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Mind the data gap: the use of unconventional data sources to assess the COVID-19 impact on people in vulnerable situations

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Candidata
dr.ssa Sara MAZZILLI

Relatore

Prof.ssa Lara TAVOSCHI

Prof. Pier Luigi LOPALCO

Prof. Dino PEDRESCHI

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"[…] achieving better health for the whole population by taking the reduction of health inequalities seriously is a banner worth rallying behind. Monitoring of the health of the population, its determinants, and its distribution is central to that societal aim."

Sir. Marmot (1)

PhD in Data Science
Scuola Normale Superiore

PhD candidate Sara Mazzilli

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Mind the data gap:

The use of unconventional data sources to assess the COVID-19 impact on people in vulnerable situations

Supervisors

Lara Tavoschi, Pier Luigi Lopalco, Dino Pedreschi

Contents

List of abbreviation

WHO	World Health Organization
HIS	Health information systems
GDPR	General Data Protection Regulation
EU	European Union
NIS	National Institute of Statistics
R&AP	Regions and Autonomous Provinces
NHS	National Health System
UNIC	Univocal Non-Invertible Code
SDH	Social Determinants of Health
CSDH	Commission on Social Determinants of Health
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2
COVID-19	Coronavirus Disease 2019
NCDs	Non-Communicable Diseases
LTCFs	Long-Term Care Facilities
IPC	Infection Prevention and Control
DI	Deprivation Index
SEP	Socioeconomic Position
ICU	Intensive Care Unit
GLM	Generalized Linear Logistic Regression Models
OR	Odd Ratio
CI	Confidence Interval
FAR	Residential and Semi-residential Care Data Flow
EEA	European Economic Area
ICD-9-CM	International Classification of Diseases Version 9
CCS	Clinical Classification System
PLP	Peopfle Living in Prison
RR	Relative Risk
POM	Prison Occupational Medicine

Abstract

According to the World Health Organization, population health monitoring is the first of ten essential public health operations. The emergence of novel data sources and monitoring approaches for public health surveillance is triggered by technological advances in data retrieval and analysis. Monitoring needs to have a central role in understanding the determinants of health and health inequalities. Health inequalities monitoring provides evidence on who is being left behind and informs equity-oriented policies, programmes and practices.

The overall aim of this thesis was to explore the potential of using existing data sources to monitor the health of people in vulnerable situations. The COVID-19 pandemic, which disproportionately affected the most disadvantaged members of society, was used as a case study in this research.

Chapter 1 aimed to compare the geographic and individual deprivation index in assessing the associations between individuals' socioeconomic position and the risk of Sars-CoV-2 infection and disease severity in the Apulia region from February to December 2020.

Chapter 2 focused on assessing the indirect impact of the COVID-19 pandemic on hospitalisation and mortality rates among residents of long-term care facilities in two Italian regions, Tuscany and Apulia, during 2020, compared to the pre-pandemic period.

Chapter 3 aimed to describe the extent and dynamics of the COVID-19 pandemic within the prison system of a large Italian region, Lombardy, and to report the infection prevention and control measures implemented.

This research serves as a proof of concept, demonstrating that with the right analytical capabilities and a commitment to utilizing existing administrative data, it is possible to monitor health outcomes even in neglected and highly vulnerable populations. Administrative data have the potential to drive high-quality empirical research and deepen our understanding of the relationships between human behavior, social phenomena, and health in unprecedented ways. Health surveillance in these populations enables governments and other stakeholders to support evidence-informed action to tackle health inequities. There is an urgent need to improve data collection, transfer, reporting, analysis, and interventions related to the environmental and social determinants of health in order to reduce health inequities.

Introduction

Big Data and the Monitoring of Health Inequities

Health Information Systems

According to the World Health Organization (WHO) Regional Office for Europe, population health monitoring is the first of ten essential public health operations (2). Public health surveillance activity is defined as the systematic and continuous collection, analysis and interpretation of data essential to the planning, implementation and evaluation of public health practice, closely integrated with the timely dissemination of these data and assessment to stakeholders and policymakers to facilitate action to be taken (3). Public health surveillance systems are crucial instruments to support governments and other stakeholders to act in an evidence-informed manner when identifying health needs, adjusting health policy actions and allocating resources, reacting to certain health threats, or assessing progress with regard to certain health targets (4).

Health information systems (HIS) are defined as complex, multi-layered systems aimed at producing health intelligence. National HIS compile evidence on population health, the determinants of health and health system performance within countries. They are usually generated through data collected from population health registers, health facilities, and national health surveys (5–7). However, ensuring that routinely collected data are fit-for-use and relevant for decision-making can be a challenge. Public health is a highly heterogeneous context of information systems and data. HIS collect dispersed data from various sources, including systems which were not initially established for public health surveillance purposes (7). Every structure that manages or processes patient information frequently has its patient registry, an encoding system and a series of archives with the data managed by computer programmes. There are often different systems in a local healthcare unit, very heterogeneous in terms of architecture, technologies, and functions. The quality of routinely collected HIS can also vary.

The emergence of novel data sources and monitoring approaches for public health surveillance is triggered by technological advances in data retrieval and data analysis. Today, new sources of data are potentially available, such as those related to mobile telephony, or apps that collect individual information on daily activities. There are also relevant experiences in some countries and specific contexts from which we can learn to improve the management of complex surveillance systems (4). Given this increase in complexity, now more than ever it is recommended to implement an information management strategy at the highest possible level. To this must be added the implementation of solid, content and universally applicable information standards to enable the exchange of information within and between countries and interoperability with new data sources.

New Data Sources for the HIS

Big data is heralded as a powerful new resource for surveillance and healthcare (8,9). The enthusiasm for big data stems from the recognition of the opportunities they can offer to improve the health threat monitoring, the healthcare offered to populations and, consequently, enhance their health status (9).

There is no consensus on the definition of big data. The most well-known definition describes them in terms of (i) volume, the amount of data; (ii) variety, the range of data formats available such as text, pictures, video, financial or social transactions; and (iii) velocity, the speed of data generation. To which were subsequently added: (iv) value, by the added-value, that the collected data can bring; (v) variability, data change during processing and lifecycle; (vi) veracity, data are consistent and trustworthy (in the public health sector, veracity is the goal, not yet the reality) (9–11). Big data in health encompasses high volume, high diversity biological, clinical, environmental, and lifestyle information collected from single individuals to large cohorts, concerning their health and wellness status, at one or several time points. Big data useful for health surveillance can originate from sources such as commercial transactions, for instance purchases in-store from supermarkets (12) or bank transactions; as sensors, for example satellite and GPS tracking data from mobile phones (13). Genome data is a source of big data and programs such as the '100 000 Genomes Project' in the UK and the 'Precision Medicine Initiative' in the US have resulted in the collection of massive amounts of data for genome sequencing (14). Administrative data, for example education records, medical records, and tax records, can also be a valuable source for studying the health of populations and its determinants (15).

Usually, possible end-users of big data have no input into their design, this results in governments and researchers not using the available data sources to their full potential. Concerning public health data, it would be convenient to use a unique personal identification number that allows accurate linkage between all sources of data (16). Big data can only be dealt with by adopting a strong governance model and best practices of new technologies, e.g., in large-scale data production compliant with community-based quality standards, coupled with interoperable data storage, data integration, and advanced analytics solutions (17).

However, for extensive use of big data in public health surveillance and research, legal and ethical issues must be consciously managed. On the one hand, the public may have concerns over their privacy, the linkage of their data from different sources, and the use of their data for research purposes. On the other hand, researchers often struggle to access data and, when data are accessible, the procedures to obtain them can be complicated and time-consuming. Even when available, data by themselves explain little. To be useful in public health surveillance, response and research, data should be processed, analyzed, and interpreted with the appropriate tools. One of the biggest bottlenecks and challenges is the availability of public health professionals and researchers that can use the latest information technologies developed in the big data analytics era (18,19). Data managers with good insight into the specificities of the public health application domain are rare, vice versa there is a lack of trained public health scientists able to deal with big data. Cross-

disciplinary education and training are necessary for the advancement of epidemic surveillance and public health research (17).

The Italian HIS

In Italy, health (or indirectly health-related) information systems have developed independently across various contexts, resulting in a diverse array of data sources. Examples include mortality information systems, hospital discharge forms, pharmacological prescribing records, electronic medical records, electronic health records, disease-specific registers, such as cancer registers, or genomics databases. Some of these systems cover the entire Italian population, while others are limited to specific regions, provinces, or other territorial aggregates. This diversity reflects a wealth of information but also leads to significant heterogeneity in organization, structure, and coding standards. While some systems, like the mortality registry managed by the National Institute of Statistics (NIS) and the hospital discharge records overseen by the Ministry of Health, have been well-established and validated over many years, others remain in early developmental stages, such as the disability registry. Additionally, comprehensive data on the completeness and accuracy of registration and coding for many systems are not readily available (20). Table 1 provides an overview of the national surveillance systems organized by the institutions responsible for data collection.

The current HIS refers to at least the following institutions: the Ministry of Health, which manages the national HIS; the Ministry of Economy and Finance; the Istituto Superiore di Sanità; the Italian Drug Agency; NIS and the Regions and Autonomous Provinces (R&AP). The private sector also maintains its own health data flows. Moreover, the Ministry for Technological Innovation and Digital Transition and the Agency for Digital Italy are privileged interlocutors for any reform (20).

Efforts to implement procedures that harmonize and interconnect these diverse data flows—thereby enabling the reconstruction of an individual's health history—are relatively recent and vary across regions and types of data (21). The information systems on an individual basis of the national health system (NHS), for which interconnection is permitted, are those within the national HIS and those necessary for the electronic health record (22–31). According to the Interconnection Regulation, entities supplying data to the national HIS must first validate the identification code of each individual against the health card system database. Before transmitting data to the Ministry of Health, this code is replaced with a Univocal Non-Invertible Code (UNIC). Upon data acquisition, the Ministry irreversibly substitutes the UNIC with an additional code known as the Patient's National Unique Code, generated through a secure, non-reversible encryption process exclusive to the Ministry of Health (21). Access to this interconnected data is granted to relevant organizational units within the Regions, the Ministry of Health, and the National Agency for Regional Health Services, with access levels differentiated based on the specific purposes of data processing (21).

Table 1. Overview of national health and surveillance datasets. The list is not exhaustive, see DPCM 3 March 2017 'Identification of surveillance systems and registers of mortality, cancer and other diseases (32).

Dataset name	Type of dataset (traditional name in Italian)	Type of dataset
DATASETS OF THE NATIONAL HEALTH INFORMATION SYSTEM MANAGED BY THE MINISTRY OF HEALTH		
SDO	Scheda di Dimissione Ospedaliera	Hospital Discharge Form
EMUR-PS	Pronto Soccorso	Emergency Room
EMUR-118	Sistema 119	System 119
ART50-FARMA	Assistenza Farmaceutica Convenzionata	Affiliated Pharmaceutical Assistance
TRACCIA -DD&DPC	Distribuzione Diretta e Per Conto dei medicinali	Direct and On Account Distribution of Medicines
ART50-SPA	Specialistica ambulatoriale	Specialist Ambulatory Care
SIAD	Assistenza Domiciliare	Home Care
FAR	Assistenza residenziale e semiresidenziale	Residential and semi-residential care
SIND	Dipendenze	Addictions
SISM	Salute mentale	Mental Health
HOSPICE	Hospice	Hospice
CEDAP	Certificato di assistenza al parto	Birth assistance certificate
SMU	Sistema Monitoraggio Uranio	Uranium Monitoring System
AVN	Anagrafe Vaccinale Nazionale	National Vaccination Registry
DATASETS MANAGED BY THE MINISTRY OF ECONOMY AND FINANCE		
ART50-SPA (then transmitted to the national HIS)	Specialistica ambulatoriale	Specialist Ambulatory Care
ART50-FARMA (then transmitted to the national HIS)	Assistenza Farmaceutica Convenzionata	Affiliated Pharmaceutical Assistance
ANA	Anagrafe Nazionale Assistiti	National Registry of Assisted Persons
TS	Sistema Tessera Sanitaria	Health Card System
DATASETS MANAGED BY THE NATIONAL HEALTH INSTITUTE		
AR-ISS	Antibiotico-resistenza	Antibiotic resistance
Sistema nazionale di sorveglianza	Arbovirosi	Arbovirosis
Okkio alla Salute	Stato nutrizionale bambini 6-10 anni	Nutritional status children 6-10 years
CRE	Batteriemie da Enterobatteri resistenti ai carbapenemi	Carbapenemase-resistant Enterobacteria bacteraemias
Sorveglianza integrata COVID-19	Coronavirus	Coronavirus

SEIEVA	Epatiti virali	Viral hepatitis
Infanzia	Sorveglianza bambini 0-2 anni	Child surveillance 0-2 years
Infezioni correlate all'assistenza	Infezioni correlate all'assistenza	Care-related infections
FluNews	Italia, Rapporto della sorveglianza integrata dell'influenza	Italy, Integrated influenza surveillance report
INFLUNET	Sistema nazionale di sorveglianza epidemiologica e virologica dell'influenza	National epidemiological and virological influenza surveillance system
Morbillo & Rosolia News	Morbillo e rosolia	Measles and rubella
Itoss	Mortalità materna	Maternal mortality
SPItOSS	Mortalità perinatale	Perinatal mortality
PASSI	Popolazione adulta	Adult population
PASSI D'ARGENTO	Popolazione anziana	Elderly population
HBSC	Ragazzi 11-15 anni - Comportamenti collegati alla salute in ragazzi di età scolare	Boys 11-15 years - Health-related behaviours in school-age children
GYTS	Ragazzi 11-15 anni - Sorveglianza Global Youth Tobacco Survey	Boys 11-15 years - Global Youth Tobacco Survey
	Rosolia congenita e in gravidanza	Congenital and pregnancy rubella
	Sindrome emolitico-uremica	Haemolytic uremic syndrome
	West Nile e Usutu virus	West Nile and Usutu virus

HEALTH DATA FLOWS MANAGED BY THE NATIONAL STATISTICAL INSTITUTE

	Cause di morte	Causes of death
	Cause di morte ospedaliera	Causes of hospital death
	Interruzioni volontarie di gravidanza	Voluntary terminations of pregnancy
	Aborto spontaneo	Miscarriage

This heterogeneity between HIS in Italy can be attributed to several factors, including: the evolution of information technology, changing health needs of the population over time, shifting NHS regulations and the institutional and administrative restructuring of the competent bodies. Additionally, the confusing and varied application of current legislation on personal data protection has further contributed to this heterogeneity. These factors create significant challenges in accessing and utilizing data, limiting the vast potential of the extensive health information already available on the Italian population.

While the GDPR addresses both the protection of personal data and the free movement of data, the Italian legislator has historically emphasized only one aspect: the protection of personal data. This focus dates back to the first Italian law on data protection, Law No. 675 of 31 December 1996 (now abolished) titled: 'Protection of persons and other subjects with regard to the processing of personal data' which did not mention the free movement of data in its title (33). This omission set a precedent, leading to a legislative focus almost exclusively on data protection. This focus has contributed to ongoing challenges in interpreting the GDPR and in applying the balance between data protection and data accessibility.

In Italy, health data can be processed without the consent of the data subject for purposes such as health planning, quality of care verification, and healthcare evaluation (20). Additionally, Italian national law allows for scientific research to be conducted using secondary data sources under certain conditions. However, the most effective solution to enhance data utilization and facilitate its circulation seems to be the introduction of new legislation. This new legislation should aim to abolish previous laws, streamline the regulatory framework, and better balance data protection with the free movement of data (34).

Harnessing Administrative Data to study Health Inequality and the Health of People in Vulnerable Situations

Administrative data can be generally described as data which are derived from the operation of administrative systems as data collected by private companies or public sector agencies for registration, transaction and record keeping. These data can be derived from a wide range of systems such as those used in education, taxation, housing, or vehicle licensing. They also include information from registers such as notifications of births, deaths and marriages, electoral registration, and national censuses. Despite administrative data has been largely neglected from many of the mainstream discussions of big data, they are a source of large and complex quantitative information that if analysed with appropriate methods, are particularly valuable and may provide the means to address fundamental questions in the public health sectors and contribute directly to the evidence base (e.g. answering questions relating to health inequality). Even if they are primarily generated for a purpose other than research, in some nations, such as Denmark and the UK, linkable administrative data resources have been available to researchers for many years (20). While, in other countries, the recent increased availability of administrative data for public health surveillance and research requires a step change in the data infrastructure (17).

Despite the great advances in the scale of data collected, analysed and used to improve human life, the need for better data collection, reporting, analysis and interventions on the social determinants of health (SDH) is still pressing (35). On the determinants of health and health inequalities, monitoring has to have a central focus. Health inequalities monitoring provide evidence on who is being left behind and informs equity-oriented policies, programmes and practices (1). Traditionally, two types of data have been used to monitor health inequality: data on health and data on dimensions of inequality, such as economic status, educational level, place of residence and sex (36).

The causal forces at work at the interface of disease epidemics and social inequality are complex: they are operant at the level of individuals, neighbourhoods, and local communities; certain interventions can help some but hinder others; and the underlying determinants of health inequality might differ from one location to another. Future research should therefore seek to unpack this heterogeneity and specify the conditions under which it can be appropriately addressed (37). The next step - and the remaining challenge for future research aiming to reduce health inequalities - is to identify the mechanisms that generate the empirical patterns observed to date. To this end, administrative big data can be used to derive convincing inferences geared towards discovering causal associations rather than simple correlation patterns (16,38). For example, when assessing the causal impact of a social benefits programme on population health outcomes, large sample sizes facilitate the construction of appropriate and statistically well-powered comparison groups, which avoid the need for methodologically complicated adjustments for confounding data and selection bias (39). Administrative data may also provide a mean to access information on those groups who may be the least likely to take part in primary public health research

(e.g. hard-to-reach populations) or be particularly useful for studying issues that individuals might be reticent to disclose to a primary researcher (e.g. mental health problems or substance use) (39). Moreover, greater statistical power allows researchers to study important but relatively rare events, such as the co-occurrence of multiple adverse exposures or broad policy reforms that impact some potentially vulnerable individuals but not others. In addition, the inherently longitudinal nature of administrative data allows researchers to collect many related observations over time on a wide range of key variables. This has the virtue of capturing temporal sequences that are central to social epidemiological enquiries, including individual life course trajectories or intergenerational transmissions of social advantages or disadvantages (40).

People in vulnerable situations (people with experiences of homelessness, justice involvement, addictions, psychosis, physical or cognitive impairment and disabilities) are characterised by exclusionary processes such as stigma and discrimination; restrictions on basic freedoms or rights (eg, voting, privacy, and liberty); or barriers to accessing public services (eg, health care) (41–43). Experiencing any one of these in isolation is associated with higher rates of ill health and premature death compared with unaffected peers, even after accounting for the socioeconomic position (44). Evidence suggests that these experiences frequently co-occur, although the extent of this overlap varies by context (45,46). These experiences and their co-occurrence might influence health through multiple and complex pathways. For instance, their harmful effects might combine or even synergise (37). Due to the lack of access to relevant data, the existing scientific literature has struggled to empirically demonstrate the impact of (co-existing or single) situations of vulnerability on health and health inequalities (47). However, an accurate understanding of the burden of ill health in people with these experiences is essential to inform the development and implementation of services and policies that meet their needs and tackle inequities in health.

Unfortunately, the information richness resulting from the data science revolution is not equally distributed within and across human populations. Vulnerable populations remain both under-studied and under-consulted on the use of data derived from their communities (48). Strategies to improve the use and integration of data designed for the general population may not be accessible to or as effective in disadvantaged groups and may lead to an exacerbation of health inequities (39,49). In the analysis of social science and health data, the global consequences of social exclusion are costly, including exacerbating poverty and reducing human capital. It also hampers the design of culturally coherent solutions which could be more easily adopted in specific communities.

The GDPR

This new realm of big data has made large and rich micro-level data on individuals accessible and usable by industry, governments, and academic researchers. After a long discussion, the General Data Protection Regulation (GDPR) (Regulation European Union (EU) 2016/679 of the European Parliament and of the Council) was finalised in May 2016. The purpose of the GDPR is to protect all EU citizens' data and to regulate the free circulation of these data. It came into effect on May 25, 2018, following a 2-year transitional period. With its 99 articles and 173 recitals, the GDPR is a complex regulation (50).

The first challenge created by the GDPR stems from its treatment of "anonymous" versus "pseudonymous" data. The GDPR's recitals discuss the concept of anonymized data differently from how the term "anonymous" has historically been understood. Under many privacy and research regulatory regimes data that have been key coded and are understood to be "anonymized" and thus, outside the applicable scope of regulation if the code or other means of identification is not derived from or related to information about the individual, is not otherwise capable of being translated to identify the individual; and the covered entity does not use or disclose the code or other means of identification for any other purpose and does not disclose the mechanism for reidentification (51,52). The GDPR, on the other hand, states in Recital 26 that all pseudonymized data are considered personal data, regardless of whether they are, or ever will be, in the hands of a person who holds the key needed for reidentification (50). Explicit consent is required for the processing of these personal data.

Secondary use of health data refers to the usage of health data from sources such as electronic health records, health insurance claim data and health registry data for purposes beyond standard surveillance, such as research (53). Challenges created by the expanded interpretation of the definition of "personal data" could be solved by seeking from data subjects a form of broad consent for future research uses of their personal data. Indeed, the GDPR's legislative history endorses such an approach (50), but EU and member state regulatory agency interpretations have foreclosed any such "broad consent" solution to allow research uses of personal data, even key-coded (54). The GDPR allow for risk-based evaluation and interpretation by the data controller. Unfortunately, health research does not fully benefit from this flexibility, as specific modalities of research are decided by individual EU member states (article 89 of the GDPR) and, in many cases, by individual ethics committees. Indeed, in many EU member states, compliance with data protection legislation in the scope of health research is under scrutiny by ethics committees - who might not have appropriate GDPR training - rather than the data protection authorities, which increases the level of over-interpretation (55).

The GDPR include some category of special exceptions to allow the processing of personal data, including health data for scientific research, thus avoiding the broad consent issue. Specifically, the GDPR allows the processing of special categories of personal data when "necessary for reasons of public interest in the area of public health, such as […] ensuring high standards of quality and safety of health care and medicinal products or medical devices, on the basis of Union or Member State law which provides for suitable and specific

measures to safeguard the rights and freedoms of the data subject, in particular professional secrecy" (GDPR, Art. 9(2)(i)) as well as when "necessary for archiving purposes in the public interest, scientific or historical research purposes […] in accordance with Article 89(1) based on Union or Member State law which shall be proportionate to the aim pursued, respect the essence of the right to data protection and provide for suitable and specific measures to safeguard the fundamental rights and the interests of the data subject" (50). However, laws in several EU member states do not clearly permit processing for secondary research under these provisions of the GDPR (56).

The GDPR has expanded the application of privacy law by including "pseudonymized" data in the definition of personal data. At the same time, it allows individual EU Member States to regulate the use of broad informed consent and to define exceptions. In this way, the GDPR has left the public health community and researchers without a clear basis to rely on for processing personal data. The situation is even further complicated for the cross-border transfer of personal data in the context of collaborations between researchers located in and outside the EU. Further guidance would be helpful to narrow the complexity surrounding the processing of personal data. The European Data Protection Board may be the most appropriate body to contain the heterogeneity of national implementation of the GDPR as it is comprised of representatives of each member state and provides the best reading on supervisory authorities' understanding of GDPR obligations (52).

The Health Gap

Health Inequities

The Alma-Ata Declaration of 1978 and the subsequent "*Health for All*" movement emerged as a major milestone of the twentieth century in the field of public health, and besides identifying primary health care as the key to the attainment of the goal of health for all, emphasises the unacceptability of the existing gross inequality in the health status of the people, particularly between developed and developing countries as well as within countries (57).

Health inequities and SDH are complex and interrelated issues that have been present throughout human history. These issues are rooted in social, economic, and political factors that shape the opportunities and resources available to individuals and communities, and have a profound impact on health outcomes. However, it was just between the 1980s and 1990s that this concept gained widespread attention among public health researchers and policymakers. In August 1980 the United Kingdom Department of Health and Social Security published the Report of the Working Group on Inequalities in Health, also known as the Black Report (after chairman Sir Douglas Black, President of the Royal College of Physicians) (58). The Report showed in great detail the extent to which ill-health and death are unequally distributed among the population of Britain, and suggested that these inequalities have been widening rather than diminishing since the establishment of the NHS in 1948. The Report concluded that these inequalities were not mainly attributable to failings in the NHS, but rather to many other social inequalities influencing health: income, education, housing, diet, employment, and conditions of work. Similarly, in the 1985, in the United States, a report about Black and minority people health was released by the Department of Health and Human Services (59). This report (the Heckler report) documented a higher burden of disease and a lower life expectancy among black people and other minority populations than among white populations.

Thanks to these reports researchers began to explore more and more the world of inequalities in health, there has been a growing recognition of the importance of addressing SDH in order to achieve health equity and improve overall population health (60). However, neoliberal economic models dominant during the 1980s and 1990s impeded the translation of health equity ideals into effective policies in many settings. The late 1990s and early 2000s witnessed mounting evidence on the failure of existing health policies to reduce inequities, and momentum for new, equity focused approaches grew, primarily in wealthy countries (61).

Health As a Social Phenomenon

Complexity defines health. Now, more than ever, in the age of globalization. To get to the heart of this complexity it is necessary to study how the structure of societies, through myriad social interactions, norms and institutions, are affecting population health, and what governments and public health can do about it. This implies understanding health as a social phenomenon. In particular, three main theoretical explanations are well established in "social" epidemiology, which are not mutually exclusive:

Psychosocial approaches: this school traces its origins to a classic study by Cassel (62), in which he argued that stress from the '*social environment*' alters host susceptibility, affecting neuroendocrine function. His list of relevant psychosocial factors includes: dominance hierarchies, social disorganization and rapid social change, marginal status in society, including social isolation, bereavement, and, acting as a buffer to all of the above, the 'psychosocial asset' of 'social support'. In Cassel's view, these psychosocial factors, considered together, explain the puzzle of why particular social groups are disproportionately burdened by otherwise markedly distinct diseases, e.g. tuberculosis, schizophrenia and suicide. Shifting attention from 'specific aetiology' to 'generalized susceptibility'. Cassel ultimately concludes that, in his own words, the most 'feasible' and promising interventions to reduce disease will be 'to improve and strengthen the social supports rather than reduce the exposure to stressors'.

More recent researchers, most prominently Richard Wilkinson, have sought to link altered neuroendocrine patterns and compromised health capability to people's perception and experience of their place in social hierarchies. According to these theorists, the experience of living in social settings of inequality forces people constantly to compare their status, possessions and life circumstances with those of others, engendering feelings of shame and worthlessness in the disadvantaged, along with chronic stress that undermines health. At the level of society as a whole, meanwhile, steep hierarchies in income and social status weaken social cohesion, with this disintegration of social bonds also seen as negative for health (63).

A psychosocial framework directs attention to endogenous biological responses to human interactions. Its focus is on responses to 'stress' and on stressed people in need of psychosocial resources. Comparatively less attention, theoretically and empirically, is accorded to: (1) who and what generates psychosocial insults and buffers, and (2) how their distribution—along with that of ubiquitous or non-ubiquitous pathogenic physical, chemical, or biological agents—is shaped by social, political and economic policies (64).

Social production of diseases/political economy of health: researchers adopting this theoretical approach are sometimes described as a materialist or neo-materialist position, do not deny negative psychosocial consequences of income inequality. However, they argue that interpretation of links between income inequality and health must begin with the structural causes of inequalities, and not just focus on perceptions of that inequality. Arising in part as critique of proliferating blame-the-victim 'lifestyle' theories, which emphasize individuals' responsibility to 'choose' so-called 'healthy lifestyles' and to cope better with

'stress'(65–67), these new analyses explicitly address economic and political determinants of health and disease, including structural barriers to people living healthy lives (65,66,68,69). At issue are priorities of capital accumulation and their enforcement by the state. Recast in this manner, determinants of health are analysed in relation to who benefits from specific policies and practices, at whose cost (70). The underlying hypothesis is that economic and political institutions and decisions that create, enforce, and perpetuate economic and social privilege and inequality are root causes of social inequalities in health (71). Under this interpretation, the effect of income inequality on health reflects both lack of resources held by individuals and systematic underinvestments across a wide range of community infrastructure (72–74). Economic processes and political decisions condition the private resources available to individuals and shape the nature of public infrastructure (education, health services, transportation, environmental controls, availability of food, quality of housing, occupational health regulations) that forms the "neomaterial" matrix of contemporary life. Thus income inequality per se is but one manifestation of a cluster of material conditions that affect population health. Yet, despite its invaluable contributions to identifying social determinants of population health, a social production of disease/political economy of health perspective affords few principles for investigating what these determinants are influencing (75). Biology is opaque. Focusing on relative risks across specified social groups, these analyses rely mainly on critical appraisals of population distributions of known risk and protective factors, most of which ironically are individual-level characteristics identified by conventional epidemiological research.

Eco-social frameworks: lately, Krieger's "ecosocial" approach and other emerging multi-level frameworks have sought to integrate social and biological factors and a dynamic, historical and ecological perspective to develop new insights into determinants of population distribution of disease and social inequities in health (64,76). According to Krieger, multilevel theories seek to "develop analysis of current and changing population patterns of health, disease and well-being in relation to each level of biological, ecological and social organization", all the way from the cell to human social groupings at all levels of complexity, through the ecosystem as a whole. In this context, Krieger's notion of "embodiment" describes how "we literally incorporate biological influences from the material and social world" and that "no aspect of our biology can be understood divorced from knowledge of history and individual and societal ways of living" (76).
The goal is not having a totalizing theory to explain everything (and therefore nothing), but rather to generate a set of integral principles useful for guiding specific inquiry and action, much as evolutionary theory guides biological disciplines ranging from paleontology to molecular biology (64). Specifically, in the case of eco-social theory, its fractal image deliberately fosters analysis of current and changing population patterns of health, disease and well-being in relation to each level of biological, ecological and social organization (e.g. cell, organ, organism/individual, family, community, population, society, ecosystem) as manifested at each and every scale.

