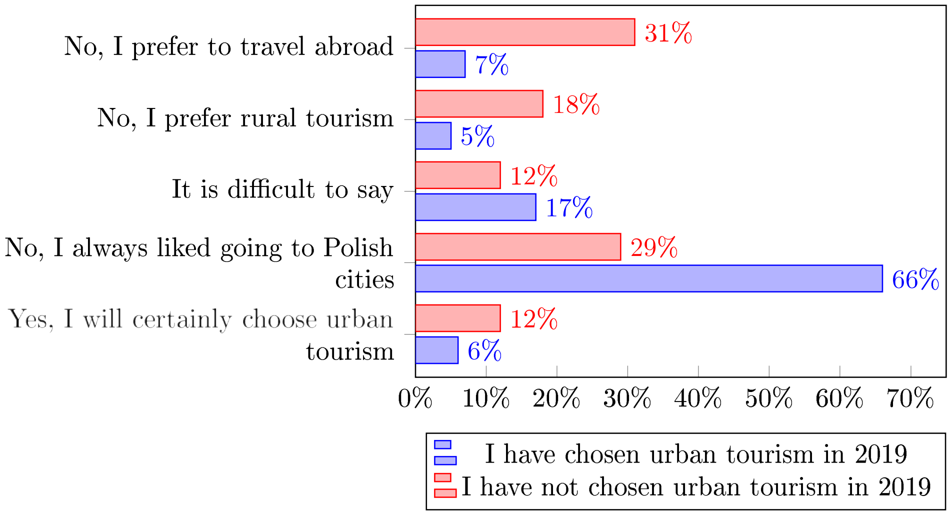
Source: Own study based on surveys, $n = 456$.

Figure 3: Factors influencing the choice of the city as a tourist destination

with the declaration of safety guarantee during the departure (3,29%), did not have such a significant impact on the decision made. Nearly 5% of the respondents also indicated other factors: slightly more than 4% of people related their decision to private issues, namely meeting family, relatives or friends, who live in or near the chosen city, 0,4% (3 people) of the respondents chose a given city because of the sporting events in which they participated, 0,2% (2 people) of the tourists considered attachment and certain family traditions as a factor, as these cities are places of regular, annual holiday trips.

In May, after the restrictions were partially lifted, 8% of respondents decided to go on holiday. However, almost 50% of this group consisted of people from single and double households. In the following month the number of respondents who decided to travel to Polish cities tripled. The peak of holiday trips fell in July and August, when 70% of the participants chose domestic urban tourism as their destination. Thus, it can be concluded that the pandemic did not change the behaviour of tourists as to the date of tourist travel. This is also confirmed by the previously indicated fact that over 70% of the respondents were not afraid of being infected with coronavirus during their travels. However, even in cases when people declared themselves afraid of the possibility of infection during the trip, in the end, visited on average as many cities as those who did not feel any fear.

More than 80% of respondents chose cities as their holiday trips, while for the rest, urban tourism was a complement to rural tourism. It would seem that, during the travels targeted at rural areas, the respondents would decide to complement their visits with smaller, less popular tourist destinations. However, the opposite happened, the list was dominated by the most attractive Polish cities such as Zakopane, Wrocław, Kraków and Gdańsk.



Source: Own study based on surveys, $n = 456$.

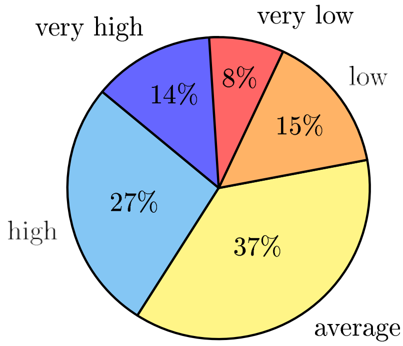
Figure 4: Preferences after a tourist trip during a pandemic

Urban tourism was not a new destination during the pandemic. Almost 90% of the respondents indicated that a year prior, they also used the tourist attractions offered by Polish city centres. For 70% of the participants, cities visited in the period from May to August were urban centres that they had already visited before (the indicated places were the most popular tourist cities in Poland, including Zakopane, Gdańsk, Gdynia, Mielno, Kraków, or Wrocław. 24% of the respondents stated that not in all cases it was a re-visit – in these cases, among the indicated, well-known cities were medium and small places (e.g. Bydgoszcz, Opole, Zamość, Toruń, Kudowa Zdrój, Supraśl, Ciechanowiec, and Drawsko Pomorskie). Only 16% of the participants visited the given cities for the first time, while almost half of the declared cities consisted of large urban centres. However, these choices may be due to the young age of the respondents who gave such an answer (18-35 years). Their choice was then focused on the most popular tourist cities.

Tourist preferences of the respondents after their trip varied, depending on whether they also benefited from urban tourism in the previous year. The surveyed tourists, who visited Polish cities in 2019, also took advantage of urban tourism during the coronavirus, due to the fact that they always preferred to go to urban centres in the country (66%). Only 6% declared a greater inclination for urban tourism in the future. However, this should be justified by the fact that this group of respondents clearly indicated that they willingly choose cities as their destination. Therefore, the opinions of people who did not opt for urban tourism a year prior can be positively assessed – such an answer was given by 12% of respondents.

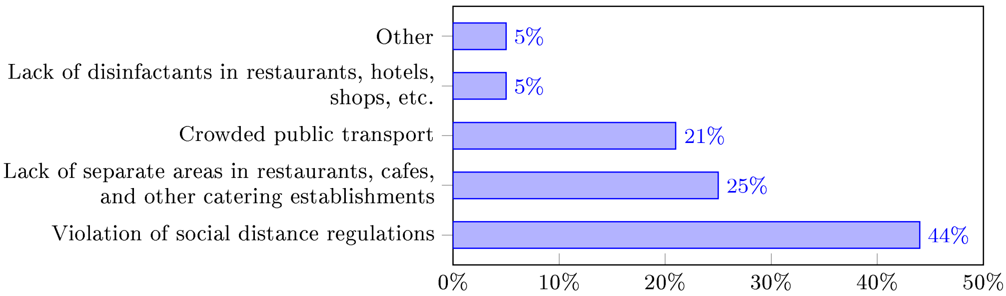
On the other hand, 31% of people (28 respondents), who did not choose urban tourism a year before, despite the fact that during the pandemic they decided on the trip, still prefer to go abroad more (Figure 4), supporting it with a fact that 15 of them travelled abroad in 2019, while 7 of them have also taken part in a trip outgoing since June 2020. This group is therefore made up of people who, with a certain degree of regularity, decide on resting places located outside the country. If we focus on the respondents in a general way, less than 60% of Polish tourists in the previous year took advantage of outgoing tourism. Moreover, during the pandemic, since June 2020, 20% of them have used the opportunity to go to another country as a holiday destination. More than 4% of the respondents who did not choose outgoing tourism in 2019, did so in 2020, during the COVID-19 pandemic. The interest in foreign trips among Poles decreased by half due to the coronavirus. As a result, for 32% of the respondents, urban tourism was compensation for the planned outgoing tourism in the holiday period.

Although more than 70% of the participants were not afraid of the coronavirus infection, they rate the level of safety relatively low – 60% of the tourists who took



Source: Own study based on surveys, $n = 456$.

Figure 5: Assessment of the safety level in cities during coronavirus threat



Source: Own study based on surveys, $n = 195$.

Figure 6: Reasons for negative assessment of urban safety levels

part in the study gave an unfavourable (very bad, bad or average) assessment of the said level in cities (Figure 5).

In this group, the most frequently indicated reason for the negative assessment of the level of security in cities (Figure 6) was a violation of the principles of social distance (44% of the respondents), 25% emphasized the lack of separate places in catering establishments.

Among other reasons given (5%), there were repeated opinions about the lack of mask coverage in places, where such a rule applied for both other tourists and staff in cafes or restaurants. The respondents pointed out negative aspects, lying both on the side of tourists and facilities or staff. Thus, one can speak of a certain underestimation of the rules, even though there were financial penalties for breaking them.

During their trips, the respondents travelled mainly by their own or rented (borrowed) car (64% of the participants), 23% opted for rail transport, while 10% opted for bus transport. Only 1% of tourists reached the city by plane. However, such a small group results from the fact that air transport is not very popular in the country and that the airports are located only in a few cities in Poland. Among the respondents, there were also people (3 participants), who only travelled by bicycle during their trip, which suggests the form of tourist travel around the cities they chose.

In connection with the introduction of the Polish tool to revive the tourism industry during the pandemic in the form of a tourist voucher, the respondents were asked whether they took advantage of such an opportunity. It was used by 2% of the respondents. However, a small percentage is due to the low number of households participating in the survey that could have used this type of tool (see Table A.1).

The survey and analysis of its results made it possible to present the tourists' suggested behaviours during the pandemic. The research has allowed us to observe that the general directions or actions taken before and during the trip do not differ significantly from those before the coronavirus outbreak, which are presented in public statistics (see the publications of Główny Urząd Statystyczny at https://stat.gov.pl/). The destinations of the largest number of tourists were large urban centres, even though they confirm a higher number of infections.

6 Discussion

Tourism in the nineteenth century is beginning to be considered as one of the basic human needs (Sala 2012), becoming, to some extent, a necessity of society (Wachyuni, Kusumaningrum 2020). The coronavirus pandemic has stopped the tourism sector (Wojcieszak-Zbierska et al. 2020), but also the society from the realization of its needs. The global blockade has shown people a new face of, among others, tourism, forcing them to, on the one hand, adapt to the current situation, and on the other, to create new solutions and search for potentials where they had not been noticed before.

As we know, it is difficult to estimate the effects of the crisis, which is not yet over. However, one can find positive aspects in it. One of them was indicated as a part of the conducted research. The potential for the Polish tourism sector is, among others, urban tourism. Cities, being attractive destinations, did not lose their relevance during the pandemic in Poland. Although the number of infected cases in cities is much higher than in rural areas, urban centres are a popular tourist destination.

The tourism industry will certainly recover from the coronavirus crisis. However, the question arises, whether it will look the same as before the pandemic. The economic revival, after the partial lifting of restrictions, may result in the formation of new patterns of holiday trips, more focused on domestic tourism among visitors.

Therefore, the representatives of the tourism industry are currently faced with a considerable challenge, as they have to carry out their tourism activities during the pandemic, and, at the same time, analyse tourists' behaviour, their requirements, expectations and preferences. According to Andreini, Mangiò (2020), the tourism sector should acquire new services to provide to tourists that focus on increasing self-esteem, meeting the needs of the higher-order and not on available promotions and discounts. This form of tourism is visible in experienced visitors, which argues for the validity of such services.

The research showed that the tourists were mostly targeting large cities during the pandemic. In individual cases, small urban centres were indicated. This is, in a way, due to the fact that the largest cities in Poland are the main tourist destinations for Poles, but also for foreign tourists, because of their advantages, which are mostly concentrated in large urban centres (Preisler 2012). Small urban centres differ significantly, when the variety of tourist attractions is concerned, with the exception of cities with high environmental values (cities located near the sea, lakes, or mountains).

Polish tourists, who took part in the survey, were not afraid of coronavirus infection during their trips. This may stem from the fact that: the group of the respondents was made up of people who rather systematically benefit from tourism, not only in Poland, but also abroad, a significant proportion of subjects were young adults who were less frequently exposed to Covid-19 and, to some extent, from the place of obtaining respondents[9]. This is also due to specific characteristics of urban tourism such as the shortness of stays or the repetitiveness of visits, among others (Lerario, Di Turi 2018, Ashworth, Page 2011, Dumbrovská, Fialová 2014).

The lack of fear of infection was also noticeable in the indicated factors determining the choice of a tourist destination (the possibility of social distancing was a factor taken into account by a little more than 10% of the respondents). Despite the lack of concern, the chosen cities were negatively assessed in terms of safety and did not discourage further trips as a part of urban tourism.

The results of the questionnaire indicated that Poles like to use domestic urban tourism (60% of the participants). Moreover, less than 10% of the tourists have decided that, in the future, after this year's trips, they will use the tourist attractions of Polish

[9]Travel and tourism groups on social networking sites are created by people who regularly travel, run blogs, websites, but also by family travel enthusiasts. In the created thematic groups, they regularly exchange information, recommending specific places, hence the established tourism trends among the respondents, despite the ongoing pandemic.

cities more often. The pandemic has therefore influenced, to some extent, the perception of national urban tourism. It is also interesting to note that the directions of the destinations were, in many cases, the cities visited in previous years, which proves a certain attachment to the holiday destination and guarantee of safety during the pandemic. The results of the surveys of people who chose several cities, and then reported that not all of them have been visited before, indicate that in the group of these urban centres there is a dominant majority of medium and small towns. Therefore, one can come to the conclusion that, due to the coronavirus, a group of respondents decided to visit less touristic cities, thus increasing the possibility of social distancing.

To sum up, the results of the research showed that the behaviour and decisions of tourists do not differ from those before the pandemic. This has its positive and negative consequences. On the list of the disadvantages is the issue of the rising number of cases of coronavirus transmission caused by increased mobility. The positive aspect of the respondents' behaviour can be considered as an advantage for the national tourism industry. Despite the pandemic, people have not changed their behaviour, they have limited it to some extent. Thus, if in the era of COVID-19, the society decides on a permanent form of vacationing, it will continue to perpetuate this pattern even after its completion. Negative assessments of the safety levels are only a signal to cities and the tourism sector to increase the quality of care for tourists during the coronavirus because it seems to be one of the main shortcomings of the industry today.

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A Appendix:

Table A.1: Metrics

Specification		Percentage of respondents
Sex	Female	82%
	Male	18%
Age	18-24 years old	36%
	25-34 years old	31%
	35-44 years old	22%
	45-54 years old	8%
	Over 55 years old	2%
Place of residence	countryside	24%
	small town	10%
	average town	15%
	big city	50%
Number of household's members	single	11%
	2-person	30%
	3-person	23%
	4-person	25%
	over 4 people	11%
Region (macroregion)	Northern	10%
	Mazowieckie voivodship	9%
	Eastern	6%
	Central	8%
	Southern	14%
	South-Western	8%
	North-Western	45%

Note: "small town" – up to 20 thousand residents; "average town" – between 20 and 100 thousand residents; "big city" – over 100 thousand residents

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Approximating the impact of COVID–19 on regional production in countries with scarce subnational data: A proposal and application for Argentina during the first wave

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Abstract. In this paper we propose an index to approximate the territorial economic impact of the COVID–19 pandemic in contexts with scarce or outdated regional data, which is often the case in developing countries. This index is based on data that are usually available in most countries: a) the sectoral productive structure of the regions, b) the operational level of each sector, c) the mobility of workers in each region, and d) the possibility of remote work among sectors. The empirical application for Argentina describes the impact of the pandemic on regional production during the second and third quarters of 2020, both for the provinces and labor market areas. Our results show that the regional impact of COVID–19 on private economic activity was highly heterogeneous between and within provinces. The proposed index is also highly correlated with sporadic official data coming from national agencies, while it has a wider geographical and temporal scope, especially in terms of labor market areas.

1 Introduction

The COVID–19 pandemic and the different regulations imposed by governments to contain the spread of the virus have produced deep transformations, as well as multiple social and economic costs (Baldwin, Weder di Mauro 2020, Barua 2020, Noguchi 2020). The trade-off between epidemiological prevention and economic activity is one of the most pressing issues that governments and societies are facing (Kok 2020). In addition, the economic impacts of the pandemic and mitigation measures have been highly uneven. Winners and losers can be identified between countries, regions, sectors, businesses, households, or workers (Adams-Prassl et al. 2020, Blundell et al. 2020, ECLAC 2020a,b, Sokol, Pataccini 2020).

Recent studies highlight that, unlike other crises such as that of 2008-2009, the impact of the pandemic has been regional rather than national, and in the case of developed countries, the territorial differences observed within them have been greater than those registered between nations (Bailey et al. 2020, Amdaoud et al. 2021). This is why the literature raises the need to adopt a regional perspective in the analysis of the economic impact of the COVID–19 pandemic, in order to understand and adequately manage the uneven impact of isolation and mobility restriction measures (Benedetti et al. 2020, Brinks, Ibert 2020, Cerqua, Letta 2020, Giannone et al. 2020, OECD 2020).

However, the study of the regional economic impact often faces several limitations, in many cases due to the limited availability of updated information at the subnational level. The abundance of real-time epidemiological statistics for multiple geographical scales – countries, regions, cities, neighborhoods – contrasts with the scarcity of economic statistics, which in developing countries are often non-existent or very outdated. On the other hand, available estimates of the economic impact of COVID–19 are usually presented at an aggregate level, that is, by country or by sector.

In this paper we intend to make a contribution especially relevant for the developing world, which is often missing in the urban and regional economics literature (Castells-Quintana, Herrera-Idárraga 2019). In particular, we explore how to approximate the territorial economic impact of the COVID–19 pandemic in contexts with scarce or outdated regional data. Argentina is a good example of this, since there are no homogeneous and updated statistics on GDP or sectoral value added at the territorial level. The latest official data, available only for provinces, correspond to 2004. In addition, there are no regional input-output tables to analyze the interactions between activities in the different regions, or factor intensities in the different sectors and regions.

In this context, it is necessary to introduce some caveats. First, based on the limited data available in Argentina, we can only approximate the regional impact of COVID–19 on private economic activity. Secondly, we will address the territorial economic impact from the supply side, considering the immediate or short-term impact on private production in each region, and not from the measurement of the different components of regional demand.

Bearing in mind these caveats, we propose the calculation of an index that, with some adjustments or adaptations to each context, could be used to approximate the regional economic impact of the pandemic and isolation measures, based on data or statistics that are usually available in most countries. Our index of territorial economic impact by COVID–19 (ITEI-COVID) takes into account: a) the sectoral production structure of the different regions, based on pre-pandemic data, b) the operational level of each sector, based on secondary post-pandemic information at the national level, c) the mobility of workers in each region, based on the easily accessible data from Google Mobility Reports, and d) the possibility of remote work across different activities or sectors, based on recent studies that have been carried out in many countries. Unlike other very interesting studies that require, for example, the availability of regional input-output tables (Bonet-Morón et al. 2020, Haddad et al. 2020, Porsse et al. 2020, Haddad et al. 2021), the relative simplicity and lower data requirements of the index could facilitate the implementation in broader contexts.

As an application, we will show the results of the ITEI-COVID for the 24 provinces and the main 85 Labor Market Areas (LMAs) of Argentina, according to the evolution of the national and regional restrictions imposed both on people's mobility and on different economic activities. In Argentina, the provinces are the first subnational political-administrative level, followed on a much smaller scale by the municipalities or local governments. Meanwhile, the LMAs are defined as the portion of territory delimited by workers' daily movements between their workplace and their home (Borello 2002, Rotondo et al. 2016). In this sense, they are made up of a central city or node and a set of other localities linked in labor terms. A similar geographical unit has also been analyzed in other Latin American countries, such as Chile, for example (Rowe et al. 2017).

The results of the ITEI-COVID shown in this paper cover the six months – or two quarters – of greatest economic contraction in Argentina, from April to September 2020. This period also coincides with the first wave of the pandemic in the country. According to official indicators from the National Institute of Statistics and Censuses (INDEC, in Spanish), the year-on-year fall in national GDP in the second quarter of 2020 was 19.1% – exceeding the 16.3% fall recorded in the first quarter of 2002, at the epicenter of the convertibility crisis – and 10,2% in the third quarter of 2020. The year-on-year fall in the monthly economic activity estimator (EMAE, in Spanish) was above 25% in April, 20% in May, around 12-13% from June to August, and about 7% in September.

The paper is structured as follows. After a brief review of recent literature (Section 2), we contextualize the Argentinean case (Section 3) and present both the methodology and data used for the calculation of the index (Section 4). In Section 5 we first show the results obtained for the different provinces and LMAs and then present some validation exercises, comparing these results with regional official indicators that have been published discontinuously. Finally, we close with some conclusions.

2 The regional economic impact of the pandemic across the literature

In the same way that the pandemic increases individual and sectoral inequalities (either between workers in essential and non-essential sectors, between activities that can be carried out remotely and those that cannot, between formal and informal wage earners, or between companies that have invested in new technologies and the ones that do not find resources to do so in this context), it is also expected to affect regional inequalities. This uneven territorial impact is, to some extent, predictable. It is due in part to the different speeds of regional circulation of the virus, but also to differences in terms of the timing of public policies, the intensity and duration of quarantine or isolation measures, the restrictions on mobility within and outside each region, the composition of local production structures, and other characteristics of the regions, such as labor and income inequalities among the population or the regional dependence on international trade and global value chains (Aalbers et al. 2020, Bailey et al. 2020, Bonaccorsi et al. 2020, Cerqua, Letta 2020, Inoue et al. 2020, Kapitsinis 2020, Ponce et al. 2020, Shen et al. 2020, Ascani et al. 2021, Beyer et al. 2021).

The study of the regional economic impact of the COVID–19 pandemic is relevant for several reasons. First, it is a basic input for designing and executing place-based responses (Friedman et al. 2020, Rahman et al. 2020), rather than centralized (one-size-fits-all) policies that have failed in many countries (Morrison, Doussineau 2019, Bailey, Tomlinson 2020, Benedetti et al. 2020, Giannone et al. 2020, OECD 2020). As highlighted by Giannone et al. (2020), isolation measures established evenly at the national level can be very early in some cities – mainly small, where the virus takes longer to spread – or very late in others, such as large urban centers. The possibility of mitigating the direct economic impact and the indirect effects of the recession depends crucially on the existence of place-based policies and targeted instruments, which generally imply a greater decentralization of functions, powers, and resources at the regional level. Secondly, the economic problems caused by the pandemic also tend to be region-specific, such as higher unemployment and poverty rates, business closures, and multiple impacts on local production systems, among others. Finally, the systematization of empirical evidence in different countries will allow us to better understand the regional patterns whose stylized features are still unknown (Bailey et al. 2020). In this sense, the analysis of the short-term impact of the pandemic is a necessary starting point for future studies regarding the expected effects in the medium- and long-term, such as changes in the configuration of global value chains, impacts on internal migration, greater diseconomies of agglomeration, changes in values of the real estate, and geography of discontent, among others.

Since the outbreak of COVID–19, and given its global scope, several papers have analyzed the regional economic impact of the pandemic. For example, it is possible to identify studies for the United States (Barrot et al. 2020, Chetty et al. 2020, Muro et al. 2020), for different countries or regions in Europe (Bachtrögler et al. 2020, Bustos Tapetado, Solla Navarro 2020, Cerqua, Letta 2020, De la Fuente 2020, González Laxe et al. 2020, Kitsos 2020, Pérez, Maudos 2020, Prades Illanes, Tello Casas 2020, Gombos et al. 2021), for China and India (Gong et al. 2020, Huang et al. 2020, Beyer et al. 2021), for Marruecos (Haddad et al. 2020), and for Colombia and Brazil (Bonet-Morón et al. 2020, Hernández-Díaz, Quintero 2020, Porsse et al. 2020, Haddad et al. 2021), among others. For Argentina, the few studies on the territorial economic impact of the pandemic are based on national and sectoral surveys with highly aggregated geographical units, such as the five or six geographical macro-regions in which the 24 provinces are usually grouped (FOP 2020a,b,c, UIA 2020). Other studies estimate the impact on the GDP of a single province, such as Santa Fe (BCSF 2020), or at best of the different municipalities within Buenos Aires Province (Lódola, Picón 2020).

As we show in the next section, the ITEI-COVID combines some topics that come from different strands of literature. For example, the analysis and definition of operational or vulnerability levels for the different economic sectors has been a common step in several of the papers mentioned (Bachtrögler et al. 2020, Bonet-Morón et al. 2020, Bustos Tapetado, Solla Navarro 2020, González Laxe et al. 2020, Haddad et al. 2020, Hernández-Díaz, Quintero 2020, Lódola, Picón 2020, Pérez, Maudos 2020, Prades Illanes, Tello Casas 2020, Haddad et al. 2021).

Another line of research that has quickly become popular is the estimation of models that relate local epidemiological statistics with data on people's mobility from the location of their mobile devices (Badr et al. 2020, Kraemer et al. 2020, Lai et al. 2020, Weill et al. 2020). The use of mobility data, from Google Mobility or similar sources, has also been a frequent input in several papers that analyze the regional impacts of the pandemic (Bonaccorsi et al. 2020, Chetty et al. 2020, Haddad et al. 2020, Huang et al. 2020, Campos-Vazquez, Esquivel 2021, Marcén, Morales 2021), as well as in some cross-country studies (Askitas et al. 2020, Chen et al. 2020, König, Winkler 2020, Maloney, Taskin 2020, Sampi, Jooste 2020).

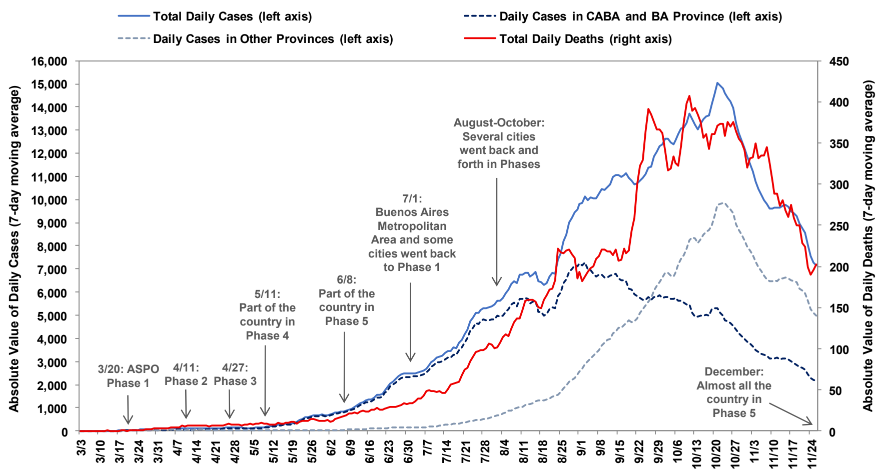
Finally, as we have mentioned, the analysis of the potential for remote work or teleworking as a possible response to certain economic activities and especially of some types of workers to mobility restrictions, has been the subject of numerous international studies (Crowley, Doran 2020, Delaporte, Peña 2020, Del Río-Chanona et al. 2020, Dingel, Neiman 2020, Garrote Sanchez et al. 2020, Hatayama et al. 2020, Saltiel 2020). In the particular case of Argentina, we can also find some specific studies on this topic (Albrieu 2020, Gasparini, Bonavida Foschiatti 2020, Red ISPA 2020).

3 The COVID–19 pandemic and isolation measures in Argentina

The first imported case of COVID–19 in Argentina was confirmed on March 3rd. A few days later, the national government established a mandatory quarantine for travelers entering or returning to the country, suspended all artistic and sports shows, as well as classes at all educational levels, and finally closed the national borders. On March 19th, when confirmed cases in the country were barely 130 and there were still no signs of community circulation (80% of cases were imported and the remaining 20% were close contacts), the President announced the beginning of a strict and mandatory quarantine for the entire country, the phase 1 of the Preventive and Compulsory Social Isolation (ASPO, in Spanish). Only those activities and workers considered essential were exempted, such as medical services and supplies, security personnel, food production, pharmacies, local food and cleaning supplies stores, public services, public transportation for essential workers, and fuel dispensing, among others. It is worth noting that on the day of the announcement, about half of the 24 Argentinean provinces had not yet registered any positive cases. Moreover, in more than half of the provinces with cases, there were only one or two infected people. In most cities, there were no confirmed cases for several weeks or even months. However, during the first phases of strict quarantine and isolation, no territorial criteria were taken into account.

During this first stage and phase 2 of administrative isolation – end of March and practically all of April – the restrictions and exceptions to economic activity were established at the level of sectors. While the economic activities considered essential continued in a relatively normal way (food and beverage processing, health services), there were others whose operations were significantly reduced (transportation) or indefinitely suspended (tourism, recreation, cultural services). On the other hand, despite mobility restrictions, some activities could be adapted and carried out remotely (various professional services, education), but others that required a physical presence in the workplace (manufacturing, construction) were naturally much more affected (Albrieu 2020, Gasparini, Bonavida Foschiatti 2020, Red ISPA 2020).

From the beginning of May, with the passage to phase 3 of geographic segmentation, the quarantine administration and especially the exempted activities began to take into account the context and epidemiological evolution of each region. The latter was deepened when some parts of the country advanced to phase 4 of progressive re-opening. In June the isolation measures were further relaxed in many regions, and even several cities moved



Source: Authors' calculation based on data reported by the Ministry of Health.

Figure 1: COVID–19 daily cases and deaths in Argentina (7-day moving average)

to phase 5 of social distancing (called DISPO), in which the circulation and development of a large number of additional activities were allowed. On the other hand, other cities with a marked community circulation of the virus, such as the Metropolitan Area of Buenos Aires, Resistencia, or San Salvador de Jujuy, among others, continued under the ASPO measures and even went back in phases by the end of June or beginning of July.

Until June the vast majority of cases were concentrated in the city of Buenos Aires (CABA, in Spanish) and its surroundings (Figure 1), which explains the gradual relaxation of the restrictions on mobility and economic activities in different parts of the country. Since July and especially during August and September, the epidemiological situation in many cities became more complicated and complex, but despite the setbacks in ASPO phases and the re-imposition of de jure restrictions, the levels of de facto mobility did not necessarily respond in the same way (Levy Yeyati, Sartorio 2020).

This evolution allows us to anticipate an unequal regional impact of the pandemic and the consequent isolation measures during the first wave in Argentina. On the one hand, when the exemptions were established at the sectoral level (phases 1 and 2), the territorial impact could be conditioned by the heterogeneous sectoral distribution of production and employment in the country, which is reflected in different regional productive specializations. On the other hand, in the later stages of ASPO, the unequal health impact of the virus in the different regions was an extra source of heterogeneity and, associated with this, the advances and setbacks in phases, as well as the tension between de jure restrictions and de facto mobility.

4 Data and methods

During the month t of April (phases 1 and 2 of ASPO, with restrictions and exceptions defined at the sectoral level), the ITEI-COVID in region j is calculated as:

$$ITEI_{jt} = 100 - \sum_{i=1}^{n} S_{ij} * OP_{it}$$

where S_{ij} is the weight of sector i in region j and OP_{it} is the operational level of sector i in the country in this month.

Meanwhile, for the months t from May to September, where mobility restrictions were relaxed or re-imposed with different (de jure or de facto) intensities, according to the regional context, the *ITEI* for each region j is obtained as follows:

$$ITEI_{jt} = 100 - \sum_{i=1}^{k} S_{ij} * OP_{it} - \sum_{i=k+1}^{n} S_{ij} * OP_{it} * LMI_{jt} * RWI_j$$

where we distinguish, on the one hand, the k sectors that showed a high operational level during April – the stage of greatest restrictions – and therefore also in the following months regardless of the regional context, and on the other hand, the rest of the sectors whose operational level effectively depended on the flexibility or not of labor mobility in each region. In this sense, LMI_{jt} is an index of people's mobility to their workplace – or labor mobility index – in region j, based on Google Mobility Reports, during the working days of month t. RWI_j is a remote work index, which reflects in what proportion the workers in region j could carry out their work activities from their home, so they would not need to go to their workplace[1].

Given that in Argentina there is no complete, homogeneous, and updated sectoral value-added statistics at the territorial level, we use data on formal salaried employment in the private sector to define the sectoral weights (S_{ij}). This information comes from the databases of provinces and LMAs elaborated by the Employment and Business Dynamics Observatory (EBDO), under the Ministry of Labor, Employment, and Social Security. In particular, we use average employment data from the year 2019 and we calculate the weight of formal private employment in each sector (ISIC at 2 digits) over the total formal private employment in each province or LMA.

It is worth noting that the regional data offered by EBDO cover the entire universe of formal salaried employment in the private sector in each province or LMA,[2] based on the crossing of administrative records of the Argentinean Integrated Pension System and the Federal Administration of Public Revenues (AFIP, in Spanish). It is not an estimate or projection according to sample data, as it happens with the National Population Survey (NHS) of INDEC. Obviously, the limitation of using data on formal salaried employment in the private sector to describe the regional (private) production structure is that informal salaried employment and self-employed workers are not considered[3]. However, in a previous working paper (Niembro, Calá 2020) we show that the general patterns for April remain relatively unchanged when we incorporate data on informality and self-employment using information from NHS.

The operational level of each sector in each month (OP_{it}) ranges from a maximum of 100 (complete) to a minimum of 0 (null), going through intermediate values of 75 (high), 50 (medium), and 25 (low). In order to carry out a simple sensitivity analysis – and since we cannot affirm a specific and exact level – we define for each sector a hypothesis of minimum operational level and another of maximum level, based on the search and interpretation of secondary information, such as recent statistics published by INDEC and other official agencies, reports from consultants and research centers, and information from various surveys and sectoral chambers[4]. The Appendix presents the list of the sectors considered (the k sectors of the second formula are highlighted) the two possible hypotheses defined, and the sources reviewed in each case. As mentioned, the definition

[1]Since we can consider the impact of the pandemic on regional production during April–September 2020 as a short-term impact, we can also assume that substitution between production factors may have been limited during the first months of the pandemic. In this sense, we are implicitly assuming that production functions behind the index would resemble a fixed-proportions production function. Therefore, in those production processes that require the physical presence of workers who cannot work remotely, the reduction of mobility and attendance at the workplace would also translate into lower production, regardless the labor intensity of each sector.

[2]Although some localities are not included within the main 85 LMAs, these LMAs account for around 95% of formal salaried employment in the private sector in Argentina. Obviously, in the case of the 24 provinces, all the national universe is covered.

[3]Employment in the public sector is not taken into account either, although it is not the purpose of this paper to analyze the impact of the pandemic and isolation measures on the production of services in this sector.

[4]For several sectors, official statistics are available at the national level, such as the Manufacturing Industrial Production Index published by INDEC. In these cases, we can analyze year-on-year variations. According to the ranges (100, 75, 50, 25, 0), we define the hypotheses of minimum and maximum operational level -that is, a lower and upper bound of operational level-. For example, a 40% drop translates into an operational level between 50 and 75. A similar procedure is followed with the percentages of production or sales decline reported by different sectoral surveys or business chambers.

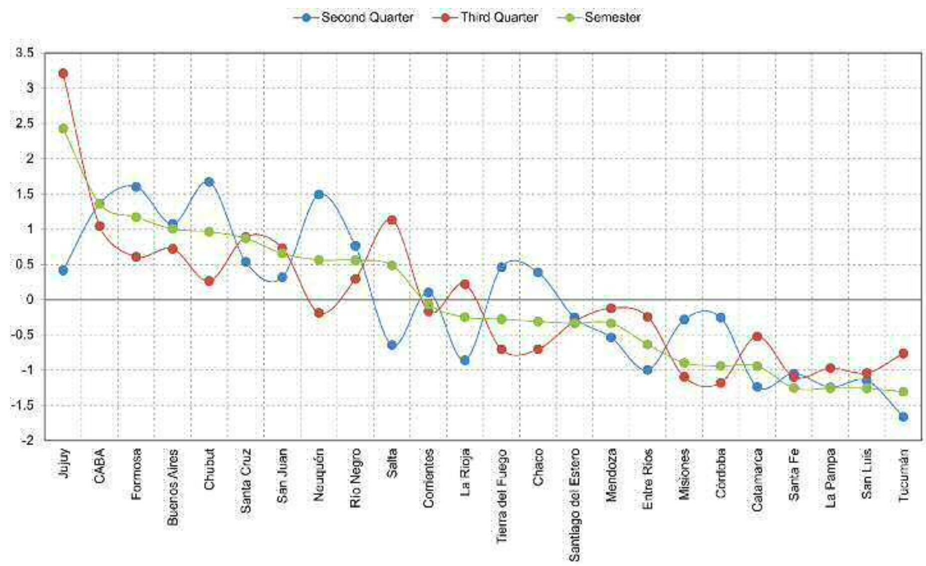


Figure 2: ITEI for provinces: standardized values per quarter and semester

of operational or vulnerability levels for each sector has been common in recent studies on the economic impact of the pandemic.

To account for people's mobility to their workplace (LMI_{jt}) in the different regions and months, we use data from Google Mobility Reports which, in the case of Argentina, is published for the provinces and the main departments within them[5]. These calculations reflect how mobility and permanence in different places – shops and leisure spaces, supermarkets and pharmacies, parks, transport stations, residential areas and, what interests us here, workplaces – have changed in percentage terms with respect to a pre-pandemic baseline value (the median for each day of the week during the 5 weeks from January 3rd to February 6th). As mentioned, the use of data from Google Mobility or similar sources has become very popular. First, we obtain for each province or department the average mobility to workplaces for the working days of each month, excluding weekends, holidays, and non-working days. Second, taking as a benchmark the value of April (mobility explained mainly by the sectoral restrictions and exceptions and the different regional production structures), we obtain the differences in mobility from May to September; that is, the recovery of mobility depending on the different evolution of each region. Then, based on a correspondence table that we have prepared, we obtain the respective values for the different LMAs, weighing the departments according to their population when it is necessary to combine two or more departments. Finally, the values for each province and LMA are divided by the national value. In other words, the labor mobility index indicates the greater or lesser recovery in mobility (above or below 1, the national level) in the provinces and LMAs with respect to the whole country.

It should be taken into account that less territorial mobility to workplaces could reflect both less flexibility in isolation measures and a greater ability of workers in that region to perform their activities from home. Therefore, the last component of the ITEI (RWI_j) accounts for the potential of remote work in each region, based on the Remote Work Indicator (RWI) proposed by Red ISPA (2020) in the case of Argentina. In general, the methodology for the RWI calculation (inspired by Del Río-Chanona et al. 2020) consists of identifying the tasks performed by a worker in each one of the occupational categories that companies declare for their employees, and detecting which of them can be carried out under a telework model. The RWI then indicates the possibility of a worker performing their activities from home, being 0 if none of the tasks can be carried out by teleworking, and 1 if all the tasks can be carried out under this modality. The RWI, which in principle

[5]In Argentina, the provincial territory is divided into departments, which generally include different localities or municipalities and also rural areas.

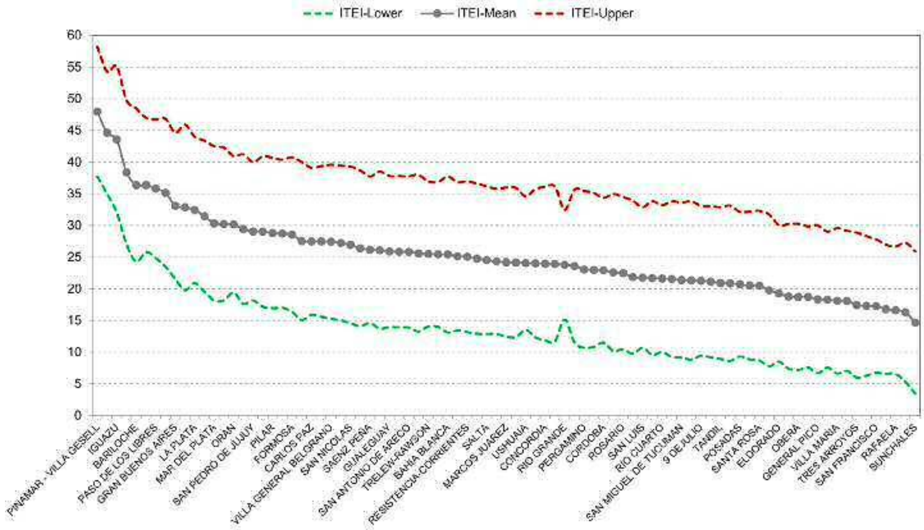


Figure 3: Lower, upper, and average ITEI for LMAs (semester)

characterizes each job position (accountant, mechanical engineer, waiter, bricklayer), can then be added to characterize the different sectors or Argentinean provinces (Red ISPA 2020). For the different LMAs, we obtain a local proxy of the RWI_j based on the RWI for each sector and the respective sectoral weights (S_{ij}). As with the labor mobility index, the values for each province and LMA are divided by the national value[6].

Due to its form of calculation, the ITEI must be interpreted as a negative index – that is, it takes higher values if the economic (private) activity has been greatly affected by the pandemic and isolation measures, and vice versa. As with any other index, the ITEI should be interpreted with some caution, prioritizing a relative comparison between regions and not an interpretation of the absolute values in each case.

5 Results

5.1 Economic impact on Argentinean provinces and LMAs

Table 1 shows the average values of the ITEI by province, for each month, quarter, and the whole semester. It is the average between the minimum and maximum values of the index, corresponding to the hypotheses of maximum and minimum operational level, respectively. Meanwhile, the quarterly and six-monthly values are obtained as a simple average of the respective monthly values. In line with the evolution of the EMAE, our index shows, in the aggregate of all provinces (last row), a very considerable negative impact in the first month, but also a sustained recovery in economic activity between April and June – a substantial fall in the index. From June onwards, this value remains relatively stable in the range of 21–23 points.

In general, there is considerable stability in the relative position of the most and least affected provinces. For example, the five most affected provinces in the semester (from Jujuy to Chubut) were among the worst ten positions in most of the months. At the other extreme, of the ten least affected provinces in the semester (from Tucumán to Santiago del Estero), half of them never were in the top ten of the most affected, and the other half only appeared there in one of the six months analyzed.

[6]It is possible to obtain a result greater than 100 -value that defines complete operativity- when multiplying the operational level of each sector (OP_{it}) by the labor mobility index LMI_{jt}) and the remote work index (RWI_j). Since this does not make sense, on such occasions the value is truncated at the upper limit of 100.

