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Socioeconomic Inequalities in Health. Evidence from Italy Before and During the SARS-CoV-2 Pandemic

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If systematic differences in health for different groups of people are avoidable by reasonable action, their existence is, quite simply, unfair.

Sir Marmot et al. (2008)

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Acknowledgments

What a crazy journey this has been. In this section, I would like to briefly thank the people who helped and supported me during this 4-year-long experience.

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Last, but never least, huge thanks to Serena. I never thought that it would be possible to find love during a PhD, but here we are. From complete stranger to fellow student, from fellow student to weird roomie, from weird roomie to now. I owe you much, and I really hope to be able to give you back all the love and support you gave me during the last year. Anywhere with you (but please, not Dresda).

As per tradition, I would like to conclude these acknowledgments by quoting a statistician much more famous than me.

> I hope to return all these favors someday. I will start by buying the first beer for anybody on this list, and the first three for anybody who should have been, but isn't.

Cheers to you all,

Luca

Introduction

In 2015, all United Nations Member States adopted the 2030 Agenda for Sustainable Development (United Nations, 2018). The resolution outlines 17 goals and 169 targets which aim to reduce poverty, promote peace, and protect people's rights and the environment. The third goal of the 2030 Agenda for Sustainable Development is to "Ensure healthy lives and promote well-being for all at all ages", highlighting the need to reduce health differentials between and within countries. Although the goal does not explicitly mention health inequalities, many of its targets can be reached only by tackling the differentials in health that disadvantage the poorest countries and the lowest strata of each country's population. Reducing mortality from non-communicable diseases and suicides (3.4), preventing drug and alcohol use (3.5), halving deaths and injuries from car accidents (3.6), achieving universal health coverage (3.8), and reducing tobacco use (3.a) are all targets that would significantly improve the health of people in lower socioeconomic positions either directly or indirectly if achieved. In Europe, individuals with lower socioeconomic positions are the ones suffering the most from non-communicable diseases (Lübker and Murtin, 2022), suicides (Lorant et al., 2018), alcohol and tobacco use (Loring, 2014b,a), car accidents (Borrell et al., 2005; Mőller et al., 2021), and financial hardship after using health services (WHO Regional Office for Europe, 2022). In 2017, the WHO (2017) Regional Office of Europe proposed a roadmap to achieve the goals outlined in the 2030 Agenda for Sustainable Development, based on further developing the policy for health and well-being "Health 2020". First approved in 2012, Health

2020 expressly aimed at reducing health inequalities across Europe, and in 2013 its implementation was defined as "the fundamental top-priority challenge for the Region" (WHO Regional Office for Europe, 2013).

Focusing on health differentials between different socioeconomic groups is important, as outlined by Woodward and Kawachi (2000). In their work, they argue that: 1) inequalities are unfair; 2) inequalities affect everyone; 3) inequalities are largely avoidable; 4) cost-effective interventions exist. With these four arguments in mind, in this thesis I try to understand, describe and find evidence about health differentials in Italy before and during the COVID-19 pandemic started in 2020. This thesis is composed of an introductory chapter and three chapters that will focus on different facets of health inequalities. The first section will give an overview of the existing literature on the topic, describing previous methodologies, definitions, and findings about inequalities in Europe and Italy. It will end by introducing the research questions I answered in the subsequent chapters. The second chapter brings new evidence about health inequalities in Rome before the COVID-19 pandemic, focusing on both individual and area-level differences. The third section will show how different levels of economic disadvantage shaped the transmission of the SARS-CoV-2 virus, in a period of differential restrictions. The fourth chapter will disentangle the effect of area-level deprivation and pre-existent chronic conditions on COVID-19 mortality. I will end the thesis with a short conclusion, discussing my main findings and their implications.

Chapter 1

An overview of health inequalities

1.1 Definitions of health and socioeconomic position

The concept of "health" is instinctively clear to everyone. However, its definition is actually quite complicated. In 1948, the WHO defined health as "a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity" (WHO, 1948). Although still used by the WHO, this multidimensional definition is difficult to operationalize, and many researchers proposed other definitions (McCartney et al., 2019). Some definitions depict health as something that people experience or as the ability to participate in society, as a dichotomy or as a continuum, at the individual or at the population level. No single or best definition exists, and different facets of health could be assessed in research.

The concepts of "health inequalities" (or differentials) and "health inequities" (or disparities) derive from the concept of health. While the first generally refers to mere (mathematical) differences in health outcomes, the latter incorporates a moral judgement about the fairness of these differences (Kawachi, 2002). In these terms, differences in health between the young and the elderly in a population can be labeled as "inequalities" but not as "iniquities": these differences are not unfair as the aging process is not modifiable and will affect everyone with the passage of time. On the other hand, differences in health between those in the highest and the lowest income deciles are both inequalities and iniquities because they are generated by an unequal distribution of earnings, rather than by an uncontrollable biological process, and therefore unfair. However, the term "health inequalities" is used differently around the world, and often an unfair differential is meant (McCartney et al., 2019). As shown by McCartney et al. (2019), other definitions of health inequalities/iniquities have been proposed in the literature, but they are more homogeneous and similar than those concerning health.

It is also necessary to address the measures and the concept of socioeconomic position. In this thesis, when talking about the concept rather than the measure, I will use the term socioeconomic "position" (SEP) instead of "status" (SES) or "social class". Although similar, the three terms differ slightly in meaning. Both socioeconomic position and status refer to all economic and social factors that shape the position held by an individual or a group in a society. The two terms are often used interchangeably, but it is preferable to use "socioeconomic position" instead "socioeconomic status" (Krieger et al., 1997; Krieger, 2002). Semantically, "position" is a more neutral and comprehensive word, whereas "status" emphasizes the importance of prestige or rank over the resources owned by the individual. Finally, the term "social class" refers to the position of the individual within structured economic groups. These groups only exist in relationship to each other and co-define each other, so the social class of an individual is not based on the individual's characteristics but on his relationship to his and others' work.

There are various indicators of socioeconomic position, each describing different aspects that determine an individual's position in a society (Galobardes et al., 2006a,b). While area-level measures indicate the available opportunities in terms of services, social networks, and describe the context in which an individual lives, the individual-level measures depict knowledge, social capital, and resources owned by the individual.

In this thesis, health will be measured through the presence or absence of chronic conditions, mortality, and the infectivity rate. Although I use various measures of health, many others were necessarily neglected, such as self-rated health, physical ability, body mass index, or emotional health, among others. The measures of socioeconomic position used in this thesis are heterogeneous. I use an individual-level measure, educational attainment, and several area-level measures: the average real estate price in the neighborhood, the share of people with a yearly income lower than 10,000€, and a composite deprivation index of the census block of residence. The measures were chosen with regard to the purpose of each analysis and/or the availability of data. Although my analyses will hardly imply causality between socioeconomic position and health, I will often refer to inequalities as avoidable and unjust differences in health status or mortality. It should be noted that an inverse causal pathway going from health to socioeconomic position is also plausible: those with worse health could have difficulties reaching higher educational levels, therefore being hired in low-paid positions, and being relegated to cheaper, underserved neighborhoods. Hoffmann et al. (2018) found that in early adulthood the effect of socioeconomic position on health was similar to the inverse effect going from health to socioeconomic position. The importance of the first path over the second increased with age, when older individuals have a relatively stable socioeconomic position that can be hardly influenced by their health status. However, the authors pointed out two important factors: 1) Both directions of the association between socioeconomic position and health are unfair; 2) throughout the life course, socioeconomic position and health are strongly associated with their own previous status, with socioeconomic position having a stronger association with itself than health. The first point is self-explicative: a fair social system would prevent both the effect of socioeconomic position on health, avoiding disparities between people with different resources, and the effect of health on socioeconomic position, making it possible for everyone to have the same opportunities. The second point is more subtle. If socioeconomic position is strongly associated with its past levels, there is small room for other factors to change its course, including health.

1.2 Health inequalities in Europe

Inequalities in health exist both between and within countries, and this is true in Europe as in the rest of the world (Lübker and Murtin, 2022; Marmot et al., 2012; Murtin et al., 2017). In terms of mortality and inequalities, Europe can be divided into roughly homogeneous macro-regions (Mackenbach et al., 2018). While Eastern Europe has high mortality rates and high inequalities ("the Eastern disaster"), Western, Northern, and Southern Europe have low mortality rates and low inequalities. Southern countries have the lowest inequalities in health despite not being as egalitarian as Nordic countries, a phenomenon termed "the Southern miracle" and "the Nordic paradox" (Mackenbach, 2020).

As described by Mackenbach (2019), the mortality trends of the macro-regions have historically been very different. In the first half of the 20th century, Western and Northern Europe benefited from lower infant and communicable disease mortality compared to Southern and Eastern Europe. Northern and Western European countries were generally more industrialized and with higher levels of literacy than the Southern and Eastern regions and at the beginning of the 1900s, they were also forerunners in increasing life expectancy and reducing mortality. However, around the middle of the century, Mediterranean countries eliminated infectious diseases and reduced infant mortality at the levels of top-performing countries. At the same time, Southern Europe benefited from lower cardiovascular mortality because of the protective effect of the Mediterranean diet and a delay in the diffusion of smoking. This combination brought life expectancy in Southern European countries to the highest levels worldwide at the end of the 20th century. Eastern Europe, on the other hand, had a more troubled path. Under the communist regimes, there were first great reductions in mortality driven by the successful control of communicable diseases. However, due to the underfunding and lack of renovation of the healthcare system, in the second half of 1900s, improvements in health lagged behind those of the rest of Europe. Then, at the end of the century and especially after the dissolution of the Soviet Union, life expectancy started plateauing or even decreasing. The most disadvantaged strata of the population in particular faced a rapid increase in mortality due to the disruptive political and economic changes. On the contrary, absolute within-country inequalities in mortality declined in most other European countries between the 1990s and the 2010s, up to magnitudes of -25% or -35% for nations like Spain or England and Wales. At the same time, relative inequalities increased significantly (up to 25%) even in the notoriously equal Scandinavian countries (Mackenbach et al., 2016, 2019). This opposite trend was driven by an overall decrease in mortality for both men and women that was faster for higher than lower socioeconomic groups. Between and within inequalities interact to create a complex geography. As an example, in the 2010s a low-educated Czech man of 25 years of age had about 45 years of life expectancy, while his Italian peer had 55 years. If the two men had been highly educated, their remaining life expectancy at 25 would have instead been of 53 and 60 years respectively (Lübker and Murtin, 2022). Inequalities are generally lower for females than for males. In fact, while there is an 8-year educational difference in life expectancy for Czech males and a 5-year difference for Italian males, females have differentials of 6 (58 and 52 years) and 3 years (63 and 60 years) respectively. While these patterns are disparate, their underlying causes are not. Mackenbach et al. (2017) identified smoking, alcohol consumption, and structural factors as the main drivers of differences in mortality both between and within countries. Popham et al. (2013) emphasized the importance of structural factors, attributing differences in health to differences in the healthcare systems among countries, with Eastern European and Ex-Soviet welfare states consistently showing both the highest mortality and the highest inequalities. Mackenbach et al. (2015) found that mortality inequalities in Europe are driven by inequalities in preventable causes, rather than by non-preventable causes, with mortality preventable through behavioral changes being particularly high in Eastern European countries.

Britain has a long, probably the longest, tradition of studies, reports, and policies about mortality inequalities, which needs to be addressed. The first estimates of mortality rates broken down by occupation can be traced back to the census of 1851. However, research interest and concerns about health inequalities started increasing after the publication of the so-called "Black Report" in August 1980 (Department of Health and Social Security, 1980; Macintyre, 1997). This report was drafted by a working group on inequalities in health chaired by Sir Douglas Black and set up by the Labour government of the United Kingdom (UK) in 1977. The working group analyzed differences in mortality and healthcare utilization between 5 social classes (I = Professional to V = Unskilled) using data from England and Wales. In their final report, they showed higher all-cause and cause-specific mortality rates at every age and lower use of preventive services for lower social classes. This is illustrated in Table 2.1, where I show age-standardized mortality rates for men aged 15-64 from England and Wales in 1951, 1961, and 1971, reproducing table 3.2 of the Black Report (Department of Health and Social Security, 1980). The working group also produced 37 recommendations to tackle the observed mortality gaps emphasizing the importance of lowering poverty during the ante-natal, post-natal, and infancy periods. When the report was released, it received a cold reception from the Conservative government of Margaret Thatcher: reportedly, only 260 copies were printed and there was no press release (Smith et al., 1998). As stated by Macintyre (1997), the results showed in the Black report were not completely unexpected. Maybe, the fame of the report was generated more by the treatment it received from the UK government of the time than by its results. However, it became a key study in the field and its grasp on the scientific community is underlined by editorials, publications, and complete journal issues made in its honor 10 (Smith et al., 1990; Strong, 1990; Morris, 1990) and 25 years (Sim and Mackie, 2006) after its release.

After the Black report, the Whitehall studies brought new evidence about health inequalities in Britain. First between 1967 and 1970 (Whitehall I) and then from 1985 to 1988 (Whitehall II), 18 and 10 thousand civil servants respectively received a health screening and were followed until their death (Reid et al., 1974; Marmot et al.,

Table 1.1. Age-standardized death rate per 100,000 living at ages 15-64, replica of Table 3.2 from the Black Report (Department of Health and Social Security, 1980)

Occupational Class	1951	1961	1971
I Professional	103	82	79
II Managerial	108	87	83
III Skilled manual and non manual	116	106	103
IV Partly skilled	119	108	113
V Unskilled	137	134	123
Ratio V/I	1.33	1.63	1.56

1991). Even in this selected group of individuals[1], people with lower employment grades were found to have more unhealthy habits and to experience higher mortality and morbidity rates than those with higher grades in both cohorts (Marmot et al., 1984, 1991). When the authors accounted for all observed risk factors, mortality was twice as high for individuals in the lowest employment grade than for those in the highest, highlighting the existence of inequalities beyond the mere distribution of unhealthy habits and/or pre-existent morbidity.

Since the second Whitehall study, every 10 years an independent review summarizes and updates the evidence, although substantial health differentials were consistently found over the years. In 1998, the Acheson report showed that Britain had experienced an overall improvement in health. However, those with the lowest social class had improved the least, resulting in a wider health gap (Acheson et al., 1998). The report also gave 39 sets of recommendations that found a favorable reception from Blair's Labour Government of the time. The priorities were similar to those set two decades before in the Black report: 1) reducing poverty in families with children; 2) evaluating health policies for their impact on health inequalities; 3) reducing income inequalities and improving the living standards of poorer households. The 13-year-long Labour Government of the time programmed and then implemented many policies addressing these issues (Macintyre, 1999; Mackenbach, 2010). Despite the favorable political climate, however, the independent review of 2008 chaired by Sir Michael Marmot reported little to no change in health inequalities, showing

[1] Quoting, "These men are all in stable, sedentary jobs in one location (London), and are not exposed to industrial hazards." (Marmot et al., 1984)

the failure of the policies of the previous decade (Mackenbach, 2010; Department of Health, 2010). Reportedly, the interventions were ineffective mainly because of the inaccurate definition of the targets, the neglect of the background causes of inequalities, and the failed delivery of the policies themselves (Mackenbach, 2010). Nevertheless, what would have happened to inequalities without these interventions remains an open question. The last report released in 2018 evidenced that inequalities in health further increased in Britain during the 2010s (Marmot et al., 2020; Marmot, 2020). The causes of this deterioration probably lay in the austerity programs implemented after the Great Recession, which cut public expenditure, together with the increasing wealth inequalities.

1.3 Health inequalities in Italy

Like other Southern European countries, Italy has low levels of health inequalities compared to other parts of Europe (Marmot et al., 2012; Murtin et al., 2017; Mackenbach et al., 2016, 2019). The presence of low inequalities is attributed to the similarity in behaviors between higher and lower socioeconomic groups (Mackenbach et al., 2017). Nevertheless, differentials in mortality are still visible in Italy (Petrelli et al., 2019). Between 2012 and 2014, the mortality of Italian men with low and medium educational attainment was 35% and 18% higher, respectively, when compared to graduates. Females had lower inequalities: women with low and medium educational levels had respectively 24% and 12% higher mortality than those with a high level of education. Geographical differences are also present for both sexes at age 30, with longer life expectancies in North-eastern and Central Italy than in North-western and Southern regions, as shown in Figure 1.1. Health inequalities also exist within local areas as lower-educated individuals suffer from higher mortality in every region, with particularly marked differences for men (Petrelli et al., 2019). The proportions of avoidable death attributable to differences in educational level vary between 15-25% for males in most regions, while it is limited to 5-15% for females.

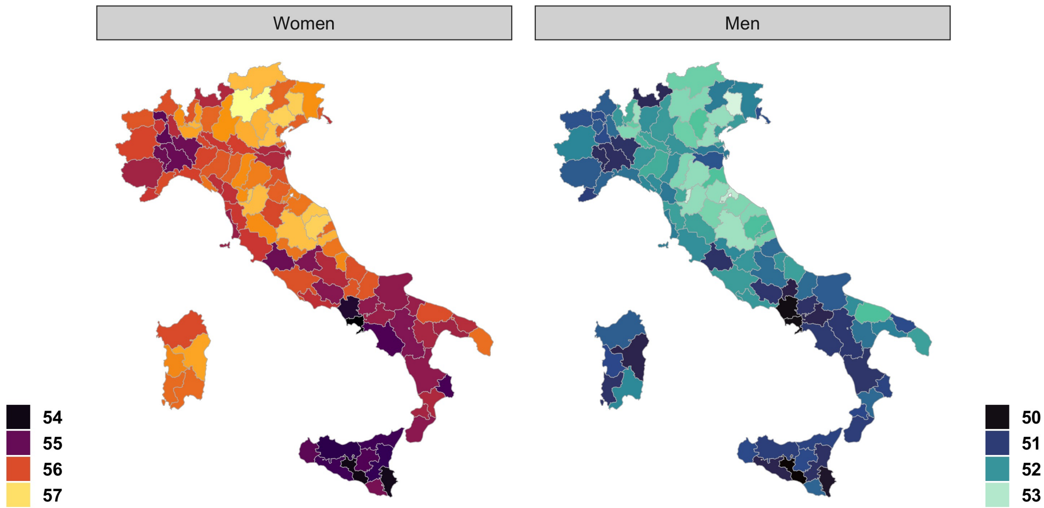

Figure 1.1. Life expectancy at 30 years for Women and Men by province in Italy. 2019 data from Istituto Nazionale di Statistica (2013).

In Italy, much of the research about health and inequalities is based on metropolitan or regional longitudinal studies. These studies link information about residents from the censuses with municipal, mortality, and hospital discharge registries. The oldest metropolitan study is based in Turin, which retrospectively traces individuals back to the census of 1971 up to the latest one in 2011, gathering 40 years of demographic and health data. A report in 2017 showed that all residents of Turin had an overall health improvement during this period thanks to a decline in cardiovascular and preventable mortality (Costa et al., 2017). This reduction in mortality produced a reduction of inequalities for females and a small increase of inequalities in males due to a faster reduction for higher-educated men. Differences in health and mortality were also related to the neighborhood, the type of employment, and the income, always disadvantaging the lowest socioeconomic positions. More deprived areas located in the North of the city were consistently affected by higher mortality compared to the richer Southern neighborhoods, managers had longer lives than employees, and those who were born into the richest families had up to 7 years higher life expectancies than those born in the poorest.

Similarly, a 2022 report about health inequalities in the Lazio Region found health differentials between higher and lower socioeconomic positions (Cesaroni and Davoli, 2022). Inequalities existed when considering overall and cause-specific mortality, the prevalence of most chronic conditions, as well as unhealthy habits. While overall mortality was 1.3 and 1.2 times higher for low- than high-educated males and females, cause-specific mortality showed different patterns. Inequalities were found for several cause-specific deaths such as cancer, cardiovascular, and respiratory diseases for males. In contrast, females showed similar cancer mortality through educational levels and more than two-fold mortality due to diabetes, disadvantaging those with low educational attainment. Equality in cancer mortality was attributed to more homogeneous smoking habits across socioeconomic strata, and to older-age fertility of more educated women, which is a risk factor for breast cancer. Chronic conditions and multimorbidity were always more frequent in individuals with lower socioeconomic positions regardless of sex. The higher shares of chronic diseases in those with low educational attainment were also reflected in the higher intake of drugs at every age. All of these adverse health outcomes can be partly traced back to inequalities in risky habits, such as smoking, alcohol consumption, sedentary lifestyle, and diet. Risky habits are highly associated with the socioeconomic position of the parents and are developed early in life. Young adults with parents with a university degree were less likely to be smokers, alcohol consumers, overweight or obese, and to adopt a sedentary lifestyle.

Rome is the largest municipality in Italy for extension, and Roman residents roughly account for half of the residents of the whole Lazio Region. Unsurprisingly, inequalities also exist in Rome and are similar to those described for the wider Region. Specifically, a study found widening inequalities in mortality from 2006 to 2017 in both men and women (Badaloni et al., 2020). At the beginning of the study period, those with low educational attainment had a life expectancy at birth of 76.8 years on average, which increased to 78.3 by 2017. At the same time, highly educated individuals passed from 80.2 to 82.2 years, widening inequalities from 3.4 to 3.9 years. A similar pattern was found for women, although differences in life expectancy increased from 1.8 to 2.2 years (lower educated: 82.4 to 83.2, highly educated 84.2 to 85.4). The study also found geographical differences of up to 3 years for men and 2.2 years for women. Rome is well-known to be geographically unequal. The city is surrounded by the Grande Raccordo Anulare ("Great Ring Junction") which has a circumference of 68.2km and an average radius of 11km, separating the city center from the periphery. As shown in Figure 1.2, the city center has a richer cultural offer with more services per capita (libraries, cinemas, theaters), is well served by public transports, and has residents with higher educational attainment. All these disparities are summarized by one simple indicator: the average real estate price in the neighborhood, which is in turn strongly associated with mortality and health. Gentrification and social exclusion are evident from the maps where is always clear what is inside and what is outside, what is the center and what is the periphery. Those who live in the cheapest neighborhoods have up to 22% more risk of all cause-mortality independently of education than those who live in the most expensive neighborhoods (Cesaroni et al., 2020).

Other than geographical and educational inequalities in health, Rome also has diverse mortality by work type (Paglione et al., 2020) and type of contract (Nardi et al., 2022). Paglione et al. (2020) showed that non-specialized manual workers have 68% more risk of all-cause mortality than high-qualified non-manual workers, 56% higher cancer mortality, and more than twice the risk to die from accidents. Instead, Nardi et al. (2022) found a greater all-cause mortality risk for men with temporary contracts compared to those with permanent contracts working in the industry, construction, and social services sectors.

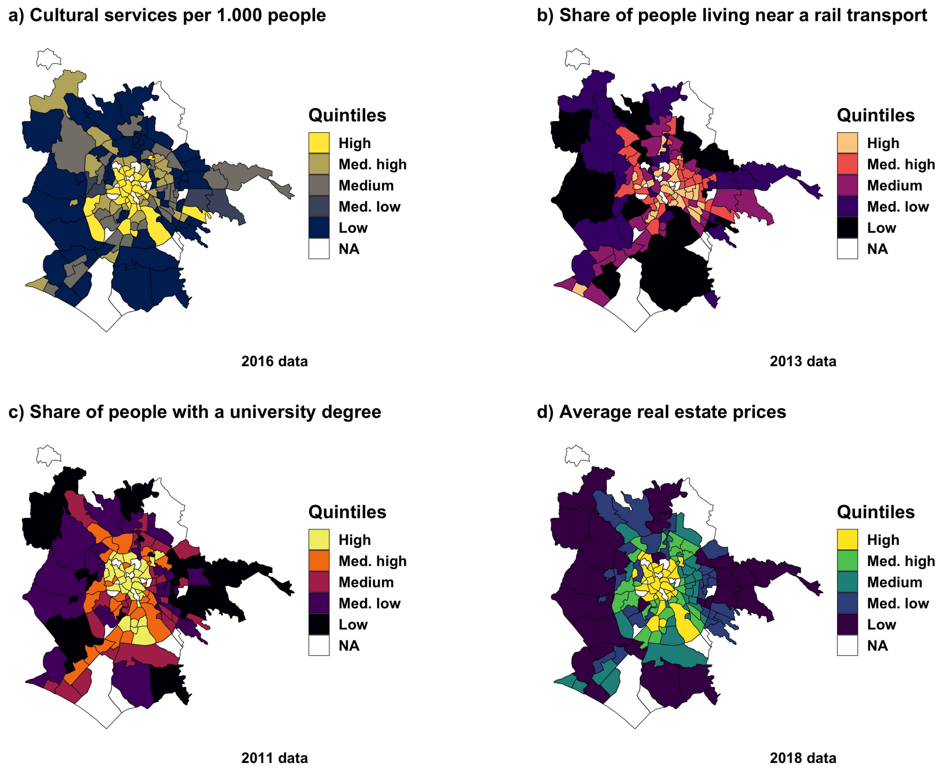

Figure 1.2. Differences between city center and periphery in Rome: a) Cinemas, theaters, and libraries per thousand people. b) Percentage of residents living within 10-minute walk from a rail transport. c) Percentage of people aged 20 or more with a bachelor's degree or higher. d) Average €/m2 real estate prices. All data from Mapparoma Lelo et al. (2019). NA = Non-residential Areas.