All three of these theoretical traditions, use the following main pathways and mechanisms to explain causation: (1) "social selection" or social mobility: the basis of this selection is that health exerts a strong effect on the attainment of social position, resulting in a pattern of social mobility through which unhealthy individuals drift down the social gradient and the healthy move up; (2) "social causation": from this perspective, social position determines health through intermediary factors. Longitudinal studies in which socioeconomic position

has been measured before health problems are present, and in which the incidence of health problems has been measured during follow-up, show higher risk of developing health problem in the lower socioeconomic groups, and suggest "social causation" as the main explanation for socioeconomic inequalities in health (77); and (3) life course perspectives: it explicitly recognizes the importance of time and timing in understanding causal links between exposures and outcomes within an individual life course, across generations, and in population-level diseases trends. Adopting a life course perspective directs attention to how SDH operate at every level of development (early childhood, childhood, adolescence and adulthood) both to immediately influence health and to provide the basis for health or illness later in life (78).

Each of these theories strongly emphasizes the concept of "social position", which is found to play a central role in the SDH inequities. A very convincing explanation of how differences in social position account for health inequities is found in the Diderichsen's model of "the mechanisms of health inequality"(79). Didierichsen's work identifies how the following mechanisms stratify health outcomes:

- Social contexts, which includes the structure of society or the social relations in society, create social stratification and assign individuals to different social positions.
- Social stratification in turn engenders differential exposure to health-damaging conditions and differential vulnerability, in terms of health conditions and material resource availability.
- Social stratification likewise determines differential consequences of ill health for more and less advantaged groups (including economic and social consequences, as well differential health outcomes per se).

Social Determinants of Health: a Conceptual Framework

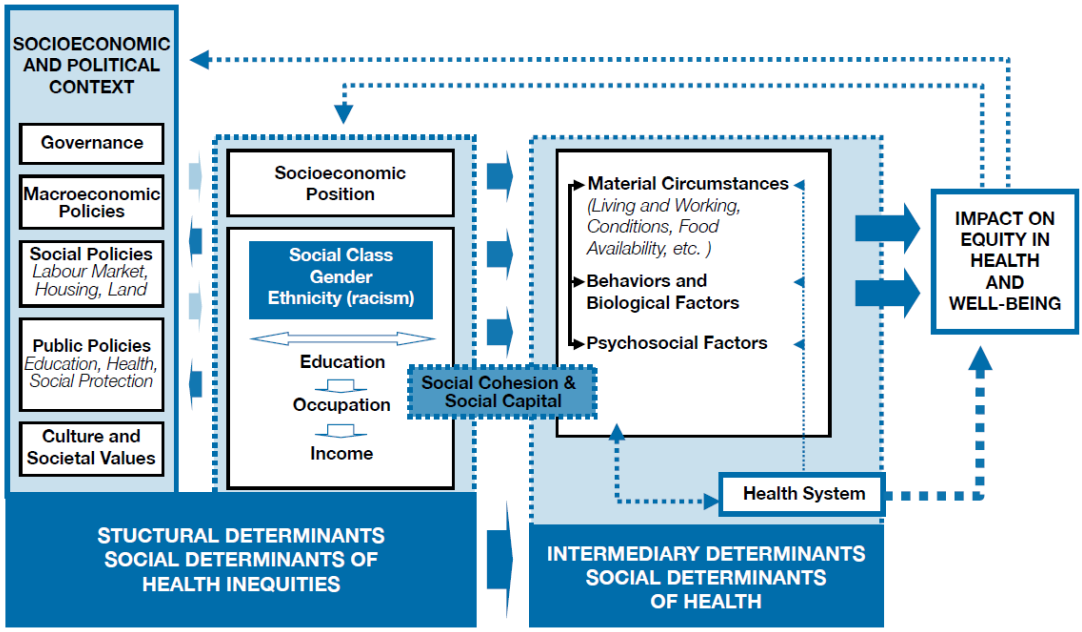
In 2008, the WHO established the Commission on Social Determinants of Health (CSDH) to develop a conceptual framework on the SDH (61). The SDH framework (figure i1) developed by the CSDH present three core components including:
(1) Socioeconomic and political context: this is an intentionally broad term that refers to the spectrum of factors in society that cannot be directly measured at the individual level. "Context", therefore, encompasses a comprehensive set of structural, cultural and functional aspects of a social system whose impact on individuals tends to elude quantification but which exert a powerful formative influence on patterns of social stratification and, thus, on people's health opportunities. In this stated context, one will find those social and political mechanisms that generate, configure and maintain social hierarchies (e.g. the labor market, the educational system and political institutions including the welfare state) (80). In the framework, six points are included in the "context" component: (i) governance in the broadest sense and its processes; (ii) macroeconomic policy; (iii) social policies; (iv) public policy in other relevant areas such as education, medical care, water and sanitation; (v) culture and societal values; and (vi) epidemiological conditions, particularly in the case of major epidemics.

(2) Structural determinants of health inequities: the CSDH adopt the term "structural determinants" to refer specifically to interplay between the socioeconomic-political context, structural mechanisms generating social stratification and the resulting socioeconomic position of individuals. This concept corresponds to Graham's notion of the "social processes shaping the distribution" of downstream social determinants (81). The CSDH framework posits that structural determinants are those that generate or reinforce social stratification in the society and that define individual socioeconomic position. These mechanisms configure the health opportunities of social groups based on their placement within hierarchies of power, prestige and access to resources (economic status). Income, education and occupation in the framework are included as proxies to measure social stratification. However, these proxies may not adequately capture disparities in working and living conditions across divisions of race/ ethnicity and gender, which in the framework are included separately among the structural stratifiers.

(3) Intermediary determinants: the structural determinants operate through a series of what we will term intermediary SDH. The social determinants of health inequities are causally antecedent to these intermediary determinants, which are linked, on the other side, to a set of individual-level influences, including health-related behaviors and physiological factors. The intermediary factors flow from the configuration of underlying social stratification and, in turn, determine differences in exposure and vulnerability to health-compromising conditions. The main categories of intermediary determinants of health are: (i) material circumstances including factors such as housing and neighborhood quality, consumption potential and the physical work environment; (ii) psychosocial circumstances including psychosocial stressors, stressful living circumstances and relationships, and social support and coping styles; (iii) behavioral and/or biological factors including nutrition,

physical activity, tobacco consumption and alcohol consumption, which are distributed differently among different social groups. Biological factors also include genetic factors. Moreover, the health system, playing an important role in mediating the differential consequences of illness in people's lives, can be define itself as a social determinant.

Figurei1. CSDH conceptual framework.



The concepts of social cohesion and social capital occupy a conspicuous place in discussions of SDH. Social capital cuts across the structural and intermediary dimensions, with features that link it to both. Influential researchers have proclaimed social capital a key factor in shaping population health (82,83). Yet focus on social capital, depending on interpretation, risks reinforcing depoliticized approaches to public health and the SDH, when the political nature of the endeavour needs to be an explicit part of any strategy to tackle the SDH. Certain interpretations have not depoliticized social capital, notably the notion of "linking social capital", which have spurred new thinking on the role of the state in promoting equity, wherein a key task for health politics is nurturing cooperative relationships between citizens and institutions. According to this literature, the state should take responsibility for developing flexible systems that facilitate access and participation on the part of the citizens.

The arrows in the framework are positioned to contemplate the fact that the disease can 'feed-back' on a given individual's social position, for example by impairing job opportunities and reducing income; some epidemic diseases can also 'feed-back' on the functioning of social, economic and political institutions (61).

People in Vulnerable Situations

In public health, the term “vulnerable population” simply implies the disadvantaged sub-segment of the community requiring utmost care, specific ancillary considerations and augmented protections (84). People living in vulnerable conditions include individuals who face systemic exclusion and discrimination based on their age, disability, ethnicity, gender, income level, religion, caste or creed, gender identity, sexual orientation, and migratory status, in addition to individuals who are caught up in conflict and are stateless, populations who are incarcerated, individuals with chronic health conditions (eg, mental illness), people living in inadequate housing, and people who are exposed to environmental degradation, air pollution, and at risk due to climate change (85). Experiencing any one of these in isolation is associated with higher rates of ill health and premature death compared with unaffected peers, even after accounting for socioeconomic position (44). Evidence suggests that these experiences frequently co-occur, although the extent of this overlap varies by context (45,46).

Across Europe there has been a growing recognition of the particular health and social inequalities faced by the most vulnerable communities and individuals. While each group faces its own specific challenges, there are common issues experienced by all groups and individuals facing vulnerable situations. These include, among others, limited or no access to health care systems and services; pressures due to co-financing requirements in some Member States, leading to increased poverty rates; growing levels of poor mental health and wellbeing; escalating isolation particularly for people who are homeless or in insecure housing conditions, and for those people who are unemployed or in very low-income employment. These issues have been exacerbated in recent years (86).

In addition to the study of the SDH at the population level, an accurate understanding of the burden of ill health in people in vulnerable situations is essential to inform the development and implementation of services and policies that address more broadly health inequities (37).

COVID-19: a Syndemic

COVID-19 Pandemic

In 2020, a new public health crisis threatened the world with the emergence and spread of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the seventh human coronavirus. In December 2019, adults in Wuhan, capital city of Hubei province and a major transportation hub of China started presenting to local hospitals with severe pneumonia of unknown cause (87). Many of the initial cases had a common exposure to the Huanan wholesale seafood market that also traded live animals. The surveillance system (put into place after the SARS outbreak) was activated and respiratory samples of patients were sent to reference labs for etiologic investigations. On 7th January, the virus was identified as a coronavirus that had > 95% homology with the bat coronavirus and > 70% similarity with the SARS-CoV (88). The number of cases started increasing exponentially, some of which did not have exposure to the live animal market, suggestive of the fact that human-to-human transmission was occurring (89). The massive migration of Chinese during the Chinese New Year fuelled the epidemic. Cases in other provinces of China, other countries were reported in people who were returning from Wuhan. Transmission to healthcare workers caring for patients was described on 20th January 2020. By 23rd January, the 11 million population of Wuhan was placed under lockdown with restrictions of entry and exit from the region. Soon this lockdown was extended to other cities of Hubei province. Cases of Coronavirus Disease 2019 (COVID-19) in countries outside China were reported in those with no history of travel to China suggesting that local human-to-human transmission was occurring in these countries. Soon it was apparent that the infection could be transmitted from asymptomatic people and before symptoms' onset (90).

As of March 17, 2023, the WHO reports a total of 760,360,956 confirmed cases and 6,873,477 confirmed deaths in 236 countries or territories Worldwide (91). The global case fatality rate range between 0.1 and 1.9% (92,93), with concrete evidence showing case fatality rate to sharply increase with age and comorbidities (94), and by territory (92). Although there were a few countries, such as New Zealand and Vietnam, that achieved almost complete control of the initial spread through rigorous surveillance efforts (95,96), community transmission quickly took off in many other countries. Globally, the list of worst-affected countries includes the United States (102+ million cases; 1+ million deaths), Brazil (37+ million cases; 699 000+ deaths), India (44+ million cases; 530 000+ deaths), and Russian Federation (22+ million cases; 396 000+ death) (91). The spread of COVID-19 has not been proportional to the sizes of the regional populations, which may indicate a range of contributing factors, from containment and screening measures to population demographics. During the progression of the outbreak, the situation in Italy had been particularly concerning, with a case fatality rate of 14.44% (95% CI 14.29–14.58) on May 26, 2020 (97). Additionally, it was reported that Italian infection rates mimic an exponential curve, with unease and doubt regarding whether the Italian healthcare system would be

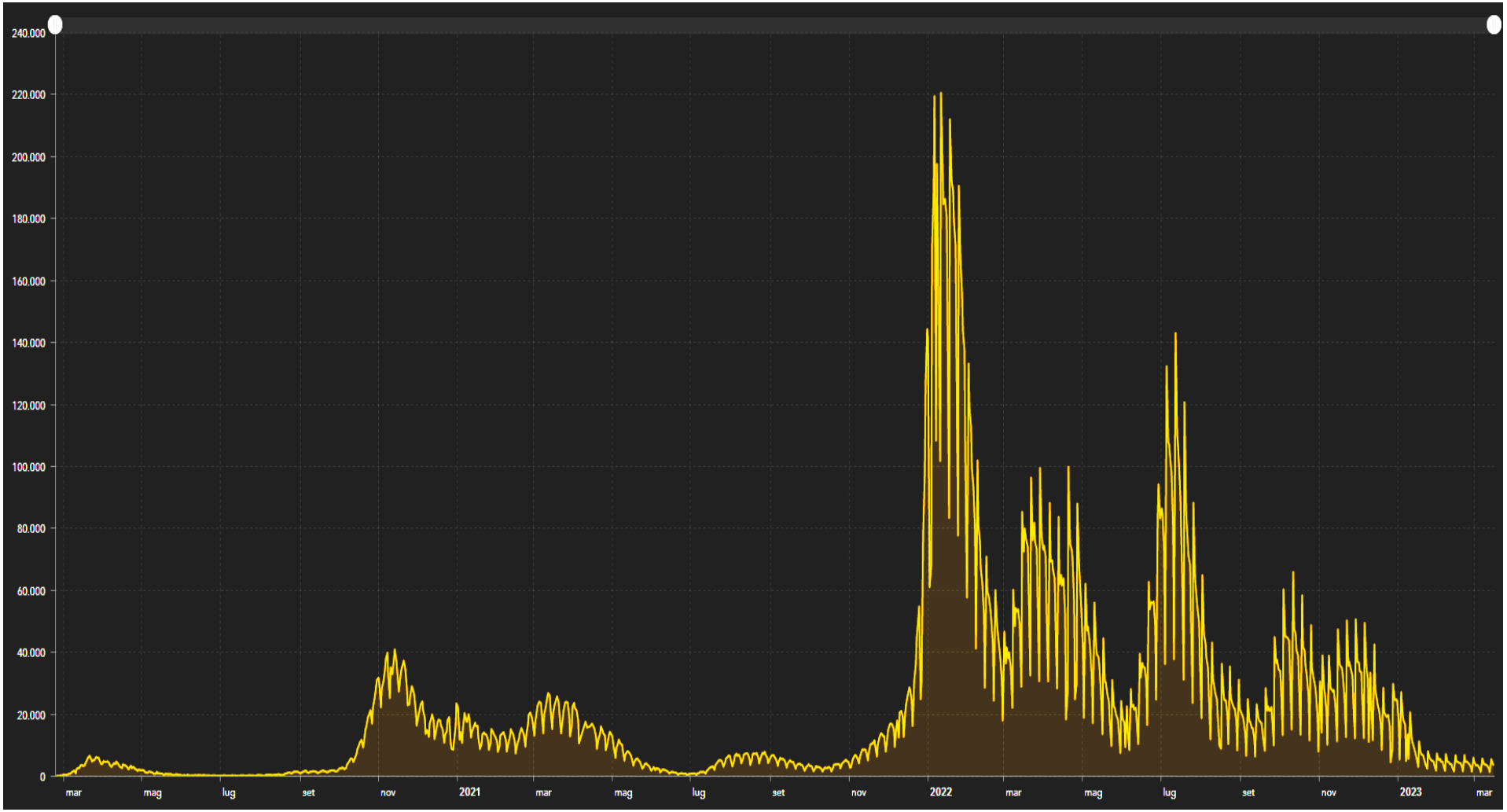
able to cope (98). The epicentre of the COVID-19 pandemic has been, and continues to be, dynamic in nature. It had begun in Asia, before transitioning to Europe, then the Americas, and back to Europe (UK) with a variant strain (91,99). Indeed, after the initial “wild type” variant (alpha: B.1.1.7), other variants of concerns have been identified (100). The WHO had warned that Africa’s increasing infection rates may possibly place it as the next epicentre for the pandemic (101), but that did not seem to manifest.

COVID-19 Pandemic in Italy

On February 20th, 2020, the first case of autochthonous COVID-19 was confirmed in the Lombardy region, Italy (102). The patient was a 38-year old healthy man (patient 1), admitted to the Hospital of Codogno, with a mild pneumonia resistant to therapy, no relevant travel history and no apparent exposure to diseased contacts. Starting with the morning of February 21st, a strict proactive intervention for tracing and testing all patient' contacts was set up. Although the patient zero could not be detected, an initial outbreak was identified around the city of Codogno. In the week that followed, Codogno area, as well as several neighbouring towns in southern Lombardy, experienced a very rapid increase in the number of detected cases, which rose to over 530 positive samples by February 28th and 7,375 by March 8th (103). With the increase in the number of detected cases, also their spatial distribution expanded, reaching several other areas in northern Lombardy. Over this period, the regional health system, local health authorities the Lombardy reference virology laboratories, and the National Health Institute collaborated to introduce coordinated actions to limit the spread of the infection. Among these, isolation of cases, contact tracing, intensive testing, and the definition of a "red" quarantined area around the most affected towns. In response to a rapid rise in the number of cases also beyond the restricted area, the Italian government announced on March 7th a complete lockdown for Lombardy and some provinces of Piedmont, Emilia-Romagna, Veneto and Marche. Since the epidemic had sparked also in other Italian regions, the government declared a nation-wide lockdown with immediate effect on the 10th of March 2020 (104).

As of 17 March 2023, Italy had 25 864 032 confirmed cases, and 187 211 deaths, with a case fatality rate of 0.7% (105). During the first pandemic year, the temporal course of the epidemic was characterized by 3 distinct phases: the first epidemic wave was from March to June 2020, followed by a summer period with a relatively low incidence, and a second wave that started in September and peaked in November 2020 (106). Two more waves occurred in the following year: the third from July 2021 to September 2021, and the fourth from October 2021 to February 2022. The second wave was characterized by the highest share of deaths, while most cases were registered during the fourth wave, probably thanks to the spread of more contagious virus variants and the discontinuation of the adoption of non-pharmaceutical containment measures (107). Throughout 2022, several epidemic waves occurred, of lesser magnitude than the fourth (Figure i2).

Figure i2. Epidemic curve of new confirmed cases in Italy (March 2020- March 2023). Source: (108)



The Disease

Regarding the pathogenesis, the virus is inhaled through respiratory droplets and acquires entry into the respiratory tract through the nasopharyngeal mucosal membranes (109). In about 80% of cases, the virus resides in the upper respiratory tract leading to an innate immune response that is mild and requires conservative symptomatic therapy. The remaining 20% of cases experience a much severe form of the disease; the virus diffusely invades and destroys lung alveolar cells, leading to a systemic inflammatory response with 'cytokine storm', followed by healing and fibrosis (110). Regarding extra-pulmonary manifestations, the virus may disseminate into the blood and affect organs that express ACE2 receptors, such as the lungs, heart, kidneys, and gastrointestinal tract (109,111). Disease severity ranges from asymptomatic to severe, with the latter shown to be associated with older age and presence of comorbidities. The most common symptoms being reported are fever and cough (112). Severe disease involves acute respiratory distress syndrome, which can also be associated with severe pneumonia. In fact, the most commonly reported cause of death is respiratory failure (113). The pneumonia most commonly presents with bilateral multiple lobular and subsegmental areas of ground-glass opacities on computerized tomography scan (114). Non-respiratory complications of COVID-19 may include septic shock (reported in 81.2% of nonsurvivors in one case series) (115), acute liver injury (116), acute kidney injury (117), ocular problems (118), neurological manifestations (119), and resemblances of disseminated intravascular coagulation (reported in 71% of non-survivors in a case series) (120). Another complication of increasing concern is the formation of diffuse microvascular thrombi (121). COVID-19 has also been linked with chemosensory dysfunction; loss of sense of taste and smell has been widely reported in cases of COVID-19, sometimes as the only symptom (122).

Strategies to Contain the Pandemic

Adoption of containment measures during the first wave of the pandemic served to flatten the curve; that is, to extend the period over which cases occurred. Flattening the curve was desirable for three reasons. First, it would prevent the healthcare system from being overwhelmed because the peak number of beds occupied at any one time would be lower under a flatter curve. Second, it would slow the momentum of the outbreak, reducing the overshoot of cases after the outbreak peak. Third, it allowed time to improve clinical care strategies and capacity and to evaluate therapeutics (123,124).

Non-pharmaceutical interventions

The most important public precaution initially applied to contain the outbreak was social distancing. It was advised to remain at home except for necessity, which has prompted the implementation of various travel bans and curfews. Moreover, mass gatherings were discouraged. Finally, it was advised to keep a minimum of 2 m distance between individuals to minimise transmission. Universal face covering/masking was also adopted as a public health tool in curtailing community transmission (125,126).

Screening and diagnosis

The COVID-19 pandemic response has led to the use of testing outside of health-care settings on an unprecedented scale. At the beginning of the pandemic, successful containment was heavily reliant on its accurate diagnosis and efficient and strict screening (followed by self-isolation or governmental/hospital quarantine of positive cases). Subsequently, diagnostic tests were used as a public health tool to ensure a safe environment for schools, workplaces, and mass gatherings for sports, music, religious, and social events. Governments and airlines have mandated testing to allow the resumption of travel in a safe manner. There are two major methods for the detection of SARS-CoV-2 infection and their role has evolved during the course of the pandemic. Molecular tests such as PCR are highly sensitive and specific at detecting viral RNA, and are recommended by WHO for confirming diagnosis in individuals who are symptomatic and for activating public health measures. Antigen rapid detection tests detect viral proteins and, although they are less sensitive than molecular tests, have the advantages of being easier to do, giving a faster time to result, of being lower cost, and able to detect infection in those who are most likely to be at risk of transmitting the virus to others. Antigen rapid detection tests can be used as a public health tool for screening individuals at enhanced risk of infection, to protect people who are clinically vulnerable, to ensure safe travel and the resumption of schooling and social activities, and to enable economic recovery (127).

Vaccinations

By December 2020, vaccines against SARS-CoV-2 were developed, trialed, and approved for emergency use; a timeline unparalleled in the history of vaccinology. Epidemiological factors facilitated the accelerated timeline of these pivotal trials. With little acquired immunity to SARS-CoV-2 and a high incidence of COVID-19 in mid-2020 when trials were underway, the studies reached their prespecified end points rapidly and ahead of anticipated schedule. As is widely appreciated now, the trials demonstrated excellent protection against COVID-19 and severe outcomes, like hospitalization and death (123).

Seven COVID-19 vaccine candidates have now been approved by the European Medicines Agency (128).

Unequal Health Impacts of the COVID-19 Pandemic

The impacts of COVID-19 have not been felt equally. Neither the direct burden of the disease nor the indirect effects of the control measures were evenly spread across the population, with the greatest impacts falling on the least privileged in society (129).

Older people, men, people with chronic non-communicable diseases (NCDs), and people with disabilities appear to have greater biological susceptibility to SARS-CoV-2 infection, and, or, propensity to develop harmful pulmonary inflammation from COVID-19 (130,131). However, the wide inequities seen in infection, hospitalization and mortality rates between population groups were mostly driven by social factors overlaid on these biological risks (132,133). Groups that have experienced increased rates of COVID-19 morbidity and mortality include: poorer people (134); marginalised ethnic minorities (135,136); low-paid essential workers (137,138); migrant and populations affected by emergencies (139); older people living in residential care homes (140); incarcerated populations (141); and homeless people (142). There are multiple mechanisms to explain the inequities for these groups, but in summary unfavourable SDH for these groups have meant higher rates of chronic disease (143) that increase their risk of poor outcomes from COVID-19 and poorer access to health services for treatment and vaccination (144).

While existing predisposing susceptibility to COVID-19 is a product of pre-existing SDH, there is growing evidence that the ability of disadvantaged groups to adhere to public health and social measures that reduce viral transmission and to deal with the aftermath of the pandemic, is also linked to social determinants (145). Difficult living and working conditions make adherence to preventive measures more difficult for disadvantaged populations, thus increasing their exposure to risk of infection (146). And the economic fallouts from the pandemic are hitting disadvantaged population groups harder.

Health-care facilities, staff capacity, equipment and resources have been overstretched by the pandemic (147). Decreased use of health services because of fear of infection and service disruptions gives rise to an increased burden for other illnesses, particularly for disadvantaged communities (148). The pandemic and associated public health and social measures have also had specific effects on a range of health conditions, mental health and well-being. Isolation for instance worsens mental health and deteriorates health behaviours of disadvantaged groups (149).

Beyond its direct effect on health and disruptions to the health sector, COVID-19 has had dramatic and unequal social and economic consequences for individuals, families and nations. These will exacerbate future health inequities. The consequences arise from the disease itself (e.g. families with multiple deaths, increased poverty due to health expenditure) but also because people have changed their behaviour due to fear of contracting the virus or of stigmatization. Public health and social measures have also required businesses and schools to close and restricted cultural and social gatherings and travel. Unequal changes in these circumstances have implications for health inequity (150).

An Integrated Approach to Respond to a Syndemic

Richard Horton, based on the theoretical assumptions made in the previous paragraph, has highlighted that COVID-19 is not a pandemic, but should more correctly be called a syndemic. Two categories of disease are interacting within specific populations: infection with SARS-CoV-2 and an array of NCDs. These conditions are clustering within social groups according to patterns of inequality deeply embedded in our societies. The aggregation of these diseases on a background of social and economic disparity exacerbates the adverse effects of each separate disease (144).

The notion of a syndemic was first conceived by Merrill Singer, writing in The Lancet in 2017, she argued that a syndemic approach reveals biological and social interactions that are important for prognosis, treatment, and health policy (151). Limiting the harm caused by SARS-CoV-2 will demand far greater attention to NCDs and socioeconomic inequality than has hitherto been admitted. A syndemic is not merely a comorbidity. Syndemics are characterised by biological and social interactions between conditions and states, interactions that increase a person's susceptibility to harm or worsen their health outcomes. In the case of COVID-19, attacking NCDs will be a prerequisite for successful containment.

The most important consequence of seeing COVID-19 as a syndemic is to underline its social origins. For people in vulnerable situation, no matter how effective a treatment or protective a vaccine, the pursuit of a purely biomedical solution to COVID-19 will fail. A syndemic approach provides a very different orientation to clinical medicine and public health by showing how an integrated approach including devise policies and programmes to reverse profound disparities can be far more successful than simply controlling epidemic disease or treating individual patients. Approaching COVID-19 as a syndemic implies taking a larger vision, one encompassing education, employment, housing, food, and environment. Viewing COVID-19 only as a pandemic excludes such a broader but necessary prospectus.

Objectives

General Objective

To inform the development and implementation of services and policies that address the needs of people in vulnerable situations and tackle inequities in health, it is crucial to accurately understand the burden of ill health in these population subgroups. The overall aim of this thesis was to explore the potential of using existing data sources to monitor the health of people in vulnerable situations.

Given that the impacts of COVID-19 were unevenly distributed across the population, with the most significant effects on the least privileged, the pandemic was used as a case study in this research. The following chapters focus on assessing the direct and indirect impacts of the pandemic on population groups in vulnerable situations. The study was conducted in Italy, specifically examining vulnerable populations in the Lombardy, Tuscany, and Apulia regions. The information systems utilized in this research were derived from administrative data routinely collected or developed during the COVID-19 pandemic.

Specific Objective

Chapter 1

COVID-19 has been shown to disproportionately affect people at a socioeconomic disadvantage. Previous studies investigating the association between geographical deprivation and COVID-19 outcomes in Italy found no significant differences in case hospitalization and case fatality according to deprivation. However, the use of the DI of the municipality or census area as a proxy for the level of individual social disadvantage carries with it the inevitable potential ecological bias that can arise from attributing a collective measure to an individual.

The specific objective of Chapter 1 was to assess the associations between the spread, morbidity, and mortality of COVID-19 and both individual and geographical DI, as well as their interaction, in the Apulia region from the beginning of the pandemic (February 2020) until December 2020.

Chapter 2

Residents of long-term care facilities (LTCFs) typically suffer from multiple chronic conditions, cognitive impairments, and various medical and social vulnerabilities. Beside this background of vulnerabilities, long-term-care facility residents experienced reduced healthcare access during the pandemic. Therefore, it was expected that people living within LTCFs were also more likely to develop worse health outcomes for non-COVID conditions during the first phase of the pandemic. While numerous studies have examined the impact of the pandemic on NCDs in the general population, research specifically focused on LTCF residents is limited.

The specific objective of Chapter 2 was to assess the indirect impact of the COVID-19 pandemic on hospitalisation and mortality rates among LTCF residents in two Italian Regions, Tuscany and Apulia, during 2020, compared to the pre-pandemic period.

Chapter 3

Individuals in contact with the criminal justice system often come from marginalized groups of society with a higher burden of poverty and discrimination, and with limited access to healthcare. Due to infrastructural and population characteristics, prison setting is at increased risk for the transmission of SARS-CoV-2 and severe clinical outcomes. Yet, conducting robust research in prison settings is challenging due to structural and operational constraints, and most available studies are mono-centric with limited temporal coverage.

The specific objective of Chapter 3 was to describe the extent and dynamics of the COVID-19 pandemic within the prison system of a large Italian region, Lombardy, and to report the infection prevention and control (IPC) measures implemented. This chapter also aimed to use scientific evidence gathered from administrative data sources to formulate guidelines and advocate for better health practices in prison settings.

Chapter 1

Executive summary

COVID-19 has disproportionately impacted socioeconomically disadvantaged populations. To effectively address social determinants of health (SDH) both in the current context and for future pandemic preparedness, it is essential to understand the relationship between socioeconomic deprivation and the impact of pandemics.

In Italy, the available deprivation index (DI) serves as a multidimensional measure of disadvantage, reflecting both social and material resource deficiencies among residents in specific census sections, akin to neighborhoods. Previous research by Mateo-Urdiales et al. explored the relationship between deprivation and COVID-19 outcomes in Italy during the pre-lockdown, lockdown, and post-lockdown phases, using the Italian DI as a contextual measure. Their findings revealed no significant differences in case-hospitalization and case-fatality rates based on deprivation. Similarly, a study in Barcelona found no significant increase in hospitalization and mortality rates in areas with higher geographical DI. However, using geographical DI as a proxy for individual social disadvantage can introduce ecological bias, as it attributes a collective measure to individuals. The interplay between disease epidemics and social inequality is complex, operating at individual, neighborhood, and community levels.