Table 1: ITEI for provinces: monthly, quarterly, and six-monthly values and ranking

	April		May		June		**Second Quarter**		July		August		September		**Third Quarter**		**Semester**	
	ITEI (mean)	Rank	ITEI (mean)	Rank	ITEI (mean)	Rank	**ITEI (mean)**	**Rank**	ITEI (mean)	Rank	ITEI (mean)	Rank	ITEI (mean)	Rank	**ITEI (mean)**	**Rank**	**ITEI (mean)**	**Rank**
Jujuy	37.9	22	27.9	17	37.2	1	**34.3**	**9**	45.9	1	44.3	1	38.1	2	**42.7**	**1**	**38.5**	**1**
CABA	45.2	8	37.2	2	33.0	4	**38.5**	**4**	33.8	2	29.7	4	22.5	10	**28.7**	**3**	**33.6**	**2**
Formosa	48.0	5	37.5	1	33.1	3	**39.5**	**2**	29.7	4	25.0	10	22.7	9	**25.8**	**7**	**32.7**	**3**
Buenos Aires	44.8	9	35.9	5	30.9	6	**37.2**	**5**	31.2	3	27.4	6	21.0	15	**26.5**	**6**	**31.9**	**4**
Chubut	48.6	4	35.3	6	35.5	2	**39.8**	**1**	24.8	6	20.7	13	25.2	6	**23.6**	**9**	**31.7**	**5**
Santa Cruz	51.3	3	32.6	8	20.7	15	**34.9**	**7**	24.4	7	31.9	2	26.5	5	**27.6**	**4**	**31.3**	**6**
San Juan	46.2	7	31.5	11	24.1	9	**33.9**	**11**	18.6	14	31.4	3	29.8	3	**26.6**	**5**	**30.3**	**7**
Neuquén	53.4	2	36.4	4	27.3	8	**39.0**	**3**	21.4	10	19.9	15	20.6	17	**20.6**	**13**	**29.8**	**8**
Río Negro	41.0	18	36.6	3	30.0	7	**35.9**	**6**	23.4	8	25.6	8	22.3	11	**23.8**	**8**	**29.8**	**9**
Salta	40.0	21	26.5	18	22.6	11	**29.7**	**17**	20.7	11	25.9	7	41.0	1	**29.2**	**2**	**29.5**	**10**
Corrientes	43.5	12	31.7	10	23.7	10	**33.0**	**12**	20.1	12	19.0	17	23.3	8	**20.8**	**12**	**26.9**	**11**
La Rioja	41.4	17	29.6	14	15.3	19	**28.8**	**18**	17.5	16	25.2	9	27.2	4	**23.3**	**10**	**26.0**	**12**
Tierra del Fuego	55.5	1	34.7	7	13.4	23	**34.5**	**8**	11.1	24	28.8	5	11.9	23	**17.3**	**18**	**25.9**	**13**
Chaco	42.1	15	29.2	16	31.3	5	**34.2**	**10**	23.2	9	16.2	19	12.4	22	**17.3**	**17**	**25.7**	**14**
Santiago del Estero	46.2	6	29.6	13	18.4	17	**31.4**	**13**	12.6	21	24.7	11	22.2	12	**19.8**	**15**	**25.6**	**15**
Mendoza	40.6	19	29.2	15	20.8	14	**30.2**	**16**	18.0	15	21.3	12	24.0	7	**21.1**	**11**	**25.6**	**16**
Entre Ríos	36.5	23	25.6	20	22.4	12	**28.2**	**19**	20.0	13	20.2	14	20.6	16	**20.3**	**14**	**24.2**	**17**
Misiones	40.4	20	31.7	9	21.7	13	**31.3**	**15**	16.2	17	15.4	20	12.6	21	**14.7**	**22**	**23.0**	**18**
Córdoba	43.8	11	31.3	12	19.1	16	**31.4**	**14**	13.8	19	14.7	21	14.0	20	**14.2**	**24**	**22.8**	**19**
Catamarca	43.3	13	23.8	23	14.3	22	**27.1**	**22**	26.4	5	11.6	24	17.3	19	**18.4**	**16**	**22.8**	**20**
Santa Fe	43.2	14	25.7	19	15.0	20	**28.0**	**20**	12.0	22	13.6	22	18.6	18	**14.7**	**23**	**21.3**	**21**
La Pampa	41.9	16	23.2	24	16.2	18	**27.1**	**23**	15.3	18	19.5	16	11.7	24	**15.5**	**20**	**21.3**	**22**
San Luis	44.6	10	24.7	21	13.3	24	**27.5**	**21**	11.6	23	11.7	23	22.0	13	**15.1**	**21**	**21.3**	**23**
Tucumán	36.3	24	24.5	22	15.0	21	**25.3**	**24**	12.9	20	16.6	18	21.2	14	**16.9**	**19**	**21.1**	**24**
Provincial Average	**44.0**		**30.5**		**23.1**		**32.5**		**21.0**		**22.5**		**22.0**		**21.9**		**27.2**	

Notes: Dark red (green) shows the five most (least) affected provinces. Light red (green) shows the next five most (least) affected provinces. Yellow shows the remaining four provinces in an intermediate position.

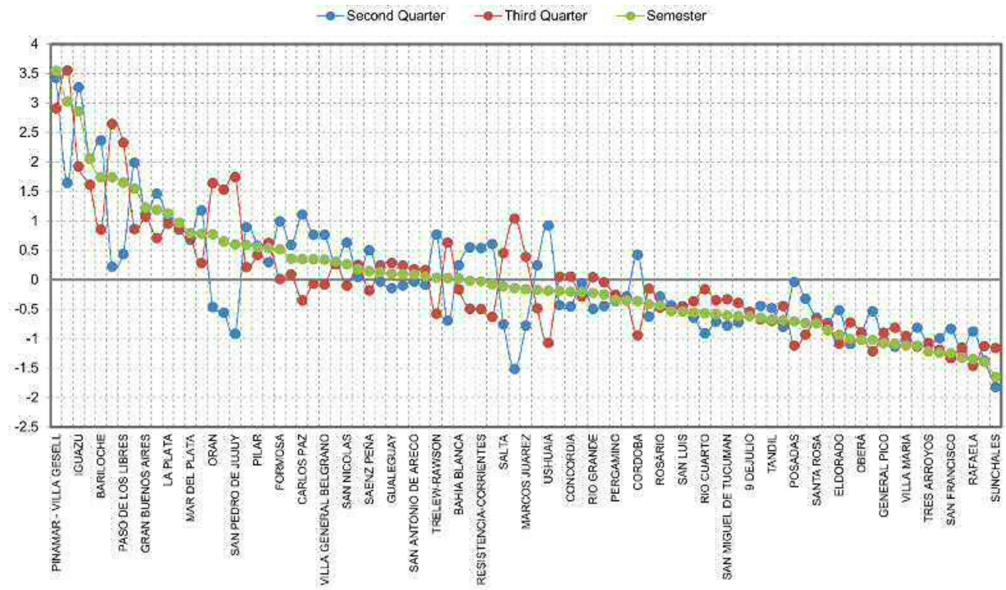


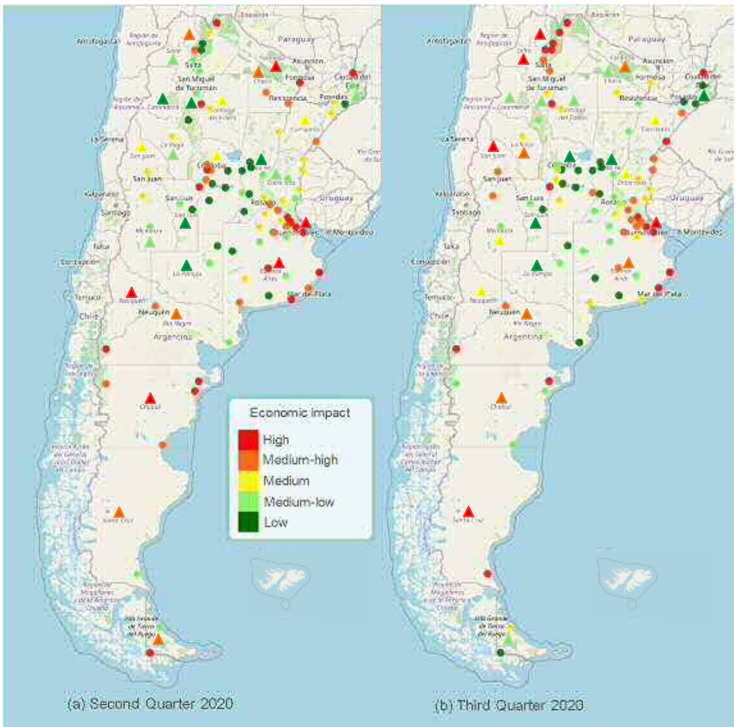
Figure 4: ITEI for LMAs: standardized values per quarter and semester

Figure 2 shows only the quarterly and six-monthly values of the ITEI in standardized values (ITEI minus the average of all provinces, divided by the standard deviation). The marked stability of the ten least affected provinces is again evident, as they are consistently below the provincial average. It can also be seen that the most affected provinces tend to have ITEI values above the average, although the fluctuations between quarters are a little more marked – Jujuy is the case with the greatest variability.

Figure 3 shows, for the whole semester, the lower and upper value of the ITEI and the average of both for the main 85 LMAs in the country. In a simple robustness analysis, we verify that the main results at the extremes of the distribution remain relatively unchanged even if we bring, on the one hand, the sectoral operational level closer to its maximum hypothesis for the most affected LMAs, and on the other hand, we bring the operational level to the minimum hypothesis for the least affected LMAs. The ITEI-Lower for the 8 most affected LMAs is 28.8 on average, while the ITEI-Upper for the 8 least affected LMAs is on, average, 27.6.

Figure 4 shows the quarterly and six-monthly standardized values of the ITEI for each LMA, analogous to Figure 2 for provinces. Several of the above-mentioned fluctuations at the provincial level are also reflected in variations of the main LMAs in each province. For example, the situation within the province of Jujuy (San Salvador de Jujuy, San Pedro de Jujuy, Libertador General San Martín) worsened between the second and third quarter, mainly due to health problems, restrictions, and reductions in labor mobility. Another interesting issue in Figure 4 is that the variability among the least affected LMAs is much lower than the most affected ones, indicating that the situation of the former barely changed along the semester. In terms of the regional productive structure, touristic areas continuously appear among the most affected LMAs throughout the whole semester. On the other hand, among the least affected LMAs, there are some areas specialized in agri-food production and several other areas with a more diversified agro-industrial profile.

Finally, and as a kind of summary, the maps in Figure 5 show the provinces and LMAs distributed throughout the country, according to the average economic impact in the second and third quarters. Apart from emphasizing some of the previous results, such as the deteriorating situation in the northwest of the country (Jujuy and Salta), the figure highlights the heterogeneity among the LMAs within the provinces. This is evident not only in large and diverse provinces, such as Córdoba or Buenos Aires, but also in smaller ones, such as Misiones or Tierra del Fuego.



Notes: the triangle indicates the economic impact in each province. The point shows the location of the central city or node of each LMA, but not its entire geographical scope.

Figure 5: Quarterly maps of economic impact: quintiles for provinces and LMAs

5.2 Comparison and validation against official indicators

As mentioned, few regional data are periodically produced in Argentina. However, given the severity of the crisis caused by the COVID–19 pandemic, some national agencies have sporadically calculated and published some indicators that could be taken as proxies of the regional economic impact of the pandemic and isolation measures. The comparison of these statistics with the ITEI values allows us to analyze their degree of correspondence and reliability (as in Fezzi, Fanghella 2020).

For the moment, the most interesting official statistic, and also the most comprehensive in territorial terms, is the percentage of companies with zero or minimum sales. This indicator was calculated for the 24 provinces and several cities in the country between April and August, based on data from all formal companies that pay taxes to AFIP (CEPXXI 2020). In order to compare this indicator of cities with the ITEI for LMAs, we weighted the data by the population of each city in those cases where one LMA covers more than one of these cities. It is worth noting that, in this way, we have information for only 50 of the 85 LMAs, showing the greater geographical and temporal coverage of the ITEI.

Figure 6 contrasts the values of the ITEI and the percentage of companies with zero or minimum sales for the two months of greatest economic impact in the country (April and May) and the latest available (August). In all cases, there is a positive relationship between the two indicators. Higher levels of the ITEI, both for provinces and LMAs, generally coincide with higher percentages of companies in a critical situation. In dynamic terms there is also a certain correspondence between these indicators, especially for the provinces. The shift, month by month, from the top to the bottom, i.e., a reduction in the economic impact measured by the ITEI, corresponds to a shift from the right to the left, i.e., a reduction in the percentage of companies with zero or minimum sales. For the LMAs the correspondence is a little weaker, above all in the comparison with August, showing a greater heterogeneity in the situation of the companies among the different localities.

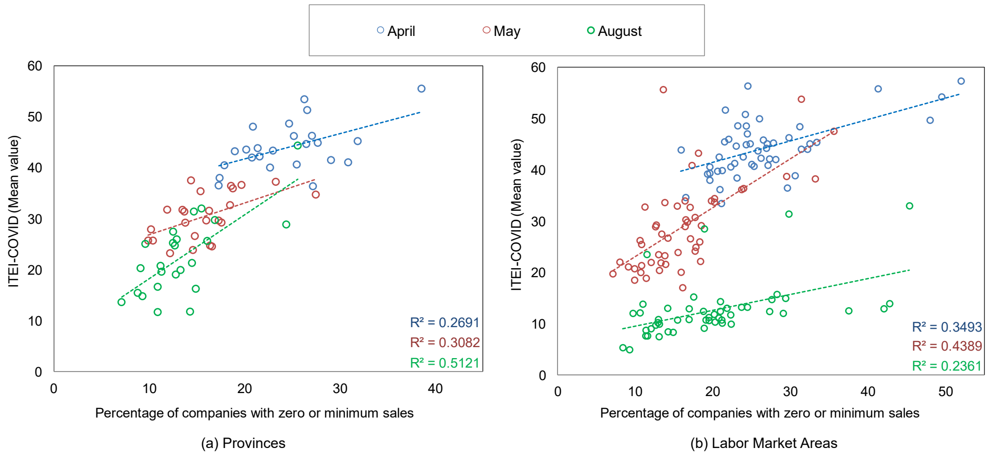


Figure 6: ITEI values versus the percentage of companies in a critical situation

The previous linkages are also evident when computing Pearson's correlations between the two indicators, as can be seen, in particular, along the diagonals highlighted in bold in Table 2. These correlations are positive and significant in all months in the case of the LMAs, and in April, May, and August for the provinces. If, instead of comparing the absolute values, we analyze the percentage changes with respect to April – that is, the recovery of both indicators against the month of greatest economic impact – we can appreciate positive and significant correlations for all months, both for provinces and LMAs (Table 3).

Table 2: Pearson's correlations between ITEI values and companies in a critical situation

		ITEI for Provinces				
		April	May	June	July	August
% of companies with zero or minimum sales	April	**0.5188*** **	0.4323**	-0.1501	-0.1622	0.2293
	May	0.5935***	**0.5551*** **	-0.0382	-0.0564	0.2707
	June	0.519***	0.5629***	**0.1839**	0.1158	0.378*
	July	0.4808**	0.4289**	0.1269	**0.1463**	0.3604*
	August	0.2408	0.2179	0.2491	0.4024*	**0.7156*** **

		ITEI for Labor Market Areas				
		April	May	June	July	August
% of companies with zero or minimum sales	April	**0.5910*** **	0.6026***	0.359**	0.3104**	0.3594**
	May	0.5944***	**0.6625*** **	0.4150***	0.3547**	0.3382**
	June	0.5960***	0.6972***	**0.5252*** **	0.4570***	0.4124***
	July	0.5755***	0.6665***	0.5119***	**0.4731*** **	0.4294***
	August	0.5685***	0.6044***	0.4524***	0.4261***	**0.4859*** **

Notes: Significance level: *p <0.10, **p <0.05, ***p <0.01.

Table 3: Pearson's correlations between ITEI and companies in a critical situation, measured as percentage changes with respect to April

		Change in ITEI for Provinces			
		May	June	July	August
Change in companies with zero or minimum sales	May	**0.3754***	0.1172	0.0714	0.0257
	June	0.3286	**0.5813*****	0.4847**	0.3525*
	July	0.1192	0.506**	**0.5558*****	0.3768*
	August	0.0719	0.5391***	0.703***	**0.7391*****

		Change in ITEI for Labor Market Areas			
		May	June	July	August
Change in companies with zero or minimum sales	May	**0.5563*****	0.3352**	0.2517*	0.1025
	June	0.5354***	**0.5405*****	0.4583***	0.2776*
	July	0.4418***	0.494***	**0.4879*****	0.2988**
	August	0.2737*	0.405***	0.4689***	**0.5396*****

Notes: Significance level: *p <0.10, **p <0.05, ***p <0.01.

6 Conclusions

In this paper we propose the construction of an index to approximate the territorial economic impact of the COVID–19 pandemic and the consequent isolation measures in contexts with scarce or outdated regional data. This can be particularly useful for developing countries, where not only national and regional statistical systems are usually weaker, but also tend to focus mainly on sectoral data. This sectoral bias is explained by the high degree of productive specialization of some regions – frequently related to the exploitation of natural resources – and often leads to reducing the analysis of the territorial impact to what happens only in a few sectors in which each region is specialized. However, contexts as disruptive as the COVID–19 pandemic require both a comprehensive sectoral view (since the vast majority of the economic activities have been affected to some extent) and a recognition of territorial particularities in terms of the political management of the pandemic.

With some adjustments or adaptations to each context, the proposed index can be used to analyze the uneven territorial economic impact of the pandemic elsewhere, based on data or statistics that are usually available in most countries: a) the sectoral production structure of the different regions (pre-pandemic data), b) the operational level of each sector (post-pandemic data at the national level), c) the mobility of workers in each region (post-pandemic data from Google Mobility Reports or other available sources), and d) the possibility of remote work among the different sectors (calculated by several recent studies).

In line with recent literature, the empirical application for Argentina showed the uneven impact of the COVID–19 pandemic on regional (private) production or economic activity. In this sense, the ITEI revealed large disparities between the 24 provinces and the main 85 LMAs of the country, as well as the heterogeneity within some provinces, which revalues the use of smaller geographical units. The results also showed that, although the economic impact of the pandemic has been decreasing over the months for the country as a whole, there is considerable stability in the relative position of the most and least affected regions. Finally, the comparison with sporadic official indicators of the regional impact of the pandemic has emphasized the validity of the proposed index, which also has a higher geographical and temporal coverage.

Although in this paper we have proposed a relatively simple and descriptive exercise, the calculation of an index of territorial economic impact can be a relevant input for the design, implementation, and monitoring of targeted and place-based policies, which seek to mitigate the harmful economic impacts of the pandemic and isolation measures. In the future, the collection of evidence on the immediate or short-term impacts of the pandemic may give rise to other studies that analyze the medium- and long-term impacts, especially concerning the evolution of regional asymmetries. Likewise, economic impact indicators such as the ITEI can be the starting point (or the dependent variable) for future studies that seek to analyze with more detail the regional factors behind this phenomenon.

As mentioned, given the limited subnational data available in Argentina, the ITEI also has some limitations that could be taken into account in future research or in applications for other countries. For example, the use of regional demand indicators could be an alternative avenue to explore, instead of analyzing the territorial economic impact from the supply side. On the other hand, the use of employment or labor data could also be expanded or complemented, taking into account the different labor intensities in the different sectors and the importance of other inputs and intermediary products. The construction of regional input-output tables would be a necessary step to consider these inter-sectoral and inter-regional linkages.

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Appendix: Sectoral operational hypotheses applied to EBDO data (ISIC)

Classification of economic activities used by EBDO (ISIC)		April		May		June		July		August		September		Based on statistics, surveys or reports from chambers, centers or organizations
2 digit		Min	Max	Min	Max	Min	Max	Min	Max	Min	Max	Min	Max	
1	Agriculture, livestock farming, hunting and related service activities	75	100	75	100	75	100	75	100	75	100	75	100	INDEC-EMAE; INDEC-ICA; CONINAGRO; Fund. Observ. PYME (FOP); CENE-UB
2	Forestry, wood extraction and related service activities	50	75	50	75	75	100	75	100	75	100	75	100	INDEC-EMAE; INDEC-ICA; AFOA; ASORA; FAIMA
5	Fishing and fishing-related activities	50	75	75	100	50	75	25	50	75	100	75	100	INDEC-EMAE; INDEC-ICA; Subsecr. de Pesca y Acuic.; Intercám. Ind. Pesquera
11	Extraction of crude oil and natural gas; activities related to oil and gas extraction, except prospecting activities	25	50	50	75	50	75	75	100	75	100	75	100	INDEC-EMAE; Secr. de Energía; CEPH; CEIPA; Ecolatina; Revista Trama
13	Extraction of metalliferous minerals	25	50	25	50	50	75	50	75	75	100	75	100	INDEC-ICA; INDEC-EMAE; CAEM
14	Exploitation of other mines and quarries	25	50	25	50	50	75	50	75	75	100	75	100	INDEC-ICA; INDEC-EMAE; CAEM
15	Foods	75	100	75	100	75	100	75	100	75	100	75	100	INDEC-IPIM; CAME; FIEL; FOP; UIA
16	Tobacco	25	50	50	75	75	100	75	100	75	100	75	100	INDEC-IPIM; CIT; FIEL; UIA
17	Textile products	25	50	50	75	75	100	50	75	75	100	75	100	INDEC-IPIM; CAME; FIEL; UIA
18	Confections	0	25	25	50	50	75	50	75	50	75	75	100	INDEC-IPIM; CAME; CIAI; FIEL; UIA
19	Leather	0	25	25	50	50	75	50	75	50	75	50	75	INDEC-IPIM; CAME; FIEL; UIA
20	Wood	50	75	75	100	75	100	75	100	75	100	75	100	INDEC-IPIM; AFOA; ASORA; FAIMA
21	Paper	75	100	75	100	75	100	75	100	75	100	75	100	INDEC-IPIM; FIEL; UIA
22	Edition	75	100	75	100	75	100	75	100	75	100	75	100	INDEC-IPIM; UIA
23	Petroleum products	50	75	50	75	75	100	75	100	75	100	75	100	INDEC-IPIM; FIEL; UIA
24	Chemical products	75	100	75	100	75	100	75	100	75	100	75	100	INDEC-IPIM; CAME; FIEL; UIA
25	Rubber and plastic products	50	75	50	75	75	100	75	100	75	100	75	100	INDEC-IPIM; CAME; UIA
26	Other non-metallic minerals	25	50	50	75	75	100	75	100	75	100	75	100	INDEC-IPIM; INDEC-ISAC; FIEL; UIA
27	Common metals	25	50	25	50	50	75	50	75	50	75	75	100	INDEC-IPIM; CAA; FIEL; UIA
28	Other metal products	25	50	50	75	75	100	75	100	75	100	75	100	INDEC-IPIM; ADIMRA; FIEL; UIA
29	Machinery and equipment	50	75	50	75	75	100	75	100	75	100	75	100	INDEC-IPIM; ADIMRA; FIEL; UIA
30	Office machinery	0	25	25	50	75	100	75	100	50	75	75	100	INDEC-IPIM; CAME; UIA
31	Electric appliances	0	25	25	50	50	75	50	75	50	75	75	100	INDEC-IPIM; CAME; UIA
32	Radio and television	0	25	25	50	75	100	75	100	50	75	75	100	INDEC-IPIM; CAME; UIA
33	Medical instruments	50	75	75	100	75	100	75	100	75	100	75	100	INDEC-IPIM; ADIMRA; UIA
34	Automotive	0	25	25	50	50	75	50	75	75	100	75	100	INDEC-IPIM; ADEFA; FIEL; UIA
35	Other transport equipment	0	25	25	50	50	75	50	75	50	75	50	75	INDEC-IPIM; UIA
36	Furniture	25	50	50	75	75	100	75	100	75	100	75	100	INDEC-IPIM; ASORA; CAME; FAIMA
37	Waste and scrap recycling	50	75	50	75	75	100	75	100	75	100	75	100	INDEC-IPIM
40	Electricity, gas and water	75	100	75	100	75	100	75	100	75	100	75	100	INDEC-ISSP; INDEC-EMAE; Secr. de Energía; ENARGAS;
41	Collection, purification and distribution of water	75	100	75	100	75	100	75	100	75	100	75	100	INDEC-ISSP; Ecolatina
45	Building	0	25	25	50	50	75	50	75	50	75	50	75	INDEC-ISAC; INDEC-EMAE; CAMARCO; FOP
50	Sale, maintenance and repair of motor vehicles and their parts, pieces and accessories; sale, maintenance and repair of motorcycles and their parts, pieces and accessories; retail sale of fuel for motor vehicles and motorcycles	25	50	50	75	50	75	50	75	50	75	75	100	ACARA; CECHA
51	Wholesale trade	25	50	50	75	75	100	75	100	75	100	75	100	INDEC-EMAE; CAC; CADAM
52	Retail trade and repair of personal and household goods	25	50	50	75	50	75	75	100	75	100	75	100	INDEC-EMAE; CAC; CACE; CAME; FOP
55	Hotel and restaurant services	0	25	0	25	25	50	25	50	25	50	25	50	INDEC-EOH; INDEC-ETI; INDEC-EMAE; FEHGRA; INPROTUR
60	Rail, automotive and pipeline transportation service	50	75	50	75	50	75	50	75	50	75	50	75	INDEC-ISSP; INDEC-EMAE; CNRT; FADEEAC
61	Sea and river transport service	50	75	50	75	75	100	75	100	75	100	75	100	INDEC-ISSP; CAPYM
62	Air transport service for cargo and passengers	0	25	0	25	0	25	0	25	0	25	0	25	ANAC
63	Cargo handling, storage and warehousing services; complementary services for transportation; travel agency services and other complementary tourist support activities; management and logistics services for the transport of goods	50	75	50	75	50	75	50	75	50	75	50	75	INDEC-ISSP; INDEC-EMAE
64	Postal and telecommunications services	75	100	75	100	75	100	75	100	75	100	75	100	INDEC-ISSP; Ecolatina; Lódola & Picón (2020); Red ISPA (2020)
65	Financial intermediation and other financial services	75	100	75	100	75	100	75	100	75	100	75	100	INDEC-EMAE; ADEBA; Albrieu (2020); Bonavida Foschiatti & Gasparini (2020); Lódola & Picón (2020); Red ISPA (2020)
66	Insurance services, retirement and pension fund management services	75	100	75	100	75	100	75	100	75	100	75	100	INDEC-EMAE; CENE-UB; Albrieu (2020); Bonavida Foschiatti & Gasparini (2020); Lódola & Picón (2020); Red ISPA (2020)
67	Auxiliary services to financial activity, except insurance and pension fund management services	75	100	75	100	75	100	75	100	75	100	75	100	INDEC-EMAE; CENE-UB; Albrieu (2020); Bonavida Foschiatti & Gasparini (2020); Lódola & Picón (2020); Red ISPA (2020)
70	Real estate services	0	25	25	50	50	75	50	75	50	75	50	75	CAC; CECBA; CIA; Reporte Inmobiliario; Lódola & Picón (2020)
71	Rental of transport equipment and machinery and equipment n.c.p. rental of personal and household goods n.c.p.	0	25	25	50	50	75	50	75	50	75	50	75	CENE-UB; Lódola & Picón (2020)
72	Computer activities: Consultant services, data processing, maintenance and repair of office, accounting and computer machinery	50	75	75	100	75	100	75	100	75	100	75	100	CAC; CESSI; CENE-UB; FOP; Albrieu (2020); Bonavida Foschiatti & Gasparini (2020); Red ISPA (2020)
73	Research and experimental development in the field of engineering and of the exact and natural sciences and of the social sciences and humanities	75	100	75	100	75	100	75	100	75	100	75	100	CAC; CENE-UB; FOP; Albrieu (2020); Bonavida Foschiatti & Gasparini (2020); Red ISPA (2020)
74	Legal and accounting, bookkeeping and auditing services; tax advice; market research and public opinion polls; business and management advice; architectural and engineering services and technical services n.c.p. advertising services; business services n.e.c.	50	75	75	100	75	100	75	100	75	100	75	100	CAC; CENE-UB; FOP; Albrieu (2020); Bonavida Foschiatti & Gasparini (2020); Red ISPA (2020)
75	Temporary employment agencies	0	25	25	50	25	50	25	50	25	50	50	75	CENE-UB
80	Teaching: initial, primary, secondary, higher and postgraduate training; adult education and educational services n.e.c.	75	100	75	100	75	100	75	100	75	100	75	100	INDEC-EMAE; Ecolatina; FOP; Albrieu (2020); Bonavida Foschiatti & Gasparini (2020); Lódola & Picón (2020); Red ISPA (2020)
85	social and Health Services	75	100	75	100	75	100	75	100	75	100	75	100	INDEC-EMAE; Lódola & Picón (2020)
90	Waste and sewage disposal, sanitation and similar services	75	100	75	100	75	100	75	100	75	100	75	100	INDEC-ISSP
91	Services of business, professional and employers organizations; union services; association services n.c.p.	75	100	75	100	75	100	75	100	75	100	75	100	CAC; CENE-UB; FOP; Bonavida Foschiatti & Gasparini (2020); Red ISPA (2020)
92	Cinematography, radio and television services and entertainment and artistic entertainment services n.e.c. news agency services; library, archive and museum services and cultural services n.c.p. services for sports and entertainment practice n.e.c.	0	25	25	50	25	50	25	50	25	50	50	75	SICA; CENE-UB; Red ISPA (2020)
93	Services n.c.p.	0	25	0	25	25	50	25	50	25	50	50	75	INDEC-EMAE; CENE-UB; Bonavida Foschiatti & Gasparini (2020)

Note: The (k) sectors highlighted in gray are those considered essential, of rapid recovery, or reconversion to teleworking, which is reflected in the fact that during April, the month of greatest restrictions, the hypothesis of maximum operational level was already equal to 100, or 75 in April but in May and June it already reaches 100; the latter only occurs in 3 sectors.

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Isolation and well-being in the time of lockdown

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Abstract. In response to the Covid 19 health crisis, the French government has imposed various measures, referred to as social-distancing measures, including a lockdown with the primary objective of reducing face-to-face interactions between people in order to limit the spread of the virus. This paper seeks to determine whether social-distancing measures and lockdown lead to social isolation for certain groups of people and if they have an impact on French people's well-being. First, it reveals that feelings of social isolation have substantially increased in France during the lockdown and regional differences have occurred. Second, it shows a change in the geography of well-being in France induced by lockdown – with Southerners, originally the happiest, exhibited a strong decline in well-being. Third, estimations show that acclimation to social isolation slows the decline in well-being during lockdown; and that the increase in people's feelings of social isolation during lockdown is a factor which negatively impacts their level of well-being. Fourth, it reveals certain positive influences of residence geographic location on changes in well-being levels.

JEL classification: I31, I30, I14

Key words: health, France, French regions, social isolation, well-being, Covid-19

1 Introduction

In response to the Covid 19 health crisis, the French government has imposed various measures, referred to as social-distancing measures. In spatial terms, these have resulted in the emptying of public spaces, the closure of places where people habitually meet and gather – bars, cafés, restaurants, live-music venues, libraries – and silence, and sometimes sound of birdsong, in urban environments. The most emblematic measure, however, was probably the lockdown of the French population – that is to say, an injunction to stay at home for all but essential reasons – which came into force at noon on Tuesday 14th March 2020 and ended on Monday 11th May 2020. The primary objective of this lockdown was to reduce face-to-face interactions between people in order to limit the spread of the virus.

The effects of lockdown on individuals have been numerous. At the collective level, by restricting the possibilities for meeting other people, it caused a contraction of social life and led people to find new ways of making social interactions possible.

Individually, lockdown can lead to what is known as social isolation. Indeed, according to De Jong Gierveld et al. (2006, p. 486) "social isolation concerns the objective characteristics of a situation and refers to the absence of relationships with other people. [...] There is a continuum running from social isolation at the one end to social participation at the other. Persons with a very small number of meaningful ties are, by definition, socially isolated." Social isolation has negative effects on people's mental, physical, and cognitive states of well-being (House et al. 1988, Hawkley, Capitanio 2015, Berkman, Syme 1979). Several studies have demonstrated that social isolation can lead to depression, reduce cardiovascular capacity, cause changes in immune responses and sleep patterns, and reduce the life expectancy of affected individuals (Berkman, Syme 1979, Alcaraz et al. 2019). And a recent study conducted in the United States, among a sample of 580,000 adults, showed that social isolation increases the risk of premature death (Alcaraz et al. 2019). We also know that, in general, the proportion of individuals reporting low levels of well-being is higher for those who feel lonely than among other groups (Helliwell 2006). In France, this proportion stands at 45% compared with 16% for other groups (Beasley, Perona 2020).

Consequently, through the reduction in face-to-face interactions among the French population, who are by nature social and sensitive beings, by confining them to a reduced living space – within the parameters of their home – and by restricting their freedom of movement and depriving them of contact with nature, social-distancing measures and lockdown can lead to social isolation for certain groups of people and have an impact on French people's well-being.

The aim of our paper is to contribute to the debate on the effects of social isolation on people's well-being by focusing on the French case on a regional scale, in an exceptional context. In the spring of 2020, the "great lockdown" was decided upon, and a large proportion of the country's economic activity was consequently shut down. This situation is unprecedented, and studying its effects is particularly welcome. We are in a position to do this because, during this great lockdown, we conducted a survey on the effects of lockdown on individuals' daily lives among French people and across different regions of France. We developed two hypotheses: first, lockdown has increased feelings of social isolation among the French population, with regional disparities; and second, the increase in people's feelings of social isolation is a factor that had a negative impact on their level of well-being.

Our paper is organized as follows. First, we present our survey methodology. Accordingly, we show that feelings of social isolation have substantially increased in France during the lockdown period and that these have not affected all people in mainland France in the same way. In particular, we will underline a number of regional differences (Section 2). We will then reveal the effects of lockdown on French people's well-being, and regional disparities in this regard. Next, using multiple linear regression, we will estimate the effects of changes in feelings of social isolation on changes in the reported level of well-being of French respondents during lockdown. We tested the following hypothesis: the increase in feelings of social isolation has a negative impact on changes in levels of well-being (Section 3). To conclude, we discuss the generalizability of our results.

2 Evaluating the effects of social-distancing measures on French people's sense of social isolation

2.1 An online survey boosted by the media and an adjusted sample

During the first week of lockdown in France, on 23rd March 2020, we have announced the launch of a national survey on three social networks: Twitter, LinkedIn, and Facebook. In these different posts, we invited internet users to go to the same independent internet page to complete the questionnaire. The next day, a daily online newspaper, Lyon Capitale, ran a headline on the research conducted by an academic from Lyon University and shared the link to the survey with its readers. From that day on, many journalists brought attention to the subject. We have been interviewed by a variety of media: television (BFM TV, France 3, Arte), radio (including RMC, RCF and Radio Virgin), and national and regional newspapers (20 Minutes, Le Monde, Le Progrès). The survey was also disseminated by a number of scientific bodies and organizations, such as the European Regional Science Association, the French National Centre for Scientific Research (CNRS), and French healthcare information-systems company VIDAL. Thus, a large number of French people became aware of the survey and responded to it by going to the web page. As a result, by 10th May, more than 10,976 French people had answered the questionnaire.

The survey was a self-administered questionnaire. This type of survey presents certain advantages. For example, as Sudman, Bradburn (1974) observe, compared with interviews, self-administered surveys reduce respondents' tendency to present themselves in a favorable light.

The aim of this survey was to record the changes that had taken place in French people's day-to-day lives – pace of life, daily habits, social relations, working conditions, employment situations, etc. – and more specifically to evaluate the impact of these factors on their well-being and health. To this end, the questionnaire comprises nine sections. The first introduces the aims of the survey; the second relates to "Life satisfaction and pace of life"; the third deals with "external activities and ICT use"; the fourth with "accommodation"; the fifth focuses on respondents' "situation with regard to work"; the sixth on "assistance during lockdown"; the seventh on "feelings/experiences"; the eighth concerns the personal situation of the interviewee; and the final section thanks respondents for their participation.

Owing to the mode of dissemination of the survey, we had to adjust the sample. To do this, a number of calibration methods exist. These methods enable us to adjust a sample by (re)weighting individuals, using ancillary information available on a number of variables, called calibration variables (Deming, Stephan 1940). The weights produced by these methods are used to calibrate the sample on known population totals in the case of quantitative variables, and on known category frequencies in the case of qualitative variables (Deville, Särndal 1992). The adjustment consists of replacing the initial weights (or "sampling weights") with new weights such that: for a categorical (or "qualitative") calibration variable, the estimated category frequencies for the sample, after adjustment, will be equal to the known population size; and for a numerical (or "quantitative") variable, the estimated total for the variable in the sample, after adjustment, will be equal to the known population total for the variable. This calibration method reduces sampling variance, and in some cases reduces bias due to total non-response.

To adjust the sample, we used an adapted version of the Calmar method. Calmar is an acronym for CALibration on MARgins. This method is "an adjustment technique which adjusts the margins (estimated from a sample) of a contingency table of two or more qualitative variables to the known population margins. However, the program is more general than mere 'calibration on margins,' since it also calibrates on the totals of quantitative variables" (Sautory 1993, p. 2)(Sataury, 1993, 2). We developed the program using IBM's Statistical Package for the Social Sciences (SPSS) software. The linear method was sufficient, as we did not get negative values.

Consequently, we corrected the biases to ensure better representativeness for our sample compared to the adult population of mainland France, who was our target population. Accordingly, we not only eliminated the biases induced by non-response but also reduced comparability concerns. The chosen criteria were age, gender, educational qualifications, and the region of residence adjusted to the population margins of the data from the French National Institution of Statistics and Economic Studies (INSEE). The selected categories were those of the French National Institute of Statistics and Economic Studies (INSEE).

In this way, we obtained a sample of 10,976 individuals, who are representative of the adult population of mainland France in terms of age (Table 1), gender (52.5% female, 47.5% male), educational qualifications (below second degree 56.0%, second degree 16.4%, Diploma Advanced Technician 10.0%, Bachelor 8.6%, Master or higher 8.9%), and region of residence during the spring lockdown from 23rd March to 10th May 2020.

2.2 The spread of feelings of social isolation through French society during lockdown

During the great lockdown, feelings of social isolation spread considerably throughout French society (Table 2). While more than 60% of respondents in France declared that

Table 1: Distribution of age in our adjusted sample

Age (years)	Percent
18-30	17.5
31-39	13.6
40-49	13.8
50-59	18.1
60-69	17.1
70+	20.0
Total	100.0

Table 2: Frequency of feelings of isolation among French people

	Before lockdown	Since lockdown
Never	60.2	32.9
Rarely	29.6	24.2
Often	7.7	27.1
All the time	1.3	14.2
Don't know	1.2	1.6
Total	100%	100%

Notes: The difference between the two periods is significant (Fisher-Freeman-Halton test with p-value = 0.000)

they never felt socially isolated before lockdown, this figure fell to just under a third during the lockdown period. It should also be noted that 41.3% of French people reported that they felt socially isolated often or all the time during lockdown, compared to only 9% before lockdown. However, certain differences can be observed within the French population, particularly with regard to employment situation, age, gender, and region of residence.

2.3 2.3 Visible differences within the French population with regard to social isolation during lockdown

Differences were observed between individuals who work and those who do not work. For example, 63.5% of those who do not usually work reported never feeling socially isolated before lockdown, compared to 58.6% of those who do work (Table 3). During lockdown, these figures dropped to 38% of those who do not work, compared with 32% of those who do. Another noteworthy fact is that, for those who habitually work, maintaining one's activity during lockdown, i.e., by working from home or continuing to go into the workplace, reduces the frequency of feelings of social isolation. In the case of our study in France, therefore, it was those respondents who usually work but were not able to do so under lockdown who tended to feel socially isolated either often or all of the time. This was the case for almost 47.7% of this group, whereas only slightly more than a third (34.7%) of remote workers and 40.7% of those who continued to go into their workplace reported similar feelings.

As we can see, being integrated into professional networks is a factor that helps reduce feelings of social isolation during lockdown. The effects of such professional networks are therefore just as favorable in lockdown as in non-lockdown periods (Dykstra 1990, Silverstein, Chen 1996).

Differences in feelings of social isolation were also observed among French respondents according to the type of housing in which they spent lockdown (Table 4). Those who lived in an apartment without a view were the most affected by feelings of social isolation: 56.6% of this group reported feeling socially isolated often or all the time during lockdown, compared with less than 40% of people living in a house with a garden. This group of respondents (i.e., in apartments without a view) also experienced the greatest deterioration

Table 3: Frequency of feelings of isolation among French people according to their employment situation

	Does not generally work	Generally works	Worked from home during lockdown	Went to workplace during lockdown	Did not work during lockdown
			Before lockdown		
Never	63.5	58.6	58.3	59.7	58.4
Rarely	26.9	32.7	34.3	30.7	32.2
Often	8.4	7.3	6.7	9.0	7.0
All the time	1.3	1.4	0.7	0.6	2.4
Total	100%	100%	100%	100%	100%
			During lockdown		
Never	38.3	32.0	32.7	30.8	24.9
Rarely	19.1	32.6	32.5	28.5	27.4
Often	25.6	32.3	25.8	31.8	31.4
All the time	17.0	13.2	8.9	8.9	16.3
Total	100%	100%	100%	100%	100%

Notes: The difference between workers and non-workers, as between groups of workers in both periods is significant (Fisher-Freeman-Halton tests with p-value = 0.000).

in terms of feelings of social isolation, with the proportion reporting never being affected by such feelings falling from 51.7% before lockdown to 19% during.

Table 4: Frequency of feelings of isolation among French people according to their type of accommodation

	Apartment without a view	Apartment with a view	Apartment with a balcony or terrace	House with a garden/outdoor space
		Before lockdown		
Never	51.7	52.3	57.7	64.8
Rarely	31.7	33.7	32.4	28.1
Often	13.0	10.1	8.6	6.5
All the time	3.7	3.9	1.3	0.6
Total	100%	100%	100%	100%
		During lockdown		
Never	19.0	32.5	29.6	36.8
Rarely	24.4	25.4	27.3	23.4
Often	39.7	29.1	31.6	24.3
All the time	16.9	12.9	11.5	15.5
Total	100%	100%	100%	100%

Notes: The difference between accommodation type is significant in both periods (Fisher-Freeman-Halton tests with p-value = 0.000).

Fewer women than men reported never feeling socially isolated. During lockdown, 29.2% of women came into this category, compared with 37% of men (Table 5). This is in line with a result observed in France under normal conditions: women generally report feeling isolated more often than men (Beasley, Perona 2020).

Living alone appears to be a factor that fosters social isolation (De Jong Gierveld et al. 2006, Waite, Gallagher 2000, Coleman et al. 2000, Dannenbeck 1995, Wenger et al. 1996). However, only 22.3% of French people who spent lockdown alone reported never feeling socially isolated during lockdown, compared with 36.5% of the remainder of the population.

We also observed variations in the frequency of French people's feelings of social isolation between different regions of France (Table 6). Almost 50% of respondents in the

Table 5: Frequency of feelings of isolation among French people according to their gender

	During lockdown		Before lockdown	
	Frequency	%	Frequency	%
		Male		
Never	1,962	37.0	3,357	63.3
Rarely	1,290	24.3	1,425	26.9
Often	1,170	22.1	389	7.3
All the time	826	15.6	115	2.2
Don't know	58	1.1	19	0.4
Total	5,305	100	5,305	100
		Female		
Never	1,653	29.2	3,250	57.3
Rarely	1,368	24.1	1,824	32.2
Often	1,808	31.9	457	8.1
All the time	728	12.8	30	0.5
Don't know	113	2	110	1.9
Total	5,671	100	5,671	100

Notes: Fisher test p-value = 0.000; significant difference between male and female.

Hauts-de-France region, in northern France, declared that they never felt socially isolated during lockdown, compared with just 15.2% of respondents in the western Pays de la Loire region. At the other end of the spectrum, 31.3% of respondents in Brittany and 32.8% of respondents in Nouvelle-Aquitaine (in southwestern France) said they felt isolated all the time, compared with 7.5% of respondents in the Grand Est region (covering most of eastern France) and 8.4% of respondents based in Île-de-France (the Paris region).

Table 6: Frequency of feelings of isolation among French people according to their region of residence during lockdown (%)

	Never	Rarely	Often	All the time	Don't know	Total
Auvergne–Rhône-Alpes	35.0	26.6	26.8	9.9	1.7	100
Bourgogne–Franche-Comté (Burgundy–Franche-Comté)	23.2	21.1	41.1	13.6	1.0	100
Bretagne (Brittany)	23.0	18.0	27.4	31.3	0.4	100
Centre-Val de Loire	37.0	18.4	33.5	9.5	1.7	100
Grand Est	38.8	25.8	24.4	7.5	3.5	100
Hauts-de-France	49.2	16.6	20.8	9.8	3.7	100
Île-de-France (Paris region)	34.8	26.3	28.6	8.4	1.9	100
Normandie (Normandy)	36.7	19.5	30.5	12.6	0.7	100
Nouvelle-Aquitaine	15.8	25.1	25.9	32.8	0.3	100
Occitanie	37.4	27.3	22.5	12.3	0.5	100
Pays de la Loire	15.2	28.7	33.4	22.4	0.3	100
Provence-Alpes-Côte d'Azur	37.1	24.4	26.8	10.0	1.6	100

Overall, during lockdown, more French people than usual felt socially isolated at least some of the time (i.e., rarely, often, or all of the time). However, lockdown did not have the same effect on everyone.