1.4 The SARS-CoV-2 pandemic

At the end of 2019, an outbreak of pneumonia from unknown causes in the city of Wuhan, China, raised the attention of the scientific community all around the world (Wang et al., 2020). The pneumonia cases were at first clustered around the seafood market of Wuhan City, but then rapidly spread to Thailand, the USA, Italy, and the whole world. The novel coronavirus named SARS-CoV-2 and its related coronavirus disease, COVID-19, are responsible for an estimated 6.5 million deaths worldwide (approaching 7 at the time of writing, WHO 2020). Soon became clear that those at higher risk of dying from COVID-19 were the males, the elderly, and those with chronic conditions (Acuti Martellucci et al., 2020). Males had almost twice the risk of dying than females, those older than 50 had a 15-fold higher risk compared to those younger than 50, and several chronic conditions such as diabetes, hypertension, and respiratory diseases, roughly doubled the mortality (Biswas et al., 2021). Despite all the containment measures implemented world-wide, the mortality shock produced by COVID-19 was visible in many countries as a loss of life expectancies, which were brought back to levels observed in 2015 (Aburto et al., 2022). The greatest reductions in health among the countries in the study were observed in the United States of America (USA) and Eastern Europe. Countries in Western and Southern Europe still experienced single-year losses in life expectancies comparable to those of the Second World War. Only Nordic European countries avoided increases in mortality during 2020. Many countries continued to experience this mortality shock also in 2021 (Schöley et al., 2022). The USA and countries in Eastern Europe experienced further losses in life expectancy, while Western and Southern Europe countries partially bounced back but without being able to reach pre-pandemic levels of life expectancy.

After an initial period of rhetoric about the fairness of the pandemic, under the motto “we are all in this together”, it became clear that the virus was hitting the lower socioeconomic groups the hardest (WHO, 2021). Poorer people, migrants, the homeless, and low-paid essential workers were among those most affected by the adverse outcomes of COVID-19. The social factors characterizing these groups were imposed mobility for essential workers, crowded housing, and a general lack of social protection. Some authors started using the term “syndemic pandemic” to describe the simultaneous raging pandemics of COVID-19, chronic diseases, and socioeconomic inequalities, each affecting the same disadvantaged strata of the populations (Bambra et al., 2020). Moreover, the pandemic increased pre-existent economic inequalities increasing the wealth of the rich and the difficulties in meeting basing needs for the poor (Wright et al., 2020b; Adams-Prassl et al., 2020).

1.5 Thesis structure

The main goal of this Ph.D. thesis is to further analyze inequalities in health found in Italy, with a focus on the ongoing SARS-CoV-2 pandemic. Specifically, I aim to answer the following questions:

1. Are individual and contextual socioeconomic positions independently associated with health status?
2. Is socioeconomic position associated with survival when accounting for baseline health status?
3. Was the effect of the restrictions implemented to mitigate the spread of SARS-CoV-2 equal between provinces with different socioeconomic levels?
4. How much do inequalities in chronic conditions drive the inequalities in COVID-19 mortality?

The first two questions are answered in Chapter 2, the third point is analyzed in Chapter 3, and the fourth question is tackled in Chapter 4. All studies were made in collaboration with the Department of Epidemiology of the Regional Health Service (ASL Roma 1), specifically with the multispecialty group "Health Status of the Population", and Dr. Giulia Cesaroni who was my external supervisor.

Chapter 2 answers the first two questions using data from the Rome Longitudinal Study, and from the mortality, and the co-payment exemption registries. I used logistic regression models to analyze the association between individual (educational attainment) and contextual socioeconomic positions (neighborhood real estate price quintiles) with the health status (presence/absence of one certified chronic condition). To investigate the role of the individual and contextual socioeconomic positions with 5-year survival, I used Accelerated Failure Time models. I found inequalities in baseline health and survival for females and males. Educational attainment had a clear negative gradient with the likelihood of having a chronic condition. Both medium and low-educated people, either females or males, were more likely to have at least one chronicity than their highly educated counterparts. Also, those living in the cheapest neighborhoods were almost twice as likely to have a chronic condition than people in the most affluent ones. The associations remained significant when both measures were considered in the same model, indicating an independent association of individual and contextual levels of socioeconomic positions with baseline health. Inequalities were also present in 5-year survival for both sexes. The higher the socioeconomic position, either individual or contextual, the longer the survival independently of the baseline health status. However, when considering both measures of socioeconomic position in the same model, only the association of educational attainment with survival remained statistically significant. The contents of Chapter 2 were developed in collaboration with Enrico Calandrini, Dr. Anna Maria Bargagli, Prof. Viviana Egidi (Sapienza University of Rome), Dr. Marina Davoli, Dr. Nera Agabiti, and Dr. Giulia Cesaroni. The results are reported in a paper published on BMJ Open in August 2022, see Dei Bardi et al. (2022b).

Chapter 3 analyzes the effect of the three-tier restriction system implemented in Italy since the second pandemic wave of November 2020, answering question 3. I used multilevel linear models with random intercepts on data at the province level gathered from the Ministry of Economy and Finance, the Civil Protection Department, the National Institute of Statistics, and the Italian Ministry of Health. Results show that higher levels of restrictions were more effective in reducing the spread of SARS-CoV-2, but every tier had statistically different effects on different levels of the province's economic disadvantage. While less strict tiers were more effective in more economically disadvantaged provinces, the highest level of restrictions (that is, a complete lockdown) was more effective in less economically disadvantaged provinces. The contents of Chapter 3 were made in collaboration with Dr. Anna Acampora, Dr. Laura Cacciani, Dr. Mirko Di Martino, Dr. Nera Agabiti, Dr. Marina Davoli, and Dr. Giulia Cesaroni. The results are reported in a published paper on BMC Public Health in February 2023, see Dei Bardi et al. (2023).

Chapter 4, answers question 4 using data from the Integrated Surveillance System of SARS-CoV-2 infections, the mortality registry, and the regional health information system. I implemented Generalized Linear Models to analyze the association between socioeconomic position and chronic conditions, and between chronic conditions and COVID-19 mortality. Then, I used the product method to estimate the mediation effect of chronic conditions on the effect of socioeconomic position on COVID-19 mortality. Results showed that more than 20% of inequalities in COVID-19 mortality can be explained by pre-existent inequalities in chronic conditions while, among single morbidities, hypertension and diabetes mediated around 10%. Other chronic conditions had either non-significant or small mediated proportions, as well as severity. The contents of Chapter 4 were made in collaboration with Enrico Calandrini, Dr. Nera Agabiti, Dr. Mirko Di Martino, and Dr. Giulia Cesaroni.

In all three studies composing the main chapters of this thesis, I was the first author. As such, I conceived and formalized the ideas, analyzed the data and the results. I was also responsible for writing the manuscripts and producing all figures. My coauthors and my external supervisor Dr. Giulia Cesaroni supported me through this work. They were responsible for the collection, linkage, anonymization, and acquisition of all micro-data, they helped me understand complex methodologies, especially in terms of the interpretation of the results, and gave insightful inputs for the data analysis.

Appendix A, B, and C report the supplementary material for chapters 2, 3, and 4 respectively.

Chapter 2

Socioeconomic inequalities in health status and survival: a cohort study in Rome

2.1 Background

Multiple factors such as sex, socioeconomic position, citizenship, and ethnicity are associated with differences in health. Some inequalities are unavoidable, others represent disparities in opportunities, knowledge, and resources that could be reduced or avoided by ad-hoc policies (Marmot et al., 2008; Marmot, 2005). Among the characteristic of a population, socioeconomic position (SEP) is often used to tackle avoidable disparities in health. Overall and cause-specific mortality appear to be inversely correlated with SEP (Paglione et al., 2020; Mackenbach et al., 2019; Murtin et al., 2017; Cesaroni et al., 2020), as well as the prevalence of different diseases (Bashinskaya et al., 2012; Gershon et al., 2012; Reiss, 2013), multimorbidity (Cassell et al., 2018; Barnett et al., 2012), and access to healthcare (Barone et al., 2009; Cylus and Papanicolas, 2015). There are several, valid, indicators of SEP (Galobardes et al., 2006a,b), each representing different facets of individual wealth, resources, and human capital. While personal SEP represents actual material or immaterial resources directly owned by the individual, contextual SEP expresses the reality and opportunities of the context in which the person lives. Both individual and contextual measures are found associated with health outcomes either used alone (Paglione et al., 2020; Cassell et al., 2018; Barnett et al., 2012), or used together (Cesaroni et al., 2020; Foraker et al., 2019; Ferré et al., 2014).

In Italy, there is a universal healthcare system, where healthcare is publicly funded and there is general access and comprehensive coverage under the National Health Service. All subjects have free access to hospital care, general practitioner visits, screening programs, and maternity care. However, all individuals contribute to payments for drugs (especially to brand-name drugs when a generic drug exists), to emergency room visits in absence of an emergency, and to outpatient care, both for specialist visits and diagnostic tests and procedures (Ferré et al., 2014). As in several other countries, there are cost-sharing exemptions for people economically disadvantaged established by the law 537/1993. Moreover, with the Ministerial Decree 329/1999, the National Health Service set up a co-payment exemption for people with chronic or rare diseases. This measure helps people to cover expenses for outpatient specialist services to monitor the disease and to prevent further aggravations. The recognition of the co-payment exemption right is obtained after a request to the local health unit of residence with a certificate, issued by a medical doctor from a public hospital, attesting the presence of the disease.

This study had two main goals. The first was to analyze the association between individual and contextual SEP with health status, as the presence of a chronic or rare condition from the Disease-Related Co-payment Exemptions Registry. The second goal was to investigate the role of (individual and contextual) SEP on survival, considering the baseline health status in a cohort of 1.8 million adults followed for five years.

2.2 Methods

Design, setting, and participants

In this study, we used a cross-sectional design to investigate the association between SEP and health status at baseline. Then, we implemented a cohort design taking into account the baseline health status to analyze the role of SEP on survival.

Rome is the largest Italian city, with a surface of 1,290 km^2 and a population of 2.5 million residents at the 2011 census. The Rome longitudinal study included the residents in Rome who filled in the 2011 census questionnaire. The census included several individual information, such as sex, age, achieved education, and residential census area. Through an anonymous identifier, the subjects enrolled were linked to the Municipal Registry database and the Regional Health Information System, which includes the Mortality Registry and the Disease-Related Co-payment Exemption Registry. The record-linkage procedures were performed under strict control to protect individual privacy. The Rome longitudinal study is part of the National Statistical Program 2019 and was approved by the Italian Data Protection Authority. The study excluded subjects without an identifier, the homeless, and those living in institutions (such as prisons, nursing homes, monasteries, or convents), overall, the 1.43% of the census population.

The interest in this study was to have both individual and contextual measures of SEP. Hence, we excluded residents in census areas located in non-residential neighborhoods and those with discording addresses in the census and the Municipal Registry database. This step excluded 2.35% of the census population. Finally, only Italian citizens aged 25-99 years at the census reference date (09 October 2011) were selected.

Variable of interest

We considered two different measures of socioeconomic position: the educational attainment achieved at the census date (individual SEP) and the quintiles of the distribution of neighborhood real estate prices (contextual SEP).

The individual SEP was categorized considering the differences between birth cohorts. The variable was defined as “Low” for compulsory education, i.e., primary education for individuals born before 1 January 1952 and lower secondary education for individuals born after. It was defined as “Medium” for degrees higher than compulsory education but lower than tertiary degrees. Finally, individual SEP was defined as “High” for tertiary education, i.e., bachelor’s, master’s, or Ph.D. degrees independently of the cohort.

The contextual SEP was obtained by assigning to all residents the average 2010 housing price (€/m^2) of the neighborhood, disseminated publicly by Lelo et al. (2019). Then, we calculated the quintiles of the housing price distribution weighted on the population, to have 20% of individuals under study in each quintile.

The number of chronic or rare conditions was derived from the Disease-Related Co-payment Exemptions Registry from 01 January 2008 to 09 October 2011. We used a binary variable indicating the presence of a chronic or rare condition to characterize the baseline health status of the population.

Age in complete years at the census date, categorized in 10-years age groups, and sex have also been included in the analyses.

Statistical analyses

For descriptive analyses, we used frequencies and graphical displays. To estimate the association between the presence of chronic or rare diseases (1 = one or more, 0 = none) with the measures of SEP, we implemented binary logistic regression models. Odds ratios (OR) and their 95% Confidence Intervals (95%CI) adjusted for age and stratified for sex have been estimated and reported along with those stratified by sex and adjusted for every other variable in the analysis.

Subjects were followed from the census reference day (09 October 2011) to the first event of censoring, that was, the date of emigration outside Rome, the 100$^{\text{th}}$ birthday, the date of death, or the 31 December 2016, whichever came first.

Accelerated Failure Time (AFT) models assuming Weibull distribution for the log-time have been used and shown, the results were reported in terms of Time Ratios (TR) along with 95%CI. Estimations of expansion (shrinkage) of times reported in the manuscript were adjusted for age and presence of chronicity, and stratified for sex, along with estimates stratified by sex and adjusted for every other variable in the study.

In all models, we analyzed significance trends across categories of both SEP using Wald tests. Also, all models were checked for multicollinearity through the estimation of Variance Inflation Factors (VIF). All analyses were performed using R 4.0 or higher (R Core Team, 2019).

Sensitivity analyses

As sensitivity analyses, we ran ordinal and non-proportional odds models using a three-category chronicity (0 - 1 - 2+) instead of the dichotomic variable as the response. we also implemented sensitivity analyses on survival models analyzing the lost at follow-up due to emigration using logistic models. Last, we ran AFT models using the three-category chronicity variable in place of the dichotomic variable. All sensitivity analyses are reported in Appendix A.

2.3 Results

Descriptive analysis

A total of 1,780,243 individuals, resulting from the above-mentioned selection, have been analyzed.

Table 2.1 shows the socio-demographic characteristics of the study population and the prevalence of chronic diseases. The population was mostly composed of females (54.2%), people aged between 45 and 54 years (19.5% of the female population, 21.2% of the male population), and individuals with medium educational level (45.8% of females, 47.9% of males). The percentage of people with at least one chronic

Table 2.1. Description of the study population by demographic characteristics, Socioeconomic Positions, and presence of Chronic or Rare Disease (CRD). Rome, 09 October 2011, 25-99 year-olds.

		FEMALES			MALES		
		N	%	CRD%	N	%	CRD%
total		964,284	100.0	22.6	815,959	100.0	20.5
age group	25-34	111,020	11.5	7.3	109,249	13.4	4.1
	35-44	183,215	19.0	11.4	168,718	20.7	6.8
	45-54	188,238	19.5	18.0	172,612	21.2	13.5
	55-64	161,308	16.7	29.2	139,744	17.1	27.0
	65-74	155,190	16.1	35.3	123,719	15.2	38.8
	75-84	117,525	12.2	34.8	80,142	9.8	43.4
	85-99	47,788	5.0	26.4	21,775	2.7	35.4
education	High	222,564	23.1	13.8	202,431	24.8	13.5
	Medium	441,904	45.8	22.5	390,909	47.9	21.7
	Low	299,816	31.1	29.4	222,619	27.3	24.9
real estate price	1 (highest)	194,493	20.2	18.5	153,399	18.8	17.2
	2	195,388	20.3	21.1	159,989	19.6	19.6
	3	198,106	20.5	24.1	165,548	20.3	21.9
	4	188,765	19.6	24.7	162,473	19.9	22.0
	5 (lowest)	187,532	19.4	24.9	174,550	21.4	21.6

condition increased with age, it was higher in females than in males and was inversely related to educational attainment and quintile of real estate prices.

The most common chronic conditions recognized for the co-payment exemption were hypertension, diabetes, and cancer. Although these conditions were in the top three for all educational levels, some differences in the prevalence were seen. In the low educated, hypertension was the most common cause of chronicity (9.9% of the low educated population) followed by diabetes (8.5%) and cancer (5.2%). In the highly educated, the main cause of disease was cancer (3.6% of the highly educated), followed by hypertension (2.9%) and diabetes (2.2%). The same pattern was found using the contextual SEP variable.

Figure 2.1 shows the percentage of individuals with chronic or rare diseases by age group, sex, and educational attainment. Although there was a clear increasing pattern over age as well as the differences between SEP categories in both sexes, the gap across levels of education was more marked for females than for males. It is possible to compare the proportion of subjects with at least one chronic condition by

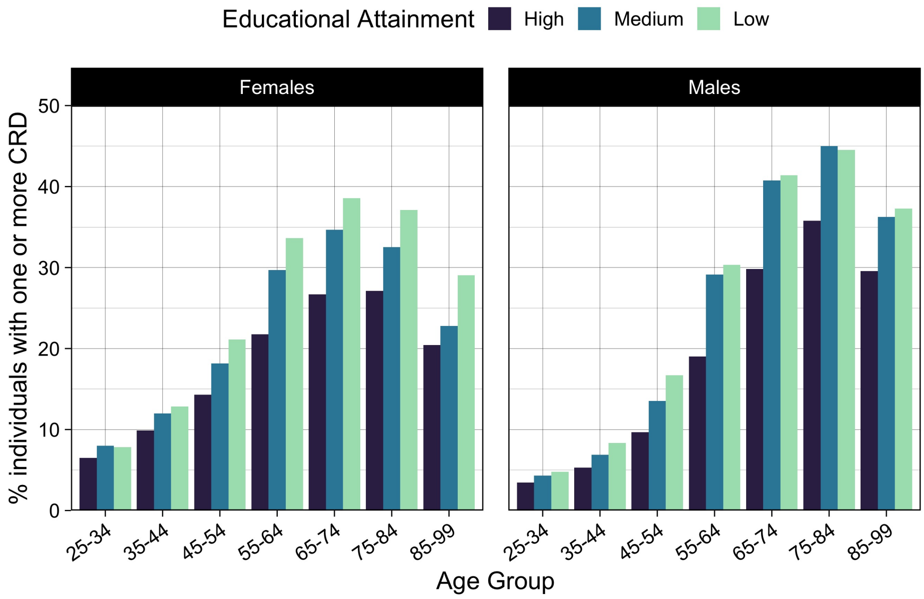

Figure 2.1. Percentage of individuals with Chronic or Rare Diseases (CRD) by age, sex, and educational attainment.

age and educational level. For example, the 22% of highly educated females in the age group 55-64 had at least one disease, while in the group of low educated, roughly the same proportion was reached in those aged 45-54 (21%). Similar patterns can be observed for the other sex: low educated males with 55-64 years had the same proportion of chronic conditions as highly educated individuals in the age group 65-74 (30%).

Figure 2.2 shows the percentage of individuals with chronic or rare diseases by age group, sex, and real estate price quintiles. The differences between the lowest and the highest contextual SEP increased steadily with increasing age group. Given a proportion of individuals affected by chronicity, in this figure is also possible to compare the differences in age group by SEP. Similar to Figure 2.1, the lowest SEP group aged 45-54 had a proportion of chronic conditions like those of the highest SEP in the age group 55-64 for both females (22% lowest, 21% highest) and males (17% lowest, 19% highest).

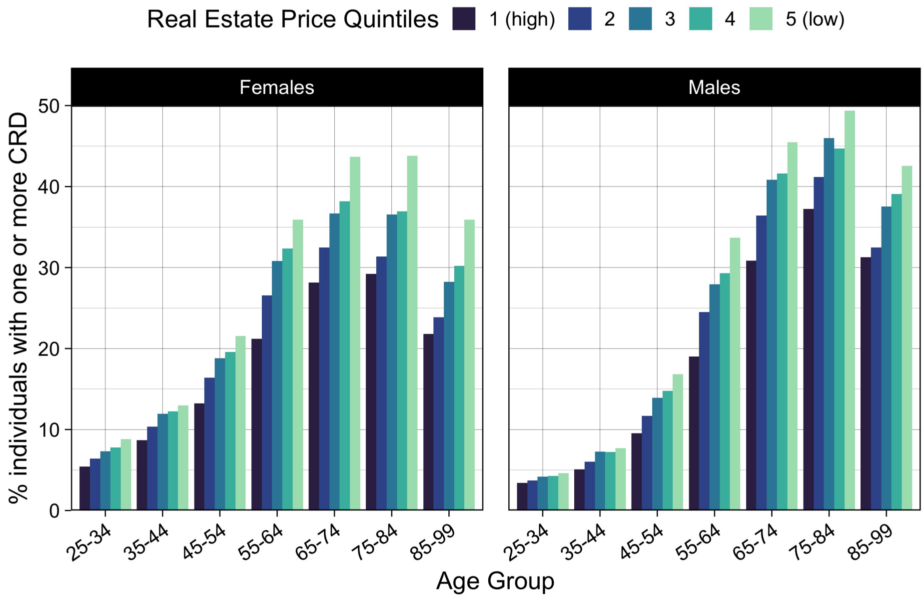

Figure 2.2. Percentage of individuals with Chronic or Rare Disease (CRD) by age, sex, and real estate price quintiles.

Cross-sectional analysis

Table 2.2 shows the results from logistic regression implemented to identify the association between the two measures of SEP and the presence of chronic or rare diseases on the census reference day. Age-adjusted and sex-stratified OR are reported with 95%CI. Educational attainment had a clear negative gradient, both medium and low educated people, either female or male, are shown as more likely to have at least one chronicity than the reference category of highly educated (low educated females: OR 1.61, 95%CI 1.59-1.64; low educated males: OR 1.67, 95%CI 1.64-1.70). It should be noted that OR for males with medium education was closer to OR for lower educated than females were. The contextual SEP showed a strong negative association with the response variable. Those living in the least expensive neighborhoods (fifth quintile) were almost twice as likely to have chronic conditions than people in the most affluent quintile (females OR 1.86, 95%CI 1.83-1.89; males OR 1.83, 95%CI 1.80-1.87).

The strength of the association for both individual and contextual SEP decreased

Table 2.2. Association between indicators of socioeconomic position and presence of Chronic or Rare Diseases, logistic models. Italian residents aged 25-99 years. Rome, 09 October 2011. Odds Ratios (OR) adjusted for age group and reported with their 95% Confidence Interval (95%CI).

		FEMALES (N= 964, 284)			**MALES** (N= 815, 959)		
		OR	**95%CI**		**OR**	**95%CI**	
age group	25-34	*ref.*	-	-	*ref.*	-	-
	35-44	1.63	1.59	1.67	1.70	1.64	1.76
	45-54	2.78	2.71	2.86	3.64	3.53	3.77
	55-64	5.24	5.11	5.37	8.61	8.33	8.89
	65-74	6.93	6.76	7.10	14.80	14.34	15.28
	75-84	6.76	6.59	6.94	17.85	17.27	18.45
	85-99	4.54	4.40	4.68	12.79	12.28	13.32
education	High	*ref.*	-	-	*ref.*	-	-
	Medium	1.35	1.33	1.37	1.54	1.52	1.57
	Low	1.61	1.59	1.64	1.67	1.64	1.70
		p-trend < 0.001			p-trend < 0.001		
real estate price	1 (highest)	*ref.*	-	-	*ref.*	-	-
	2	1.23	1.21	1.25	1.25	1.23	1.28
	3	1.49	1.47	1.51	1.52	1.49	1.54
	4	1.57	1.55	1.60	1.56	1.53	1.59
	5 (lowest)	1.86	1.83	1.89	1.83	1.80	1.87
		p-trend < 0.001			p-trend < 0.001		

when the complete model was considered, but all associations remained significant as well as the overall trends as shown in Table 2.3. The check for multicollinearity showed VIF always lower than 2.5 in every logistic model, indicating the absence of strong correlations among variables.