This chapter aims to compare geographic and individual DI in assessing the association between SEP and the risk of SARS-CoV-2 infection and disease severity in the Apulia region from February to December 2020.

The findings of this study underscore that the COVID-19 pandemic has been experienced unevenly, with the most disadvantaged communities bearing a heavier burden. During the first wave, no significant associations were observed between COVID-19 outcomes and either geographic or individual DI. However, during the second wave, associations between COVID-19 outcomes and individual DI emerged. Geographic DI was not associated with an increased risk of hospitalization and death, except among the most disadvantaged groups.

The results of this study highlight the need for caution when using geographical DI as a proxy for individual social disadvantage, as it may lead to inaccurate assessments. Future research and data collection should prioritize enhancing surveillance systems by incorporating individual measures of inequality into national health information systems.

Comparison of geographical and individual deprivation index to assess the risk of Sars-CoV-2 infection and disease severity: a retrospective cohort study

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Link to the article.

It has been shown that COVID-19 afects people at socioeconomic disadvantage more strongly. Previous studies investigating the association between geographical deprivation and COVID-19 outcomes in Italy reported no diferences in case-hospitalisation and case-fatality. The objective of this research was to compare the geographic and individual deprivation index (DI) in assessing the associations between individuals' deprivation and risk of Sars-CoV-2 infection and disease severity in the Apulia region from February to December 2020.

This was a retrospective cohort study. Participants included individuals tested for SARS-CoV-2 infection during the study period. The individual DI was calculated employing principal component analysis (PCA) on four census variables. Multilevel logistic models were used to test associations between COVID-19 outcomes and individual DI, geographical DI, and their interaction.

In the study period, 139,807 individuals were tested for COVID-19 and 56,475 (43.5%) tested positive. Among those positive, 7,902 (14.0%) have been hospitalised and 2,215 (4.2%) died. During the frst epidemic wave, according the analysis done with the individual DI, there was a signifcant inversely proportional trend between the DI and the risk of testing positive. No associations were found between COVID-19 outcomes and geographic DI. During the second wave, associations were found between COVID-19 outcomes and individual DI. No associations were found between the geographic DI and the risk of hospitalisation and death. During both waves, there were no association between COVID-19 outcomes and the interaction between individual and geographical DI.

Evidence from this study shows that COVID-19 pandemic has been experienced unequally with a greater burden among the most disadvantaged communities. The results of this study remind us to be cautious about using geographical DI as a proxy of individual social disadvantage because may lead to inaccurate assessments. The geographical DI is often used due to a lack of individual data. However, on the determinants of health and health inequalities, monitoring has to have a central focus. Health inequalities monitoring provides evidence on who is being left behind and informs equity-oriented policies, programmes and practices. Future research and data collection should focus on improving surveillance systems by integrating individual measures of inequalities into national health information systems.

Introduction

The newly emerged virus SARS-CoV-2 was initially reported in China in December 2019 (152). On February 20, 2020, the first major COVID-19 outbreak in Europe was detected in the Lombardy region, Italy (102). On March 11, 2020, WHO declared the SARS-CoV-2 outbreak a pandemic (153). As of August 30, 2023, the WHO reports a total of 770 085 713 confirmed cases and 6 956 173 confirmed deaths worldwide (91); while the Italian NHS reported 26 175 146 confirmed cases, and 190 644 deaths (105). During the first pandemic year, the temporal course of the epidemic in Italy was characterized by 3 distinct phases: the first epidemic wave from March to June 2020, followed by a summer period with a relatively low incidence, and a second wave that started in September and peaked in November 2020 (4).

Evidence shows that males, aged over 65 and smoking patients might face a greater risk of developing more critical or lethal conditions if infected with SARS-CoV2. Comorbidities, such as hypertension, diabetes, cardiovascular disease or respiratory diseases, could also greatly affect the prognosis of the COVID-19 patients (154). A study carried out in a large community cohort has also shown associations between adverse lifestyles and a higher risk of COVID-19 (155). However, it is now well known that lifestyle plays a mediating role in the relationship between SEP and health (156). Literature reports that the wide inequalities seen in infection, hospitalization and mortality rates between population groups were mostly driven by social factors overlaid on biological risks (132,133). Multiple mechanisms explain the increased impact of COVID-19 among people with a higher level of socio-economic disadvantage, but in summary, unfavourable social determinant of health (SDH) and associated higher rates of chronic disease (143) increased their risk of poor outcomes from COVID-19 and poorer access to health services for treatment and vaccination (144). While existing predisposing susceptibility to COVID-19 is a product of pre-existing SDH, there is growing evidence that the ability of disadvantaged groups to adhere to public health and social measures that reduce viral transmission and to deal with the aftermath of the pandemic, is also negatively affected by unfavourable SDH (145). Difficult living and working conditions make adherence to preventive measures more difficult for disadvantaged populations, thus increasing their exposure to the risk of infection (146). For instance, most deprived individuals usually carry out manual labour professions or work in the informal sector and therefore, resulting in limited opportunities for working from home. Health and socioeconomic inequality mutually influence each other by triggering and feeding vicious circles (144). The economic fallouts from the pandemic are hitting disadvantaged population groups harder. The pandemic itself has accentuated these already existing social and health inequalities, widening the gap among individuals with different SEP. This is a crucial point for the present but also for the future. Assessment and mitigation of SDH cannot be neglected in a pandemic response and prevention programme.

The available Italian deprivation index (DI) is a multidimensional measure of the disadvantage in the ownership of both social and material resources among residents in each census sections, which are comparable to neighbourhoods as described elsewhere (157,158). Mateo-Urdiales et al. investigated the association between deprivation and COVID-19 outcomes in Italy during pre-lockdown, lockdown and post-lockdown periods using the

Italian DI as a contextual measure of deprivation. No differences in case-hospitalisation and case-fatality according to deprivation were observed (159). Similarly, in a study on the city of Barcelona, the increase in hospitalisation and mortality rates was not significant among people living in areas characterised by higher geographical DI (160). However, the use of geographical DI measures as a proxy for the level of individual social disadvantage is subject to potential ecological bias that can arise from attributing a collective measure to an individual.

The overall objective of this research was to compare the geographic and individual DI in assessing the associations between individuals' SEP and risk of Sars-CoV-2 infection and disease severity in the Apulia region from February to December 2020.

Methods

Study setting

The Italian 'Servizio Sanitario Nazionale' (SSN) was introduced in 1978 to ensure that healthcare is accessible to all Italian citizens without socio-economic barriers, according to a principle of horizontal equity (161). The system is organized into three levels: national, regional, and local. The national level is responsible for establishing the general objectives and fundamental principles of the NHS. The nineteen regions and two autonomous provinces (R&AP) are then responsible for organizing and delivering health care (162). In this scenario, through ministerial decrees, the Ministry of Health has taken the lead in the fight against the COVID-19 epidemic. Then, the R&AP were in charge of organizing and implementing the monitoring and prevention strategy at the local level based on national guidelines.

Pandemic stages and preventive measures

In Italy, after the detection of the first locally acquired Covid-19 case in Lombardy on February 20, 2020, the number of cases increased greatly in the following weeks, although unevenly among regions, forcing the government to adopt unprecedented restrictive measures. In particular, during the first year of the pandemic, the following phases can be defined: (1) first comprehensive national lockdown from 9 March to 3 May (closure of schools and most workplaces, and the implementation of quarantines, border closings, and restriction on public gatherings) (163), (2) gradual reopening phase from 4 May to 14 June (restrictions were gradually rolled back) (164), (3) Few restrictions from 15 June to 7 October (Covid-19 incidence remained low) (165), (4) new restrictions from 8 October to 5 November (166), and (5) lockdowns on a regional basis from 6 November until the end of 2020 (closure of regional borders) (167). During the first epidemic wave, the number of diagnostic tests (Polymerase Chain reaction - PCR) available was limited, while availability increased considerably during the second wave (168).

Study design and Data Sources

This is a retrospective cohort study conducted by analysing and merging the following electronic health records from the Apulia regional health-care information systems: (i) laboratory registry of individuals tested for Sars-CoV-2 infection; (ii) registry of COVID-19 confirmed cases; (iii) healthcare workers' registry; (iv) 2011 census dataset. Figure 1.1 explains how the final dataset was obtained. In the study, a COVID-19 confirmed case was defined as an individual who resulted positive to a PCR test. The study period goes from 20 February to 31 December 2020. The cohort in this study includes all the individuals tested for SARS-CoV-2 infection during the study period in the Apulia region, in which a total of 3.95 million inhabitants were registered as of December 31, 2019 (169). Since the census data date back to 2011, we decided to exclude persons under 35 years of age, for whom part of the census data (i.e. education) may have changed. Individuals tested from 20 February 2020 to 31 May 2020 were included in the first epidemic wave, while those tested from 16 September 2020 to 31 December 2020 were included in the second epidemic wave (91).

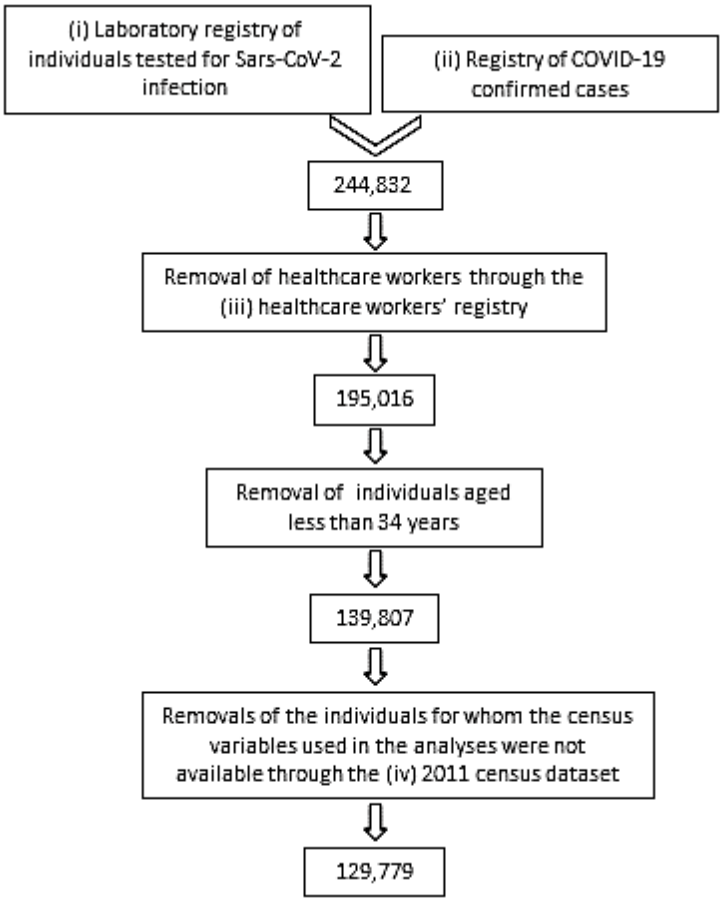
The laboratory registry tracked: identification code; age; sex; province of residence; date of the test; PCR test result. The COVID-19 confirmed cases registry reported the following information: identification code, COVID-19 related hospitalization; admission to the intensive care unit (ICU) and death. From the census variables available, the following were selected to perform this study: identification code; education; the number of family members; citizenship; family type; and employment status.

Charlson comorbidities index, extensively described previously (170), and the geographical DI (157,158) were added to the characteristics of individuals in the final dataset. The Italian geographical DI is the sum of the z score of five simple indicators: x_1: % of population among 15 and 60 years old with education equal to or less than elementary school; x_2: % of the active population unemployed or seeking their first job; x_3: % of housing occupied for rent; x_4: % of single-parent families (and consisting of a single-family unit) with children under 18 years old; x_5: population density (occupants per 100 m^2).

Through the use of the healthcare workers' registries, healthcare workers were removed from the dataset as their risk of acquisition of infection was strongly related to their professional exposure to the virus.

The merging of the data information system has been carried out by the regional health agency through a numeric identification code. All the health data used in the study were anonymous.

Figure 1.1 Data linkage to obtain the study cohort.



Definition of the individual deprivation index through the census data

For the definition of the individual DI, polychoric principal component analysis (PCA) was employed, and four census variables were used: citizenship, family type, employment status, and education. Table 1.1 reports the value attributed to each individual variable category.

Table 1.1. Census variables used to define the individual DI.

Citizenship	Family Type	Employment Status	Education
1 - Italian	1 - Couple without children	1 - Employed	1 - Academic Diploma 2nd Level/Academy of Fine Arts Diploma/Master degree
2 - Foreigner	2 – Single-person households	2 - Recipient(s) of one or more pensions due to previous employment or investment income	2 - Academic 1st Level Diploma/Bachelor degree
	3 - Couple with children	3 - Students /Housewives/In other status	3 - High school graduation
	4 - Single parent	4 - First-time job seekers	4 - Middle school graduation
	5 - Households with 2 or more families	5 - Unemployed	5 - Elementary school diploma
			6 -Illiterates/Literate without educational qualification

The coordinates of the observation over the PCA were used as the DI and based on this new variable the population was divided in quintiles. The geographical and individual DI range from 1 (lowest deprivation level) to 5 (highest deprivation level).

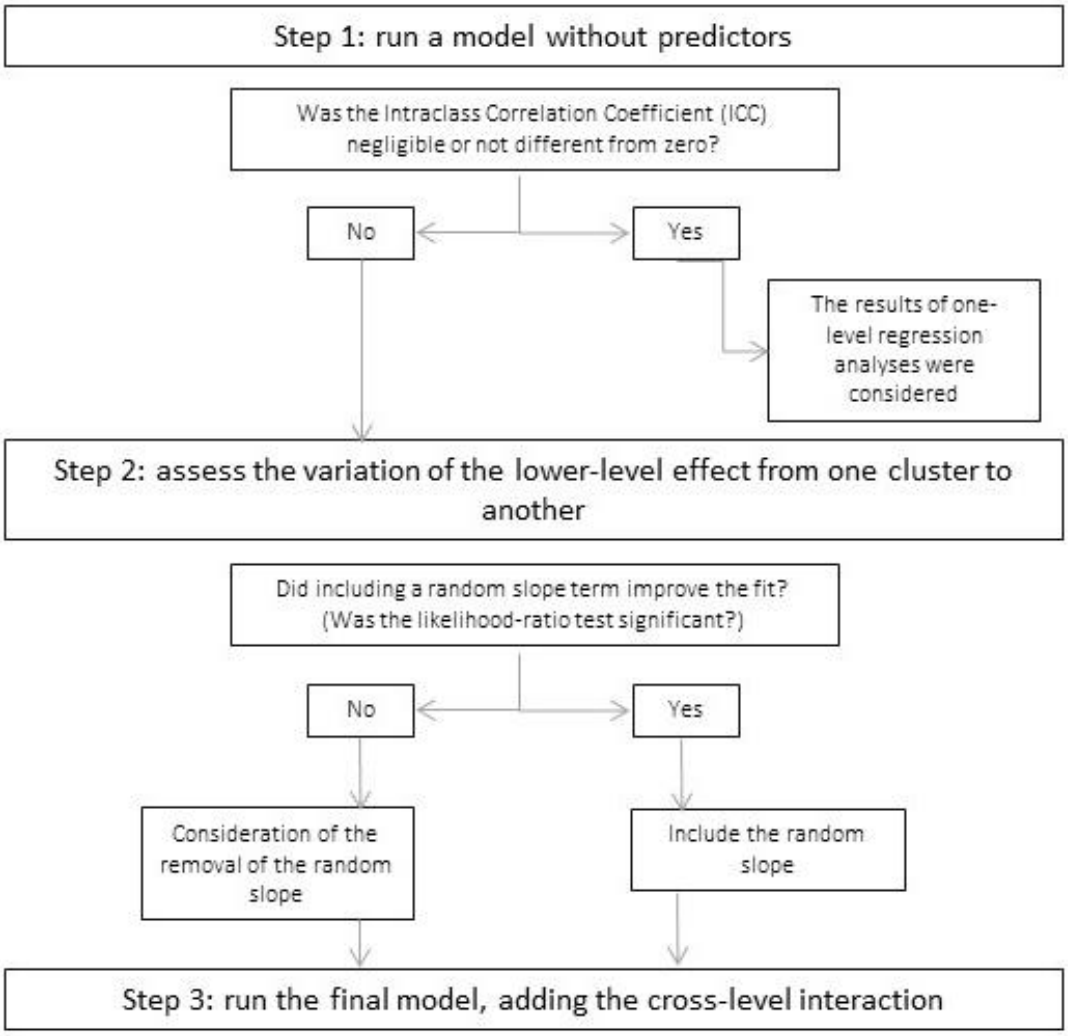
Statistical Analysis

Generalized linear logistic regression models (GLM) were used to test associations between COVID-19 outcomes (tested positive, being hospitalised due to COVID-19, being admitted in ICU and death) and geographical or individual DI. Age, sex and Charlson comorbidity index were included in the model as covariates. Multilevel logistic models were used to test associations between COVID-19 outcomes and PCA individual DI, geographical DI, and their interaction. Census sections were used as clusters for the model, each of which was assigned a geographical DI. Age, sex and Charlson comorbidity index were included in the model as covariates. To build the model, we followed the following steps also explained in Figure 1.2: Preliminary step: Data preparation (centring of variables); Step1: Construction of an empty model to assess the variation of log-odds from cluster to cluster. This model did not contain the covariates. Step2: Assessment of the variation of lower-level effects from cluster to cluster. In order to perform the assessment, first, a constrained intermediate model was run, secondly, an augmented intermediate model was run and finally both were compared by performing a likelihood- ratio test. Both models contained the covariates, geographical and PCA individual DI. The augmented intermediate included also the residual term associated with the PCA individual DI, thereby estimating the random slope. Step3: Construction of a final model adding the cross-level interaction. The methodology is described in detail in the work of Morselli et al. (171). When the variation of log-odds from

cluster to cluster was not significant, the results of one-level regression analyses were considered. The statistical analysis has been carried out separately for the first epidemic wave and the second epidemic wave.

R (version 4.2.0) was used for all statistical analysis and a p-value of 0.05 was applied for testing statistical significance.

Figure 1.2. Summary of the three steps performed to build the multilevel logistic regression.



Results

In the study period, 139 807 individuals aged more than 34 (49.1% female and 50.9% male) were tested for COVID-19: 7 876 (5.6%) during the first wave, 22 270 (15.9%) during the summer and 109 661 (78.4%) during the second wave (Figure 1.3). In our study population, the median age was 60. 24 560 (18.9%) individuals lived in a census area whose geographical DI was 1, 23 665 (18.2%) in a census area whose geographical DI was 2, 25 579 (19.6%) in a census area whose geographical DI was 3, 27 742 (21.3%) in a census area whose geographical DI was 4, 28 606 (20.5%) in a census area whose geographical DI was 5. Table 1.2 describes study population characteristics by epidemic wave.

Figure 1.3. Epidemic courve of positive COVID-19 PCR test results (7 days moving average).

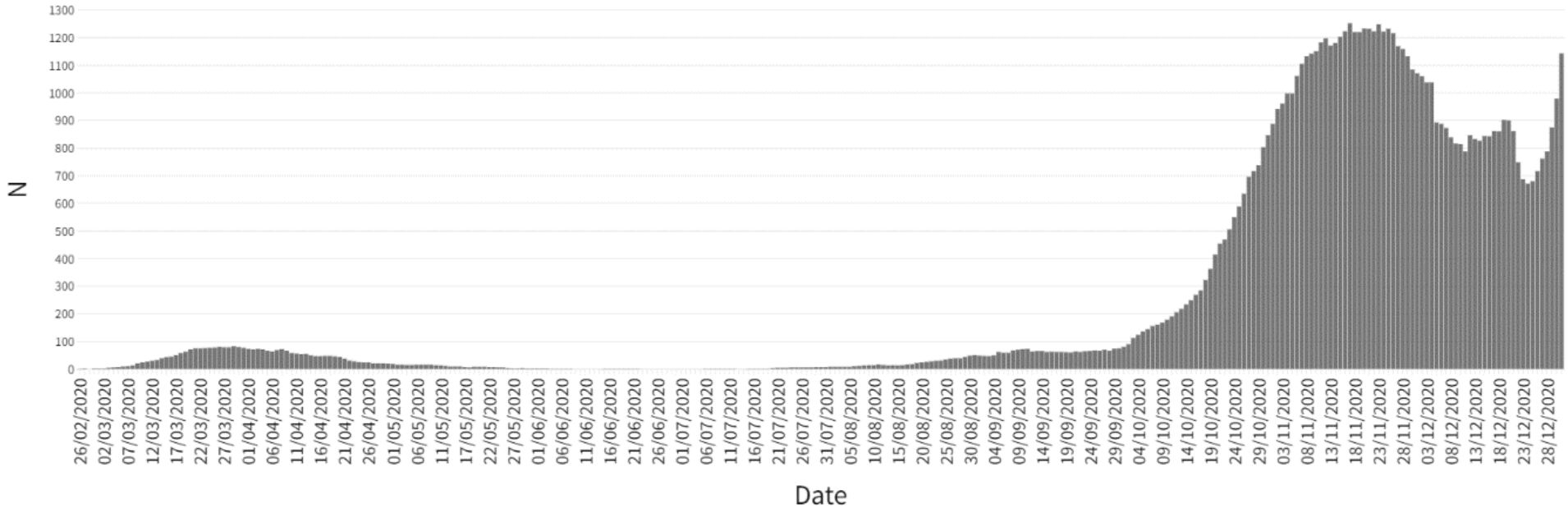


Table 1.2. Description of the study population by wave of epidemics. Proportion calculated only on complete data.

	1st Wave										2nd Wave									
	Negative		Positive		Hospitalization		ICU		Death		Negative		Positive		Hospitalization		ICU		Death	
	N	%	N	%	N	% Hosp/pos	N	% ICU/pos	N	% Death/ pos	N	%	N	%	N	% Hosp/pos	N	% ICU/pos	N	% Death/ pos
Sex																				
Male	2 279	(63.3%)	1 322	(36.7%)	750	(56.7%)	165	(12.5%)	273	(20.7%)	24 075	(48.7%)	25 356	(51.3%)	3 753	(14.8%)	718	(2.8%)	1 027	(4.1%)
Female	2 200	(63.6%)	1 259	(36.4%)	575	(45.7%)	69	(5.5%)	223	(17.7%)	25 197	(47.9%)	27 428	(52.1%)	2 542	(9.3%)	323	(1.2%)	636	(2.3%)
Age group																				
35-69	2 316	(62.2%)	1 410	(37.8%)	536	(38.0%)	97	(6.9%)	73	(5.2%)	32 982	(45.7%)	39 241	(54.3%)	2 773	(7.1%)	480	(1.2%)	307	(0.8%)
>69	2 236	(65.1%)	1 198	(34.9%)	802	(66.9%)	140	(11.7%)	431	(36.0%)	16 318	(54.6%)	13 555	(45.4%)	3 524	(26.0%)	561	(4.1%)	1 357	(10.0%)
Comorbidity index																				
0	3 658	(61.2%)	2 321	(38.8%)	1 144	(49.3%)	214	(9.2%)	395	(17.0%)	44 636	(47.2%)	49 996	(52.8%)	5 523	(11.0%)	927	(1.9%)	1 379	(2.8%)
1	666	(74.8%)	224	(25.2%)	150	(67.0%)	17	(7.6%)	81	(36.2%)	3 512	(62.0%)	2 148	(38.0%)	615	(28.6%)	98	(4.6%)	224	(10.4%)
2	190	(79.8%)	48	(20.2%)	38	(79.2%)	5	(10.4%)	26	(54.2%)	745	(68.7%)	340	(31.3%)	128	(37.6%)	13	(3.8%)	50	(14.7%)
3	29	(90.6%)	3	(9.4%)	3	(100.0%)	0	(0.0%)	2	(66.7%)	67	(82.7%)	14	(17.3%)	4	(28.6%)	1	(7.1%)	1	(7.1%)
Geographical deprivation index																				
1	893	(63.0%)	525	(37.0%)	267	(50.9%)	45	(8.6%)	107	(20.4%)	10 954	(58.5%)	7 761	(41.5%)	898	(11.6%)	140	(1.8%)	234	(3.0%)
2	834	(63.4%)	481	(36.6%)	256	(53.2%)	52	(10.8%)	93	(19.3%)	9 839	(53.4%)	8 576	(46.6%)	1 005	(11.7%)	162	(1.9%)	282	(3.3%)
3	889	(61.8%)	549	(38.2%)	269	(49.0%)	40	(7.3%)	93	(16.9%)	9 752	(48.5%)	10 357	(51.5%)	1 215	(11.7%)	185	(1.8%)	325	(3.1%)
4	919	(65.3%)	489	(34.7%)	255	(52.1%)	51	(10.4%)	97	(19.8%)	9 472	(42.6%)	12 784	(57.4%)	1 435	(11.2%)	237	(1.9%)	355	(2.8%)
5	1 013	(64.2%)	564	(35.8%)	291	(51.6%)	49	(8.7%)	114	(20.2%)	9 277	(41.1%)	13 302	(58.9%)	1 741	(13.1%)	316	(2.4%)	467	(3.5%)
PCA individual deprivation index																				
1	812	(59.8%)	546	(40.2%)	232	(42.5%)	47	(8.6%)	47	(8.6%)	13 129	(51.0%)	12 611	(49.0%)	923	(7.3%)	155	(1.2%)	113	(0.9%)
2	527	(59.8%)	355	(40.2%)	150	(42.3%)	25	(7.0%)	23	(6.5%)	7 764	(44.0%)	9 884	(56.0%)	713	(7.2%)	129	(1.3%)	86	(0.9%)
3	938	(65.7%)	490	(34.3%)	245	(50.0%)	58	(11.8%)	85	(17.3%)	10 045	(50.0%)	10 028	(50.0%)	1 345	(13.4%)	266	(2.7%)	385	(3.8%)
4	1 098	(63.8%)	622	(36.2%)	358	(57.6%)	59	(9.5%)	187	(30.1%)	9 922	(48.6%)	10 481	(51.4%)	1 604	(15.3%)	261	(2.5%)	532	(5.1%)
5	1 177	(66.4%)	595	(33.6%)	353	(59.3%)	48	(8.1%)	162	(27.2%)	8 440	(46.3%)	9 792	(53.7%)	1 709	(17.5%)	229	(2.3%)	547	(5.6%)

PCA individual deprivation index

The census variables selected to build the individual DI were available for a subpopulation of 129 779 individuals. We have retained two principal components in our PCA: the variance explained by the principal component 1 was 34.1% and the variance explained by the principal component 2 was 25.5% (Figure 1.4). The coefficients forming these components can be found Table 1.3.

Figure 1.4. Scree plot of PCA performed on census variables.

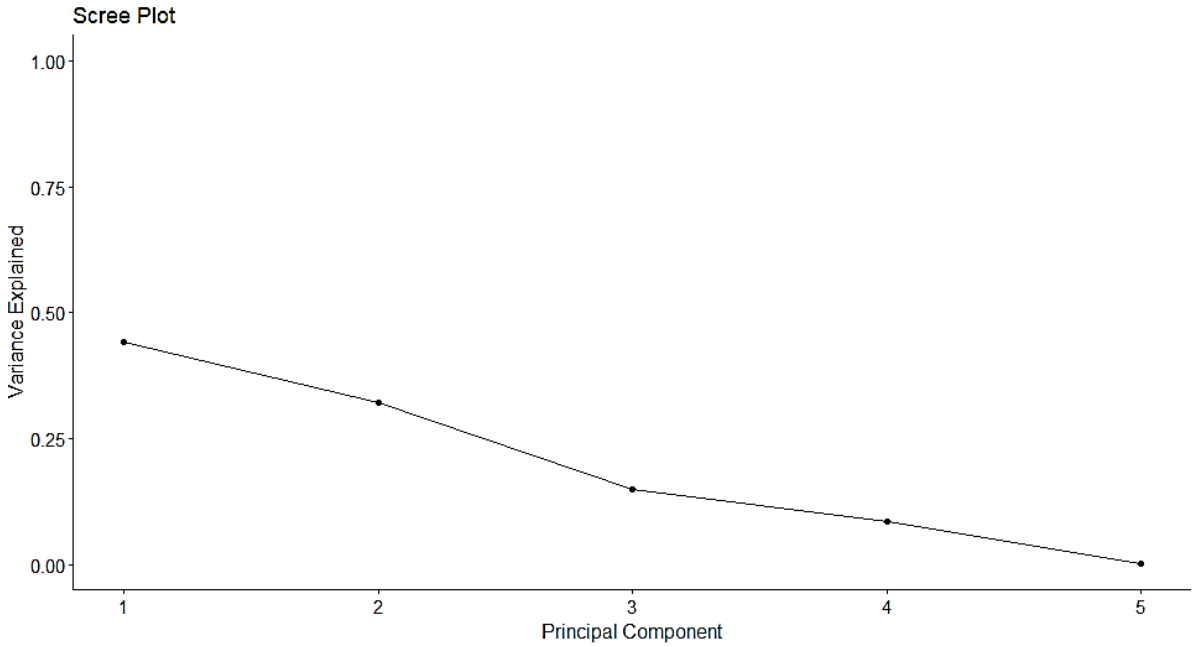


Table 1.3. Coefficients forming components retained in the PCA.

	PC1	PC2
Citizenship	0.08	0.62
Family Type	-0.16	0.79
Employment Status	0.81	0.15
Education	0.79	-0.21

Outcomes of interest by type of deprivation index

Figure 1.5 shows the counts of positive tests, COVID-19 hospitalisations, intensive care unit admissions and deaths among the DI groups per 100 000 tests or positive tests during the first or second wave respectively.

