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## TITOLO TESI / THESIS TITLE

# Analysis of hospital activity during the COVID-19 pandemic: population-based evidence from highly impacted provinces in northern Italy

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# Abstract

At the close of 2019, the COVID-19 pandemic caught the world off guard, promptly becoming the most severe health crisis of the past 100 years. The rapid surge in cases worldwide has impacted health systems, which, together with restriction measures such as lockdowns, has caused substantial disruptions in the provision of care for non-COVID-19 patients.

To understand the extent of this indirect impact on the provision of hospital care for other conditions, this research investigated hospital and emergency department admissions during the pandemic period (up to June 2021) in the areas of Bergamo and Brescia, two densely populated provinces in northern Italy which were hardly hit during the first epidemic wave in February-April 2020.

Longitudinal retrospective analyses were conducted using time-series data to model variations in hospitalizations and emergency department visits over the study period, using 2017–2019 as a reference. The indirect impact of COVID-19 on hospital care pathways was also evaluated by fitting time-series of their proxies (i.e., hospital access, hospitalization and mortality) of high-volume, non-deferrable clinical conditions. Furthermore, data on COVID-19-attributable excess of health events (hospital admissions and emergency department visits) were analysed through epidemic surveillance systems to learn whether there was evidence of SARS-CoV-2 transmission in Bergamo and Brescia provinces in the period preceding the recognized epidemic outbreak in late February 2020 using healthcare administrative database.

This dissertation provides complete estimates of hospital activity during the pandemic period and accurately details the impact that COVID-19 has had on the health services in Bergamo and Brescia, as well as on the Lombardy Regional Health Service in general. The results provide population-based evidence that expands our understanding of the disruptions caused by the COVID-19 pandemic; findings could also be used to inform policy and management decisions to ensure that the most appropriate health service responses and preparedness are implemented.

# **Abstract** *(ITALIANO)*

La pandemia da COVID-19, sviluppatasi in Cina alla fine del 2019, ha subito rappresentato la più devastante crisi sanitaria dagli inizi del XX secolo. La rapida trasmissione di SARS-CoV-2 e le restrizioni imposte per tenere sotto controllo il contagio hanno causato interruzioni e ritardi nell'assistenza a condizioni cliniche diverse dal COVID-19 stesso.

Al fine di meglio comprendere l'impatto della pandemia sull'assistenza ospedaliera, questa ricerca è andata ad esaminare gli accessi ospedalieri e in pronto soccorso dagli inizi della pandemia (e fino a giugno 2021) nelle province di Bergamo e Brescia, due aree primariamente e duramente colpite durante la prima ondata pandemica tra febbraio e aprile 2020.

Sono state condotte analisi longitudinali retrospettive sulle serie storiche degli accessi in ospedale e pronto soccorso, usando il triennio 2017-2019 come riferimento. L'impatto indiretto del COVID-19 sui percorsi assistenziali ospedalieri è stato ulteriormente esaminato attraverso *proxy* di cura (accessi in ospedale, ricoveri e mortalità) di condizioni cliniche caratterizzate da alti volumi e necessità di assistenza in emergenza-urgenza. Infine, i flussi amministrativi degli eventi che hanno mostrato un eccesso dovuto alla pandemia sono stati analizzati con strumenti di sorveglianza epidemica per stabilire se fosse possibile tracciare eventuali *cluster* epidemici nei territori bergamaschi e bresciani prima del riconoscimento dei primi casi di infezione alla fine di febbraio 2020.

Nel complesso, questa tesi offre stime esaustive dei cambi nell'attività ospedaliera nel periodo pandemico, descrivendo accuratamente l'impatto che il COVID-19 ha avuto sul sistema sanitario nelle province di Bergamo e Brescia e, più ampiamente, sul Servizio Sanitario Regionale lombardo. I risultati forniscono, quindi, un'evidenza basata su dati di popolazione che aiuta a comprendere i disagi causati a pazienti e utenti dei servizi di salute. Le conclusioni di questo lavoro possono, quindi, servire da riferimento per orientare decisioni strategiche nella futura organizzazione dei servizi sanitari—non solo ospedalieri—nonché per sviluppare elementi di preparazione e risposta a COVID-19 e ad altri possibili eventi a carattere epidemico.

# Acknowledgements

I would like to thank the following people, without whom I would not have been able to complete my PhD journey.

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I am deeply indebted to the VICES-SMIRE team, especially to Sara Conti, Fabiana Madotto and Carla Fornari, whose insight and knowledge into the subject matter steered me through this research.

And my biggest thanks to my family for all the support you have shown me through the culmination of these three years.

# List of abbreviations

| Abbreviation | Definition |
|---|---|
| 95% CI | 95% Confidence Interval |
| ACE-2 | Angiotensin-Converting Enzyme 2 |
| AIDS | Acquired Immunodeficiency Syndrome |
| AIFA | Italian Medicines Agency (IT: Agenzia Italiana del Farmaco) |
| APC | Antigen-presenting Cell |
| ARDS | Acute Respiratory Distress Syndrome |
| BDA | Banca Dati Assistiti (registry of patients with chronic diseases) |
| C-PAP | Continuous Positive Airway Pressure |
| CAC | COVID-19-associated coagulopathy |
| CDC | US Centers for Disease Control and Prevention |
| CFR | Case–Fatality Ratio |
| CKD | Chronic Kidney Disease |
| CNS | Central Nervous System |
| COPD | Chronic Obstructive Pulmonary Disease |
| COVID-19 | Coronavirus Disease 2019 |
| CVD | Cardiovascular Disease |
| DAD | Diffuse Alveolar Damage |
| DRG | Diagnosis Related Group |
| EARS | Early Aberration Reporting System |
| ECDC | European Centre for Disease Prevention and Control |
| ECMWF | European Centre for Medium-Range Weather Forecasts |
| ED | Emergency Department |
| EMA | European Medicines Agency |
| EOHSP | European Observatory on Health Systems and Policies |
| HAD | Healthcare Administrative Database |