Results obtained from sensitivity analyses with ordinal models and non proportional odds models were very similar and never differed in meaning and trend from those obtained with logistic models. Ordinal models stratified by sex and adjusted by age group are reported in Table A.1, while Ordinal models stratified by sex and adjusted by every variable in the table are shown in Table A.2. Both tables can be found in Appendix A. Estimates from non proportional odds models stratified by sex and adjusted for every variable in the table are reported in Table A.3, in Appendix A.

Table 2.3. Association between indicators of socioeconomic position and presence of Chronic or Rare Diseases, logistic models. Italian residents aged 25-99 years. Rome, 09 October 2011. Odds Ratios (OR) adjusted for every other variable in the table and reported with their 95% Confidence Interval (95%CI).

		FEMALES (N= 964, 284)			MALES (N= 815, 959)		
		OR	**95%CI**		**OR**	**95%CI**	
age group	25-34	*ref.*	-	-	*ref.*	-	-
	35-44	1.61	1.56	1.65	1.69	1.63	1.75
	45-54	2.70	2.63	2.77	3.62	3.50	3.74
	55-64	5.11	4.98	5.24	8.68	8.40	8.96
	65-74	6.66	6.49	6.83	14.91	14.44	15.40
	75-84	6.41	6.24	6.58	17.88	17.29	18.48
	85-99	4.42	4.28	4.56	13.32	12.78	13.88
education	High	*ref.*	-	-	*ref.*	-	-
	Medium	1.23	1.22	1.25	1.40	1.38	1,42
	Low	1.36	1.33	1.38	1.43	1.40	1,46
		p-trend < 0.001			p-trend < 0.001		
real estate price	1 (highest)	*ref.*	-	-	*ref.*	-	-
	2	1.18	1.17	1.20	1.18	1.16	1.20
	3	1.40	1.38	1.43	1.38	1.36	1.41
	4	1.46	1.44	1.48	1.40	1.38	1.43
	5 (lowest)	1.69	1.67	1.72	1.62	1.59	1.65
		p-trend < 0.001			p-trend < 0.001		

Survival analysis

During the study period (09 October 2011 – 31 December 2016) 64, 978 females and 58, 680 males died (for a total of 123, 656 deaths), 55, 702 were lost due to emigration outside the municipality of Rome (27, 537 females and 28, 165 males), 1, 578 females and 378 males reached the 100th birthday and were censored, and 1, 598, 929 were still alive at the end of the follow-up (870, 193 females and 728, 736 males).

Table 2.4 shows the results from accelerated failure time models, TR adjusted for age and presence of chronicity and stratified by sex are reported with 95%CI. Individual SEP was found directly associated with survival: people with both medium and low education had shorter survival than the reference category either females or males. Educational attainment had a stronger effect on males than on females (low educated females TR 0.79, 95%CI 0.77-0.81; low educated males TR 0.71, 95%CI 0.70-0.73). Contextual SEP showed an impact on survival across each category, compared to the highest, the lowest quintile had a survival time of 93% in

Table 2.4. Association between indicators of socioeconomic position and survival, accelerated failure time models. Italian residents aged 25-99 years. Rome, 2011-2016. Time Ratios (TR) adjusted for age group and chronicity, reported with their 95% Confidence Intervals (95%CI).

		FEMALES			MALES		
		TR	95%CI		TR	95%CI	
age group	25-34	*ref.*	-	-	*ref.*	-	-
	35-44	0.44	0.37	0.51	0.51	0.46	0.58
	45-54	0.18	0.16	0.21	0.22	0.20	0.25
	55-64	0.08	0.07	0.09	0.10	0.09	0.11
	65-74	0.04	0.03	0.04	0.04	0.04	0.05
	75-84	0.01	0.01	0.01	0.02	0.01	0.02
	85-99	0.00	0.00	0.00	0.01	0.01	0.01
education	High	*ref.*	-	-	*ref.*	-	-
	Medium	0.87	0.84	0.89	0.84	0.82	0.86
	Low	0.79	0.77	0.81	0.71	0.70	0.73
		p-trend < 0.001			p-trend < 0.001		
real estate price	1 (highest)	*ref.*	-	-	*ref.*	-	-
	2	0.96	0.94	0.98	0.96	0.94	0.98
	3	0.95	0.93	0.97	0.91	0.89	0.93
	4	0.95	0.93	0.97	0.90	0.88	0.92
	5 (lowest)	0.93	0.91	0.95	0.88	0.86	0.91
		p-trend < 0.001			p-trend < 0.001		
chronicity	none	*ref.*	-	-	*ref.*	-	-
	one or more	0.73	0.72	0.74	0.69	0.67	0.70

females (TR 0.93, 95%CI 0.91-0.95) and 88% in males (TR 0.88, 95%CI 0.86-0.91). The variable with the strongest association with survival was the presence of chronic conditions at baseline: females having chronicity shortened the mean survival time approximately by a fourth compared to females without chronic conditions (TR 0.73, 95%CI 0.72-0.74). A similar effect was found in males (TR 0.69, 95%CI 0.67-0.70) for which having certified chronicity was comparable to having low educational attainment.

All the associations lost some strength in the fully adjusted model shown in Table 2.5, but they remained statistically significant and there was only a slight change in the effect size. The only exception was the effect of the real estate price quintiles that became non-significant. All AFT models showed lower VIF than the chosen threshold of 2.5.

As sensitivity analyses, we studied the association between emigration and

Table 2.5. Association between indicators of socioeconomic position and survival, accelerated failure time models. Italian residents aged 25-99 years. Rome, 2011-2016. Time Ratios (TR) adjusted for every other variable in the table and reported with their 95% Confidence Intervals (95%CI).

		FEMALES			MALES		
		TR	**95%CI**		**TR**	**95%CI**	
age group	25 – 34	*ref.*	-	-	*ref.*	-	-
	35 – 44	0.44	0.38	0.52	0.52	0.47	0.59
	45 – 54	0.19	0.16	0.22	0.23	0.21	0.26
	55 – 64	0.08	0.07	0.10	0.10	0.09	0.11
	65 – 74	0.04	0.03	0.04	0.04	0.04	0.05
	75 – 84	0.01	0.01	0.02	0.02	0.02	0.02
	85 – 99	0.00	0.00	0.01	0.01	0.01	0.01
education	High	*ref.*	-	-	*ref.*	-	-
	Medium	0.87	0.85	0.89	0.84	0.83	0.86
	Low	0.79	0.77	0.81	0.71	0.70	0.73
		p-trend < 0.001			p-trend < 0.001		
real estate price	1 (highest)	*ref.*	-	-	*ref.*	-	-
	2	0.98	0.97	1.00	1.00	0.98	1.03
	3	0.99	0.97	1.02	0.99	0.96	1.01
	4	1.00	0.98	1.02	0.99	0.97	1.01
	5 (lowest)	0.99	0.97	1.02	1.00	0.98	1.03
		p-trend $= 0.74$			p-trend $= 0.66$		
chronicity	none	*ref.*	-	-	*ref.*	-	-
	one or more	0.74	0.73	0.75	0.70	0.68	0.71

characteristics at the baseline with logistic models stratified by sex. Also, we ran AFT models replacing the dichotomic chronicity variable with a three-level variable. Table A.3, in Appendix A, shows that younger people were more likely to emigrate, as well as lower educated and those living in wealthier neighborhoods. The strength of the association between indicators of SEP and survival was comparable to results presented in Tables 2.4 and 2.5. Having two or more chronicity had a higher impact on survival than having one. In the sex-stratified AFT models adjusted for age group and presence of chronicity reported in Appendix A, Table A.4, females with one chronic condition had survival times shortened by a fifth (TR 0.79, 95%CI 0.77-0.80) and those with two or more about a third (TR 0.66, 0.65-0.67). Similarly, males with one chronicity had TR= 0.75 (95%CI 0.74-0.77) and TR= 0.62 (95%CI 0.61-0.64). Results from AFT models stratified by sex and adjusted for every other variable in the study are reported in Table A.5, which is shown in Appendix A. OR were similar to those obtained from the main models and did not differ in meaning.

2.4 Discussion

Principal findings

Our analysis of the 2011 Rome cohort found an inverse association between both individual and contextual SEP indicators with having a chronic or rare disease, an inverse association of chronicity with survival, and a direct association between individual and contextual SEP with survival. These associations enlighten the presence of multiple levels of inequalities in the Rome cohort of 2011 always disadvantaging the lower strata of SEP. The first level of inequality is at the individual level: highly educated individuals have an advantage in health as less likely to suffer from a chronic condition. They also have an advantage in survival taking account of baseline health status, as more likely to live longer than low educated. These advantages could be due to immaterial resources (knowledge and awareness attained from education itself), but also to material resources (wealth obtained from better-paid jobs, resulting in the possibility to afford healthier life conditions). The second level of inequality is at the neighborhood level: people living in wealthier neighborhoods are more likely to be in better health and to live longer than individuals who are living in more disadvantaged areas. A worse and shorter life characterizes the more disadvantaged groups of the population in Rome.

This work shows a difference in baseline health of about 10 years in middle-aged between low and high SEP (either individual or contextual), for both sexes. The percentage of individuals with a chronic or rare disease reaches a plateau and then a reduction at old ages. The author attribute this phenomenon to two possible explanations. The first is the action of a selection effect, by which only healthier individuals reach older ages. The second explanation is that a competing action of the most common type of income-related co-payment exemption, acquirable after 65 years of age and not considered in this study, could have occurred. However, a strong competing action between the two types of exemptions is considered unlikely. In fact, income-related co-payment exemption does not cover drug expenditures. Moreover, 37.7% of 65+ year-olds who had an income exemption had also an exemption in the Disease-Related Co-payment Exemption Registry, and the exemption right based on the income is given by the Tax Agency independently on the health condition of the user. On the assumption that Income-exemptions compete with Disease-Related Co-payment Exemptions, underestimation of inequalities in baseline health and overestimation of the effect of SEP on survival might exist.

Every analysis reported in this work shows that individual and contextual SEP are inversely associated with having at least one chronic condition. The association between SEP and having a Disease-Related Co-payment Exemption was stronger for contextual than individual SEP, this result is unexpected because individual indicators are generally more strongly associated with health than the contextual ones (Foraker et al., 2019; Schüle et al., 2016; Cesaroni et al., 2003). Results on inequalities in the presence of chronic conditions, although not fully comparable, show similar patterns to a study based on 2007 Scottish data by Barnett et al. (2012), which found a higher prevalence of multimorbidity in lower area-deprivation deciles.

Results of survival analysis are consistent with previous works on the Rome population and general studies on inequalities. In the Rome census cohort of 2001, Cacciani et al. (2015) found an inverse association between education and overall or cause-specific mortality, while Nardi et al. (2022) found higher overall mortality in temporary workers. Moreover, Cesaroni et al. (2020) found association between real estate price quintiles and mortality when the educational level was considered. In the complete survival model, the contextual SEP had no association with survival times, when the other measure of SEP was considered. In both logistic and survival analyses, we found stronger inequalities for males than for females as already reported in the literature for similar cohorts (Paglione et al., 2020).

Strength and weakness

This work has its limitations. Mainly, chronicity data should only be considered as a proxy of morbidity but not as a substitutive measure due to a possible underestimation of mild forms of chronic conditions. The measure was obtained from the Disease-Related Co-payment Exemption Registry, an administrative dataset implemented to help people with chronic or rare diseases to receive appropriate and free-of-charge assistance. The dataset was not intended for medical or statistical purposes, leading to rough definitions of chronicity and the possibility to observe only the more severe conditions. Nevertheless, good reliability over severe forms of illnesses is expected because a medical certificate is needed and the economic advantage deriving from the co-payment exemption should incentivize all the people with chronic or rare diseases to apply for it. However, people with multiple chronicity may not be interested in multiple certificates as the expenses for specialist visits or diagnostic tests could be already covered, totally or partially, by the first certificate. This might result in marked differences between who owns a chronicity certificate and who does not, and in smaller differences between who has one certification and who owns more. From this last point comes our choice to dichotomize the variable in this study. Finally, a small proportion of the well-off population could rely on private insurance companies and not use the National Health Service. However, the proportion of the wealthy population leaning on private insurances is expected to be small as in 2011 the voluntary health insurances covered around 1% of the whole health expenditure (Ferré et al., 2014). Under the assumption that higher SEP were less likely to request co-payment exemptions for conditions with non-expensive treatments, an overestimation of inequalities in baseline health might exist. On the opposite, the same assumption would result in an underestimation of the association between SEP and mortality. In this work, we explicitly or implicitly stated that SEP (individual and contextual) acts on health, but a reverse pathway is plausible (Hoffmann et al., 2018). Individuals in bad health conditions during their youth may have more difficulties attending school, thus, limiting their instruction to lower levels. Those individuals could also have fewer opportunities to find well-paid jobs that would allow them to afford houses in wealthy neighborhoods. Moreover, we considered as lost to follow-up all subjects who moved from Rome during the study period. In logistic regressions, implemented to analyze differences in baseline characteristics between those lost to follow-up and the rest of the population, showed that younger people, individuals with lower education, residents in higher quintiles neighborhoods, and people in good health were more likely to emigrate. However, in a previous work by Cacciani et al. (2015), the results obtained using an inverse probability approach to weight for the characteristics of the population were very similar to those from the unweighted analysis. Finally, changes in neighborhood during the follow-up were not considered, but bias would happen only if individuals would have changed neighborhood quintiles.

The main strengths of this work are the huge statistical power, the good reliability of the two measures of SEP, and the robustness of the results to sensitivity analyses. Thanks to the access to administrative Roman databases, we could use almost all the Italian adult population residing in Rome, basing our estimates on more than 1.7 million individuals. Data on educational attainment came from the census, one of the most reliable data sources. Unobserved changes over time of the measure are possible but unlikely since we only analyzed individuals aged 25 or more. Moreover, the real estate price is one of the main factors in selecting a population within a city (McDonald and McMillen, 2010). The average real estate price has the strength to be openly and easily available and has the potential to synthesize in one measure the quality of life in the neighborhood with its services and infrastructures, but also in terms of perception and social prestige. Finally, sensitivity analyses using a different categorization for the chronicity data and/or based on the implementation of different models showed minimal differences in the results and none in the meaning or the trend.

These results highlight the need for ad-hoc policies aimed to help the most disadvantaged strata of the Rome population, to reduce socioeconomic inequalities in health that exist even in a universal healthcare coverage setting. Further studies using comorbid conditions estimated using different datasets could improve the quality of the analysis, reducing the bias and making results comparable in terms of diseases and multiple diseases with international literature.

Conclusions

Inequalities are present in both health and survival, with lower SEP having always worse outcomes than higher SEP. Lower SEP undergo a double inequality in health: the higher likelihood of being affected by at least one chronic condition, which is associated with shorter survival per se, and a shorter survival independently of the presence of chronicity.

Chapter 3

SARS-CoV-2 spread and area economic disadvantage in the Italian three-tier restrictions: a multilevel approach

3.1 Background

It is well known that socioeconomic level is associated with health outcomes (Marmot et al., 2008; Barnett et al., 2012). SARS-CoV-2 pandemic is no exception, as it exacerbated pre-existent socioeconomic inequalities regarding finances and basic needs (Wright et al., 2020b; Adams-Prassl et al., 2020). Moreover, evidence from the first outbreak showed associations between the spread of the virus and socioeconomic level in the US (Chang et al., 2021; Lewis et al., 2020; Abedi et al., 2021), Europe (Morrissey et al., 2021; Aguilar-Palacio et al., 2021; Wachtler et al., 2020), and Italy (Mateo-Urdiales et al., 2021; Consolazio et al., 2021). In addition, lockdown and other measures to prevent the spread of SARS-CoV-2 had a different impact on mobility depending on individual and contextual socioeconomic levels, showing lower compliance to stay-at-home orders by poorer neighborhoods (Pullano et al., 2020; Gauvin et al., 2021; Glodeanu et al., 2021).

After one of the longest lockdowns worldwide, Italy gradually lifted all restrictions with the Decree of the Prime Minister of 11 June 2020, leaving in place an indoor mask mandate only. In November 2020, when facing the second outbreak, Italy implemented a three-tier restriction system based on a pandemic threat assessed at the regional level (NUTS-2). This system defined the pandemic threat and the restrictions combining three levels of risk based on 21 indicators and four transmission levels (Presidente del Consiglio dei Ministri, 2020). The pandemic threat could be either "moderate" (yellow; default level), "elevated" (orange; high risk and medium-high transmission), or "maximum" (red; high risk and transmission), where each level had a set of increasing restrictions and was named according to the color scheme. Specifically, in the yellow tier, the limitations were: mandatory face masks indoors and outdoors, halved public transport capacity, distance learning in high schools and universities, closure of shopping malls on weekends and holidays, closure of some indoor activities like cinemas, exhibitions, museums and gyms, stop to service in bars and restaurants at 18:00, and a curfew between 22:00-5:00. The additional restrictions in the orange tier were the stop to travels between municipalities and regions and the suspension to all non-delivery food-service activities. Last, the red level had a complete lockdown where only essential workers were allowed to move, and only primary schools kept their in-presence everyday activities. In mid-January 2021, the pandemic threat assessment procedure was updated introducing a threshold of 50 weekly cases per 100.000 into the evaluation. This revision allowed the implementation of higher restrictions in regions with high incidence but a medium level of risk or low transmission (Ruffino, 2021). In the same period, the system added a new lowest level of restrictions: when regions reached the so-called "low" pandemic threat (white, low risk, low transmission, and low incidence), only a mask mandate indoors was in place. A more in-depth description can be found elsewhere (Ruffino, 2021; Manica et al., 2021; Vespe et al., 2021; Bonifazi et al., 2021).

Manica et al. (2021) and Vespe et al. (2021) showed that this restriction system systematically reduced mobility between and within regions when higher tiers were implemented. Moreover, Bonifazi et al. (2021) made a study on the nine most populated Italian regions and showed stronger reductions in transmissibility with increasing tiers. However, it is unknown whether these effects were equal among provinces characterized by different levels of economic disadvantage. It is well known that adherence to stay-at-home orders implemented during the SARS-CoV-2 pandemic differs among socioeconomic groups (Pullano et al., 2020; Gauvin et al., 2021; Glodeanu et al., 2021; Jay et al., 2020; Wright et al., 2020a). However, whether this remains true for less strict mandates remains an open question.

Our main goal was to investigate the association between the province's economic disadvantage and SARS-CoV-2 spread by the level of restriction.

3.2 Methods

Study design and setting

We conducted an ecological study at the province level, corresponding to the NUTS-3 regions. Due to the timing of the restrictions' implementation (beginning of November 2020) and a disruptive change in the pandemic threat assessment procedure in mid-May 2021, we analyzed the second pandemic wave. Specifically, the period from Sat 6 Nov 2020 to Sun 9 May 2021.

Unit of observation and variables

In this study, the units of observation are the 107 Italian provinces. For each province, we measured the exposure (economic disadvantage), the daily outcome (infection spread), the potential confounders (population density, population age structure, and geographical repartition), and the number of days into each restriction tier. We measured the provinces' economic disadvantage (PED) using data on total yearly income from the Ministry of Economy and Finance (2020). We calculated the PED using the percentage of taxpayers in 2019 with a total yearly income lower than €10,000. The total yearly income includes all gross incomes from work (employment, self-employment, and pensions) and other sources (capital, land, and business). To measure the SARS-CoV-2 spread, we used the cumulative number of SARS-CoV-2 infections disseminated daily by the Italian Civil Protection Department (2020). The dataset contains information about the cases confirmed through Reverse Transcription-Polymerase Chain Reaction (RT-PCR). We estimated the SARS-CoV-2 spread through the daily reproduction number (R_t) using the "instantaneous R_t" methodology proposed by Fraser (2007) and developed by Cori et al. (2013). In this setting, R_t is the sum of infection incidences observed in the previous period weighted by the infectivity function. We assumed that the infectivity function followed a Gamma Distribution with parameters estimated in the first outbreak in Lombardy (Cereda et al., 2020). We observed the provinces' extensions and population age structure from the National Institute of Statistics (2022b,a, 2021). We estimated the population density for every province and then we divided the provinces into quartiles. To account for the mask mandate exemption for children, we used the percentage of individuals aged 0-5 (population age structure). Last, to account for the geographical repartition of the provinces, we aggregated the five NUTS-1 classifications in three groups, considering Northeast and Northwest as "Northern" Italy and South and Insular as "Southern" Italy. The Italian Ministry of Health communicated weekly the change in pandemic threat assessments and restrictions in each region, and we gathered the information from the Ministry of Health's web page about the novel coronavirus and the SKY TG24 news archive (Italian Ministry of Health, 2020; Sky TG24, 2018). We did not analyze the "low" level of pandemic threat, namely the white, because only the five Sardinia's provinces reached the level in the study period.

Statistical analysis

We used graphical displays for descriptive geographical analysis, timing of restriction by region, and trend of R_t and incidence at the national level. We also plotted R_t trends for each province in the single restriction episode by PED tercile and tier of restriction along with their average trend and 90% credible interval. The average trend is calculated through multilevel linear regression models stratified by restrictions and economic disadvantage terciles with days as the only covariate. The 90% credible intervals are obtained through simulation of the posterior distribution of the day parameters (Korner-Nievergelt et al., 2015).

We used Multilevel Linear Regression (MLR) models with random intercepts stratified by restriction tier to analyze the association between PED and R_t. That is, per every restriction we defined R_t as: $R_{t\,ij} = \alpha + \underline{x}'_{ij}\beta + u_i + e_{ij}$ where i indicates the cluster and j the observation. In the formula, α is the fixed intercept, $\underline{x}'_{ij}$ is the vector of variables observed in cluster i at the j-th observation, β the vector of fixed effects (common for every cluster and observation), u_i the specific random intercept of cluster i assumed to be normally distributed, and e_{ij} the usual error term of linear regressions assumed to be normally distributed as well. Since provinces faced the same restriction several times in different pandemic contexts, we choose to not define the cluster i of MLR models as the province. Rather, we preferred to define a finer cluster i as the province in the single episode of restriction. Hence, every province in each color limitation has different intercepts every time it faces the restriction. To check whether MLR models were needed, we estimated the Intraclass Correlation Coefficient (ICC) for every restriction level. We ran four sets of MLR models. First, we ran days models to estimate the overall effect of each tier. The estimates for the number of days into the restriction allowed us to identify the average daily effect of the restriction itself. Second, we ran PED models to study the average association of PED with our response variable. Third, we ran MLR models with the linear effects of PED, the linear effect of and days, and their interaction. In this setting, studying the interaction term gives insights into the differential effect of PED by tier. While linear effects represent changes in the R_t starting level, the interaction term represents a change in the R_t trend, that is, the slope. Fourth, we added all the confounders to the models with interaction, obtaining adjusted models. All the model equations are reported in the supplementary material in the

Appendix B. For all models, we reported estimates, standard errors, and p-values, considering estimates with $p < 0.05$ as statistically significant. Moreover, to ease the interpretation of interaction terms in the models, we calculated the turning points for both PED and days. Turning points are the values at which the first-order partial derivative of the function equals zero. As in typical function studies, it is possible to know whether the outcome variable increases or decreases with larger or smaller values than the turning point.

Finally, we ran two sensitivity analyses. First, we removed restrictions shorter than a week and ran MLR full models to check whether short restrictions can affect the results. Then, we ran MLR full models weighted by the provinces' populations, giving more weight to more populated provinces which in turn have more stable and reliable R_t. In the analyses, we centered the economic disadvantage and the share of people aged 0-5 to their minimum observed values (19.8 and 3.4 respectively). This allows the intercepts to have a theoretically observable value in all models. We used the software R for data preparation and analyses (R Core Team, 2019). All data and codes are available in an online repository to guarantee full access and reproducibility to our results (Dei Bardi et al., 2022a).

3.3 Results

In Italy, there are 107 provinces (NUTS-3 level) heterogeneous by extension, population, and income distribution. These three variables varied between 203-7,692 square kilometers, 83-4,253 thousand people, and 19.8-48.5 percent of people with low income (PED), respectively.