1st epidemic wave

According to the results of the logistic GLMs, during the first wave, the risk of testing positive for Sars-CoV-2 infection was not significantly different in people with a level of geographical deprivation higher than 1 when compared with the less deprived population group. The models that used PCA individual ID reported that in sub groups with higher level pf deprivation the OR of testing positive was lower than in the subgroup of the population with the lowest DI. The OR of being hospitalised, admitted to the ICU or dying when positive in the subgroups of the population with the highest DI was not significantly different from the subgroup of the population with the lowest DI. No substantial differences were found between the analyses performed using the geographical DI and those performed using the PCA individual DI. (Figure 1.6, table 1.4).

2nd epidemic wave

According to the results of the logistic GLMs, during the 2nd epidemic wave the risk of testing positive for Sars-CoV-2 infection was significantly higher in people with a level of deprivation higher than 1 when compared with the less deprived population group, with generally homogeneous results disregarding the DI used in the model. For what concern the OR of being hospitalised and dying if positive, considering the geographical DI, the subgroup with deprivation level 5 had a higher OR of being hospitalised (OR: 1.23; 95% CI: 1.12-1.35) and dying (OR: 1.34; 95% CI: 1.05-1.58) if positive than the subgroup with deprivation level 1. Calculating GLMs with the PCA individual DI, the OR of being hospitalised and dying if positive increased with increasing individual deprivation level also in population subgroups with a DI less than 5. The models that used individual ID reported that as deprivation increased, the risk of hospitalisation and death increased, which was not evident in the models that used geographic ID. The OR of being admitted to the ICU when positive in the subgroups of the population with the highest DI was not significantly different from the subgroup of the population with the lowest DI, irrespective of the type of DI used (Figure 1.6, table 1.4).

Figure 1.5. Counts per 100 000 of positive tests, hospitalisations, ICU admissions, and deaths per DI level.
Panel A: 1st wave (20 February 2020 to 31 May 2020). Panel B: 2nd wave (16 September 2020 to 31 December 2020).

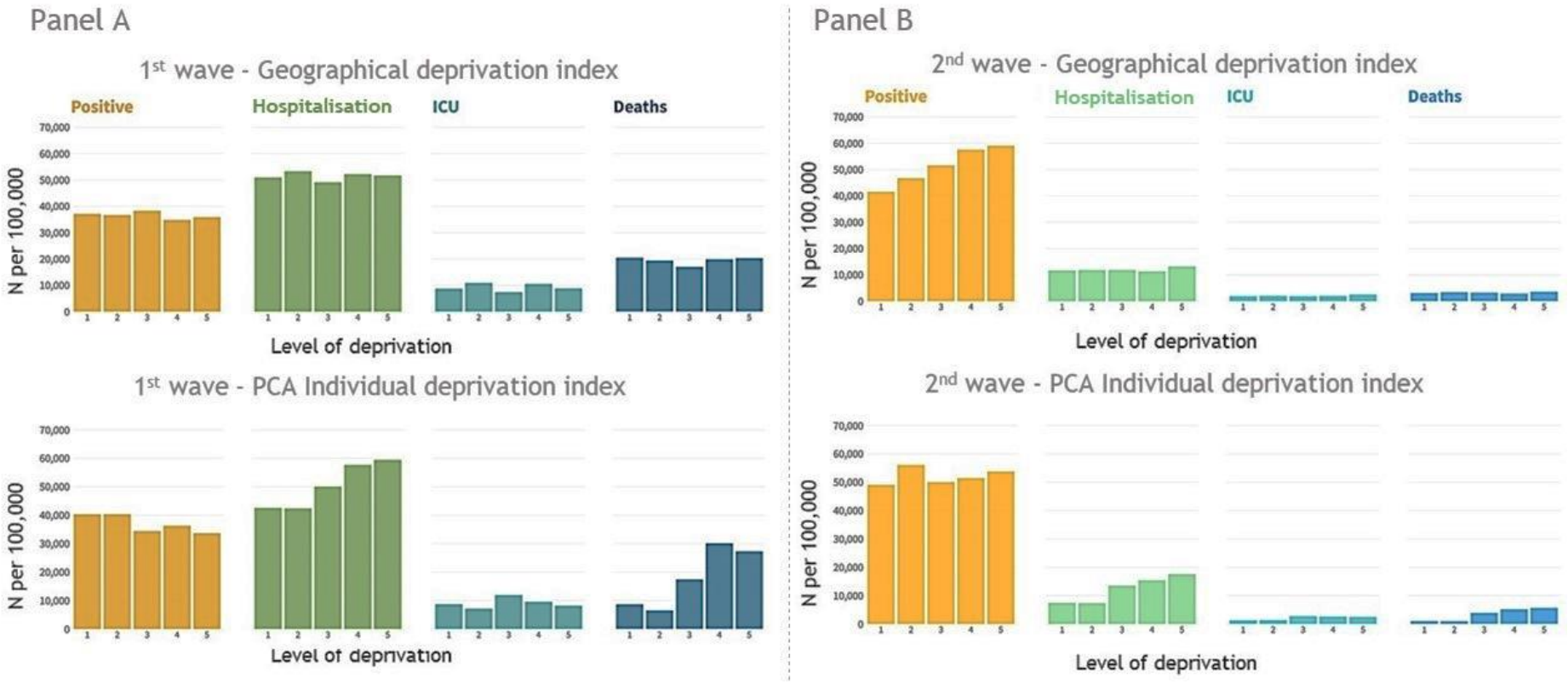


*Figure 1.6. Adjusted ORs per increase in the geographical, PCA individual DI for the counts of positive tests, hospitalisations, ICU admissions, and deaths. *IDI: individual deprivation index.*

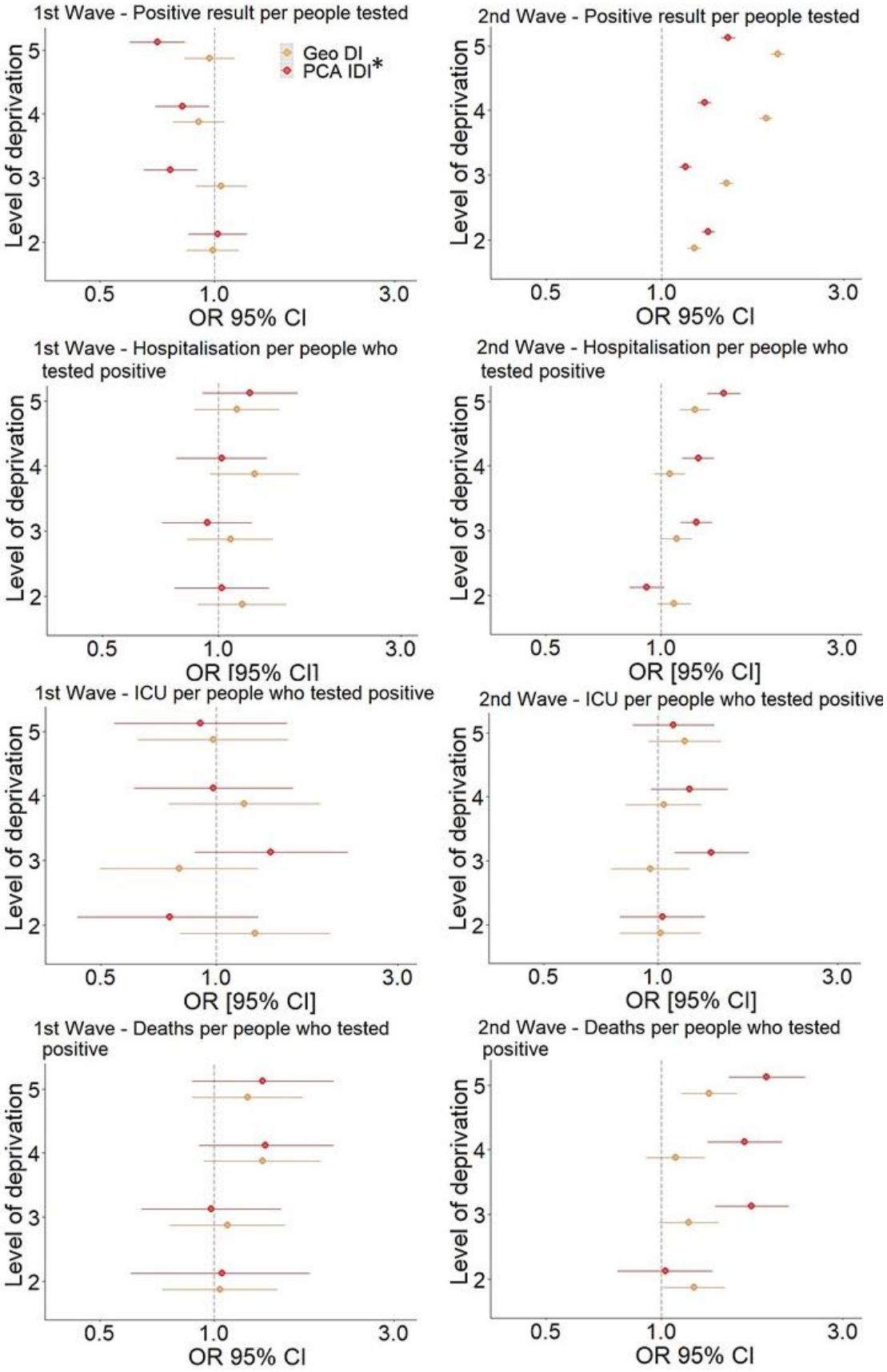


Table 1.4. Associations between geographical and individual DI and risk of Sars-CoV-2 infection and disease severity.

	1st Wave					2nd Wave				
	Positive per tested	Hospitalisations per positive tests	ICU per positive tests	Deaths per positive tests		Positive per tested	Hospitalisations per positive tests	ICU per positive tests	Deaths per positive tests
Geo DI	OR CI 95%	OR CI 95%	OR CI 95%	OR CI 95%	Geo DI	OR CI 95%	OR CI 95%	OR CI 95%	OR CI 95%
1	ref	ref	ref	ref	1	ref	ref	ref	ref
2	0.99 (0.84-1.16)	1.16 (0.89-1.51)	1.27 (0.81-1.99)	1.04 (0.73-1.48)	2	1.22 (1.17-1.27)	1.08 (0.98-1.20)	1.02 (0.79-1.30)	1.22 (1.01-1.47)
3	1.04 (0.90-1.21)	1.08 (0.83- 1.39)	0.80 (0.50-1.28)	1.09 (0.77-1.54)	3	1.48 (1.42-1.54)	1.10 (0.99-1.21)	0.96 (0.75-1.21)	1.18 (0.99-1.42)
4	0.91 (0.78-1.06)	1.24 (0.95-1.63)	1.19 (0.75.-1.87)	1.34 (0.94-1.92)	4	1.88 (1.80-1.95)	1.06 (0.96-1.16)	1.04 (0.83-1.31)	1.09 (0.91-1.30)
5	0.97 (0.84-1.13)	1.12 (0.87-1.45)	0.98 (0.62-1.55)	1.23 (0.88-1.73)	5	2.02 (1.94-2.10)	1.23 (1.12-1.35)	1.18 (0.95-1.47)	1.34 (1.05-1.58)
PCA Individual DI					PCA Individual DI				
1	ref	ref	ref	ref	1	ref	ref	ref	ref
2	1.02 (0.86-1.22)	1.02 (0.77-1.36)	0.76 (0.44-1.30)	1.05 (0.61-1.81)	2	1.33 (1.28-1.38)	0.92 (0.83-1.36)	1.03 (0.79-1.33)	1.02 (0.77-1.36)
3	0.77 (0.65-0.90)	0.94 (0.72-1.23)	1.40 (0.88-2.21)	0.98 (0.64- 1.51)	3	1.16 (1.11-1.20)	1.24 (1.13-1.38)	1.39 (1.11-1.74)	1.73 (1.38-2.16)
4	0.83 (0.70-0.97)	1.02 (0.78- 1.34)	0.98 (0.61-1.59)	1.37 (0.91-2.06)	4	1.30 (1.25-1.35)	1.26 (1.14-1.62)	1.21 (0.96-1.54)	1.65 (1.32-2.07)
5	0.71 (0.60-0.84)	1.21 (0.91-1.61)	0.91 (0.54-1.53)	1.34 (0.88-2.06)	5	1.49 (1.43-1.56)	1.46 (1.32-1.84)	1.10 (0.86-1.41)	1.89 (1.50-2.37)

Multilevel Logistic Modelling

1st epidemic wave

The proportion of the between-cluster variation (ICC) in the probability of being positive if tested during the first wave was 9.9 (Table 1.5). This indicates that 9.9% of the chances was explained by between the census section differences. The deviance of the augmented intermediated model was significantly lower than the deviance of the constrained model. Table 1.5 reports multilevel logistic regression results. The model showed that higher level PCA individual DI were significantly associated with lower probability of being positive if tested. Figure 1.7, Panel A shows the interaction between geographical and individual DI in the prospective prediction of being positive if tested. Although the association between geographical and individual DI was not significant, the coefficient (ß) was negative. The proportion of the between-cluster variation in the probability of being hospitalised, admitted to ICU and dying if positive during the first wave was respectively 5.4, 4.9 and 2.1. Therefore, the results for the one-level regression model were considered.

2nd epidemic wave

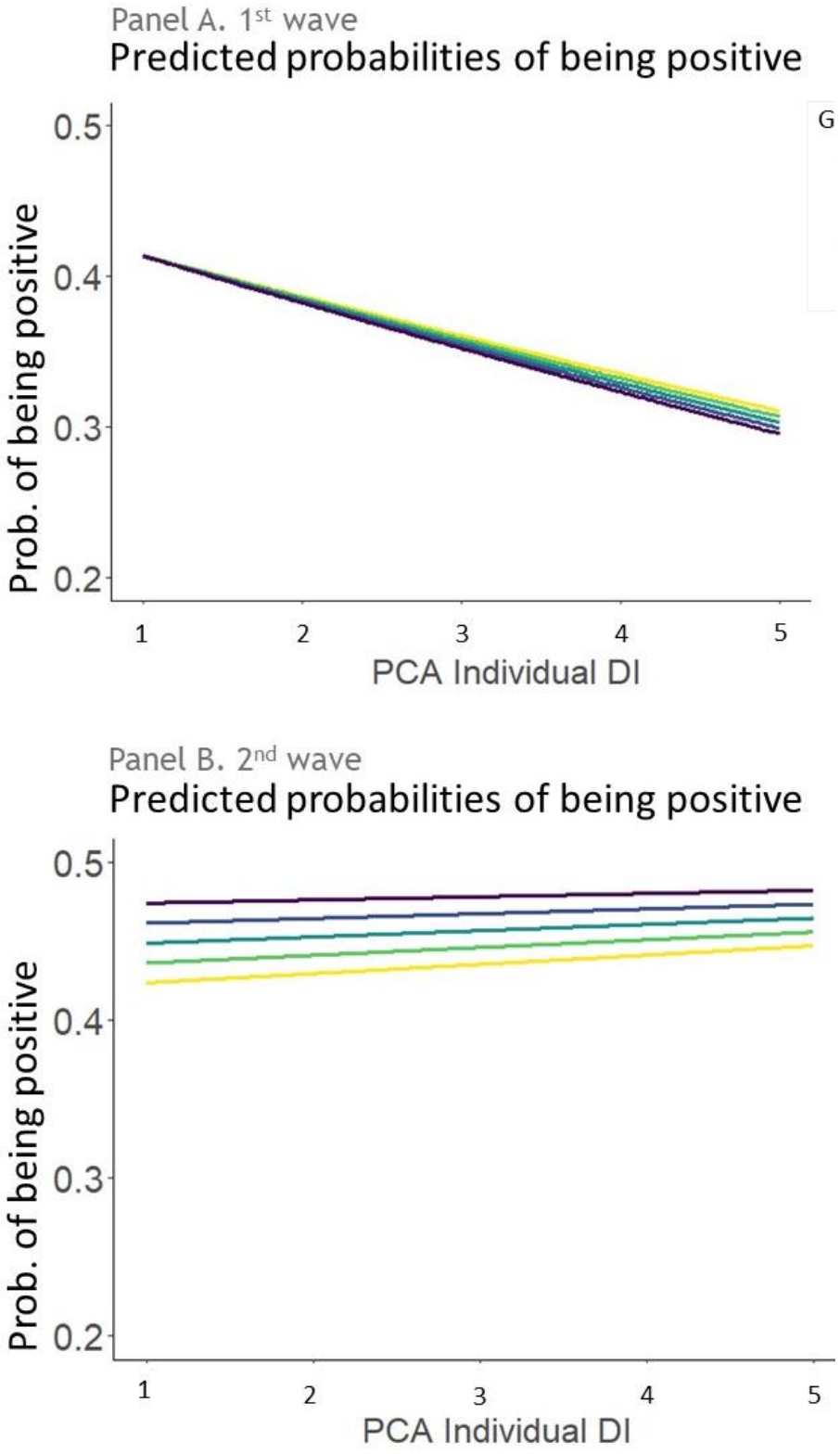
The proportion of the between-cluster variation in the probability of being positive if tested during the first wave was 15.2. This indicates that 15.2% of the chance was explained by the census section differences. The deviance of the augmented intermediated model was significantly lower than the deviance of the constrained model. The model shows that both higher level PCA individual DI or geographical DI were significantly associated with higher probability of being positive if tested (Table 1.5). Figure 1.7, Panel B shows the interaction between geographical and individual DI in the prospective prediction of being positive if tested. Although the association between geographical and individual DI was not significant, the coefficient (ß) was positive. The proportion of the between-cluster variation in the probability of being hospitalised, admitted to ICU and dying if positive during the first wave was respectively 1.3, 2.4 and 1.9. Therefore, the results for the one-level regression model were considered.

Table 1.5. Results of multilevel logistic regression or GLM models including geographical and individual DI interaction.

	1st Wave		2nd Wave	
	Outcome: being positive if tested			
ICC for empty models	**0.10**		**0.15**	
	ß	**SE**	**ß**	**SE**
PCA Individual DI	-0.12***	0.03	0.02°	0.01
Geo DI	-0.01	0.02	0.04***	0.01
Female	-0.02	0.05	-0.01	0.01
Age	0.01**	0.00	-0.01***	0.00
Charlson comorbidity index 1	-0.66***	0.09	-0.61***	0.03
Charlson comorbidity index 2	-0.96***	0.17	-0.89***	0.07
Charlson comorbidity index 3	-1.69**	0.62	-1.77***	0.30
Geo x Individual DI	0.00	0.01	0.00	0.00

*** p-value<0.001; ** p-value=0.001; * p-value=0.01; ° p-value=0.05

Figure 1.7. Interaction between geographical and individual DI in the prospective prediction of being positive if tested. Estimated values reflect statistical adjustment for sex, age, and Charlson comorbidity index.



Discussion

This study reports results from a large population-wide cohort of people tested for COVID-19 in the Apulia region, Italy, during the first and second wave of the pandemic in 2020. To our knowledge, this was the first study to investigate the role of individual DI on COVID-19 outcomes in Italy. Previous studies were limited to the use of an area-based DI or the individual component of socioeconomic deprivation as a proxy of individual deprivation (159,172–174). Although for the first wave, the geographic DI and the individual DI calculated in this study show no differences in the non-significance of the association with COVID-19 outcomes, the results were different for the second wave.

According to the findings of this study, the association between the risk of testing positive for Sars-CoV-2 and the level of socioeconomic deprivation in the Apulia region changed between the first and second waves. According to the analysis done with the PCA individual DI, there was a significant inversely proportional trend between the DI and the risk of testing positive. As deprivation increased, the risk of being positive when tested decreased. During the second wave, individuals with a higher level of socio-economic deprivation had a higher statistically significant probability of testing positive. This may be explained by the fact that during the early stages of the epidemic outbreak, with affected geographical areas still circumscribed, most of the cases in the Apulia region were due to returning residents (175). Indeed, the gradual implementation of control measures in Italy sparked substantial movements of people travelling from northern regions at the epicentre of the epidemic toward other regions, such as Apulia. Then, the swift extension of lockdown to the entire country (163) mitigated the impact of these COVID-19 seeding events and the epidemic in Apulia region was successfully contained. For these reasons, during the first wave in Apulia, the epidemic probably spread mainly among individuals who had the financial means to travel or who were economic migrants in Lombardy or northern regions, areas of intense economic activities. During the first wave, individuals with a higher level of socio-economic deprivation did not have a statistically significant higher probability of being hospitalised or dying if positive. These results were in line with those reported by Furtunato et al (176). During the second wave, individuals with a higher level of socio-economic deprivation had a higher statistically significant probability of being hospitalised or dying if positive.

Concerning the second wave, the two DI showed a clear association between the probability of testing positive and the level of deprivation. However, the geographic DI showed a stronger trend. The results of this study showed that most people with a higher individual DI live in the most deprived census areas. Since people with a higher individual DI were more often in jobs that were less amenable to remote working and so they benefited less from lockdown restrictions than those able to work from home; they had a higher likelihood of acquiring the infection (177). Moreover, they generally live in higher-density environments where family members could be infected secondarily (178). This may have meant that in more deprived areas the virus circulated more widely than in less deprived areas. As individual DI increased, so did the probability of hospitalisation and death. The same trend was not observed for geographical DI, which showed a significantly increased probability of being hospitalised or dying if positive only for the highest level of deprivation. In accordance with our results, Mateo-Urdiales and colleagues, using the same geographical DI used in this

study, but at the municipality level, found a higher incidence of cases in the most deprived municipalities compared with the least deprived ones and no differences in case-hospitalisation and case-fatality according to deprivation were observed in any period under study. The same result has also been reported by other studies using geographical measures of deprivation conducted in Spain (179,180). While many factors could explain this finding, an alternative could be that hospitalisation and death cases were similar across areas with different levels of deprivation in a well-developed universal healthcare system, such as Italy and Spain.

The use of individual DI enabled to understand that actually, the most disadvantaged people had a higher risk of hospitalisation and death, regardless of the area in which they lived. To avoid exacerbating existing social inequalities and marginalisation, it is essential to be able to monitor them. According to our results, using geographical DI as a proxy for individual DI may lead to inaccurate assessments. However, the geographic DI can have a relevance in providing insight into the distribution of infection within different neighbourhoods, accounting for their heterogeneity. This may have important implications for public health action planning.

Understanding the relationship between deprivation and COVID-19 outcomes is multifaceted and complex. This is why the secondary objective of this manuscript was to test the hypotheses about how individual and geographical DI interact to predict COVID-19 outcomes. According to the results of the multilevel logistic and GLM models, there was no association between COVID-19 outcomes and the interaction between PCA individual DI and geographical DI. Although this may seem at odds with the robust evidence in the literature demonstrating an interaction between socioeconomic status in one's neighbourhood, individual deprivation and health, this evidence is mainly based on health outcomes of non-communicable chronic diseases (181–184).

The COVID-19 pandemic has been described as a syndemic (185). Originating in anthropology, a syndemic describes a set of closely intertwined and mutual enhancing health problems that significantly affect the overall health status of a population within the context of a perpetuating configuration of noxious social conditions (151). Deprivation— which is an area measure of poverty, low income, and a reflection of the wider social determinants of health (such as housing, working conditions, unemployment, health-care access, etc.)— results in multiple, interacting, and additive adverse risk factors for COVID-19 outcomes. These can be summarised by way of four inter-related pathways: unequal exposure, unequal transmission, unequal vulnerability, and unequal susceptibility (186). Living in a more deprived neighbourhood may increase the likelihood exposure and transmission. Although it has been proven that individuals living in more deprived neighbourhoods have worse profiles on many components of subjective health, more risk factors and higher morbidity and mortality rates than their counterparts living in less deprived neighbourhoods, the level of neighbourhood deprivation does not influence to a high extent the health of those with low individual DI compared to those with a higher individual DI (184). This could be the reason why not all individuals living in the most deprived neighbourhoods have a higher vulnerability and susceptibility to COVID-19 and would explain why the analyses in this study give different results when using geographical DI than when using individual DI.

This study had some limitations. Firstly, policies for the execution of the diagnostic test changed during the period under study. During the first wave, the diagnostic capacity was limited, and the number of positives could be under-reported, whereas for the second wave data could represent laboratory-confirmed COVID-19 cases who sought care. Secondly, the death status only reflects deaths occurring in individuals diagnosed with COVID-19, but this number may be underestimated due to non-diagnosis. Third, the DI is a composite measure of deprivation, and it is difficult to know which of its constituent factors are driving associations.

Conclusion

Historically, pandemics have been experienced unequally with higher rates of infection and mortality among the most disadvantaged communities (187). Evidence from a variety of countries suggests that these inequalities are being mirrored in the COVID-19 pandemic (177,188) and this study also adds to this evidence. The causal forces at work at the interface of disease epidemics and social inequality are complex: they are operant at the level of individuals, neighbourhoods, and local communities. The results of this study remind us to be cautious about using geographical DI as a proxy for the level of individual social disadvantage because of the inevitable potential ecological bias that can result from attributing a collective measure to an individual and may lead to inaccurate assessments.

The geographical DI is often used due to a lack of individual data. However, on the determinants of health and health inequalities, monitoring has to have a central focus. Health inequalities monitoring provides evidence on who is being left behind and informs equity-oriented policies, programmes and practices (1). The emergence of novel data sources and monitoring approaches for public health surveillance is triggered by technological advances in data retrieval and data analysis. Unfortunately, the information richness resulting from the data science revolution is not exploited to better understand health inequities and inform the development and implementation of services and policies that tackle inequities in health (16,38).

Reducing these inequalities - and those that may result from future pandemics - requires long-term action to improve equity in health and wealth. Future research and data collection should focus on improving surveillance systems, for example by integrating individual measures of inequalities into national health information systems. Understanding the social nature of emerging infectious disease pandemics will ultimately help reduce the burden of disease.

Chapter 2

Executive summary

Long-term-care facility residents typically suffer from multiple long-term conditions, cognitive impairment, and medical and social vulnerabilities. Due to the characteristics of this population and structural or organisational features of the facilities – such as staff working in multiple facilities and high rates of staff turnover – the risk of contracting COVID-19 or developing subsequent severe outcomes were high among people living in LTCFs.

Despite the general knowledge that LTCFs were affected by a high COVID-19 burden, the actual number of COVID-19 cases among residents has been difficult to assess due to the lack of a specific surveillance system for LTCFs. Furthermore, in the COVID-19 Integrated Surveillance System established by the Istituto Superiore di Sanità, the place of infection of confirmed COVID-19 cases was not always reported.

The FAR (Residential and semi-residential care) data flow collected by the Ministry of Health's HIS reports the anonymised identifiers of LTCF residents and their access and discharge data. If FAR were interoperable with the COVID-19 Integrated Surveillance System it would have been possible to estimate the real number of cases in Italian LTCFs on a national scale. Unfortunately, the flows collected by NHS are not interoperable with those of the Ministry of Health. Additionaly, although the FAR data flow is collected by all Italian regions, not many use it for periodic analyses and are aware of the type and quality of the data it contains.

To get an estimate of the direct impact of COVID-19 on LTCFs, the Istituto Superiore di Sanità dedicated a survey to the issue. A dramatic picture emerged, with LTCFs reporting high infection rates.

People living in LTCFs are characterised by poor health and experienced reduced health access during the pandemic. This may have resulted in a further deterioration of their health status. Although many studies have examined the impact of the pandemic on NCDs in the general population, investigations on LTCF resident population are scarce.

This study aimed to assess the indirect impact of the COVID-19 pandemic on hospitalisation and mortality rates among LTCF population in two Italian Regions, Tuscany and Apulia, during 2020 in comparison with the pre-pandemic period.

The existing administrative flow (FAR) interoperable with the hospital discharge form flow was used to achieve this goal.

We invited six Italian regions to participate in the study, but only two agreed. The regions that declined either lacked confidence in the quality of the FAR data flow and preferred not to share it, or were unwilling to allocate staff to this research, which was viewed as low priority and too time-consuming due to the complexity of analyzing a relatively unknown data flow (FAR).

This research serves as a proof of concept, demonstrating that with the necessary willingness and analytical capability to extract evidence from administrative data, it is possible to monitor health outcomes even in neglected and extremely fragile populations.

Hospital admission and mortality rates for non-COVID-19 diseases among residents of the Long-term care facilities before and during the pandemic: a cohort study in two Italian regions

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Link to the article.

Long-term-care facility residents are a vulnerable population who experienced reduced healthcare access during the pandemic. This study aimed to assess the indirect impact of the COVID-19 pandemic, in terms of hospitalisation and mortality rates, among this population in two Italian Regions, Tuscany and Apulia, during 2020 in comparison with the pre-pandemic period.

We conducted a retrospective cohort study on people residing in long-term-care facilities from 1 January 2018 to December 2020 (Baseline period: 1 January 2018-8 March 2020; and pandemic period: 9 March-31 December 2020). Hospitalisation rates were stratified by sex and major disease groups. Standardised weekly rates were estimated with a Poisson regression model. Only for Tuscany, mortality risk at 30-days after hospitalisation was calculated with the Kaplan-Meier estimator. Mortality risk ratios were calculated using Cox proportional regression models

19,250 individuals spent at least 7 days in a long-term-care facility during the study period. The overall mean non-COVID-19 hospital admission rate per 100 000 residents/week was 144.1 and 116.2 during the baseline and pandemic periods, with a decrease to 99.7 and 77.3 during the first (March-May) and second lockdown (November-December). Hospitalisation rates decreased for all major disease groups. 30-day mortality risk ratios for non-COVID-19 conditions increased during the pandemic period (1.2, 1.1 to 1.4) compared with baseline.

The pandemic resulted in worse non-COVID-19 related health outcomes for long-term-care facilities' residents. There is a need to prioritise these facilities in national pandemic preparedness plans and to ensure their full integration into national surveillance systems.