2.4 *Differentiated changes in feelings of social isolation throughout France*

Some French people – to be precise, 442 out of the 10,976 individuals in our sample – felt less socially isolated than usual. This was the case for 5.4% of women and 2.8% of men, who reported feeling less socially isolated during lockdown than before lockdown. Others – 5,256 individuals – felt no difference: for nearly 56% of men and 42% of women, lockdown had no effect on their feelings of social isolation. This means that 5,574 of our

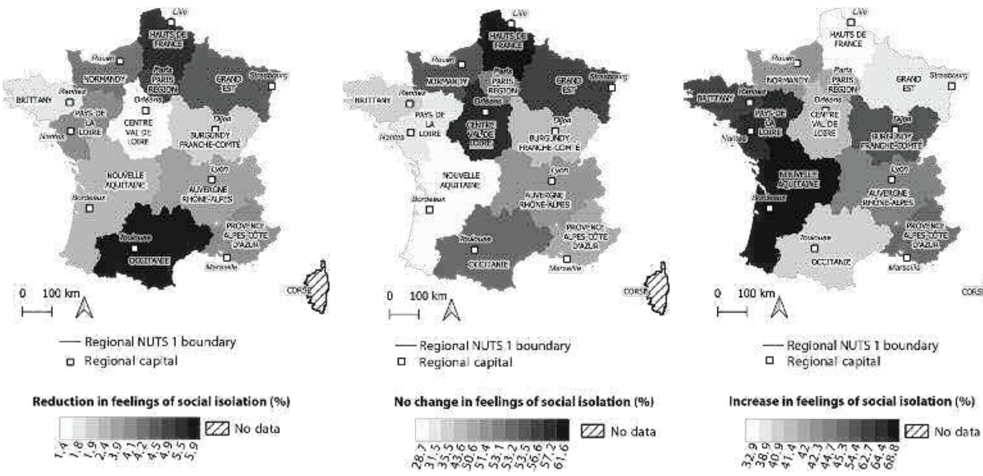
Table 7: Change in feelings of social isolation, by gender and age, among the French population during the spring 2020 lockdown

	Total numbers of French respondents		Male	Female	Age 18-34	Age 35-54	Age 55-74	Age 75+
Less isolated	442	4.1%	2.8%	5.4%	5.9%	5.0%	2.6%	3.5%
No change	5,256	48.8%	55.9%	42.0%	39.2%	42.4%	53.0%	65.7%
More isolated	5,074	47.1%	41.3%	52.6%	54.8%	52.5%	44.5%	30.8%
Total	10,771*	100%	100%	100%	100%	100%	100%	100%

Notes: *205 individuals out of the 10,976 individuals did not give an opinion.

respondents saw their situation deteriorate, or 47.1% of the people in our sample; more specifically, 41.3% of French men and 52.6% of French women reported an increase in their feelings of social isolation (Table 7).

If we take age group into consideration, we can see that 18- to 34-year-olds were the group most affected. Indeed, almost 55% of this age group reported an increase in feelings of social isolation, followed closely by 35- to 54-year-olds (52.5%). This result is particularly interesting because, in a normal context, young people are less inclined to report feeling isolated, especially when they are students. Consequently, in a lockdown situation, young people feel isolated more intensely than others, perhaps because at this period in their lives the gregarious instinct is very strong; when physically cut off from their friend groups and/or professional networks, they thus feel isolated.



Note: This survey garnered a sample population of 10.976 individuals, who are representative of the adult population of mainland France in terms of age, gender, educational qualifications, and region of residence during the great lockdown from 23rd March to 10th May 2020.

Figure 1: Regional disparities in feelings of social isolation in France during the great lockdown

There are also regional differences in the way feelings of social isolation have changed. In particular, 68% of respondents from Nouvelle-Aquitaine, 64.4% of those from Pays de la Loire, and 62.7% of those from Brittany experienced an increase in feelings of social isolation during lockdown, compared with just 32.9% of respondents in Hauts-de-France or 38.9 of those of Grand Est (Figure 1).

Thus, residents on the west coast of France were more affected by social isolation during lockdown than other French people. Proportionally, more inhabitants of these regions reported greater social isolation during lockdown than before, compared with other French people. This may be due to the structure of economic activity of these regions. We know that the western coast regions have a significant tourist activity. With the lockdown, this activity has stopped, and workers no longer worked. As a result, people lost touch with their clients and colleagues and felt very isolated. In other regions such as Paris Region, teleworking was important during lockdown and people were able to maintain social relations. Thus, the economic structure has probably played a role in the evolution of the feeling of social isolation. But these are just assumptions. Regional cultural differences also matter.

This finding immediately raises a question: how do these changes in feelings of social isolation affect people's well-being? This is the question we shall answer in the next section.

3 Estimating the effects of feelings of social isolation in terms of French people's well-being

We can now address the final question that we proposed to answer in this paper: that of the influence of feelings of social isolation on the level of well-being of French people during lockdown. We shall test our hypothesis that individuals who showed an increase in their feelings of social isolation during lockdown experienced a decrease in their level of well-being. But first, we must examine the effect of lockdown on French people's well-being according to their region of residence.

3.1 Effects of lockdown on French people's well-being. Some regional differences

In order to gauge respondents' level of well-being and the extent to which this level has changed, we mobilized the World Values Survey method, which, since 1981, has used the Cantril scale to assess well-being (Inglehart et al. 2020). We asked respondents two questions:

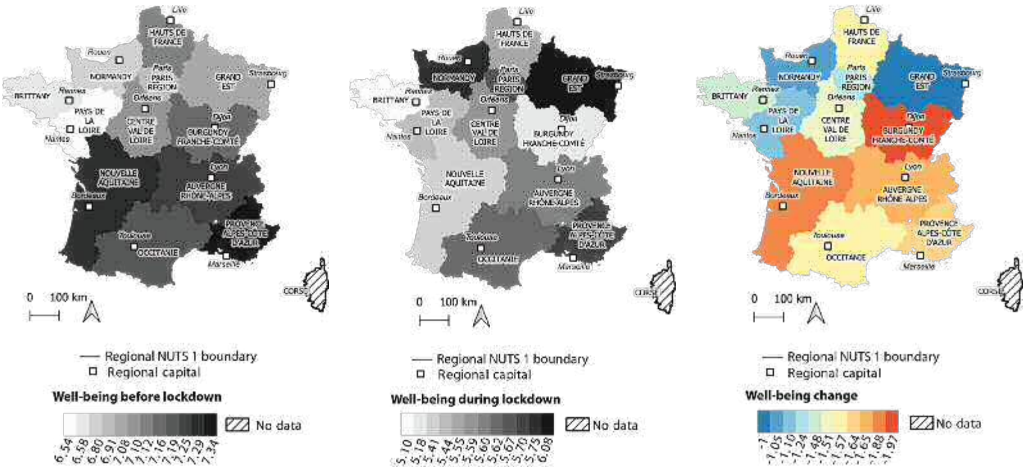
1. Using this card, on which 1 means you are "completely dissatisfied" and 10 means you are "completely satisfied", all things considered, how satisfied were you with your life as a whole up until lockdown began?

2. Using this card, on which 1 means you are "completely dissatisfied" and 10 means you are "completely satisfied", all things considered, how satisfied have you been with your life since the beginning of lockdown?

Before analyzing the levels of well-being reported by French people (before and during lockdown), we ensured the reported levels of well-being were comparable between individuals, as we know that not all individuals were necessarily in the same frame of mind when they responded to the survey: certain external factors may have played on their attitude and affected how they responded to the questionnaire. In addition, studies in psychology tell us that some people tend to be more forgiving in their rating than others because their scale of values is not the same, for example. We eliminated the effect induced by variability of state of mind and personality within society. Therefore, a simple adaptation of the item response theory, the Rasch-model (also known as right centering or centering by row) was applied (Füstös et al. 2004)(Füstös et al., 2004). As we did not have information about the general (average) psychological status of each respondent, a larger set of questions positively related to well-being was used. After centering, the variables were rescaled to the original scale by a min-max rescaling process (Bro, Smilde 2003). Thus, we use the term "calibrated level of well-being" to indicate the fact that the level of well-being is comparable between individuals. The change of the calibrated well-being is the difference between the calibrated well-being in the two periods.

The first observation is that during the great lockdown, the well-being of French people was rapidly deteriorating. The calibrated level of well-being decreased from 7.07 (before lockdown) to 5.6 (during lockdown) on a scale of 1 to 10, a decrease of 1.47.

The second remark is that lockdown has redistributed the regional cards of well-being within the country. Whereas before lockdown, Southerners were the most satisfied with their lives (their level of well-being varying between 7.25 and 7.34), during the lockdown there are those in the Grand Est (6.08) and Normandy (5.75) regions who were less affected and are now the most satisfied (Figure 2).



Note: This survey garnered a sample population of 10.976 individuals, who are representative of the adult population of mainland France in terms of age, gender, educational qualifications, and region of residence during the great lockdown from 23rd March to 10th May 2020.

Figure 2: Regional disparities in well-being (calibrated level of well-being)

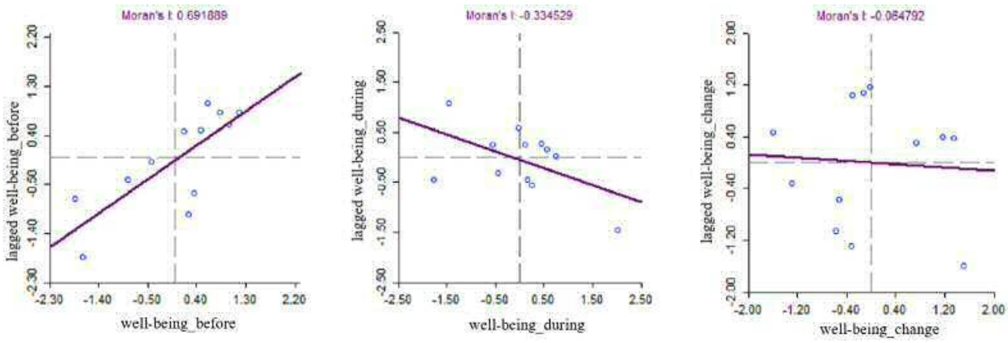


Figure 3: Moran's I coefficient

Before lockdown, the level of well-being exhibited a strong positive spatial autocorrelation, with a Moran's I of 0.691889 significant at 1% (Figure 3). This means that the well-being differential between advantaged and disadvantaged regions reflected their geographical distance.

This was no longer the case during lockdown. Indeed, the level of well-being exhibited a negative spatial autocorrelation; The pattern of the regions was close to a checkerboard.

But the drop-in well-being levels did not affect all regions in the same way. Residents of Burgundy–Franche-Comté and Nouvelle-Aquitaine displayed the greatest decreases in well-being, while Grand Est and Normandy residents exhibited the smallest decreases. The change in well-being did not present significant spatial autocorrelation: Moran's I was equal to -0.064792. The change in well-being was therefore random.

3.2 The relationship between feelings of social isolation and level of well-being

We can now test the hypothesis that social isolation has a negative impact on the reported level of well-being in any situation. To do this, we must first analyze the link between feelings of social isolation (before and since lockdown) and the reported level of well-being of individuals using linear regression. It transpires that the level of social isolation has a strong influence on the level of well-being.

Thus, our hypothesis is validated in that social isolation clearly has a negative impact on the reported level of well-being in any situation. Accordingly, before and during lockdown, those respondents who were most socially isolated were also those who reported the lowest levels of well-being. Both before and after lockdown, being more isolated

Table 8: Linear regression of change in well-being

	Coefficients
Constant	4.643***
	(0.077)
Did you feel socially isolated before lockdown?	0.254***
	(0.019)
Have you felt socially isolated since lockdown began?	-0.517***
	(0.012)
Calibrated level of well-being before lockdown	-0.794***
	(0.010)

Notes: Dependent variable: change in calibrated level of well-being. Standard errors in parentheses, *** = p-value <0.01. We use the term "calibrated level of well-being" to indicate the fact that the level of well-being is comparable between individuals.

reduces well-being by about 0.5 units. An interesting element is to be noted: more isolation before lockdown may partially compensate for this loss of well-being (0.27 units).

The next hypothesis we shall test is acclimation to being socially isolated slows the decline in well-being during lockdown. For this, a linear regression was estimated to establish the general relationship between social isolation and the decrease in well-being (Table 8).

Following our observations of the link between the frequency of feelings of social isolation before lockdown and change in levels of well-being (Table 8), we are inclined to say that a person used to being socially isolated will experience a lesser change in his or her level of well-being during lockdown than others. Indeed, people with a higher level of social isolation before lockdown are those who experienced a smaller reduction in their level of well-being than others (for a person with a one-unit higher isolation before the lockdown, the fall of well-being was 0.254 units less). Our hypothesis is therefore validated.

By contrast, people who experienced a higher level of social isolation during lockdown than others experienced a greater fall in their level of well-being than others. Thus, social isolation prior to lockdown has a small but positive impact on the level of well-being during lockdown, while social isolation during lockdown has a negative impact on the level of well-being.

But how do changes in feelings of social isolation affect changes in levels of well-being? Does it have a positive or negative effect on changes in people's level of well-being? In other words, will a person who feels more socially isolated during lockdown than usual see their level of well-being decrease?

Studies show that, in general, an increase in feelings of social isolation leads to a decrease in individuals' level of well-being, in particular because humans are beings with a gregarious instinct. We therefore hypothesize that the increase in feelings of social isolation is a determinant of the decrease in levels of well-being during lockdown.

3.3 *The impact of changes in feelings of social isolation on changes in levels of well-being*

To test our hypothesis, we conducted multiple linear-regression analysis. Our dependent variable was the change in the calibrated level of well-being, denoted by Y. We used a number of explanatory variables from our questionnaire; specifically, we made use of 21 variables, denoted by X_j: being more or less isolated during lockdown than before lockdown; boredom; the level of well-being reported before lockdown; having a pet to walk; frequency of physical exercise before and during lockdown; age; gender (reference group: male); region of residence (reference group: Île-de-France, i.e. the Paris region); employment situation (reference group: does not work in general); activities undertaken at home: music, relaxation, reading, physical exercise; changes in sleep duration (positive if someone sleeps more); information on the health crisis; feeling safe at home; presence of noise nuisance before lockdown; presence of plants at home; presence of pets at home; alcohol consumption; and changes in dietary habits. We encoded the qualitative variables using dummy variables, omitting the reference group indicated above. The large quantity of control variables is explained by the intent to avoid biased estimation of the impact of the isolation. However, in the interpretations, we focus only on the most influential ones.

Our model can be expressed in the following way:

$$Y = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \ldots + \beta_k X_k + \epsilon \quad (1)$$

where:

Y represents the change in the calibrated level of well-being;

X_j represents the explanatory variables mentioned above;

β represents regression coefficients;

ϵ represents random error.

After the initial regression, we applied a backward elimination with a probability threshold of 10%. Removing the not significant variables has not changed the conclusion, the coefficient of the isolation variables in other model versions was ± 0.02 different from the reported coefficients in Table 9.

Table 9: Regression parameters of change in well-being

Variables	Unstandardized coefficients	Standardized coefficients
Calibrated well-being before lockdown	-0.787*** (0.010)	-0.571
Have you at times been bored since lockdown began?	-0.506*** (0.014)	-0.281
Do you have a pet with you in lockdown that must be taken out for walks?	-0.649*** (0.028)	-0.153
More isolated during lockdown	-0.432*** (0.025)	-0.132
Do you have a pet with you in lockdown that does not need to be taken out for walks?	-0.433*** (0.023)	-0.129
In general, how many times per week have you exercised since lockdown began?	-0.087*** (0.006)	-0.117
Do you have plants in your home during lockdown?	-0.377*** (0.027)	-0.094
Age (in years)	-0.007*** (0.001)	-0.076
Since lockdown began, have you undertaken the following activities at home: relaxation/yoga?	0.185*** (0.027)	0.048
Less isolated during lockdown	0.384*** (0.054)	0.047
Normally works but has not been working during lockdown	0.170*** (0.028)	0.043
In general, how many times per week did you exercise before lockdown?	0.032*** (0.006)	0.039
Region=Hauts-de-France	-0.199*** (0.039)	-0.034
Region=Auvergne–Rhône-Alpes	-0.161*** (0.032)	-0.034
Region=Grand Est	0.184*** (0.039)	0.032
Since lockdown, have you felt safe at home?	0.181*** (0.040)	0.031
Would you say that, since the start of lockdown, you have been kept informed about the health crisis and about what you should be doing?	0.057*** (0.013)	0.030
Since lockdown began, have you undertaken the following activities at home: music (playing an instrument)?	0.105*** (0.025)	0.028

Continued on next page

Table 9: Regression parameters of change in well-being – continued

Variables	Unstandardized coefficients	Standardized coefficients
Are you (male = 0, female = 1)?	0.087*** (0.022)	0.027
Since lockdown began, have you undertaken the following activities at home: physical exercise (working out, weight-lifting, cycling, etc.)?	0.087*** (0.024)	0.027
Working from home during lockdown	0.100*** (0.029)	0.025
Since lockdown began, have you consumed more alcoholic drinks than usual, compared to before lockdown?	0.096*** (0.027)	0.024
Change in sleep duration (hours)	0.024*** (0.009)	0.018
Region=Normandie (Normandy)	0.125*** (0.047)	0.017
Before lockdown, did you experience noise nuisance (street noise, noise from neighbors, etc.) when at home?	-0.060** (0.023)	-0.017
Since lockdown began, have you changed your dietary habits, compared with before lockdown?	-0.050** (0.023)	-0.015
Constant	5.293*** (0.105)	

Notes: Dependent variable: change in calibrated level of well-being. Standardized coefficients are calculated as the unstandardized coefficient divided by the standard deviation of the independent variable and multiplied by the standard deviation of the dependent variable. These unitless coefficients show the comparable effect size. The model was tested for multicollinearity issues, the highest VIF = 1.529 for the age variable, thereby no disturbing multicollinearity was detected. Heteroskedasticity corrected standard errors in parentheses, * = p-value <0.1, ** = p-value <0.05, *** = p-value <0.01.

The results show that our hypothesis is validated (Table 9). Specifically, people who felt more isolated during lockdown than before experienced a decrease in their level of well-being of 0.432 units compared to those who did not experience a change in their level of social isolation. Conversely, people who felt less isolated during lockdown than before experienced an increase in their level of well-being of 0.384 units compared to those who did not experience a change in their level of social isolation.

So, changes in feelings of social isolation do indeed have an influence on changes in levels of well-being (Table 9). It is the third most important factor in determining changes in levels of well-being, after the level of well-being before lockdown, boredom since lockdown, and before having a pet to be taken out. The result concerning "ownership of pets that need to be walked" is interesting. Ordinarily, the company of a pet is recommended to improve people's levels of well-being, especially for the elderly (Cherniack, Cherniack 2014, McNicholas 2014). It helps them feel less alone and forces them to go outside regularly and take exercise. In this way, they create links with the outside world, sometimes talking to other pet owners, all of which may help them feel better. Pet therapy also reinforces this point. During lockdown, however, these pets did not produce the same effects as usual, perhaps because social-distancing measures prevented people from engaging in the activities they usually would with their pets: walking in the forest, meeting neighbors in their local area during outings with their pet, etc. Such explanations are mere speculation on our part, though, as a qualitative survey of pet owners would be required to provide definitive answers.

Other results deserve our attention. Indeed, we observed that, in certain cases, the region of residence can have a positive or negative impact on changes in levels of well-being. For example, people who live in the Hauts-de-France, Auvergne–Rhône-Alpes, and Bourgogne-Franche-Comté regions experienced, respectively, decreases in their level of well-being of 0.133, 0.161 and 0.231 units compared to those who live in the Île-de-France (Paris) region. Conversely, people who live in the Grand Est and Normandy regions experienced increases in their level of well-being of 0.184 units and 0.125 units, respectively, compared to those who live in the Paris region.

4 Conclusion

We have shown that social-distancing measures have had a significant effect on the degree to which French people feel socially isolated. This feeling of social isolation has spread throughout France, especially in western regions. Residents of Nouvelle-Aquitaine, Pays de la Loire, and Brittany have been particularly affecting during lockdown compared to those of the Hauts-de-France and Grand Est regions. Our study therefore reveals that certain categories of French people are more vulnerable than others to social-distancing measures.

We highlighted a change in the geography of well-being in France induced by lockdown. While residents of southern regions had the highest levels of well-being before lockdown, this is no longer the case during lockdown. Residents of the Normandy and Grand Est regions exhibited the highest well-being levels.

Our study shows that, in a context of lockdown, the link between feelings of social isolation and reported well-being among French people continues to exist. Indeed, our study also demonstrated that the increase in people's feelings of social isolation during lockdown was a factor that had a negative impact on their level of well-being during lockdown. We were also able to reveal certain positive influences of residence location on changes in well-being levels.

Some of our results are hard to generalize because the cultural context plays a major role in people's evaluation of feelings of social isolation De Jong Gierveld et al. (2006). For example, sociocultural factors must be taken into account. Discussions on the theme of the UCLA (University of California Los Angeles) loneliness scale or De Jong Gierveld scale remind us of this (Russell et al. 1980, Russell 1996, De Jong Gierveld et al. 2006).

However, our results regarding the drop in well-being levels due to lockdown have been observed in other studies. This is the case for the study conducted by van Leeuwen, Bourdeau-Lepage (2020), for instance, which shows that, with lockdown, the average level of well-being (on a scale of 1 to 10) of Dutch people decreased from 8 to 6.7 (a drop of 1.3 points). This study also revealed territorial differences in well-being levels, especially between urban and rural areas.

But what has been the impact of social-distancing measures and lockdown on the physical, emotional and cognitive health of French people? A paper by Brooks et al. (2020) reveals that the psychological impact of lockdown is negative on individuals, and more specifically that lockdown generates anger, confusion and post-traumatic stress. Our questionnaire included questions on individuals' emotional, cognitive and physical state. It would be interesting to try to see whether there is a link between French people's feelings of isolation, levels of well-being, and states of health, in order to make progress in understanding the effects of lockdown on individuals.

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Regional Innovation Systems of Medical Technology: A knowledge production function of cardiovascular research and funding in Europe

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Abstract. We investigated the role of public funding in cardiovascular device innovation across 31 countries in Europe. We rely on the knowledge production function (KPF) framework that establishes the knowledge output of a region as a function of innovatory effort and other characteristics of that region. In a cross-sectional analysis, we investigated regional variation in knowledge production by the number of publications in cardiovascular device research obtained from the bibliometric data of the world's largest biomedical library, the US National Library of Medicine, 2014–2017. We mapped these publications to product categories of medical devices approved for cardiovascular diseases by the US Food and Drug Administration. Considering spatial correlation across regions of Europe in our estimates of the KPF, we investigated the impact of two types of public funding mechanisms: the volume of European Union (EU) Framework Programme (FP) 7 funding received by the innovating regions and that of its successor the EU Horizon 2020 funding. We obtained 123,487 cardiovascular device-related publications distributed across 1,051 (75% of total) regions (NUTS-3 level). Receiving public funding strongly contributes to a region's knowledge output. The estimated elasticities of innovatory effort by FP7 range between 0.36 and 0.40 while the estimated elasticities of Horizon 2020 range between 0.13 and 0.17. Estimated elasticities remain robust after controlling for country level fixed effects. When accounting for additional inputs to the KPF by private funding and health system related factors, the elasticity estimates for FP 7 and Horizon 2020 reduced, but remained significant. We documented spillover from neighboring regions, albeit at small scale. Our results conclude that innovatory efforts in the form of public research investments are effective for promoting innovation in the medical device industry at the regional level.

JEL classification: R11, R12, O32, O52

Key words: Innovation, Regional Innovation System, Medical Technology, Cardiovascular Devices, Innovatory Spillover, Spatial Spillover

1 Introduction

In a learning economy, innovation is recognized as new knowledge resulting from user-producer interaction. In the medical device industry, knowledge generation has led to a better clinical understanding of diseases, resulting in improved medical procedures in addition to technological advancements. For example, the evolution of the left ventricular assist device began with advances in understanding heart failure, leading to improvements in the medical procedures, further improving the design of the device (Morlacchi, Nelson 2011). As in other industries, such user-producer interaction in the medical device industry may tend to cluster innovation systems that, in turn, accelerates knowledge production (Cooke et al. 1997, Asheim, Isaksen 1997, Asheim, Coenen 2005).

In this study, we analyzed regional innovation systems (RIS) of cardiovascular medical devices by accounting for the spatial distribution of knowledge and quantifying the role of public funding as an innovatory effort in a knowledge production function (KPF). The medical device industry typically ranks high in terms of its patent share in Europe – 7.7% of all patents to the European Patent Office are filed for medical devices (MedTech 2020a). The European market is the second largest in the global medical device industry (27% of revenues), with a trade surplus of about 11.7 billion Euro in 2018. However, industry activities are spread unevenly across different clusters in terms of market, employment, and trade shares. Of the roughly 32,000 companies active in the industry, 95% are small and medium-sized enterprises (SMEs) employing more than 730,000 employees across Europe. A geographical variation exists in terms of implant/usage rates of devices at both regional and country levels in Europe (Tarricone et al. 2017).

New medical devices develop from the interplay of scientific advancements, learning in medical practice, and technological development where physicians are often key contributors to device development as entrepreneurs (Morlacchi, Nelson 2011, Smith, Sfekas 2013). When interactive involvement of physicians is considered in advancing medical device innovation, the question remains how and which investments in research and development (R&D) contribute. The SMEs and physicians in Europe have depended on public and private investments, of which public funding contributes a substantial proportion (MedTech 2020b). Targeted scientific research funding and coordination by research institutes have been identified as the strongest opportunities (Maresova et al. 2015). While the distribution of public research funding on cardiovascular research is heterogeneous (Pries et al. 2018), the effectiveness of public funding from national and supranational levels such as the European Union's Framework 7 and Horizon 2020 programs on knowledge output is unclear. Previous evidence, irrespective of the industry, demonstrates the effectiveness of innovatory efforts by measuring R&D investments, human capital, and intermediary scientific institutes on the knowledge output of patents (Moreno et al. 2005, Marrocu et al. 2013, Fritsch, Franke 2004). Understanding what leads to new knowledge and subsequent innovation in the medical device industry is important because the patients with access to highly innovative clinicians and firms in their region will likely benefit from these innovatory efforts. For example, significant regional level differences in use, along with hospital mortality, were documented in the case of transcatheter aortic valve implantation by region in the United States (Gupta et al. 2017).

This study aimed to investigate the role of public funding in cardiovascular device innovation. We relied on the KPF framework that establishes regional knowledge output as a function of innovatory effort that we examined by public funding. We investigated regional variation in knowledge production by the number of publications in cadiovascular device research from bibliometric data obtained from the world's largest biomedical library, the US National Library of Medicine (NLM). We evaluated the effectiveness of receiving public funding mainly through the European Union (EU)'s funding programs on regional level knowledge production in Europe (31 countries consisting of EU-27, the UK, Switzerland, Iceland, and Norway). We further accounted for variation in private funding by capturing sponsorship received by randomized controlled trials in our publication data. In addition, we performed subgroup analyses in four countries to capture additional healthcare system level variation. We expected to find that receiving public research funding positively influences the regional knowledge output for innovation in cardiovascular devices.

2 Background

2.1 Innovation pathways in cardiovascular device research and development and health outcomes

Our study setting emphasizes cardiovascular devices because, within the medical device industry, many significant advancements have been made to improve the treatment and diagnosis of cardiovascular diseases. These include various diseases linked to heart and blood vessels, such as heart failure, stroke, arrhythmia, heart disease, and heart valve problems. Besides cancer research, advancements in cardiovascular research contributed to an increase in life expectancy of around 3.73 years in the US from 1950 to 2000 (Murphy, Topel 2006). Many cardiovascular devices are products of this research contributing to health gains; several important cardiovascular device innovations – such as electrocardiogram, cardiac catheterization, computed tomography, and magnetic resonance – were products of Noble Prize-winning research (Mesquita et al. 2015).

Our focus is on the innovation stage that lies beyond the invention of a medical device, since they undergo incremental innovation in multiple tests and validation stages before market launch and commercialization, but also post-marketing approval phases (Dziallas, Blind 2019, Tarricone et al. 2017). In this way, the innovation activity of a device is observed during the "design-build-test-redesign" cycle instead of the preliminary prototype stage. It often takes place in collaboration with physicians who experience unmet needs in their clinical practice. Physicians also take part in clinical studies where the safety and efficacy of a new medical device need to be demonstrated before adopting it into clinical practice (Kaplan et al. 2004, EMA 2019). For example, the coronary artery stents, invented by physicians and researchers, became widespread only after various clinical trials demonstrated them to be safe and effective (Xu et al. 2012, Mckavanagh et al. 2018). Moreover, user-producer interaction in the post-market approval phase is crucial (Ciani et al. 2016). In this phase, technology scope is often refined with physicians' feedback long after the initial device-design was invented. For example, the device scope of cardiac resynchronization therapy widened because clinical studies revealed its applications in new and diverse patient groups (Boriani et al. 2018). Such user-oriented and process-oriented innovations are often recorded as results of clinical studies and scientific publications. In terms of financing, such stages of testing, validation, and redesign involve academic centers that rely on various funding sources. Public funding of individual inventors and clinicians is acknowledged to foster innovation in the medical device domain (Xu et al. 2012).

Analyzing innovative activity in cardiovascular research not only has implications for knowledge production and subsequent innovation but also for cardiovascular disease-related health outcomes. More than 1.8 million deaths were attributed to cardiovascular diseases in 2016 in Europe alone (Eurostat 2016, WHO 2017). Cardiovascular morbidity and mortality are highly variable across regions, even within the same country. Patient's access to new devices remains higher in areas where adopting new devices is more likely. The role of the supply side and related physician behavior is emphasized in explaining regional variation in health outcomes in the health-economic literature (Bech et al. 2009, Cutler et al. 2019). Therefore, patients in regions with higher innovative activity have higher health benefits from the early use of innovation. As the financial burden of cardiovascular diseases is high, €196 billion in 2013 in Europe (Komajda et al. 2013), the potential of efficiency gains from knowledge production translating to the bedside is high. Although we will focus on knowledge production occurring at the incremental innovation phases (testing, validating, and post-marketing feedback), our results may have wider implications on the regional variation in the productivity of health care systems.

2.2 Regional Innovation Systems for Research and Development

Innovation systems develop via interventions received at regional levels and are typically analyzed by regional-level R&D activities (Buesa et al. 2010, Moreno et al. 2005, Cooke et al. 1997). Hence, we assume that cardiovascular device innovations emerge from regional R&D activities involving vertically interconnected actors, such as medical device manufacturers, physicians, and academia. By considering the availability of R&D investments, particularly of public funding mechanisms at the regional level, we can analyze if such opportunities promote the innovative capacity of a region.

Analyzing this capacity requires accounting for the spillover effects by innovative activities in neighboring regions as previous evidence suggests it influences the knowledge output of a region (Moreno et al. 2005, Gumbau-Albert, Maudos 2009, Marrocu et al. 2013, Bottazzi, Peri 2003). Out of four types of proximities explored in the literature that consider possible spillovers, we focus on geographical proximity (Usai et al. 2015). Previous evidence suggests that technological proximity can be even more impactful than geographical proximity when considering innovatory effort across many industrial sectors (Marrocu et al. 2013). However, we focus on geographical proximity, by analyzing regional variation in knowledge production, within the same technological field, i.e., cardiovascular devices. Social and organizational proximities are known to be less impactful when performing cross-regional comparisons (Marrocu et al. 2013).

2.3 Knowledge Production Function to Investigate the Innovatory Effort by Public Research Investments

To understand how public funding influences knowledge production regarding cardiovascular devices, we based our analysis on the knowledge production function (KPF) framework developed by Griliches and Jaffe (Jaffe 1989, Grillitsch, Asheim 2018).

$$K_r = f(R_r, Z_r) \tag{1}$$

K_r refers to knowledge production in terms of innovative output in region r that is a function of two inputs. R_r is the innovatory effort of region r based on the endogenous growth model, which implies that production output is a function of endogenous (regional) factors (Furman et al. 2002). Z_r are additional regional indicators of this same region, such as the economic and financial capacity.

To measure knowledge production K_r, we rely on a bibliometric measure of innovation by capturing the number of publications in the field of cardiovascular devices. Although literature-based innovation measures were initially preferred as direct measures, most previous approaches have captured knowledge production by either R&D inputs or patents (Acs et al. 2002, Acs, Audretsch 1993, Coombs et al. 1996). R&D investments represent allocated investments but not necessarily innovation and must be considered inputs instead of outputs (Pavitt et al. 1987). Patents reflect the state of the invention but do not necessarily reflect the innovation it perpetuates as it continues to develop and diffuse. Patents, also, cannot capture innovation arising from daily practices that are often not patented (Pakes, Griliches 1980, Acs, Audretsch 1993). Since innovative activities of cardiovascular devices involve physicians in both pre- and post-launch phases, we rely on publications to capture the innovative activities most likely expressed in terms of clinical studies, scientific guidelines, or case reports. It is reflected by the globally increased number of publications in cardiovascular research, with Europe having outpaced the US and China in the 1990s and 2000s (Gal et al. 2017).

We considered innovatory effort R_r as the regional level research investments as funding received by the EU Framework 7 and EU Horizon 2020 programs. Previous studies have empirically identified positive effects of financing mechanisms (mostly, as the share of internal R&D) or human capital on the knowledge output of regions (Gumbau-Albert, Maudos 2009, Charlot et al. 2015, Tappeiner et al. 2008). Public funding is an important type of investment in research because it is pre-investment, similar to venture capital investment, in which future outcomes are yet unclear. An advantage of using public funding by EU programs is that it can be traced to the regions receiving it. We also account for variation in private investments by the number of clinical trials receiving sponsorship from private companies in our empirical approach.

3 Data and Methods

To empirically analyze the impact of research investments on knowledge output, we composed a cross-sectional data set of innovation activity in the years 2014–2017 by linking multiple data sources. Our investigation covered 27 EU member countries as of September 2020 plus the UK, Switzerland, Iceland, and Norway, summing up to a list of 31 countries[1]. In the final data set, all the data was uniquely assigned and aggregated to the level of 1,394 regions defined by NUTS-3. We then implemented an empirical strategy that accounts for potential confounding on the effects of funding mechanisms on knowledge output by considering additional regional characteristics and spatial dependency across neighboring regions as additional inputs to the knowledge production function.

3.1 Data Sources

To capture variations in knowledge output measured by publication activity due to investments in research and regional environment according to their corresponding regions, we extracted data from seven different sources [Supplement 1 – Source Data]. We collected bibliometric data from the US NLM MEDLINE/PubMed baseline database as the primary data source. It contains 26 million and 30 million publication records from MEDLINE and PubMed, respectively (Amelung 2017). We relied on the 2018 version of the baseline database that provides 4,374,797 citation records that we obtained via bulk download (NLM 2020a,c).

Although the US NLM is from the US, it is the prime source for biomedical research globally. Journals not included in the PubMed/Medline possibly do not meet the quality standards set by the US NLM (NLM 2021). Our captured publications, therefore, ensure that the knowledge generated is incremental. We further ensure that the coverage of Europe-origin journals is high, given that Europe-based authors may prefer to publish in them. Using the SCImago Journal & Country Rank database that lists 173 journals in cardiology and cardiovascular medicine with publishing offices in EU-28 countries, we found 141 journals (i.e., 81%) included in the PubMed/Medline baseline database as of 2021. The other 19% may not have met PubMed/Medline's quality standards.

To select relevant records from MEDLINE/PubMed, we used NLM's thesaurus classification of Medical Subject Headings (MeSH). The MeSH terms are NLM's in-house developed keywords for cataloging each publication depending on its subject matter (NLM 2019a). MeSH terms are assigned to each publication by a team of indexers who systematically scan the title, abstract, and publication. The MeSH classification is provided by a hierarchical tree structure containing 16 main branches, including diseases, drugs, therapeutic equipment, and processes, and each branch contains hierarchical sub-branches[2] In addition to its definition, each MeSH is described by a "DescriptorName" for one word/phrase description and is accompanied by "DescriptorUI", a unique ID number for that particular MeSH (NLM 2019b). Per publication, multiple MeSH terms may be assigned (NLM 2020b). We relied on the 2019 version of the MeSH tree.

Third, we used the U.S. Food and Drug Administration's (FDA) Product Code Classification Database to classify cardiovascular devices (FDA 2018). Most importantly, this database provides generic definitions of a set of approved medical devices by disease indication and the typical classification of medical devices by their risk. Fourth, we collected gross domestic product (GDP) per region for the years of 2014 to 2017 from Eurostat (Eurostat 2020) and national statistical offices in Switzerland (BFS 2019) and Iceland (Statistics Iceland 2019). Fifth, we obtained data on research funding received under EU Framework 7 and Horizon 2020 program at regional level as provided by the official online dashboard of the European Commission (European Commission 2020b).

[1] Liechtenstein was excluded from the dataset as no publications were recorded on cardiovascular devices.

[2] For example, the main branch "Analytical, Diagnostic and Therapeutic Techniques, and Equipment" includes "Surgical Procedures, Operative" as a sub-branch containing additional sub-branches such as "Cardiovascular Surgical Procedures" that has "Heart Valve Prosthesis Implantation" as a sub-branch that in turn has "Transcatheter Aortic Valve Replacement."

Sixth, we collected data about funding status of registered clinical trials reported in the extracted publications from the database provided by ClinicalTrials.gov (2021). Seventh, we collected additional characteristics of the region to account for health system related factors in a subset of four countries, relying on a publicly available previous data collected for these variables (Rabbe et al. 2021).

3.2 Classification of Publications of Cardiovascular Devices

We developed a programming algorithm to extract all publications from MEDLINE/PubMed that cover medical devices for cardiovascular diseases [Supplement 2 – Additional External Variables] [Supplement 3 – Program Code for Data Extraction and Preparation]. First, based on the MeSH tree, we classified publications as to whether they refer to medical devices in general. Second, we restricted the sample to publications with those MeSH terms for which we could attribute an approved medical device definition for a cardiovascular specialty by the U.S. FDA. Although our study focused on Europe, we relied on the classification of medical devices provided by the FDA because the recently published European medical device nomenclature was under development at the time of data-collection (European Commission 2020a).

To focus on publications about medical devices, using the MeSH tree, we included all MeSH terms that cover analytical, diagnostic, and therapeutic techniques and equipment [Supplement 4 – Auxiliary Data Created]. Specifically, we selected all the MeSH terms of the sub-branches E01 (diagnosis), E02 (therapeutics), E04 (surgical procedures, operative), E06 (dentistry), and E07 (equipment and supplies), with 2,178 unique MeSH terms in total.

To retain publications on medical devices explicitly for use in cardiovascular disease, as a second step, we mapped the identified MeSH terms with cardiovascular devices authorized by the U.S. FDA's Product Code Classification Database (FDA 2018). In this way, we ensured that the selected publications are linked to the FDA approved products to maintain our focus on those that succeeded the approval process (Stern 2017). The U.S. FDA medical device classification is based on risks posed by the devices on patients, I being the lowest and III being the highest risk. In the Product Code Classification Database, we selected all product definitions attributed to cardiovascular disease (medical specialty "CV"). To focus on devices that are likely part of cardiovascular interventions and avoid devices that mostly contain accessories to support interventions, we excluded class I devices, which includes devices such as forceps and scissors, for example. We included all 276 devices with moderate (class II, for example, cardiovascular blood flow meter) and greatest risk (class III, for example, pacemaker/cardiac resynchronization therapy) to patients (FDA 2017). The mapping exercise left us with 86 MeSH terms [Supplement 4 – Auxiliary Data Created].

3.3 Assigning Publication Geolocations to Identify Regional Innovation Systems and Knowledge Output

In total, we extracted data on 123,487 publications that we could assign to at least one MeSH term relating to a cardiovascular device and to a geocode in Europe [Supplement 4 – Auxiliary Data Created]. To obtain the geographical distribution of the publications of cardiovascular devices, we used the publicly available tool MapAffil to assign geocodes (latitudes and longitudes) to each publication based on the authors' affiliations (Torvik 2015). MapAffil is capable of correctly identifying 97.7% of the geolocation of a city reported in the author's affiliation variable provided by PubMed.

We restricted our analysis to publications published between 2014 and 2017 because MEDLINE/PubMed's indexing method started in 2014 to include information about affiliations of multiple authors (NLM 2019b). We assumed that not accounting for authors and their location beyond the first authors would heavily underestimate regional contribution to the knowledge output. Medical device research is often performed in networks of authors from different locations. In 2012, 40% of studies reported authors from two or more countries (Gal et al. 2017). Based on the assigned geocodes, we aggregated publications by regional level.

To identify distinguished regions in the RIS of knowledge production of cardiovascular devices, we relied on the geographical classification of regions defined by the Nomenclature of Territorial Units for Statistics (NUTS), provided by Eurostat and the Organisation for Economic Co-operation and Development (OECD) (Damanpour, Schneider 2009, OECD 2005). NUTS is a hierarchical geographical classification based on regional administrative structures of countries and territories to perform socio-economic and statistical analysis. Across all analyses, we used the 2016 version of the NUTS classification at the lowest level 3 as it refers to small regions for diagnosis of specific questions (Damanpour, Schneider 2009).

We distributed the geocodes of multiple affiliations of the same publication by equal weight. For example, a publication with three authors referring to geolocations in Milan, Munich, and Zurich was assigned three sets of geocodes corresponding to each of these cities. If the publication included authors from outside Europe, we discarded the affiliations from outside Europe to focus on innovation output located in Europe.

Data extraction was performed using SAS Enterprise Guide 9.4 (SAS Institute, Cary, NC, USA). Statistical analysis was performed using R, version 4.0.2. All program codes to extract and analyze all data sources and the data set for analysis are provided via the Open Science Framework (OSF) repository.