Figure 3.1 shows the Italian maps by provinces of the variables we considered: the percentage of people with a gross yearly income lower than €10,000; the SARS-CoV-2 cases per 10,000 inhabitants in the period 06 Nov 2020 – 09 May 2021; the percentage of people aged 0-5 years; and the population density quartiles. In the figure, a remarkable north-south gradient in yearly income is visible. Southern provinces

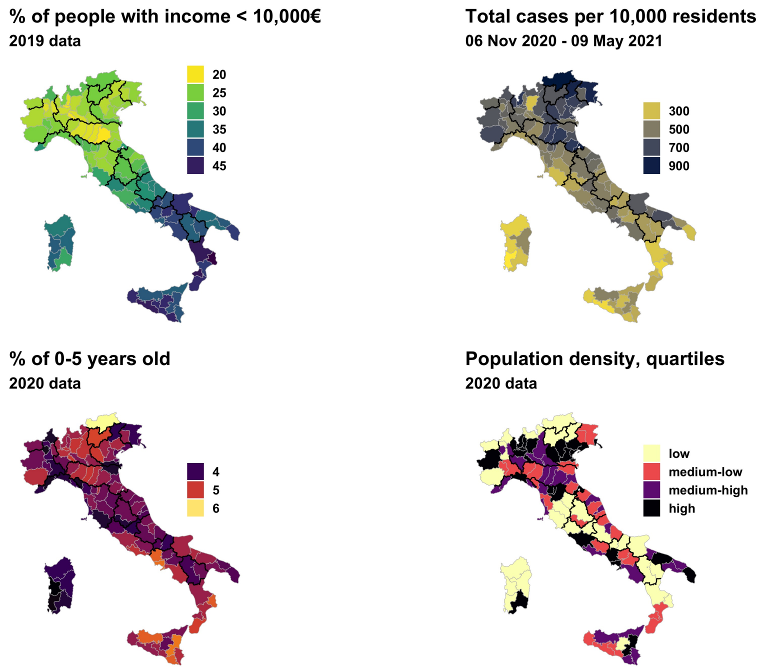

Figure 3.1. Selected variables by province (NUTS-3 level): the percentage of people with a gross yearly income lower than €10,000 (top-left); the SARS-CoV-2 cases per 10,000 inhabitants in the period 06 Nov 2020 – 09 May 2021(top-right); the percentage of people aged 0-5 years (bottom-left); and the population density quartiles (bottom-right)

consistently show a larger share of low-income people than northern provinces. However, the reverse is observed for SARS-CoV-2 infections per 10,000 inhabitants. Higher values in cumulative incidence of cases were observed in the north, suggesting an inverse relationship between our measure of PED and the spread of SARS-CoV-2 infection. The share of the population aged 0-5 is generally higher in the north and south of Italy, with lower values observed in Sardinia and the center. Finally, population density is the lowest in mountainous provinces and the highest in provinces with the largest cities in Italy.

Figure 3.2 reports the regional daily measures in place from 1 Nov 2020 to 17 May 2021, highlighting the date when the pandemic threat assessment started including the weekly incidence threshold (16 January 2021). Restrictions changed frequently and were heterogeneous by duration and implementation, showing no association with the geographical repartition of the regions. Country-wide restrictions not based on the pandemic threat of the regions are visible during Christmas, new year, and

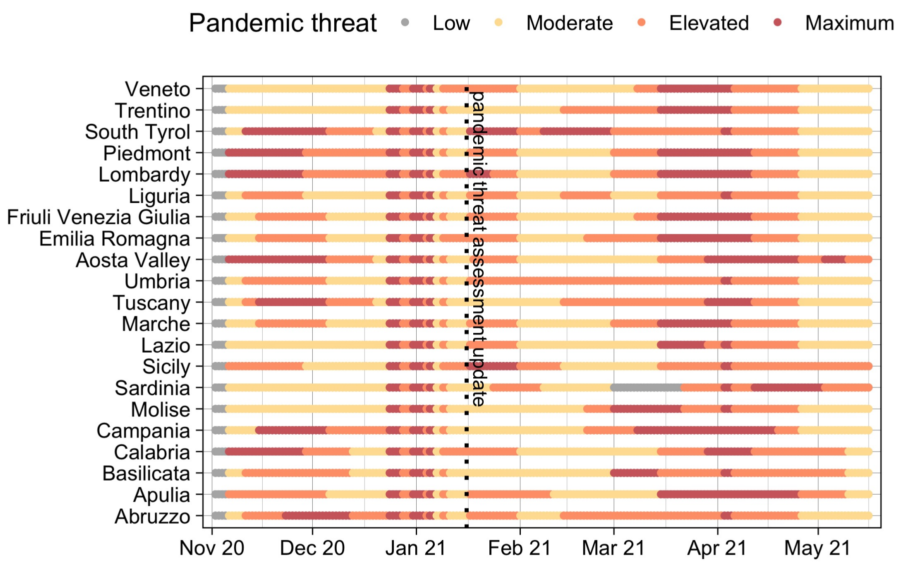

Figure 3.2. Pandemic threat and restriction levels by Italian regions Nov 2020 - May 2021. Nation-wide measures were imposed during the holiday season (Christmas, new year, Epiphany) and Easter (04 April). On 16 January 2021, the pandemic threat assessment started including a weekly incidence threshold.

Easter (4 Apr 2021) periods. Figure 3.3, displays the trends of R_t and SARS-CoV-2 incidence from the beginning of data collection on positives in Italy (24 Feb 2020) to 31 Dec 2021, highlighting the study period. Confronting Figure 3.2 and Figure 3.3 is visible that the Italian Government implemented the first restrictions right before November's pandemic peak. Also, a new peak occurred in mid-March, this led many regions to the orange or the red restrictions before the so-called "Easter lockdown" was imposed at the national level.

Figure 3.4 shows the R_t trends observed from the restriction implementation by PED terciles and restriction level. Overall, the yellow tier showed increases in R_t, while the orange and the red reduced the spreading of the virus with greater reductions in the red compared to the orange tier. However, we can observe very different slopes between the least and the most economically disadvantaged in every level of restriction. While the overall trend in the yellow tier was rapidly increasing for the least disadvantaged provinces, the other two terciles showed slower growths. Also, the most economically disadvantaged appeared to have the sharpest decreasing

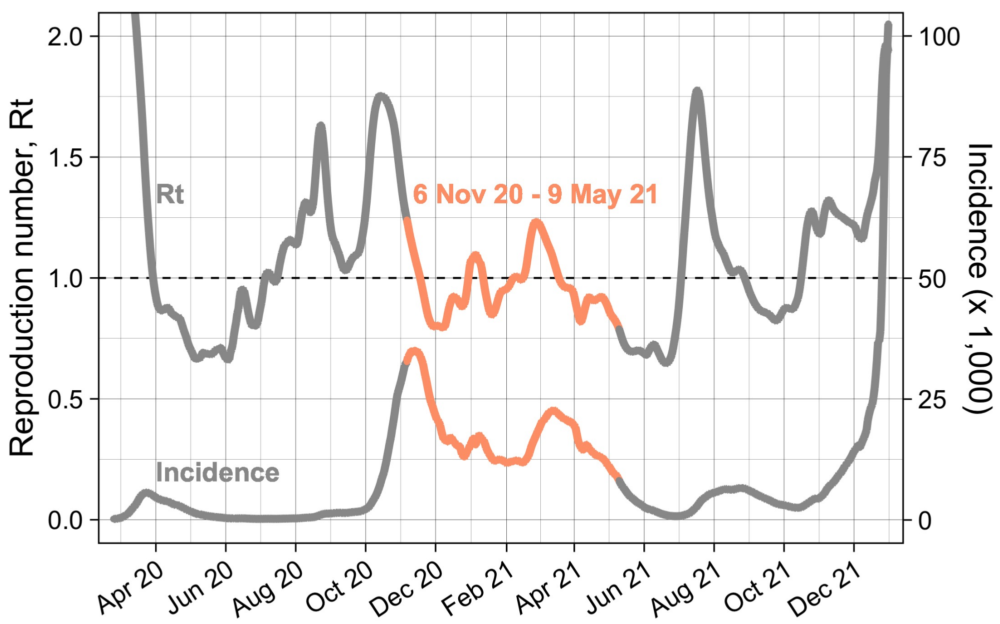

Figure 3.3. SARS-CoV-2 incidence and Cori's Reproduction number (R_t) in Italy. February 2020 - December 2021. The period under analysis is highlighted in orange.

slope in the orange tier. The opposite is visible in the highest restriction level, where the reduction in R_t is less steep in provinces with the highest share of people with low income.

Table 3.1 shows the results from MLR models with fixed effects and random intercepts stratified by level of restriction. To account for the strong correlation of subsequent R_t, we defined the cluster as the single episode in which the province entered a tier. Estimates of the Intraclass Correlation Coefficient (ICC) reported in the table confirm the need for a multilevel analysis as clusters explained 42-63% of the R_t variability (ICC yellow = 0.42; ICC orange = 0.63; ICC red = 0.55). Results from days models (Table 3.1.A) showed an increasing R_t trend for the yellow tier (days = 0.004 $p < 0.01$), a small restrictive effect in the orange tier (days = -0.005 $p < 0.01$), and a strong effect in the red tier, where every day of restriction contributed to reducing the R_t by 0.014 ($p < 0.01$). On average, R_t increased from 0.99 to 1.08 after three weeks in the yellow level, decreased from 1.03 to 0.93 in the orange restriction, and reduced from 1.05 to 0.76 in the red tier. Table 3.1.B shows

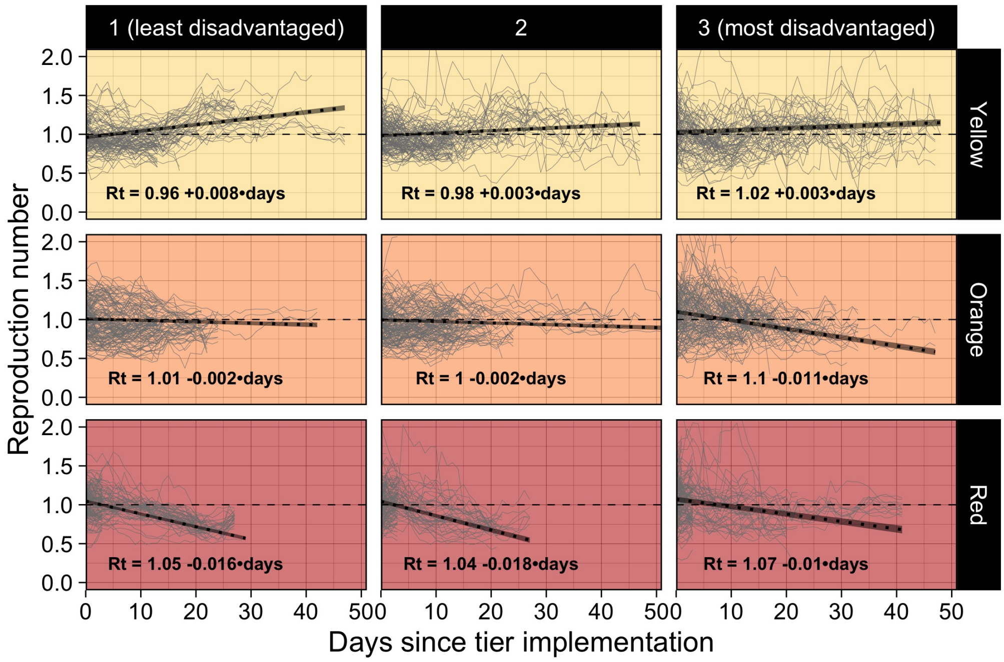

Figure 3.4. Daily reproduction number (R_t) trend of every province in a tier occasion by deprivation tercile and tier of restriction.

that provinces with higher PED have always higher R_t in every restriction level, although non-significant in the lowest tier (yellow = 0.001 $p = 0.19$; orange = 0.002 $p = 0.02$; red = 0.004 $p < 0.01$). Interaction MLR models in Table 3.1.C confirmed the trends observed in Figure 3.4. The yellow tier model shows a positive effect of days and PED and a negative statistically significant interaction term, representing a slower increase in R_t for more economically disadvantaged provinces. The positive effects of both PED and days were reversed at the turning points PED = 64.7, outside the observed range, and days = 16.4. These estimates and the negative sign of the interaction effect show an increasing daily trend of R_t for all PED levels and a lower R_t for higher PED after 17 days in the yellow tier. The interaction model of the orange level reports a significant change in the direction of the effect of days. However, this inversion is completely balanced by the statistically significant interaction effect of days and PED. The negative estimate for the interaction term reverses the two positive estimates for the single terms at PED = 21.9 and days = 10.4. Given that the minimum observed share of low-income people is 19.8, a few

Table 3.1. Association between economic disadvantage and SARS-CoV-2 spread by restriction tier. Estimates from Multilevel Linear Model with random intercepts stratified by restriction tier. ICC = Intraclass Correlation Coefficient; Est. = Estimate; SE = Standard Error; PED = Province's Economic Disadvantage. *Models were adjusted for population density, share of people aged 0-5, and geographical repartition.

	Yellow (ICC = 0.418)			**Orange (ICC = 0.632)**			**Red (ICC = 0.553)**		
	Est.	**SE**	**p**	**Est.**	**SE**	**p**	**Est.**	**SE**	**p**
A) days models									
Intercept	0.989	0.008	< 0.01	1.032	0.008	< 0.01	1.050	0.009	< 0.01
days	0.004	2E-04	< 0.01	-0.005	2E-04	< 0.01	-0.014	3E-04	< 0.01
B) PED models									
Intercept	1.008	0.013	< 0.01	0.981	0.013	< 0.01	0.942	0.015	< 0.01
PED	0.001	0.001	0.19	0.002	0.001	0.02	0.004	0.001	< 0.01
C) interaction models									
Intercept	0.967	0.014	< 0.01	0.973	0.013	< 0.01	1.026	0.015	< 0.01
days	0.006	4E-04	< 0.01	0.001	4E-04	< 0.01	-0.018	0.001	< 0.01
PED	0.002	0.001	0.07	0.006	0.001	< 0.01	0.002	0.001	0.04
PED x days	-1E-04	3E-05	< 0.01	-5E-04	3E-05	< 0.01	3E-04	4E-05	< 0.01
D) adjusted models*									
Intercept	0.928	0.028	< 0.01	0.985	0.026	< 0.01	0.993	0.030	< 0.01
days	0.006	4E-04	< 0.01	0.001	4E-04	< 0.01	-0.018	0.001	< 0.01
PED	-0.002	0.003	0.55	0.005	0.002	0.05	0.009	0.003	< 0.01
PED x days	-1E-04	3E-05	< 0.01	-5E-04	3E-05	< 0.01	3E-04	4E-05	< 0.01

provinces had a slightly increasing trend while every other province had a reduction in the spread of the virus when in the orange tier. The reduction in R_t had growing strength with greater PED. On average, after 11 days into the orange level, the starting gap between more and less economically disadvantaged provinces was filled and reversed.

Finally, the interaction model of the red tier confirmed the slower reductions in R_t for more economically disadvantaged provinces observed previously. The negative effect of days on R_t was eased by the positive effect of both PED and the interaction term. Turning points happened to be outside the observed range of the variables (PED = 71.8, days = -7.2), meaning that provinces with a higher share of people with low income always had both higher R_t levels and slower reductions in the red tier. When adjusting the estimates for potential confounders, we observed little to no differences in our variables of interest (Table 3.1.D). The estimate of PED in the yellow tier model became negative but remained non-significant causing a sign change in the turning point of days as well (days = -11.6). The adjusted model for the yellow tier thus shows that provinces with a higher share of low incomes always had lower starting R_t (although non-significant) and lower increasing trends, thus resulting constantly advantaged in the lowest tier. The orange level adjusted model showed no meaningful difference with its non-adjusted peer. Last, the red tier adjusted model differed in the effect size of PED only (PED $= 0.009$; $p < 0.01$), but do not differ in meaning from the non-adjusted.

The confounding variables did not have statistically significant effects (not shown). It is worth underlining two exceptions: 1) the effect of the share of children aged 0-5 in the yellow tier model (estimate $= 0.054$ $p < 0.01$), and 2) the significant effect of NUTS-1 regions in the red tier model (Central vs Northern -0.078 $p < 0.01$; Southern vs Northern -0.138 $p < 0.01$) that numerically represent what showed in Figure 2.1.

Sensitivity analyses performed on adjusted models are reported in Table B.1 and showed no substantial change in the reported results. Models without restrictions in place for less than 7 days, shown in Table B.1.1 in the Appendix B, did not have different estimate directions or significance of the adjusted models. Also, weighting the adjusted models for the population of the provinces did not change our estimates, as reported in Table B.1.2 in the Appendix B.

3.4 Discussion

Principal Findings

In our analysis of Italian provinces, we found differential effects of the provinces' economic disadvantage on SARS-CoV-2 spread by restriction level. We found statistically significant interaction effects between the number of days into the restriction and the PED. Overall, in the lowest tier (yellow), R_t had an increasing trend, but more economically disadvantaged provinces had slower R_t increases than less disadvantaged. This different behavior resulted in generally higher R_t values for the latter. Conversely, a moderate level of restrictions (orange) led to a general decrease in R_t values. The more economically disadvantaged provinces resulted particularly benefited from the orange tier, as their R_t downward trend was steeper than less disadvantaged provinces. The average level of R_t was lower in more disadvantaged than less disadvantaged provinces after 9 days in the orange level. However, in the highest level of restriction (red) the higher the PED, the higher the R_t, and the slower the reduction.

Our results suggest the presence of different behaviors in the three levels of restrictions depending on the PED. The yellow level of restrictions was mainly characterized by the nocturnal curfew, mandatory stop to services in bars and restaurants at 18:00, and closure of social indoor activities (i.e., cinemas, gyms, museums) and shopping malls on non-working days. However, many social activities were still allowed during the day. When these restrictions were in place, we could expect that people with a wider economic availability enjoyed more frequently the restaurants, bars, shopping centers, and all the other available social venues. In contrast, disadvantaged people could spontaneously stay more at home, resulting in lower transmissibility. This could result in a higher number of social contacts and higher chances of contagion in less economically disadvantaged provinces compared to more disadvantaged ones and might explicate the faster increasing R_t trends for the least disadvantaged provinces when the lowest level of restrictions was applied.

The orange tier, in addition to the restrictions applied in yellow, introduced a suspension to most social activities and limited the mobility between municipalities and regions. However, those limitations did not demonstrate a higher impact in less compared to more economically disadvantaged provinces. A possible explanation of the observed trend for less disadvantaged could be that in the orange tier, although stricter, the measures did not introduce a stay-at-home order, did not forbid private gatherings, and did not mandate smart working. That is, "non-essential" in-person working activities could continue. Moreover, it is plausible that the restricted mobility between municipalities impacted more residents in small towns than those living in big cities, and provinces with large provincial capitals have lower percentages of people with low income than those composed of small conurbations. However, albeit it is safe to attribute the reduced spread of SARS-CoV-2 to the reduced mobility between municipalities and the take-away-only mandate to restaurants and bars, the reasons why these measures resulted more effective in more economically disadvantaged provinces remain an open question.

The highest level of restrictions (red) corresponds to a complete lockdown, where only essential workers were allowed to leave home. In this case, we could speculate that more economically disadvantaged provinces have higher shares of essential low-skilled workers who do not have the chance to work at home whilst limiting contacts and rapidly reducing the R_t (Glodeanu et al., 2021; Bambra et al., 2020). In addition, essential low-skilled workers could also have limited access to personal protective equipment and safe working conditions are generally less guaranteed (Rao et al., 2021).

In summary, while more advantaged people would have more contacts with lower restrictions, those with less economic availability would have more unavoidable social contacts during lockdowns increasing the chance of infections occurring.

The results about the red tier are comparable to previous studies about the effect of lockdowns during the first wave. For example, several studies found lower efficacy of lockdowns in poorer neighborhoods or disadvantaged areas in the United States (Chang et al., 2021; Lewis et al., 2020; Abedi et al., 2021), Europe (Morrissey et al., 2021; Aguilar-Palacio et al., 2021; Wachtler et al., 2020), and Italy (Mateo-Urdiales et al., 2021; Consolazio et al., 2021). Furthermore, our results are coherent with a European Commission report on the impact of the Italian three-tier system on mobility, which found lower mobility with increasing restriction levels (Vespe et al., 2021). Also, our findings on the restrictions' effects are consistent with previous studies that found increasing R_t trends with the yellow restrictions, little to no reduction in the orange tier, and sharp declines in R_t with the red level (Manica et al., 2021; Bonifazi et al., 2021).

Strength and Weakness

This work has its limitations. First, it was an ecological study, and ecological fallacy can lead to associations not necessarily true at the individual level. Although we used the lowest-available data reaching the NUTS-3 level, the granularity remains high, and it is not possible to account for individual confounders. Second, the restrictions were decided based on the assessed pandemic threats at the regional level (NUTS-2) while our analyses were at a lower level (NUTS-3). This means that provinces of the same region with different spread and control of the virus could face the same restriction, potentially modifying the strength of our estimates unpredictably. Third, our measure of PED based on the gross yearly income did not consider the difference in the cost of living, the unofficial labor, and other forms of socioeconomic disadvantage. The same yearly income could have very different purchasing power in different parts of Italy. In fact, a report by the Bank of Italy estimated that the cost of living is roughly 17% lower in south-insular than in north-central Italy (Cannari and Iuzzolino, 2009). Unofficial labor is also more widespread in southern Italy. Both phenomena could affect our measure of PED by showing more people with low income than the actual value. However, Pittau et al. (2011) found that price differentials do not compensate for the differences in incomes, although they reduced the north-south gradient. Regardless, the threshold we used of €/y 10,000 is very low, and gross incomes lower than this threshold are hardly considered adequate for living in any part of Italy. Moreover, informal work could also be intended as a form of disadvantage for its lack of economic security and absence of sick leave. Fourth, during the study period, the vaccination campaign began (27/12/2021), and the new alpha variant (lineage B.1.1.7) became predominant, replacing the original SARS-CoV-2 strain. We choose to not account for those two variables in our analyses because it is easy to assume that the share of vaccinated people is a mediator of the PED on SARS-CoV-2 spread, thus, adjusting our analyses for the vaccinal status of the population would remove part of the total effect we are interested in. Also, to the best of our knowledge, the alpha variant was associated with higher spread, but there is no evidence that it was associated with the economic disadvantage of the province, making it not a confounder between the two measures. Moreover, public data on the vaccinal status of the population and the spread of the alpha variant are only available at the regional level (Italian Commissioning Structure for the COVID-19 Emergency, 2021; European Centre for Disease Prevention and Control, 2022). Fifth, the data on SARS-CoV-2 infections might have some delay in the notification that is hardly quantifiable and may be affected by diverse under-notification by province. The former could assign infections that occurred previously to a sequent tier, affecting the starting and ending R_t we observed in each restriction and province. Regarding the latter, it is possible that smaller or more economically disadvantaged provinces were more affected by the under-notification of cases due to lower detection capability. This would result in lower reported infections during outbreak peaks and underestimations of R_t. Sixth and last, we assumed linear trends for R_t in every tier. This does not account for a plateau effect of the tiers or pandemic fatigue by the population. However, as visible in Figure 3.4, implementation periods were relatively short and trends, on average, appear as linear.

Our work also has some strengths. First, to our knowledge, this is the first study to look at inequalities in the effects of tiered restrictions. It underlines differential behaviors from areas characterized by different incomes, analyzing the effect on the spread of SARS-CoV-2. Second, our study is based on a reliable measure of R_t, widely used in the literature and the daily reports of the Italian National Institute of Health (Gostic et al., 2020; Guzzetta and Merler, 2020; Italian National Institute of Health, 2022). The instantaneous R_t does not need any assumption except the distribution of the infectivity function and, intrinsically, that the observed past trend will hold in the close future. Mainly, the use of this measure does not require any assumption about the growth of the epidemic, often assumed to be exponential, which is rarely met in context with changing restricting measures such as the one we analyzed. Finally, our estimates were robust to sensitivity analyses either with removed shorter periods of restrictions or weighted by provinces' population. To ease the replicability to the readers, the full code and data can be found in an online repository (Dei Bardi et al., 2022a). Our results suggest the importance of improving public policies at area levels that make it possible to account for the composition of the population. Consequently, resources could be allocated based on evaluated needs. In more economically disadvantaged areas, these policies could pay particular attention to workers in essential services that cannot work at home by implementing, for example, specific preventive measures aimed to limit virus circulation within the workplace (Rao et al., 2021; Hammonds and Kerrissey, 2020). As suggested by some authors, workers with symptoms or known contact with a positive person should be encouraged to stay at home without the risk to lose their job, and free onsite testing could be offered also facilitating access to diagnosis (Rao et al., 2021). Also, in less economically disadvantaged areas more efforts could be oriented to strengthen the opportunity to work at home and to implement education and information campaigns in the context of social activities.