Introduction

People living within long-term care facilities (LTCFs) typically suffer from multiple long-term conditions, cognitive impairment, and medical and social vulnerabilities (189). Due to characteristics of this population and structural or organisational features of the facilities – such as staff working in multiple facilities and high rates of staff turnover (190) – risks of contracting COVID-19 or developing subsequent severe outcomes, especially before the introduction of COVID-19 vaccination, were high among LTCF resident population (191,192). In a report published in May 2020 by the European Centre for Disease Prevention and Control, it was estimated that deaths among LTCF residents accounted for 37-66% of all COVID-19-related deaths in EU/European economic area (EEA) countries, depending on the country. No data was provided on the Italian LTCF situation (193).

In Italy, the first confirmed autochthonous cases of COVID-19 were detected in Lombardy, a region in the North of Italy, in late February 2020, with subsequent spread to other regions at different times and rates (175,194). During the first phase of the pandemic, the real number of COVID-19 cases among LTCF residents was difficult to assess due to the lack of a surveillance system specifically for LTCFs and context and time-specific features (e.g. low or absent testing capacity and undertrained staff (189). To fulfil these gaps, in March 2020, the Italian National Health Institute dedicated a survey to the issue. A dramatic picture emerged from it, with LTCFs reporting high infection rates (195). Besides, results from studies conducted at the national and local levels in 2020 suggest that the impact of the pandemic in terms of mortality among LTCF residents was large (196,197). In particular, a study evaluating mortality rates of older adults in LTCF across different Italian regions during the first four months of 2020, highlighted that the risk of death among LTCF residents increased about four times during the study period when compared to the same period in the previous years. Moreover, the mortality rates of LTCF residents were significantly higher when compared to age-specific mortality rates of the general population (197). Another national study highlighted that the COVID-19 incidence rate does not fully explain the differences of mortality impact among different regions (198).

Although less broadly investigated, it is expected that people living within LTCFs were also more likely to develop worse health outcomes for non-COVID conditions during the first phase of the pandemic. The non-medical measures enforced by Governments during the pandemic, including dramatic restrictions on individual liberties and prioritisation of healthcare services to reduce risks of system collapse (199,200), influenced access to healthcare services and hospital admissions for the entire population. In particular, in Italy, in March 2020, the Government asked regions to postpone outpatient and hospital scheduled activities that were not considered of high priority during the emergency, with a progressive re-activation from June 2020 (201).

As highlighted by a systematic review by Moynihan et al on 20 countries worldwide, including Italy, such restrictive measures along with fear of becoming infected or inability to access

care, resulted in an overall decrease of one-third of healthcare utilisation by the general population (202). No information was provided on LTCF resident population.

In the literature, the effects of the pandemic on NCDs have been extensively studied. In the UK, according to a retrospective serial cross-sectional study, total admissions and emergency department attendances for selected cardiovascular diseases dropped between 31% and 88% during the first lockdown in 2020 in comparison with 2019 (203,204) and excess in acute cardiovascular mortality (+8%) was observed in England and Wales during the first semester of 2020 compared with the expected historical average in the same period of the year (205–207). Similar results have been observed in the US, with a national increase in deaths by ischemic heart diseases and hypertensive diseases in the first semester of 2020 compared with 2019 (208). Further studies conducted worldwide, including in Italy (209,210), investigating the indirect impact of the pandemic on a vast range of NCDs – especially cardiovascular diseases and cancer – showed similar results, with a decrease in hospital admissions for NCDs and an increase in disease burden after the onset of the pandemic compared to the pre-pandemic period (199,211–214).

Although many studies have examined the impact of the pandemic on NCDs among the general population, investigations on LTCF resident population are scarce. A study conducted among Canadian LTCF residents during the first six months of the pandemic, observed that hospital admissions for non-COVID-19 diseases dropped by 27% during the study period in comparison with the same period in 2019, with the largest decrease in hospital transfers for chronic conditions requiring a doctor's order to seek hospital care, such as heart failure and chronic respiratory conditions, while deaths for all causes increase of 19% in comparison with five-year average period (215).
Studies on the effects of the pandemic on the utilisation of healthcare services for non-COVID-19 diseases among LTCF residents in Italy are missing, and on mortality for all causes are limited.

This study is a retrospective cohort study aimed to assess the indirect impact of the COVID-19 pandemic on the health outcomes of LTCFs residents in Italy. Hospital admission and mortality rates among LTCF residents in two Italian regions, Tuscany and Apulia, were monitored during the first year of the pandemic and in the pre-pandemic period to identify significant changes.

Methods

Setting and study population

The Italian healthcare system is a regionally based NHS. The system is organized into three levels: national, regional, and local. The national level is responsible for establishing the general objectives and fundamental principles of the NHS. The nineteen regions and two autonomous provinces are then responsible for organising and delivering health care (162). In this scenario, the R&AP are in charge of organising the long term-care facilities at the local level based on national guidelines.

Long-term care facilities have been established in Italy in the mid-nineties, after the release in 1989 of a governmental policy act for the creation of residential health care facilities for the elderly (216). With the release of two more decrees in 2001 (217), the Government endorsed the role of social protection of the LTCFs, promoting integration between social and health care services within the facilities, and included assistance in LTCFs among those essential services that the NHS guarantees to non-self-sufficient people who do not have the possibility to care for themselves at home (218). LTCFs can be administered by the public (NHS or the municipality) or by the private sector (alone or in affiliation with the NHS). The percentage of LTCFS administered by the public or private sector can vary widely among Regions.

In 2020, in Tuscany, there were 312 LTCFs with 13.997 beds. Of these facilities, 115 were public and 197 private (219); in Apulia, there were 140 LTCFs with 6,937 beds of which 97% were administered by the private sector (220). Most private facilities are contracted by the public system that partially subsidise the cost of resident stay. In Italy, the state provides all residents with free and unrestricted access to healthcare (221). Data are recorded prospectively in regional registries, allowing longitudinal surveillance of the entire population. This cohort study included individuals residing in the LTCFs from 1 January 2018 to 31 December 2020. The individuals included in the study were residing for at least seven consecutive days in the LTCFs of Tuscany and Apulia regions during the study period.

Pandemic stages and preventive measures

In Italy, after the detection of the first locally acquired COVID-19 case in Lombardy on February 20, 2020, the number of cases increased greatly in the following weeks, although unevenly among regions, forcing the government to adopt unprecedented restrictive measures (104,222). In particular, during the first year of the pandemic, the following phases can be defined: 1. first comprehensive national lockdown from 9 March to 3 May (closure of schools and most workplaces, and the implementation of quarantines, border closings, and restriction on public gatherings) (222); 2. gradual reopening phase from 4 May to 14 June (restrictions were gradually rolled back) (164); 3. few restrictions from 15 June to 7 October (COVID-19 incidence remained low) (223); 4. new restrictions from 8 October to 5 November (166); 5. L3.1ockdowns on a regional basis from 6 November until the end of 2020 (closure of regional borders) (167).

The Italian government issued specific provisions aimed at minimising the risk of introducing and transmitting diseases within LTCFs. In particular, with a decree released in April 2020, along with measures regulating the entry of new residents and visits from family members, it was decided to avoid the access of LTCFs residents to hospitals as far as possible, even if for specialist visits or diagnostic or therapeutic procedures (224). In August 2020, the use of telemedicine in delivering care to LTCF residents was promoted and general practitioners' access to in-person visits was recommended for essential cases only (225). These national recommendations were endorsed by Tuscany and Apulia regions that adapted them to the local context with the implementation of more stringent restrictions if needed.

Data sources and study period

We conducted a retrospective cohort study by analysing and merging two electronic health records from the Tuscany and Apulia healthcare information systems: the regional registries of people admitted in the public and the contracted private LTCFs and the regional hospital discharge dataset (≥ 95% of all LTCF beds available). The study period ran from 1 January 2018 to 31 December 2020. We defined the period between the 1st January 2018 and the 8th March 2020 as pre-COVID-19 baseline period, while the period between the 9th of March and the 31st December 2020 as COVID-19 pandemic period.

The regional registries of people admitted in the LTCFs track age, sex, LTCF admission and discharge date. Only for Tuscany, this data source provided data also on the vital status of LTCFs residents. The regional hospital discharge form dataset includes hospital admission and discharge date, sex, and principal diagnosis of discharge coded according to the WHO's international classification of diseases version 9 (ICD-9-CM) (226).

Through a numeric identification code, we linked the LTCFs residents' registries with the hospital discharge dataset. All the health data used in the study were anonymous administrative health data routinely collected through the regional health information systems.

The study protocol was approved on October 10, 2021, by the Joint Ethical Committee for research of the Scuola Normale Superiore (Pisa, Italy) and the Sant'anna School for Advanced Studies (Pisa, Italy). Number of approval: 39/2021.

Outcomes

From 1 January 2018 to 31 December 2020, all hospital admissions of people residing in LTCFs were identified by principal diagnosis codes in the hospital discharge form. These codes were subsequently grouped according to the multi-level diagnosis clinical classification system (CCS) (227) which is based on the ICD-9-CM classification. In 2020, in the ICD-9-CM diagnosis group the category "COVID-19" has been added.

Only for people residing in LTCFs in Tuscany, we computed the overall weekly average mortality rate per 1 000 LTCF residents before and after the pandemic, and the 30-day mortality risks for hospital admissions investigated overall and according to major disease groups by pandemic period.

Statistical Analysis

We examined overall hospital admission rates stratified by sex and major disease groups. We used a Poisson regression model to estimate standardised weekly hospital admission rates.

We computed hospital admission rate ratios and 95% CI by using the pre-COVID-19 baseline period (1st January 2018 – 8th March 2020) as reference. We then repeated the analyses for the two regional study population cohorts.

For the Tuscany region, we assessed mortality risk at 30 days after hospital admission by using the Kaplan-Meier estimator, with censoring at LTCF discharge or end of follow-up whichever occurred first. Mortality risk ratios and 95% CIs were calculated using Cox proportional regression models, and the pre-COVID-19 baseline period (1st January 2018 – 8th March 2020) as competing risk.

Stata MP version 15 was used for all statistical analysis and a p-value of 0.05 was applied for testing statistical significance.

Results

A total of 19 250 individuals that spent at least 7 days in a LTCF from 1 January 2018 to 31 December 2020 were included in the study cohort. Of these individuals 11,806 (median age 87, 28% male) were LTCFs residents in Tuscany and 7 444 (median age 84, 29% male) in Apulia. Table 2.1 shows the weekly average population in the LTCFs in the pre-pandemic period and in the different pandemic phases overall and by region. The number of (non-COVID-19) hospital admission among LTCFs residents in 2018 were 4 883 (3 570 in Tuscany; 1 313 in Apulia); in 2019 were 4 914 (3 667 in Tuscany; 1 247 in Apulia) and 2020 were 3 456 (2,583 in Tuscany; 873 in Apulia). During the study period, the median age of individuals hospitalised was 85 in Tuscany and 83 in Apulia.

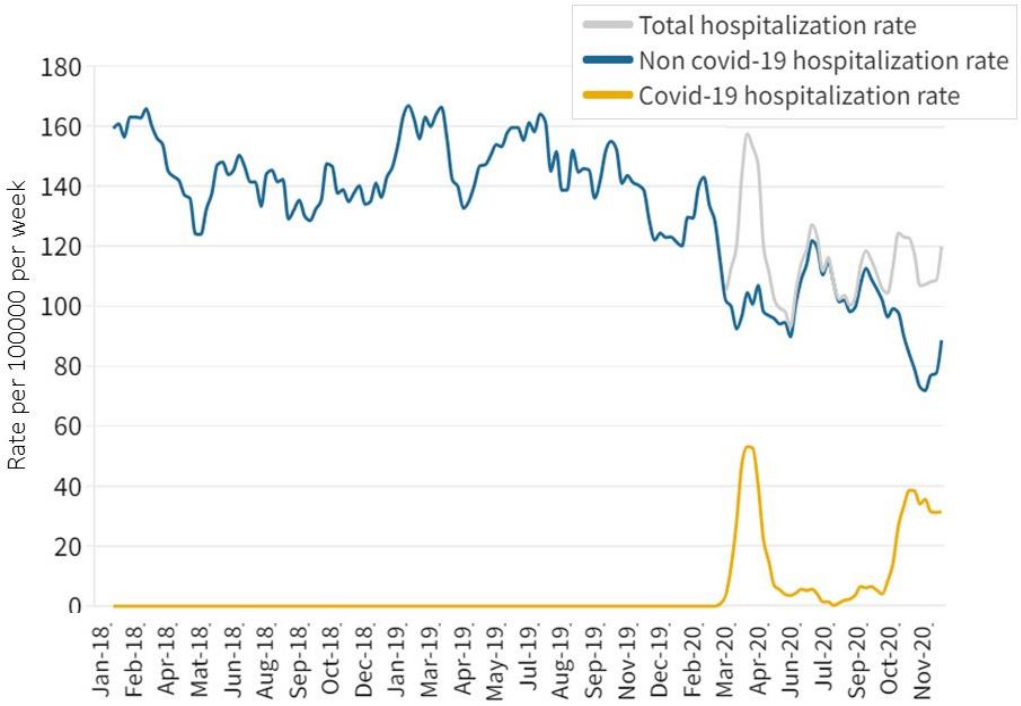
Hospital admission rates

The overall mean non-COVID-19 hospital admission rate was 144.1 (198.4 males; 123.2 females) per 100 000 LTCF residents/week during the baseline period and 116.2 (138.9 males; 82.5 females) per 100 000 LTCF residents/week during the pandemic period (Figure 2.1). The overall mean non-COVID-19 hospital admission rate was 155.8 in Tuscany and 114.5 in Apulia during the baseline period and 123.5 in Tuscany and 56.8 in Apulia during the pandemic period (Table 2.2 and Table 2.3). The mean hospital admission rate for non-COVID-19 conditions decreased to 99.7 (rate ratio 0.7; 95% CI: 0.6 to 0.8) during the first national lockdown, 92.1 (0.6; 95% CI: 0.6 to 0.7) during the gradual reopening phase, 108.9 (0.8; 95% CI: 0.7 to 0.8) during the period with few restrictions, 90.1 (0.6, 0.5 to 0.7) during the period with new restrictions, and 77.3 (0.5; 95% CI: 0.5 to 0.6) during regional lockdown phase. The mean hospital admission rate for non-COVID-19 conditions in men decreased to 149.6 (0.8; 95% CI: 0.7 to 0.9) during the first national lockdown, 121.7 (0.6; 95% CI: 0.5 to 0.7) during the gradual reopening phase, 153.3 (0.8; 95% CI: 0.7 to 0.9) during the period with few restrictions, 133.2 (0.7; 95% CI: 0.5 to 0.8) during the period with new restrictions, and 109.5 (0.6; 95% CI: 0.5 to 0.7) during regional lockdown phase (Figure 2.2.A). In female LTCF residents, the mean hospital admission rate for non-COVID-19 conditions decreased to 80.7 (0.7; 95% CI: 0.6 to 0.7) during the first national lockdown, 85.3 (0.7, 0.6 to 0.8) during the gradual reopening phase, 91.6 (0.7; 95% CI: 0.7 to 0.8) during the period with few restrictions, 73.3 (0.6; 95% CI: 0.5 to 0.7) during the period with new restrictions, and 64.2 (0.5; 95% CI: 0.4 to 0.6) during regional lockdown phase (Figure 2.2.B) (Table 2.2). Similar results were obtained when the analysis was repeated by region (Table 2.2 and Table 2.3).

Table 2.1. The weekly average population in LTCFs during the pre-pandemic period and in the different pandemic phases by age and gender, Apulia and Tuscany, 2018-2020

	Baseline Before 9 Mar 2020			First national lockdown 9 Mar-3 May 2020			Gradual reopening phase 4 May-14 Jun 2020			Few restrictions 15 Jun-7 Oct 2020			New restrictions 8 Oct-5 Nov 2020			Lockdowns on a regional basis 6 Nov-31 Dec 2020		
Tuscany																		
	Tot	*F*	*M*	*Tot*	*F*	*M*	*Tot*	*F*	*M*	*Tot*	*F*	*M*	*Tot*	*F*	*M*	*Tot*	*F*	*M*
65-74	817	378	438	767	355	412	737	344	394	723	331	392	696	318	378	661	301	360
75-84	1 837	1 178	659	1 654	1 075	579	1 568	1 027	542	1 523	990	532	1 460	948	512	1 372	897	475
85-94	2 935	2 364	571	2 712	2 156	555	2 566	2 064	503	2 444	1 979	465	2 322	1 881	441	2 133	1 748	385
>94	785	713	72	809	740	68	765	703	61	713	654	58	658	599	59	581	532	49
Tot	6 374	4 634	1 740	5 941	4 326	1 615	5 636	4 137	1 499	5 402	3 954	1 448	5 135	3 746	1 390	4 747	3 478	1 270
Apulia																		
	Tot	*F*	*M*	*Tot*	*F*	*M*	*Tot*	*F*	*M*	*Tot*	*F*	*M*	*Tot*	*F*	*M*	*Tot*	*F*	*M*
65-74	435	201	234	430	199	231	434	202	232	443	202	241	450	206	244	452	206	246
75-84	835	535	300	780	507	273	790	517	273	812	528	284	825	536	289	828	541	287
85-94	1 005	809	196	922	733	190	923	742	181	943	764	179	956	775	181	963	789	174
>94	121	110	11	122	112	10	119	109	10	117	108	9	119	108	11	116	106	10
Tot	2 395	1 656	739	2 255	1 551	704	2 266	1 571	695	2 315	1 602	713	2 350	1 624	726	2 359	1 642	717

Figure 2.1. Overall non-COVID-19 (blue line) and COVID-19 (yellow line) hospital admission rates among LTCFs residents in Apulia and Tuscany, 2018-2020.



Hospital admission rates for major disease groups

For all other major diagnosis groups, the hospital admission rate decreased markedly during the pandemic period compared with the baseline period. The decreased rate remained statistically significant in all the pandemic phases only for hospital admission with a cardiovascular disease, endocrine, nutrition, and metabolism diseases and respiratory diseases diagnosis (Table 2.4, Figure 2.3).

Table 2.2. Hospital admission rates (per 100 000/week) among LTCFs residents in Tuscany during COVID-19 pandemic compared with pre-pandemic baseline period, 2018-2020.

	Baseline (reference)	COVID-19 pandemic period			First national lockdown			Gradual reopening phase			Few restrictions			New restrictions			Lockdowns on regional basis		
	Rate	Rate	RR	(95% CI)	Rate	RR	(95% CI)	Rate	RR	(95% CI)	Rate	RR	(95% CI)	Rate	RR	(95% CI)	Rate	RR	(95% CI)
Any cause (including COVID-19)	155.8	146.9	0.9	0.9 1.0	155.8	1.0	0.9 1.1	111.9	0.7	0.6 0.8	141.0	0.9	0.8 1.0	169.4	1.1	1.0 1.2	168.3	1.1	1.0 1.2
Any cause (excluding COVID-19)	155.8	123.5	0.8	0.8 0.8	114.9	0.7	0.7 0.8	107.2	0.7	0.6 0.8	137.9	0.9	0.8 0.9	117.6	0.8	0.6 0.9	115.9	0.7	0.7 0.8
Male	214.7	178.2	0.8	0.8 0.9	182.9	0.9	0.7 1.0	147.0	0.7	0.6 0.8	194.1	0.9	0.8 1.0	178.4	0.8	0.7 1.1	160.5	0.7	0.6 0.9
Female	133.8	103.6	0.8	0.7 0.8	89.7	0.7	0.6 0.8	92.9	0.7	0.6 0.8	117.4	0.9	0.8 1.0	95.3	0.7	0.6 0.9	99.7	0.7	0.6 0.9
ICD-10																			
Cardiovascular disease	25.2	18.1	0.7	0.6 0.8	18.6	0.7	0.6 0.9	18.2	0.7	0.5 1.0	20.3	0.8	0.7 1.0	16.7	0.7	0.4 1.0	13.0	0.5	0.4 0.7
Haematological disorders	1.9	1.4	0.8	0.5 1.2	0.9	0.5	0.2 1.5	0.8	0.5	0.1 1.9	2.5	1.3	0.8 2.3	1.4	0.8	0.2 3.1	0.0	0.0	0.0 .
Injury or poisoning	17.6	19.2	1.1	1.0 1.2	16.4	0.9	0.7 1.2	15.7	0.9	0.6 1.2	22.2	1.3	1.1 1.5	14.7	0.8	0.5 1.3	20.7	1.2	0.9 1.6
Endocrine, nutrition, and metabolism diseases	8.3	4.6	0.6	0.4 0.7	3.3	0.4	0.2 0.7	4.7	0.6	0.3 1.0	6.3	0.8	0.6 1.1	2.8	0.3	0.1 0.9	2.6	0.3	0.1 0.7
Diseases of the digestive system	14.3	9.0	0.6	0.5 0.8	7.9	0.6	0.4 0.8	9.3	0.7	0.4 1.0	10.7	0.7	0.6 1.0	7.6	0.5	0.3 1.0	6.5	0.5	0.3 0.8
Diseases of the genitourinary system	11.4	10.9	1.0	0.8 1.1	10.6	0.9	0.7 1.3	11.0	1.0	0.7 1.4	12.2	1.1	0.8 1.4	8.4	0.7	0.4 1.3	9.1	0.8	0.5 1.2
Infectious diseases	8.8	5.9	0.7	0.5 0.8	5.1	0.6	0.4 1.0	6.4	0.7	0.4 1.2	7.7	0.9	0.7 1.2	4.2	0.5	0.2 1.1	3.0	0.3	0.2 0.7
Bone, muscle, and connective tissues diseases	1.1	0.4	0.4	0.2 0.8	0.0	0.0	0.0 .	0.4	0.4	0.1 2.7	0.6	0.5	0.2 1.5	0.7	0.6	0.1 4.4	0.4	0.4	0.1 2.7
Neoplasms	7.1	5.5	0.8	0.6 1.0	0.9	0.1	0.0 0.4	4.7	0.7	0.4 1.2	7.6	1.1	0.8 1.4	5.5	0.8	0.4 1.6	6.5	0.9	0.5 1.5
Diseases of the nervous system	3.2	2.8	0.9	0.6 1.2	2.1	0.7	0.3 1.4	0.8	0.3	0.1 1.1	4.2	1.3	0.9 2.0	2.1	0.7	0.2 2.1	2.5	0.8	0.4 1.8
Mental and behavioural disorders	2.5	1.8	0.7	0.5 1.0	1.8	0.7	0.3 1.6	1.3	0.5	0.2 1.6	1.7	0.7	0.4 1.2	1.4	0.6	0.1 2.2	2.6	1.0	0.5 2.3
Respiratory diseases	49.0	40.2	0.8	0.7 0.9	42.9	0.9	0.1 1.0	29.2	0.6	0.5 0.8	39.0	0.8	0.7 0.9	48.7	1.0	0.8 1.3	44.5	0.9	0.7 1.1
Other causes	5.7	4.0	0.7	0.5 0.9	4.3	0.8	0.4 1.3	4.7	0.8	0.5 1.5	3.6	0.6	0.4 1.0	3.5	0.6	0.3 1.5	4.4	0.8	0.4 1.4

Table 2.3. Hospital admission rates (per 100 000/week) among LTCFs residents in Apulia during COVID-19 pandemic compared with pre-pandemic baseline period, 2018-2020.

	Baseline (reference)	COVID-19 pandemic period			First national lockdown			Gradual reopening phase			Few restrictions			New restrictions			Lockdowns on regional basis		
	Rate	Rate	RR	(95% CI)	Rate	RR	(95% CI)	Rate	RR	(95% CI)	Rate	RR	(95% CI)	Rate	RR	(95% CI)	Rate	RR	(95% CI)
Any cause (including COVID-19)	114.5	65.0	0.6	0.5 0.6	91.1	0.8	0.7 0.9	68.2	0.6	0.5 0.7	63.7	0.6	0.5 0.6	52.5	0.5	0.3 0.6	42.5	0.4	0.3 0.5
Any cause (excluding COVID-19)	114.5	56.8	0.5	0.5 0.5	70.2	0.6	0.5 0.7	64.4	0.6	0.5 0.7	59.5	0.5	0.5 0.6	45.8	0.4	0.3 0.6	31.1	0.3	0.2 0.4
Male	160.2	78.3	0.5	0.4 0.6	90.5	0.6	0.4 0.8	79.3	0.5	0.3 0.7	89.5	0.6	0.5 0.7	67.6	0.4	0.3 0.7	42.6	0.3	0.2 0.4
Female	95.6	46.8	0.5	0.4 0.6	63.4	0.7	0.5 0.8	59.2	0.6	0.5 0.8	46.2	0.5	0.4 0.6	35.0	0.4	0.2 0.6	25.3	0.3	0.2 0.4
ICD-10																			
Cardiovascular disease	22.8	11.9	0.7	0.5 0.8	12.2	0.5	0.4 0.8	12.4	0.6	0.3 0.9	13.2	0.6	0.4 0.8	12.3	0.5	0.3 1.0	7.6	0.3	0.2 0.6
Haematological disorders	1.5	0.3	0.7	0.6 1.0	0.6	0.4	0.1 2.8	0.0	0.0	0.0 .	0.3	0.2	0.0 1.3	0.0	0.0	0.0 .	0.6	0.4	0.1 3.0
Injury or poisoning	20.2	7.5	0.6	0.5 0.7	7.5	0.4	0.2 0.7	8.5	0.4	0.2 0.8	9.8	0.5	0.3 0.7	5.6	0.3	0.1 0.7	1.9	0.1	0.0 0.3
Endocrine, nutrition, and metabolism diseases	4.6	3.7	0.5	0.6 1.2	5.8	0.7	0.4 1.3	5.4	0.6	0.3 1.3	7.3	0.8	0.6 1.3	6.7	0.8	0.3 1.7	1.3	0.1	0.0 0.6
Diseases of the digestive system	8.8	3.3	0.5	0.4 0.7	2.9	0.3	0.1 0.8	7.0	0.8	0.4 1.5	2.4	0.3	0.1 0.5	4.5	0.5	0.2 1.4	1.9	0.2	0.1 0.7
Diseases of the genitourinary system	6.9	2.4	0.8	0.3 0.7	2.3	0.3	0.1 0.9	3.9	0.6	0.2 1.4	2.7	0.4	0.2 0.7	1.1	0.2	0.0 1.2	1.3	0.2	0.0 0.7
Infectious diseases	4.5	3.2	0.5	0.6 1.2	2.9	0.7	0.3 1.6	2.3	0.5	0.2 1.7	4.4	1.0	0.6 1.7	5.6	1.3	0.5 3.2	0.0	0.0	0.0 .
Bone, muscle, and connective tissues diseases	1.6	0.8	0.5	0.3 0.7	0.6	0.4	0.1 2.8	2.3	1.5	0.5 5.0	0.3	0.2	0.0 1.3	0.0	0.0	0.0 .	1.3	0.8	0.2 3.5
Neoplasms	5.1	2.5	0.6	0.3 0.7	1.2	0.2	0.1 0.9	3.1	0.6	0.2 1.7	3.9	0.8	0.4 1.3	2.2	0.4	0.1 1.8	0.0	0.0	0.0 .
Diseases of the nervous system	3.8	1.4	0.9	0.4 0.9	2.3	0.6	0.2 1.7	0.0	0.0	0.0 .	1.6	0.4	0.2 1.0	2.2	0.6	0.1 2.4	0.6	0.2	0.0 1.2
Mental and behavioural disorders	2.5	1.5	0.7	0.7 1.2	1.7	0.7	0.2 2.3	1.5	0.6	0.2 2.6	1.1	0.4	0.2 1.2	1.3	1.4	0.4 4.4	1.3	0.5	0.1 2.1
Respiratory diseases	26.4	14.1	0.4	0.6 0.9	27.3	1.0	0.8 1.4	13.2	0.5	0.3 0.8	12.0	0.4	0.3 0.6	4.5	0.2	0.1 0.5	10.1	0.4	0.2 0.6
Other causes	6.1	4.3	0.8	0.6 1.1	5.8	1.0	0.5 1.8	5.4	0.9	0.4 1.9	4.4	0.7	0.4 1.2	2.2	0.4	0.1 1.5	2.5	0.4	0.2 1.1

Table 2.4. Hospital admission rates (per 100 000/week) among LTCFs residents in Tuscany and Apulia during COVID-19 pandemic compared with the pre-pandemic baseline period

	Baseline (reference)	COVID-19 pandemic period			First national lockdown			Gradual reopening phase			Few restrictions			New restrictions			Lockdowns on a regional basis		
	Rate	Rate	RR	(95% CI)	Rate	RR	(95% CI)	Rate	RR	(95% CI)	Rate	RR	(95% CI)	Rate	RR	(95% CI)	Rate	RR	(95% CI)
Any cause (including COVID-19)	144.1	116.2	0.8	0.8 0.8	133.7	0.9	0.9 1.0	96.5	0.7	0.6 0.7	112.4	0.8	0.7 0.8	124.5	0.9	0.8 1.0	117.3	0.8	0.7 0.9
Any cause (excluding COVID-19)	144.1	98.2	0.7	0.7 0.7	99.7	0.7	0.6 0.8	92.1	0.6	0.6 0.7	108.9	0.8	0.7 0.8	90.1	0.6	0.5 0.7	77.3	0.5	0.5 0.6
Male	198.4	138.9	0.7	0.7 0.8	149.6	0.8	0.7 0.9	121.7	0.6	0.5 0.7	153.3	0.8	0.7 0.9	133.2	0.7	0.5 0.8	109.5	0.6	0.5 0.7
Female	123.2	82.5	0.7	0.6 0.7	80.7	0.7	0.6 0.7	83.5	0.7	0.6 0.8	91.6	0.7	0.7 0.8	73.3	0.6	0.5 0.7	64.2	0.5	0.4 0.6
ICD-9-CM																			
Cardiovascular disease	24.5	15.8	0.6	0.6 0.7	16.4	0.7	0.5 0.8	16.2	0.7	0.5 0.9	17.7	0.7	0.6 0.8	15.0	0.6	0.4 0.9	10.8	0.4	0.3 0.6
Haematological disorders	1.8	1.0	0.6	0.4 0.9	0.8	0.5	0.2 1.2	0.5	0.3	0.1 1.3	1.7	0.9	0.6 1.6	0.9	0.5	0.1 2.0	0.3	0.1	0.0 1.0
Injury or poisoning	18.2	14.8	0.8	0.7 0.9	13.3	0.7	0.6 0.9	13.2	0.7	0.5 1.0	17.7	1.0	0.8 1.1	11.2	0.6	0.4 0.9	13.1	0.7	0.5 0.9
Endocrine, nutrition, and metabolism diseases	8.4	5.0	0.6	0.5 0.7	4.2	0.5	0.3 0.8	4.9	0.6	0.4 0.9	6.7	0.8	0.6 1.0	4.3	0.5	0.3 1.0	2.1	0.2	0.1 0.5
Diseases of the digestive system	12.8	6.9	0.5	0.5 0.6	6.2	0.5	0.3 0.7	8.5	0.7	0.5 1.0	7.7	0.6	0.5 0.8	6.4	0.5	0.3 0.8	4.6	0.4	0.2 0.6
Diseases of the genitourinary system	10.1	7.8	0.8	0.7 0.9	7.8	0.8	0.6 1.1	8.5	0.8	0.6 1.2	8.7	0.9	0.7 1.1	5.6	0.5	0.3 1.0	5.9	0.6	0.4 0.9
Infectious diseases	7.6	4.9	0.7	0.5 0.8	4.4	0.6	0.4 0.9	4.9	0.7	0.4 1.0	6.5	0.9	0.7 1.1	4.7	0.6	0.3 1.1	1.8	0.2	0.1 0.5
Bone, muscle, and connective tissues diseases	1.3	0.6	0.4	0.3 0.8	0.2	0.2	0.0 1.1	1.1	0.9	0.3 2.4	0.5	0.4	0.2 1.0	0.4	0.3	0.0 2.5	0.8	0.6	0.2 1.9
Neoplasms	6.5	4.3	0.7	0.5 0.8	1.0	0.2	0.1 0.4	4.1	0.6	0.4 1.1	6.2	0.9	0.7 1.2	4.3	0.7	0.4 1.2	3.9	0.6	0.4 1.0
Diseases of the nervous system	3.5	2.3	0.7	0.5 0.9	2.2	0.7	0.4 1.2	0.5	0.2	0.0 0.7	3.2	1.0	0.7 1.4	2.1	0.6	0.3 1.6	1.8	0.5	0.3 1.1
Mental and behavioural disorders	2.5	1.7	0.7	0.5 0.9	1.8	0.7	0.4 1.4	1.4	0.5	0.2 1.3	1.5	0.6	0.3 1.0	2.1	0.9	0.4 2.1	2.1	0.8	0.4 1.7
Respiratory diseases	42.7	30.4	0.7	0.7 0.8	37.6	0.9	0.8 1.0	23.6	0.6	0.4 0.7	29.0	0.7	0.6 0.8	31.7	0.7	0.6 0.9	30.6	0.7	0.6 0.9
Other causes	5.8	4.1	0.7	0.6 0.9	4.8	0.8	0.6 1.3	4.9	0.9	0.5 1.4	3.8	0.7	0.5 0.9	3.0	0.5	0.2 1.1	3.6	0.6	0.4 1.1

Figure 2.2. Overall non-COVID-19 (blue line) and COVID-19 (yellow line) hospital admission rates by gender and region.