3.4 Empirical Knowledge Production Function Model

The aim of our empirical strategy was to quantify the effect of research investments on knowledge production measured by the number of publications assigned to one region, accounting for potential confounding of other characteristics of the region as a secondary input to knowledge production, and spatial dependency across regions. Considering the specification of the KPF as stated by equation (1), we specified the following linear regression model:

$$K_r = \hat{\beta}_1 X_r + \hat{\beta}_2 Z_r + \epsilon_r \tag{2}$$

K_r refers to knowledge output (number of publications) of region r. X_r is our variable of interest and captures innovatory effort of region r. Z_r represents characteristics of the region r itself that are reflected by suitable regional indicators. In our case, we captured economic performance by considering the GDP of that region. ϵ_r captures the error term. For all input and output variables, we provided specifications per capita by dividing absolute values by the number of inhabitants in the region. The estimate of $\hat{\beta}_1$ captures the effectiveness of innovatory effort by two types of measures. Our primary measure of innovatory effort is the monetary volume of funding received in the region via the 7th EU framework programme (FP7). It was rolled out from 2007 to 2013 as part of European Commission's research and innovation funding promotion to boost economic growth in the European Union. The program offers financial aid to EU member countries and a list of associated countries, including all countries in our analysis, and, subsequently, research activities taking place in those countries eligible for it (European Commission 2020c). It is the largest framework program for promoting research and innovation across Europe. Controlling for other factors of the region Z_r, we hypothesize that innovatory effort made through FP7 causes knowledge production between 2014 and 2017 to increase. In addition, we include a separate variable for its successor EU Horizon 2020, spanning from 2014 to 2020 (European Commission 2020d). That way, we account for lags of innovatory effort and hypothesize that higher current innovatory effort is associated with higher levels of knowledge production. In addition, we accounted for country fixed effects to compare estimates with and without heterogeneity that may persist due to first and second nature advantages between national environments. First nature advantages relate to geography of the region while second nature advantages relate to agglomeration economies that have advantages due to proximity of customers and suppliers, technological externalities and better matching between employers and employees (Charlot et al. 2015).

To account for other factors of the region that define knowledge output, we considered GDP in region r for the years 2014 to 2017 such that $\hat{\beta}_2$ is the estimate of the effectiveness of other characteristics of the region as input to the KPF. To provide a uniform measure of GDP, values were obtained at current market prices by million Euro, or other applicable local currencies, and converted to units of per million US Dollars by dividing them with purchasing power parities obtained using data provided by the OECD (2020b). We calculated averages to receive one mean and uniform GDP value for the period 2014–2017.

Finally, to account for proximity effects in innovatory effort and other characteristics of the region, we considered the spatial dependency of neighboring regions, assuming that knowledge production is not only influenced by the inputs of the KPF of the region itself but also by the inputs of the neighboring regions (Moreno et al. 2005, Charlot et al. 2015). We consider spatial proximity and the related correlations of dependent and independent variables as important given the role of user-producer interactions in the development process of medical devices and the fragmented nature of the medical device industry across geographical regions. Most importantly, we do not account for any collaborating clusters across neighboring regions ex-ante in our data, so we need to allow for knowledge and innovatory efforts to flow not only locally, but also across neighboring regions. Accordingly, equation (2) can be extended to a spatial form as follows:

$$\begin{aligned} K_r &= \hat{\rho}\, \boldsymbol{WK} + \hat{\beta}_1 X_r + \hat{\theta}_1 \boldsymbol{WX} + \hat{\beta}_2 Z_r + \hat{\theta}_2 \boldsymbol{WZ} + u \\ u &= \hat{\lambda}\, \boldsymbol{Wu} + \epsilon_r \end{aligned} \tag{3}$$

Spatial lags of these variables are denoted by $\boldsymbol{WK}$ referring to knowledge outputs of the neighboring regions, $\boldsymbol{WX}$ to funding mechanism received by the neighbor regions, $\boldsymbol{WZ}$ to GDP of the neighbor regions, and $\boldsymbol{Wu}$ to unobserved environmental characteristics of the neighbor regions. $\boldsymbol{W}$ is the weight matrix of the neighboring regions, for which we defined a contiguity neighborhood matrix that assigns equal weight to all neighbors with row-standardized values (Tosetti et al. 2018).

To assess the degree of spatial dependency across data reporting knowledge production and research investments across regions, we first performed Moran's I test for our specified models (Lesage 2008, Elhorst 2010, Tosetti et al. 2018). We accounted for the spatial dependency of both dependent and independent variables (Manski 1993): endogenous interaction by knowledge output in the number of publications of neighboring regions (ρ), exogenous interaction by inputs to the knowledge production function of the neighboring regions (θ), and correlated effects by unobserved environment of the neighboring regions (λ) (Elhorst 2010, Floach, Le Saout 2018). We followed a combined approach which included parts of both bottom-up and top-down approaches for the selection of order of spatial effects proposed (Elhorst 2010, Floach, Le Saout 2018). The purpose of the approach is to account for spatial lags of the dependent variable and the error term with robust Lagrange multiplier tests as a first step. As the second step, we specified a Durbin model, which refers to the baseline model as described in (3), including lags of independent variables and either ρ or λ. We then performed a likelihood ratio test, comparing the model specifications with and without spatial autocorrelation of the independent variables (θ) (Floach, Le Saout 2018). We only report relevant type of spatial model specified in case where spatial effects were confirmed. All spatial tests and analyses were performed using R version 4.0.2 (packages spdep, SDraw, spatialreg, rgeos) [Supplement 5: Spatial Analysis and Results].

To estimate the elasticity of innovatory effort and other characteristics of the region, we estimated models at the log scale (Moreno et al. 2005, Gumbau-Albert, Maudos 2009). Here, we needed to account for regions that do not report EU Horizon 2020 or FP7 funding. Estimating models at the log scale is particularly challenging for values of zero; we explicitly accounted for the lack of innovatory effort by including a dummy variable (Battese 1997). In the appendix (Tables A.1 and A.2), we report another version of the spatial KPF that excluded regions with zero innovatory effort in terms of public funding received.

3.5 Robustness analyses by input and output variables

To assess whether our results hold across different specifications, we performed additional analyses accounting for non-public innovatory efforts to fund randomized clinical trials that were part of the publications, the number of grants reported in the publications as innovatory efforts, and observed healthcare system-related factors of the region besides GDP.

To account for regional variation of innovatory effort from private sources, we measured receipts of private funding by capturing sponsorship of clinical trials by the industry. We relied on the reporting of clinical trials in the publications captured in the MEDLINE/PubMed database[3] to link them with sponsorship information in ClinicalTrials.gov (2021). In total, 1,242 clinical trials were reported in the publications. Accounting for both lead and collaborative sponsors types that include industry, government, and non-governmental agencies, we created a binary variable – "private funding." For publications corresponding to clinical trials with sponsorship from at least one industry sponsor, "one" was assigned, otherwise "zero." We counted the number of publications reporting private funding by region.

To account for an alternative measure of innovatory effort from public funding sources, we replaced the measure of innovatory effort by public funding with the number of grants reported in the publications in the MEDLINE/PubMed dataset. We relied on the reported element "GrantList" corresponding to those articles for which the authors reported grant funding. It includes the name of the grant-funding agency along with additional grant identifying details (NLM 2019b). These funding agencies are part of the list maintained by the NLM and consist of US government health organizations, US non-governmental funding organizations, and non-US funding agencies/organizations (NLM 2019b). We created a binary variable, "grant received," coded as "one" for a publication that reported at least one grant-funding agency and "zero" for no reported grant funding. We grouped and aggregated the binary variable corresponding to the regions where the published work was performed; thus, calculating the total number of publications that received grants per region. This variable allows us to account for both public and non-public grants as reported by the authors, while the EU Horizon 2020 and FP7 funding volume allows us to account for public funds only. As this variable was collected only from published studies, the grant variable does not account for funds acquired that did not end up in publication.

We considered factors related to the regional health care environment to account for additional confounding of the elasticities of public funding by other regional factors. For cardiovascular care, potential confounders of public funding are the intensity of hospital care in the region. In addition, there may be regional variations in unmet medical needs, driving clinicians to develop new products and seek funding opportunities. In a subset covering 422 regions of four countries (Germany, Italy, Switzerland, and Hungary), we relied on a publicly available and recently extracted data set of hospital counts and life expectancy at NUTS-level 3 (Rabbe et al. 2021). We first separately specified the baseline model from equation (2) for these subsets of regions and then added hospital counts and life expectancy to control for the regional health care system environment.

4 Results

4.1 Exploratory Spatial Data Analysis

Of the 1,394 regions in the 31 countries that we considered, 1,051 (75%) regions were active in knowledge production as they had at least one cardiovascular device-related publication between 2014 and 2017. Figures 1a and 1b provide an overview of the exploratory spatial data analysis that demonstrates the regional variation in knowledge output by number of publications in multiple western and southern European countries. The figures depicting the remaining countries from our dataset are provided in the appendix.

[3]In MEDLINE / Pubmed, an element named "DataBankList" provides ClinicalTrials.gov identifier (i.e., NCT number) in cases when publication reports results of a clinical trial (NLM 2019b).

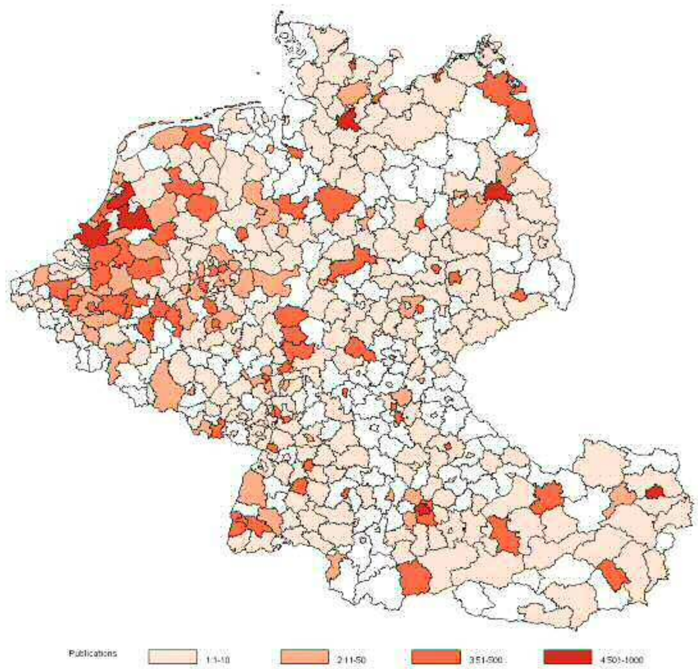

Figure 1a: Publication Output for Cardiovascluar Medical Devices at Regional levels of NUTS-3 in Europe: Netherlands, Belgium, Luxembourg, Germany, and Austria

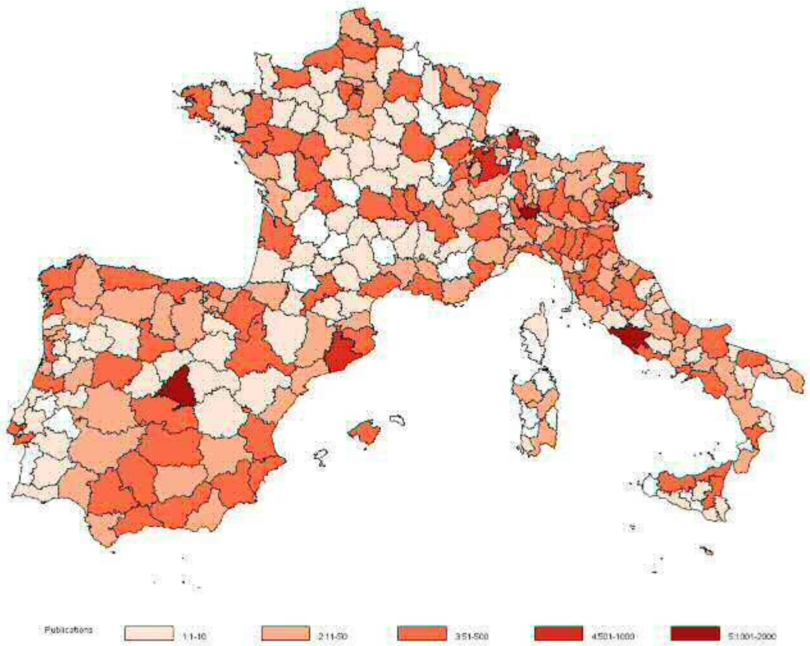

Figure 1b: Publication Output for Cardiovascluar Medical Devices at Regional levels of NUTS-3 in Europe: Switzerland, France, Portugal, Spain, Italy, and Malta

Table 1a: The ten Most Active Regions in Cardiovascular Device Knowledge Output by number of publications, 2014-2017

Region (NUTS-3)	No. of Publications	Share of Total Publications	EU 2020 Horizon Funding Volume in Million Euro	EU FP7 Funding Volume in Million Euro
Milano	1,730	2.58%	541	613
Westminster	1,674	2.50%	563	795
Paris	1,421	2.12%	2,558	3,168
Rome	1,380	2.06%	960	953
Madrid	1,195	1.78%	1,223	1,162
Barcelona	997	1.49%	1,023	1,005
Munich	911	1.36%	1,621	1,695
Groot-Amsterdam	905	1.35%	877	745
Groot-Rijnmond	828	1.24%	146	178
Berlin	812	1.21%	492	565

Note: Data on publications was obtained from the US NLM capturing 123,487 publications in the field of cardiovascular devices, 2014-2017. A region is defined by NUTS level 3.

Table 1b: The ten Most Active Regions in Cardiovascular Device Knowledge Output by number of publications per capita, 2014-2017

Region (NUTS-3)	Publications per Inhabitant	Share of Total Publications per Inhabitant	EU 2020 Horizon Funding Volume in Euro	EU FP7 Funding Volume in Euro
Westminster	709	5.36%	2,382	3,366
Erlangen	316	2.39%	625	725
Heidelberg	263	1.99%	1,854	2,342
Basel-Stadt	169	1.28%	620	998
Camden and City of London	152	1.15%	2,381	2,938
Jena	135	1.02%	460	481
Würzburg	134	1.01%	448	612
Freiburg im Breisgau	128	0.97%	254	69
El Hierro	121	0.92%	0	0
Regensburg	119	0.90%	220	424

Note: Data on publications was obtained from the US NLM capturing 123,487 publications in the field of cardiovascular devices, 2014-2017. A region is defined by NUTS level 3.

The descriptive analysis suggests that knowledge production is highly distributed across space (Table 1a and Table 1b). Even the region of Milano (Italy), producing the highest number of publications ($n = 1,730$), is responsible for only 2.58% of the total publication output of Europe. For the absolute number of publications, Italy (Milano, $n = 1,730$; Roma, $n = 1,380$), the United Kingdom (Westminster, $n = 1,674$), France (Paris, $n = 1,421$), and Spain (Madrid, $n = 1,195$) are the countries with the most active regions. For the number of publications per capita, the UK (Westminster, $n = 709$; Camden and City of London, $n = 152$), Germany (Erlangen, $n = 316$; Heidelberg, $n = 263$), and Switzerland (Basel, $n = 169$) were found to be the countries with the most active regions.

When we consider the country level, Germany ($n = 11,971$), Italy ($n = 10,250$), the UK ($n = 10,079$), France ($n = 7,302$), and the Netherlands ($n = 4,941$) are the most active countries (Table 2). The geographical span across the European Economic Area and adjacent countries further uncovers the regional level variation in knowledge production of cardiovascular devices. For example, Germany had the highest number of total publications ($n = 11,971$) whereas only two regions (Munich, $n = 911$; Berlin, $n = 812$) fell into the top ten highest publications producing regions, indicating that the knowledge production activity of cardiovascular device research in Germany is widespread rather than clustered in one or a few regions. On the contrary, Spain also has two

Table 2: Inputs and Outputs of the Knowledge Production Function of Cardiovascular Device Research by country, Europe 2014-2017

Country	Active Regions	Total Publi-cations	Publi-cations / Region	Publi-cations / Capita	H2020 funding (mill. €)	FP7 funding (mill. €)	No. of grants	No. of private funding
Germany	283	11,971	42	4,238	6,455	7,591	1,862	384
Italy	103	10,250	100	1,292	3,791	3,714	895	131
United Kingdom	164	10,079	61	2,728	5,846	8,020	6,122	191
France	86	7,302	85	644	4,997	5,832	545	174
Netherlands	37	4,941	134	702	3,431	3,847	1,188	158
Spain	53	4,920	93	582	4,100	3,468	422	129
Switzerland	21	2,673	127	503	1,408	2,500	341	64
Sweden	19	1,855	98	270	1,536	1,904	438	50
Denmark	10	1,813	181	292	1,151	1,095	222	55
Belgium	28	1,799	64	366	2,219	1,984	256	77
Poland	43	1,678	39	222	280	415	203	33
Greece	30	1,354	45	311	1,032	1,009	98	7
Austria	23	1,294	56	232	1,266	1,278	289	47
Portugal	20	824	41	109	701	540	71	4
Finland	17	758	45	176	1,013	904	361	20
Norway	17	756	44	160	1,007	789	113	22
Czech Republic	13	650	50	64	319	277	112	33
Ireland	8	508	64	68	501	640	118	4
Hungary	15	461	31	60	266	319	82	23
Romania	17	301	18	36	179	120	9	3
Croatia	11	167	15	38	64	71	1	0
Slovenia	8	147	18	35	236	157	11	1
Lithuania	5	99	20	15	56	46	0	3
Slovakia	6	97	16	15	83	68	22	1
Cyprus	1	71	71	8	212	100	32	0
Bulgaria	5	57	11	7	21	94	0	1
Latvia	2	51	26	8	67	44	8	7
Iceland	2	49	25	24	99	64	126	0
Estonia	2	28	14	7	93	93	2	2
Luxembourg	1	23	23	4	125	60	0	0
Malta	1	18	18	4	23	21	0	0

Note: Data on publications was obtained from the US NLM capturing 123,487 publications in the field of cardiovascular devices, 2014-2017. A region is defined by NUTS level 3.

regions, Madrid ($n = 1,195$) and Barcelona ($n = 997$), in the top ten absolute number of publication output, but it lags behind many other countries in terms of the total number of publications ($n = 4,920$), suggesting clustering of research only in very active centers. Table 2 further provides insights into country-level variations for the number of active regions (i.e., producing at least 1 cardiovascular device related publication), total publications, publications per region, publications per capita, total amount of EU Horizon 2020 and FP7 funding by million Euro, total number of publications reporting grants and private funding.

4.2 *Estimates of the spatial Knowledge Production Function*

The estimates of the (spatial) KPF models across the 1,051 regions reporting publication output suggest that innovatory effort in the form of EU FP7 program funding between 2007 and 2013 increases knowledge production of cardiovascular devices from 2014 to 2017. The elasticity was 0.40 ($p < 0.0001$). It declined to 0.36 ($p < 0.0001$) when we added country-fixed effects to the OLS specification and considered spatial dependency.

The EU Horizon 2020 program, that was active between 2014 and 2020, is positively related to knowledge production of cardiovascular devices, with an elasticity of 0.13–0.17 (Table 3). For the EU Horizon 2020 program, our OLS-based estimate of the elasticity was 0.17 ($p < 0.0001$). It declined to 0.13 ($p < 0.001$) when adding country-fixed effects and accounting for spatial dependency.

The estimates of spillovers generated by neighboring regions were reported as the indirect impacts of independent variables. Compared to the elasticity estimates in the focal region, these were negative and small, both for receiving funding from FP7 and EU

Table 3: Estimates of (Spatial) Knowledge Production Function by scientific publications per capita, considering funding from EU FP7 and EU Horizon 2020 program as innovatory effort – Inputs and outputs per capita (log-scale incl. zero)

	OLS	OLS	SAR
EU FP7 program	0.40***	0.36***	0.36***
	(0.04)	(0.04)	(0.04)
EU Horizon 2020 program	0.17***	0.13**	0.13*
	(0.04)	(0.04)	(0.04)
GDP	0.14***	0.86***	0.92***
	(0.03)	(0.13)	(0.13)
Spillover_FP7	-	-	-0.06
Spillover_Horizon2020	-	-	-0.02
Spillover_GDP	-	-	-0.16
Total_Impact_FP7	-	-	0.30
Total_Impact_Horizon2020	-	-	0.11
Total_Impact_GDP	-	-	0.77
Observations	1051	1051	1051
Country Fixed Effects	No	Yes	Yes
Adjusted R-squared	0.41	0.71	-
Moran's I	0.02	-0.03	-
LM test: lags of Y	1.34	14.01**	-
LM test: lags of e	0.76	2.43	-
ρ in SDEM (model with ρ and θ)	-	-0.15*	-
ρ in constrained SDM (model with ρ only)	-	-0.20***	-
LR test: lags of Y and X (ρ and θ)	-	50.17	-

Note: Data on cardiovascular device related publications in Europe from US NLM for the period 2014-2017. Outcome variable in each regression is the log value of number of publications per capita. GDP: gross domestic product; OLS: ordinary least squares; LM: Lagrange multiplier test; LR: likelihood ration test; SAR: Spatial Durbin Model; Y: dependent variable; ϵ: error term; ρ: estimate of spatial effect by dependent variable of the neighboring regions; θ: estimate of spatial effect by independent variables of the neighbor regions; λ: estimate of spatial effects by error variables of the neighboring regions. p-values: " $p < 0.05$, * $p < 0.01$, ** $p < 0.001$, *** $p < 0.0001$.

Horizon 2020 (Table 3, column 3). In the assessment of the spatial dependency, Moran's I was insignificant. However, the Lagrange multiplier tests and their robust counterparts indicated possible interaction with knowledge outputs of neighboring regions (ρ). The likelihood ratio tests in the second step between SDM (model with ρ and θ) and its constrained form (model with ρ only) indicated the likelihood of only ρ to be present, leading to specification of a spatial auto-regression (SAR) model, often termed as a spatial lag model. Our estimate of the elasticity for the EU Horizon 2020 program remained at 0.13 ($p < 0.01$) in the SAR model. Considering that we capture fixed effects of all 31 countries to control for unobserved heterogeneity by the country, these elasticities are sizeable. The elasticities of GDP estimate in the KPF were at a range of 0.14–0.92. Here, we also find negative spillover of neighboring regions.

4.3 Estimates of the Knowledge Production Function controlling for additional inputs

Our estimates remain robust when considering additional inputs as confounders. As we cannot rule out that higher knowledge production has led to better funding opportunities of EU Horizon 2020 in the same period, only the estimates of EU FP7 can be validly interpreted as a causal effect of innovatory effort on knowledge production. When we additionally controlled for innovatory efforts by private funding for the clinical studies present in our dataset (Table 4, column 1), the estimate of the elasticity of the EU FP7 program reduced to 0.22 ($p < 0.0001$). These results demonstrate that even after controlling for private funding received by clinical trial sponsorship in our dataset, the effect of innovatory effort by EU FP7 program persists, although at a smaller magnitude.

Table 4: Estimates of (Spatial) Knowledge Production Function by scientific publications per capita, additional inputs by number of grants reported, private funding, health system related factors – Inputs and outputs per capita (log-scale incl. zero)

			4 countries Subgroup Analysis	
	OLS	OLS	OLS	OLS
EU FP7 program	0.22***	-	0.34***	0.34***
	(0.04)	-	(0.06)	(0.06)
EU Horizon 2020 program	0.08*	-	0.13'	0.14*
	(0.04)	-	(0.06)	(0.06)
Grants reported	-	0.49***	-	-
	-	(0.03)	-	-
Private Funding reported	0.49***	-	-	-
in clinical trials	(0.06)	-	-	-
GDP	0.54***	0.97***	1.26***	1.20***
	(0.11)	(0.10)	(0.20)	(0.20)
Number of Hospitals	-	-	-	0.55***
				(0.12)
Life Expectancy	-	-	-	-3.54***
				(4.88)
Observations	1051	1051	422	422
Country Fixed Effects	Yes	Yes	Yes	Yes
Adjusted R-squared	0.79	0.78	0.72	0.73
Moran's I	0.00	0.00	0.00	0.00
LM test: lags of Y	8.3*	5.94	0.59	0.19
LM test: lags of e	0.04	0.02	0.03	0.00

Note: Data on cardiovascular device related publications in Europe from US NLM for the period 2014-2017. Outcome variable in each regression is the log value of the number of publications per capita. GDP: gross domestic product, OLS: ordinary least squares, LM: Lagrange multiplier test, LR: likelihood ration test, SDM: Spatial Durbin Model; Y: dependent variable; ϵ: error term; ρ: estimate of spatial effect by dependent variable of the neighboring regions; θ: estimate of spatial effect by independent variables of the neighbor regions; λ: Estimate of spatial effects by error variables of the neighboring regions. p-values: ' $p < 0.05$, * $p < 0.01$, ** $p < 0.001$, *** $p < 0.0001$.

When we consider innovatory effort by the number of grants reported in the context of cardiovascular device research (Table 4, column 2), we find a higher elasticity of 0.49 ($p < 0.0001$) as compared to our baseline models with the estimates of the EU FP7 and Horizon 2020 measures of innovatory effort. Considering other regional characteristics as additional inputs to the KPF with grants reported, we also find sizeable elasticity by the regional GDP at 0.97 ($p < 0.0001$).

Accounting for additional factors of the region that relate to the health care environment, we find similar estimates for the elasticities of the EU FP7 program in the subgroup of regions in Germany, Italy, Switzerland, and Hungary (Table 4, columns 3–4). At baseline, the elasticity of the EU FP7 program was 0.34 ($p < 0.0001$). When we controlled for the number of hospitals and life expectancy in the region, this estimate of elasticity remained the same at 0.34 ($p < 0.0001$) for the EU FP7 program.

5 Discussion

Our estimates of the (spatial) KPF for cardiovascular publication output in the 1,051 active regions across 31 European and adjacent countries suggest that innovatory effort via public funding substantially increases knowledge output. The estimates of the elasticities ranged between 0.36 and 0.40 for the EU FP7 program. The underlying (and considerable) heterogeneity in knowledge output that we documented is similar to the uneven distribution of medical device usage and companies across Europe (MedTech 2020a, Tarricone et al. 2017). We also uncovered small but negative spillover in innovatory effort and other characteristics of the neighboring regions on the regional knowledge production. We also find positive associations of 0.13–0.17 for the EU Horizon 2020 program, FP7's successor, although they cannot be interpreted as a causal effect of innovatory effort on knowledge production.

Contrary to our focus on cardiovascular devices that also has implications for patients receiving innovation faster, previous studies have identified the role of innovatory efforts by pooling input and output variables from several industries. The estimates of elasticities of knowledge output in these studies ranged from 0.24 to 0.90 (Moreno et al. 2005, Bottazzi, Peri 2003, Marrocu et al. 2013, Greunz 2003). Thus, our estimates of the elasticities for the FP7 funding (0.36-0.40) are in middle of this range. In their factorial analysis approach, Buesa et al. (2010) estimated the increase in the number of patents by about 400–1,100 due to a regional environment consisting of economic and human resources variables, about 200–270 due to innovatory firms' internal R&D investment, and about 25–80 due to the national economic environment. Some studies, such as Gumbau-Albert, Maudos (2009) and Charlot et al. (2015), estimated R&D elasticities on innovation outputs at 0.17–0.27 in Spanish and 0.26 in European regions, respectively; the associations we find for the EU Horizon 2020 funding are aligned more closely to this range (0.13–0.17). While these studies also capture innovatory effort by R&D investments, measurement variables differed as they capture R&D investments mainly by share of GDP or by internal R&D investment of the manufacturing firms. The relatively high elasticity for estimates of the FP7 funding program (0.36-0.40) is possibly due to a cumulative effect. Regions already receiving higher funding in the past had a higher potential of producing research activities resulting in publications 2014-2017.

Our estimates confirm that the public funding brought to a region has a considerable role in its innovation output in the medical device industry. For the medical device industry-specific evidence, several regional clusters have been described on a descriptive level, for example, the Medical Valley Nuremberg, Germany, or the Emilia Romagna region in Italy (Klein et al. 2015, Valley 2020). However, few studies focus on quantitative spatial analysis of the regions' inputs and outputs related to the medical device industry. The choice of innovation measure will also play an important role; analyzing elasticities of public funding may not have similar effects for early intervention measure such as patents that may predominantly rely on other funding sources such as venture capital. However, recent industry reports suggest that the European medical device industry, unlike that of the US, still heavily depends on public or semi-public grants (MedTech 2020b). In addition, even when private funding by the industry was controlled in case of some publications reporting clinical trials, the estimates of the elasticities of the EU FP7 program remained significant, albeit smaller.

The spatial spillovers of innovatory efforts on knowledge output are consistently negative, albeit on a small scale. It indicates that higher knowledge output in one region resulting from its regional innovatory efforts indirectly and negatively influences the knowledge output of neighboring regions. Innovative activity may withdraw innovative activity from neighbor regions. The small to non-significant estimates of spillovers that we detect are in line with previous evidence that uncovered the role of spatial proximity in knowledge production. While Moreno et al. (2005) has demonstrated that spillovers are significant for neighbors, as well as neighboring regions of the neighbors, Tappeiner et al. (2008) showed that spatial correlation did not exist after controlling for all traditional variables of the KPF. Finally, considering a semi-parametric approach, Charlot et al. (2015) demonstrated that spillover effects are significant only for certain thresholds of R&D expenditure.

The study had some limitations. First, our estimates of the elasticities of the KPF for the innovatory effort captured by EU Horizon 2020 program may be subject to reverse causality (Charlot et al. 2015). Most importantly, we cannot rule out that highly active regions in terms of publication output successfully attract more R&D resources in the form of grants or EU funding received. We aimed to accommodate this endogeneity issue by considering innovatory efforts provided by the EU FP7 program. Considering the estimates of the EU FP7 program, the threat of reverse causality is minimized as the publications we captured were published after regions could acquire funding for this program. In this way, we can rule out that the knowledge production we observe coincides with obtaining research funds from the same publication output. However, the regions that received more funding for EU FP7 may also contain more human resources in the academic activities that are more likely to attract public research funds in the first place. Thus, for EU Horizon 2020, we cannot fully separate the effects of receiving funding from the level of human resources dedicated to cardiovascular device research that are a prerequisite to attract funds. Previous studies have considered this type of endogeneity by capturing alumni representation in evaluation boards of funding institutions as an instrument of receiving grants (Payne, Siow 2003). Estimates of the applied instrumental variable regressions were similar in effect to those disregarding such type of endogeneity. Such data was not readily available at the European level in the context of this study.

Second, our funding measure by the number of grants reported in one of our robustness analyses may be subject to publication bias and bias if authors of one region would more actively report their grants than authors in another region. It would lead to a problem only in the case when there is a cultural practice in some regions for (not) reporting the grants with the publications compared to others.

Third, as we focus only on funding mechanisms as innovatory effort and GDP as a proxy for other regional characteristics, we cannot disentangle the relative elasticities of other types of innovatory efforts (most importantly internal R&D investments and human resources) and other regional economic or financial characteristics. For example, Buesa et al. (2010) identified the relative importance of multiple input factors in the KPF. Our primary aim was to evaluate the elasticities of public research funding relative to other inputs, such as regional characteristics. However, as GDP is the single-most-important indicator for economic activity of a region (OECD 2020a), one concern is that adding additional regional characteristics leads to biases in the estimate of the elasticity as these are intermediate variables on the path between GDP and publication output and may cause collider-stratification biases. Our subgroup analyses that include health system-related factors suggest that the estimates of the elasticities appear not strongly biased when we exclude additional factors related to innovatory effort.

Fourth, we exclude the regions for which no publication output was documented so that the estimated elasticities are conditional on some minimum degree of knowledge production. In our data, we find that the 472 regions that did not publish a cardiovascular device-related article received approximately 365 million Euro by EU FP7 funding compared to about 47 billion Euro received by the regions with at least one publication, that is about 1% of the total funding volume. Similarly, 588 million Euro in EU Horizon 2020 funding was received by these 472 regions, compared to 43 billion Euro in EU Horizon 2020 funding received by the regions with at least one publication – about 1% of the total funding volume. As documented earlier, innovation systems in the regions not generating knowledge output are likely very different from the other regions, such that our estimated elasticities may not be transferrable to these regions (Charlot et al. 2015).

Fifth, funding by EU Horizon 2020 and EU FP7 programs is targeted for multidisciplinary research. Therefore, the possibility of knowledge spillover from other technologies may moderate the effectiveness of the innovatory effort that we study for cardiovascular device related research only.

Our study provides implications for R&D policymakers as well as the industry. Given the high burden of disease in cardiovascular conditions, the global demand for R&D in cardiovascular research is high (Komajda et al. 2013). When considering promoting certain regions in their activity for knowledge production, most medical device innovators, especially SMEs, have already been relying on public funding to innovate (MedTech 2020b). We show that targeting the levels of innovatory effort in the form of providing funds does effectively increase knowledge production of a region and the underlying networks. This finding is also relevant to justify related health and R&D policies or non-profit initiatives that aim to improve the innovatory output of a region. While our results point to a large geospatial heterogeneity in access to novel treatments from medical device innovation, to what extent this innovatory effort leads to early adoption of new and effective technologies in daily clinical use needs further investigation. With such an analysis one could find out how much of the knowledge supported by public funded in a region benefits that region. This way, policy makers could assess the spatial rootedness of the knowledge production and thus, direct benefits to the region.

Our approach in extracting publications for a particular medical field and assign author affiliations may also be used to capture variation in knowledge production in other medical areas where user-producer interactions are important, and patents may not fully reflect the innovative activity beyond the first invention of the device. Location of knowledge production may also be linked to other regional level health-related variables such as mortality from cardiovascular diseases. This will allow studying, for example, whether having an innovating expert in the region would also lead to quicker adoption of health technology in routine care of cardiovascular patients and changes in the networks of these experts.

6 Conclusion

Knowledge production of cardiovascular devices is largely spread across the regions of Europe. Even the most active regions contribute relatively small shares of publications that document innovation in cardiovascular devices. Receiving funding as a form of innovatory effort is effective for generating new ideas and, subsequently, devices because large parts of the industry are organized in small and medium enterprises, which rely on the knowledge of clinicians and academics. Our results support the notion that the regional innovation systems in Europe can be fostered by public research investments to promote innovation in the medical device industry.

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A Appendix:

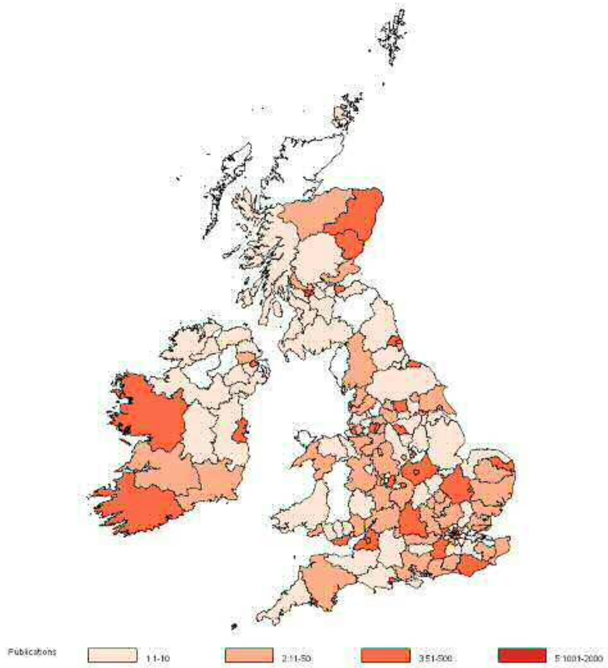

Figure A.1: Publication Output for Cardiovascluar Medical Devices at Regional levels of NUTS-3 in Europe: UK & Ireland

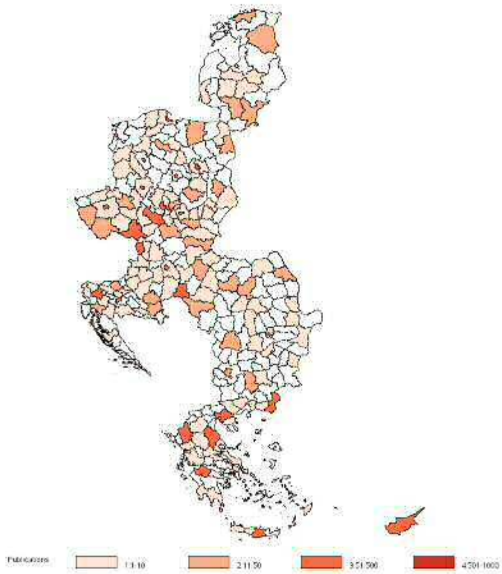

Figure A.2: Publication Output for Cardiovascluar Medical Devices at Regional levels of NUTS-3 in Europe: Bulgaria, Cyprus, Czech Republic, Estonia, Greece, Croatia, Hungary, Lithuania, Latvia, Romania, Slovakia, Slovenia

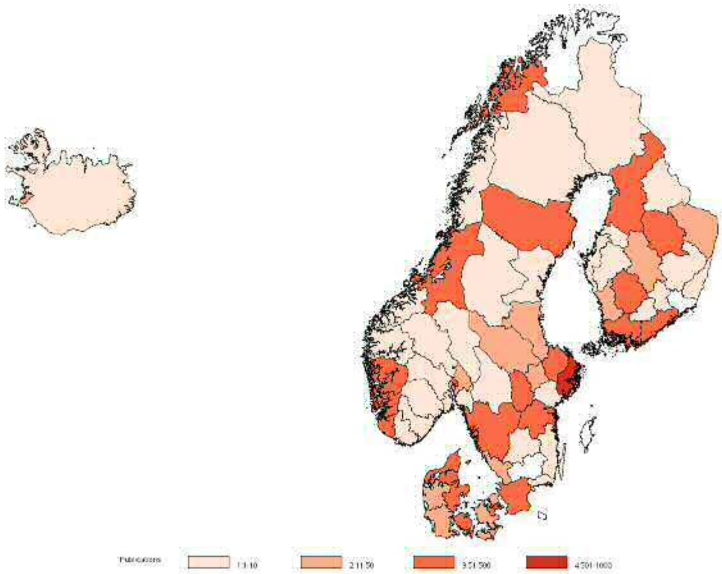

Figure A.3: Publication Output for Cardiovascluar Medical Devices at Regional levels of NUTS-3 in Europe: Iceland, Finland, Denmark, Sweden, Norway

Table A.1: Estimates of (Spatial) Knowledge Production Function by scientific publications per capita, excluding values with zero, considering funding from EU Horizon 2020 and EU FP7 program as innovatory effort – Inputs and outputs per capita (log-scale, excluding values with zero)

	OLS	OLS	SAR
EU FP7 program	0.41***	0.38***	0.37***
	(0.04)	(0.04)	(0.04)
EU Horizon 2020 program	0.17***	0.13**	0.13*
	(0.04)	(0.05)	(0.04)
GDP	0.10**	0.86***	0.92***
	(0.04)	(0.14)	(0.13)
Spillover_FP7	-	-	-0.07
Spillover_Horizon2020	-	-	-0.03
Spillover_GDP	-	-	-0.19
Total_Impact_Horizon2020	-	-	0.10
Total_Impact_FP7	-	-	0.30
Total_Impact_GDP	-	-	0.75
Observations	914	914	914
Country Fixed Effects	No	Yes	Yes
Adjusted R-squared	0.41	0.41	-
Moran's I	0.02	-0.04	-
LM test: lags of Y	1.35	3.3807	-
LM test: lags of e	1.20	17.90***	-
ρ in SDEM (model with ρ and θ)	-	-0.16*	-
ρ in constrained SDM (model with ρ only)	-	-0.24***	-
LR test of SDEM and SDM (ρ and θ)	-	52.62	-

Note: Data on cardiovascular device related publications in Europe from US NLM for the period 2014-2017. Outcome variable in each regression is the log value of number of publications per capita. GDP: gross domestic product; OLS: ordinary least squares; LM: Lagrange multiplier test; LR: likelihood ration test; SAR: Spatial Durbin Model; Y: dependent variable; ϵ: error term; ρ: estimate of spatial effect by dependent variable of the neighboring regions; θ: estimate of spatial effect by independent variables of the neighbor regions; λ: estimate of spatial effects by error variables of the neighboring regions. p-values: " $p < 0.05$, * $p < 0.01$, ** $p < 0.001$, *** $p < 0.0001$.

Table A.2: Estimates of (Spatial) Knowledge Production Function by scientific publications per capita, additional inputs by number of grants reported, private funding, health system related factors – Inputs and outputs per capita (log-scale incl. zero)

			4 countries Subgroup Analysis	
	OLS	OLS	OLS	OLS
EU FP7 program	0.29***	-	0.35***	0.34***
	(0.06)	-	(0.07)	(0.07)
EU Horizon 2020 program	0.04	-	0.14	0.15*
	(0.06)	-	(0.07)	(0.07)
Grants reported	-	0.55***	-	-
		(0.03)		
Private Funding reported in clinical trials	0.57***	-	-	-
	(0.05)			
GDP	0.16	0.61***	1.08***	1.06***
	(0.15)	(0.13)	(0.22)	(0.22)
Number of Hospitals	-	-	-	0.62***
				(0.14)
Life Expectancy	-	-	-	-2.74
				(5.22)
Observations	321	393	354	354
Country Fixed Effects	Yes	Yes	Yes	Yes
Adjusted R-squared	0.94	0.92	0.74	0.48
Moran's I	-0.01	-0.04	0.00	0.01
LM test: lags of Y	1.33	4.67	1.18	0.36
LM test: lags of e	0.04	1.49	0.01	0.04

Note: Data on cardiovascular device related publications in Europe from US NLM for the period 2014-2017. Outcome variable in each regression is the log value of the number of publications per capita. GDP: gross domestic product, OLS: ordinary least squares, LM: Lagrange multiplier test, LR: likelihood ration test, SDM: Spatial Durbin Model; Y: dependent variable; ϵ: error term; ρ: estimate of spatial effect by dependent variable of the neighboring regions; θ: estimate of spatial effect by independent variables of the neighbor regions; λ: Estimate of spatial effects by error variables of the neighboring regions. p-values: " $p < 0.05$, * $p < 0.01$, ** $p < 0.001$, *** $p < 0.0001$.

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EU funds as a catalyst of change for the Slovak healthcare system?

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Abstract. In the programming period 2007-2013, the European Structural and Investment Funds (ESIF) invested €237 million in Slovak hospitals. We investigate whether this injection of additional funds has improved the quality of healthcare in the targeted hospitals. As a measure of healthcare quality, we use the readmission rate (ratio of readmissions within 30 days over total hospitalizations) and the mortality rate. Our results show a statistically significant but small effect of ESIF on the readmission rate but not on the mortality rate. We argue that these results suggest that the main problem in Slovak healthcare is low productivity rather than a lack of funding.

JEL classification: H51, H87, I18, F36

Key words: healthcare, public finance, productivity, difference in differences

1 Introduction

The quality of healthcare provision in Slovakia is underwhelming. Despite Slovakia undergoing a substantial degree of development since its accession to the EU, its healthcare system continues to lag behind those of other EU Member States. This can be seen especially in terms of its relatively high amenable mortality rate, which is among the highest in the EU. Furthermore, Slovakia lags behind other EU countries in preventative healthcare and in the quality of primary care provision, which, in turn, leads to unnecessarily frequent admissions to hospital (OECD, European Observatory on Health Systems Policies 2017).

In this paper, we seek to identify the causes for the underperformance of the Slovak healthcare system. The basic premise motivating this analysis is that poor performance of healthcare could be attributable to one of the following two reasons. First, the healthcare system could be underfunded. If this is the case, some patients may not receive the required treatment because of a lack of funds. They may instead receive treatment that is cheaper but less effective than the best-possible course of action, or the healthcare providers lack the necessary equipment to diagnose and treat patients appropriately.

Second, the resources within the healthcare system could be used inefficiently. For example, healthcare providers may be allocating a significant share of available funds to relatively unproductive aspects of their work. This could include filling out forms and reporting, instead of looking after patients. Expensive equipment may also be allocated to hospitals that do not need it while hospitals that could better utilize them remain without. The remedy aimed at improving the quality of healthcare should address the cause of its deficiency. If the healthcare system is underfunded, then injecting additional funds would be productive. In contrast, inefficient use of existing resources will not be improved by giving the hospitals additional funds; instead, the underlying causes of inefficiency should be identified.