Conclusions

This study found that the associations between area-level economic disadvantage and the spread of SARS-CoV-2 differed for diverse levels of restriction implemented to prevent the spread of the virus. While lower restrictions curbed more the spread in more economically disadvantaged provinces, the lockdown reduced more the spread in less disadvantaged provinces. We hypothesize that these results could be linked to different shares of people with low income and essential workers. This study suggests the importance of further differentiating actions, aiming at both minimizing the burden on the population and maximizing the impact of the restrictions on the spread of epidemics/pandemics. This would allow for early ease or early implementation of restrictions, as well as aimed policies shaped for specific contexts, optimizing the outcomes. This work calls for new studies to investigate whether associations found at the province level are also present at the municipal or individual level.

Chapter 4

The mediating role of chronic conditions between COVID-19 mortality and socioeconomic status. Findings from 2 years of the SARS-CoV-2 pandemic in the Lazio Region.

4.1 Background

The trilateral relationship between Socioeconomic Position, the prevalence of chronic conditions, and COVID-19 mortality has been well known since the first wave of the SARS-CoV-2 pandemic. The literature shows that people living in neighborhoods with higher shares of poor, non-white, low-educated, and unemployed individuals are more likely to die from COVID-19 (Feldman and Bassett, 2021; Kontopantelis et al., 2021, 2022). Those with chronic conditions have a higher likelihood of dying or being hospitalized (Yang et al., 2020; Richardson et al., 2020; Reyes-Sánchez et al., 2022; Dessie and Zewotir, 2021). And finally, evidence of social inequalities in the prevalence and incidence of chronic diseases was well known way before the SARS-CoV-2 pandemic (Agardh et al., 2011; Gershon et al., 2012; Potter et al., 2019; Barnett et al., 2012). Similar patterns of inequalities in COVID-19 mortality (Alicandro et al., 2021; Angelici et al., 2022), the effect of chronic conditions on COVID-19 adverse outcomes (Gobbato et al., 2020; Profili et al., 2020), and inequalities in chronic conditions (see Chapter 1, Chapter 2, and Cesaroni and Davoli 2022), have also been documented in the Italian context. As Nepomuceno et al. (2020) stated, studies on COVID-19 mortality should go further than mere age differences between individuals and also account for epidemiological and social characteristics.

Some studies have found that inequalities in COVID-19 severe outcomes persist after adjusting for chronic conditions. In Sweden, hospitalization, intensive care unit admission, and death show differences by income, even after considering other measures of socioeconomic position, age, sex, and the Charlson Comorbidity Index (Gustafsson et al., 2022). Similar results were previously observed in Canada, where individuals tested positive who lived in the richest neighborhoods had a 20% lower risk of dying from COVID-19 than those living in the poorest areas (Ge et al., 2021). However, little is known about why higher COVID-19 mortality is observed for more deprived populations. Some authors attribute these differentials in mortality to concomitant and unequal factors, which combine to create a "syndemic pandemic" (Bambra et al., 2020; McGowan and Bambra, 2022). According to this hypothesis, those living in more deprived areas are affected by four pathways of inequalities: 1) Unequal exposure to the virus, 2) Unequal transmission due to difficulties to self-isolate, 3) Unequal vulnerability due to non-communicable diseases, and 4) Unequal susceptibility due to chronic exposure to the social determinants of health (McGowan and Bambra, 2022). While the first two are related to the likelihood of being in contact with the virus and therefore of being infected, the last two refer to the diverse development of the disease itself once the infection has taken place.

In this study, we will focus on the third of the four pathways, related to inequalities in COVID-19 mortality due to the higher burden of pre-existent chronic conditions.

Focusing on the unequal vulnerability pathway, we make three hypotheses that could explain variations in COVID-19 mortality by deprivation level. 1) Individuals living in more deprived areas have higher prevalence of chronic conditions than those living in less deprived areas (prevalence hypothesis). 2) Residents of more deprived areas have a higher prevalence of chronic conditions specifically related to COVID-19 mortality than residents of less deprived areas (composition hypothesis). 3) Individuals in more deprived areas have higher mortality for the same morbidity due to more severe conditions than individuals in less deprived areas (severity hypothesis). The three hypotheses are not mutually exclusive and each or a mixture of some could be possible. Our main goal is to test these three different hypotheses in the context of the Lazio Region.

As international readers may not be familiar with the Lazio Region, a brief description follows. The Lazio Region is located in Central Italy and it is the second most populated Italian Region with 5.76 million residents at 01 Jan 2020. Most of its population resides in the Metropolitan City of Rome (2.8 million), the Italian Capital and largest city. While it remained largely unaffected by the first wave of SARS-CoV-2 pandemic in early 2020, it was hit by following waves, totaling 10.4 thousand COVID-19 deaths by 01 Mar 2022 (Italian Civil Protection Department, 2020).

4.2 Methods

We conducted a longitudinal study in the Lazio Region, gathering data on 961,017 reported SARS-CoV-2 first infections from February 2020 until February 2022. For every reported infection, we observed the exposure (Socioeconomic Position), the outcome (COVID-19 mortality), the potential confounder (age at testing), the possible effect modifier (sex), and the potential mediator (health status). We removed from our analyses those younger than 50 or older than 99 years, resulting in a study population of 330,092 individuals.

Variables

We measured the socioeconomic position using a composite deprivation index estimated at the census block level with data from the 2011 census (Rosano et al., 2020). Briefly, the index summarizes different proxy indicators of socioeconomic position: low educational attainment, unemployment, tenancy, single-parent households, and housing density.

To measure COVID-19 mortality, we gathered information about the date of death of the individuals from the regional mortality registry. We defined all deaths within 30 days from a positive SARS-CoV-2 test as deaths due to COVID-19, coherently with other studies (Iavarone et al., 2020; Ge et al., 2021; Panagiotou et al., 2021)

The health status was assessed through the regional health information systems. Combining data about hospitalizations, specialist visits, long-term drug use, and chronicity certifications, we estimated the presence/absence of 23 chronic conditions, grouped into 11 groups: **Cancer**, **Cardiopathies** (ischemic and valvular heart disease, arrhythmic, and non-arrhythmic myocardiopathy, congestive heart failure), **Chronic Kidney Disease** (CKD), **Chronic Obstructive Pulmonary Diseases** (and Respiratory failure, COPD), **Dementia** (and Alzheimer), **Diabetes** (type II), **Digestive Diseases** (hepatitis, pancreatitis, cirrhosis), **Hypercholesterolemia** (High Blood Lipids, HBL), **Hypertension**, **Neurologic Diseases** (epilepsy, Parkinson's, multiple sclerosis), and **Vasculopathies** (arterial, venous, and cerebral vasculopathy). A more in-depth description of the datasets used to estimate the chronic conditions is reported in the Appendix C.

Among the 11 groups of chronic conditions, we could estimate two levels of severity (non-severe/ severe) for Diabetes (without/ with organ damage) and cardiopathies (cardiopathies/ congestive heart failure).

Statistical analysis

We reported frequencies to describe the data, while we used logistic regression (presence/ absence of single morbidity) or negative binomial models (count of chronic conditions) to assess the association between the deprivation index and the health status, adjusting our estimates by age and stratifying by sex. We estimated the association between each chronic condition and mortality using sex-stratified logistic models, adjusted first for age and the deprivation index; and then for age, deprivation index, and every other morbidity. To assess the role of the mediator, we needed to estimate the indirect effect, that is, the part of the total effect of the exposure over the outcome passing through the mediator. There are two families of methodologies to do this: the difference method and the product method. The difference method focuses on the plain relation between exposure and outcome, comparing their direct relationship with its changes when adjusting for the mediator (MacKinnon, 2012). In practice, the effect of the exposure on the outcome adjusted by the mediator is deducted by the unadjusted effect. On the contrary, the product method studies the relationship between exposure and mediator and then between mediator and outcome, focusing on the indirect path going from the exposure to the outcome through the mediator (MacKinnon, 2012). In practical terms, the effect of the exposure on the mediator is multiplied by that of the mediator on the outcome. We used the product method which yields better estimates (Cheng et al., 2022), reporting the ratio between the indirect effect and the total effect (Mediated Proportion, MP). We first adjusted the MP estimates for age, and then for age and all other morbidities in the study. The 95% Confidence Interval (95%CI) for the MP was computed via the delta method. A more in-depth description of the natural indirect effect, the MP, and the delta method can be found elsewhere (Cheng et al., 2021). To answer the "severity hypothesis" we restricted the analyses to people with selected chronic conditions, i.e., Diabetes or cardiopathies. To test whether the deprivation index is an effect modifier in the relationship between chronic conditions and COVID-19 mortality, we ran age-adjusted sex-stratified logistic models. Last, we ran sensitivity analyses defining our outcome as 90-day all-cause mortality in all mediation analyses, adjusting our estimates by age and all morbidities in the study. We used the software R for data preparation and analyses (R Core Team, 2019).

4.3 Results

Descriptive results

In the Lazio region, 330,092 people (53.4% females) resulting from the above-mentioned selection got infected by SARS-CoV-2 from Feb 2020 to Feb 2022. We had information about 17,728 deaths (48.9% females) that occurred in our study population. The median day of death was 27 days after a positive swab, 25% of deaths happened within 13 days, and 75% within 87 days. 54% of deaths happened within 30 days, that is our definition of deaths due to COVID-19. If we only consider these, the 25%, 50%, and 75% of deaths happened within 8, 14, and 20 days respectively. In our study population, the deprivation index ranged between -5.79 and 27.98, with 80% of people having a deprivation index between -1.73 (least deprived decile) and 2.25 (most deprived decile). The median deprivation index was -0.14 and the interquartile range was 1.89 (first quartile = -1.02, third quartile = 0.87). Table 4.1 shows some descriptive statistics of the study population, reporting numerosity, proportions of deaths, and the mean deprivation index. Roughly half of the individuals were in the youngest age group 50-59, which suffered the lowest lethality for SARS-CoV-2. Lethality was higher for males than for females in all age groups, and reached its peak in the oldest population, killing more than 10% of females and almost 20% of males aged 80-99. Half of the study population was not affected by chronic conditions while more than 10% and 15% of females and males respectively had three or more comorbidities. Crude COVID-19 lethality was increasingly higher for increasing number of chronic conditions passing from less than 1% deaths for people without chronic conditions to more than 9% deaths for people with 3 or more. Finally, the most common morbidities were hypertension,

Table 4.1. Description of the study population. CC = Chronic Condition, DI = Deprivation Index, HBL = High Blood Lipids (hypercholesterolemia).

	Females			Males		
	N	**% deaths**	**mean DI**	**N**	**% deaths**	**mean DI**
total	176,188	2.42	0.25	153,904	3.40	0.21
50-59	79,965	0.13	0.20	71,377	0.38	0.18
60-69	43,769	0.75	0.30	41,624	1.84	0.25
70-79	27,043	3.21	0.29	25,271	6.02	0.26
80-99	25,411	11.70	0.25	15,632	17.14	0.14
0 CC	91,188	0.57	0.14	72,874	0.92	0.12
1 CC	44,465	2.22	0.29	38,195	2.72	0.23
2 CCs	21,853	4.59	0.38	19,604	5.25	0.30
3+ CCs	18,682	9.04	0.51	23,231	10.57	0.38
hypertension	64,367	4.97	0.39	63,325	5.95	0.29
HBL	19,691	4.75	0.43	22,313	6.83	0.31
cardiopathies	18,742	8.75	0.43	23,924	9.35	0.31

hypercholesterolemia, and cardiopathies for both sexes. Of these three, cardiopathies were the chronic condition with the highest lethality both in females and males, with crude estimates close to those of the population with three or more comorbidities.

As reported in Table C.1, in the Appendix C, hypertension, cardiopathies, and hypercholesterolemia were also the most common morbidities in those affected by multimorbidity. On the other hand, the chronic conditions which were more frequently present with other conditions were CKD (97% and 96% for females and males), vasculopathies (93% and 95%), and cardiopathies (93% and 94%). These chronic conditions have among their risk factors other morbidities (such as hypertension, hypercholesterolemia, and diabetes) and their frequent appearance in multimorbid settings could be linked with more frequent but less serious conditions. Hypertension, cancer, and digestive diseases were the conditions that most often occurred alone, appearing in multimorbid settings around 56%-66% of the time for females and 60%-74% for males.

Prevalence and composition hypotheses

To assess whether a higher prevalence of chronic conditions increases COVID-19 mortality inequalities, we had to check that 1) our study population had inequalities in health, and 2) that chronic conditions increased 30-day mortality in people who tested positive to SARS-CoV-2.

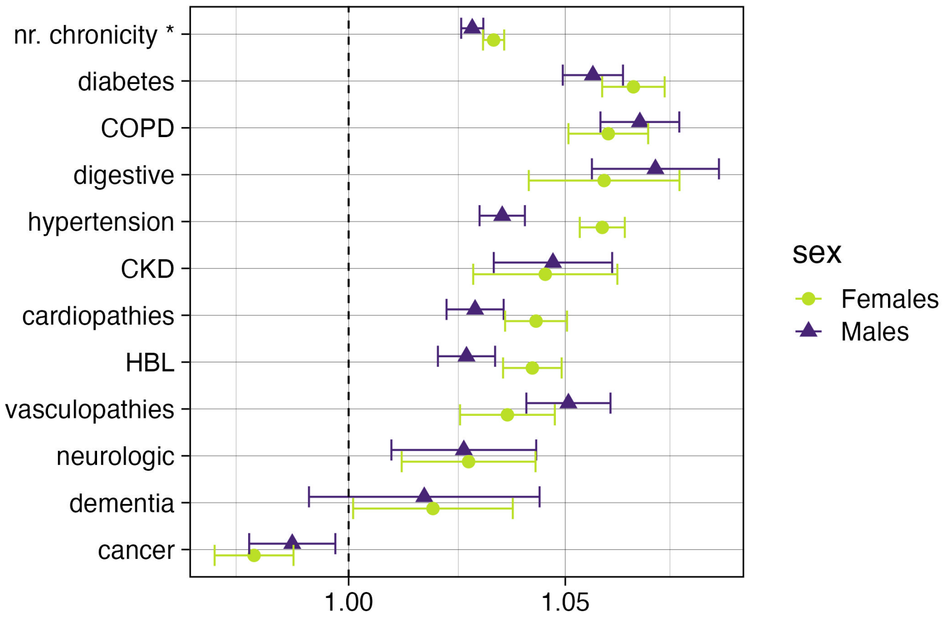

Figure 4.1. Age-adjusted odds ratios from logistic models (* = risks ratio from negative binomial), expressing the association between a composite indicator of deprivation (exposure) and chronic conditions (outcome). CKD = Chronic Kidney Disease, COPD = Chronic Obstructive Polmunary Disease, HBL = High Blood Lipids (hypercholesterolemia).

Figure 4.1 reports associations between the deprivation index and chronic conditions. Estimates come from age-adjusted and sex-stratified logistic regressions (negative binomial for number of chronic conditions, expressed as count), with morbidity as the outcome and the deprivation index as the exposure. Most of the models show a statistically significant association of single chronic conditions and the count of chronic conditions with the deprivation index. Dementia (males only) shows no significant association, while cancer shows a negative association with the deprivation index for both sexes. The positive associations indicate that people who tested positive and lived in areas with high values of the deprivation index had a higher likelihood of having any chronic condition than those living in areas with lower values of the deprivation index. Negative Binomial models show that every point increase in the deprivation index increases the chances of having a chronic condition by 3% both for females and males. That is, the higher the deprivation index, the higher the likelihood of having most of each morbidity and the higher the likelihood of having a higher number of chronic conditions.

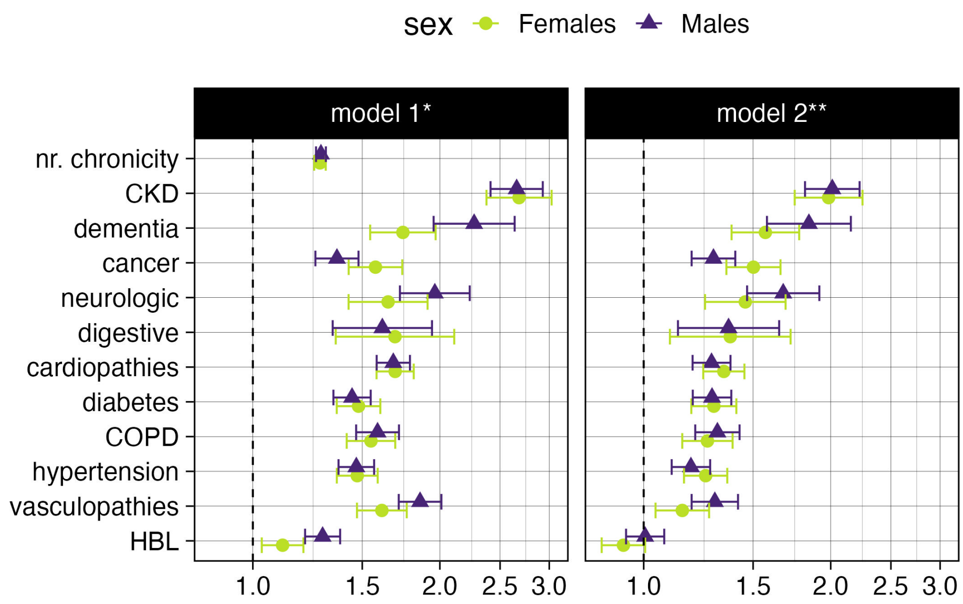

Figure 4.2. Odds ratios from logistic models, expressing the association between chronic conditions (exposure) and COVID-19 mortality (outcome). Estimates are adjusted by age and deprivation index (*) and by age, deprivation index and all other chronic conditions (**). CKD = Chronic Kidney Disease, COPD = Chronic Obstructive Polmunary Disease, HBL = High Blood Lipids (hypercholesterolemia).

Figure 4.2 shows estimates from logistic models stratified by sex and adjusted for age and deprivation index (left panel); and age, deprivation index, and all other morbidities (right panel). The models' outcome was death within 30 days from a positive test and the exposure was the chronic condition/ number of conditions. The number of chronic conditions and all single morbidities were positively associated with 30-day mortality in both sexes, but hypercholesterolemia became non-significant after adjusting for other comorbidities. Every additional chronic condition increases the odds of dying by 29% for both sexes. That is, individuals with two comorbidities had 66% higher mortality than those with no chronic condition and those with three

Table 4.2. Mediated Proportions (MP) for the indirect effect of deprivation on COVID-19 mortality passing through the chronic condition (CC). Estimates adjusted by age. CKD = Chronic Kidney Disease, COPD = Chronic Obstructive Polmunary Disease, HBL = High Blood Lipids (hypercholesterolemia).

	Females			**Males**		
	MP%	**95% CI**		**MP%**	**95% CI**	
nr. CCs	19.82	12.07	27.57	20.15	13.60	26.70
cancer	-1.73	-4.65	1.19	-0.89	-3.18	1.40
cardiopathies	5.39	1.61	9.18	5.22	1.16	9.29
CKD	1.81	-4.24	7.85	3.44	-3.64	10.51
COPD	3.66	0.61	6.71	5.52	1.44	9.59
dementia	0.19	-3.25	3.63	0.10	-5.83	6.03
diabetes	6.11	2.58	9.65	6.58	2.80	10.35
digestive	1.21	-2.07	4.50	2.16	-1.39	5.71
HBL	1.27	0.06	2.48	2.49	0.36	4.62
hypertension	11.07	6.08	16.06	8.33	4.17	12.50
neurologic	0.71	-2.37	3.79	0.93	-3.88	5.74
vasculopathies	1.63	-1.32	4.57	4.81	0.06	9.57

conditions more than twice higher mortality. The chronic condition associated with the highest mortality was CKD for both males and females whether or not the model was adjusted for other morbidities. Most chronic conditions substantially increased mortality with odds ratios statistically higher than 1.4. When adjusting for other comorbidities, only CKD for females and CKD, dementia, and neurologic diseases for males remained statistically above 1.4, although all odds ratios remained positive and statistically significant but those of hypercholesterolemia.

Table 4.2 shows the percentual MP of the indirect effect of the deprivation index on COVID-19 mortality passing through chronic conditions. The higher the MP, the more pre-existent inequalities in chronic conditions explain the inequalities in COVID-19 mortality. The highest MP is shown by the count of morbidity, mediating the effect of the deprivation on COVID-19 mortality by up to 20% for females (95%CI = 12-28) and males (95%CI = 14-27). The single morbidities that mediate the most are hypertension and diabetes in both sexes, roughly driving 10% and 6% of inequalities respectively. Apart from cardiopathies and COPD for both sexes and vasculopathies for males, the other chronic conditions have small or non-statistically significant MP. For both sexes, cancer has a negative (although not statistically

Table 4.3. Mediated Proportions (MP) for the indirect effect of deprivation on COVID-19 mortality passing through the chronic condition. Estimates adjusted by age and every other chronic condition. CKD = Chronic Kidney Disease, COPD = Chronic Obstructive Polmunary Disease, HBL = High Blood Lipids (hypercholesterolemia).

	Females			**Males**		
	MP%	**95% CI**		**MP%**	**95% CI**	
cancer	-1.88	-5.12	1.36	-0.98	-3.54	1.58
cardiopathies	3.44	0.73	6.14	3.12	0.34	5.91
CKD	1.42	-3.38	6.23	2.93	-3.20	9.06
COPD	2.32	0.12	4.52	3.90	0.62	7.18
dementia	0.19	-3.27	3.65	0.09	-5.67	5.86
diabetes	4.55	1.53	7.58	5.35	1.79	8.90
digestive	0.80	-1.44	3.03	1.74	-1.31	4.79
HBL	-1.35	-2.87	0.17	-0.20	-1.13	0.73
hypertension	7.15	2.85	11.44	4.49	1.24	7.74
neurologic	0.65	-2.19	3.49	0.94	-3.95	5.84
vasculopathies	0.56	-0.55	1.68	2.50	-0.25	5.25

significant) MP, meaning that it reduces inequalities in COVID-19 mortality. Since lower deprivation indexes are associated with a higher cancer prevalence in our study population, and cancer is associated with higher mortality, theoretically removing cancer from our study population would result in an overall increase in COVID-19 mortality differentials.

Adjusting the MP of single morbidities by age and the other morbidities reduced all the estimates reported previously, as shown in Table 4.3. The MP of hypercholesterolemia became non-significant in both sexes, and the lower bound for the MP of COPD and cardiopathies got close to zero for females and males. Diabetes and hypertension remained the most mediating morbidities in both sexes, although the MP for hypertensive males was reduced by roughly half. For males, diabetes and hypertension mediated respectively around 5% (95%CI: 2%-9%) and 4% (95%CI: 1%-8%) respectively of inequalities in COVID-19 mortality. For females, diabetes mediated 5% of inequalities (95%CI: 2%-8%) and hypertension 7% (95%CI: 3%-10%).

Severity hypothesis

To assess the severity hypothesis, we replicated the analyses made for the prevalence and composition hypotheses, restricting the study population to those with chronic conditions for which we could assess severity, namely, cardiopathies and diabetes. The response variable when considering inequalities in severity and the mediator variable when analyzing the effect on mortality was having severe/ non-severe chronic condition. 5,283 females out of 18.742 had the severe form of cardiopathies (28.2%) while numbers for males these were 5,423 out of 23,924 (22.7%). Shares were lower for diabetes: 7% (1,028) and 8.1% (1,370) of females and males respectively had organ damage due to severe diabetes. Females and males who resided in areas with high values of the deprivation index were more likely to have severe cardiopathies (females OR = 1.04, 95%CI = 1.03-1.06; males OR = 1.05, 95%CI = 1.04-1.07) and severe diabetes (females only, OR = 1.04, 95%CI = 1.01-1.06). Both chronic severe conditions showed higher mortality than their non-severe form in females (cardiopathies OR = 1.67, 95%CI = 1.50-1.86; diabetes OR = 1.68, 95%CI = 1.35-2.10) and males (cardiopathies OR = 1.69, 95%CI = 1.54-1.86; diabetes OR = 1.59, 95%CI = 1.33-1.91). The MP for the severe forms were not statistically significant and showed wide confidence intervals due to the low numerosity in the restricted population affected by the morbidity (results not shown).

Supplementary analyses

In the supplementary material, Table C.2 reports estimates of the interaction effects between chronic condition and deprivation index over mortality. Both sexes show non-significant estimates for every interaction term, indicating the absence of an effect modification. Table C.3 shows sensitivity analyses performed on the MP adjusted by age and all other chronic conditions. When changing the outcome from 30-day to 90-day mortality, MP estimates remained similar to those showed in our main analyses.