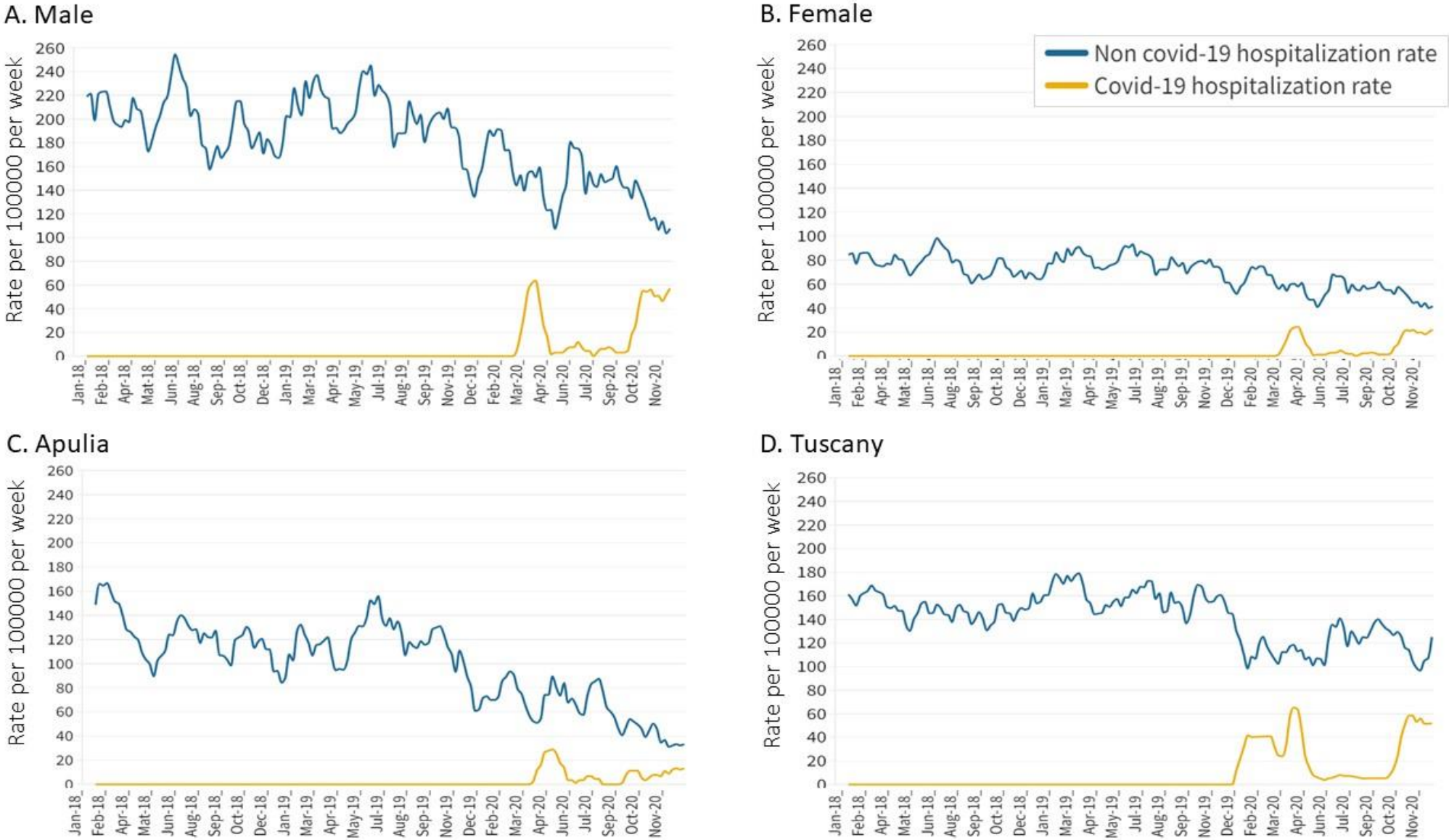
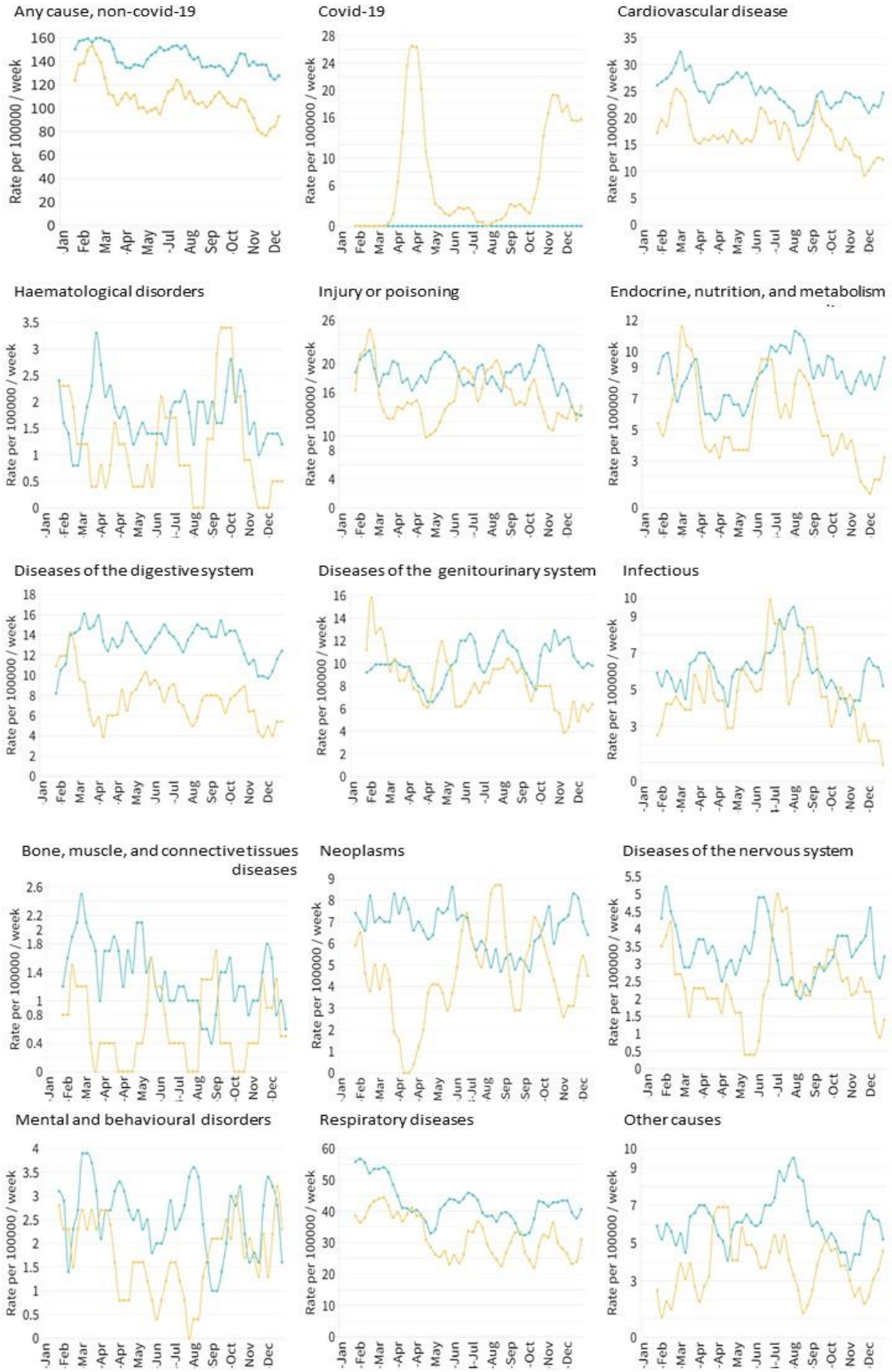


Figure 2.3. Weekly hospital admission rates by ICD-9-CM (international classification of diseases version 10) among LTCF residents in Tuscany and Apulia. Blue line: 2018-2019 average rate; yellow line: 2020 rate



Mortality among LTCF residents in Tuscany

The overall weekly average mortality rate for 1 000 LTCF residents in Tuscany was 8.9 before the start of the pandemic and 12.5 during the pandemic. The proportion of deaths at 30 days after hospitalisation was 40.3% in the pre-pandemic period and decreased to 34.5% in the pandemic period, excluding COVID-19 related hospitalisation. The overall 30-day mortality risk ratios among people admitted to hospital for non-COVID-19 causes increased during the first national lockdown (1.4, 1.2 to 1.7), during the period with new restrictions (1.5, 1.2 to 1.9) and the regional lockdown (1.5, 1.2 to 1.9) compared with the pre-pandemic baseline period. The increase in mortality risk was higher among males than females for the first pandemic phases, while we have the opposite scenario in the last reported pandemic phases (Table 2.5).

Table 2.5. 30-day mortality risk and risk ratio among LTCF residents admitted to hospital for non-COVID-19 medical conditions during COVID-19 pandemic in Tuscany compared with the pre-pandemic baseline period, 2018-2020

	Baseline (reference)	COVID-19 pandemic period			First national lockdown			Gradual reopening phase			Few restrictions			New restrictions			Lockdowns on a regional basis		
	Risk	Risk	HR	(95% CI)	Risk	HR	(95% CI)	Risk	HR	(95% CI)	Risk	HR	(95% CI)	Risk	HR	(95% CI)	Risk	HR	(95% CI)
Any cause (including COVID-19)	21.9	29.1	1.4	1.3 1.5	32.2	1.6	1.3 1.9	27.5	1.2	1.0 1.6	23.5	1.1	0.9 1.2	40.1	2.0	1.6 2.4	31.5	1.8	1.5 2.2
Any cause (excluding COVID-19)	21.9	26.4	1.2	1.1 1.4	29.7	1.4	1.2 1.7	26.7	1.2	0.9 1.5	23.6	1.1	0.9 1.2	33.0	1.5	1.2 1.9	26.1	1.5	1.2 1.9
Male	22.6	27.9	1.3	1.1 1.5	33.1	1.6	1.2 2.1	32.2	1.5	1.0 2.2	24.3	1.1	0.9 1.4	29.3	1.3	0.9 2.0	26.8	1.4	1.0 2.1
Female	21.5	25.4	1.2	1.1 1.4	27.2	1.3	1.0 1.7	23.6	1.0	0.8 1.5	23.2	1.0	0.9 1.3	35.5	1.7	1.2 2.3	25.7	1.6	1.1 2.1
ICD-9-CM																			
Cardiovascular disease	21.7	27.4	1.3	1.0 1.7	26.4	1.2	0.7 2.1	33.3	1.6	0.9 2.7	26.0	1.2	0.8 1.7	19.2	0.8	0.3 2.0	33.3	2.1	1.1 3.8
Haematological disorders	16.1	26.1	1.5	0.5 4.1	0.0	0.0	0.0 .	0.0	0.0	0.0 .	31.3	1.8	0.6 5.3	50.0	6.1	0.7 51.2	.		
Injury or poisoning	20.8	27.9	1.4	1.1 1.9	23.5	1.1	0.6 2.0	40.0	2.3	1.3 3.9	24.6	1.3	0.9 1.8	26.9	1.2	0.6 2.6	33.3	2.0	1.2 3.4
Endocrine, nutrition, and metabolism diseases	23.7	19.7	0.8	0.4 1.4	44.4	2.1	0.8 5.7	9.1	0.3	0.0 2.3	12.2	0.5	0.2 1.1	25.0	0.9	0.1 6.2	50.0	4.2	1.3 13.3
Diseases of the digestive system	10.2	12.3	1.0	0.6 1.8	23.8	1.6	0.5 5.2	9.1	0.4	0.1 3.2	10.9	1.0	0.5 2.3	6.7	0.6	0.1 4.5	12.5	1.6	0.4 6.5
Diseases of the genitourinary system	19.6	15.6	0.8	0.5 1.3	34.5	2.1	1.1 4.0	12.0	0.6	0.2 1.9	10.3	0.5	0.2 1.0	18.2	0.9	0.2 3.8	12.5	0.8	0.3 2.6
Infectious diseases	30.0	28.4	1.0	0.6 1.5	41.2	1.6	0.7 3.3	26.7	0.9	0.3 2.4	20.4	0.7	0.3 1.2	28.6	0.9	0.2 3.8	57.1	2.9	1.1 7.9
Bone, muscle, and connective tissues diseases	9.4	0.0	0.0	0.0 1.0	.			0.0	0.0	1.0 0.0	0.0	0.0	1.0 0.0	0.0	0.0	1.0 0.0	0.0	0.0	1.0 0.0
Neoplasms	16.7	17.6	1.1	0.6 1.9	0.0	0.0	0.0 .	9.1	0.5	0.1 3.9	25.5	1.5	0.8 2.9	10.0	0.6	0.1 4.1	6.7	0.5	0.1 4.0
Diseases of the nervous system	12.1	22.7	2.2	1.0 4.7	16.7	1.6	0.2 12.2	0.0	0.0	0.0 .	22.2	2.2	0.8 5.5	33.3	2.6	0.3 19.7	33.3	3.8	0.9 16.5
Mental and behavioural disorders	13.6	3.6	0.3	0.0 1.9	0.0	0.0	. .	0.0	0.0	. .	9.1	0.6	0.1 4.7	0.0	0.0	. .	0.0	0.0	. .
Respiratory diseases	27.4	34.1	1.3	1.1 1.5	36.1	1.3	1.0 1.8	32.4	1.2	0.8 1.8	32.9	1.2	1.0 1.5	47.9	2.0	1.4 2.8	25.9	1.2	0.8 1.8
Other causes	40.5	54.8	1.6	1.1 2.3	61.5	1.7	0.8 3.6	60.0	2.0	0.9 4.5	41.7	1.0	0.5 2.0	100.0	2.9	1.2 7.0	50.0	1.9	0.8 4.6

Discussion

Although there is extensive literature describing COVID-19 outbreaks in LTCFs and the excess mortality that occurred during the pandemic (140,193,197), to our knowledge, this is the first attempt to extensively study the indirect impact of the COVID-19 pandemic on hospital care provided to LTCFs residents in Europe.

Here, we analysed regional health registers that include residents of LTCFs in Tuscany and Apulia regions and observed a lower overall hospitalisation rate during the first year of the pandemic compared with the pre-pandemic period, combined with an increased risk of mortality within 30 days of hospital admission.

During the study period we observe that the LTCFs weekly average population gradually decreased and this is in line with the Ministry of Health's recommendations (224) to limit new admissions of residents to urgent and unavoidable cases, in order to allow for a reduction in the number of residents to facilitate management of COVID-19 cases in isolation. In these recommendations, it is suggested to avoid sending residents to hospitals for specialist visits and instrumental examinations as much as possible.

This may be one of the reasons why, in our study, we observe a significant reduction in hospital admission rate during the pandemic period compared to the previous two years. This reduction has also been reported in the general population in Italy as in other countries (228–232). Furthermore, our results are in line with the findings of Betini et al. who reported a drop by 27% of LTCF resident transfers to hospitals for the treatment of chronic conditions and infections (215).

According to our results, the decrease in the admission rate is particularly pronounced in the second epidemic wave. This may be due to the fact that, although the hospitals were better prepared, the second epidemic wave was more extensive than the first (233). Moreover, teams of healthcare workers periodically accessed the LTCFs to deal mainly with COVID-19 patients, allowing the nursing home staff and general practitioners who periodically visit the facilities to devote themselves to other patients (224).

The magnitude of the reduction in the hospitalisation rate for the major disease groups was homogenous (around 30-40%) if we compare the pre-pandemic period with the pandemic period as a whole. In specific periods, the reduction in the rate of hospitalisation for specific diseases was more pronounced. For instance, for neoplasms during the first lock-down the reduction in hospitalisation rates is about 80%, about twice the reduction reported for the same period in the Italian population (228). The two Italian regions in our study have different hospitalisation rates for both the baseline and pandemic periods. In particular, the Apulia region reported lower hospitalisation rates and has experienced a more drastic reduction in access to hospital during the pandemic. This may be due to various factors: the healthcare provided in LTCFs may be dissimilar in the two regions or criteria for hospitalisation may be different. Further studies are needed for a proper understanding of the reasons behind these differences as well as a harmonisation of data collection systems.

During the pandemic period, the mortality risk at 30 days after non-COVID-19 hospital admission increased of about 20%, higher when compared to age-specific mortality rates of the general population (234), and this is consistent with what previous studies have reported (215,230,235,236).

Even before the crisis, the Italian LTCFs have been characterized by weaknesses, due to a strong level of fragmentation both in terms of competencies among institutional and non-institutional actors, and unheard struggles to enter the policymakers' agenda. LTCFs were not conceived and developed as a comprehensive model, rather they emerged from multiple legislative interventions that aimed intermittently at integrating what existed already (235). LTCFs governance structure is, at the central level, somewhere in the middle between the Ministry for Labour and Social Policy and the Ministry of Health.

Moreover, R&AP implement the dual ministerial policies by organising the LTCFs at the local level defining network of services; ultimately, local health authorities and municipalities manage services and interventions at the local and individual level. This fragmented situation is further compromised by the insufficient level of coordination that exists among all the actors involved in LTCFs: the absence of national awareness and lack of strategic vision inevitably inhibits dialogue, cooperation and joint actions even in non-crisis times. This fragmentation also affects the information monitoring system, which is not integrated with national health data collection systems and is heterogeneous among regions. Although imperfect, these registers are available at regional level. Using them allows us not only to evaluate the health care performance of LTCFs, but also to advocate for the development of unified and comparable data collection systems across regions.

Limitations

This study has limitations. First, while we acknowledge that data regarding age-specific mortality, comorbidities and cause of death of older residents would allow a more detailed assessment of the indirect impact of COVID-19 pandemic in LTCFs, we decided not to further stratify by age groups in order to increase accuracy of estimates. Second, the epidemic burden and organisation of LTCFs differ among Italian regions, therefore it is not possible to translate our findings into the Italian context. Finally, we have no information on the type of LTCFs in which the subjects reside. This does not allow us to assess whether there are differences between privately and publicly managed LTCFs that might have had implications on the outcome during the COVID-19 pandemic.

Conclusion

COVID-19 pandemic had strong direct and indirect impact on LTCFs. They are vulnerable places for structural reason and the residents' characteristics; therefore, LTCFs need to be prioritized in pandemic preparedness plans.

Besides the pandemic, it is important to monitor LTCFs potential threats and health performance. This implies integrating LTCF health registries within national surveillance and implement possible sentinel sites for syndromic surveillance for early warning. These registries are available, can be harmonised among regions and used to build a monitoring system against key indicators reflecting healthcare quality, but also appropriate use of the health system resources, including access to specialised services and hospitalisation.

Chapter 3

Executive summary

Healthcare in Italian prisons is managed by the Ministry of Health, yet there is a significant lack of healthcare surveillance and integration between prisons and the community. During the COVID-19 pandemic, no national or regional data were collected on confirmed cases within the prison population, revealing a critical gap in public health monitoring.

Structural and operational challenges make conducting research in prison settings difficult. Most available studies on COVID-19's impact in these environments were limited in scope and duration. Comprehensive health data on the pandemic's effects in prisons were largely unavailable, with information scattered across isolated paper records or individual prison information systems.

For this study, COVID-19 data were compiled from daily reports by Lombardy's prisons, which were forwarded to the Lombardy Region Superintendency for surveillance. These reports were consolidated into a single database to enable analysis.

The study reveals the significant COVID-19 burden among prisoners and staff, highlighting the challenges of implementing effective prevention and control measures in prisons and the heightened risks this population faces from airborne diseases. This underscores the necessity of including prison settings in emergency preparedness frameworks and standard surveillance activities.

In the second section, (FROM EVIDENCE TO PRACTICE), national guidelines developed from this evidence are presented, outlining priorities and strategies for implementing COVID-19 vaccination in residential communities across Italy. The third section, (FROM EVIDENCE TO ADVOCACY), discusses how the experience of COVID-19 vaccination in prisons can be used to advocate for better healthcare access for adolescents in juvenile institutions, using vaccination as a gateway to broader preventive care.

Infections with COVID-19 Among Prison Inmates and Staff in Lombardy, Italy March 2020-February 2021

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Link to the article.

Due to infrastructural and population characteristics, prison setting is at increased risk for transmission of SARS-CoV-2, and for severe clinical outcomes. Yet, due to structural and operational reasons, conducting solid research in prison settings is challenging and often available studies are mono-centric and with limited temporal coverage. This chapter aims to describe the extent and dynamics of the COVID-19 pandemic within the prison system of a large Italian region, Lombardy, and to report the infection prevention and control (IPC) measures implemented.

This was a repeated cross-sectional study carried out between March 2020 and February 2021 in the prison system of Lombardy constituted of 18 detention facilities for adult individuals. The main exposures of interest were the weekly average number of people living in prison placed in quarantine in single/shared isolation rooms, the rate of symptomatic/asymptomatic sick leave of prison staff notified by the prison occupational medicine on a weekly basis and the level of overcrowding.

The primary study outcome measurements were: weekly COVID-19 crude case rates, weekly test positivity rate and the relative risk of acquiring the infection for prison staff, people in prison, and the general population.

During the study period among an average of 7 599 people in prison and 4 591 prison staff, 1 564 and 661 COVID-19 cases were reported respectively. Of these cases, most were reported during the second wave, when stringent measures previously enforced were relaxed. During both epidemic waves, people in prison and prison staff had a higher relative risk than the general population (First wave: respectively 1.30 95% CI: 1.06-1.58 for people living in prison (PLP), 3.23 95% CI: 2.74-3.84 for prison staff. Second wave: 3.91 95% CI: 3.73-4.09 for PLP, and 2.61 95% CI: 2.41-2.82 for prison staff).

Prisons were an element of fragility during the COVID-19 pandemic, with a high burden of COVID-19 cases. Therefore, prison setting and prison population need to be included and possibly prioritised in the response during epidemic events.

Introduction

On February 20, 2020, the first COVID-19 major outbreak in Europe was detected in the Lombardy region, Italy (102). The Lombardy region is home to a sixth of the Italian population (10.03 million inhabitants (237)) and accounted for 20% of cases and 27% of deaths in the country, as of June 23, 2021 (238). The temporal course of the epidemic was characterized by three distinct phases: the first epidemic wave from March to June 2020, followed by a summer period with relatively low incidence and a second wave which started in September and peaked in November 2020 (238).

The evidence shows that the risk of transmission of SARS-CoV-2 is much higher in prisons and other closed settings (239). Multiple large outbreaks of COVID-19 have been documented in detention facilities worldwide (240,241).

Individuals in contact with the criminal justice system often come from marginalized groups of society with a higher burden of poverty and discrimination, and with limited access to healthcare, who represent perfectly the COVID-19 syndemic concept, for which the biological, economic and social interactions between NDCs and COVID-19 increase a person's susceptibility to infection and worse health outcomes (144). The high turnover of people coming from the most disadvantaged segments of the population, together with the daily inflow/outflow of prison staff, increases the risk of virus introduction within prisons. Once the virus enters the detention facilities, proximity, overcrowding and infrastructural constraints facilitate the spreading of the infection (242).

Italy has the highest prison density in the European Union, with an occupancy rate of 120%, and old penitentiary infrastructures (243). According to the latest available data, PLP in Italy are largely constituted of male smokers (80%) with disproportionately higher rates of acute and chronic physical and mental illnesses, including diabetes, cardiovascular and chronic respiratory diseases (244). Therefore, PLP are more likely to suffer severely from COVID-19.

Lombardy had 7 766 PLP as of February 28, 2021 (245). During the first pandemic wave, Italian detention facilities implemented a number of preventive interventions including (i) hygiene and sanitary measures (i.e. use of personal protective equipment, handwashing, environmental disinfection); (ii) IPC measures (triage and COVID-19 test for new arrivals, isolation for symptomatic negative individuals, suspected or confirmed cases); (iii) measures to restrict access to essential staff, banning visitors and discontinuing PLP activities that required contact with individuals/communities from outside the prison; (iv) early release and alternatives to incarceration for low-risk offenders (246,247).
With the conclusion of the first epidemic wave, the restrictive measures have gradually been lifted, with the exception of hygiene and IPC measures (248,249), although with considerable variability between detention facilities.

In this study, we aimed to describe the progression of the COVID-19 epidemic in prison settings in Lombardy, Italy, during the first pandemic year (March 2020-February 2021), and to report the IPC measures implemented during the same period.

Methods

Study setting

In Lombardy there are 18 detention facilities for adult individuals: 14 are correctional facilities where pre-trial detainees and individuals with sentences shorter than three years are incarcerated; four are detention facilities for individuals with sentences longer than three years.

Data collection

COVID-19 prison data

COVID-19 data covering the period 1 March 2020-28 February 2021 were sourced from daily reports produced by each prison and submitted to the Prison Superintendence of the Lombardy region for surveillance purposes. The following variables were available: COVID-19 confirmed cases among PLP, number of naso-pharyngeal swabs, the daily number of PLP in quarantine in single or shared cells, COVID-19 confirmed cases among prison staff, and registered sick leaves taken by symptomatic and asymptomatic prison staff.

A detailed analysis of intra-facility outbreak was performed for selected prisons (Milan Opera, a detention facility for long-sentenced individuals, Milan San Vittore and Monza correctional facilities for pre-trial and short-sentenced individuals) during the first and second epidemic waves. We accessed routine clinical registries to source additional data including infection outcome, defined as: the presence of symptoms compatible with COVID-19, hospitalization, death.

The prison population

Due to the unavailability of more accurate data, the prison population was estimated using the number of individuals detained in each facility on the last day of the month, serving as a proxy for the monthly prison population. We used the average number of individuals detained in each imprisonment facility on the last day of the month to calculate the average annual number of PLP. In the absence of more accurate data, we used information on prison staff employed at each detention facility, obtained from the regional social security/occupational health database as of March 1, 2020, as a proxy for the entire study period.

COVID-19 General population data

The total number of inhabitants in Lombardy was sourced from the National Institute of statistics (237). COVID-19 data of the general population of Lombardy were sourced from a publicly accessible dataset from the GitHub repositories developed by the Italian Presidency of the Council of Ministers and the Italian Department of Civil Protection (250). The following variables were available: COVID-19 confirmed cases among PLP, the number of naso-pharyngeal swabs.