We model the provision of healthcare as a production process transforming measurable inputs into measurable outcomes. Thus, we estimate a production function to observe the effect of injecting additional funds on hospital-specific readmission and mortality rates. During the 2007-2013 programming period, around €265 million from the European Structural and Investment Funds (henceforth ESIF or EU Funds) were invested in Slovak healthcare facilities, of which the vast majority (€237 million) went to hospitals[1]. We investigate the impact of the overall amount of ESIF spent, and the impact of spending according to the different categories of ESIF (infrastructure, equipment, and personnel and other expenses).

Our results reveal a small but statistically significant favorable effect of the ESIF on the readmission rate one year after the allocation of the funds. In contrast, we find no effect on the overall mortality rate. When we divide the EU funds according to the expenditure categories, we find that only investments into construction and reconstruction of hospitals have had a statistically significant effect on the readmission rate. Furthermore, while the ESIF seem to affect some sub-categories of mortality, the results are mixed – we find both positive and negative effects. Moreover, even when the results are statistically significant, they are very small in magnitude.

The small magnitude of the estimated effects suggests that the Slovak healthcare system is on the predominantly flat segment of the production function, where injections of additional funds are associated only with limited improvements in the quality of outputs. Therefore, the unfavorable performance of the Slovak healthcare system does not seem to be primarily due to underfunding. Rather, the problem is inefficient use of the available funds: what is needed is an improvement that would shift the production function upwards.

2 Conceptual Framework

A popular way of evaluating the impact of spending on healthcare quality is by means of a production function, which relates the amount of spending on healthcare (inputs) to the health of the inhabitants of an economy (output). The main input factor is typically the expenditure on healthcare. To control for specific conditions and other inputs, socio-economic, lifestyle and environmental factors can also be used in the model. Outcomes are usually measured in terms of life expectancy, hospital readmissions, or mortality. Life expectancy can be either estimated at birth or at a higher age (such as 65+ life expectancy, life expectancy adjusted for quality of life, or considering only healthy life expectancy). Life expectancy measures are the most comprehensive indicators of health and quality of life, reflecting the combined effect of healthy lifestyles, nutrition, healthcare and other factors, over long periods (Thornton 2002, Lubitz et al. 2003, Nixon, Ulmann 2006, Gallet, Doucouliagos 2016). As such, they are well suited for analyses of long-term trends or comparative multi-country analyses. On the other hand, short-lasting interventions are unlikely to be reflected in changes in life expectancy. Therefore, to analyze short-term aspects of healthcare provision, hospital readmission and mortality rates may be more suited. Hospital readmissions, typically measured as readmission of

[1] Although the 2007-2013 Programming period ended in 2013, EU Member States had the possibility to draw on funds allocated within this period until 2015 under the so-called "n+2 rule", with Romania and Slovakia gaining an extension to n+3, to mitigate the possible risk of losing funds. See http://europa.eu/rapid/press-release_IP-13-446_en.htm.

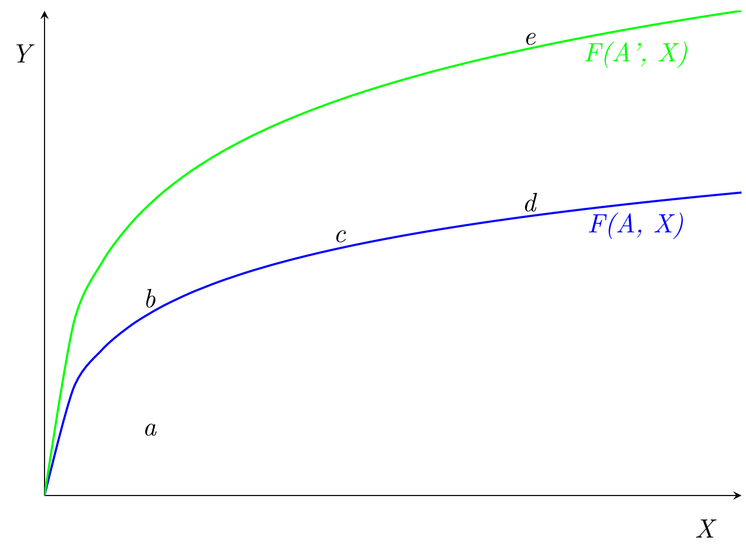
the same patient with 30 days of having been discharged, are a particularly good measure, as a significant proportion of such readmissions have been found to be avoidable: more than half, according to some studies (Benbassat, Taragin 2000, Van Walraven et al. 2011). Because of this, hospital readmissions were chosen as a criterion of quality of hospital performance under the US Affordable Care Act (McIlvennan et al. 2015, Zuckerman et al. 2016). Finally, mortality – either overall or by specific cause of death – is another valuable indicator of quality of healthcare, which is also suited for analyses of short-term trends and variations (Or 2001, Nolte, Mckee 2004, Prentice, Pizer 2007). A potential downside is that it can be subject to endogeneity and measurement/reporting issues (Dreger, Reimers 2005). For example, a poorly run healthcare system may result in a large share of the elderly dying in their homes rather than in hospitals, with their passing attributed to old age rather than to the true cause of death. Inasmuch as healthcare improvements lead to an increase in hospital admissions of the elderly, such improvements can actually translate into an increase in reported mortality in hospitals and/or mortality due to specific ailments.

In their meta-analysis of production function-based models, Gallet, Doucouliagos (2016) show that healthcare spending has a greater impact on mortality than on life expectancy: the elasticities of spending with respect to mortality rate and life expectancy are around -0.13 and 0.04 respectively. Gallet, Doucouliagos (2016) note that these relatively low elasticities may be due to other factors (income, demographics and lifestyle choices) playing significant roles. Similarly, Nixon, Ulmann (2006), looking at the 15 Member States of the European Union in 1980-1995, find that increases in healthcare expenditure are significantly associated with lower child mortality, but only with modest improvements in life expectancy. At the same time, however, they note that these relatively low elasticities may signify an importance of other factors (income, demographics and lifestyle choices). Martin et al. (2008) looked at spending on two special care programs, cancer patients and patients with cardiovascular diseases, with the latter having a higher elasticity of spending with respect to disease related deaths. Thornton (2002) also points out that the additional spending on medical care is relatively ineffective in reducing patient mortality and prolonging life expectancy; with the most important factors affecting mortality rates being socio-economic status and lifestyle. They also suggest that the effect of healthcare spending may have diminishing returns.

A number of analyses aim to define, measure and improve the organizational efficiency of healthcare facilities around the world. Palmer, Torgenson (1999) define three main aspects of efficiency in healthcare facilities: technical, allocative and productive efficiency. Technical efficiency refers to the use of given inputs in the most efficient way, given the currently available technology. A production process is technically efficient if reducing the amount of any input would lead to a reduction in output. Productive efficiency, in turn, refers to achieving a given outcome with the lowest possible cost. For example, if the same outcome could be achieved with two or more different combinations of inputs, the least costly input combination is productively efficient. Allocative efficiency, finally, reflects the ability to allocate its resources in a manner that maximizes social welfare.

The generally low estimated elasticities of healthcare spending suggest that the production of healthcare may be inefficient: the available resources and technologies are not used optimally, so that the same outputs could be produced with lower cost. Injections of additional funds have the potential to improve all three aspects of efficiency. New healthcare infrastructure and equipment can improve the quality of healthcare, new skills and techniques acquired through additional training help improve the utilization of available resources, and improvements in the provision of healthcare can help remove disparities in the quality of healthcare received by different individuals.

The previous literature assessing the impact of EU funds on healthcare in Slovakia relies primarily on descriptive analyses. The evaluation of the impact of EU funds on healthcare by KPMG (2013) concludes that the EU funds from Operational Programme Health (OPH) improved the healthcare in Slovakia by 58% in terms of quality, 24% in terms of efficiency, and 18% in terms of availability. The authors had to deal with several limitations. First, the OPH does not define criteria for quality, availability or efficiency. For that reason, the authors themselves had to define these terms and the causal links



Notes: The graph depicts output, Y, as a function of a factor of production, X, and technology (efficiency) A. An increase in inputs corresponds to moving to the right along the horizontal axis. An improvement in technology is associated with a vertical shift of the production function profile. Points a through d thus correspond to outcomes with different inputs but the same technology (efficiency), while point e is on a production function associated with more advanced technology (higher efficiency).

Figure 1: Production function and injection of additional funds

between them. This was undertaken through a structured approach of identifying the relationship and contribution of projects and their outputs to the quality, effectiveness, and availability of healthcare. It is, however, questionable whether descriptive analysis is a suitable method for finding causal linkages.

Furthermore, there is also a lack of quantitative assessments of the effect of ESIF on healthcare in other EU countries. Murauskiene, Karanikolos (2017) use a simple comparison of targeted indicators before and after the 2007-2013 programming period in Lithuania, such as the number of beds or life expectancy. A more common approach is to evaluate case studies: for instance, Pasowicz et al. (2009) look at the role of ESIF in the modernization of John Paul II Hospital in Krakow, while Glinos, Baeten (2014) mention the function of ESIF in their case studies of cross border hospital cooperation in the EU.

Our study aims to address this dearth of quantitative assessments of the impact of spending on healthcare. We follow the rest of the literature by adopting the production-function approach: we relate the outputs of healthcare establishments to the available inputs (equipment, labor, and financial resources). The health outcomes we consider are the rate of readmission within 30 days, and the mortality rate (both overall and by different causes of death). We depict our conceptual framework in a stylized form in Figure 1, wherein the graph shows the production function transforming healthcare inputs, X, into an output (health), Y, using available technology, A. The magnitude of the impact that the injection of funds achieves thus depends on where the healthcare system is situated relative to the production function. Consider points a through e; points a and b are both associated with the same (relatively low) level of inputs, while a is well below the production function, suggesting that the available resources are spent inefficiently. An injection of additional resources that moves the economy from point b to c is associated with a significant improvement in the level of output. The additional funds help move the healthcare system from the upward sloping segment of the production function (an indication that the healthcare system may be underfunded), to a flatter segment. In contrast, a similar injection of funds moving the healthcare system from c to d only leads to a modest increase in output. At c, the healthcare system is not particularly deprived of resources and is already on the flat segment of the production function. A more substantial increase in output can be achieved only by a productivity improvement, signified by an upward shift in the production function. This would occur if the injection of additional funds is associated with the adoption of a more efficient technology (A' instead of A). The healthcare system can thus move from c to e instead of d. Indeed, adopting a more efficient technology alone could lead to a significant increase in output: movement from d to e, even without additional resources (although the resource injection may prove a catalyst of an improvement in productivity).

In line with the preceding discussion, we hypothesize that finding evidence of small returns to spending increases would indicate that the healthcare system is on the relatively flat part of the production function. As such, it would not appear substantially underfunded. In contrast, finding large increases in the quality of healthcare outputs would be ambiguous. It could either imply that the healthcare system was on the upward sloping part of the production function (that is, that it was originally underfunded), or that the spending increase translated into a significant productivity improvement. In the latter case, further analysis would be required to identify which of these two cases applies to Slovak healthcare.

3 Overview of the Slovak Healthcare System

The Slovak healthcare system[2] is based on statutory health insurance, which guarantees the same basic benefit package for all insured individuals. The insurance works by means of selective contracting between health insurance companies and healthcare providers. Health insurance companies are obliged to ensure adequate healthcare for their insurant, and compete on both quality and prices. There are three health insurance companies, one public and two private. The Ministry of Health mandates the basic benefit package and maximum waiting lists, and ensures that the health insurance companies contract sufficient numbers of healthcare providers.

Healthcare services can be distinguished as either ambulatory (outpatient) care, or inpatient and other healthcare. Ambulatory care provides care to patients not admitted to the healthcare institutions. Inpatient care includes all types of hospitals, professional medical institutions and specialized sanatoriums, palliative care, spas and health resorts. Other care includes emergency medical services, home nursing care and dialysis centers. Thus, a broad range of establishments are involved in providing healthcare services, from general practitioners, through narrowly-focused clinics to hospitals with a large number of diverse wards.

When comparing Slovakia to neighboring countries or the EU as a whole, the Slovak healthcare sector appears to underperform on a number of criteria. The Ministry of Health of the Slovak Republic (2007) notes that healthcare infrastructure is often outdated. For instance, medical equipment had an average age of 10 years, in some regions even 12 years. As a result, Slovakia lags behind the other EU countries in terms of the health status of its population. According to Medeiros, Schwierz (2015), if Slovakia were to reduce its inefficiencies in healthcare, life expectancy could be 6.4 years higher at birth and 3.2 years higher at age 64. Hence, EU Funds have the potential to improve the quality of healthcare and increase the effectiveness.

Overall, €237 million were invested in Slovak hospitals during the 2007-2013 programming period, 95% of which was disbursed under Operational Programme Health (OPH). The stated objectives of OPH included, according to the Ministry of Health of the Slovak Republic (2007), improving the quality, accessibility and effectiveness of healthcare and health support, and to reduce the relatively high morbidity and mortality rates due to circulatory system diseases, carcinomas, respiratory system diseases, digestive system diseases and external causes. It aims to achieve this by investing into healthcare infrastructure (construction of new capacities, reconstruction of buildings, delivery of medical equipment and IT equipment).

Allocated EU funds have to be accompanied by matching spending from domestic sources (private, public, or a combination of the two)[3]. The co-financing share was

[2]For further details about Slovak healthcare, see Kuenzel, Solanič (2018).

[3]Specific rules on the co-financing rate depend on the specific fund of the EU budget, from which the finances stem. For details consult Council Regulation (EC) No. 1083/2006 of 11 July 2006 available at

between 15% and 19.25% of the projected amount, depending on the ownership structure (Ministry of Health of the Slovak Republic 2007). For privately held hospitals, the EU contribution was 80.75%, with 14.25% contributed from national public sources and the remaining 5% by the hospital itself. In the case of publicly owned hospitals, the EU contribution was 85%, with 15% coming from governments at the federal and local levels.

4 Data and methodology

Our goal is to investigate the impact of the ESIF on the performance of hospitals in Slovakia. To observe the impact of the ESIF, we have obtained a detailed list of all ESIF-financed projects in Slovakia during the 2007-2013 programming period. The data were provided by the Central Coordination Body, a department at the Deputy Prime Minister's Office[4] responsible for the oordination of the ESIF in Slovakia, who extracted this information from the central information systems of EU funds (ITMS). For the purposes of our analysis, we define a hospital as a healthcare facility that contains at least the following departments: internal medicine, surgical department, central admissions office, and department of anesthesia and intensive medicine. In this way, we exclude small and narrowly focused establishments such as dermatology clinics, cosmetic surgery clinics, or centers treating addiction. Based on these criteria, we identify 67 hospitals in Slovakia.

We used the hospitals' identification numbers to match EU funds received with each individual hospital. However, we encountered some cases in which several hospitals had the same identification number; this was due to some of them having the same owner. This problem was solved by contacting the managerial authorities responsible for the operational programs and asking them about the recipient of the funds. Furthermore, one project involved two separate hospitals. In this case, we divided the total amounts based on the number of doctors working in each hospital[5].

Overall, 30 of the 67 hospitals received EU funds during the 2007-2013 programming period. Figure 2 presents the number of hospitals that have drawn ESIF in each year as well as the amount that was disbursed in each year[6]. The absorption of funds by Slovak hospitals was quite low at the beginning of the 2007-2013 programming period, with peak spending occurring in 2012[7].

Figure 3 presents the regional distribution of the ESIF. Hospitals in Prešov, Banská Bystrica, and Košice regions received the greatest funding levels. On the other hand, no funds were allocated to hospitals in the Bratislava region. This is due to its status as a more developed region, meaning its GDP per capita exceeds 90% of the EU average[8]. Therefore, the Bratislava region was eligible for support only under the regional competitiveness and employment objectives, making it more difficult to invest ESIF in hospitals in this region.

Figure 3 also depicts the regional distribution of ESIF by categories of expenditure. Notice that the bulk of ESIF were spent on infrastructure (construction and reconstruction work) and medical equipment. Only in two regions, Trnava and Trenčín, were more ESIF invested in medical equipment than in infrastructure[9]. Investments in personnel,

https://eur-lex.europa.eu/legal-content/EN/ALL/?uri=CELEX:32006R1083. In this paper we summed all sources of finance together.

[4]From 1 July 2020, the Deputy Prime Minister's Office has been transformed to Ministry of Investments, Regional Development and Informatisation of the Slovak Republic.

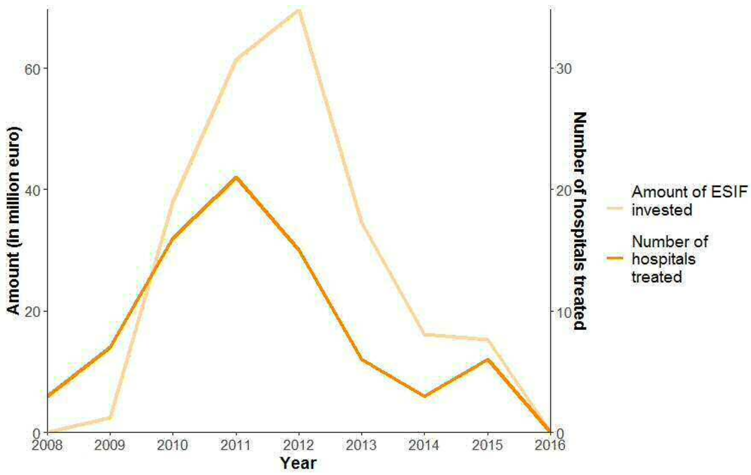
[5]The project "Further education of hospital staff", No. 27140130038, financed educational and training sessions in hospitals in Žiar nad Hronom and Rimavská Sobota.

[6]A hospital applying for ESIF at first finances the expenditure by themselves, and submits a request for reimbursement that is then assessed by the managing authority. In Figure 4 as well as throughout the whole paper we allocate the funds to the year in which the beneficiary paid the contractor.

[7]Recall that EU allowed Member States to draw unspent funds allocated in the 2007-2013 budget also during the 2-3 years immediately following the end of the programming period (see footnote 1).

[8]The EU classifies regions into less developed (with GDP per capita up to 75% of the EU average), transition regions (75 to 90%) and more developed regions (GDP per capita exceeding more than 90% of the EU average).

[9]This reflects a government assessment of the needs of the individual regions, which found that Trnava and Trenčín were especially in need of new medical equipment (see Ministry of Health of the Slovak Republic 2007).



Data source: ITMS.

Figure 2: Development of absorption of ESIF in hospitals

comprising spending on wages and training, and other expenditures, were comparatively small. As the distribution by categories suggests, the highest amount, €225 million or 95 % of the whole allocation, was drawn from the OPH. The main objective of this operational programme was to improve the quality of healthcare through construction and reconstruction of healthcare infrastructure.

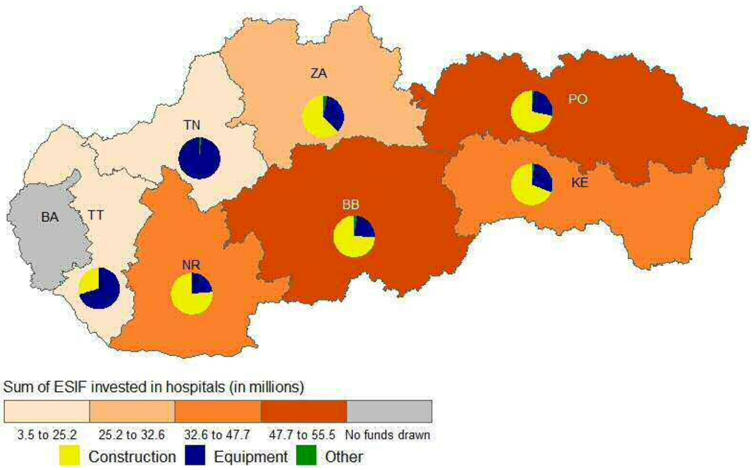
As the majority of the ESIF were spent on modernizing hospital infrastructure (construction or reconstruction), the impact on readmission rates is not entirely straightforward. Staying in a newly built or refurbished building might increase the enjoyability of one's stay in a hospital, but the improved infrastructure should only have a limited impact on the quality of the treatment provided. However, infrastructure improvements also serve to decrease a hospital's running costs, and such savings can be used to improve the quality of healthcare. Furthermore, in as much as the improvements were necessary to maintain the functionality of a hospital, obtaining external financing reduces the need to finance such planned expenditure from a hospital's own budget. Thus, funds freed up in this way can be redirected to other uses where they can have a direct impact on the readmission or mortality rates[10].

Although many previous studies used life expectancy as the outcome variable, as we discuss above, life expectancy can be attributed to numerous other factors besides the quality of healthcare system or the expenditure on it. It is also a long-term measure, and as such it would be ill-suited for an analysis of the impact of a relatively short-lasting intervention. Instead, we use the readmission rate, which we define as the rate of readmissions within 30 days of the original hospitalization, and the mortality rate, including its subcategories.

Data on readmission and mortality rates in Slovak hospitals during 2010-2017 cover the healthcare treatments recorded by Všeobecná zdravotná poisťovňa (VšZP, the public health insurance company) and were provided to us by the Ministry of Health of the Slovak Republic. VšZP is the oldest and largest health insurance provider, with a market share of 57.73% as of 1.1.2020 (this share was even higher during the years covered by the analysis)[11]. The data show insurance claims by clients of the VšZP at the level

[10]Such spillover effects are similar to the crowding out of investment by development aid. The literature studying the effect of aid on investment in less developed countries routinely finds that receiving aid for investment projects leads to a reduction in investment by the recipient country and an increase in government consumption. In other words, the aid received allows the recipient country to free up some of its own resources originally earmarked for investment and redirect them to other uses (see Section 5 in Doucouliagos, Paldam 2009). It is reasonable to expect a similar pattern at the level of hospitals.

[11]Since 2013 around 200,000 switched to one of the two private insurance companies. For more information see: https://www.vszp.sk/showdoc.do?docid=2219&forceBrowserDetector=blind and http://www.udzs-sk.sk/documents/14214/29608/OZNAMENIE_podiel+PP_web_1.1.2020.pdf/d1b10048-34f5-4a0a-ba72-83c85c51bd30.



Data source: ITMS.
Note: Hospitals in Bratislava region were not eligible for EU funds. The abbreviations in Figure 3 represent the names of the regions: Bratislava region (BA), Trnava region (TT), Trenčín region (TN), Nitra region (NR), Žilina region (ZA), Prešov region (PO) and Košice region (KE).

Figure 3: ESIF invested in hospitals (in millions of Euros) and breakdown by type of expenditure

of hospital departments; these were added up to compute the hospital-level aggregates. However, the data on readmission rates are incomplete for 17 hospitals. We imputed the missing observations by bootstrapping from the existing data using the hospitals trends.

We have also included various additional control variables to ensure the model is well specified and free of omitted variable bias by accounting for the possible impact of hospital specific factors on the readmission and mortality rates. Quality of healthcare might be affected by the nature of ownership of the healthcare facility (Czypionka et al. 2014, Berger, Messer 2002) and the number of medical devices available at the hospital (Retzlaff Roberts et al. 2004, Samut, Cafri 2016, Stefko et al. 2018). Hospitals with an oncology department or an intensive care unit tend to deal with more serious cases so they are likely to have higher readmission and mortality rates. Similarly, the capacity and occupancy of the hospital might influence the readmission rate. Furthermore, we also control for the effects of several socio-economic variables at the district level: the average wage, perinatal mortality, economic dependency ratio (number of people in retirement age divided by the number of people of working age), population density, and the share of people of the Roma ethnicity (who tend to suffer from significant economic and social exclusion) in the district's population. We obtained these data from the Statistical Office of the Slovak Republic[12].

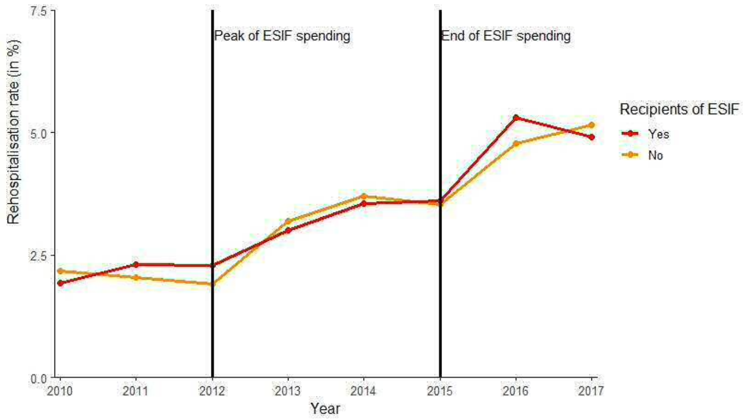
In order to estimate the impact of ESIF investments on the quality of healthcare, we estimate the production function of healthcare quality for hospital i located in district j in time period t:

$$\ln Y_{it} = \beta_0 + \beta_1 \ln ESIF_{it} + \gamma hos\_controls_{it} + \delta socecon\_controls_{jt} + \tau_t + \mu_i + u_{it}$$

ESIF denotes the cumulative sum of all ESIF invested by period t in a given hospital: adding-up the EU funds in this way allows us to evaluate their long-term effect. The reason is that the expenditure should not only impact the quality of healthcare in the same year but also in the following years[13]. Furthermore, *hosp_controls* and *soc-*

[12] In the discussion of our findings below, we focus on the ESIF effect. The full regression results for all control variables can be found in the Appendix.

[13] The alternative would have been to consider different lag length to see which yields the best results. However, as we explain above, we are precluded from doing this by the changes in how the data were collected in 2016 and subsequent years.



Data source: National health information center.

Figure 4: Development of the readmission rate in Slovak hospitals in 2010-2017

econ_controls represent the hospital and district controls, respectively[14]. Lastly, τ_t denotes the time fixed effects and μ_i stands for the individual fixed effects.

As we are also interested in the impact of different categories of ESIF, we also estimate the following model:

$$\begin{aligned} \ln Y_{it} \quad = \quad & \beta_0 + \beta_1 \ln constr_{it} + \beta_2 \ln equip_{it} + \beta_1 \ln persother_{it} + \\ & \gamma hos\_controls_{it} + \delta socecon\_controls_{jt} + \tau_t + \mu_i + u_{it} \end{aligned}$$

where *constr*, *equip* and *persother* represent the ESIF invested in infrastructure, equipment, and other expenses (which also includes personnel expenses that are too small to be used as a separate category), all expressed as cumulative sums.

We adjust the data in a number of ways. First, although the hospitals were also receiving EU funds in 2008 and 2009, due to limited availability of data on the quality of healthcare in hospitals in these years we cannot include them in our model. However, not considering the funds utilized by hospitals in 2008 and 2009 should not affect our results much because, as Figure 2 shows, the drawing rate of ESIF in these two years was negligible. Second, we exclude the years 2016 and 2017 from our model, because in these two years the ESIF from the programming period 2007-2013 were no longer drawn. As can be seen in Figure 4, the readmission rate increased in 2016 and 2017. This increase is not caused by changes in Slovak healthcare, but rather by an improvement in data collection. Hence, the inclusion of these two years might distort the results. Due to missing data on the hospital controls we have an unbalanced panel[15]. Lastly, we take logarithms of variables, with the exception of binary variables, and added 1 to the variables expressed as ratios before taking logarithms of them to prevent additional loss of data as they contained numerous zeros.

We estimate models with contemporaneous cumulative ESIF and with its first lag. All in all, our two models cover 67 hospitals, of which 30 were drawing ESIF over the period 2010-2015.

In Table 1, we present the descriptive statistics for both groups of hospitals, that is, hospitals that were recipients of funds, and those that did not receive any funds during our observation period. The two groups of hospitals are similar, but some important differences stand out. The hospitals that drew EU funds have a higher capacity in terms of beds as well as more medical personnel and specialized medical

[14]Some of the control variables at the hospital level (new patients, capacity of the hospital and the number of medical devices) were divided by the number of medical personnel to control for the size of the hospital.

[15]Out of the 67 hospitals in our dataset we are missing complete times series for several variables in the case of seven hospitals, with two of them belonging to the treatment group. For approximately ten others we have incomplete time series.

Table 1: Comparison of mean values of variables between ESIF recipients and other hospitals

		2010			2015	
ESIF recipients	Yes	No	Difference	Yes	No	Difference
Number of hospitals	17	50	-33	30	37	-7
ESIF [euros]	1,346,473.15	0.00	1,346,473.15	7,913,732.23	0.00	7,913,732.23
Readmission rate1	1.83%	2.15%	-0.32 p.p.	3.50%	3.41%	0.10 p.p.
Mortality rate2	2.06%	2.53%	-0.48p.p.	2.07%	2.27%	-0.21 p.p.
Capacity3	493.52	368.80	124.72	452.75	327.86	124.89
Occupancy4	66.99%	61.83%	5.16 p.p.	67.46%	64.87%	2.59 p.p.
Intensive Care [0/1]	0.53	0.49	0.05	0.67	0.59	0.07
Oncology [0/1]	0.10	0.03	0.07	0.03	0.03	0.01
CT5	1.13	0.73	0.40	1.17	0.91	0.26
MR5	0.52	0.15	0.37	0.38	0.15	0.23
Perinatal mortality6	5.87	5.54	0.33	5.96	5.15	0.82
Average wage7	730.50	814.84	-84.34	884.07	956.62	-72.55
Population density8	205.49	514.93	-309.45	201.83	505.92	-304.09
Old age dependency9	17.22	18.12	-0.91	20.91	21.64	-0.73
Roma share10	2.32	2.21	0.11	2.41	1.95	0.46
State hospital [0/1]	0.67	0.32	0.34	0.67	0.38	0.29
Regional hospital [0/1]	0.20	0.57	-0.37	0.07	0.38	-0.31

Data source: National health information center and Statistical Office of the Slovak Republic.
Notes: Hospital controls: 1 Percentage of patients readmitted within 30 days after being discharged from hospital. 2 Percentage of patients who pass away while in hospital. 3 Capacity in terms of number of patients that can be accommodated. 4 Patients admitted as percentage of capacity. 5 Number of devices in the hospital. District controls: 6 Perinatal mortality in the district the hospital is located in. 7 Average salary in the district the hospital is located in. 8 Persons per square kilometer in the district the hospital is located in. 9 Old persons (65+), as percentage of population in economically active age in the district the hospital is located in. 10 Percentage of Roma ethnicity in the population of the district the hospital is located in.

equipment (MRI scanners and CT scanners). Apart from that, we can see that they are located in poorer regions (in terms of the average wage). The OPH prioritized hospitals that urgently needed repairs or construction works or were located in regions that had high mortality rates due to cardiovascular, respiratory and oncological diseases (Ministry of Health of the Slovak Republic 2007). Therefore, our model may suffer from endogeneity bias due to omitted variables. Because of the lack of data, we are not able to control for all these characteristics. Nevertheless, if endogeneity is present, it would bias the estimates downwards, given that EU funds were prioritized for poorly performing hospitals. Therefore, our results can be interpreted as the lower bound of the impact of ESIF.

Besides the overall mortality rate, we also have information on the main causes of death. These are summarized in Table 2. Note that, given some hospitals have a limited range of departments, not all causes of death are observed in each hospital.

5 Results

Table 3 presents the results with contemporaneous effect of the cumulative EU funds on the rate of readmission of patients within 30 days. Columns (1-2) present the results obtained with hospital fixed effects only, while columns (3-4) also feature time fixed effects. In Columns (1) and (3), we report the regression results obtained with the total ESIF, while the results with subcategories of spending are reported in Columns (2) and (4) [16]. The effect of EU spending overall is insignificant; when looking at subcategories, only ESIF invested into construction and reconstruction of hospitals seem to have a statistically significant negative effect on the readmission rate. Thus, it appears that investing more funds in construction and reconstruction of hospital premises results in a lower rate of patient readmissions. Controlling for time fixed effects makes little difference, which is reassuring. Our results do not capture some unobserved nation-wide

[16] In the main body of the paper, we only report the coefficient estimates for the EU Funds. The full results, with all control variables, are available in the Appendix.

Table 2: Descriptive statistics: mortality by cause of death and other indicators

Variable	Obs.	Mean	Std. Dev.	Min	Max
Mortality after femur fracture (age over 65)	283	0.11	0.08	0	1
Mortality caused by myocardial infarction after emergency (age 35-74)	292	0.07	0.09	0	1
Mortality after acute stroke	320	0.14	0.10	0	1
Mortality after interventions	329	0.02	0.02	0	0.10
Mortality in ICUs	309	0.05	0.04	0	0.25
Ratio of transfers to ICUs	308	0.22	0.25	0	2.00
Mortality in regular wards after transfer from ICU	352	0.00	0.00	0	0.01
Pressure ulcer	353	0.00	0.00	0	0.08
Ratio of transfers to ICUs *	308	0.22	0.25	0	2.00
Operation rate **	299	0.57	0.17	0	1

Data source: National health information center.
Notes: * Ratio of patients transferred to an ICU over total number of hospitalizations. ** Ratio of patients undergoing surgery over total number of hospitalizations.

Table 3: Contemporaneous effect of cumulative ESIF on the readmission rate

	(1) Readmission rate 30 days	(2) Readmission rate 30 days	(3) Readmission rate 30 days	(4) Readmission rate 30 days
Constant	-0.265543*	-0.269996*	0.373888	0.329155
	(0.138624)	(0.136596)	(0.225511)	(0.215518)
ESIF	0.000219		0.000092	
	(0.000437)		(0.000416)	
Construction		-0.001070***		-0.001093***
		(0.000291)		(0.000332)
Equipment		0.000627*		0.000713*
		(0.000323)		(0.000367)
Persother		0.000860		0.000585
		(0.000636)		(0.000620)
Hospital controls	Yes	Yes	Yes	Yes
Socioeconomic controls	Yes	Yes	Yes	Yes
Observations	333	333	333	333
Individual FEs	Yes	Yes	Yes	Yes
Time FEs	No	No	Yes	Yes
R-squared	0.2675	0.2936	0.3667	0.3919
Adjusted R-squared	0.230362	0.253093	0.323977	0.346663
F statistics	475.65***	40.68***	5.33***	6.02***

Notes: Robust standard errors in parentheses. Full results in the Appendix. *** $p < 0.01$, ** $p < 0.05$, * $p < 0.1$.

policy trends in the organization or financing of healthcare.

In Table 4, we lag the EU funds by one year: this is intended to allow for a delay in the investments bearing fruit. The impact of EU funds now appears stronger and is more precisely estimated. In Column (3), when time fixed effects are taken into account, a one-percent increase in the EU funds reduces the readmission rate in the following year by 0.000775%. If we consider that the average readmission rate was 2.68% during this period, then this is equivalent to a decline of 0.0021 percentage points. Without including time effects, the impact falls just short of being statistically significant. We obtain a slightly higher coefficient when we divide the EU funds into three categories, among which construction and equipment are the most significant. Interestingly, their estimated effects have the opposite signs. Investment in construction, which is the category with the largest proportion of EU funds, lowers the readmission rate, as expected. The positive coefficient for EU funds invested in equipment can be rationalized as an effect of an increased capacity of the hospital. After installing new and more modern equipment, the hospital may receive additional patients and/or is likely to admit patients with more complicated ailments. Being required to treat more complicated cases may then translate into a higher incidence of readmissions.

We also examine the impact of EU funds on the overall mortality rate as well as the main causes of death (Tables 5-7). In case of the overall mortality rate, the results

Table 4: Lagged effect of cumulative ESIF on the readmission rate

	(1) Readmission rate 30 days	(2) Readmission rate 30 days	(3) Readmission rate 30 days	(4) Readmission rate 30 days
Constant	-0.785390	-0.792601	1.154970	1.178965
	(0.626623)	(0.629372)	(0.852947)	(0.842379)
Lag_ ESIF	-0.000463		-0.000757***	
	(0.000287)		(0.000272)	
Lag_construction		-0.000775***		-0.000906***
		(0.000192)		(0.000237)
Lag_equipment		0.000652***		0.000740***
		(0.000239)		(0.000250)
Lag_persother		-0.000407		-0.000771**
		(0.000370)		(0.000324)
Hospital controls	Yes	Yes	Yes	Yes
Socioeconomic controls	Yes	Yes	Yes	Yes
Observations	279	279	279	279
Individual FEs	Yes	Yes	Yes	Yes
Time FEs	No	No	Yes	Yes
R-squared	0.3214	0.3322	0.4365	0.4497
Adjusted R-squared	0.279996	0.285952	0.392766	0.402433
F statistics	4.11 ***	5.45 ***	16.42 ***	13.96 ***

Notes: Robust standard errors in parentheses. Full results in the Appendix. *** $p < 0.01$, ** $p < 0.05$, * $p < 0.1$.

show no statistically significant relationship with the EU funds (Table 5). Looking at the various sub-categories of mortality, we find that the absorption of financial resources in hospitals is positively correlated with mortality after femur fracture in the case of patients over 65, mortality due to myocardial infarction and mortality after transfers from ICU. Femur fracture is a common injury among the elderly associated with significant morbidity, mortality and disability (Bouchard et al. 1996). The positive effects for these two categories could be explained by the fact that hospitals that underwent improvements are likely to receive additional and more serious cases which, in turn, are more likely to end up with the patient passing away. On the other hand, additional financial resources in hospitals are negatively correlated with mortality in ICUs. The remaining categories appear unaffected by EU funds[17]. The mixed effects of investments financed by the ESIF on the various categories of mortality can explain the lack of significance of EU funds with respect to the overall mortality rate.

6 Conclusions

In this paper, we evaluate the impact of injecting additional EU funding into hospitals on the quality of healthcare in Slovakia. Between 2010 and 2015, €237 million of EU grants were invested in 30 Slovak hospitals, with most of these funds utilized for reconstruction of hospital premises or construction of new buildings. We measure the quality of hospital care by means of the readmission rate, defined as the ratio of readmissions within 30 days over total hospitalizations, and the mortality rate. These are outcomes that are unambiguously important for the patients' wellbeing and quality of life. Slovakia is a particularly well-suited subject for such analysis as the performance of its healthcare system compares rather unfavorably to similar countries in the region and to the EU as a whole. One possible explanation for this is lack of funding, as Slovakia spends a lower share of its GDP on healthcare compared to the EU average. In this paper, we aim to shed light on whether the poor performance of the Slovak healthcare system is indeed

[17] When we again split the ESIF by categories (construction, equipment, and personnel/other), we find that mortality after femur fracture is positively correlated with ESIF spending on equipment. Mortality due to myocardial infarction shows a negative correlation with purchases of equipment and a positive (and larger) correlation with spending on personnel and other uses. Mortality after interventions falls with expenditure on construction and equipment but increases with personnel and other spending. Mortality in ICUs is weakly negatively correlated with equipment spending, and, finally, the ratio of transfers to ICUs depends negatively on ESIF in construction. These results are available upon request.

Table 5: Contemporaneous and lagged effects of cumulative ESIF on the mortality rate

	(1) Mortality rate	(2) Mortality rate	(3) Mortality rate	(4) Mortality rate
Constant	-0.0164	-0.0167	0.2276	0.2346
	(0.0263)	(0.0262)	(0.1441)	(0.1469)
ESIF	0.0000			
	(0.0001)			
Lag_ESIF			0.0000	
			(0.0001)	
Construction		-0.0000		
		(0.0001)		
Equipment		0.0000		
		(0.0001)		
Persother		0.0001		
		(0.0001)		
Lag_construction				0.0000
				(0.0001)
Lag_equipment				0.0000
				(0.0001)
Lag_persother				-0.0001
				(0.0001)
Hospital controls	Yes	Yes	Yes	Yes
Socioeconomic controls	Yes	Yes	Yes	Yes
Observations	344	344	289	289
Individual FEs	Yes	Yes	Yes	Yes
R-squared	0.0851	0.0880	0.1352	0.1384
Adjusted R-squared	0.0403	0.0376	0.0843	0.0809
F statistics	1.93**	1.51	2.39***	2.17**

Notes: Robust standard errors in parentheses. *** $p < 0.01$, ** $p < 0.05$, * $p < 0.1$. Regressions with time-fixed effects did not differ significantly from those with individual fixed effects.

caused by the low level of funding, or whether it is a sign of low overall productivity of healthcare facilities.

Our results indicate that the injection of EU funds has led to a significant but small decrease in the readmission rate in the following year. An increase in EU funds by one percent is associated with a decrease in the readmission rate by 0.0007% in the following year. When looking at the break-down of EU-financed investments by category of spending, we see that the favorable impact is driven primarily by spending on the construction and reconstruction of hospital premises. In contrast, we find that investments in equipment are correlated with slightly higher readmission rates in the next year. We think that this latter result may be caused by hospitals with new equipment receiving more acute patients from other hospitals. The impact of ESIF on mortality rates is statistically insignificant. When we look at the various subcategories of mortality, the results are mixed: we observe some positive but also negative effects, all of which tend to be rather small.

How are we to make sense of the result that injections of EU funds are associated with only small improvements in healthcare outcomes? First, it suggests that the Slovak healthcare system is at present on the relatively flat segment of the production curve. For this reason, increases in inputs lead only to modest gains in performance. In turn, that means that the healthcare system is not at present underfunded, had that been the case, we would expect much larger gains after the hospitals received additional resources. Rather, what the Slovak healthcare system needs is efficiency improvements. Returning to the production-function paradigm, what is needed is an upward shift in the production function, not movement alongside the existing (and low) production function.

The small gains can also be related to the fact that the bulk of EU funds were spent on construction and reconstruction of hospital facilities, that is, on purposes not directly related to provision of healthcare. Such funding can affect the quality of healthcare only indirectly, by freeing up hospitals' own funds to be redirected to other uses. Our findings suggest that such indirect effects are not present or very limited. Nevertheless, it is important to note that several other contributions also find small or zero effects of

Table 6: Contemporaneous effect of ESIF on the mortality rate in selected categories (part 1)

	(1) Mortality after femur fracture (age over 65)	(2) Mortality caused by myocardial infarction after emergency (age 35-74)	(3) Mortality after acute stroke	(4) Mortality after interventions
Constant	-1.4762*	0.0512	2.3563	0.0355
	(0.8261)	(0.8355)	(1.4376)	(0.1353)
ESIF	0.0027*	0.0028**	0.0015	-0.0001
	(0.0014)	(0.0012)	(0.0022)	(0.0002)
Hospital controls	Yes	Yes	Yes	Yes
Socioeconomic controls	Yes	Yes	Yes	Yes
Observations	271	282	306	319
Individual FEs	Yes	Yes	Yes	Yes
R-squared	0.1142	0.0974	0.0781	0.1212
Adjusted R-squared	0.0585	0.0429	0.0271	0.0747
F statistics	441.71***	4.19***	22.90 ***	335.94 ***

Notes: Robust standard errors in parentheses. *** $p < 0.01$, ** $p < 0.05$, * $p < 0.1$.