4.4 Discussion

Principal findings

We found that differences in COVID-19 mortality between those living in more and less deprived areas can be explained by up to 20% for females and males by differences in the prevalence of pre-existing chronic conditions. Diabetes and hypertension were the conditions that mediate the most, while other single morbidities were not as important for either females or males. Finally, we did not find any evidence about the role of chronic conditions' severities in mediating the effect of census tract deprivation on COVID-19 mortality.

Our results indicate that: 1) those living in deprived areas have higher rates of COVID-19 mortality due to a higher prevalence of pre-existent chronic conditions, confirming our prevalence hypothesis. 2) Inequalities in the higher prevalence of diabetes and hypertension may drive inequalities in COVID-19 mortality, partially supporting the composition hypothesis. 3) The severity of pre-existing conditions did not appear to mediate inequalities in COVID-19 mortality, not endorsing the severity hypothesis.

Overall, our results suggest that what drives inequalities in COVID-19 mortality the most is the quantity rather than the type of chronic conditions. That is, while inequalities in single morbidities or in severity account for a smaller or negligible percentage of all inequalities in COVID-19 mortality, the higher risk of having a higher count of chronic conditions explains more than a fifth of the differences in COVID-19 mortality by deprivation. The number of chronic conditions indicates increasingly complex medical needs, polypharmacy, and, potentially, multiple body systems affected (Wallace et al., 2015). This can explain why inequalities in the number of chronicity so easily influence inequalities in COVID-19 mortality (29% higher odds of dying for every additional chronic condition). Although inequalities in the likelihood of having each single morbidity exist, only inequalities in diabetes and hypertension seem to drive COVID-19 mortality inequalities substantially. Both chronic conditions have their own important mediating effect even after adjusting for the effects of the other morbidities. Hypertension was a main driver of inequalities in COVID-19 mortality although inequalities in its prevalence and its association with COVID-19 mortality were not larger compared to those of other morbidities. We could speculate that its diffusion among the population (N $\simeq$ 128,000) could play a role in its mediating power. The low numerosity of the restricted populations with diabetes or cardiopathies could explain why there were no statistically significant result when considering the mediating role of severity between inequalities in health and COVID-19 mortality.

To the best of our knowledge, this is the first study that has the main goal of estimating the mediating effect of pre-existent chronic conditions between socioeconomic position and COVID-19 mortality, trying to quantify and test the idea of the "syndemic pandemic" (Bambra et al., 2020; McGowan and Bambra, 2022).

As far as we are aware, only a study by Marra et al. (2022) investigated this relationship, estimating a reduction of between 15%-25% of the relative index of inequalities after adjusting for a comorbidity index, in line with our MP estimates. However, they did not perform a mediation analysis and the aim of the studies, the period of analyses, the measures of inequalities, and the measure of chronic conditions differ. Therefore, comparisons between our study and Marra and colleagues' should be made with caution. Still, we can compare our results about inequalities in chronic conditions and the adverse effect they have on COVID-19 mortality with international and Italian studies. In our population of first-time SARS-CoV-2 infections, we found the well-known association between socioeconomic position and chronic conditions (Agardh et al., 2011; Gershon et al., 2012; Potter et al., 2019; Barnett et al., 2012), the widely reported association between chronic conditions and COVID-19 adverse outcomes (Yang et al., 2020; Richardson et al., 2020; Reyes-Sánchez et al., 2022; Dessie and Zewotir, 2021; Zhou et al., 2020), and the unequal burden of COVID-19 death in more disadvantaged socioeconomic groups (Feldman and Bassett, 2021; Kontopantelis et al., 2021, 2022; Sun et al., 2021; Chen and Krieger, 2021; Yoshikawa and Kawachi, 2021; Vanthomme et al., 2021).

Strength and Weakness

Our study presents some limitations and strengths. First, the core assumption of mediation analyses is that the exposure causes the mediator, and the mediator causes the outcome. This hypothesis requires that exposure, mediator, and outcome are temporally ordered. In our study, there is no doubt that our exposure (socioeconomic position) as well as our mediator (chronic conditions) both happen before the outcome (COVID-19 mortality). However, the temporality between exposure and mediator could be problematic. The onset of a health condition might force an individual to move from a less deprived to a more deprived area, i.e., change his level of socioeconomic position. Nevertheless, the inverse causality between area of residence and chronic condition is unlikely in the Italian context for two reasons. 1) Italy has low shares of renters and big shares of homeowners, resulting in one of the lowest residential mobility among OECD countries (Caldera Sánchez and Andrews, 2011). 2) The chronic conditions considered in our analyses have onsets that generally occur at older ages when the residential mobility is lower (Caldera Sánchez and Andrews, 2011). Although these two points do not completely rule out the possibility of reverse causality between exposure and mediator, we are confident that only a small fraction of events might be affected by inverse temporality.

Second, regarding the exposure, we used a composite deprivation index estimated with data from the 2011 census as our exposure. The index could not be updated and the 2011 remain the latest version available. Although the values of the deprivation index may have varied over the years, it is implausible that formerly deprived areas could have become non-deprived areas, although a more recent measure would be more accurate and desirable.

Third, we defined the outcome as 30-day all-cause mortality from a positive swab, analyzing roughly 54% of deaths that occurred in our study population of first-time infected. This means that 1) we mainly focused on short-term, acute, COVID-19 mortality, without considering long-term mortality; 2) we considered as COVID-19 mortality also deaths that would have occurred without the SARS-CoV-2 infection, mainly for individuals with many comorbidities. Regarding the first point, although rarer, long-term COVID-19 mortality has been documented (Uusküla et al., 2022), and roughly 25% of deaths in our study population occurred between 30 and 90 days. At the same time, the increase in mortality after a month from a positive swab is minimal (Günster et al., 2021), and we choose to limit the analyses to a specific time frame to use logistic instead of survival models. Moreover, measuring COVID-19 mortality as 30-day all-cause mortality from a positive swab is consistent with previous studies (Iavarone et al., 2020; Ge et al., 2021; Panagiotou et al., 2021). Regardless, sensitivity analyses using 90-day all-cause mortality (roughly 76% of deaths) gave the same results as our main analyses. Concerning the second point, the possible inclusion of individuals that would have died anyway in the same period, even without the infection, is likely minimal, and this can hardly affect the results.

Fourth, we had information about 23 chronic conditions that we grouped into 11 categories. While the former 23 chronic conditions are many, they are not a comprehensive list of morbidities, nor do they account for broader chronic habits such as smoking, obesity, or alcohol abuse. Our choice in grouping the conditions included in the study were to some extent subjective. However, it was necessary to simplify the analyses and to allow an easier interpretation of the results. Moreover, we relied on the help of a clinician to make the grouping.

Fifth, we used the delta method to estimate its 95%CI of the MP instead bootstrapping procedures for computing power and time reasons. However, simulation studies showed that with a study population bigger than 20,000 and more than 500 events, the nominal coverage of the confidence intervals obtained via the delta method is satisfactory (Cheng et al., 2021). Every analysis we ran had more than seven times the population and eight times the cases than the minimal numerosity indicated by the simulation study. The only exceptions were the severity analyses which, however, had N $\simeq$ 20,000 and $\simeq$ 2,000 outcomes.

Our work also has several strength. First, to the best of our knowledge, this is the first study that specifically analyzes (part of) the "syndemic pandemic" idea proposed by Bambra et al. (2020) using a mediation analysis. It enumerates the proportion of inequalities in COVID-19 mortality that can be explained by pre-existent inequalities in chronic conditions. Second, although we could not compare our main results, estimates regarding inequalities in chronic conditions and increased mortality by morbidities follow the previous literature, as we already discussed. Third, we used the product method instead of the difference method, which has been proven to give better estimates than the latter for dichotomous outcomes (Cheng et al., 2022). Fourth and last, our estimates were robust to different adjustments, supplemental analyses, and sensitivity analyses with 90-day all-cause mortality instead of 30-day overall mortality.

Although we explained 20% of the inequalities in COVID-19 mortality with pre-existent inequalities in chronic conditions, the remaining 80% of inequalities remains unexplained. Future studies should aim to further disentangling the effect of socioeconomic position on COVID-19 mortality analyzing the mediating effect of vaccinations, health literacy/ early access to best-practice cures, and viral load, among others. Finding the most-mediating factor between socioeconomic position and COVID-19 mortality could "kill two birds with one stone", making it possible to reduce inequalities in the mediating factor and consequently on COVID-19 mortality with just one intervention.

Conclusions

More than 20% of inequalities in COVID-19 mortality for people who tested positive could be explained by pre-existent inequalities in chronic conditions. The most influential mediators between socioeconomic position and COVID-19 mortality were hypertension and diabetes, both accounting more than 5% of the total effect. Inequalities in the prevalence and the composition of chronic conditions play an important role in mediating the effect of socioeconomic position on COVID-19 mortality. On the contrary, we could not find any evidence in support of the hypothesis that inequalities in the severity of the chronic conditions explains COVID-19 mortality inequalities.

Conclusions

In the last half century, relative health inequalities in Europe have stagnated, at best, while absolute inequalities reduced (Mackenbach, 2020). The overall improvement in health observed over this period was driven by faster advancements for individuals in higher rather than lower socioeconomic positions, who instead had slower mortality declines. After the 2008 financial crisis, healthcare systems were fragile and strained by the austerity policies. In this scenario, a new coronavirus emerged, highlighting pre-existent inequalities, and further amplifying differentials in health between socioeconomic positions (WHO, 2021). The most disadvantaged benefited less from the measures implemented to mitigate the spread of the SARS-CoV-2. It was more difficult for them to self-isolate when infected, due to smaller habitations, and those who could not avoid working in person during lockdowns suffered either a higher infection rate or a higher likelihood of job loss. Although Italy had lower inequalities in health compared to other European countries, differentials in mortality and health between socioeconomic positions were evident before and during the ongoing SARS-CoV-2 pandemic.

The present thesis had the goal to analyze health inequalities in the Italian setting. Specifically, I aimed to analyze inequalities in pre-COVID-19 times, how SARS-CoV-2 spread differently among socioeconomic positions, and what drove COVID-19 mortality differentials between socioeconomic levels.

The results I show in Chapter 2 underline the presence of multiple and independent levels of inequalities in the pre-pandemic period. This study highlights the heterogeneous forces that shape health. Individuals with a lower socioeconomic position had shorter survival expectations regardless of their baseline health status. Moreover, the likelihood of having a chronic condition was always higher for people in lower socioeconomic positions, both at the individual and at the contextual level. In fact, these two measures of socioeconomic positions were independently associated with health. Addressing and mitigating inequalities at the individual and contextual levels is a harder challenge than acting on just one level, but it is needed. Similarly, preventing inequalities in health status without considering underlying inequalities in the socioeconomic position would not completely prevent inequalities in mortality, as confirmed also by the analyses in 4.

Chapter 3 analyzes the diverse effects of the Italian three-tier restriction system in provinces with different economic disadvantages. While the highest restriction level, that is, a complete lockdown, was particularly effective in provinces with lower levels of economic disadvantage; the moderate and the lowest set of restrictions were more effective in more economically disadvantaged provinces. This study underlines the importance of preventive measures aimed at reducing the spread of viruses, but also the inequalities they produce. As previously discussed, the spread of SARS-CoV-2 is tightly linked to the habits and the movements of the population. Probably, in times of less-strict measures, those with higher economic availability were more likely to enjoy social activities and resulted disadvantaged in terms of infections. On the contrary, essential workers had a higher spread in times of stay-at-home orders when they had to continue working without the chance to avoid contacts. It is important to know that different levels of restriction affect areas with different levels of socioeconomic position differently. This allows to program ad-hoc policies in disparate contexts. For example, giving essential workers privileged access to vaccinations or free-of-charge high-quality masks could help reduce disparities in times of pandemic peaks, giving more protection to those who cannot follow stay-at-home orders. Conversely, improved ventilation in social venues such as restaurants, malls, and bars, could have mitigated the spread during lower-risk periods, mainly in wealthy areas.

Finally, results from Chapter 4 show that a fifth of socioeconomic inequalities in COVID-19 mortality can be explained by pre-existent inequalities in chronic conditions. These results give an insight into what happens after the diverse spread of the virus shown in Chapter 3. I found that the unequal prevalence of comorbidities is the most mediating factor among those in analysis, meaning that it explains the greatest portion of inequalities in COVID-19 mortality. The different composition of chronic conditions had an important but less relevant role, and the inequalities in morbidity's severity showed no evidence to be a mediator of inequalities in COVID-19 mortality. These results are the first step to disentangling the relationship between socioeconomic position and COVID-19 mortality. Finding the most mediating factor between the two measures would help focus interventions on reducing disparities in the mediator, obtaining positive outcomes both on the mediator and on COVID-19 mortality. As an example, I show that differences in the number of chronicity mediates 20% of inequalities in COVID-19 mortality. It would be ideal, but rather difficult, to reduce inequalities in every chronic condition to reduce the overall difference in the count of morbidities. However, my results also showed that diabetes alone mediates around 7-9% of COVID-19 mortality inequalities. That is, interventions aimed at reducing the prevalence of diabetes among lower socioeconomic positions would reduce an important part of inequalities in COVID-19 mortality. Results also combine with those of Chapter 2, when I showed an independent association between chronic conditions and socioeconomic status. That is, some inequalities in mortality could be addressed by inequalities in baseline health but some other remained unexplained by the difference in chronic conditions alone.

To conclude, inequalities in health highlight unjust differences in health literacy, living conditions, opportunities, and well-being that could be avoided. Comparing health outcomes between socioeconomic positions can give us important insights into what could be improved and to reach a reasonable, achievable standard of health that would give benefits to the whole population. The inequalities revealed by extensive studies in Britain gave rise to a robust policy response in the 2000s aimed at redressing the situation. Their ineffectiveness should not discourage further actions to prevent unequal health among the population. On the contrary, they can and should become lessons on the importance of reducing the "background causes" of health inequalities (that is, the wealth inequalities), together with the "proximal causes" (i.e., risky habits).

Beyond any ethical concerns, removing differentials in chronic conditions would mean reducing the cost of avoidable utilization of drugs and healthcare services. This would allow us, as a society, to focus and optimize resources to tackle non-avoidable conditions. The absence of inequalities indicates the fairness of the system and represents the best health status the population could reach at that moment. The main goal that every National Healthcare System should aim to.

Appendix A

Supplementary material of Chapter 2

Table A.1. Association between indicators of socioeconomic position and presence of Chronic or Rare Diseases, ordinal models. Italian residents aged 25-99 years. Rome, 09 October 2011. Odds Ratios (OR) adjusted for age group and reported with their 95% Confidence Intervals (95%CI).

		FEMALES (N= 964, 284)			MALES (N= 815, 959)		
		OR	**95%CI**		**OR**	**95%CI**	
age group	25-34	*ref.*	-	-	*ref.*	-	-
	35-44	1.62	1.58	1.67	1.69	1.63	1.75
	45-54	2.77	2.70	2.84	3.63	3.51	3.75
	55-64	5.32	5.19	5.45	8.72	8.44	9.00
	65-74	7.22	7.04	7.40	15.34	14.86	15.83
	75-84	7.13	6.95	7.32	18.76	18.15	19.38
	85-99	4.77	4.63	4.92	13.47	12.93	14.02
education	High	*ref.*	-	-	*ref.*	-	-
	Medium	1.36	1.34	1.38	1.55	1.53	1.58
	Low	1.64	1.62	1.67	1.68	1.65	1.71
real estate price	1 (highest)	*ref.*	-	-	*ref.*	-	-
	2	1.23	1.21	1.25	1.25	1.23	1.27
	3	1.51	1.49	1.54	1.52	1.50	1.55
	4	1.60	1.58	1.63	1.58	1.55	1.61
	5 (lowest)	1.90	1.87	1.93	1.84	1.81	1.88

Table A.2. Association between indicators of socioeconomic position and presence of Chronic or Rare Diseases, ordinal models. Italian residents aged 25-99 years. Rome, 09 October 2011. Odds Ratios (OR) adjusted for every other variable in the table and reported with their 95% Confidence Intervals (95%CI).

		FEMALES (N= 964, 284)			**MALES** (N= 815, 959)		
		OR	**95%CI**		**OR**	**95%CI**	
age group	25-34	*ref.*	-	-	*ref.*	-	-
	35-44	1.60	1.56	1.64	1.68	1.62	1.74
	45-54	2.68	2.61	2.75	3.61	3.50	3.73
	55-64	5.19	5.06	5.32	8.81	8.53	9.10
	65-74	6.95	6.77	7.13	15.48	14.99	15.98
	75-84	6.76	6.59	6.95	18.82	18.21	19.46
	85-99	4.65	4.51	4.80	14.05	13.48	14.63
education	High	*ref.*	-	-	*ref.*	-	-
	Medium	1.24	1.22	1.26	1.41	1.38	1.43
	Low	1.37	1.35	1.39	1.43	1.40	1.45
real estate price	1 (highest)	*ref.*	-	-	*ref.*	-	-
	2	1.19	1.17	1.21	1.18	1.15	1.20
	3	1.42	1.40	1.45	1.39	1.37	1.42
	4	1.49	1.46	1.51	1.42	1.39	1.44
	5 (lowest)	1.73	1.70	1.76	1.63	1.60	1.66

Table A.3. Association between indicators of socioeconomic position and presence of Chronic or Rare Diseases, non proportional odds models. Italian residents aged 25-99 years. Rome, 09 October 2011. Odds Ratios (OR) adjusted for every other variable in the table and reported with their 95% Confidence Intervals (95%CI).

		FEMALES (N= 964, 284)			**MALES** (N= 815, 959)		
1 vs 0		**OR**	**95%CI**		**OR**	**95%CI**	
age group	25-34	*ref.*	-	-	*ref.*	-	-
	35-44	1.54	1.50	1.59	1.59	1.53	1.65
	45-54	2.41	2.34	2.47	2.97	2.87	3.08
	55-64	3.82	3.71	3.92	5.85	5.65	6.06
	65-74	4.46	4.33	4.58	8.77	8.46	9.08
	75-84	4.13	4.01	4.26	9.85	9.49	10.21
	85-99	2.86	2.76	2.97	7.41	7.06	7.78
education	High	*ref.*	-	-	*ref.*	-	-
	Medium	1.18	1.16	1.20	1.32	1.29	1.34
	Low	1.26	1.23	1.28	1.37	1.34	1.40
real estate price	1 (highest)	*ref.*	-	-	*ref.*	-	-
	2	1.15	1.13	1.17	1.19	1.16	1.22
	3	1.30	1.28	1.33	1.32	1.29	1.35
	4	1.34	1.31	1.37	1.32	1.29	1.35
	5 (lowest)	1.52	1.49	1.55	1.51	1.47	1.54
2+ vs 0							
age group	$25-34$	*ref.*	-	-	*ref.*	-	-
	$35-44$	2.10	1.95	2.25	2.41	2.19	2.65
	$45-54$	4.89	4.57	5.23	8.50	7.78	9.30
	$55-64$	14.42	13.51	15.40	30.07	27.55	32.82
	$65-74$	22.42	21.00	23.92	61.58	56.45	67.19
	$75-84$	22.61	21.17	24.15	79.09	72.44	86.35
	$85-99$	15.59	14.54	16.73	58.49	53.28	64.21
education	High	*ref.*	-	-	*ref.*	-	-
	Medium	1.44	1.40	1.48	1.56	1.52	1.60
	Low	1.65	1.61	1.70	1.55	1.50	1.59
real estate price	1 (highest)	*ref.*	-	-	*ref.*	-	-
	2	1.25	1.22	1.28	1.16	1.13	1.19
	3	1.63	1.59	1.67	1.48	1.43	1.52
	4	1.74	1.69	1.78	1.54	1.49	1.58
	5 (lowest)	2.12	2.06	2.18	1.81	1.76	1.86

Table A.4. Association between baseline characteristics and emigration, logistic models. Italian residents aged 25-99 years. Rome, 2011-2016. Odds Ratios (OR) adjusted for every variable in the table and reported with their 95% Confidence Intervals (95%CI).

		FEMALES (N= 927, 537)			**MALES** (N= 28, 165)		
		OR	**95%CI**		**OR**	**95%CI**	
age group	25-34	*ref.*	-	-	*ref.*	-	-
	35-44	0.47	0.46	0.49	0.61	0.59	0.63
	45-54	0.35	0.33	0.36	0.46	0.44	0.47
	55-64	0.37	0.35	0.38	0.49	0.47	0.51
	65-74	0.29	0.28	0.31	0.39	0.37	0.41
	75-84	0.31	0.29	0.32	0.27	0.26	0.29
	85-99	0.32	0.30	0.34	0.24	0.21	0.26
education	High	*ref.*	-	-	*ref.*	-	-
	Medium	1.09	1.06	1.12	1.08	1.04	1.11
	Low	1.20	1.16	1.25	1.10	1.06	1.14
		p-trend < 0.001			p-trend < 0.001		
real estate price	1 (highest)	*ref.*	-	-	*ref.*	-	-
	2	0.91	0.88	0.95	0.92	0.89	0.96
	3	0.87	0.83	0.90	0.88	0.84	0.91
	4	0.84	0.81	0.88	0.84	0.81	0.87
	5 (lowest)	0.81	0.78	0.84	0.82	0.79	0.85
		p-trend < 0.001			p-trend < 0.001		
chronicity	none	*ref.*	-	-	*ref.*	-	-
	one or more	0.90	0.87	0.93	0.90	0.87	0.93

Table A.5. Association between indicators of socioeconomic position and survival, accelerated failure time models. Italian residents aged 25-99 years. Rome, 2011-2016. Time Ratios (TR) adjusted for age group and reported with their 95% Confidence Intervals (95%CI).

		FEMALES			**MALES**		
		TR	**95%CI**		**TR**	**95%CI**	
age group	25-34	*ref.*	-	-	*ref.*	-	-
	35-44	0.43	0.37	0.51	0.51	0.46	0.58
	45-54	0.18	0.16	0.21	0.22	0.20	0.25
	55-64	0.08	0.07	0.09	0.10	0.09	0.11
	65-74	0.04	0.03	0.04	0.04	0.04	0.05
	75-84	0.01	0.01	0.01	0.02	0.01	0.02
	85-99	0.00	0.00	0.01	0.01	0.01	0.01
education	High	*ref.*	-	-	*ref.*	-	-
	Medium	0.87	0.85	0.89	0.84	0.82	0.86
	Low	0.79	0.77	0.81	0.71	0.70	0.73
		p-trend < 0.001			p-trend < 0.001		
real estate price	1 (highest)	*ref.*	-	-	*ref.*	-	-
	2	0.96	0.94	0.98	0.96	0.93	0.98
	3	0.96	0.94	0.98	0.91	0.89	0.94
	4	0.95	0.93	0.97	0.90	0.88	0.92
	5 (lowest)	0.94	0.91	0.96	0.88	0.86	0.91
		p-trend < 0.001			p-trend < 0.001		
chronicity	none	*ref.*	-	-	*ref.*	-	-
	one	0.79	0.77	0.80	0.75	0.74	0.77
	two or more	0.66	0.65	0.67	0.62	0.61	0.64

Table A.6. Association between indicators of socioeconomic position and survival, accelerated failure time models. Italian residents aged 25-99 years. Rome, 2011-2016. Time Ratios (TR) adjusted for every variable in the table and reported with their 95% Confidence Intervals (95%CI).

		FEMALES			**MALES**		
		TR	**95%CI**		**TR**	**95%CI**	
age group	25-34	*ref.*	-	-	*ref.*	-	-
	35-44	0.44	0.38	0.52	0.52	0.47	0.59
	45-54	0.19	0.16	0.22	0.23	0.21	0.26
	55-64	0.08	0.07	0.10	0.10	0.09	0.11
	65-74	0.04	0.03	0.05	0.04	0.04	0.05
	75-84	0.01	0.01	0.02	0.02	0.02	0.02
	85-99	0.00	0.00	0.01	0.01	0.01	0.01
education	High	*ref.*	-	-	*ref.*	-	-
	Medium	0.87	0.85	0.89	0.84	0.83	0.86
	Low	0.79	0.77	0.81	0.71	0.70	0.73
		p-trend < 0.001			p-trend < 0.001		
real estate price	1 (highest)	*ref.*	-	-	*ref.*	-	-
	2	0.99	0.97	1.01	1.00	0.98	1.02
	3	1.00	0.98	1.02	0.99	0.96	1.01
	4	1.01	0.98	1.03	0.99	0.97	1.02
	5 (lowest)	1.00	0.97	1.02	1.00	0.98	1.03
		p-trend < 0.001			p-trend < 0.001		
chronicity	none	*ref.*	-	-	*ref.*	-	-
	one	0.79	0.78	0.81	0.76	0.75	0.78
	two or more	0.67	0.66	0.68	0.63	0.62	0.64

Appendix B

Supplementary material of Chapter 3

Models' equations

$R_{t\,ij} = \alpha + \underline{x}'_{ij}\beta + u_i + e_{ij}$ where i indicates the cluster and j the observation. In the formula, α is the fixed intercept, $\underline{x}'_{ij}$ is the vector of variables observed in cluster i at the j-th observation, β the vector of fixed effects (common for every cluster and observation), u_i the specific random intercept of cluster i assumed to be normally distributed, and e_{ij} the usual error term of linear regressions assumed to be normally distributed as well. Specifically, we run four different models per tier, as reported in Table 1 in the manuscript. Models were defined as follows.