Data analysis

For the data analysis we used Stata 13.0 and R version 4.2.0. The number of confirmed cases minus the number of recovered cases and deaths was defined as active cases. This was the number of cases considered to be still infectious. We examined the weekly COVID-19 crude case rates per 1 000 for prison staff, PLP, and the general population. We examined the weekly testing rate (number of executed nasopharyngeal over 1 000 individuals) and the weekly test positivity rate (the percent of tests that returned positive) in PLP and the general population. We calculated the weekly average number of PLP placed in quarantine in single/shared isolation rooms per 1 000 PLP. We calculated the rate of symptomatic/asymptomatic sick leave of prison staff notified by the prison occupational medicine on a weekly basis. We assessed the level of overcrowding by calculating the percentage of individuals detained exceeding the regulatory capacity of the facility (9 square metres per person). We calculated the relative risk (RR) of acquiring the infection of PLP and prison staff compared to the general population during the first (March -June 2020) and the second (July 2020-February 2021) epidemic waves.

For the second epidemic wave (October - February 2021), we studied the time series of the daily number of new COVID-19 cases among PLP; the daily number of new COVID-19 cases among staff members; the daily number of PLP in preventive isolation in single or shared rooms; the daily number of new asymptomatic or symptomatic sick leaves among staff. For each time series, data from all prisons were aggregated. To remove the long-time trend from each of these series, negative binomial regression models were fitted with the effect of time modelled by B-spline functions (Figure 3.1, Figure 3.2). The number of degrees of freedom of B-splines was selected with the Akaike Information Criterion. The total number of PLP or staff members was used as offsets. The deviance residuals of each negative binomial regression model were extracted, and the Spearman correlation coefficients were estimated for each couple of time series. The deviance residuals were fitted with linear models to estimate the lagged effect of each variable and the synchronous and lagged effects of the others.

The exposure variable overcrowding was available on monthly basis and it presented small variability over time compared to the variability by prison; therefore, its effect on the incidence of new cases among PLP was evaluated using the prison-specific data, instead of prison-aggregated data. The monthly incidence of new cases among PLP was modelled with a negative binomial model with the person-days of PLP as offset and month as a factor; the deviance residuals were then extracted and fitted with a linear model including overcrowding as a predictor. The threshold p-value considered for statistical significance was $p < 0.01$.

The study was conducted at the request of regional authorities. This analysis used routine monitoring data collected in collaboration with the local health authorities for the purpose of containing the COVID-19 outbreak. This is the standard operating procedure for medical interventions during public health emergencies. The authorisation was obtained from the Ministry of Justice (no. 12107 of 27 February 2020) before data collection. The privacy and confidentiality of patients were ensured. All data were anonymised or aggregated when entered into the database and it was not necessary to obtain informed consent from individuals. No ethnic or other sensitive identifying information was encoded. This

retrospective description of programme data is exempt from review by the ethical review board.

Figure 3.1. The trend of the number of new daily confirmed cases among incarcerated individuals from October 1 to February 28: observed values (black line), predicted values (red line), 95% confidence band (shaded pink area) and 95% predicted band (shaded grey area).

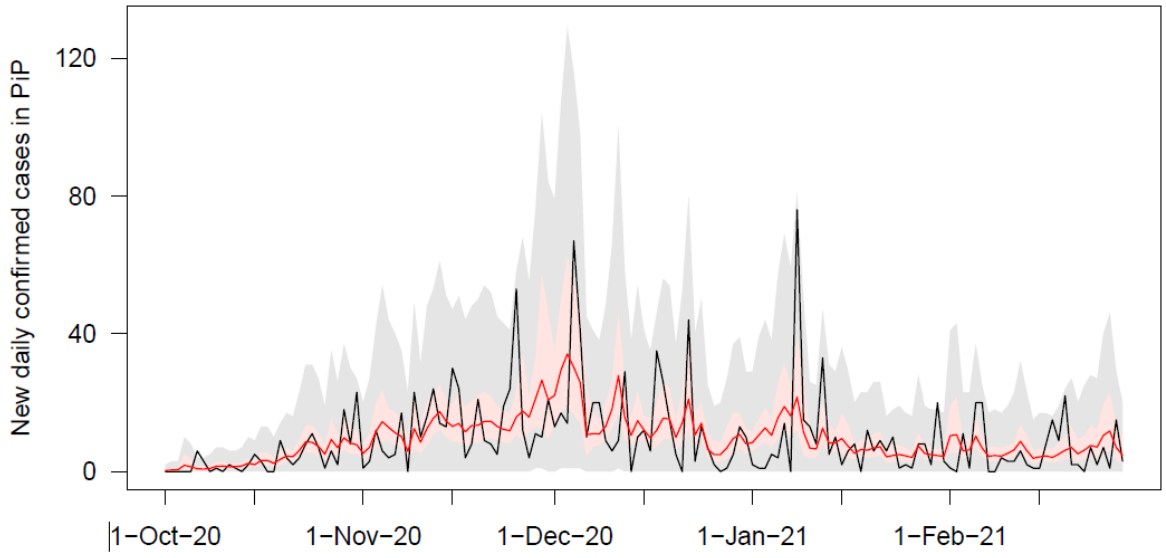
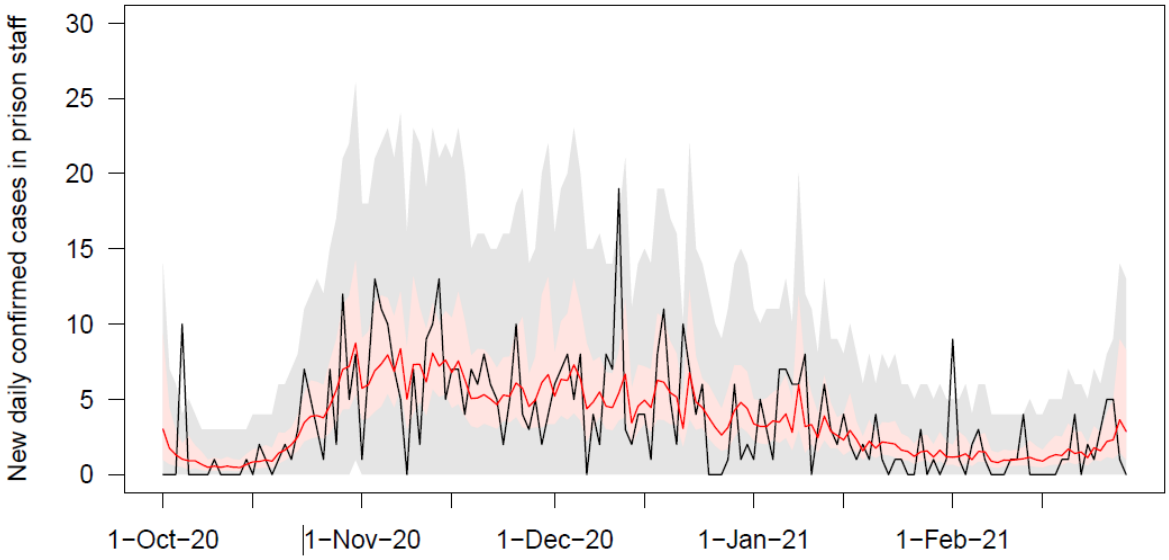


Figure 3.2. The trend of the number of new daily confirmed cases among prison staff from individuals from October 1 to February 28: observed values (black line), predicted values (red line), 95% confidence band (shaded pink area) and 95% predicted band (shaded grey area).



Results

From 1 March 2020 to 28 February 2021, an annual average of 7 599 individuals were detained in the 18 prisons of Lombardy, where 4 591 prison staff were employed. The overcrowding rate of the imprisonment system of Lombardy was 131% at the start of the pandemic, then fell to 119% in April 2020 and afterwards gradually increased to 126% in October remaining stable until the end of the study observation period (Figure 3.3). The overcrowding rate was heterogeneous among different prisons (range: 91%-202%), with all prisons exceeding the overcrowding rate of 100% for at least a month during the study period.

Between March 2020 and February 2021, a total of 1 564 cases were reported among PLP in the Lombardy region, and an additional 661 among prison staff. At the end of the first wave, 90 confirmed cases of COVID-19 were reported among PLP and 132 among prison staff. Two of the 18 prisons reported no cases of COVID-19, neither among PLP nor among the prison staff. In six prisons, although cases were reported among prison staff, no infections were detected among PLP. From July 2020 to February 2021, 1474 COVID-19 confirmed cases were reported among PLP and 529 among prison staff. At least one case was recorded among both prison staff and PLP in all prisons (Figure 3.4).

Figure 3.3. Overcrowding level in the penitentiary system of the Lombardy region.

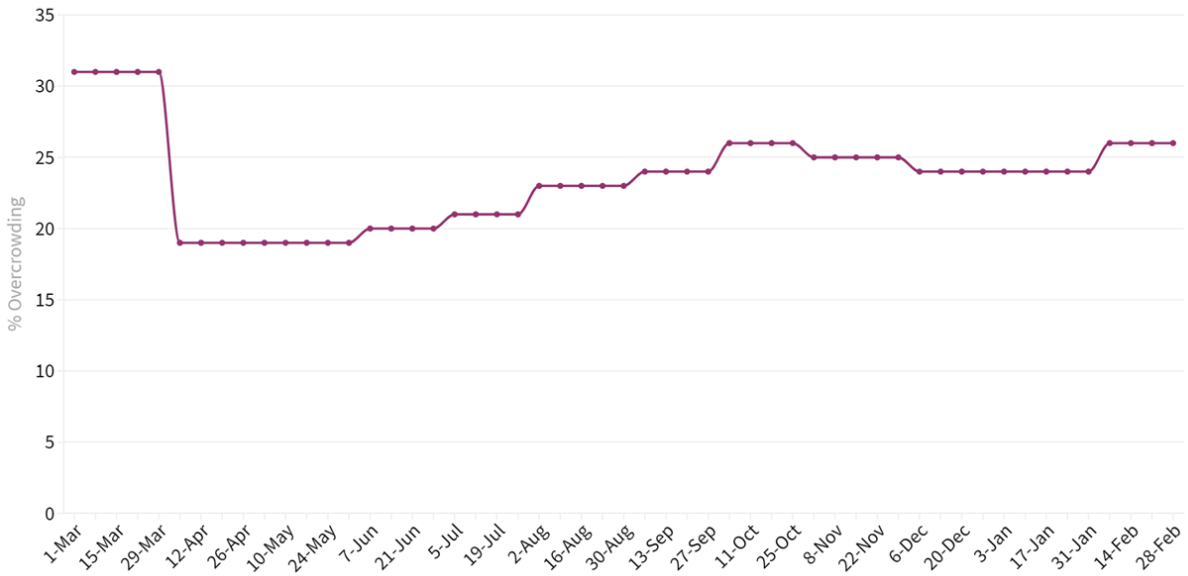
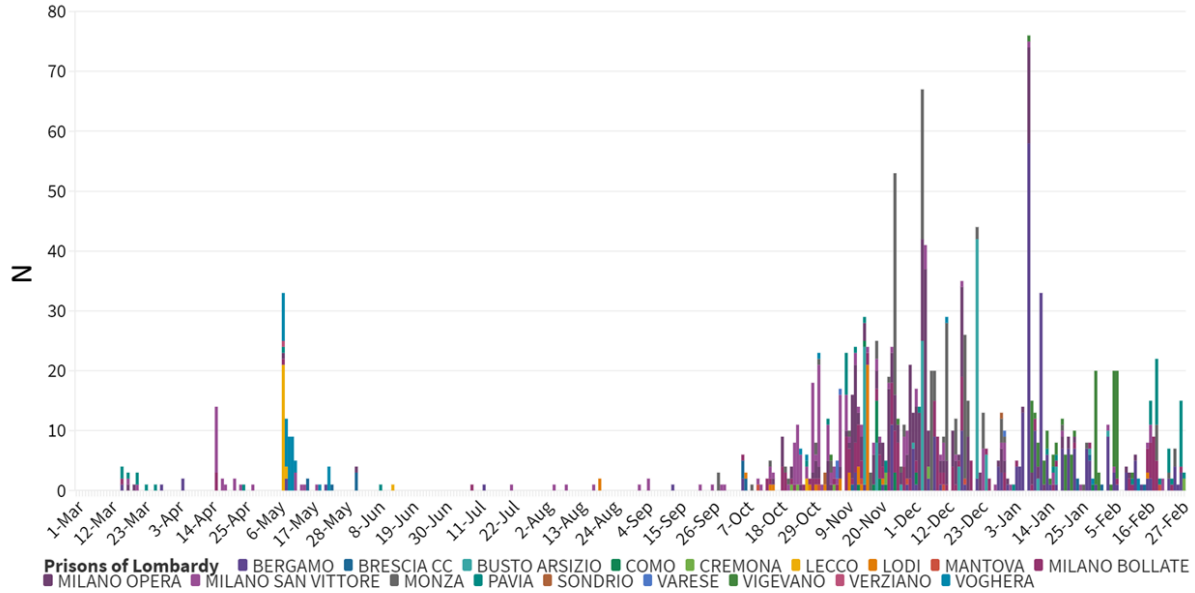


Figure 3.4. New daily confirmed cases among PLP in the 18 prisons of Lombardy region (March 1, 2020 – February 28, 2021)

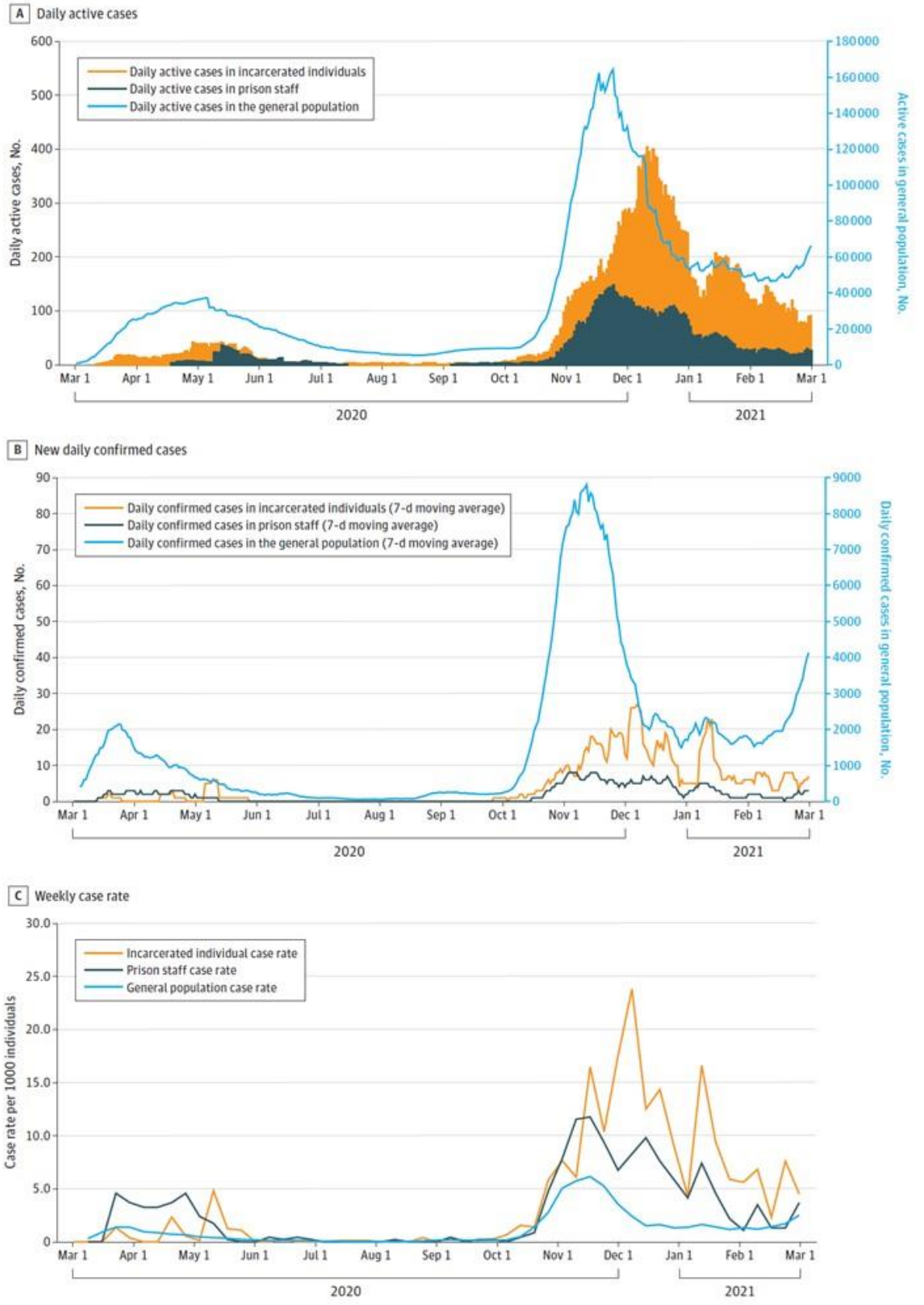


The epidemic trend in PLP, prison staff and the general population

During the first epidemic wave, there was a lag time of about 10 days between the start of the epidemic in the general population and the start of the epidemic in PLP. While, the temporal gap between the epidemic peak in the general population and in PLP was of more than 30 days (Figure 3.5A, 3.5B). Regarding prison staff, the trend of the epidemic curve of the first wave was unusual due to the sub-optimal level of access to diagnostics during the initial weeks of the outbreak, as described elsewhere (246).

In PLP and prison staff, the second epidemic wave began after a lag time of fifteen days compared to the general population. The number of new cases per day in the general population and prison staff reached its peak in the first two weeks of November. Instead, the PLP epidemic curve was characterized by two peaks, the first occurred on December 5th and the second on January 9th (Figure 3.5B).

Figure 3.5. COVID-19 cases among incarcerated individuals, prison staff, and the general population



Trends from March 1, 2020, to February 28, 2021, in daily active cases (A), new daily confirmed cases (B), and weekly case rates (C).

Case rates in PLP, prison staff, and the general population

During both epidemic waves, both PLP and prison staff had a higher case rate than the general population. While prison staff had the highest case rate during the first wave, PLP had the highest case rate during the second wave (Figure 3.5C).

During the first wave, the RR of acquiring the infection compared with the general population was respectively 1.30 (95% CI: 1.06-1.58) for PLP, 3.23 (95% CI: 2.74-3.84) for prison staff. During the second wave, the RR of acquiring the infection compared with the general population was 3.91 (95% CI: 3.73-4.09) for PLP, and 2.61 (95% CI: 2.41-2.82) for prison staff.

According to the linear model, when the mutual synchronous and lagged effects were accounted for, the number of new cases among PLP and new cases among staff presented a synchronous positive association (p=0.03). These results were confirmed by the Spearman correlation coefficient (Table 3.1)

Table 3.1. Spearman correlation coefficients between the residuals of each time series under different negative binomial regression models[a]

Characteristic	New cases among incarcerated individuals	New cases among staff	Quarantined incarcerated individuals
New cases among staff			
Model 1	0.48[b]	NA	NA
Model 2	0.24[b]	NA	NA
Incarcerated individuals in quarantine			
Model 1	0.41[b]	0.43[b]	NA
Model 2	-0.15	-0.08	NA
New sick leave among staff			
Model 1	0.24[b]	0.36[b]	0.28[b]
Model 2	-0.01	0.02	0.22[b]

Abbreviation: NA, not applicable.
[a] *Model 1, time series correlation; model 2, time series correlation after removing the long-term time association.*
[b] *P < .01.*

Testing rate and positivity rate in PLP and the general population

During the first epidemic wave, the average weekly testing rate per 1000 individuals was 61.09 (range: 0-115.44) in PLP and 6.11 (range: 1.16-10.41) in the general population. During the second wave, the average weekly positivity rate was 258.43 (range: 123.92-573.08) in PLP and 19.73 (range: 11.68-30.09) in the general population (Figure 3.6). During the first epidemic wave, the average weekly positivity rate per 100 individuals was 1.76 (range: 0.00-10.68) in PLP and 9.55 (range: 1.21-37.50) in the general population. During the second wave, the average weekly positivity rate was 4.46 (range: 0.00-17.92) in PLP and 8.71 (range: 1.16-20.71) in the general population (Figure 3.7).

Figure 3.6. The weekly testing rate among 1 000 PLP and 1 000 individuals of the general population.

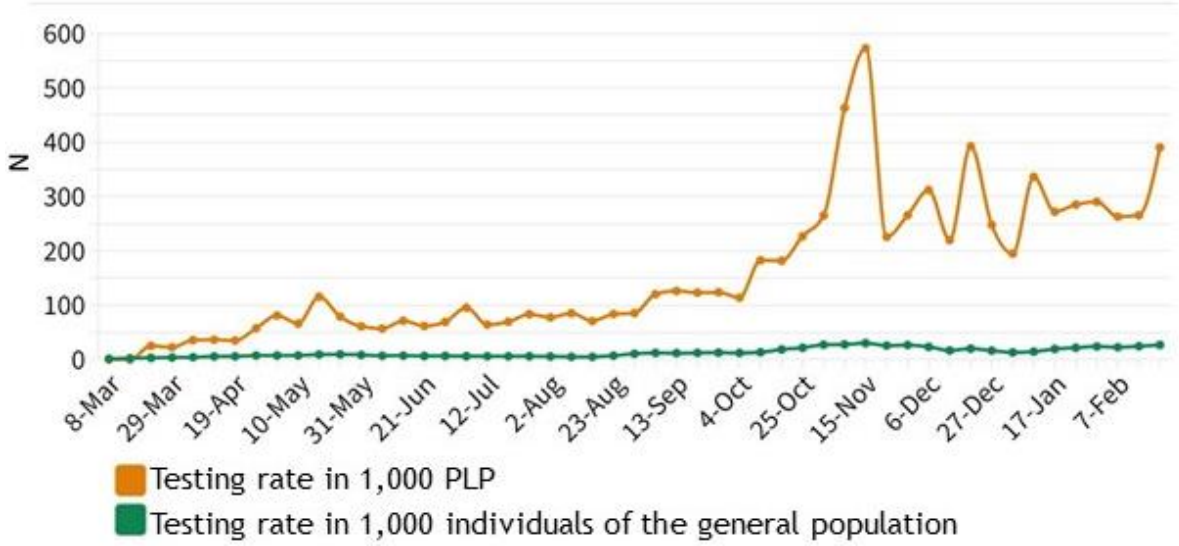
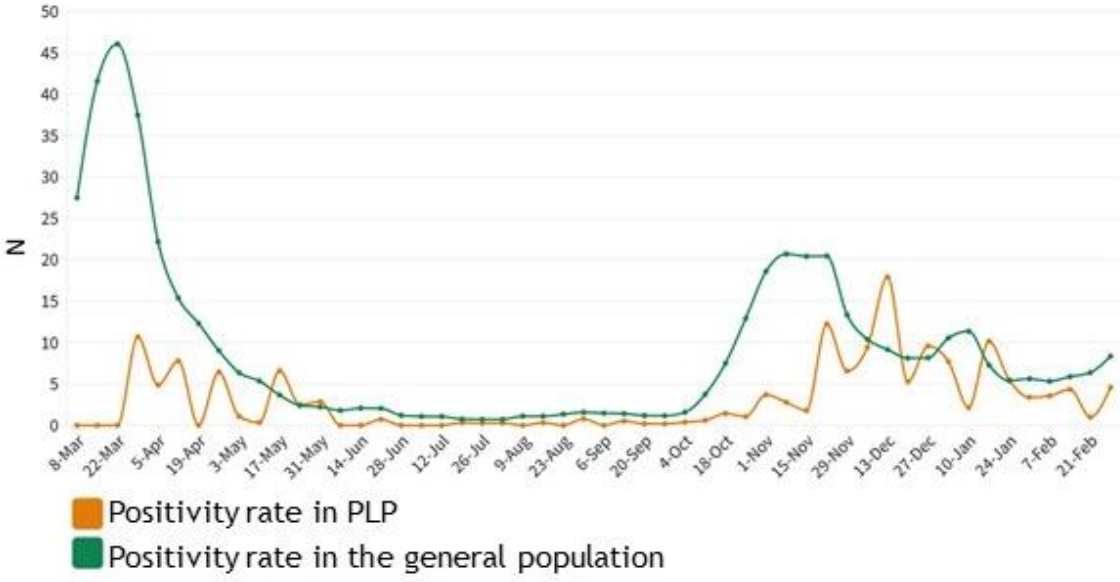


Figure 3.7. Weekly positivity rate among PLP and the general population.



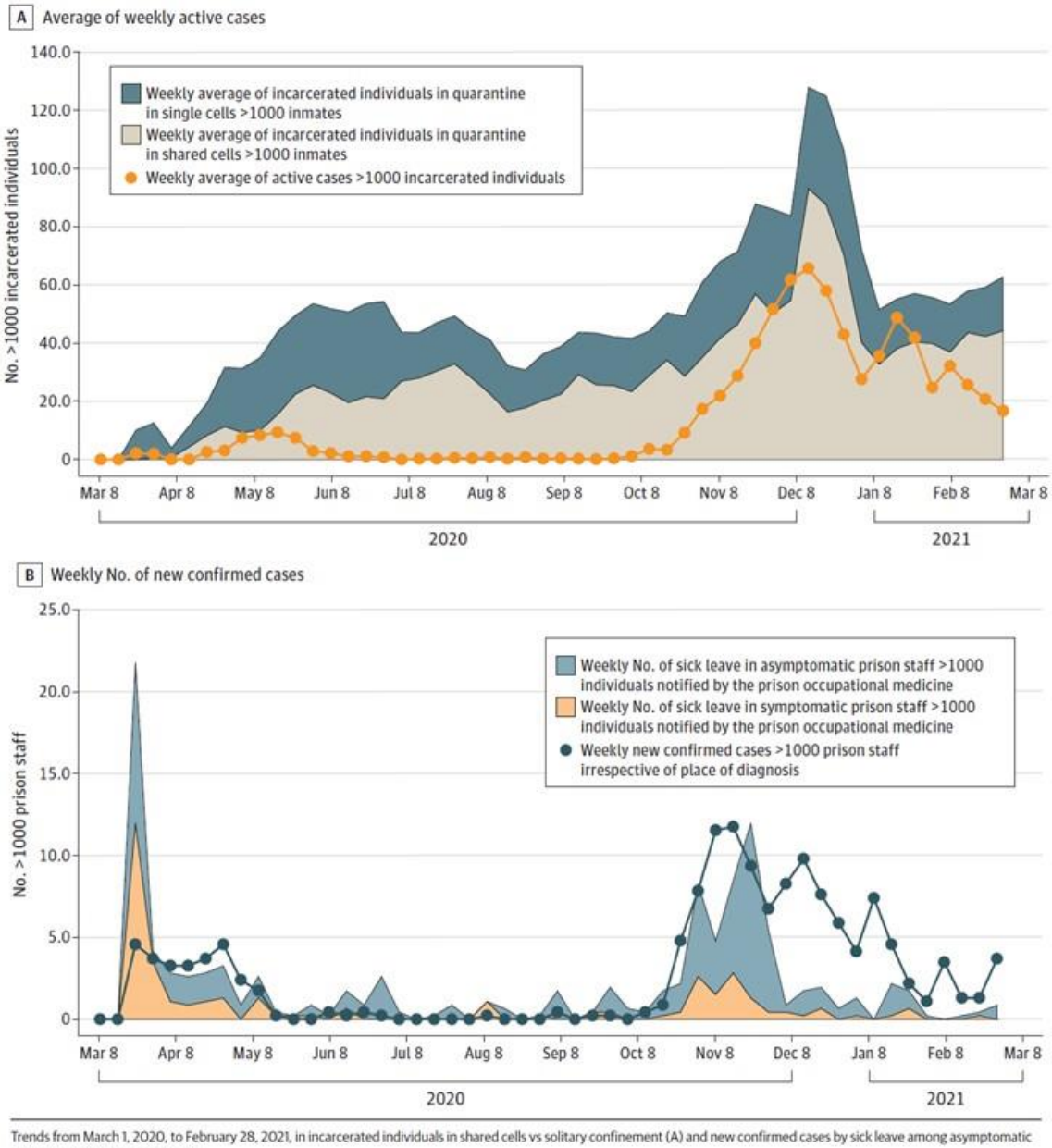
Containment measures

The measure of quarantine in single or shared cells was introduced on April 5th 2020 for PLP who were COVID-19 suspected or confirmed cases. The weekly average of PLP placed in quarantine increased until the end of June then had an irregular trend until the start of the second wave. Quarantine in single or shared cells was used evenly over time, except for the second epidemic wave when an increase in active cases (Figure 3.5A) led to an increase in PLP quarantined in shared cells (Figure 3.8A).

At the beginning of the pandemic, the number of asymptomatic and symptomatic individuals on sick leave notified by the prison occupational medicine (POM) was far greater than the number of confirmed cases (Figure 3.8B). Starting from April, the number of staff on sick leave dropped and became comparable with the number of confirmed cases. On the

contrary, during the second wave, the number of asymptomatic and symptomatic individuals on POM registered sick leave was lower than the number of confirmed cases (Figure 3.8B). No statistically significant association was observed between the incidence of new cases among PLP and prison-specific overcrowding (p = 0.43). The Spearman correlation among containment measures (the daily number of PLP in preventive isolation in single or shared rooms; the daily number of new asymptomatic or symptomatic sick leaves among staff) and the daily number of new COVID-19 cases among PLP and among staff members was significant when the long-term time effect was not removed, but became not significant after removing the long-term time effect.

Figure 3.8. Containment measures.