Table 7: Contemporaneous effect of ESIF on the mortality rate in selected categories (part 2)

	(5) Mortality in ICUs	(6) Ratio of transfers to ICUs	(7) Mortality in regular wards after a transfer from ICU	(8) Pressure ulcer	(9) Operation rate
Constant	0.3189	-5.3445*	-0.0042	0.0107	-0.1128
	(0.1901)	(2.9647)	(0.0085)	(0.0091)	(2.7022)
ESIF	-0.0014**	-0.0072	0.0000477*	0.0000	-0.0043
	(0.0005)	(0.0044)	(0.0000259)	(0.0000)	(0.0029)
Hospital controls	Yes	Yes	Yes	Yes	Yes
Socioeconomic controls	Yes	Yes	Yes	Yes	Yes
Observations	220	220	221	339	291
Individual FEs	Yes	Yes	Yes	Yes	Yes
R-squared	0.1465	0.3663	0.1405	0.0541	0.1399
Adjusted R-squared	0.0838	0.3198	0.0776	0.0072	0.0897
F statistics	31.97***	41.83***	4.45***	1.91**	5.23***

Notes: Robust standard errors in parentheses. *** $p < 0.01$, ** $p < 0.05$, * $p < 0.1$.

spending increases on the quality of healthcare (Or 2001, Nixon, Ulmann 2006, Gallet, Doucouliagos 2016).

Our analysis sheds light on correlation between the EU funds and the quality of healthcare; it does not reflect a causal relationship. Nevertheless, our findings suggest that the unfavorable performance of the Slovak healthcare system (in international comparison) is not due to lack of funding but is attributable to low efficiency. This likely reflects the general lack of qualified healthcare practitioners, both doctors and especially nurses. The lack of qualified staff will worsen over time as a significant proportion of existing doctors and nurses are above 60 years old (ÚHP 2019). Graduates of medical schools tend to migrate to other countries, which will further exacerbate the shortage of medical personnel in Slovakia (Haluš et al. 2017). The low efficiency also reflects a misallocation of resources, with the ratio of general practitioners to specialists at 3 compared to the EU average of 0.6 (ÚHP 2019). If the objective of EU Funds is to generate significant improvements in the quality of healthcare, then future funding programs should focus on fostering knowledge transfer, technology acquisition, and training healthcare professionals rather than (or in addition to) rebuilding facilities. Future research, and the attention of policy makers, should therefore be directed towards identifying potential avenues to improve efficiency and to ensure the healthcare system does not suffer staff shortages.

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A Appendix:

Table A.1: Contemporaneous effect of cumulative ESIF on the readmission rate – full model

	(1) Readmission rate 30 days	(2) Readmission rate 30 days	(3) Readmission rate 30 days	(4) Readmission rate 30 days
Constant	-0.265543*	-0.269996*	0.373888	0.329155
	(0.138624)	(0.136596)	(0.225511)	(0.215518)
ESIF	0.000219		0.000092	
	(0.000437)		(0.000416)	
Construction		-0.001070***		-0.001093***
		(0.000291)		(0.000332)
Equipment		0.000627*		0.000713*
		(0.000323)		(0.000367)
Persother		0.000860		0.000585
		(0.000636)		(0.000620)
Capacity	-0.000310	-0.000326	0.000049	0.000017
	(0.000385)	(0.000351)	(0.000407)	(0.000372)
Occupancy	0.042628	0.039042	0.036114	0.030490
	(0.035229)	(0.035018)	(0.034315)	(0.034642)
New patients	-0.014553*	-0.014867*	-0.009925	-0.010003
	(0.007949)	(0.007624)	(0.007703)	(0.007448)
Medical devices	0.004416	0.007104	-0.000381	0.002303
	(0.012546)	(0.012119)	(0.011726)	(0.011287)
IC	0.002146	0.003078	-0.002637	-0.001697
	(0.005749)	(0.005934)	(0.005070)	(0.005225)
Oncology	0.014272*	0.013181	0.011428**	0.010773*
	(0.007332)	(0.008856)	(0.004535)	(0.005455)
CT	0.000586	0.001850	0.001625	0.002864
	(0.002468)	(0.002517)	(0.002456)	(0.002480)
MR	-0.006358	-0.006880*	-0.006177**	-0.006728**
	(0.003985)	(0.003935)	(0.002540)	(0.002545)
State hospital	-0.010493***	-0.010833***	-0.016054***	-0.016175***
	(0.001885)	(0.001961)	(0.004352)	(0.004235)
Regional hospital	-0.000886	-0.000823	0.003683	0.003296
	(0.002866)	(0.002919)	(0.003071)	(0.003208)
Perinatal mortality	0.001077	0.000593	0.000693	0.000276
	(0.001689)	(0.001648)	(0.001611)	(0.001579)
Average wage	0.018057	0.016919	-0.026035	-0.023398
	(0.021607)	(0.020930)	(0.024024)	(0.023672)
Roma share	0.007260	0.008703*	0.003990	0.005766
	(0.004546)	(0.004468)	(0.004398)	(0.004298)
Econ dependency	0.071239**	0.069779**	-0.006601	-0.005288
	(0.031568)	(0.029800)	(0.025260)	(0.023932)
Population density	-0.000585	0.002908	-0.025804	-0.020925
	(0.020684)	(0.020219)	(0.019709)	(0.018752)
Observations	333	333	333	333
Individual FEs	Yes	Yes	Yes	Yes
Time FEs	No	No	Yes	Yes
R-squared	0.2675	0.2936	0.3667	0.3919
Adjusted R-squared	0.230362	0.253093	0.323977	0.346663
F statistics	475.65 ***	40.68 ***	5.33 ***	6.02 ***

Notes: Robust standard errors in parentheses. *** $p < 0.01$, ** $p < 0.05$, * $p < 0.1$.

Table A.2: Lagged effect of cumulative ESIF on the readmission rate – full model

	(1) Readmission rate 30 days	(2) Readmission rate 30 days	(3) Readmission rate 30 days	(4) Readmission rate 30 days
Constant	-0.785390	-0.792601	1.154970	1.178965
	(0.626623)	(0.629372)	(0.852947)	(0.842379)
Lag_ ESIF	-0.000463		-0.000757***	
	(0.000287)		(0.000272)	
Lag_construction		-0.000775***		-0.000906***
		(0.000192)		(0.000237)
Lag_equipment		0.000652***		0.000740***
		(0.000239)		(0.000250)
Lag_persother		-0.000407		-0.000771**
		(0.000370)		(0.000324)
Capacity	0.000052	0.000091	0.000427	0.000459
	(0.000312)	(0.000297)	(0.000334)	(0.000314)
Occupancy	0.050533	0.042946	0.025954	0.015898
	(0.039044)	(0.039733)	(0.033427)	(0.032614)
New patients	-0.021922***	-0.022567***	-0.013669*	-0.014256*
	(0.007937)	(0.007844)	(0.008074)	(0.008105)
Medical devices	0.004876	0.003975	0.000499	-0.000901
	(0.011617)	(0.011693)	(0.010795)	(0.010615)
IC	-0.000544	-0.000401	-0.007310	-0.007221
	(0.005786)	(0.005946)	(0.004887)	(0.005034)
Oncology	0.007604	0.008716	-0.002632	-0.000670
	(0.009528)	(0.009006)	(0.006267)	(0.005412)
CT	-0.001968	-0.001622	-0.000822	-0.000425
	(0.003111)	(0.003101)	(0.002922)	(0.002855)
MR	-0.006329	-0.005996	-0.005077**	-0.004690**
	(0.003889)	(0.003829)	(0.002339)	(0.002260)
State hospital	-0.011444***	-0.011232***	-0.016106***	-0.015946***
	(0.003733)	(0.003830)	(0.002924)	(0.002899)
Regional hospital	-0.004278	-0.004157	0.000508	0.000717
	(0.003745)	(0.003809)	(0.003117)	(0.003150)
Perinatal mortality	0.001440	0.001366	0.000229	0.000119
	(0.001615)	(0.001652)	(0.001431)	(0.001443)
Average wage	0.029405	0.033204	0.004548	0.008963
	(0.028528)	(0.028508)	(0.027010)	(0.026846)
Roma share	-0.056345	-0.054630	-0.047380	-0.045273
	(0.037615)	(0.037073)	(0.029981)	(0.028874)
Econ dependency	0.083215**	0.080566**	-0.015373	-0.019533
	(0.040359)	(0.040026)	(0.035883)	(0.034995)
Population density	0.077464	0.076632	-0.209844	-0.216376
	(0.128693)	(0.129861)	(0.156662)	(0.155700)
Observations	279	279	279	279
Individual FEs	Yes	Yes	Yes	Yes
Time FEs	No	No	Yes	Yes
R-squared	0.3214	0.3322	0.4365	0.4497
Adjusted R-squared	0.279996	0.285952	0.392766	0.402433
F statistics	4.11 ***	5.45 ***	16.42 ***	13.96 ***

Notes: Robust standard errors in parentheses. *** $p < 0.01$, ** $p < 0.05$, * $p < 0.1$.

Table A.3: Contemporaneous and lagged effect of cumulative ESIF on the mortality rate – full model

	(1) Mortality rate	(2) Mortality rate	(3) Mortality rate	(4) Mortality rate
Constant	-0.0164	-0.0167	0.2276	0.2346
	(0.0263)	(0.0262)	(0.1441)	(0.1469)
ESIF	0.0000			
	(0.0001)			
Lag_ESIF			0.0000	
			(0.0001)	
Construction		-0.0000		
		(0.0001)		
Equipment		0.0000		
		(0.0001)		
Persother		0.0001		
		(0.0001)		
Lag_construction				0.0000
				(0.0001)
Lag_equipment				0.0000
				(0.0001)
Lag_persother				-0.0001
				(0.0001)
Capacity	0.0000	0.0000	-0.0000	-0.0000
	(0.0001)	(0.0001)	(0.0001)	(0.0001)
Occupancy	0.0015	0.0014	-0.0102*	-0.0106*
	(0.0078)	(0.0078)	(0.0055)	(0.0057)
New patients	-0.0020	-0.0020	-0.0032**	-0.0031**
	(0.0017)	(0.0017)	(0.0014)	(0.0014)
Medical devices	-0.0004	-0.0003	-0.0020	-0.0022
	(0.0030)	(0.0030)	(0.0036)	(0.0037)
IC	-0.0004	-0.0003	-0.0011	-0.0011
	(0.0015)	(0.0016)	(0.0015)	(0.0015)
Oncology	0.0002	0.0002	-0.0003	0.0000
	(0.0007)	(0.0007)	(0.0009)	(0.0007)
CT	0.0005	0.0005	0.0011	0.0011
	(0.0009)	(0.0009)	(0.0009)	(0.0009)
MR	0.0001	0.0001	0.0005	0.0006
	(0.0005)	(0.0005)	(0.0005)	(0.0005)
State hospital	-0.0025**	-0.0025**	-0.0026**	-0.0026**
	(0.0011)	(0.0011)	(0.0012)	(0.0012)
Regional hospital	-0.0008	-0.0009	-0.0006	-0.0006
	(0.0007)	(0.0007)	(0.0007)	(0.0007)
Perinatal mortality	-0.0001	-0.0002	-0.0003	-0.0003
	(0.0003)	(0.0003)	(0.0003)	(0.0003)
Average wage	-0.0025	-0.0026	-0.0035	-0.0035
	(0.0024)	(0.0025)	(0.0032)	(0.0032)
Roma share	0.0029*	0.0030*	0.0027	0.0020
	(0.0016)	(0.0016)	(0.0067)	(0.0069)
Econ dependency	0.0039	0.0037	0.0038	0.0037
	(0.0024)	(0.0024)	(0.0024)	(0.0024)
Population density	0.0102**	0.0105**	-0.0335	-0.0349
	(0.0047)	(0.0048)	(0.0298)	(0.0305)
Observations	344	344	289	289
Individual FEs	Yes	Yes	Yes	Yes
R-squared	0.0851	0.0880	0.1352	0.1384
Adjusted R-squared	0.0403	0.0376	0.0843	0.0809
F statistics	1.93**	1.51	2.39***	2.17**

Notes: Robust standard errors in parentheses. *** $p < 0.01$, ** $p < 0.05$, * $p < 0.1$. Regressions with time-fixed effects did not differ significantly from those with individual fixed effects.

Table A.4: Contemporaneous effect of cumulative ESIF on the mortality rate in selected categories – full model (part 1)

	(1) Mortality after femur fracture (age over 65)	(2) Mortality caused by myocardial infarction after emergency (age 35-74)	(3) Mortality after acute stroke	(4) Mortality after interventions
Constant	-1.4762*	0.0512	2.3563	0.0355
	(0.8261)	(0.8355)	(1.4376)	(0.1353)
ESIF	0.0027*	0.0028**	0.0015	-0.0001
	(0.0014)	(0.0012)	(0.0022)	(0.0002)
Capacity	-0.0006	-0.0036**	-0.0028	0.0005*
	(0.0010)	(0.0015)	(0.0033)	(0.0002)
Occupancy	-0.1777	0.0600	0.2163	0.0412
	(0.2148)	(0.1696)	(0.2471)	(0.0274)
New patients	0.0385	0.0403	-0.0690	-0.0019
	(0.0486)	(0.0508)	(0.0934)	(0.0062)
Medical devices	-0.0143	-0.0379	0.0016	0.0014
	(0.0479)	(0.0592)	(0.0819)	(0.0089)
IC	-0.0016	0.0355	-0.0359**	0.0034
	(0.0356)	(0.0477)	(0.0145)	(0.0045)
Oncology	0.0306**	0.0522***	0.0138	-0.0041*
	(0.0138)	(0.0190)	(0.0270)	(0.0022)
CT	-0.0218	0.0255*	-0.0125	0.0037*
	(0.0164)	(0.0139)	(0.0095)	(0.0021)
MR	-0.0044	0.0310**	-0.0246*	0.0008
	(0.0084)	(0.0147)	(0.0128)	(0.0018)
State hospital	-0.1664***	0.0049	-0.1163**	0.0163***
	(0.0431)	(0.0329)	(0.0447)	(0.0048)
Regional hospital	0.0048	0.0072	-0.1025	0.0001
	(0.0183)	(0.0158)	(0.0774)	(0.0033)
Perinatal mortality	-0.0092	-0.0040	0.0075	-0.0001
	(0.0088)	(0.0104)	(0.0070)	(0.0017)
Average wage	-0.0798	-0.2210**	0.0081	0.0025
	(0.0885)	(0.0882)	(0.0929)	(0.0158)
Roma share	0.0374	-0.0368	-0.0125	-0.0036
	(0.0292)	(0.0249)	(0.0243)	(0.0036)
Econ dependency	-0.0027	-0.0051	-0.1712*	0.0174
	(0.0941)	(0.0809)	(0.0983)	(0.0110)
Population density	0.4375***	0.2483	-0.2909	-0.0217
	(0.1611)	(0.1558)	(0.2536)	(0.0203)
Observations	271	282	306	319
Individual FEs	Yes	Yes	Yes	Yes
R-squared	0.1142	0.0974	0.0781	0.1212
Adjusted R-squared	0.0585	0.0429	0.0271	0.0747
F statistics	441.71***	4.19***	22.90***	335.94***

Notes: Robust standard errors in parentheses. *** $p < 0.01$, ** $p < 0.05$, * $p < 0.1$.

Table A.5: Contemporaneous effect of cumulative ESIF on the mortality rate in selected categories – full model (part 2)

	(5) Mortality in ICUs	(6) Ratio of transfers to ICUs	(7) Mortality in regular wards after a transfer from ICU	(8) Pressure ulcer	(9) Operation rate
Constant	0.3189	-5.3445*	-0.0042	0.0107	-0.1128
	(0.1901)	(2.9647)	(0.0085)	(0.0091)	(2.7022)
ESIF	-0.0014**	-0.0072	0.0000477*	0.0000	-0.0043
	(0.0005)	(0.0044)	(0.0000259)	(0.0000)	(0.0029)
Capacity	0.0010	0.0009	-0.0000	-0.0000	-0.0028
	(0.0006)	(0.0049)	(0.0000)	(0.0000)	(0.0025)
Occupancy	-0.0022	0.0468	-0.0039	-0.0007	-0.0237
	(0.0275)	(0.4603)	(0.0042)	(0.0028)	(0.2116)
New patients	0.0076	-0.0163	0.0003	0.0004	0.0896
	(0.0133)	(0.1331)	(0.0006)	(0.0006)	(0.0933)
Medical devices	0.0443**	-0.1093	-0.0008	-0.0002	0.0162
	(0.0200)	(0.1892)	(0.0018)	(0.0017)	(0.1275)
IC				-0.0003	0.1389**
				(0.0003)	(0.0546)
Oncology	-0.0088	0.0023	-0.0001	0.0001	0.0667
	(0.0065)	(0.0428)	(0.0002)	(0.0003)	(0.0486)
CT	0.0055	0.0214	-0.0002	-0.0005	0.0103
	(0.0056)	(0.0306)	(0.0002)	(0.0004)	(0.0183)
MR	0.0059*	-0.0004	0.0000	-0.0002	-0.0395
	(0.0030)	(0.0320)	(0.0001)	(0.0003)	(0.0241)
State hospital	-0.0368***	-0.1181***	0.0008	0.0007	0.0022
	(0.0034)	(0.0372)	(0.0008)	(0.0008)	(0.0307)
Regional hospital	0.0039	0.0402	-0.0009***	-0.0004	-0.0678**
	(0.0053)	(0.0495)	(0.0002)	(0.0003)	(0.0272)
Perinatal mortality	-0.0018	0.0196	0.0001	0.0001	0.0000
	(0.0021)	(0.0186)	(0.0001)	(0.0001)	(0.0135)
Average wage	-0.0470	0.1083	0.0004	-0.0035*	-0.1388
	(0.0286)	(0.2938)	(0.0018)	(0.0018)	(0.1133)
Roma share	0.0011	0.0802	-0.0012	-0.0000	0.1027**
	(0.0068)	(0.0660)	(0.0007)	(0.0004)	(0.0432)
Econ dependency	0.0623	1.5466***	-0.0020	0.0028	0.2990**
	(0.0519)	(0.4045)	(0.0034)	(0.0017)	(0.1409)
Population density	-0.0322	0.0825	0.0020	0.0009	0.0783
	(0.0231)	(0.4155)	(0.0012)	(0.0017)	(0.5028)
Observations	220	220	221	339	291
Individual FEs	Yes	Yes	Yes	Yes	Yes
R-squared	0.1465	0.3663	0.1405	0.0541	0.1399
Adjusted R-squared	0.0838	0.3198	0.0776	0.0072	0.0897
F statistics	31.97 ***	41.83 ***	4.45 ***	1.91 **	5.23 ***

Notes: Robust standard errors in parentheses. *** $p < 0.01$, ** $p < 0.05$, * $p < 0.1$.

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Antibiotic Self-Medication and Antibiotic Resistance: Multilevel Regression Analysis of Repeat Cross-Sectional Survey Data in Europe

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Abstract. Antibiotic resistance is a global public health issue with several anthropogenic drivers, including antibiotic consumption. Recent studies have highlighted that the relationship between antibiotic consumption and antibiotic resistance is contextualised by a variety of socioeconomic, cultural, and governance-related drivers of consumption behaviour and contagion that have been underexamined. A potential complication for research and policy is that measures of antibiotic consumption are often reliant on prescribing or sales data which may not easily take into account the dynamics of community consumption that include self-medication; for example, the preservation and use of leftover medication or the obtaining of antibiotics without a prescription. This study uses repeated cross-sectional survey data to fulfil two core aims: firstly, to examine the individual-level and national-contextual determinants of self-medication among antibiotic consumers in European countries, and secondly, to examine the relationship between self-medication behaviour and antibiotic resistance at the national level.

This study is particularly novel in its application of a multilevel modelling specification that includes individual-level factors with both time-variant and persistent national characteristics to examine antibiotic consumption behaviours. The key findings of the study are that survey respondents in countries with persistently higher levels of inequality, burdens of out-of-pocket health expenditure, and corruption have an increased probability of self-medicating with antibiotics. The study also highlights that overall levels of antibiotic consumption and antibiotic self-medication do not correlate and are associated heterogeneously with changes in different pathogen/antibiotic pairs. In summary, the study emphasises that antibiotic stewardship and antibiotic resistance, whilst related by biological mechanisms, are also inherently social issues. Attempts to improve antibiotic stewardship and address the challenge of antibiotic resistance should also attend to structural challenges that underlie challenges to antibiotic stewardship in the community, such as the effects of inequality and reduced access to healthcare services.

1 Introduction

Antibiotic resistance is a global public health problem that poses significant challenges to modern medical infrastructure. The WHO (2019) lists antimicrobial resistance as one of the top ten threats to global public health, alongside issues such as climate change and vaccine hesitancy. In the UK Government Cabinet Office (2017, p. 8) National Risk Register, antimicrobial resistance is listed alongside climate change as a long-term trend that is likely "to change the overall risk landscape," making current risks more severe and leading to the emergence of completely new risks.

Antibiotic resistance is the social manifestation of a biological process. The biological process at the heart of antibiotic resistance is the evolution of evasion strategies by bacteria to overcome chemical and environmental challenges, such as exposure to antibiotic medication (Wright 2007). Bacteria that survive exposure to antibiotics are then able to grow and spread due to a lack of competition from other strains. There is an inevitability to the evolutionary selection pressure that antibiotic consumption generates, meaning it is important that antibiotics are used prudently in order to mitigate the speed at which resistance develops. Understanding the relationship between unregulated off-prescription antibiotic use, such as over-the-counter (OTC) sales or the use of leftover antibiotics, and levels of antibiotic resistance is consequently important for both policy and research agendas.

OTC sales of antibiotics are generally prohibited in EU Member States with the exception of some specific antibiotics in some countries; nevertheless, antibiotics are still accessible OTC or online in some Member States (Paget et al. 2017, Machowska, Lundborg 2019). There are some healthcare-system drivers associated with the ability to access antibiotics without a prescription, including a lack of enforcement of laws prohibiting OTC sales of antibiotics and requirements to dispense whole pre-packaged packages of antibiotics rather than specific quantities. Whilst the prevalence of resistance has been shown to correlate with prescribed outpatient antibiotic use, it has also been argued that the actual total consumption level includes self-medication which is not accounted for in prescription statistics and whose burden may be underestimated by sales figures (Grigoryan et al. 2006, 2010). For example, if an antibiotic course is not completed in order to keep a supply of the medication for a second course, this could lead to two sub-optimal courses. Patients' having access to antibiotics prior to visiting a healthcare professional can also drive regional variation in stewardship-related resistance drivers, as evidenced in qualitative research into clinicians' accounts of factors shaping antibiotic prescribing decisions (Brookes-Howell et al. 2012).

This study has two central aims. Firstly, to examine the determinants of self-medication among antibiotic consumers in European countries. This aim is addressed through consideration of both individual-level characteristics and national-level contexts, with an analysis approach that accounts for both time-variant and time-invariant contexts. Secondly, to examine the relationship between self-medication behaviour and antibiotic resistance at the national level.

These aims have implications not only for policies aimed at mitigating antibiotic resistance through consumption behaviours, but also for research into this issue, since off-prescription antibiotic use may not be captured by other measures, such as prescription statistics. If the level of self-medication in a country is associated with variations in antibiotic resistance measures between countries, this influence might not be captured by measures that do not account for this type of community consumption. By utilising a survey series that employs random probability sampling, this study is able to examine the association between unregulated antibiotic consumption and antibiotic resistance measures in a way that avoids the pitfalls associated with prescribing or sales data and may illuminate this methodological challenge.

2 Literature

2.1 Drivers of Antibiotic Use and Self-Medication

There are many individual-level factors associated with self-medication using antibiotics in Europe. Some of these determinants are related to individuals' feelings of illness, with multiple studies noting that self-medication is triggered in particular by upper respiratory tract symptoms, fevers, common colds, sore throats, or conditions with similar symptoms to a previous illness for which antibiotics were prescribed (Scicluna et al. 2009, Skliros et al. 2010, Shabani, Redican 2018, Druică et al. 2021). More recently, research in Australia has also found that COVID-19 pandemic-induced psychological distress has been a trigger for preventive self-medication with antibiotics (Zhang et al. 2021).

Further drivers are associated with the combination of healthcare professionals' prescribing practices (such as providing antibiotics without a prescription, over-prescribing, and dispensing by packet rather than by number of pills), patient behaviour, and poor access to healthcare, resulting in leftover antibiotics which are then stored for later use (Eggermont et al. 2018, McNulty et al. 2006, 2007b, Grigoryan et al. 2007, Lescure et al. 2018, Guinovart et al. 2018, Machowska, Lundborg 2019). In summary, several of the factors associated with self-medication relate to the individual experience of ill health in combination with contextual and healthcare system influences.

Demographic and knowledge-related correlations with self-medication behaviours have been inconsistent across studies in Europe. McNulty et al. (2006, 2007b), for example, found in the UK that higher levels of knowledge about antibiotics were associated with both higher course completion and also the storing of antibiotics for self-medication, whilst other studies in Europe have found that lack of knowledge is associated with greater propensity for self-medication (Horvat et al. 2017, Machowska, Lundborg 2019) or had no significant bearing (Druică et al. 2021). Again, there are discrepancies in European studies regarding the association of self-medication with demographic characteristics. For example, whilst Pavydė et al. (2015) found that male, rural, and childless respondents were more likely to self-medicate in Lithuania, McNulty et al. (2006) found that younger and female respondents in the UK were more likely to hold leftover drugs. In summary, at the individual-level self-medication has a complex set of determinants, with heterogeneity among previous studies in European contexts.

More broadly, a number of socio-economic national characteristics have been associated with variations in antibiotic use, demonstrating the importance of understanding both the contextual and individual factors associated with appropriate or otherwise antibiotic use. The quality of national governance, and in particular the level of corruption, has been found to persistently associate positively with national levels of antibiotic consumption (Rönnerstrand, Lapuente 2017, Mueller, Östergren 2016, Gaygisiz et al. 2017). Additionally, national cultural dimensions have repeatedly been associated with levels of antibiotic consumption both appropriate and otherwise – especially Uncertainty Avoidance, Masculinity, and Power Distance (Gaygisiz et al. 2017, Borg 2012, Deschepper et al. 2008). Antibiotic use is more common in countries with lower tolerance for uncertainty, an emphasis on cooperation and caring for vulnerable members of society, and in countries where unequal distributions of power are less welcome. Cultural dimensions may explain why educational campaigns are not universally successful in all countries, as the messaging of responsible antibiotic use may work against rather than with the grain of national cultures established over long periods of time (Borg 2012). These same cultural dimensions also influence the healthcare workers who gatekeep access to antibiotics in most instances (Borg 2012). Intolerance for uncertainty for example, may underpin practices like more defensive medicine on the part of healthcare professionals, and unwillingness of the patient to wait out what could be a self-limiting cold and refrain from requesting antibiotics. These cultural differences, if associated causally with different patterns of antibiotic prescribing and consumption, would be indicative of the need for international policymakers to locally tailor interventions by increasing focus on, for example, on societal educational narratives or tightening regulatory mechanisms.

Variation in socio-economic and demographic factors has also been found to associate with differences in national antibiotic consumption. Countries with higher average levels of education among their populations tend to have lower levels of antibiotic consumption, and the proportions of the population above 65 years of age and below 14 years of age have both been positively associated with higher antibiotic consumption (Gaygisiz et al. 2017, Blommaert et al. 2014). The relationship between variation in national income measures and antibiotic consumption relative to other national indicators is not completely clear in high-income settings. Klein et al. (2018) argue that Gross Domestic Product (GDP) is primarily associated with antibiotic consumption in lower- and middle-income countries, and that in higher-income countries economic growth is not a factor driving variation in antibiotic consumption between countries. However, the amount spent on healthcare expressed as a percentage of GDP has been positively associated with antibiotic consumption (Blommaert et al. 2014). This suggests that in higher income settings such as those examined in this study, issues of culture and governance described above including resource allocation for healthcare may be more important for explaining variation in antibiotic consumption than general economic comparisons. The question of resource allocation is particularly pertinent given the context of the time period for this study, in which many countries in Europe implemented austerity measures that impacted healthcare expenditure and access (Reeves et al. 2014, Stuckler et al. 2017, ECDC 2013). Economic inequality, exacerbated by austerity measures, is also associated with the distribution of health outcomes (Mackenbach et al. 2011, EC 2013b, Chauvel, Leist 2015, Detollanaere et al. 2018) and behaviours (Kino et al. 2017) in Europe, including higher risk of infections among deprived groups and areas (ECDC 2013, Charani et al. 2021).

2.2 Social and Economic Drivers of Antibiotic Resistance

Antibiotic use is one among several drivers of levels of antibiotic resistance. Temporal variation in antibiotic use has been shown to correlate positively with various antibiotic resistances, such as the incidence of methicillin-resistant *Staphylococcus aureus* (MRSA) in hospitals and the community (Lawes et al. 2015, Aldeyab et al. 2008, Lafaurie et al. 2012, Parienti et al. 2011), with sub-national spatial variation in antibiotic prescribing also being shown to strongly positively correlate with MRSA bloodstream infections (Andreatos et al. 2018). However, there are other societal factors beyond antibiotic consumption that may compound or exacerbate the issue of antibiotic resistance by maintaining environments in which antibiotic resistance is able to develop.

Policy proposals for addressing antibiotic resistance include awareness-raising and the strengthening of antimicrobial stewardship alongside other measures such as the development of 'One Health' surveillance, improving infection prevention and control, and limiting the environmental exposure of antimicrobial resistant pathogens (Anderson et al. 2019). In previous studies, national characteristics such as levels of development, infrastructure quality, inequality, and levels of regulation have been found to explain antibiotic resistance alongside, or occasionally with better fit than, levels of antibiotic consumption (Collignon et al. 2015, 2018, Collignon, Beggs 2019, Savoldi et al. 2019, Pärnänen et al. 2019, Hay et al. 2018, Bryce et al. 2016). These social and economic conditions matter for the consideration of infection control, sanitary conditions, food handling, waste treatment, water quality, and other areas that might influence the contagion of antibiotic resistance rather than simply the development of resistance as driven by antibiotic consumption. Collignon et al. (2018) in particular argue that the use and overuse of antibiotics are drivers of the emergence and maintenance of antimicrobial resistance, whilst other social, economic, and infrastructural factors contribute with greater effect to the year-on-year changes in levels of resistance. This relationship is, however, mediated by countries' levels of economic development, for example with the volume of antibiotic use only correlating with antibiotic resistance in more economically developed regions rather than at a global scale (Collignon et al. 2018). Consequently, when considering the relationship between national-level antibiotic consumption and levels of antibiotic resistance, either cross-sectionally or longitudinally, it is necessary to also consider the factors that may aid contagion as part of the analysis in order to minimise the confounding of the consumption/resistance relationship by factors associated with greater propensity for contagion.

In summary, antibiotic consumption and antibiotic resistance are more than purely biological issues: they are deeply embedded in personal, socio-economic, and cultural contexts. Understanding variation in either specific antibiotic consumption behaviours – such as self-medication in the case of this study – or antibiotic resistance requires an appreciation of the human contexts in which these phenomena take place. By providing evidence regarding the relationship between context and behaviour, this study may inform both future research into these behaviours and future policymaking aiming to address challenges to antibiotic stewardship in European contexts.

3 Methods and Materials

3.1 Data sources

Survey data were from the Eurobarometer survey series. Eurobarometer surveys covering European countries in 2009 (EC 2013a), 2013 (EC 2017), 2016 (EC 2019a), and 2018 (EC 2019b) posed questions about antibiotic use. Each survey sampled approximately 1,000 individuals per country (except in Cyprus, Luxembourg, and Malta, where 500 individuals are sampled per wave) using a random probability methodology and face-to-face mode. The survey dataset covers 28 countries, but for the waves used in this study Croatia (2013, 2016, 2018) was only sampled three times for the survey; Slovakia (2013, 2016, 2018) and Slovenia (2009, 2013, 2016) only had complete antibiotic resistance data covering three years each, and Cyprus had no Hofstede Cultural Dimension data.

Country-level independent variable data were sourced from multiple locations. GDP as a time-variant measure of economic prosperity (World Bank 2020a), Out-of-Pocket health expenditure as a time-variant measure of the financial burden of healthcare for individuals (World Bank 2020b), and World Governance Indicator (World Bank 2020c) data for a time-variant measure of corruption (Control of Corruption) were sourced from World Bank datasets. Gini data as a time-variant measure of economic inequality within countries were sourced from Eurostat (2019). Hofstede's Cultural Dimensions as time-invariant measures of cultural differences between countries were sourced from Geert Hofstede (Hofstede 2015). The Hofstede Cultural Dimensions are one way of capturing cultural factors at the national level, and they position countries relative to one another along six statistically distinct dimensions of culture that describe relationships to authority, conceptions of self, and ways of dealing with dilemmas of conflict (Hofstede 2011).

Antibiotic resistance variables were selected initially based on the World Health Organisation's global priority list of antibiotic-resistant bacteria (WHO 2017) and then filtered based on the availability of data for the countries and years available in the survey data. Final bacteria-antibiotic combinations used were *Escherichia coli* and *Klebsiella pneumoniae* resistant to third-generation cephalosporins (3GCR *E. coli* and *K. pneumoniae*), MRSA, and carbapenem resistant *Pseudomonas aeruginosa* (CRPA). National-level antibiotic resistance data were sourced from the ECDC (2020) Surveillance Atlas.

These country-level data were linked to the four-wave survey dataset by country and wave for time-variant variables, and by country for the time-invariant variable. This combined dataset included 25 sets of country-level data covering all four Eurobarometer waves and two sets of country-level data covering three waves. Cyprus was excluded from the analysis due to the lack of Hofstede Cultural Dimension data. The variables linked to the survey dataset, which were all numerically continuous, are described in Table 1. These descriptive statistics demonstrate not only that there are sizeable variations in the persistent differences between European countries for these variables, but that there are also a variety of different country-wave trajectories revealed by the ranges of the differenced variables. The construction of these differenced variables is explained in the 'Analysis' section as part of the modelling approach.

3.2 Survey Variable Specification

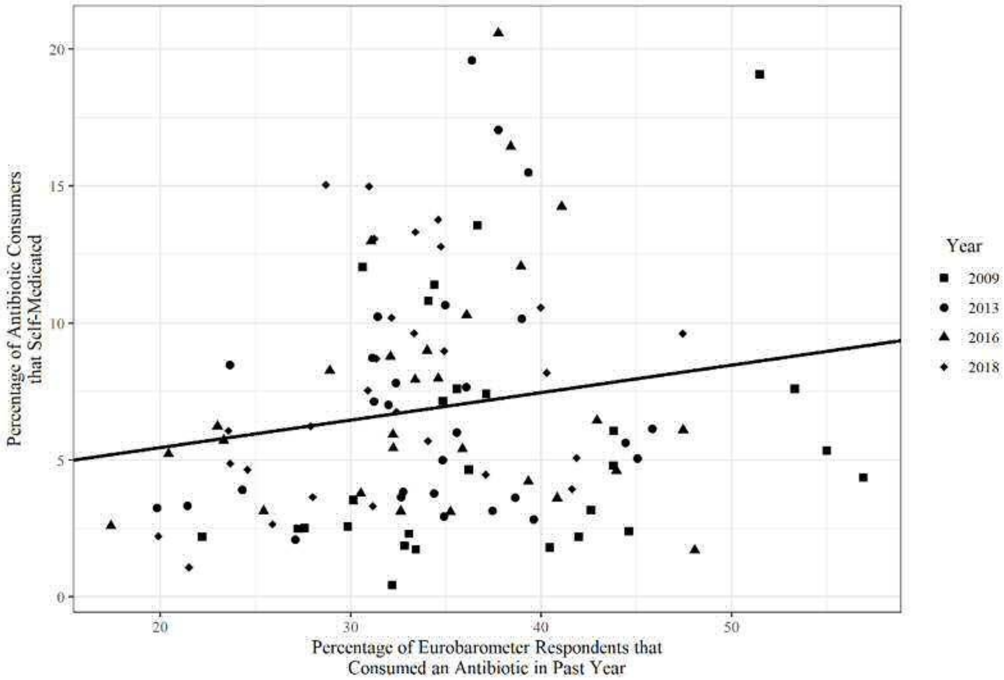
The binary dependent variable used to examine self-medication in this study covered respondents that reported having taken an antibiotic in the past 12 months, separating respondents who obtained the last course of antibiotics they used from a medical prescription or had them administered by a medical practitioner, and respondents who either used leftover antibiotics from a previous course or obtained them without a prescription. This variable was based on a question that was asked in all four Eurobarometer waves used in this study, which directed participants to reflect on their behaviour within the past year. This temporal bounding mitigates the possibility of recall issues that have been previously demonstrated with regard to antibiotic consumption questions (Anderson 2019) and improves the value of the variable as a temporal barometer for behaviour. A limitation of this variable is that it does not capture the specific antibiotic

Table 1: Descriptive statistics for country-level and outcome variables

Variable	Source	Enduring/Differenced Variable	Mean	Standard Deviation	Minimum	Maximum	Countries	Observations
Antibiotic Self-Medication	Eurobarometer Survey	Enduring	6.91	3.80	2.56	16.91	28	111
(% of Antibiotic Consumers)		Differenced	0.00	2.27	-6.22	6.51		
Antibiotic Consumption	Eurobarometer Survey	Enduring	34.51	6.91	19.83	47.94	28	111
(% of Pop. in prev. 12 Months)		Differenced	0.00	3.23	-10.39	12.41		
GDP/capita (1,000s USD)	World Bank	Enduring	37.24	15.69	17.56	101.30	28	276
		Differenced	0.22	5.45	-18.96	33.39		
Gini	Eurostat	Enduring	30.05	3.58	23.80	36.40	28	276
		Differenced	-0.02	1.13	-4.40	4.80		
OOP Health Expenditure	World Bank	Enduring	51.66	25.49	9.70	92.30	28	276
per Capita (1,0s USD)		Differenced	0.30	6.86	-17.95	28.60		
Control of Corruption	World Governance Indicators	Enduring	1.01	0.79	-0.22	2.31	28	276
	(World Bank)	Differenced	0.01	0.11	-0.30	0.37		
Power Distance	Geert Hofstede	Enduring	51.05	20.41	11.00	104.00	27	266
Individualism		Enduring	58.89	17.48	27.00	89.00	27	266
Masculinity		Enduring	46.02	24.56	5.00	110.00	27	266
Uncertainty Avoidance		Enduring	71.28	22.65	23.00	112.00	27	266
Long-Term Orientation		Enduring	57.40	16.40	24.00	83.00	27	266
Indulgence		Enduring	44.54	19.72	13.00	78.00	28	276
MRSA Percentage	European Centre for Disease	Enduring	19.10	14.51	0.98	50.03	28	275
	Prevention and Control	Differenced	0.22	3.85	-15.99	20.81		
CRPA Percentage		Enduring	18.95	12.73	3.38	59.26	28	274
		Differenced	0.44	4.72	-13.80	23.95		
3GCR *E. coli* Percentage		Enduring	14.11	8.11	5.56	38.62	28	275
		Differenced	-0.16	3.60	-19.45	21.06		
3GCR *K. pneumoniae* Percentage		Enduring	33.85	22.22	2.71	74.92	28	274
		Differenced	-0.44	5.74	-26.60	26.50		

Source: ¡The source¿

Notes: ¡The notes¿



Note: $R^2 = 0.030$

Figure 1: Antibiotic consumption against the level of self-medication among antibiotic consumers for country-waves

being consumed, which does have bearing on the relationship between antibiotic consumption and resistance development (Pouwels et al. 2019). The independent antibiotic-related knowledge variables used in this study were derived from a set of four true/false questions asked in all four surveys covering whether antibiotics kill viruses (correct = false), whether antibiotics are effective against colds and flu (false), whether unnecessary use of antibiotics makes them become ineffective (true), and whether taking antibiotics often has side-effects such as diarrhoea (true). These were included as binary variables in the analyses. Overall antibiotic consumption was calculated from the Eurobarometer data to create an aggregate continuous measure for each country-wave to be controlled in the regression model.

Figure 1 shows the relationship between the outcome variable (aggregated to the country-wave level) and the aggregate overall consumption measure. A cluster-robust linear regression of self-medication against total consumption (Estimate = 0.100, p = 0.166, R^2 = 0.03), illustrated with a regression line in Figure 1, confirmed that these measures were insignificantly correlated, with 3.0% of the variation in self-medication among antibiotic consumers explained by the overall level of consumption in each country-wave. This supports the rationale that self-medication may be a source of variation in actual antibiotic consumption not captured by official sources such as prescription data.

3.3 Analysis

The aim of the analysis was firstly to examine individual- and national-level associations with self-medication behaviour and secondly to examine whether self-medication behaviour was associated with four resistance measures from the WHO priority list.

Variable selection to control for known associations with antibiotic resistance – such as correlates relating to contagion – was informed by the literature discussed above, and bivariate cluster-robust regressions examining associations between national characteristics and nationally-aggregated self-medication behaviour. In each of these regressions, the clusters were countries, and the observations were individual years in each country.

Following these tests, a mixed-effects logistic regression model was fitted with self-medication as the outcome variable. The model used a technique reported by Fairbrother

(2014) (see also Schmidt-Catran, Fairbrother 2016) for the analysis of repeated cross-sectional survey data, with a three-tier structure of respondents nested within country-waves, nested within countries, to examine both time-variant and enduring national effects. By using models with random intercepts, this study is able to analyse overall associations across Europe through the regression coefficients for independent variables (fixed effects) whilst allowing the mean of the coefficients to vary across country-waves and countries. The regression model is specified by Fairbrother (2014) with $\bar{X}_j$ as the enduring cross-national effect, X_{tjM} as the centred longitudinal component calculated by subtracting X_{tj} from $\bar{X}_j$, and $time_{tj}$ as the temporal control (in this case Year), in the following equation:

$$y_{itj} = \beta_0 + \beta_1 X_{itj} + \beta_2 X_{tjM} + \beta_3 \bar{X}_j + \beta_4 time_{tj} + u_j + u_{tj} + \epsilon_{itj}$$

In this study, a respondent from the UK in 2009, for example, would be nested within the 2009 UK sample, which would itself be nested within the UK country level. National-level effects were separated into enduring country-level differences calculated as the median of available data for all years between 2009 and 2018 ($\bar{X}_j$), and differenced effects within countries over time calculated as the value for a specific country-year (X_{tj}) with the enduring median value for that country subtracted (X_{tjM}). This approach models persistent differences between countries as well as differential trajectories in the time period, acknowledging not only that respondents within countries are more likely to be similar than between countries but that respondents sampled in the same year within a country are more likely to be similar than in different years within the same country. The exceptions to this separation were variables that were time-invariant for the study period; specifically, the Hofstede cultural dimensions.

In summary, this modelling approach provides the ability to distinguish between consistent differences between national contexts alongside differences in trajectories between countries. For example, this approach could show firstly whether countries that are persistently more economically equal are a significantly different context than those that are less equal in the context of self-medication, and also whether countries that have had large changes in inequality are a significantly different context than those that have seen little change.

Further individual-level variables were included to control for country composition, including: age interacted with gender, age respondents left education compared to the median for their country-year, presence of children in the household, local geography, and antibiotic-related knowledge. Interviewer-coded respondent cooperation was also included, as this has been found to associated with antibiotic-related outcome variables in other studies using survey data (Anderson 2020a) along with mode effects (Anderson 2020b). By controlling for individual-level variables within the analysis, including those discussed in the Literature section and these protocol variables, the effects of demographic distributions on antibiotic consumption behaviour are mitigated when analysing the higher-level associations.