Model A) in Table 3.1

$$R_{t\,ij} = \alpha + days_{ij}\beta + u_i + e_{ij}$$

$days_{ij}$ is the cardinal number of days (0, 1, 2, ...). Since the models are stratified per each restriction, β indicates the effect of passing days in each tier, that is, the overall effect of the restriction.

Model B) in Table 3.1

$$R_{t\,ij} = \alpha + PED_i\beta + u_i + e_{ij}$$

PED_i is the average effect of the province's economic disadvantage over the R_t.

Model C) in Table 3.1

$$R_{t\,ij} = \alpha + days_{ij}\beta_{days} + PED_i\beta_{PED} + days_{ij} \cdot PED_i\beta_{int} + u_i + e_{ij}$$

$days_{ij} \cdot PED_i$ indicates the interaction term between the number of days into the restriction and the province's economic disadvantage. It is a cross-level interaction because the variable days changes per every cluster i per every observation j, while the PED is constant in every observation once the cluster is defined.

Model D) in Table 3.1

$$\begin{aligned} R_{t\,ij} = \alpha &+ days_{ij}\beta_{days} + PED_i\beta_{PED} + days_{ij} \cdot PED_i\beta_{int} + \\ &+ age_i\beta_{age} + density_i^{ML}\beta_{ML} + density_i^{MH}\beta_{MH} + density_i^{H}\beta_{H} + \\ &+ repartition_i^{C}\beta_{C} + repartition_i^{S}\beta_{S} + u_i + e_{ij} \end{aligned}$$

age_i indicates the share of people aged 0-5. $density_i^{ML}$, $density_i^{MH}$, and $density_i^{H}$ are three dichotomic variables representing, respectively, the Medium-Low, Medium-High, or High population density of the cluster. Their betas are effects compared to provinces with Low population density. $repartition_i^{C}$ and $repartition_i^{S}$ are two dichotomic variables that indicate, respectively, the provinces belonging to the Central or Southern geographical repartition. Their betas are effects compared to Northern provinces.

Supplementary table

Table B.1. Association between economic disadvantage and SARS-CoV-2 spread by restriction tier. Estimates from Multilevel Linear Model with random intercepts stratified by restriction tier. Est. = Estimate; SE = Standard Error; PED = Province's Economic Disadvantage. *Models were adjusted for population density, share of people aged 0-5, and geographical repartition.

	Yellow			Orange			Red		
	Est.	**SE**	**p**	**Est.**	**SE**	**p**	**Est.**	**SE**	**p**
1) restriction $\geq$ 7 days*									
Intercept	0.967	0.014	< 0.01	0.973	0.013	< 0.01	1.026	0.015	< 0.01
days	0.006	4E-04	< 0.01	0.001	4E-04	< 0.01	-0.018	0.001	< 0.01
PED	0.002	0.001	0.07	0.006	0.001	< 0.01	0.002	0.001	0.04
PED x days	-1E-04	3E-05	< 0.01	-5E-04	3E-05	< 0.01	3E-04	4E-05	< 0.01
2) weighted models*									
Intercept	0.928	0.028	< 0.01	0.985	0.026	< 0.01	0.993	0.030	< 0.01
days	0.006	4E-04	< 0.01	0.001	3E-04	< 0.01	-0.018	0.001	< 0.01
PED	-0.002	0.003	0.55	0.005	0.002	0.05	0.009	0.003	< 0.01
PED x days	-1E-04	3E-05	< 0.01	-5E-04	3E-05	< 0.01	3E-04	4E-05	< 0.01

Appendix C

Supplementary material of Chapter 4

Data sources for the estimation of chronic conditions

A selection of chronic and acute clinical conditions that occur frequently in the general population is considered in this study. The diseases identification algorithms used in this study came from a review of the scientific literature and an analytical study of Italian and international data.

The following sources were used to assess the prevalence of diseases in the Lazio Region:

- ISTAT survey of the resident population by sex, year of birth and marital status on 1ST January of the year under study.

- The Hospital Information System of the Lazio Region (Sistema Informativo Ospedaliero del Lazio, SIO), which records data on hospital admissions that occur each year in the region. The system has satisfactory coverage since 1997. Clinical information is coded using the International Classification of Diseases ICD-9-CM.

- The Pharmaceutical Prescription Information Systems (available since 2004): the FARM and the FarmED. The FARM contains all the prescriptions sent by public and private pharmacies for the residents in the Lazio Region and reimbursed by the SSN (class A drugs). Medicines are registered with the marketing authorization code (codice dell'Autorizzazione dell'Immissione in Commercio, AIC). The AIC makes it possible to identify the active ingredient (ATC code - Anatomical-Therapeutic-Classification) and the quantity dispensed. For each prescription, the delivery date of the drug and the patient's data are recorded. The FarmED records the direct dispensing with the same detail as the FARM, i.e., the distribution of drugs that took place in the hospital at the time of discharge.

- The Register of Co-payment Exemptions, which collects the exemptions from co-payment of drugs for certified chronic conditions or low income of residents in Lazio since 2005.
- The Registry of Assisted Patients of the Lazio Region updated at 31/12/2016. This archive contains, for each patient, an indicator of presence/ absence in the archive on a specific date (updated every three months), and information on the residence of the patient.
- The Lazio Register of Causes of Death (Registro Nominativo delle Cause di Morte, ReNCaM). The ReNCaM contains for each death the socio-demographic information, the place, the date, and the cause of death (ICD-9 codes).
- The Regional Register of Dialysis and Transplantation of Lazio (Registro Regionale Dialisi e Trapianti del Lazio, RRDTL), active since the 1990s, records all dialysis patients. The nephrology clinics of the Lazio Region are obliged to provide annual updates on all their patients.
- The Special Care Information System (Sistema Informativo dell'Assistenza Specialistica, SIAS) is an archive of all services provided by outpatient clinics, family counseling centers, the instrumental, and the laboratory diagnostic procedures. Since 2000, it records all services from public or accredited private institutions that are either covered by the Regional Health Service or that require a co-payment participation.

Supplementary tables

Table C.1. Prevalence of chronic conditions (CC) in the study population and in the multimorbid population. CKD = Chronic Kidney Disease, COPD = Chronic Obstructive Polmunary Disease, HBL = High Blood Lipids (hypercholesterolemia).

	Females		**Males**	
	N	**in 2+ CCs**	**N**	**in 2+ CCsin**
2+ CCs	40.535	40.535	42.835	42.835
cancer	12.339	6.950	10.163	7.472
cardiopathies	18,742	17,407	23,924	22,427
CKD	2,476	2,400	3,681	3,531
COPD	8,524	6,714	8,423	6,895
dementia	2,344	2,054	1,109	1,006
diabetes	14,754	12,382	16,919	14,234
digestive	2,149	1,427	2,661	1,767
HBL	19,691	16,498	22,313	19,965
hypertension	64,367	36,417	63,325	38,104
neurologic	3,186	2,317	2,676	2,010
vasculopathies	6,535	6,076	7,844	7,432

Table C.2. Estimates of interaction terms between chronic conditions (CC) and the deprivation index over COVID-19 mortality. CKD = Chronic Kidney Disease, COPD = Chronic Obstructive Polmunary Disease, HBL = High Blood Lipids (hypercholesterolemia).

	Females			**Males**		
	OR	**95% CI**		**OR**	**95% CI**	
nr. CCs	1.00	0.99	1.01	1.01	1.00	1.01
cancer	1.01	0.98	1.05	1.02	0.99	1.05
cardiopathies	1.03	0.99	1.08	1.00	0.97	1.04
CKD	1.01	0.98	1.03	1.02	0.99	1.04
COPD	1.02	0.97	1.08	1.02	0.98	1.06
dementia	0.98	0.93	1.03	0.96	0.90	1.02
diabetes	0.97	0.94	1.00	1.02	1.00	1.05
digestive	1.00	0.92	1.09	1.00	0.93	1.07
HBL	1.01	0.98	1.05	1.03	1.00	1.06
hypertension	0.99	0.96	1.02	1.03	1.00	1.06
neurologic	0.98	0.92	1.04	0.97	0.92	1.03
vasculopathies	1.02	0.98	1.06	1.00	0.97	1.03

Table C.3. Mediated Proportions (MP) for the indirect effect of deprivation on 90-day COVID-19 mortality passing through the chronic condition (CC). Estimates adjusted by age and every other chronic condition.CKD = Chronic Kidney Disease, COPD = Chronic Obstructive Polmunary Disease, HBL = High Blood Lipids (hypercholesterolemia).

	Females			**Males**		
	MP%	**95% CI**		**MP%**	**95% CI**	
nr. CCs	20.9	13.97	27.76	21.34	14.39	28.28
cancer	1.95	0.17	3.74	3.84	0.89	6.78
cardiopathies	- 1.98	- 5.34	1.38	- 0.87	- 3.13	1.38
CKD	3.03	0.79	5.28	2.96	0.51	5.41
COPD	1.36	- 3.23	5.96	2.78	- 2.99	8.55
dementia	0.23	- 3.99	4.45	0.10	- 6.10	6.31
diabetes	4.22	1.68	6.77	4.47	1.75	7.19
digestive	0.98	- 1.69	3.64	1.67	- 1.16	4.49
HBL	- 1.26	- 2.53	0.02	- 0.40	- 1.21	0.42
hypertension	6.09	2.79	9.40	3.28	1.00	5.56
neurologic	0.82	- 2.71	4.35	1.09	- 4.54	6.71
vasculopathies	0.90	- 0.77	2.56	2.75	- 0.09	5.59

Bibliography

Abedi, V., Olulana, O., Avula, V., Chaudhary, D., Khan, A., Shahjouei, S., Li, J., and Zand, R. (2021). Racial, Economic, and Health Inequality and COVID-19 Infection in the United States. *Journal of Racial and Ethnic Health Disparities*, 8(3):732–742.

Aburto, J. M., Schöley, J., Kashnitsky, I., Zhang, L., Rahal, C., Missov, T. I., Mills, M. C., Dowd, J. B., and Kashyap, R. (2022). Quantifying impacts of the COVID-19 pandemic through life-expectancy losses: a population-level study of 29 countries. *International Journal of Epidemiology*, 51(1):63–74.

Acheson, D., Barker, D., Jacky, C., Marmot, M., and Whitehead, M. (1998). Independent Inquiry into Inequalities in Health Report. *The Stationery Office*.

Acuti Martellucci, C., Flacco, M. E., Cappadona, R., Bravi, F., Mantovani, L., and Manzoli, L. (2020). SARS-CoV-2 pandemic: An overview. *Advances in Biological Regulation*, 77:100736.

Adams-Prassl, A., Boneva, T., Golin, M., and Rauh, C. (2020). Inequality in the impact of the coronavirus shock: Evidence from real time surveys. *Journal of Public Economics*, 189:104245.

Agardh, E., Allebeck, P., Hallqvist, J., Moradi, T., and Sidorchuk, A. (2011). Type 2 diabetes incidence and socio-economic position: A systematic review and meta-analysis. *International Journal of Epidemiology*, 40(3):804–818.

Aguilar-Palacio, I., Maldonado, L., Malo, S., Sánchez-Recio, R., Marcos-Campos, I., Magallón-Botaya, R., and Rabanaque, M. J. (2021). COVID-19 Inequalities: Individual and Area Socioeconomic Factors (Aragón, Spain). *International journal of environmental research and public health*, 18(12):6607.

Alicandro, G., Corsetti, G., Battaglini, M., Prati, S., and Frova, L. (2021). Education inequalities in overall mortality during the first wave of the COVID-19 pandemic in Italy. *Epidemiologia e Prevenzione*, 45(6):463–469.

Angelici, L., Sorge, C., Di Martino, M., Cappai, G., Stafoggia, M., Agabiti, N., Girardi, E., Lanini, S., Nicastri, E., Davoli, M., and Cesaroni, G. (2022). Incidence of SARS-CoV-2 Infection and Related Mortality by Education Level during Three Phases of the 2020 Pandemic: A Population-Based Cohort Study in Rome. *Journal of Clinical Medicine*, 11(3):877.

Badaloni, C., Michelozzi, P., and Davoli, M. (2020). Variazione spazio-temporale dell'aspettativa di vita per livello socioeconomico e distretto sanitario a Roma negli anni 2006-2017. *Epidemiologia e prevenzione*, 44(5-6):342–348.

Bambra, C., Riordan, R., Ford, J., and Matthews, F. (2020). The COVID-19 pandemic and health inequalities. *Journal of Epidemiology and Community Health*, 74(11):964–968.

Barnett, K., Mercer, S. W., Norbury, M., Watt, G., Wyke, S., and Guthrie, B. (2012). Epidemiology of multimorbidity and implications for health care, research, and medical education: A cross-sectional study. *The Lancet*, 380(9836):37–43.

Barone, A. P., Fusco, D., Colais, P., D'Ovidio, M., Belleudi, V., Agabiti, N., Sorge, C., Davoli, M., and Perucci, C. A. (2009). Effects of socioeconomic position on 30-day mortality and wait for surgery after hip fracture. *International Journal for Quality in Health Care*, 21(6):379–386.

Bashinskaya, B., Nahed, B. V., Walcott, B. P., Coumans, J. V. C., and Onuma,

O. K. (2012). Socioeconomic Status Correlates with the Prevalence of Advanced Coronary Artery Disease in the United States. *PLoS ONE*, 7(9):1–7.

Biswas, M., Rahaman, S., Biswas, T. K., Haque, Z., and Ibrahim, B. (2021). Association of Sex, Age, and Comorbidities with Mortality in COVID-19 Patients: A Systematic Review and Meta-Analysis. *Intervirology*, 64(1):36–47.

Bonifazi, G., Lista, L., Menasce, D., Mezzetto, M., Pedrini, D., Spighi, R., and Zoccoli, A. (2021). Study on the effects of the restrictive measures for containment of the COVID-19 pandemic on the reproduction number Rt in Italian regions. *European Physical Journal Plus*, 136(12):1–16.

Borrell, C., Plasència, A., Huisman, M., Costa, G., Kunst, A., Andersen, O., Bopp, M., Borgan, J. K., Deboosere, P., Glickman, M., Gadeyne, S., Minder, C., Regidor, E., Spadea, T., Valkonen, T., and Mackenbach, J. P. (2005). Education level inequalities and transportation injury mortality in the middle aged and elderly in European settings. *Injury Prevention*, 11(3):138–142.

Cacciani, L., Bargagli, A. M., Cesaroni, G., Forastiere, F., Agabiti, N., and Davoli, M. (2015). Education and Mortality in the Rome Longitudinal Study. *PLOS ONE*, 10(9):e0137576.

Caldera Sánchez, A. and Andrews, D. (2011). To Move or not to Move: What Drives Residential Mobility Rates in the OECD ? *OECD Economics Department Working Papers*, page 40.

Cannari, L. and Iuzzolino, G. (2009). Le differenze nel livello dei prezzi al consumo tra Nord e Sud. Technical Report 4, Banca d'Italia.

Cassell, A., Edwards, D., Harshfield, A., Rhodes, K., Brimicombe, J., Payne, R., and Griffin, S. (2018). The epidemiology of multimorbidity in primary care. *British Journal of General Practice*, 68(669):1–7.

Cereda, D., Tirani, M., Rovida, F., Demicheli, V., Ajelli, M., Poletti, P., Trentini, F., Guzzetta, G., Marziano, V., Barone, A., Magoni, M., Deandrea, S., Diurno, G., Lombardo, M., Faccini, M., Pan, A., Bruno, R., Pariani, E., Grasselli, G., Piatti, A., Gramegna, M., Baldanti, F., Melegaro, A., and Merler, S. (2020). The early phase of the COVID-19 outbreak in Lombardy, Italy. *arXiv Populations and Evolution*.

Cesaroni, G. and Davoli, M. (2022). *Salute ed equità nella regione lazio*. Il Pensiero Scientifico Editore, Roma.

Cesaroni, G., Farchi, S., Davoli, M., Forastiere, F., and Perucci, C. A. (2003). Individual and are-based indicators of socioeconomic status and childhood asthma. *European Respiratory Journal*, 22(4):619–624.

Cesaroni, G., Venturi, G., Paglione, L., Angelici, L., Marino, C., Davoli, M., and Agabiti, N. (2020). Mortality inequalities in Rome: the role of individual education and real estate market. *European Journal of Public Health*, 30(Supplement_5):1–7.

Chang, H.-Y., Tang, W., Hatef, E., Kitchen, C., Weiner, J. P., and Kharrazi, H. (2021). Differential impact of mitigation policies and socioeconomic status on COVID-19 prevalence and social distancing in the United States. *BMC Public Health*, 21(1):1140.

Chen, J. T. and Krieger, N. (2021). Revealing the Unequal Burden of COVID-19 by Income, Race/Ethnicity, and Household Crowding: US County Versus Zip Code Analyses. *Journal of Public Health Management and Practice*, 27(Supplement 1):S43–S56.

Cheng, C., Spiegelman, D., and Li, F. (2021). Estimating the natural indirect effect and the mediation proportion via the product method. *BMC Medical Research Methodology*, 21(1):253.

Cheng, C., Spiegelman, D., and Li, F. (2022). Is the Product Method More Efficient

Than the Difference Method for Assessing Mediation? *American Journal of Epidemiology*, 00(00):1–9.

Consolazio, D., Murtas, R., Tunesi, S., Gervasi, F., Benassi, D., and Russo, A. G. (2021). Assessing the Impact of Individual Characteristics and Neighborhood Socioeconomic Status During the COVID-19 Pandemic in the Provinces of Milan and Lodi. *International Journal of Health Services*, 51(3):311–324.

Cori, A., Ferguson, N. M., Fraser, C., and Cauchemez, S. (2013). A New Framework and Software to Estimate Time-Varying Reproduction Numbers During Epidemics. *American Journal of Epidemiology*, 178(9):1505–1512.

Costa, G., Stroscia, M., Zengarini, N., and Demaria, M. (2017). *40 anni di salute a Torino. Spunti per leggere i bisogni e i risultati delle politiche.* Inferenze.

Cylus, J. and Papanicolas, I. (2015). An analysis of perceived access to health care in Europe: How universal is universal coverage? *Health Policy*, 119(9):1133–1144.

Dei Bardi, L., Acampora, A., Cacciani, L., Di Martino, M., Agabiti, N., Davoli, M., and Cesaroni, G. (2022a). GitHub Repository. https://github.com/Luca-DB/covid_provincia. Accessed: 01/02/23.

Dei Bardi, L., Acampora, A., Cacciani, L., Di Martino, M., Agabiti, N., Davoli, M., and Cesaroni, G. (2023). SARS-CoV-2 spread and area economic disadvantage in the italian three-tier restrictions: a multilevel approach. *BMC Public Health*, 23(1):329.

Dei Bardi, L., Calandrini, E., Bargagli, A. M., Egidi, V., Davoli, M., Agabiti, N., and Cesaroni, G. (2022b). Socioeconomic inequalities in health status and survival: a cohort study in Rome. *BMJ Open*, 12(8):e055503.

Department of Health (2010). Fair society, healthy lives (the Marmot Review).

Department of Health and Social Security (1980). Inequalities in health: report of a research working group. *DHSS*.

Dessie, Z. G. and Zewotir, T. (2021). Mortality-related risk factors of COVID-19: a systematic review and meta-analysis of 42 studies and 423,117 patients. *BMC Infectious Diseases*, 21(1):855.

European Centre for Disease Prevention and Control (2022). SARS-CoV-2 variants dashboard. https://www.ecdc.europa.eu/en/covid-19/situation-updates/variants-dashboard. Accessed: 01/06/22.

Feldman, J. M. and Bassett, M. T. (2021). Variation in COVID-19 Mortality in the US by Race and Ethnicity and Educational Attainment. *JAMA Network Open*, 4(11):e2135967.

Ferré, F., Giulio De Belvis, A., Valerio, L., Longhi, S., Lazzari, A., Fattore, G., Ricciardi, W., and Maresso, A. (2014). Health Systems in Transition.

Foraker, R. E., Bush, C., Greiner, M. A., Sims, M., Henderson, K., Smith, S., Bidulescu, A., Shoben, A. B., Hardy, N. C., Brien, E. O., Louis, S., and Hill, C. (2019). Distribution of Cardiovascular Health by Individual- and Neighborhood-Level Socioeconomic Status. *Global Heart*, 14(3):241–250.

Fraser, C. (2007). Estimating Individual and Household Reproduction Numbers in an Emerging Epidemic. *PLoS ONE*, 2(8):e758.

Galobardes, B., Shaw, M., Lawlor, D. A., Lynch, J. W., and Smith, G. D. (2006a). Indicators of socioeconomic position (part 1). *Journal of Epidemiology and Community Health*, 60(1):7–12.

Galobardes, B., Shaw, M., Lawlor, D. A., Lynch, J. W., and Smith, G. D. (2006b). Indicators of socioeconomic position (part 2). *Journal of Epidemiology and Community Health*, 60(2):95–101.

Gauvin, L., Bajardi, P., Pepe, E., Lake, B., Privitera, F., and Tizzoni, M. (2021). Socio-economic determinants of mobility responses during the first wave of COVID-

19 in Italy: from provinces to neighbourhoods. *Journal of The Royal Society Interface*, 18(181):20210092.

Ge, E., Li, Y., Wu, S., Candido, E., and Wei, X. (2021). Association of pre-existing comorbidities with mortality and disease severity among 167,500 individuals with COVID-19 in Canada: A population-based cohort study. *PLoS ONE*, 16(10 October):1–18.

Gershon, A. S., Dolmage, T. E., Stephenson, A., and Jackson, B. (2012). Chronic obstructive pulmonary disease and socioeconomic status: A systematic review. *COPD: Journal of Chronic Obstructive Pulmonary Disease*, 9(3):216–226.

Glodeanu, A., Gullón, P., and Bilal, U. (2021). Social inequalities in mobility during and following the COVID-19 associated lockdown of the Madrid metropolitan area in Spain. *Health and Place*, 70(April).

Gobbato, M., Clagnan, E., Burba, I., Rizzi, L., Grassetti, L., Del Zotto, S., Dal Maso, L., Serraino, D., and Tonutti, G. (2020). Clinical, demographical characteristics and hospitalisation of 3,010 patients with covid-19 in friuli venezia giulia region (Northern italy). a multivariate, population-based, statistical analysis. *Epidemiologia e Prevenzione*, 44(5-6):226–234.

Gostic, K. M., McGough, L., Baskerville, E. B., Abbott, S., Joshi, K., Tedijanto, C., Kahn, R., Niehus, R., Hay, J. A., De Salazar, P. M., Hellewell, J., Meakin, S., Munday, J. D., Bosse, N. I., Sherrat, K., Thompson, R. N., White, L. F., Huisman, J. S., Scire, J., Bonhoeffer, S., Stadler, T., Wallinga, J., Funk, S., Lipsitch, M., and Cobey, S. (2020). Practical considerations for measuring the effective reproductive number, Rt. *PLOS Computational Biology*, 16(12):e1008409.

Günster, C., Busse, R., Spoden, M., Rombey, T., Schillinger, G., Hoffmann, W., Weber-Carstens, S., Schuppert, A., and Karagiannidis, C. (2021). 6-month mortality and readmissions of hospitalized COVID-19 patients: A nationwide cohort study of 8,679 patients in Germany. *PLOS ONE*, 16(8):e0255427.