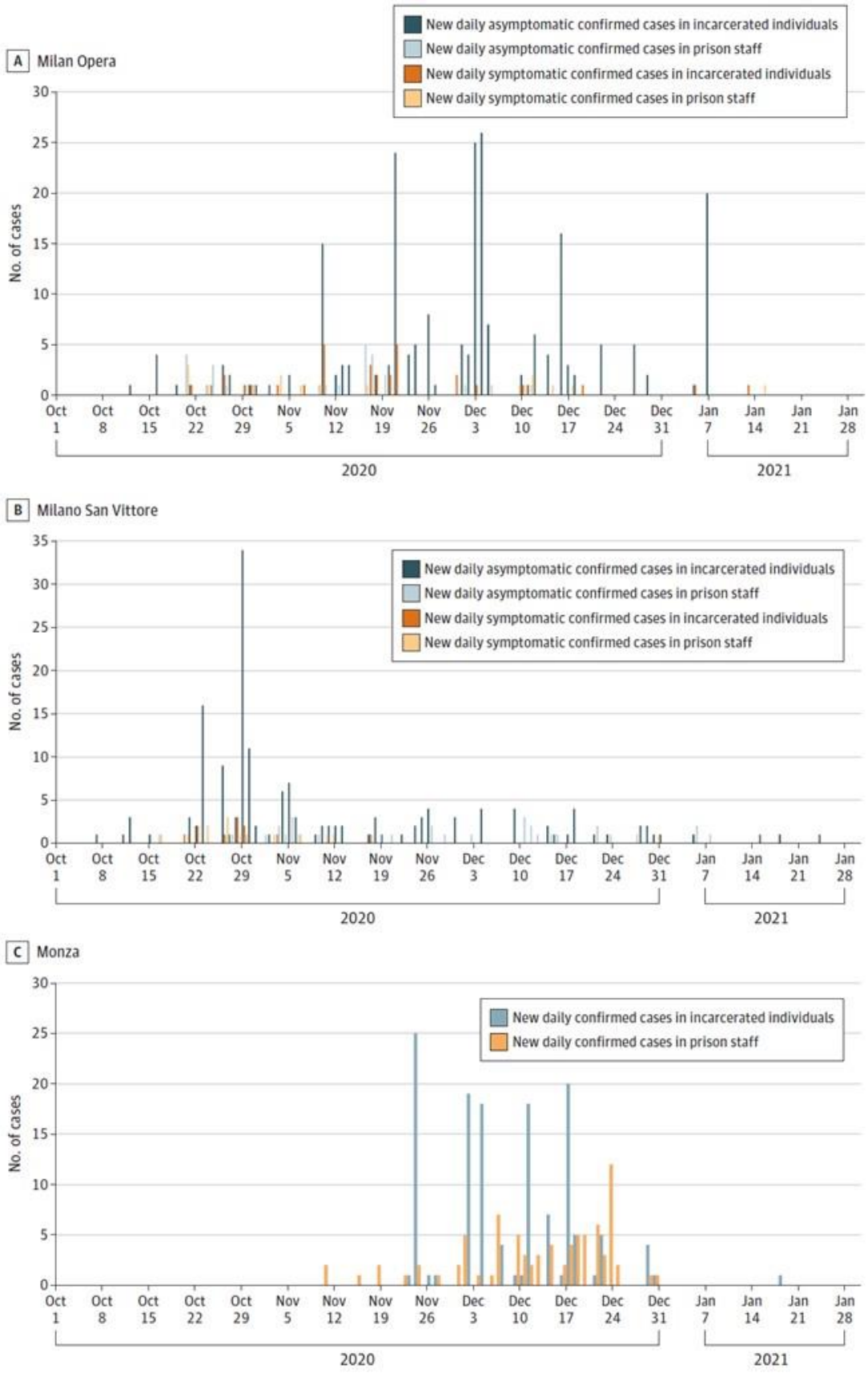


Trends from March 1, 2020, to February 28, 2021, in incarcerated individuals in shared cells vs solitary confinement (A) and new confirmed cases by sick leave among asymptomatic and symptomatic prison staff (B).

Insights from three prisons outbreaks

During October 2020-January 2021 in Milan Opera, 253 cases were confirmed among PLP, of which 12 were hospitalized and one died, and 45 cases were reported among prison staff. In Milan San Vittore, 165 cases were confirmed among PLP, of which 10 were hospitalized, and 52 cases were detected among prison staff. In Monza, 134 cases were confirmed among PLP of which 2 were hospitalized, and 83 cases were detected among prison staff (Figure 3.9). The occurrence and progression of the three outbreaks were heterogeneous and prison specific. The proportion of symptomatic confirmed cases in PLP and prison staff in Milan Opera prison were respectively 12.65% and 37.78% and in San Vittore prison were respectively 6.67% and 34.62%.

Figure 3.9 Daily confirmed cases among incarcerated individuals and prison staff in 3 prisons in the Lombardy Region. Confirmed cases of COVID-19 in the Milan Opera (A), Milan San Vittore (B), and Monza (C) prisons.



Discussion

Here we described the extent and dynamics of COVID-19 spread within the penitentiary system of Lombardy, the most populated Italian region, during the first 12-months of the global pandemic. While the evidence does exist from other countries, such as the USA (251), important differences in health care, prison systems and socio-demographic composition of the population make it challenging to translate such findings into the European context.

Among Italian regions, Lombardy was one of the most affected by COVID-19 during both the first and second waves. Yet, the COVID-19 epidemic among PLP was heterogeneous across the region and over time. During the first epidemic wave, COVID-19 spread within the prison system was largely contained and limited number of cases occurred among PLP (246). When comparing crude case rates, PLP were in fact protected from the infection as compared to residents in the region, even when considering the substantial level of under-ascertainment and underestimation that characterised the initial months of the pandemic (252). PLP enjoyed a higher coverage of testing and screening as compared to the general population during the first epidemic wave, as suggested also by the test positivity rates during the period. On the contrary, during the second epidemic wave the burden of COVID-19 among PLP was substantially higher, with over ten times more cases and an overall crude case rate greater than that observed among the general population. The distribution of PLP cases over time was also distinctive, with multiple peaks, likely due to outbreak episodes within different prison institutions. These observations confirm the assumption that PLP are at increased risk of infection from outbreak-prone airborne diseases (253). Indeed, detention facilities are often characterized by overcrowding, poor ventilation, poor access to healthcare services, and a high turnover of staff and incarcerated individuals which are features that facilitate the entry and spread of the virus (254). Due to the high prevalence of underlying health conditions, PLP are also at higher risk of developing severe clinical events when infected by SARS-CoV-2 (244,255).

The difference in the burden of COVID-19 among PLP between the two waves may be attributed to multiple factors, including the different degrees to which control interventions were implemented. Stringent measures were enforced early on with the establishment of national lockdown, the banning of virtually all activities in prison settings, including visits, and prison de-population (242,247). While effectively shielding PLP from SARS-CoV-2 entering prisons, these measures triggered revolts and may have worsened the mental health of prison residents (242,247,256). Since June 2020, containment measures were progressively relaxed in the community and the prison setting, with various degrees of limitation to inter-prison and prison/community movement being maintained throughout the period. Also, rates of incarceration, occupancy and overcrowding returned to pre-COVID-19level during the second epidemic wave, possibly increasing the overall risk of virus introduction and spreading within prison facilities (257).

We did not find any significant correlation between assessed control measures and the daily number of new COVID-19 cases among PLP during the study period. However, a previous assessment focussed on the first wave showed an association between number of cases and

quarantines in single rooms (246). During the second wave quarantines were mainly implemented in shared rooms due to space constraints, a practice that may have affected impact. Infrastructural constraints, old-fashioned buildings and overcrowding hinder the effective management of COVID-19, and potentially other communicable diseases outbreak in prison settings. Also, similar bundles of measures may have been implemented with different modalities or intensity in different prison institutions due to several reasons, including prison set-up, availability of staff or commodities, and PLP characteristics (e.g. long-term/short-term sentence). These, and possibly additional contextual factors, such as the level of virus circulation in the community or staff turnover, may have led to different distribution and intensity of intra-facility outbreaks.

Prison staff navigating between correctional facilities and their communities may incur in multiple occasions of acquiring the infection. According to our results and the existing literature (258), prison staff have an increased risk of testing positive for SARS-CoV-2 compared with the general population. From the distribution of cases over time, we observe that, during both the first and second epidemic waves, the spread of the virus in prison staff occurred earlier than in PLP. Therefore, it is likely that prison staff played a role in introducing and spreading SARS-CoV-2 in detention facilities. The prison staff may have multiple occasions for acquiring SARS-CoV-2 infection also during their occupational duties, such as escorting detainees to health services or supervising hospitalised PLP. Moreover, prison staff often live in the prison compound, sharing living space with colleagues (259). Intra-facility outbreak analysis showed a higher proportion of confirmed symptomatic cases in prison staff than in PLP. Since PLP have a worse health status (260), this result was unexpected and may possibly be explained by two reasons. First, there may have been an underestimation of symptomatic cases in PLP due to the lack of a systematic and continuous recording of follow up clinical data. Second, coverage of COVID-19 tests was lower among prison staff compared to PLP. This disproportion was already documented during the first wave (246). Asymptomatic cases among prison staff may have not been detected, further supporting the hypothesis that prison staff played a role in spreading SARS-CoV-2 into prison settings.

The study did not assess the impact of COVID-19 and related preventive measures on the mental health of PLP. However, a literature review suggests that factors such as fear of the virus, the effects of isolation, suspension of prison visits, and reduced access to mental health services likely had a negative impact on the well-being of incarcerated people (261). To effectively plan and manage future epidemic events in prison environments, it is essential to take into account the pandemic's impact on the mental health of PLP.

Study limitations

This study presents some limitations: (i) it was not possible to have information on individuals admitted, moved or released from prison during the study period. Therefore, the number of individuals who were in contact with the Lombardy detention system was approximated and most likely underestimate. Similarly, the number of prison staff was estimated from the regional social security/occupational health database and may not accurately reflect the actual number of people who worked in the prisons during the study period; (ii) the number of naso-pharyngeal swabs performed in prison staff was not available

and it was not possible to calculate the positivity rate; (iii) during the second wave, prison staff also had access to the naso-pharyngeal swab outside the prison facility and therefore, confirmed cases in this population may have been under-reported; (iv) as the general population had a lower test coverage compared to PLP and consequently a potential underestimation of the COVID-19 burden, the RR of PLP compared with the general population may be overestimated.

Conclusions

Despite the fact that healthcare provision in Italian prison is in the remit of the Ministry of Health (262), the lack of integrated healthcare and preventive services as well as surveillance activities between prison and community were an element of fragility in the pandemic response. The containment measures implemented during the first epidemic wave contributed to limit the spread of the infection. The burden of COVID-19 among PLP and prison staff during the second epidemic wave clearly demonstrated the challenges in implementing effective prevention and control measures in the prison setting as well as the increased risks and vulnerability of such population groups to airborne diseases. Prison settings and population need to be included in the framework of emergency preparedness, as well as in standard monitoring and surveillance activities.

Vaccinazione contro COVID-19 nelle comunità residenziali in Italia: priorità e modalità di implementazione ad interim: la comunità carceraria

Rapporto ISS COVID-19 • n. 16/2021
Link to the report.

Vaccination against COVID-19 in residential communities in Italy: priorities and ways of implementation ad interim: the prison community

The risk of outbreaks of respiratory infections in prisons is extremely high due to a multiplicity of factors comprising limited hygiene resources, overcrowding, inability to keep social distancing including the difficulties to isolate cases, poor ventilation, and lack of access to quality healthcare services (253).

Following the advent of SARS-CoV-2, in line with international guidelines, immediate IPC actions were implemented in Italian prisons, aimed at reducing the risk of introducing the aetiological agent into prisons and mitigating its transmission. However, the circulation of SARS-CoV-2 within Italian prisons was documented during the first epidemic wave and, with greater intensity, in the second (263). Epidemic outbreaks have highlighted the difficulties in effectively protecting the prison population through standard IPC and non-pharmaceutical measures taken, mainly due to the structural and logistical constraints of the prison system.

Considering these aspects, vaccination against SARS-CoV-2 is an essential component for the prevention and control of COVID-19 in the prison environment, as highlighted by documents of international organizations (264,265), and the scientific community (266,267). In the Italian national COVID-19 vaccination plan, both PLP and prison staff were included among the priority categories for vaccination (268).

Key characteristics of the population

Prison population

Prison populations are highly heterogeneous in terms of age, ethnicity, education level and health literacy. Moreover, the characteristics of prison populations differ depending on the type of prison institution. Correctional facilities, dedicated to individuals awaiting sentencing or with short sentences, are characterised by a younger population and a higher percentage of foreign inmates than detention facilities, where individuals with longer sentences are held (269). As of 28 February 2021, of the 53 697 inmates in Italian prisons, 32.2% (17,306) were foreign nationals (270). Foreign nationals typically have reduced access to the healthcare system, which can hardly guarantee them appropriate care and continuity of care (271,272).

Moreover, the prison population in Italy is characterised by a high burden of acute and chronic diseases, including NCDs (244,255), (known to be related to a low socioeconomic position of the individual) and embody the COVID-19 syndemic concept, i.e. the biological, economic and social interactions between NCDs and COVID-19 increase a person's susceptibility to infection and worse health outcomes (144).

Prisons can provide an opportunity for the NHS to take care of people who are otherwise difficult to reach while in the community.

In addition to being heterogeneous, the prison population is extremely dynamic with an average detention time in Italy of eight months (273). The limited time spent in prison and the high turnover of PLP facilitate the transmission of SARS-CoV-2 from prisons to the community and vice versa.

Role of custodial staff

Prison staff constitute a population with a high risk of contracting SARS-CoV-2, as in addition to being exposed to the infectious risk in prison, they sometimes reside in barracks or other service accommodations on the institution's premises. In several cases, they live with their families or share living space with colleagues. During the most critical months of the first epidemic wave, in Lombardy, the percentage of prison staff absent due to illness reached peaks of 15% (263). However, prison staff are essential workers and their absences should be kept to a minimum to ensure the proper functioning of the detention facilities. In addition, prison staff move in and out of prison premises daily, which leads to an increased risk of the introduction and spread of SARS-CoV-2 within prisons.

Health and civilian staff

In addition to the custodial staff, other professionals such as doctors, nurses, social workers and psychologists also work within the prison facilities. All of them are exposed to the same service problems with entering, leaving and, often, staying overnight in the facilities. It is likely that these staff, for their specific duties, which cannot have suspensions, may be the ones most at risk of contracting the infection, as is also the case in the community. Other

figures working in the prison system such as religious ministers, lawyers, volunteers, teachers, etc. have had their access authorisation suspended for many months.

Implementation of COVID-19 vaccination in prison communities

Objectives of COVID-19 vaccination in prison communities

Vaccination against COVID-19 in prison communities has several objectives:

I. the vaccination of the prison population, characterised by a high burden of chronic diseases, reduces the risk of severe illness and death from SARS-CoV-2 infection;
II. offering COVID-19 vaccination in prisons makes it possible to vaccinate segments of the population that would be more difficult for community health services to intercept
III. the vaccination of custodial staff, by enabling a reduction in sick leave, ensures continuity and the proper functioning of detention facilities
IV. vaccinating custodial staff and other prison staff, including healthcare staff, reduces the risk of introducing the virus inside prison facilities and in the barracks where some of these essential workers live
V. vaccinating people living and working in prisons protects the entire community and contributes to the achievement of population immunity. In fact, the high turnover of PLP, together with the daily access of prison staff to prison premises, would favour the transmission of SARS-CoV-2 from prisons to the community and vice versa in the occurrence of an epidemic outbreak.

The issue of COVID-19 vaccination in prisons has been followed with a constant commitment by the national guarantor of the rights of persons deprived of their liberty. The guarantor himself indicated as a priority objective to make prisons 'COVID-19 free' by proceeding with vaccinations institution by institution.

Planning and priority criteria

The COVID-19 Vaccine FAQs in Correctional and Detention Centres (updated 16 February 2021) by the US Centers for Diseases Control and Prevention considers issues related to vaccination in prison (274):

1. The recommendation is to vaccinate staff and PLP at the same time, and in any case to vaccinate in as short a timeframe as possible, due to the common high risk of disease. Vaccination coverage achieved almost at the same time within the prison population and the prison staff of each institution is an effective form of prevention both for those inside and outside the facility (275).
2. Particular attention must be paid to organising the administration of vaccines to staff to establish the staff rotation so that it is compatible with the need to guarantee continuity of services throughout the vaccination period. The schedule must therefore take into account an appropriate post-vaccination period of at least one day due to possible side effects and the high level of stress (276).

For PLP, it should not be necessary to establish priority criteria or do further planning on the basis of the facility or individual risk factors. Individual-level factors for prioritising vaccination include older age, high-risk medical conditions and risk of exposure to other PLP

infected with SARS-CoV-2. The small number of PLP or working within an average prison allows vaccinations to be scheduled within even very tight timeframes, and this reduces or nullifies the need to prioritise particular groups within this context. It must be remembered that even those who have contracted COVID-19 must be vaccinated starting three months after the documented infection and by the sixth month after the infection with a single dose according to the recommendations of the Ministry of Health (268).

Communication, information and informed consent

Some issues, although present in the general population, require increased attention in the prison environment. To prevent the perception that non-compulsory vaccination is unnecessary or even dangerous, clear and comprehensive information is essential. The role of communication is crucial for increasing confidence in vaccination and is certainly an essential part of the vaccination strategy. The prison and health administrations must collaboratively develop and implement a clear communication strategy to address the 'vaccination hesitancy determinants' (such as beliefs, attitudes, and socio-cultural factors) that can lead to vaccine refusal.

One significant obstacle is the language barriers and cultural diversity among foreign PLP. These difficulties can and must also be overcome with the involvement of cultural mediators who can make the information on the vaccine accessible to the person using language and modalities specific to different cultural contexts. Another communication tool could be visual communication through simple, colourful pictures describing the procedure and the objectives of vaccination.

The occurrence of side effects, such as soreness at the injection site, fever, and widespread joint pain —already documented in the relevant factsheets— could be a decisive factor in future vaccine refusals. Therefore, special attention must be given to this issue, as it may lead to post-vaccination hesitancy among other PLP or staff. Finally, it is essential to remember that vaccination is a voluntary act that requires the recipient's awareness. They need to sign an informed consent form, of both the risks of the disease and the risks and benefits of vaccination.

Mobility and tracing

Another problem peculiar to prison is the mobility of people from one institution to another, from detention to liberty and arrests from liberty. This complicates the vaccination strategy, given that some currently available COVID-19 vaccines provide for two doses, and the second dose, of the same type of vaccine as the first, must be administered 3 to 12 weeks after the first, depending on the type of vaccine.

At the organisational level, the second dose can be planned for persons who will stay in the facility long enough to receive it, but it becomes a challenge for those about to be released or transferred. In addition, health and justice facilities should share a tracking and identification system to avoid, for instance, the person being vaccinated several times in different prison communities, especially when it comes to inter-agency and inter-regional mobility, or not receiving the next dose after the first one.

Certainly, the use of single-dose vaccines should be considered to solve at least part of these problems.

Other situations of limitation of liberty

Special attention should be paid to some groups of persons with reduced personal liberty who should be taken into account in national legislation. They are represented where semi-freedom is foreseen (Articles 48-50 O.P.), admission to external work for detainees (Article 21 O.P.), semi-detention (Articles 53 and 55 of Law 689/1981), detention with permanence (even if brief) of juveniles in First Reception Centres (Article 18-bis paragraph 4 of Presidential Decree 22 September 1988 no. 448), the Juvenile Penitentiary Institutes (Presidential Decree 448/1988, DL.vo 121/2018), the Ministerial Communities for minors often attached to the First Reception Centres (art.22 of Presidential Decree 448/1988) and the Residences for the Execution of Security Measures newly established under Law 9/2012.

It is therefore clear from the above that it is advisable to consider the individual prison institution with all its specificities with respect to the rest of the territory, but also between institutions, as a particular entity to be taken care of overall and simultaneously in its various components.

Its small size compared to the rest of the territory and its structural confinement favour a comprehensive type of intervention using the usual categories present in prison facilities:

- persons detained or with restrictions of personal freedom;
- prison management (director, educators, ministerial psychologists, workers) and custodial staff;
- anyone entitled to work in prison (health, voluntary work, religious, etc.).

COVID-19 vaccine in prison: a not-to-be-missed opportunity to promote access to vaccination in adolescents

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Link to the article.

In May 2021, the European Medicine Agency and the United States' Food and Drug Administration approved the use of COVID-19 vaccine Comirnaty to 12- to 15-year-olds (277). As a result, the vaccination campaign for adolescents has begun in many countries (277,278). Meanwhile, the Strategic Advisory Group of Experts on immunization (WHO) calls for ensuring that vaccine prioritization within countries takes into account the needs of those groups that, due to underlying social, ethnic, geographic or biomedical factors, are at greater risk of getting infected or suffering COVID-19 most severe consequences (279). Since the risk of transmission of SARS-CoV-2 is considerably higher in prisons and detention facilities (266), adolescents who are detained in juvenile institutions should be given priority for vaccination.

Detained adolescents often come from marginalized groups of society with a considerable burden of ill health rooted in poverty and discrimination, and with limited access to healthcare, perfectly embodying the COVID-19 syndemic concept (144). The objectives of vaccinating adolescents in juvenile institutions include both the direct benefits to their own health and the indirect benefit of reducing onwards transmission of SARS-CoV-2 within the prison community, including prison staff, and in the community they belong. Furthermore, the implementation of the COVID-19 vaccine in juvenile institutions is essential to uphold the principle of equity of care and to guarantee the right to health for those deprived of liberty, leaving no one behind (280).

COVID-19 vaccination can also offer an opportunity to promote access to integrated care for detained adolescents, including other vaccinations and preventive services. Among adolescents transiting the juvenile prison system, a combination of age, risky health-related behaviours, overcrowded living conditions, contribute to increased vulnerability to vaccine-preventable diseases such as pertussis, human papillomavirus, hepatitis B, meningococcal disease, and others (281).

Correctional facilities offer the possibility to provide vaccination services to these adolescents, who may not otherwise engage with or have access to preventive health services.

Some of the main challenges towards vaccinating adolescents detained in juvenile institutions include: (i) lack of attention paid to children/adolescents in detention; (ii) low perception of their health risk; (iii) the absence or suboptimal link between healthcare provision and information systems in detention facilities and in the community; (iv) obtaining consent for vaccination from their parents or legal guardians (282). The latter barrier has been overcome mainly through two strategies: either the director of the juvenile penitentiary institution held the role of the legal guardian of the detained adolescents, or the detained minors directly express their consent to be vaccinated (Table 3.2).

Table 3.2. Indication of who is entitled to express consent for COVID-19 vaccination in detained adolescents and the status of the vaccination campaign in the juvenile institutions involved in the European research project: "Reaching the hard-to-reach: Increasing access and vaccine uptake among prison population in Europe – RISE-Vac" co-funded by the EU health programme.

Country	Consent for adolescents < 16 express by	Consent for adolescents ≥ 16 express by	COVID-19 campaign status
Italy	Director of the penitentiary	Adolescents themselves	Started and ongoing
France	Both parents. In adolescents with very high-risk conditions, consent by one of the two parents is sufficient.	Both parents. In adolescents with very high-risk conditions, consent by one of the two parents is sufficient.	Started but waiting for parental authorisation.
Germany	Legal guardian (at the municipal unit of social affairs)	Adolescents themselves	Started and ongoing
England	Legal guardian or adolescents themselves if deemed 'Gillick competent'	Adolescents themselves	Ongoing for clinically vulnerable aged 16 years and over and for all those aged 18 years and over
Cyprus	Adolescents <16 not present	Adolescents themselves	Started and ongoing
Moldova	Persons under 18 are not subject to the vaccination process	Persons under 18 are not subject to the vaccination process	Started and ongoing for all those aged 18 years and over

For most adolescents, prison stay is a transitional period in the course of their lives; therefore, coordination between detention facility and community healthcare services is essential to ensure accurate and timely monitoring of dose administration and completed vaccination schedules. The lack of efficient monitoring systems and integrated prison-community immunization information system not only fails to effectively protect people receiving only a single dose from vaccine-preventable diseases, but, in the case of the COVID-19 vaccine, may hinder the acquisition of the immunization passport. In many countries, starting in January 2021, an immunization passport has been required for travel and participation in social, public, and economic activites (283); therefore, to prevent exacerbating existing societal inequalities and marginalisation, it should be made available and accessible to all, including adolescents in prisons.

Universal access to available vaccines throughout the life course is a regional and global objective (284). Ensuring access to COVID-19 vaccines in juvenile facilities represents an opportunity to set up, test and implement tailored vaccination services that could be extended beyond the current pandemic and the sole COVID-19 vaccine, in order to contrast health inequities, enhance preparedness and protect public health.

Conclusion

The research activity presented in this doctoral dissertation provided an opportunity to explore the potential of using existing data sources to monitor the health of people in vulnerable situations. Specifically, this project focused on exploring the use of different administrative data to assess the impact of the COVID-19 pandemic on different population groups, including persons with a high level of individual socio-economic deprivation in the Apulia region, persons residing in LTCFs in the Apulia and Tuscany regions, and PLP and prison staff in the Lombardy region. This research provided a proof of concept demonstrating that with the willingness and analytical capacity to extrapolate evidence from existing administrative data, health outcomes can be monitored even in neglected populations and extremely fragile. Health surveillance in these populations enables governments and other stakeholders to support evidence-informed action to tackle health inequities.

Beyond the conclusions related to the individual research questions discussed at the end of each chapter, the findings of this dissertation have wider practical and theoretical implications.

Big data are a powerful new resource for public health research. The excitement around big data emerges from the recognition of the opportunities it may offer to advance our understanding of the relationship between human behaviour, social phenomenon and health in a way that has never been possible before. Despite administrative data having been largely neglected from many of the mainstream discussions of big data, administrative big data can be fruitfully harnessed for purposes of population health research. In contrast to small-scale research data, administrative data involve the assemblage of comprehensive data files comprising virtually entire populations over time. In addition, in places where for structural and operational reasons, conducting solid research is difficult, such as in prisons, the use of administrative data may be the only way to investigate health inequities.

The potential of administrative big data for improving health is enormous but, at the same time, we face a wide range of challenges to overcome urgently. HIS and databases for evaluating health determinants are diverse and fragmented. There is a lack of harmonization of data formats, processing, analysis, and data transfer, which leads to incompatibilities and lost opportunities.

For instance, in Italy there is no official health information system to monitor the health of PLP and the health services these people have access to. Each prison has its own data information system, which in some cases may also be paper-based. To carry out the study presented in Chapter Three on the direct impact of COVID-19 on PLP in the Lombardy region, it was necessary to retrieve data from the prison superintendence and organise them into a single dataset.

To enhance research on health inequalities and the health of vulnerable populations health data should be collected in a systematic electronic format. In addition, unique and consistent identification numbers should be available to enable database linkage. In some northern European countries, such as Norway, Finland and Sweden an effective infrastructure is already in place for the linkage and sharing of administrative data for research purposes. The availability of consistent unique identification numbers in these countries is a major advantage for the facilitation of administrative data research. In countries like Italy, the lack of consistent identification numbers across administrative

systems means that linking together the pieces of information required to answer a social epidemiology research question is usually much more complex.

Determining the burden of disease in marginalised and vulnerable populations remains challenging because membership of such populations (as having experienced incarceration, or being homeless) is not recorded in most demographic and health information systems. However, recording this information in administrative data is essential for studying small population subgroups and rare events.

For some populations in vulnerable situations, such as foreign nationals temporarily present in Italy (i.e. refugees or migrants), data are not routinely collected and obtaining information on the health of these people is extremely difficult. A scan of public health data shows substantial inequalities in the inclusion of those populations that are most at risk of having health inequalities. This can lead to an exacerbation of health inequalities. In the analysis of social science and health data, the overall exacerbation consequences of social exclusion are costly, including the exacerbation of poverty and the reduction of human capital. It also hinders the design of culturally coherent solutions that could be more easily adopted in specific communities.

The mobility of people within the EU has increased massively in recent years. Some of the people crossing the borders of European states are part of populations in vulnerable situations (i.e. refugees). However, European health systems and databases are different and fragmented. There is an urgent need to harmonise European health systems, not only to track vulnerable populations on the move, but also to carry out common surveillance to prevent health emergencies that, as COVID-19 has taught us, do not respect individual country borders.

The extensive use of administrative big data in public health surveillance and research is often hampered by legal barriers. The GDPR has expanded the application of privacy law by including “pseudonymized” data in the definition of personal data. At the same time, it allows individual EU Member States to regulate the use of broad informed consent and to define exceptions. In this way, the GDPR has left the public health community and researchers without a clear basis to rely on for processing personal data. The situation is even more complicated for the cross-border transfer of personal data. There are broad differences within and across Europe concerning privacy protection and data-sharing policies. Further guidance would be helpful to narrow the complexity surrounding the processing of personal data.

This dissertation demonstrates that, when effectively repurposed for scientific research, administrative data can drive high-quality empirical investigations. There is an urgent need to enhance data collection, transfer, reporting, analysis, and interventions related to environmental and social determinants of health to reduce health inequities.

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Scientific Publications

Publications Mentioned in the PhD Thesis

1. **Mazzilli** S, Scardina G, Collini F, Forni S, Gianolio G, Bisceglia L, et al. Hospital admission and mortality rates for non-Covid diseases among residents of the long-term care facilities before and during the pandemic: a cohort study in two Italian regions. J Public Heal [Internet]. 2023;(0123456789). Available from: https://doi.org/10.1007/s10389-023-01925-1

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Publications Under Review

1. **Mazzilli** S, Aslam MK, Akhtar J, Tsekeri A, de Glanville W, Zou W, et al. Feasibility study of self-testing for HCV in a high-prevalence urban informal settlement in Karachi, Pakistan. Journal of Viral Hepatitis

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I sacriféizi

Se mè ò studié
l'è stè par la mi ma,
ch'la fa una cròusa invéci de su nóm.

S'a cnòss tótt al zità
ch'u i è in chèva e' mònd,
l'è stè par la mi ma, ch'la n'à viazè.

E ir a l'ò purtèda t'un cafè
a fè du pas, ch'la n' vàid bèla pió lómm.
- Mitéiv disdài. Csa vléiv! Vléiv un bignè?

I sacrifici

Se ho potuto studiare
lo devo a mia madre
che firma con una croce.

Se conosco tutte le città
che stanno in capo al mondo
è stato per mia madre, che non ha mai viaggiato.

Ieri l'ho portata in un caffè
a far due passi
perché quasi non ci vede più niente
- Sedetevi, qua. Cosa volete? Un bignè?

Tonino Guerra

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