Following the mixed-effects modelling, cluster-robust multiple regression was used to examine variation in country-level antibiotic resistance variables and their relationship to the aggregated survey measures of antibiotic consumption and self-medication. These models included the same socio-economic and cultural variables as the mixed-effects models, with the addition of total antibiotic consumption and percentage of antibiotic consumption that was self-medication aggregated for each wave for each country. The aims of these models were to ascertain the relationship between national measures of antibiotic resistance and, principally, the survey measure of antibiotic self-medication used as an outcome variable in the mixed-effects models.

4 Results

The results of this study are broken down into multiple stages to address the two key aims. The key model for the first aim (understanding the determinants of antibiotic self-medication behaviour across European countries) is a mixed-effects logistic regression model accounting for individual-level respondent characteristics discussed in

Table 2: Results of bivariate cluster-robust linear regressions of national characteristics and the percentage of antibiotic self-medication among antibiotic consumers

Variable	Estimate	p	R^2	N
Year	0.233	0.002	0.03	111
Antibiotic Consumption (% Pop. in prev. 12 months)	0.100	0.166	0.03	111
Economic				
GDP/capita (1,000s USD)	-0.087	0.013	0.12	111
Gini (0-100)	0.581	0.000	0.26	111
Out-of-Pocket Health Expenditure/capita (10s USD)	-0.040	0.154	0.06	111
Governance (-2.5-2.5)				
Control of Corruption	-2.989	0.000	0.29	111
Cultural Dimensions (0-112)				
Power Distance	0.051	0.186	0.06	107
Individualism	-0.096	0.036	0.15	107
Masculinity	0.005	0.822	0.00	107
Uncertainty Avoidance	0.057	0.045	0.09	107
Indulgence	-0.086	0.005	0.15	111
Long-Term Orientation	0.026	0.401	0.01	107

Notes: Statistical significance ($\alpha = 0.05$) denoted by asterisk.

the Literature section and available across all four waves of survey data, and time-variant and invariant national contextual variables. National variable selection for this mixed-effects model was informed by the Literature, along with cluster-robust linear regressions of the aggregated self-medication outcome variable against the candidate national-level variables. In particular, the cluster-robust regressions were used to determine which of the six cultural dimensions were to be included alongside the other socio-economic variables. This variable selection modelling is reported first, followed by the main model. The second aim of the study is achieved through cluster-robust regression models with national-level resistance measures as the outcomes predicted by a set of national-level characteristics.

4.1 Bivariate Correlations: Self-Medication

Table 2 presents the results of bivariate cluster-robust regressions of national characteristics for each country-wave on the percentage of antibiotic self-medication among antibiotic consumers. The aim of these tests was to provide initial understanding of these variables' relationships with the self-medication outcome, and to determine which cultural variables to include in the final model. National wealth represented by GDP per capita (Est = -0.087, $p = 0.013$, $R^2 = 0.12$) was negatively associated with the percentage of antibiotic consumers reporting self-medication, whilst higher levels of income inequality represented through the Gini coefficient (Est = 0.581, $p <0.000$, $R^2 = 0.26$) were associated positively with aggregate self-medication. There was no evidence for a significant association between out-of-pocket health expenditure (Est = –0.040, $p = 0.154$, $R^2 = 0.06$) and the level of self-medication. Countries with greater control of corruption (Est = –2.989, $p <0.000$, $R^2 = 0.29$) were correlated with lower levels of self-medication among antibiotic consumers. Control of Corruption and the Gini coefficient had the best fit measured by R^2, accounting for 29% and 26% of the variation in aggregate self-medication in their respective bivariate models. Among the cultural dimensions, Uncertainty Avoidance (Est = 0.057, $p = 0.045$, $R^2 = 0.09$) was positively associated with levels of self-medication among antibiotic consumers, whilst the Individualism (Est = –0.096, $p = 0.036$, $R^2 = 0.15$) and Indulgence (Est = –0.086, $p = 0.005$, $R^2 = 0.15$) dimensions were negatively associated with self-medication. There was no evidence for a significant association between Power Distance (Est = 0.051, $p = 0.186$, $R^2 = 0.06$), Masculinity (Est = 0.005, $p = 0.822$, R^2 <0.01), or Long-Term Orientation (Est =

0.026, $p = 0.401$, $R^2 = 0.01$) and levels of self-medication. As described with Figure 1, overall levels of antibiotic consumption in the survey samples was not correlated with levels of self-medication among antibiotic consumers. Based on these results, only the Uncertainty Avoidance, Individualism, and Indulgence cultural dimensions were included in the mixed-effects model alongside the national socio-economic variables.

4.2 Multilevel Regression Results: Self-Medication

Table 3 contains the results for the full mixed-effects regression model predicting whether an antibiotic consumer self-medicated or obtained antibiotics through a prescription. Compared with the reference category (15–29 year-old female), antibiotic consumers in the 30–41 (OR = 1.281, CI = 1.059 – 1.549) year-old female respondents category were more likely to have self-medicated, whilst respondents in the 54–67 (OR = 0.792, CI = 0.647 – 0.968) and 67+ (OR = 0.477, CI = 0.379 – 0.599) year-old female category were less likely to have self-medicated. Among males, those in the 15–29 (OR = 1.699, CI = 1.437 – 2.009) year-old category were almost 1.7 times as likely to have self-medicated than 15–29 year-old females, whilst 30–41 (OR = 0.684, CI = 0.539 – 0.869), 54–67 (OR = 5.593, CI = 0.458 – 0.770), and 67+ (OR = 0.718, CI = 0.531 – 0.971) male antibiotic consumers were less likely to have self-medicated. Antibiotic consumers who had left education above the median age (OR = 1.121, CI = 1.018 – 1.236) for their country-wave were marginally more likely to have self-medicated. Antibiotic consumers who had two or more children under the age of 10 (OR = 0.797, CI = 0.672 – 0.946) were less likely to have self-medicated than antibiotic consumers without children under the age of 10, however antibiotic consumers with one child aged between 10 and 14 years (OR = 1.170, CI = 1.023 – 1.338) were more likely to have self-medicated than consumers without children between these ages. Antibiotic consumers who correctly answered that antibiotic are not useful for treating colds and influenzas (OR = 0.531, CI = 0.47 – 0.588), that unnecessary use of antibiotics can lead to them becoming ineffective (OR = 0.664, CI = 0.594 – 0.743), and that antibiotics cause side effects (OR = 0.837, CI = 0.763 – 0.919) were all less likely to have self-medicated, though the strength of the association differed between these questions. When contrasted with 'Excellent' co-operators, antibiotic consumers who interviewers coded as having 'Bad' (OR = 1.647, CI = 1.154 – 2.353) cooperation were more likely to have reported self-medicating behaviour.

Three national characteristics presented evidence for a significant association with propensity to self-medicate among antibiotic consumers once other factors were controlled. Antibiotic consumers in countries with persistently higher levels of income inequality (OR = 1.070, CI = 1.026 – 1.115) were more likely to have self-medicated than obtained their antibiotics through a prescription, however a higher rate of increase in inequality (OR = 0.931, CI = 0.871 – 0.995) was associated with being less likely to have self-medicated. This clarifies the nature of the earlier finding that aggregate levels of self-medication correlated with income inequality by separating this relationship into persistent country-level variation and within-country temporal variation. The association of persistent differences in inequality with higher levels of self-medication was further complemented by a positive association between persistent differences in the amount of out-of-pocket health expenditure per capita (OR = 1.009, CI = 1.000 – 1.018) and self-medication.

Additionally, respondents in countries perceived to have persistently higher levels of control over corruption (OR = 0.606, CI = 0.413 – 0.888) were less likely to have self-medicated in the previous 12 months. As with income inequality this finding clarifies the earlier correlation by illustrating that, for this time period, persistent differences between countries are more important for distinguishing between populations' self-medication behaviours than the rate at which change occurred within countries. There was no further evidence in the model for other national contextual associations with individuals' propensity for self-medication.

The significant results from this model are summarised in terms of their average marginal effects (AMEs) in Figure 2. In contrast to the model results, age and gender are not interacted in these AMEs. The marginal effects suggest that being a male respondent (AME = 0.015, CI = 0.009 – 0.020) increased the chance of self-medication by 1.5%, whilst being in the 42–53 (AME = –0.014, CI = –0.024 – 0.004), 54–67 (AME = –0.031,

Table 3: Results for full mixed-effects logistic regression model predicting whether an antibiotic consumer self-medicated or obtained antibiotics through a prescription

Self-Medication Mixed-Effects Model Fixed Effects Variable	OR	2.5	97.5
Individual-Level Variables			
*Age*Gender (Reference: 15-29 year old Female)*			
30-41 Female	1.281*	1.059	1.549
42-53 Female	0.902	0.737	1.105
54-67 Female	0.792*	0.647	0.968
67+ Female	0.477*	0.379	0.599
15-29 Male	1.699*	1.437	2.009
30-41 Male	0.684*	0.539	0.869
42-53 Male	0.826	0.641	1.066
54-67 Male	0.593*	0.458	0.770
67+ Male	0.718*	0.531	0.971
Age Left Education (Reference: Below Median)			
Age Left Education (Above Median)	1.121*	1.018	1.236
Still Studying	1.025	0.862	1.220
Children Under 10 years old in Household (Reference: None)			
Children Under 10 (1)	0.950	0.835	1.080
Children Under 10 (2+)	0.797*	0.672	0.946
Children 10-14 years old in Household (Reference: None)			
Children 10-14 (1)	1.170*	1.023	1.338
Children 10-14 (2+)	1.074	0.828	1.394
Local Geography (Reference: Rural)			
Large Town	1.053	0.942	1.178
Small Town	1.059	0.953	1.178
Knowledge Questions (References: Incorrect or Don't Know Response)			
Antibiotics are ineffective against viruses	1.094	0.987	1.213
Antibiotics are ineffective against colds and flu	0.531*	0.479	0.588
Unnecessary use of antibiotics makes them ineffective	0.664*	0.594	0.743
Antibiotics cause side effects	0.837*	0.763	0.919
Respondent Cooperation (Reference: Excellent Cooperation)			
Fair Cooperation	1.093	0.993	1.204
Average Cooperation	1.099	0.944	1.280
Bad Cooperation	1.647*	1.154	2.353
Country and Country-Wave Variables			
Year	1.075	1.034	1.118
Total Antibiotic Consumption (% of Pop.) (Enduring)	0.976	0.952	1.001
Total Antibiotic Consumption (% of Pop.) (Differenced)	1.019	0.993	1.045
GDP/capita (USD 1,000s) (Enduring)	1.003	0.990	1.016
GDP/capita (USD 1,000s) (Differenced)	1.001	0.982	1.021
Gini (Enduring)	1.070*	1.026	1.115
Gini (Differenced)	0.931*	0.871	0.995
OOP/capita (USD 10s) (Enduring)	1.009*	1.000	1.018
OOP/capita (USD 10s) (Differenced)	0.995	0.983	1.007
Control of Corruption (Enduring)	0.606*	0.413	0.888
Control of Corruption (Differenced)	0.814	0.429	1.547
Individualism	0.993	0.984	1.003
Uncertainty Avoidance	0.993	0.986	1.001
Indulgence	0.997	0.985	1.009
Random Effects			
	Standard Deviation (Intercepts)		
Country-Year (107 levels)	0.263		
Country (27 levels)	0.252		

Notes: Statistical significance ($\alpha = 0.05$) denoted by asterisk. $N = 35,332$.

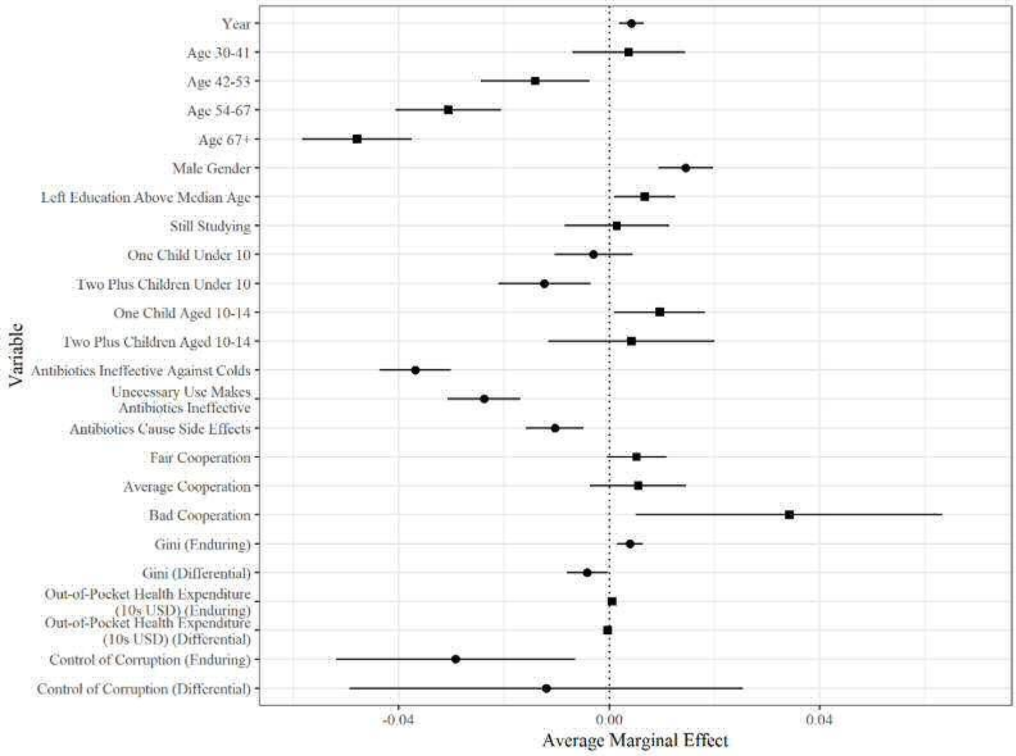


Figure 2: Average marginal effects of significant variables in the mixed-effects regression model, with 95% confidence intervals

CI = –0.041 – 0.021), and 67+ (AME = –0.048, CI = –0.0583 – 0.0376) age categories decreased the change of self-medication by 1.4%, 3.1%, and 4.8% respectively. However, as the model output in Table 3 highlights, the age quintiles do interact with gender categories to produce more nuanced trajectories across the age groups, albeit with similar interpretations. The marginal effects were generally comparable in size, for example with overlapping confidence intervals for each of having two or more children under ten years of age (AME = –0.012, CI = –0.021 – 0.004) reducing the change of self-medication by 1.2%, responding correctly regarding antibiotics being ineffective for treating colds and flu (AME = –0.037, CI = –0.044 – 0.030) reducing the chance by 3.7%, unnecessary usage of antibiotics rendering them ineffective (AME = –0.024, CI = –0.031 – 0.017) reducing the change by 2.4%, and antibiotics causing side effects (AME = –0.010, CI = –0.016 – 0.005) reducing the change by 1%. Similarly, among positive associations there were comparable magnitudes of AME for changes in year (AME = 0.004, CI = 0.002 – 0.007) with the chance of a self-medication response increasing by 0.4% per year, and having left education above the median age for the country-wave (AME = 0.007, CI = 0.001 – 0.011) increasing the chance of a self-medication response by 0.7%, and having one child aged 10–14 (AME = 0.010, CI = 0.001 – 0.018) increasing the chance of self-medication by 1%. Respondents categorised as bad co-operators (AME = 0.034, CI = 0.005 – 0.063) were 3.4% more likely to have provided a self-medication response.

At the country level, the AMEs represent continuous rather than discrete variables. For each increased point on the Gini coefficient representing a persistent difference between countries (AME = 0.004, CI = 0.001 – 0.006) the likelihood of a self-medication response increased by 0.4%, whilst for each point above the median Gini for the country in the time period (AME = –0.004, CI = –0.008 – 0.000) the likelihood of self-medication decreased by 0.4%. For each persistent 10USD increase in out-of-pocket health expenditure per capita (AME = 0.001, CI = 0.000 – 0.001) the likelihood of self-medication increased by 0.1%, and for each increased point measuring Control of Corruption as a persistent difference between countries (AME = -0.029, CI = –0.052 – 0.006) the likelihood of self-medication decreased by 2.9%. The contrasting trajectories of the

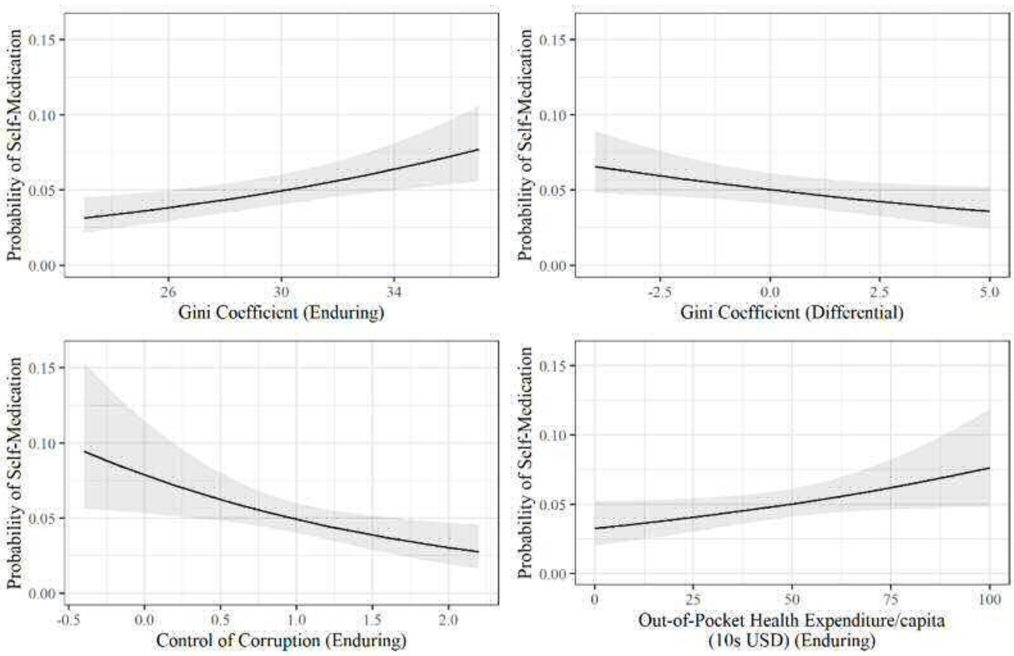


Figure 3: Predicted probabilities of self-medication for individuals in countries with persisting differences in inequality, corruption, and out-of-pocket health expenditure with 95% confidence intervals

predicted probabilities for these significant contextual variables are illustrated in Figure 3.

4.3 Cluster-Robust Linear Regressions: Antibiotic Resistance

Table 4 presents the results of cluster-robust multiple regressions of national characteristics on national-level antibiotic resistance measures for the selected antibiotic/pathogen combinations. There were multiple patterns of association across the four measures, evidencing a lack of homogeneity between the distributions of the antibiotic/pathogen combinations. Overall antibiotic consumption was only associated with the MRSA (Est = 0.633, p = 0.001) and 3GCR *K. pneumoniae* (Est = –0.670, p = 0.005) resistance measures, being associated positively with MRSA and negatively with 3GCR *K. pneumoniae*. It is worth noting that in a bivariate regression, 3GCR *K. pneumoniae* was positively and insignificantly associated (Est = 0.751, p = 0.08) with antibiotic consumption and the association only became negative and significant after the introduction of Control of Corruption, suggesting an element of confounding between consumption, 3GCR *K. pneumoniae*, and corruption measured at the national level. The proportion of self-medication within overall antibiotic consumption however was positively associated with CPRA (Est = 0.907, p = 0.013) only.

National wealth, represented as GDP/capita, was positively associated (Est = 0.398, p = 0.001) with the level of 3GCR *K. pneumoniae* at the national level, and the level of out-of-pocket health expenditure per capita was positively associated with 3GCR *E. coli* (Est = 0.084, p = 0.023). Control of Corruption was a significant variable for multiple resistance measures, with negative associations for CPRA (Est = –11.069, p = 0.004), 3GCR *E. coli* (Est = –8.516, p <0.000), and 3GCR *K. pneumoniae* (Est = –28.217, p <0.000). This means that countries perceived to have a better handle on corruption tended to have lower levels of these resistance pairings, with the association most pronounced in relation to 3GCR *K. pneumoniae*. In countries that were more Indulgent there tended to be a higher level of MRSA (Est = 0.290, p = 0.026), whilst in countries that were more prone to avoiding uncertainty there were lower levels of 3GCR *E. coli* (Est = –0.110, p = 0.034).

Table 4: Cluster-robust linear multiple regression results of national-level variables against four national resistance measures

	MRSA		CRPA		3GCR *E. coli*		3GCR *K. pneumoniae*	
Variable	Estimate	p	Estimate	p	Estimate	p	Estimate	p
Year	0.037	0.870	-0.284	0.410	0.682*	0.000	-0.575	0.150
Total Antibiotic Consumption (% of Pop. in prev. 12 Months)	0.633*	0.001	-0.099	0.511	0.115	0.173	-0.670*	0.005
Percentage of Antibiotic Consumption that is Self-Medication	-0.056	0.900	0.907*	0.013	-0.121	0.347	0.081	0.817
GDP/capita (USD 1,000s)	-0.097	0.240	0.107	0.114	0.054	0.252	0.398*	0.001
Gini	0.141	0.823	-0.670	0.185	0.005	0.989	0.506	0.287
OOP/capita (USD 10s)	0.013	0.893	-0.060	0.408	0.084*	0.023	0.004	0.967
Control of Corruption	-8.543	0.055	-11.069*	0.004	-8.516*	0.000	-28.217*	0.000
Individualism	-0.122	0.415	-0.094	0.302	-0.059	0.360	-0.084	0.536
Uncertainty Avoidance	0.163	0.143	0.001	0.992	-0.110*	0.034	0.006	0.961
Indulgence	0.290*	0.026	-0.001	0.990	-0.087	0.167	-0.108	0.346
Observations (Country-Waves)	104		104		104		103	
Adjusted R^2	0.58		0.65		0.60		0.82	

5 Discussion

Antibiotic consumption is one among a number of drivers of antibiotic resistance, and the extent to which national variation in levels of antibiotic consumption are associated with variation in levels of antibiotic resistance relative to other drivers (such as contagion-related factors) has been the subject of recent research. Antibiotic use measured through prescriptions or sales may not adequately capture consumption via self-medication however, defined in this study as the practice of using leftover antibiotics from previous prescriptions or otherwise obtaining antibiotics without a prescription. Self-medication varies between countries and does not directly correlate with overall antibiotic consumption, as demonstrated through the measures derived and correlated in this study using random-probability survey samples of self-reported behaviour. The explicit examination of associations between individual-level characteristics and macro-level contexts and self-medication among antibiotic consumers is thus the first key contribution of this study, followed by the examination of how total consumption and levels of self-medication correlate with national measures of four different antibiotic/bacteria combinations from the WHO priority list.

5.1 Self-Medication in Europe: Individual-Level Characteristics

Compliance with instructions for medication-taking is associated with several identified factors, including age, patient-physician relationship, beliefs about medications, misconceptions about disease conditions, experience and management of side-effects, and individual personality traits (Foot et al. 2016, Aslani, Schneider 2014, Axelsson 2013). The findings of this study support those of previous studies focusing on public antibiotic stewardship behaviours. The finding that higher levels of education are associated with a higher propensity for self-medicating behaviour among antibiotic consumers supports previous research that has demonstrated associations between higher levels of education and inappropriate stewardship behaviour (McNulty et al. 2007a, Shehadeh et al. 2012). The finding that among antibiotic consumers, younger age groups of both male and female genders have a higher propensity to self-medicate also supports previous studies that have found that younger age groups are more likely to report inappropriate attitudes and behaviours regarding antibiotic use (Anderson 2020a, Pechère et al. 2007, Napolitano et al. 2013, Kardas et al. 2007).

This study suggests that specific aspects of knowledge about antibiotics and antibiotic resistance are relevant to self-medication propensity within European countries. The raising of public awareness through education has been a key area of policy action addressing antibiotic resistance, aiming to inform the public about how to take antibiotics appropriately and the consequences of inappropriate antibiotic use through credible professional sources (McParland et al. 2018, Price et al. 2018). Public health interventions commonly include knowledge-based components (McParland et al. 2018, Price et al. 2018), though the relationship between individuals' knowledge and their behaviour with antibiotics has a mixed evidence base. Knowledge about antibiotics and antibiotic resistance has been associated in the literature with good stewardship attitudes and behaviours (Anderson 2018, Kim et al. 2011, Jamhour et al. 2017, Horvat et al. 2017, Vallin et al. 2016, Chan et al. 2012, McNulty et al. 2007b), as well as with negative behaviours such as self-medication or retaining leftovers (McNulty et al. 2007b, Pan et al. 2012). In addition to knowledge about antibiotics as a medication, meta-analyses of adherence to medication have shown that individuals believing that the medication is necessary for their health are more likely to follow medication-taking instructions, while individuals that have strong concerns about the medication, such as beliefs about side-effects, are less likely to follow instructions (Foot et al. 2016, Aslani, Schneider 2014, Axelsson 2013, Horne et al. 2013).

This study contributes to these previous studies, having examined the relationship between multiple aspects of individual-level knowledge about antibiotics. Specifically, and with the strength of a large multi-country and multi-year survey dataset, this study provides evidence that three specific aspects of knowledge about antibiotics and antibiotic resistance are salient with regard to self-medication behaviour in Europe. Respondents that correctly responded that antibiotics cannot treat colds, that unnecessary use of antibiotics exacerbates antibiotic resistance, and that antibiotic consumption commonly comes with side-effects, were all less likely to have provided a self-medication response. This might suggest that practical messaging linked to specific illness conditions may be more effective for curbing self-medication behaviour than what may be more abstract messages about not treating viral illness with antibiotics, for which comprehension involves some academic understanding of biology. The association between knowledge of the link between unnecessary antibiotic use and the development of antibiotic resistance and lower propensity for self-medication was a positive sign that behaviour may be associated with understanding of public health consequences. Similarly, the association between knowing about antibiotics' side-effects and lower propensity for self-medication is also positive and may suggest that this knowledge makes antibiotics a less attractive option for consumers that have not sought medical advice and may be in doubt over whether antibiotics are necessary or not. However, this discussion must be caveated by the cross-sectional nature of the data that gives these causal attributions a speculative nature, since any causal association could go both ways between the outcome (self-medication) and predictors (knowledge). For example, obtaining antibiotics via prescription necessarily entails a visit to and interaction with a health professional who may provide educational information, and this could also be a principal explanation for the positive associations discussed above.

5.2 Self-Medication in Europe: Inequality and Corruption

This study suggests that there are some contextual factors relevant to self-medication behaviour in Europe in addition to the above compositional factors. Inequality, as measured by the Gini coefficient, has been found to be an illustrative measure of inequality in the distribution of health outcomes (Mackenbach et al. 2011, EC 2013b, Chauvel, Leist 2015, Detollanaere et al. 2018) and modifiable health behaviours (Kino et al. 2017) in Europe. This study suggests that antibiotic self-medication is part of the mosaic of poor health outcomes and modifiable behaviours differentiating the health of countries with persistently higher income inequality from those with lower inequality.

Increased income inequality is associated with greater precarity for individuals at the low end of the income spectrum, referred to as, for example, the 'precariat' (Standing 2014, Greenstein 2020). In this study, persistent differences in income inequality between European countries from 2009 to 2018 were associated with variation in levels of self-medication behaviour, with people in countries experiencing persistently higher levels of income inequality over this time period more likely to be associated with self-medication behaviour. Alongside this, countries in which people bore persistently higher burdens of out-of-pocket health expenditure also saw higher levels of self-medication behaviour with antibiotics. During this time period, several countries implemented austerity measures in response to the 2007/8 financial crisis that negatively impacted upon funding, access to, and the provision of healthcare (Reeves et al. 2014, Stuckler et al. 2017, ECDC 2013). Sargent, Kotobi (2017), for example, highlight that some areas in France experienced "medical desertification" that was particularly damaging to marginalized groups. There may consequently be several non-exclusive explanations for why countries experiencing higher levels of inequality may also experience higher levels of antibiotic self-medication among their population. Charani et al. (2021, p. 2), for example, highlight that "low vaccination coverage persists in marginalized communities in many settings" and that, "socioeconomic deprivation is a risk factor for many infectious diseases including TB and meningococcal disease." Economic precarity could be associated with an inability to afford time away from work for illness, an inability to pay for medication, and higher levels of ill health prompting antibiotic consumption, whilst austerity measures that significantly affect vulnerable and deprived groups may reduce access to healthcare services and be generative of leftover-retaining behaviours. What remains unexplained, however, is why years with above average inequality over the 2009–2018 period tended to see lower levels of self-medication behaviour, or, to reverse the trend: why years with below-average inequality tended to see higher levels of self-medication behaviour. This area warrants further research using qualitative approaches that can provide more in-depth explanations of the relationship between economic precarity and antibiotic self-medication in Europe. Whilst a definitive explanation cannot be provided by this study, the results are suggestive that interventions to address antibiotic self-medication in Europe should also aim to address structural economic factors that may underly individuals' self-medication behaviour.

This study also suggest that countries with greater control of corruption have lower levels of self-medication among antibiotic consumers, which supports previous suggestions that poorly controlled corruption is associated with a higher level of undocumented antibiotic use (Collignon, Beggs 2019) in addition to general antibiotic use (Rönnerstrand, Lapuente 2017, Mueller, Östergren 2016, Gaygisiz et al. 2017). As Collignon, Beggs (2019, p. 6) articulate: "If corruption is poorly controlled, it is much more likely that there will be antibiotic use that is undocumented and so antibiotic volumes used, and their effects, will not be reflected in official figures." This study directly supports this suggestion by evidencing that countries with persistently higher levels of (perceived) corruption are associated with greater propensity for self-medication – an undocumented form of antibiotic consumption – among antibiotic consumers.

5.3 Social Correlates of Antibiotic Resistance

The findings of this study regarding the relationship between antibiotic consumption, self-medication, and national resistance levels suggest that there are different impacts across pathogen/antibiotic combinations for different aggregated levels of antibiotic-related behaviour. A strong association has been shown between the use of carbapenems to treat P. aeuruginosa infections and the development of resistance (Carmeli et al. 1999, Lepper et al. 2002, Rossolini, Mantengoli 2005, Mladenovic-Antic et al. 2016), and in particular the use of sub-inhibitory concentrations of antibiotics (Wright et al. 2013). The finding in this study that high self-medication countries also tended to have higher levels of CRPA suggests that the maintenance of CRPA levels is in part attributable to poorly enforced regulation of antibiotic consumption, as members of the public are more likely to have obtained the antibiotics they consumed in the past year off-prescription. This is further supported by the negative association presented between the perception of how well corruption is controlled in each country and the level of CRPA. These are only correlations of aggregated data about antibiotic use broadly defined however, and do not reveal the impact of specific classes of antibiotic. Indeed, the cross-sectional nature of the data could also mean that any causal pathway operates in the reverse direction to that suggested above, with higher levels of CRPA leading to higher demand for off-prescription antibiotics.

Previous research has demonstrated relationships between antibiotic stewardship interventions and the development of MRSA (Aldeyab et al. 2008, Lafaurie et al. 2012, Lawes et al. 2015), as well as regionally aggregated antibiotic consumption and MRSA bloodstream infection rates (Andreatos et al. 2018). This study provides support for these previous studies by presenting a positive association between nationally aggregated levels of antibiotic consumption and nationally-aggregated levels of MRSA. Previous studies also demonstrate a positive association between antibiotic consumption, particularly third-generation cephalosporins, and resistant *K. pneumoniae* (Joseph et al. 2015, Lombardi et al. 2015, Yang et al. 2020). The present study would seem to contradict this previous research by suggesting that there is a negative relationship between national antibiotic consumption levels and the level of 3GCR *K. pneumoniae*. However, this result is not necessarily anomalous, as a previous study by (Carlet et al. 2020) showed that in France contrasting results were found regarding the relationship between antibiotic consumption (which was reduced following a public campaign) and some antibiotic resistance pairs. Carlet et al. (2020) showed that whilst resistance levels decreased among *S. aureus*, the resistance of *K. pneumoniae* to third-generation cephalosporins increased. This study echoes this with a positive association between overall consumption and levels of MRSA and a negative association between overall consumption and 3GCR *K. pneumoniae* in the time period. Again, a clear caveat to this is that the survey-based antibiotic consumption measures in this study do not account for the consumption of specific classes of antibiotic or changing patterns of prescribing that might lead to higher or lower use of third-generation cephalosporins in different countries. However, along with the association between levels of self-medication and CRPA, and the lack of evidence for an association between antibiotic consumption (prescribed or otherwise) and levels of 3GCR *E. coli* levels, these results do illustrate heterogeneity between pathogen/antibiotic pairs in terms of their relationship to controlled or otherwise antibiotic consumption broadly measured.

Importantly, this study included a number of socio-economic and cultural factors to further contextualise the relationships between antibiotic consumption, self-medication, and resistance measures. As with the antibiotic consumption measures, this study illustrates that there are varied factors associated with different resistance measures. Indeed, 3GCR *E. coli* levels were predominantly characterised in terms of socio-economic and cultural factors, including out-of-pocket health expenditure per capita, corruption, and cultural avoidance of uncertainty, rather than the level of consumption of antibiotics. Corruption was a significant factor associated with levels of antibiotic resistance, more so than either of the measures of antibiotic consumption used, supporting the argument that poor governance (and in particular, high levels of corruption) is a significant barrier to addressing antibiotic resistance (Collignon et al. 2015, 2018, Collignon, Beggs 2019). Together these demonstrate that, socially, the challenge of 'antibiotic resistance' is a broad church, and that addressing resistance between specific pathogens and classes of antibiotic requires attention to the varied societal contexts that may aid the development of various pathogenic ecologies, as well as the improvement of antibiotic stewardship.

5.4 Limitations

This study has multiple limitations that should be acknowledged. Whilst the modelling approach distinguished between persistent and time-variant country-level differences, the data used are cross-sectional in nature. This limits the potential for causal pathways to be determined, and whilst these have been suggested in the context of existing literature, alternative and potentially opposing pathways cannot be definitively ruled out. Survey data themselves contain inherent limitations as a trade-off against large-scale data collection and analysis. Specifically for this study, whilst associations with 'antibiotic consumption' and 'self-medication' can be determined, the motivations of individuals and the specific experiences that underly these behaviours cannot be analysed in detail. For example, the relationship between inequality and self-medication was explained with a contextual rationale in this paper, but this area requires in-depth qualitative research to fully understand the conditions that precipitate higher levels of self-medication in the countries that have higher inequality. Furthermore, the survey-based measures of antibiotic consumption used in this study do not discriminate between prescribing policies concerning the use of specific classes of antibiotics, which may influence patterns of resistance between countries.

6 Conclusion

This study makes two key contributions to the literature. Firstly, it demonstrates that antibiotic consumers in European countries with persistently higher levels of income inequality, burdens of out-of-pocket health expenditure, and corruption are more likely to consume antibiotics without a prescription than consumers in countries with lower levels of inequality, out-of-pocket health expenditure, and corruption. This finding is important, as measures of national antibiotic consumption between countries that do not take into account off-prescription consumption may produce unreliable results confounded by the level of inequality or out-of-pocket health expenditure or extent of corruption in different countries. This study was able to distinguish, albeit broadly, between antibiotic consumption and self-medication by using survey-based measures rather than prescribing or sales data, and was able to distinguish between persistent and time-variant differences between countries using a mixed-effects regression technique. Secondly, the study has demonstrated that, whilst relationships between different pathogen/antibiotic pairs and antibiotic consumption, self-medication, and socio-economic and cultural factors are heterogeneous, socio-economic and cultural factors play an important role in explaining national variations in resistance. Whilst levels of corruption appear to correlate with both self-medication and resistance levels, other factors like cultural dimensions and economic variables presented different patterns across different resistance pairs. Approaches to improve antibiotic stewardship in Europe by addressing self-medication behaviours should take into account the structural factors that underlie such behaviours, in addition to individual-level approaches like educational interventions. Furthermore, these approaches should take into account that antibiotic resistance is not simply driven by antibiotic consumption, but is contextualised by social, economic, and cultural environments.

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Spatial health inequality and regional disparities: Historical evidence from Italy

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Abstract. Geography and the quality of the environment may have long lasting effects on the living standards of individuals and this, in its turn, may substantially affect the distribution of income and regional disparities. In this paper I consider exposure to malaria as a measure of "bad geography" and illustrate evidence showing that it was a major determinant of individuals' health, (as measured by the height of military conscripts) as well as its disparities between individuals and regions in Italy. To estimate the relationship between malaria exposure and height, I rely on the "fetal origins hypothesis"; I hypothesize that exposure to malaria in utero or during childhood has persistent effects on health. The periods under scrutiny in this paper are the last two decades of the XIX century, a period without major public health interventions, and the years around the malaria eradication era in the 1950s. My results support the hypothesis that geographically targeted policies may reduce health inequality between and within regions.

Key words: Health inequality, place-based policies, spatial disparities, regional development, malaria, height

1 Introduction

The quality of the environment where individuals live has long-lasting effects on their health and consequently on a variety of socio-economic outcomes, including education and labor productivity. This well-established evidence further implies that there is an association between the quality of the environment, health and local development, not only in developing, but also in developed countries. Health is also considered as a desirable outcome by individuals assessing the quality of life in their regional environments. Life expectancy and child mortality are among the variables used to construct synthetic indicators, as in the case of the EU Regional Human Development Index (Haderman, Dijkstra 2014) and the Italian regions under study (Ferrara, Nisticò 2015).

This paper contributes to the literature by presenting historical evidence from Italy, with specific reference to the burden of malaria across regions. More broadly, this paper aims to present historical evidence on spatial and individual inequality in health and living standards in Italy, a country where such inequalities are still persistent (see e.g. Franzini, Giannoni 2010, Perucca et al. 2019).

In the 19th century, most physicians believed malaria was caused by "miasma" (poisoning of the air), while others made a link between swamps, water and malaria, but did not make the further leap towards insects (Snowden 2006). As a result of these theories, little was done to fight the disease before the end of the century. Italian scientists managed to predict the cycles of fever, but it was in Rome that the naturalist Giovanni Battista Grassi found that a particular type of mosquito was the carrier of malaria. After an extraordinary series of experiments on healthy volunteers in Italy (mosquitoes were released into rooms with volunteers), Grassi was able to make the direct link between the insects (all females of a certain kind) and the disease. The use of quinine to cure malarial fevers has been known for a long time. It has been systematically used since 1922 by the Italian Government to prevent malaria. The effects in Italy were so positive that its use as a preventive extended to other similarly situated countries; i.e., highly malarious farming countries. Although effective in reducing the burden of the disease, the use of quinine did not eradicate malaria, which was only eliminated in the 1945-1950 period, when the US government and the Rockefeller Foundation introduced DDT in the country.

Because of its impact on children's health, malaria has serious impacts on the individuals' physical growth and hence on their height. By relying on the 'fetal origins of adult outcomes' hypothesis and by taking a place-based perspective, this study estimates the impact of malaria eradication in Italy on the height distribution of military conscripts between and within regions. Taller individuals generally have higher income, so height is often used as a measure of historical living standards (Floud et al. 1990, Fogel 2004, Steckel 1995, 2004). This evidence also leads us to argue that the distribution of height across regions and across individuals can be considered as a measure of health and socio-economic inequality for periods in which data are not available.

In this paper, I present two pieces of evidence regarding the effect of malaria on adult height distribution in Italy. First, I illustrate that the quality of the environment, as proxied by malaria mortality rates, is crucial in predicting future height. In this case, I consider the average height of conscripts at regional level, born between 1889 and 1900, a period with no policy interventions to eradicate the disease. The second piece of evidence shows that the eradication of malaria that occurred between 1945 and 1950 has resulted in increased average height and distribution of height across individuals within regions, hence pointing to considerable redistributive effect of the policy.

The evidence reported in this paper indicates the clear effectiveness of place-based policies aiming at improving the individuals' quality of life, even in socio-economic terms.

2 Related literature

The aim of this paper is to examine the impact of malaria exposure in utero or during early childhood on height. My theoretical starting point is the so-called 'fetal origins' hypothesis (Barker 1990), i.e. the quality of the environment and the events to which a fetus or a child is exposed have major long-run impacts on health and cognitive abilities. The first evidence concerning the importance of the persistent effects of shocks during childhood was provided by Stein, Saenger (1975), who found adverse health outcomes for Dutch children born during the famine and the Nazi occupation. Barker (1990) has systematized the medical evidence available to date, arguing in favor of the 'fetal and infant origins' hypothesis of human development. A complete review of the evidence supporting the "fetal origins" hypothesis would fall outside the scope of this paper; hence, in what follows, I will focus mainly on the literature on malaria, with special emphasis on socio-economic outcomes.

Although the 'fetal origins' hypothesis has been proposed in the field of medical science, an increasing body of economic literature has shown that in utero and early life shocks may have relevant long-term effects on adults, especially in terms of educational attainments and income (see, among others Almond 2006, Barreca 2010, Bleakley 2010, Case, Paxson 2009, 2010, Chen, Zhou 2007, Cutler et al. 2010, Kim et al. 2010, Lucas 2010, Meng, Qian 2009, Neelsen, Stratmann 2011, Percoco 2013, 2016). Besides its theoretical appeal, one of the reasons for such a surge of economic studies relying on this hypothesis is that considering an environmental variable measured early in the lives of individuals significantly reduces the confoundedness due to adults' avoidance behavior. In other words, a given cognitive- and health-related outcome for an individual observed at a given point in time is probably not the result of exposure to certain environmental conditions in the same year; rather, it is the result of a very long-term and often unobserved process in which an individual may systematically choose to avoid exposure to adverse conditions. Given these caveats in assessing the effects of exposure to pernicious diseases on adult outcomes, an increasing body of literature is focusing on the 'fetal origins' hypothesis in order to have a reliable lower bound estimate of the impact.

Regarding malaria, Bleakley (2007) finds that on average one year of exposure to the disease reduced citizens' years of schooling by approximately 0.05 in the United States, whereas Barreca (2010) shows that 10 deaths from malaria per 100,000 inhabitants decreased the length of schooling by 0.23 years for cohorts born in the United States between 1900 and 1930. Lucas (2010) investigates the effect of malaria on lifetime female educational attainment in Sri Lanka and Paraguay, finding evidence of a negative effect of the disease on years of education and literacy. Similar results have been obtained by Bleakley (2010) for Brazil, Colombia and Mexico. Percoco (2013) studies the eradication of malaria in Italian regions during the early 1950s and finds evidence of a long-term positive effect on education through inter-generational transmission channels.

In another study on malaria eradication in colonial Taiwan during the early twentieth century, Chang et al. (2011) find that malaria exposure around birth worsens old-age health status; it particularly increases the likelihood of cardiovascular diseases as well as the hazard of mortality and leads to worse cognitive functions. Similarly, Hong (2011) shows that Union Army recruits, who spent their early childhoods in malaria-endemic counties of mid-nineteenth century USA, were on average 2.8 centimeters shorter than their counterparts born in malaria free areas. A somewhat similar result was found by Bozzoli et al. (2008), who estimated an inverse relationship between post-neonatal (one month to one year) mortality, used as a measure of disease and nutritional conditions during childhood, and average adult height.