Gustafsson, P. E., San Sebastian, M., Fonseca-Rodriguez, O., and Fors Connolly, A.-M. (2022). Inequitable impact of infection: social gradients in severe COVID-19 outcomes among all confirmed SARS-CoV-2 cases during the first pandemic wave in Sweden. *Journal of Epidemiology and Community Health*, 76(3):261–267.

Guzzetta, G. and Merler, B. (2020). Stime della trasmissibilità di SARS-CoV-2 in Italia. pages 1–12.

Hammonds, C. and Kerrissey, J. (2020). "We are not heroes because it is not a choice": A Survey of Essential Workers' Safety and Security During COVID-19. page 25.

Hoffmann, R., Kröger, H., and Pakpahan, E. (2018). Pathways between socioeconomic status and health: Does health selection or social causation dominate in Europe? *Advances in Life Course Research*, 36(February):23–36.

Iavarone, M., D'Ambrosio, R., Soria, A., Triolo, M., Pugliese, N., Del Poggio, P., Perricone, G., Massironi, S., Spinetti, A., Buscarini, E., Viganò, M., Carriero, C., Fagiuoli, S., Aghemo, A., Belli, L. S., Lucà, M., Pedaci, M., Rimondi, A., Rumi, M. G., Invernizzi, P., Bonfanti, P., and Lampertico, P. (2020). High rates of 30-day mortality in patients with cirrhosis and COVID-19. *Journal of Hepatology*, 73(5):1063–1071.

Istituto Nazionale di Statistica (2013). I.Stat Data Warehouse. `http://dati.istat.it`. Accessed: 01/07/2022.

Italian Civil Protection Department (2020). Dataset of COVID-19 infected cases in Italy by province. `https://github.com/pcm-dpc/COVID-19`. Accessed: 01/06/22.

Italian Commissioning Structure for the COVID-19 Emergency (2021). Covid-19 Opendata Vaccines. `https://github.com/italia/covid19-opendata-vaccini`. Accessed: 01/06/22.

Italian Ministry of Health (2020). Nuovo coronavirus - Notizie. http://www.salute.gov.it/portale/nuovocoronavirus/archivioNotizieNuovoCoronavirus.jsp. Accessed: 01/11/22.

Italian National Institute of Health (2022). COVID-19 integrated surveillance: key national data. https://www.epicentro.iss.it/en/coronavirus/sars-cov-2-integrated-surveillance-data. Accessed: 01/06/22.

Jay, J., Bor, J., Nsoesie, E. O., Lipson, S. K., Jones, D. K., Galea, S., and Raifman, J. (2020). Neighbourhood income and physical distancing during the COVID-19 pandemic in the United States. *Nature Human Behaviour*, 4(12):1294–1302.

Kawachi, I. (2002). A glossary for health inequalities. *Journal of Epidemiology & Community Health*, 56(9):647–652.

Kontopantelis, E., Mamas, M. A., Webb, R. T., Castro, A., Rutter, M. K., Gale, C. P., Ashcroft, D. M., Pierce, M., Abel, K. M., Price, G., Faivre-Finn, C., Van Spall, H. G., Graham, M. M., Morciano, M., Martin, G. P., and Doran, T. (2021). Excess deaths from COVID-19 and other causes by region, neighbourhood deprivation level and place of death during the first 30 weeks of the pandemic in England and Wales: A retrospective registry study. *The Lancet Regional Health - Europe*, 7:100144.

Kontopantelis, E., Mamas, M. A., Webb, R. T., Castro, A., Rutter, M. K., Gale, C. P., Ashcroft, D. M., Pierce, M., Abel, K. M., Price, G., Faivre-Finn, C., Van Spall, H. G. C., Graham, M. M., Morciano, M., Martin, G. P., Sutton, M., and Doran, T. (2022). Excess years of life lost to COVID-19 and other causes of death by sex, neighbourhood deprivation, and region in England and Wales during 2020: A registry-based study. *PLOS Medicine*, 19(2):e1003904.

Korner-Nievergelt, F., Roth, T., von Felten, S., Guélat, J., Almasi, B., and Korner-Nievergelt, P. (2015). *Bayesian Data Analysis in Ecology Using Linear Models with R, BUGS, and Stan*. Elsevier.

Krieger, N. (2002). A glossary for social epidemiology. *Epidemiological bulletin*, 23(1):7–11.

Krieger, N., Williams, D. R., and Moss, N. E. (1997). Measuring social class in us public health research: Concepts, methodologies, and guidelines. *Annual Review of Public Health*, 18(1):341–378.

Lelo, K., Monni, S., and Tomassi, F. (2019). Le mappe della disuguaglianza. https://www.mapparoma.info/. Accessed: 01/05/2021.

Lewis, N. M., Friedrichs, M., Wagstaff, S., Sage, K., LaCross, N., Bui, D., McCaffrey, K., Barbeau, B., George, A., Rose, C., Willardson, S., Carter, A., Smoot, C., Nakashima, A., and Dunn, A. (2020). Disparities in COVID-19 Incidence, Hospitalizations, and Testing, by Area-Level Deprivation — Utah, March 3–July 9, 2020. *MMWR. Morbidity and Mortality Weekly Report*, 69(38):1369–1373.

Lorant, V., De Gelder, R., Kapadia, D., Borrell, C., Kalediene, R., Kovács, K., Leinsalu, M., Martikainen, P., Menvielle, G., Regidor, E., Maica, R. S., Wojtyniak, B., Strand, B. H., Bopp, M., and Mackenbach, J. P. (2018). Socioeconomic inequalities in suicide in Europe: The widening gap. *British Journal of Psychiatry*, 212(6):356–361.

Loring, B. (2014a). Alcohol and inequities: Guidance for addressing inequities in alcohol-related harm. *World Health Organization Regional Office for Europe*, pages 1–6.

Loring, B. (2014b). Tobacco and inequities - Guidance for addressing inequities in tobacco-related harm. *WHO Regional Office for Europe*, pages 1–31.

Lübker, C. and Murtin, F. (2022). Educational Inequalities in Longevity Among OECD Countries Around 2016. *OECD Papers on Well-being and Inequalities*, 8(08).

Macintyre, S. (1997). The Black Report and beyond what are the issues? *Social Science and Medicine*, 44(6):723–745.

Macintyre, S. (1999). Reducing health inequalities: An action report. *Critical Public Health*, 9(4):347–350.

Mackenbach, J. P. (2010). Has the English strategy to reduce health inequalities failed? *Social Science and Medicine*, 71(7):1249–1253.

Mackenbach, J. P. (2019). *Health Inequalities: Persistence and Change in Modern Welfare States*. Oxford University Press.

Mackenbach, J. P. (2020). *A History of Population Health*, volume 95. BRILL.

Mackenbach, J. P., Bopp, M., Deboosere, P., Kovacs, K., Leinsalu, M., Martikainen, P., Menvielle, G., Regidor, E., and de Gelder, R. (2017). Determinants of the magnitude of socioeconomic inequalities in mortality: A study of 17 European countries. *Health & Place*, 47(June):44–53.

Mackenbach, J. P., Kulhánová, I., Artnik, B., Bopp, M., Borrell, C., Clemens, T., Costa, G., Dibben, C., Kalediene, R., Lundberg, O., Martikainen, P., Menvielle, G., Östergren, O., Prochorskas, R., Rodríguez-Sanz, M., Strand, B. H., Looman, C. W., and De Gelder, R. (2016). Changes in mortality inequalities over two decades: Register based study of European countries. *BMJ (Online)*, 353.

Mackenbach, J. P., Kulhánová, I., Bopp, M., Deboosere, P., Eikemo, T. A., Hoffmann, R., Kulik, M. C., Leinsalu, M., Martikainen, P., Menvielle, G., Regidor, E., Wojtyniak, B., Östergren, O., Lundberg, O., Biggeri, A., Borrell, C., Brown, L., Costa, G., Esnaola, S., Klotz, J., Kovacs, K., Lange, A., Rodriguez-Sanz, M., Strand, B. H., and White, C. (2015). Variations in the relation between education and cause-specific mortality in 19 European populations: A test of the "fundamental causes" theory of social inequalities in health. *Social Science and Medicine*, 127:51–62.

Mackenbach, J. P., Valverde, J. R., Artnik, B., Bopp, M., Brønnum-Hansen, H., Deboosere, P., Kalediene, R., Kovács, K., Leinsalu, M., Martikainen, P., Menvielle, G., Regidor, E., Rychtaríkova, J., Rodriguez-Sanz, M., Vineis, P., White, C., Wojtyniak, B., Hu, Y., and Nusselder, W. J. (2018). Trends in health inequalities in 27 European countries. *Proceedings of the National Academy of Sciences of the United States of America*, 115(25):6440–6445.

Mackenbach, J. P., Valverde, J. R., Bopp, M., Brønnum-Hansen, H., Deboosere, P., Kalediene, R., Kovács, K., Leinsalu, M., Martikainen, P., Menvielle, G., Regidor, E., and Nusselder, W. J. (2019). Determinants of inequalities in life expectancy: an international comparative study of eight risk factors. *The Lancet Public Health*, 4(10):e529–e537.

MacKinnon, D. P. (2012). *Introduction to Statistical Mediation Analysis*. Routledge.

Manica, M., Guzzetta, G., Riccardo, F., Valenti, A., Poletti, P., Marziano, V., Trentini, F., Andrianou, X., Mateo-Urdiales, A., del Manso, M., Fabiani, M., Vescio, M. F., Spuri, M., Petrone, D., Bella, A., Iavicoli, S., Ajelli, M., Brusaferro, S., Pezzotti, P., and Merler, S. (2021). Impact of tiered restrictions on human activities and the epidemiology of the second wave of COVID-19 in Italy. *Nature Communications*, 12(1):4570.

Marmot, M. (2005). Social determinants of health inequalities. *Lancet*, 365(9464):1099–1104.

Marmot, M. (2020). Health equity in England: The Marmot review 10 years on. *The BMJ*, 368:m693.

Marmot, M., Allen, J., Bell, R., Bloomer, E., and Goldblatt, P. (2012). WHO European review of social determinants of health and the health divide.

Marmot, M., Allen, J., Boyce, T., Goldblatt, P., and Morrison, J. (2020). Health Equity in England: the Marmot review 10 years on. *The Marmot Review*.

Marmot, M., Friel, S., Bell, R., Houweling, T. A., and Taylor, S. (2008). Closing the gap in a generation: health equity through action on the social determinants of health. *The Lancet*, 372(9650):1661–1669.

Marmot, M. G., Shipley, M. J., and Rose, G. (1984). Inequalities in Death-Specific Explanations of a General Pattern? *The Lancet*, 323(8384):1003–1006.

Marmot, M. G., Stansfeld, S., Patel, C., North, F., Head, J., White, I., Brunner, E., Feeney, A., Marmot, M. G., and Smith, G. D. (1991). Health inequalities among British civil servants: the Whitehall II study. *The Lancet*, 337(8754):1387–1393.

Marra, M., Strippoli, E., Zengarini, N., and Costa, G. (2022). Inequalities in the Health Impact of the First Wave of the COVID-19 Pandemic in Piedmont Region, Italy. *International Journal of Environmental Research and Public Health*, 19(22):14791.

Mateo-Urdiales, A., Fabiani, M., Rosano, A., Vescio, M. F., Del Manso, M., Bella, A., Riccardo, F., Pezzotti, P., Regidor, E., and Andrianou, X. (2021). Socioeconomic patterns and COVID-19 outcomes before, during and after the lockdown in Italy (2020). *Health & Place*, 71(July):102642.

McCartney, G., Popham, F., McMaster, R., and Cumbers, A. (2019). Defining health and health inequalities. *Public Health*, 172:22–30.

McDonald, J. F. and McMillen, D. P. (2010). *Urban Economics and Real Estate: Theory and Policy*. John Wiley & Sons, 2010.

McGowan, V. J. and Bambra, C. (2022). COVID-19 mortality and deprivation: pandemic, syndemic, and endemic health inequalities. *The Lancet. Public health*, 7(11):e966–e975.

Ministry of Economy and Finance (2020). Tax Returns Opendata. https://www1.finanze.gov.it/finanze/analisi_stat/public/index.php?search_class[0]=cCOMUNE&opendata=yes. Accessed: 01/06/22.

Morris, J. N. (1990). Inequalities in health: ten years and little further on. *The Lancet*, 336(8713):491–493.

Morrissey, K., Spooner, F., Salter, J., and Shaddick, G. (2021). Area level deprivation and monthly COVID-19 cases: The impact of government policy in England. *Social Science & Medicine*, 289(August):114413.

Murtin, F., Mackenbach, J., Jasilionis, D., and D'Ercole, M. M. (2017). Inequalities in longevity by education in OECD countries. *OECD Statistics Working Papers*, 02.

Mőller, H., Rogers, K., Cullen, P., Senserrick, T., Boufous, S., and Ivers, R. (2021). Socioeconomic status during youth and risk of car crash during adulthood. Findings from the DRIVE cohort study. *Journal of Epidemiology and Community Health*, 75(8):755–763.

Nardi, A., Dei Bardi, L., Davoli, M., Agabiti, N., and Cesaroni, G. (2022). Differences in mortality between temporary and permanent workers: results from the Rome Longitudinal Study. *BMJ Open*, 12(5):e058594.

National Institute of Statistics (2021). Resident population by province, age, sex and marital status on 1st January 2020. https://demo.istat.it/popres/download.php?anno=2020&lingua=eng. Accessed: 01/07/22.

National Institute of Statistics (2022a). Municipalities and Provinces codes as of 01/01/2020. https://www.istat.it/it/archivio/6789. Accessed: 01/07/22.

National Institute of Statistics (2022b). Municipalities sizes and populations as of 01/01/2020. https://www.istat.it/it/archivio/156224. Accessed: 01/07/22.

Nepomuceno, M. R., Acosta, E., Alburez-Gutierrez, D., Aburto, J. M., Gagnon, A., and Turra, C. M. (2020). Besides population age structure, health and other demographic factors can contribute to understanding the COVID-19 burden.

Proceedings of the National Academy of Sciences of the United States of America, 117(25):13881–13883.

Paglione, L., Angelici, L., Davoli, M., Agabiti, N., and Cesaroni, G. (2020). Mortality inequalities by occupational status and type of job in men and women: Results from the Rome Longitudinal Study. *BMJ Open*, 10(6).

Panagiotou, O. A., Kosar, C. M., White, E. M., Bantis, L. E., Yang, X., Santostefano, C. M., Feifer, R. A., Blackman, C., Rudolph, J. L., Gravenstein, S., and Mor, V. (2021). Risk Factors Associated with All-Cause 30-Day Mortality in Nursing Home Residents with COVID-19. *JAMA Internal Medicine*, 181(4):439–448.

Petrelli, A., Di Napoli, A., Sebastiani, G., Rossi, A., Giorgi Rossi, P., Demuru, E., Costa, G., Zengarini, N., Alicandro, G., Marchetti, S., Marmot, M., and Frova, L. (2019). Italian Atlas of mortality inequalities by education level. *Epidemiologia e prevenzione*, 43(1S1).

Pittau, M. G., Zelli, R., and Massari, R. (2011). Do Spatial Price Indices Reshuffle the Italian Income Distribution? *Modern Economy*, 02(03):259–265.

Popham, F., Dibben, C., and Bambra, C. (2013). Are health inequalities really not the smallest in the Nordic welfare states? A comparison of mortality inequality in 37 countries. *Journal of Epidemiology and Community Health*, 67(5):412–418.

Potter, E. L., Hopper, I., Sen, J., Salim, A., and Marwick, T. H. (2019). Impact of socioeconomic status on incident heart failure and left ventricular dysfunction: Systematic review and meta-analysis. *European Heart Journal - Quality of Care and Clinical Outcomes*, 5(2):169–179.

Presidente del Consiglio dei Ministri (2020). Ulteriori disposizioni attuative del decreto-legge 25 marzo 2020, n. 19, recante misure urgenti per fronteggiare l'emergenza epidemiologica da COVID-19, e del decreto-legge 16 maggio 2020, n. 33, recante ulteriori misure urgenti per fronteggiare l'emergen. https://www.trovanorme.salute.gov.it/norme/dettaglioAtto?id=74482. 01/08/22.

Profili, F., Ballo, P., Balzi, D., Bellini, B., Bartalocci, S., Zuppiroli, A., Voller, F., and Francesconi, P. (2020). Malattie croniche e rischio di ammalarsi di COVID-19 sintomatica: risultati di uno studio case-population su un campione di casi in AUSL Toscana Centro. *Epidemiologia e prevenzione*, 44(56):308–314.

Pullano, G., Valdano, E., Scarpa, N., Rubrichi, S., and Colizza, V. (2020). Evaluating the effect of demographic factors, socioeconomic factors, and risk aversion on mobility during the COVID-19 epidemic in France under lockdown: a population-based study. *The Lancet Digital Health*, 2(12):e638–e649.

R Core Team (2019). A Language and Environment for Statistical Computing. http://www.r-project.org. Accessed: 01/09/2020.

Rao, A., Ma, H., Moloney, G., Kwong, J. C., Jüni, P., Sander, B., Kustra, R., Baral, S. D., and Mishra, S. (2021). A disproportionate epidemic: COVID-19 cases and deaths among essential workers in Toronto, Canada. *Annals of Epidemiology*, 63:63–67.

Reid, D., Hamilton, P., Keen, H., Brett, G., Jarrett, R., and Rose, G. (1974). Cardiorespiratory Disease and Diabetes Among Middle-Aged Male Civil Servants. *The Lancet*, 303(7856):469–473.

Reiss, F. (2013). Socioeconomic inequalities and mental health problems in children and adolescents: A systematic review. *Social Science and Medicine*, 90:24–31.

Reyes-Sánchez, F., Basto-Abreu, A., Torres-Alvarez, R., Canto-Osorio, F., González-Morales, R., Dyer-Leal, D. D., López-Ridaura, R., Zaragoza-Jiménez, C. A., Rivera, J. A., and Barrientos-Gutiérrez, T. (2022). Fraction of COVID-19 hospitalizations and deaths attributable to chronic diseases. *Preventive Medicine*, 155(May 2021).

Richardson, S., Hirsch, J. S., Narasimhan, M., Crawford, J. M., McGinn, T., Davidson, K. W., the Northwell COVID-19 Research Consortium, Barnaby, D. P., Becker, L. B., Chelico, J. D., Cohen, S. L., Cookingham, J., Coppa, K., Diefenbach,

M. A., Dominello, A. J., Duer-Hefele, J., Falzon, L., Gitlin, J., Hajizadeh, N., Harvin, T. G., Hirschwerk, D. A., Kim, E. J., Kozel, Z. M., Marrast, L. M., Mogavero, J. N., Osorio, G. A., Qiu, M., and Zanos, T. P. (2020). Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area. *JAMA*, 323(20):2052–2059.

Rosano, A., Pacelli, B., Zengarini, N., Costa, G., Cislaghi, C., and Caranci, N. (2020). Update and review of the 2011 italian deprivation index calculated at the census section level. *Epidemiologia e Prevenzione*, 44(2-3):162–170.

Ruffino, L. (2021). Un anno di zone colorate. https://www.youtrend.it/2021/11/10/un-anno-di-zone-colorate/. Accessed: 01/11/22.

Schöley, J., Aburto, J. M., Kashnitsky, I., Kniffka, M. S., Zhang, L., Jaadla, H., Dowd, J. B., and Kashyap, R. (2022). Life expectancy changes since COVID-19. *Nature Human Behaviour*, 6(12):1649–1659.

Schüle, S. A., von Kries, R., Fromme, H., and Bolte, G. (2016). Neighbourhood socioeconomic context, individual socioeconomic position, and overweight in young children: a multilevel study in a large German city. *BMC Obesity*, 3(1):25.

Sim, F. and Mackie, P. (2006). Health inequalities: The Black Report after 25 years. *Public Health*, 120(3):185–186.

Sky TG24 (2018). Sky TG24 News Archive. https://tg24.sky.it/archivio. Accessed: 01/06/22.

Smith, G. D., Bartley, M., and Blane, D. (1990). The Black report on socioeconomic inequalities in health 10 years on.

Smith, G. D., Morris, J. N., and Shaw, M. (1998). The independent inquiry into inequalities in health. *BMJ*, 317(7171):1465–1466.

Strong, P. M. (1990). Black on class and mortality: Theory, method and history. *Journal of Public Health*, 12(3-4):168–180.

Sun, Y., Hu, X., and Xie, J. (2021). Spatial inequalities of COVID-19 mortality rate in relation to socioeconomic and environmental factors across England. *Science of The Total Environment*, 758:143595.

United Nations (2018). Transforming Our World: The 2030 Agenda for Sustainable Development. In *A New Era in Global Health*. Springer Publishing Company, New York, NY.

Uusküla, A., Jürgenson, T., Pisarev, H., Kolde, R., Meister, T., Tisler, A., Suija, K., Kalda, R., Piirsoo, M., and Fischer, K. (2022). Long-term mortality following SARS-CoV-2 infection: A national cohort study from Estonia. *The Lancet Regional Health - Europe*, 18:100394.

Vanthomme, K., Gadeyne, S., Lusyne, P., and Vandenheede, H. (2021). A population-based study on mortality among Belgian immigrants during the first COVID-19 wave in Belgium. Can demographic and socioeconomic indicators explain differential mortality? *SSM - Population Health*, 14:100797.

Vespe, M., Minora, U., Iacus, S. M., Spyratos, S., Sermi, F., Fontana, M., Ciuffo, B., and Christidis, P. (2021). Mobility and economic impact of covid-19 restrictions in italy using mobile network operator data. (KJ-NA-30630-EN-N (online)).

Wachtler, B., Michalski, N., Nowossadeck, E., Diercke, M., Wahrendorf, M., Santos-Hövener, C., Lampert, T., and Hoebel, J. (2020). Socioeconomic inequalities in the risk of SARS-CoV-2 infection - First results from an analysis of surveillance data from Germany. *Journal of health monitoring*, 5(Suppl 7):18–29.

Wallace, E., Salisbury, C., Guthrie, B., Lewis, C., Fahey, T., and Smith, S. M. (2015). Managing patients with multimorbidity in primary care. *BMJ (Online)*, 350(jan20 2):h176–h176.

Wang, C., Horby, P. W., Hayden, F. G., and Gao, G. F. (2020). A novel coronavirus outbreak of global health concern. *The Lancet*, 395(10223):470–473.

WHO (1948). Constitution of the World Health Organization. *World Health Organization*.

WHO (2017). Roadmap to implement the 2030 Agenda for Sustainable Development, building on Health 2020, the European policy for health and well-being. *World Health Organization*, 5(September):11–14.

WHO (2020). WHO Coronavirus (Covid19). https://covid19.who.int/. Accessed: 01/07/2022.

WHO (2021). COVID-19 and the social determinants of health and health equity: evidence brief. *World Health Organization*, (October):1–32.

WHO Regional Office for Europe (2013). Health 2020: A European policy framework and strategy for the 21st century. *World Health Organization*, page 190.

WHO Regional Office for Europe (2022). Can people afford to pay for health care? Evidence on inequity in financial protection in Europe.

Woodward, A. and Kawachi, I. (2000). Why reduce health inequalities? *Journal of Epidemiology and Community Health*, 54(12):923–929.

Wright, A. L., Sonin, K., Driscoll, J., and Wilson, J. (2020a). Poverty and economic dislocation reduce compliance with COVID-19 shelter-in-place protocols. *Journal of Economic Behavior and Organization*, 180:544–554.

Wright, L., Steptoe, A., and Fancourt, D. (2020b). Are we all in this together? Longitudinal assessment of cumulative adversities by socioeconomic position in the first 3 weeks of lockdown in the UK. *Journal of Epidemiology and Community Health*, 74(9):jech–2020–214475.

Yang, J., Zheng, Y., Gou, X., Pu, K., Chen, Z., Guo, Q., Ji, R., Wang, H., Wang, Y., and Zhou, Y. (2020). Prevalence of comorbidities and its effects in coronavirus disease 2019 patients: A systematic review and meta-analysis. *International Journal of Infectious Diseases*, 94:91–95.

Yoshikawa, Y. and Kawachi, I. (2021). Association of Socioeconomic Characteristics With Disparities in COVID-19 Outcomes in Japan. *JAMA Network Open*, 4(7):e2117060.

Zhou, F., Yu, T., Du, R., Fan, G., Liu, Y., Liu, Z., Xiang, J., Wang, Y., Song, B., Gu, X., Guan, L., Wei, Y., Li, H., Wu, X., Xu, J., Tu, S., Zhang, Y., Chen, H., and Cao, B. (2020). Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *The Lancet*, 395(10229):1054–1062.