There are good reasons to hypothesize that height is affected by malaria. In fact, adult height is affected by the balance between the demand and supply of nutrients, by exposure to diseases and by physical exertion (Silventoinen 2003). Crimmins, Finch (2006) also argue that the inflammatory responses developed as a defense against many childhood diseases divert energy from growth and thus reduce adult height. These conditions are generally encountered in the cases of exposure to malaria, especially Falciparum malaria. The study of height is also important because it has been shown to be a good predictor of health outcomes, including mortality (Song et al. 2003) especially from strokes (McCarron et al. 2002, Song et al. 2003), and of earnings (Case, Paxson 2008).

The height of conscripts in Italy in particular has recently attracted the interest of scholars across several disciplines. Arcaleni (2006) presents a comprehensive, descriptive analysis of the height trends of Italian conscripts between 1854 and 1980, whereas Peracchi (2008) reviews the evidence on the relationship between height and economic development.

The distribution of height across individuals also points to distribution of living standards, although under relatively strict assumptions. Let us assume height of individual i, h_i, depends on his/her living standards, y_i, so that it is possible to predict height across individuals with the formula:

$$h_i = \alpha y_i^{\beta} \epsilon_i \tag{1}$$

where α and β are two scale parameters, and ϵ_i is an i.i.d. term. By considering the logarithms, it is possible to reformulate the expression as (Deaton 2008):

$$\ln h_i = \alpha + \beta \ln y_i + \epsilon_i \tag{2}$$

To achieve the linear correlation of the dispersions of height and living standards around their means, under strong assumption of orthogonality between y_i and ϵ_i, the variance of h_i can be expressed as:

$$var(\ln h_i) = \beta^2 var(\ln y_i) + \sigma_\epsilon^2 \tag{3}$$

In other words, observing and analyzing the distribution of adult height across regions and individuals, it is possible to have a picture of the distribution of living standards between and within regions. These arguments are of extreme importance for this paper, since in the following sections I propose evidence supporting the negative association between malaria and height across regions and that a place-based policy aimed at eradicating the disease has had significant impact in terms of health inequality between and within regions.

3 An overview of the diffusion of malaria in Italian history

Italy was infested with malaria for hundreds of years until 1962, when its eradication was officially declared. Unlike other pernicious but sporadic diseases, malaria has been a persistent feature of many Italian regions, especially in the South. It shaped the socio-economic development of the entire country, so it was widely considered the "Italian national disease" (Snowden 2006).

Despite its importance, the attempts to document and report malaria incidence only started taking place in 1887, when health statistics began to be collected, and when it was made compulsory to register deaths classified by cause throughout the country. Even then, however, the impact of the disease was unclear and probably underestimated, owing, among other things, to uncertainty about the nature and causes of malaria itself[1].

The influential and fascinating work by Snowden (2006) provides a social history of the malaria eradication program which can be divided into four main phases.

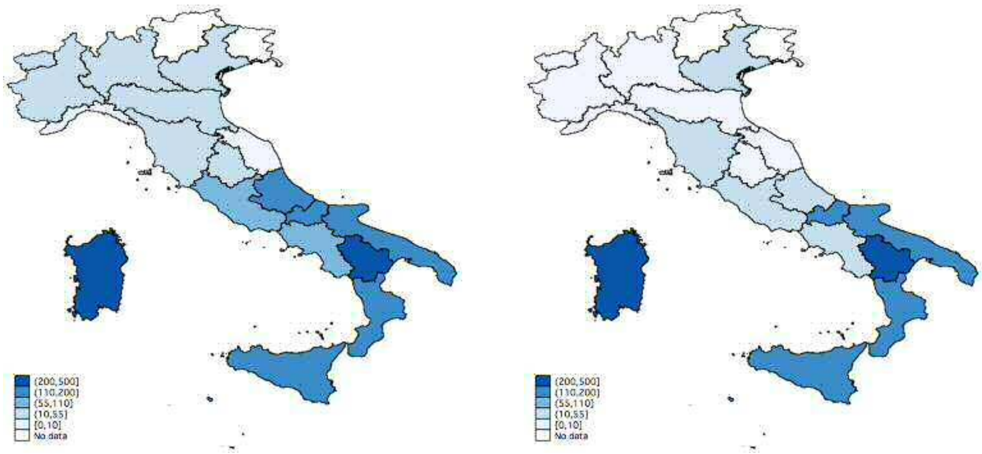
The first phase ranges from the Italian Unification to 1904. The territorial pervasiveness of malaria in Italian regions was one of the main social issues faced by the Government in the aftermath of the 1861 Unification of the country (Amorosa et al. 2005). At that time, almost one third of Italian municipalities were under malaria threat. Life expectancy, which was only 22.5 years in areas affected by malaria and 35.7 in relatively safe areas, presents a sufficient illustration of the burden imposed by the disease. As a result, the economic costs in terms of health care expenditure and loss of productivity were particularly high, so the Italian Government decided to engage in a vast scale campaign to eradicate malaria.

The second phase of the eradication process ranges from 1904 to 1928. In fact, prior to the studies carried out by the physicians Giovanni Battista Grassi and Angelo Celli, malaria was considered to be caused by a miasma, particularly as a result of some gases produced by certain types of terrain. Grassi instead argued that the disease was transmitted by mosquitoes, and that it could have been controlled by using quinine. In 1904, Grassi conducted the first large scale experiment in the Agro Pontino, in the surroundings of Rome, and convincingly demonstrated the validity of his theories. Given the declining price of quinine induced by the increase of coffee production, the Government engaged in a program called "Chinino di Stato", resulting in the free distribution of quinine through a network of health care offices. The effect of this program was very large, decreasing the number of deaths from 15,593 in 1900 to 6,333 in 1914. However, during World War I, as physicians employed in the anti-malaria program were sent to the war front, the death toll of malaria rose once again, with the number of deaths increasing up to 11,487 in 1918.

The third phase begins with the so-called "Legge Mussolini" (i.e. the Mussolini Act) in 1928. By recognizing the failure of the quinine in definitively eradicating malaria in Italian regions, Mussolini aimed to reclaim the entire marshlands in the Agro Pontino, Latium (the so-called bonifica integrale) in order to settle new cities and eradicate malaria. With the employment of advanced technology for hygienic and hydraulic control, malaria was almost eradicated in the area. However, land reclamation interventions put in place during the fascist period were limited to certain areas and insufficient to guarantee the complete eradication of malaria in Italy.

The fourth phase is the phase of the ultimate eradication of malaria by means of DDT, as firstly introduced by American troops in 1944 and massively used by the Italian

[1] Inter-regional mobility in the considered time period was almost nonexistent (Audenino, Tirabassi 2008). This is particularly relevant in my case because I use regional- and cohort-specific data matched with malaria mortality in the cohort's year of birth in the region, where height measurements took place. The substantial absence of inter-regional migration flows is important for the identification of the parameter of interest, so that the probability of birth in a given region and migration to another region where measurements took place is very low.



(a) Mortality in 1889

(b) Mortality in 1900

Figure 1: Malaria mortality in 1889 and 1900

Note: The figure illustrates the distribution of the malaria death rate in Italy during the two years. There is no data for Trentino-Alto Adige and Friuli-Venezia Giulia, which were not part of the Kingdom of Italy. *Data source*: (Istituto Centrale di Statistica 1958).

government in the years 1945-1950.

In this paper I first focus on the pre-quinine period in order to eliminate possible bias due to policy interventions which might result in lower estimates of the effect of malaria. My data particularly cover the period 1889-1900, a time interval during which the geography of the malaria death toll was remarkably stable with marginal intra-regional variations allowing for an estimation of a panel model (Figure 1). The second piece of evidence I present concerns the impact of the final eradication of malaria on the distribution of height between and within regions, that is I provide evidence of change in the distribution of height among individuals born in regions with high malaria mortality rates.

4 Data

The data for the 1889-1900 period is on the height of conscripts from Costanzo (1948), cohorts of males born between 1889 and 1900. The number of total conscripts from each region in each year and the number of conscripts whose heights were measured are also reported[2]. The regions considered are: Piemonte-Valle d'Aosta, Lombardia, Liguria, Veneto, Emilia Romagna, Marche, Umbria, Toscana, Lazio, Abruzzo-Molise, Basilicata, Campania, Calabria, Puglia, Sicilia, and Sardegna.

As for the analysis of the distribution of height within regions, the sample we used to is from the ISTAT time series[3]. It refers to data collected during the compulsory medical examinations for military service. In Italy, the latter has been mandatory until 2005 and implied a first general visit to confirm the fitness for service. The dataset provides average height for people born between 1918 and 1990 in each region, although the data used in this study is from the 1930-1960 period. Additionally, there are also frequencies for different height intervals, i.e. percentage of people (for a given year in a given region) whose height falls in the intervals: less than 150 cm, 150-154, 155-159, 160-164, 165-169, 170-174, 175-179, more than 180 cm.

Data on deaths resulting from malaria are available in the Cause di Morte: 1887-1955, published by the Istituto Centrale di Statistica (Istituto Centrale di Statistica 1958).

[2] A'Hearn et al. (2009) raise concerns about the non-normal distribution of height and propose a framework to adjust the empirical distribution. However, from their results, it seems that the adjusted time series does not significantly differ from the original one in the period considered in this paper; I therefore make use of the one observed originally.

[3] Data are available at the website: http://seriestoriche.istat.it/fileadmin/allegati/Sanita/tavole/-Tavola_4.16.1.xls.

Table 1: Summary of statistics (Italy)

	Mean	Std.Dev.	Min	Max	Median
Mean height	160.003	0.765	156.77	161.93	160.115
Malaria death rate	65.12	78.12	0.669	312.63	21.89
Average Temperature	12.958	1.83	9.46	17.04	12.87
Average Precipitation	65.733	13.39	40.37	85.98	68.16

Notes: The malaria death rate is the number of deaths per 100,000 residents. Average temperature and precipitation are annual means. The total number of observations is 224.

Table 2: Summary of statistics (Center-North vs South)

	Center-North				Non-North			
	Mean	Std.Dev.	Min	Max	Mean	Std.Dev.	Min	Max
Mean height	160.461	0.44	158.96	161.57	159.646	0.77	156.77	161.93
Malaria death rate	8.81	4.12	0.669	17.38	108.917	80.34	2.05	312.63
Average Temp.	11.868	1.42	9.46	15.5	13.805	1.67	10.13	17.04
Average Prec.	74.079	8.92	57.68	85.98	59.242	12.7	40.37	77.76

Notes: North comprises all the regions the capitals of which are located above 43° latitude. Non-north comprises all the other regions, including Latium, where Rome is located. North: Piedmont/Aosta Valley, Lombardy, Veneto, Liguria, Emilia-Romagna, Tuscany, Umbria. Non-north: Marche, Latium, Abruzzi-Molise, Campania, Apulia, Basilicata, Calabria, Sicily, Sardinia. Malaria Deaths: there are 98 observations for the North and 126 observations for the South. The malaria death rate is the number of deaths per 100,000 residents. Average temperature and precipitation are annual means.

The book reports the number of malaria deaths between 1887 and 1955 for each region. Data for previous years are not available for all regions and are unreliable: indeed, the compulsory registration of deaths classified by causes was extended to the whole country only in 1887. I construct 'annual malaria death rates' as the number of deaths due to malaria divided by the resident population of each region; the latter is estimated using census data. I have taken data on general mortality, which will be used as a further control variable, from the same source.

Data on regional population have been compiled using the Annali di statistica: Sviluppo della Popolazione Italiana dal 1861 al 1961 (anno 94, Serie VII-Vol.17), published by ISTAT[4].

Descriptive statistics on conscripts' height, malaria incidence and climatic conditions are reported in Tables 1 and 2. Table 1 reports results for the whole of Italy, whereas Table 2 distinguishes between Center-North and South.

The average malaria mortality rate for the entire Peninsula during the 1889-1900 period (i.e. the death rate averaged across all years and regions) is 69.12 deaths per 100,000 inhabitants, and the standard deviation is quite large (approximately 78 per 100,000). Indeed, as discussed above, there was considerable variation in mortality caused by fevers across areas, due to different degrees of pervasiveness of the disease and its different forms. In the North, in fact, the average number of malaria deaths per 100,000 inhabitants over the 1889-1900 period did not reach 9 units, whereas the mean malaria death rate in the South was nearly 109 units per 100,000 residents. In the North, the median malaria death rate was 9.18, whereas in the South, it was 90.77. The most malarial region was Sardinia, which recorded the highest average malaria death rate over the period under scrutiny (i.e. 265.5 deaths per 100,000), as well as the maximum number of deaths per 100,000 in a given year (i.e. 312.63 in 1889). Conversely, the least malarial region was Liguria, which had the lowest mean malaria mortality rate (i.e. 2.06) and the

[4]For each region, the book reports the resident and present population numbers recorded in census years (every ten years starting from 1861, with the exception of 1891, when no census was carried out) and the average annual growth rates of the population in the inter-census period. I estimate the resident and present population for all regions and years between 1889 and 1900 by applying the annual average inter-census growth rates to the population data from the 1881 census. Furthermore, data on GDP per capita, which will be used as a control variable, are from Daniele, Malanima (2007).

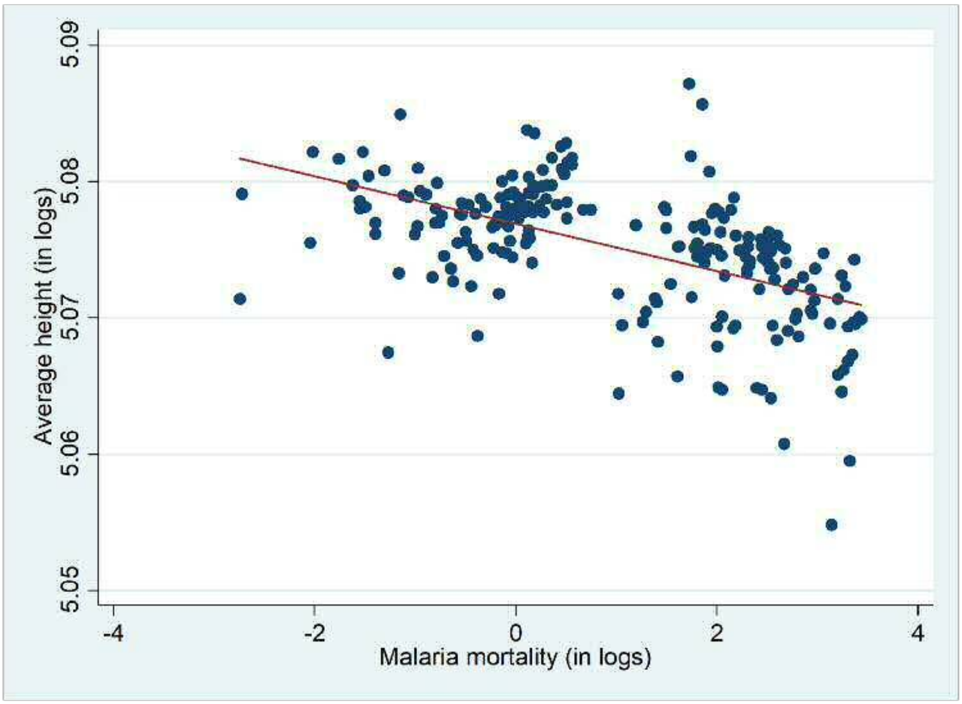


Figure 2: Malaria mortality and height

Table 3: Average height of conscripts

	Regions with high malaria mortality	Regions with low malaria mortality
Before the eradication	165.410	169.211
(1930-1944)	(1.976)	(2.167)
After the eradication	169.180	172.621
(1950-1960)	(1.998)	(1.910)

Notes: Regions with high malaria mortality: Abruzzo, Molise, Basilicata, Calabria, Lazio and Sardegna. Standard errors are in parentheses.

lowest number of deaths per 100,000 in a given year (i.e. 0.669 in 1900). Figure 2 reports the scatter plot for the pooled sample of the relationship between malaria in the year of birth and height. From the linear trend line, it seems that the correlation is negative, although far from being robust.

When it comes to climatic variables, average annual temperature was in general higher in southern regions, whereas rainfall was more abundant in the Center-North.

Table 3 reports descriptive statistics of the impact of malaria eradication on height of conscripts. In the table, regions are divided between the group with high mortality rates and the group with low mortality (i.e. above or below the national average), so the comparison is made between the averages of the 1930-1945 and 1946-1960 time periods. The difference between the two groups significantly decreased after the eradication. However, the observation of only one moment of the distribution of height may hide other, more significant changes occurring in the full distribution of the outcome of interest. To highlight those changes, Figures 3 and 4 plot kernel density for the high and the low mortality groups respectively. As evident, the most significant changes have occurred in the distribution of height of conscripts in regions with high malaria mortality with a sharp change in the tails, especially in the lower limit, implying an interesting change within regions more significantly affected by the treatment (i.e. the eradication).

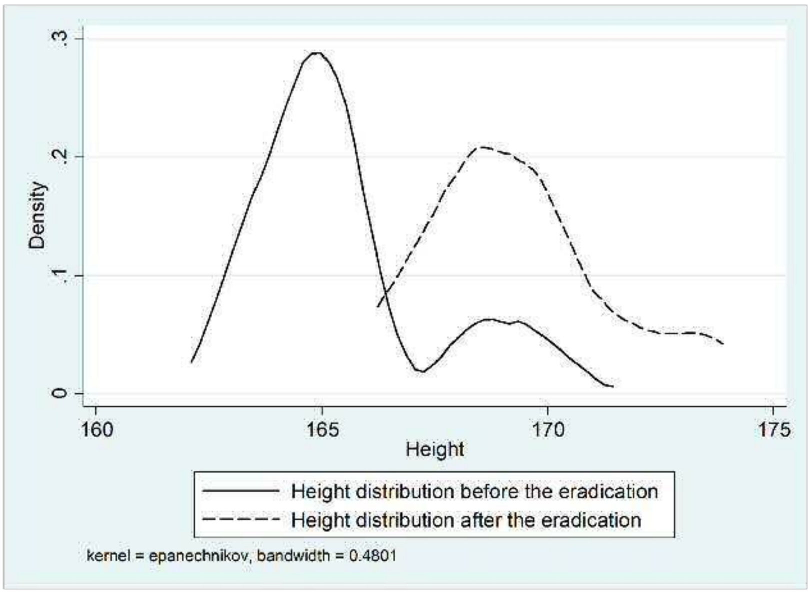


Figure 3: Change in height distribution in regions with high malaria mortality rates

5 The burden of malaria in the pre-eradication era

5.1 Methodology

I start my analysis by estimating OLS regressions where the dependent variable is the regional average height as a function of malaria mortality, controlling for region of birth fixed effects, year of birth fixed effects and region-specific time trends. The first specification is as follows:

$$MeanHeight_{it} = \beta Malaria_{it} + \delta_i Year_{cohort_t} + \gamma_t + \epsilon_{it} \quad (4)$$

where $MeanHeight_{it}$ is the average adult height of conscripts born in year t in region i; $Malaria_{it}$ is the incidence of malaria in region i in year t as measured by deaths per 100,000 inhabitants; δ_i is a set of region-of-birth fixed effects that captures features varying across regions but not across time (e.g. geographical characteristics, region-specific genetic backgrounds and even malaria endemicity); γ_t is a set of cohort (year of birth) fixed effects that accounts for birth conditions varying over time but remaining constant across regions (e.g. country-wide shocks). Finally, $\delta_i Year_{cohort_t}$ is a set of region-specific time trends used to account for the possibility that the evolution of mean height follows different linear paths in different regions, so that spurious time-series correlations may arise between height and malaria incidence. This latter set of variables is very important for the identification of β since it is meant to capture the evolution of living standards across regions, even in terms of access to healthcare facilities and local availability of food.

Equation (4) assumes that the effect of malaria on average height is only relevant in the conscripts' years of birth. In particular, this specification assumes that in utero and postnatal exposure may have an effect independent of the exposure in the following years. Equation (4) implicitly assumes that the height of individuals born in region i in year t reacts to malaria exposure only in time t, and that exposure in subsequent years is orthogonal to height by definition.

In order to relax this strong assumption, I propose an alternative specification, i.e.:

$$MeanHeight_{it} = \beta Malaria^p_{it} + \delta_i Year_{cohort_t} + \gamma_t + \epsilon_{it} \quad (5)$$

where $Malaria^p_{it}$ is a measure of malaria incidence over the time period t, which goes from the year of birth of the cohort (year 0) to some years after birth. For example, p may be a period of two years comprising the year of birth and the first year after birth, or a period of three years from the year of birth to the second year after birth, and so

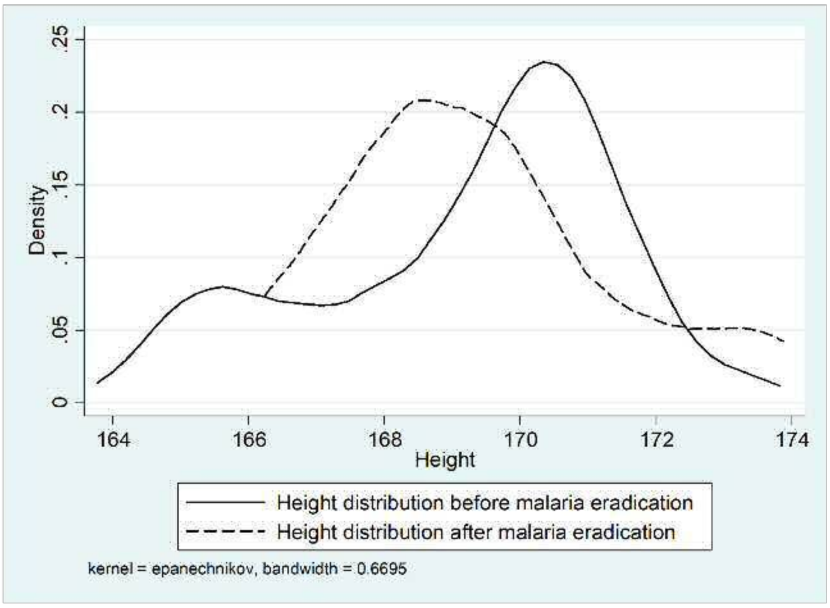


Figure 4: Change in height distribution in regions with low malaria mortality rates

on. In this way the effect of prolonged exposure to malaria during childhood is captured. As a measure of malaria over period p, I use the annual average malaria death rate (per 100,000 inhabitants) over the period under study[5].

There are good reasons to consider estimates of β via OLS to be biased. Firstly, malaria may be correlated with unobservable variables that also influence long-term health, thus creating a problem of endogeneity which would bias the estimation of the parameter β. Secondly, the way I measure malaria, i.e. by the number of deaths per 100,000 inhabitants, is only a proxy for the true incidence of the disease. Malaria deaths were often misreported and probably under-reported. Furthermore, since some forms of malaria are less deadly than others, mortality data do not capture the true pervasiveness of the disease, because the incidence of these mild forms is underrepresented by the number of deaths that they cause, so that β may be biased downward due to a measurement error. An instrumental variable estimation (IV) therefore seems more appropriate[6]. Craig et al. (1999) discuss the relationship between monthly temperature and rainfall surfaces and malaria prevalence. They argue that transmission below $18°C$ is unlikely, because few mosquitoes survive the 56 days necessary for sporogony to complete, whereas temperatures above $22°C$ are sufficient for stable transmission. The rate at which sporogony takes place increases with temperatures in the range of $15°C$-$40°C$ (Martens et al. 1995). Sporogony takes approximately 7-8 days in $30°C$, 8-10 days in $28°C$, 15-16 days in 20-$21°C$, and 200 days when the temperature is around $16°C$. Development stops below $16°C$ for Plasmodium falciparum and below $15°C$ for Plasmodium vivax, but temperatures above $32°C$ cause high vector population turnovers, weak mosquitoes and high mortality. Kirby, Lindsay (2009) find that rates of survival to adulthood are highest for mosquitoes' larvae reared at $25°C$ and decrease with increasing temperature. Furthermore, the time necessary for the development from larvae to the adult stage is also temperature dependent, taking a minimum of 7 days.

[5]A similar approach was also adopted in Percoco (2016) during the evaluation of the Spanish flu.

[6]This approach has already been taken by, among others, Barreca (2010), who uses climatic variables for instrumenting malaria, and Chang et al. (2011), who instead use the number of public health physicians and other medical personnel per 10,000 inhabitants as an instrument for measuring the malaria death rate in colonial Taiwan. Similarly, Hong (2011) predicts malaria risk using monthly average temperature. Barreca (2010) considers the malaria death rate to be a function of the fraction of the year in which the average daily temperature is between $22°C$ and $28°C$, i.e. the range in which malaria transmission is believed to be less constrained by temperature. The influence of climatic conditions on malaria transmission operates through three channels: mosquito larvae development, mosquito survival, and sporogonic duration – all of them depending on weather conditions.

Table 4: Malaria and height (OLS estimates)

	Malaria mortality					
	in $p = 0$ (1)	in $p = 0$ (2)	in $p = 3$	in $p = 3$	in $p = 5$	in $p = 5$
Malaria	0.000233	4.87e-05	–	–	–	–
			-0.00385***	-0.00465***	-0.00581***	-0.00647***
	(0.239)	(0.0512)	(-3.155)	(-2.636)	(-3.147)	(-3.280)
General mortality		0.0169**		-0.0266		-0.0204
		(2.565)		(-1.018)		(-0.524)
GDP per capita		-0.0221		0.0297***		0.0435***
		(-1.103)		(3.815)		(3.773)
R^2	0.825	0.834	0.829	0.840	0.830	0.840
# of Obs.	224	224	224	224	224	224
F test	12.84	12.30	13.62	13.80	13.46	13.41

Notes: All variables are in logarithms. Robust t-statistics are in parentheses. *** p<0.01, ** p<0.05, * p<0.1. Time dummies, region dummies and region-specific time trends are included.

According to Craig et al. (1999), it is important to use precipitation to indicate the probable presence of malaria vectors, their survival and the potential for malaria transmission. Another important aspect of malaria transmission is the fact that suitable conditions must persist for a period long enough for vector populations to increase and for the transmission period to be completed. Three months should be a long enough for transmission (Craig et al. 1999).

In the analysis presented in this paper, I follow Craig et al. (1999) and use climatic variables as instruments to explain the pervasiveness of malaria exogenously. I particularly use average temperature and average rainfall in the year and region of birth as instruments to identify β.

Data on both temperature and rainfalls are from various years of the *Annali del Regio Ufficio Centrale di Meteorologia e Geodinamica*, the data for which are available from several monitoring stations for each region. I consider the simple average across stations for both rainfall and temperature within each region.

5.2 Results

Table 4 presents estimates of OLS regressions, where the logarithm of average height is used as a dependent variable. It's important to note that I always include region and time fixed effects as well as regional time trends, although the associated coefficients are not reported. In model 1, the death rate in the year of birth is used as the only explanatory variable. The associated coefficient is not significant at conventional levels: a result that holds also when controlling for GDP per capita and general mortality (both in logarithms). In models 3 and 4, the average death rate for malaria during the first three years of life is used as an explanatory variable. Interestingly, the coefficient turns out to be highly significant and with a negative sign, a result that is confirmed also in models using average malaria mortality during the first five years of life, although with lower significance.

The results of the ordinary least square estimation prompt some considerations regarding the possible impact of childhood malaria on adult height, and hence on long-term health. In fact, it seems that only in utero or postnatal (i.e. where $p = 0$ and $p = 1$) exposure to the disease is not enough to explain differences in adult heights among different cohorts across regions. Consequently, it is necessary to consider the level of pervasiveness of malaria over a longer period of time. The average malaria death rate computed over the year of birth and the first three years after birth (or the total number of deaths per 100,000 inhabitants in the period) proved to have a statistically significant effect on mean height. The above analysis also suggests that malaria has a stronger long-term impact in the first few years of life of a cohort than in later childhood years.

Table 5: Malaria mortality and climatic variables (2SLS estimates; first stage regressions)

	Malaria mortality					
	in $p = 0$ (1)	in $p = 0$ (2)	in $p = 3$	in $p = 3$	in $p = 5$	in $p = 5$
Temperature	0.327***	0.320***	0.402***	0.293***	0.272***	0.631***
	(4.498)	(4.310)	(2.849)	(3.082)	(3.562)	(3.666)
Rainfalls	0.290**	0.201**	0.136**	0.294***	0.250**	0.307***
	(2.266)	(2.253)	(2.353)	(5.028)	(2.374)	(4.834)
General mortality		0.885		0.846		0.882
		(0.631)		(0.602)		(0.721)
GDP per capita		0.125		0.119		0.182
		(0.323)		(0.313)		(0.431)
F test	16.07	16.24	18.72	37.19	19.22	41.15

Notes: All variables are in logarithms. Robust t-statistics are in parentheses. *** p<0.01, ** p<0.05, * p<0.1. Time dummies, region dummies and region-specific time trends are included.

Table 6: Malaria and height (2SLS estimates; second stage)

	Malaria mortality					
	in $p = 0$ (1)	in $p = 0$ (2)	in $p = 3$	in $p = 3$	in $p = 5$	in $p = 5$
Malaria	0.000333	5.17e-05	–	–	–	–
			-0.00415***	-0.00517***	-0.00581***	-0.00718***
	(0.839)	(0.516)	(-4.055)	(-3.316)	(-3.147)	(-4.181)
General mortality		0.0191**		-0.0218		-0.0204
		(3.164)		(-1.182)		(-0.604)
GDP per capita		-0.0221		0.0207***		0.0421***
		(-1.200)		(3.815)		(3.443)
R^2	0.715	0.742	0.745	0.840	0.830	0.840
# of Obs.	224	224	224	224	224	224

Notes: All variables are in logarithms. Robust t-statistics are in parentheses. *** p<0.01, ** p<0.05, * p<0.1. Time dummies, region dummies and region-specific time trends are included.

As discussed in previous sections, the parameter of interest, β may be affected by endogeneity and can be instrumented by using temperature and rainfalls. To this end, Tables 5 and 6 report estimates of the first and second stages respectively. It should be noted that, in the case of 3-5 years average malaria mortality, instruments are averaged as well. This is confirmed by the results presented in Table 4, although it is important to note that the magnitude of the coefficient of interest is higher across all the six specifications with respect to the estimates in Table 4 – a result in line with the hypothesis of omitted variable bias in the OLS regressions.

The overall results presented in this section confirm the negative impact of exposure to malaria on height, although only prolonged exposure is statistically significant. The magnitude of the estimated coefficients, however, is very small. To get an idea about the magnitude, let us consider a reduction in malaria mortality from 108.917 in the South to 8.81 in the Center-North, corresponding to a reduction of approximately 91% in the mortality rate. If we consider the estimates in Table 5 as the most reliable and assume an average β coefficient of -0.05, then the increase in the height of the Southern population would be about +0.45% (0.7 centimeters), i.e. sufficient to fill the gap in height between North and South.

These calculations imply that the differences in the incidence of malaria across regions significantly affects spatial health inequality as approximated by conscripts' height.

6 Malaria eradication and health inequality

In the previous section, after accounting for several factors, I have illustrated that spatial disparities in terms of malaria incidence were a major driver of spatial health disparities. In this section, I estimate the effect of malaria eradication on spatial health inequality within and between regions.

Starting with the seminal paper by DiNardo et al. (1996), literature was focused on the impact of policy interventions on the distribution of outcome variables and on its decomposition to assess the most important factors. Recent contributions have particularly refined the use of quantile regressions and prediction decomposition or the evaluation of counterfactual distributions (Chernozhukov et al. 2008, DiNardo et al. 1996, DiNardo, Tobias 2001, Elder et al. 2011, Machado, Mata 2005, Melly 2006). This approach, however, assumes that the treatment affects only some categories, i.e. only some units belonging to some intervals in the distribution. In principle, in the case of malaria, the eradication of the disease in given regions has affected all height intervals, so a quantile regression approach is not feasible, as there is no distinction between treated and control quantiles. To circumvent this problem, and given the characteristics of the dataset, I propose the use of an equation system defined as:

$$height_{hit} = a_{ht} + \alpha_h high_{hi} + \beta_h post_{ht} + \delta_h high_{hi} \times post_{ht} + \epsilon_{hit} \tag{6}$$

where the dependent variable is the share of conscripts with height falling in interval h defined as above, in region i and in year t; α denotes a common trend; $high_{hi}$ is an indicator variable for regions with high mortality; whereas $post_{ht}$ is an indicator for the post-eradication period, i.e. after 1950. Our parameters of interest in system (6) are δ_I as they measure the shift in the distribution after treatment in the regions (i.e. those with high mortality).

According to (6), the counterfactual is defined by the share of conscripts in each interval before and after the treatment in regions with high versus low malaria mortality rates. The system of equations (6) is hence suitable to estimate the changes in the distribution of height through estimates of the movement of the share of conscripts falling in given intervals.

In order to obtain more efficient results, system (6) is estimated though SUR methodology.

We start our analysis with an estimation of the baseline system of equations in (6), the results of which are reported in Table 7. As stated in the previous section, our parameters of interest are those associated with the interaction $high_{hi} \times post_{ht}$, measuring the effect of eradication across height intervals. As documented in the table, the coefficients are significant at 99% across categories, with the sole exception of the interval 174-179 cm. Interestingly, lower categories have negative coefficients, indicating a decreasing share of conscripts falling in those height intervals. The interval 150-154 cm presents a reduction of about 2.8%, whereas the largest drop is in the 155-159 cm interval, with a contraction of 6.3%. Intervals 165-169 cm and 170-174 cm increase by 7.2% and 8.6% respectively. Interestingly enough, the coefficient associated with the highest category, i.e. those taller than 180 cm, has a negative and significant coefficient, indicating a considerable contraction in the domain of the distribution function. The Appendix reports several robustness checks confirming the results.

Overall, our results point to a robust change in the distribution of height of Italian conscripts due to the eradication of endemic malaria with the tails of that distribution becoming thinner; this is especially true of the left one, exhibiting a shift of population towards higher height intervals.

7 Conclusion

An increasing body of social science studies rely on the 'fetal origins hypothesis', according to which in utero, infant, and childhood conditions and shocks can considerably influence adult outcomes. Adult outcomes, in their turn, determine the accumulation and the quality of the human capital of regions and countries, thus influencing economic development.

Table 7: Height distribution change (SUR estimates)

	Intervals							
	<150cm	150-154	155-159	160-164	165-169	170-174	175-179	>180cm
$High_{ir}$	0.820***	3.192***	8.664***	9.086***	-0.879**	-9.579***	-7.719***	-3.590***
	(0.0356)	(0.127)	(0.340)	(0.496)	(0.372)	(0.404)	(0.464)	(0.415)
$Post_{it}$	-0.252***	-1.132***	-4.919***	-11.00***	-9.615***	3.733***	11.13***	12.04***
	(0.0302)	(0.108)	(0.289)	(0.422)	(0.316)	(0.343)	(0.394)	(0.353)
$High_{ir} \times Post_{it}$	-0.736***	-2.798***	-6.320***	-3.023***	7.181***	8.639***	1.282*	-4.214***
	(0.0536)	(0.191)	(0.512)	(0.748)	(0.561)	(0.609)	(0.699)	(0.626)
Constant	0.313***	1.373***	6.469***	18.30***	29.09***	25.51***	13.58***	5.363***
	(0.0195)	(0.0694)	(0.186)	(0.272)	(0.204)	(0.221)	(0.254)	(0.227)
R^2	0.477	0.536	0.604	0.619	0.507	0.521	0.626	0.630
# of Obs.	976	976	976	976	976	976	976	976

Notes: The share of conscripts falling in the interval is the dependent variable for each regression. Significance: ***: p<0.01; **: p<0.05 *: p<0.1.

With the present paper I add to this body of literature by analyzing the experience of Italy.

I particularly focused on the last twelve years of the nineteenth century, examining whether the conscripts born in regions and years with high malaria incidence were on average significantly shorter as adults than those born in years when the incidence was relatively lower.

I used aggregate data at regional level, and found, through both OLS and IV regression estimates, that exposure to malaria during the year of birth (in utero or postnatal exposure according to the quarter of birth) does not significantly influence mean adult height. However, the average level of exposure experienced by conscripts during the first three to five years of life does have a causal and negative effect on height. My estimates suggest that if the South had had the same malaria mortality as the North of Italy, then the difference in conscripts' height would have been almost nonexistent.

Furthermore, by considering cohorts of conscripts born before and after the eradication of malaria in Italian regions, I documented a shift in the distribution of height with an increase in its average and a convergence towards the interval of 164-174 centimeters. This result is suggestive of the redistributive impact of malaria eradication, although some further work on the topic is still needed. The results in the specific case of malaria in Italy point to intra- and interregional redistributive effects of policies addressing issues related to geography of regions. Furthermore, the evidence presented in this study suggests that place-based policies might successfully address spatial health inequality.

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A Appendix: Robustness checks

To test the robustness of the baseline specification results (3), I have run several checks. Firstly, the term $high_{ir} \times post_{it}$ can be confounded with an eventual process of height convergence across cohorts and regions because of a general improvement in living standards. In Table A.1, I present estimates of a version of (3) in which regional GDP per capita is used as a further regressor (the time series are taken from Daniele, Malanima 2007 and are in constant 2002 prices). Notably, all estimates maintain their signs and significance, although the coefficients associated with higher intervals have slightly lower point values with respect to the ones reported in Table 2.

Table A.1: Height distribution change – Robustness checks (SUR estimates)

	Intervals							
	<150cm	150-154	155-159	160-164	165-169	170-174	175-179	>180cm
$High_{ir}$	0.769***	2.915***	7.440***	6.750***	-2.314***	-8.405***	-5.489***	-1.674***
	(0.0388)	(0.137)	(0.340)	(0.427)	(0.291)	(0.420)	(0.373)	(0.255)
$Post_{it}$	-0.160***	-0.705***	-2.885***	-6.157***	-4.587***	3.207***	5.987***	5.289***
	(0.044)	(0.155)	(0.386)	(0.484)	(0.330)	(0.477)	(0.423)	(0.289)
$High_{ir} \times Post_{it}$	-0.736***	-2.771***	-6.290***	-3.427***	6.004***	7.935***	1.910***	-2.613***
	(0.058)	(0.204)	(0.508)	(0.638)	(0.434)	(0.627)	(0.557)	(0.381)
GDP per capita	-0.001***	-0.001***	-0.002***	-0.00511***	-0.004***	0.001***	0.005***	0.006***
	(2.44e-05)	(8.59e-05)	(0.001)	(0.001)	(0.001)	(0.001)	(0.001)	(0.001)
Constant	0.420***	1.926***	8.949***	23.34***	32.87***	23.59***	8.602***	0.313
	(0.029)	(0.102)	(0.254)	(0.319)	(0.217)	(0.314)	(0.279)	(0.191)
R^2	0.487	0.554	0.662	0.749	0.707	0.561	0.780	0.863
# of Obs.	976	976	976	976	976	976	976	976

Notes: The share of conscripts falling in the interval is the dependent variable for each regression Significance: ***: $p<0.01$; **: $p<0.05$ *: $p<0.1$.

Table A.2: Height distribution change – Excluding treatment cohorts (SUR estimates)

	Intervals							
	<150cm	150-154	155-159	160-164	165-169	170-174	175-179	>180cm
$High_{ir}$	0.769***	2.915***	7.440***	6.750***	-2.314***	-8.405***	-5.489***	-1.674***
	(0.0388)	(0.137)	(0.340)	(0.427)	(0.291)	(0.420)	(0.373)	(0.255)
$Post_{it}$	-0.160***	-0.705***	-2.885***	-6.157***	-4.587***	3.207***	5.987***	5.289***
	(0.0440)	(0.155)	(0.386)	(0.484)	(0.330)	(0.477)	(0.423)	(0.289)
$High_{ir} \times Post_{it}$	-0.736***	-2.771***	-6.290***	-3.427***	6.004***	7.935***	1.910***	-2.613***
	(0.058)	(0.204)	(0.508)	(0.638)	(0.434)	(0.627)	(0.557)	(0.381)
GDP per capita	-0.001***	-0.001***	-0.002***	-0.005***	-0.004***	0.001***	0.005***	0.006***
	(2.44e-05)	(8.59e-05)	(0.001)	(0.001)	(0.001)	(0.001)	(0.001)	(0.001)
Constant	0.420***	1.926***	8.949***	23.34***	32.87***	23.59***	8.602***	0.313
	(0.029)	(0.102)	(0.254)	(0.319)	(0.217)	(0.314)	(0.279)	(0.191)
R^2	0.487	0.554	0.662	0.749	0.707	0.561	0.780	0.863
# of Obs.	854	854	854	854	854	854	854	854

Notes: The share of conscripts falling in the interval is the dependent variable for each regression. Cohorts of conscripts born between 1945 and 1950 are excluded. Significance: ***: p<0.01; **: p<0.05 *: p<0.1.

Table A.3: Height distribution change – Excluding treatment cohorts and testing for pre-existing trends (SUR estimates)

	Intervals							
	<150cm	150-154	155-159	160-164	165-169	170-174	175-179	>180cm
$High_{ir}$	0.610***	2.316***	5.773***	4.593***	-2.800***	-6.468***	-3.565***	-0.465*
	(0.0388)	(0.135)	(0.329)	(0.411)	(0.309)	(0.412)	(0.357)	(0.249)
$Post_{it}$	-0.241***	-1.008***	-3.729***	-7.250***	-4.834***	4.188***	6.961***	5.901***
	(0.0417)	(0.145)	(0.353)	(0.440)	(0.331)	(0.442)	(0.383)	(0.267)
$High_{ir} \times Post_{it}$	-0.724***	-2.726***	-6.165***	-3.264***	6.041***	7.789***	1.765***	-2.704***
	(0.0540)	(0.188)	(0.458)	(0.571)	(0.429)	(0.574)	(0.497)	(0.346)
GDP per capita	-3.15e-05	-0.001***	-0.001***	-0.0041***	-0.004***	0.001**	0.004***	0.005***
	(2.37e-05)	(8.25e-05)	(0.000)	(0.001)	(0.001)	(0.000)	(0.000)	(0.001)
Trend * $High_{ir}$	0.001***	0.001***	0.002***	0.002***	0.001***	-0.002***	-0.002***	-0.001***
	(1.65e-05)	(5.73e-05)	(0.001)	(0.001)	(0.000)	(0.000)	(0.001)	(0.001)
Constant	0.300***	1.474***	7.689***	21.71***	32.50***	25.05***	10.06***	1.227***
	(0.029)	(0.101)	(0.247)	(0.308)	(0.231)	(0.309)	(0.267)	(0.186)
R^2	0.554	0.620	0.725	0.798	0.713	0.633	0.825	0.887
# of Obs.	854	854	854	854	854	854	854	854

Notes: The share of conscripts falling in the interval is the dependent variable for each regression. Cohorts of conscripts born between 1945 and 1950 are excluded. Significance: ***: p<0.01; **: p<0.05 *: p<0.1.

Regression estimates in Tables A.2 and A.3 report estimates of functions in which the cohorts of individuals born between 1945 and 1950, i.e. during the treatment period, are included. Table A.2 reports estimates in which those cohorts are excluded, and it is quite surprising to see that there is no change in the magnitude of estimated parameters. Finally, the specification, the results of which are in Table A.3, considers a time trend specific to regions with high mortality (i.e. an interaction term between a time trend and height). It is important to note that, in this case, results also do not significantly change from my baseline specification.

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