| | |
|---|---|
| HCoV | Human Coronavirus |
| HCRU | Healthcare Resource Utilization |
| HDR | Hospital Discharge Records (IT: Scheda di Dimissione Ospedaliera, SDO) |
| HIV | Human Immunodeficiency Virus |
| HPA | Health Protection Agency (IT: Agenzia di Tutela della Salute, ATS) |
| ICD-9 | 9th revision of the International Statistical Classification of Diseases |
| ICD-9-CM | ICD-9 Clinical Modification |
| ICU | Intensive Care Unit |
| IFN | Interferon |
| Ig | Immunoglobin |
| IHEM | Institute for Health Metrics and Evaluation |
| IL | Interleukin |
| ILI | Influenza-like Illness |
| IQR | Interquartile Range |
| IRR | Incidence Rate Ratio |
| ISS | Italian National Institute of Health |
| ISTAT | Italian National Institute of Statistics (IT: Istituto Nazionale di Statistica), |
| LHS | Lombardy Regional Health Service |
| LMWH | Low Molecular Weight Heparin |
| MDC | Major Diagnostic Category |
| MERS | Middle East Respiratory Syndrome |
| MERS-CoV | Middle East Respiratory Syndrome Coronavirus |
| MI | Acute Myocardial Infarction |
| MIS-A | Multisystem Inflammatory Syndrome in Adults |
| MIS-C | Multisystem Inflammatory Syndrome in Children |
| NCD | Noncommunicable Disease |
| NHS | National Health Service |
| NIH | US National Institute of Health |
| NPI | Nonpharmaceutical Interventions |
| NSAID | Non-Steroidal Anti-Inflammatory Drug |
| PANGO | Phylogenetic Assignment of Named Global Outbreak Lineages |

| | |
|---|---|
| PNRR | National Recovery and Resilience Plan |
| PSM | Propensity Score Matching |
| $R_0$ | Basic Reproduction Number (or R naught) |
| $R_e$ or $R_{eff}$ | Effective Reproduction Number |
| RBD | Receptor-Binding Domain |
| RNA | Ribonucleic Acid |
| RR | Relative Risk |
| RT-PCR | Reverse Transcription Polymerase Chain Reaction |
| mRNA | messenger Ribonucleic Acid |
| SARI | Severe Acute Respiratory Infection |
| SARS | Severe Acute Respiratory Syndrome |
| SARS-CoV-1 | Severe Acute Respiratory Syndrome Coronavirus 1 |
| SARS-CoV-2 | Severe Acute Respiratory Syndrome Coronavirus 2 |
| SII | Systemic Immune-Inflammation Index |
| SD | Standard Deviation |
| T1DM | Type 1 Diabetes Mellitus |
| T2DM | Type 2 Diabetes Mellitus |
| TMPRSS2 | Type 2 Transmembrane Serine Protease |
| TNF | Tumour Necrosis Factor |
| VOC | Variant of Concern |
| VOI | Variant of Interest |
| WHO | World Health Organization |
| WHO Europe | World Health Organization – Regional Office for Europe |

# Table of contents

# Preamble

*Project motivation*

The emergence and spread of communicable diseases with pandemic potential has afflicted humanity multiple times (Diamond, 1997). Agricultural communities developed as recently as 10,000 years ago facilitated the spread of infections and epidemics. Smallpox is believed to be the first such example, although the earliest evidence of skin lesions consistent with disease was recently found in Egyptian mummies, including the mummy of the pharaoh Ramses V, who died in 1157 BC (Tulchinsky, 2018). Other diseases that appeared during agrarian life (or earlier) still affect human societies, such as malaria and tuberculosis.

The first evocative narrative of a possible epidemic has been dated to around 1350 BC in ancient Egypt and is based on a letter in the Amarna tablets (Amarna letters EA 244) in which the mayor of Megiddo tells Pharaoh Amenhotep III that his city was 'consumed by death, by plague, by dust' (Hanson, 1995).

In the 5th century BC, Thucydides described the cross-country spread of a νόσος—termed 'the plague of Athens' (430–427/425 BC)—that ''ἤρξατο δὲ τὸ μὲν πρῶτον, ὡς λέγεται, ἐξ Αἰθιοπίας τῆς ὑπὲρ Αἰγύπτου, ἔπειτα δὲ καὶ ἐς Αἴγυπτον καὶ Λιβύην κατέβη καὶ ἐς τὴν βασιλέως γῆν τὴν πολλήν. ἐς δὲ τὴν ᾿Αθηναίων πόλιν ἐξαπιναίως ἐσέπεσε *[…]*'[1], which has been recognized as typhus or viral haemorrhagic fever (Olson, 1996).

Several large pandemics have subsequently been documented over the course of human history. Owing to its impact, the COVID-19 pandemic has been ranked amongst the five most deadly (considering both the direct and indirect impacts on general population mortality; see *section* 2.2). The Black Death has been the deadliest pandemic, with *Yersinia pestis* killing approximately 75–200 million people in Eurasia and North Africa between 1346 and 1353. Other major pandemics were the 1918 Spanish H1N1 influenza, which caused between 17 and 50 million deaths globally (although possibly up to 100 million) during 2 years, the Plague of Justinian, the first confirmed bubonic plague that killed an estimated 15–100 million people in North

[1] Thucydides. *History of the Peloponnesian War*, Bk. 2, chs. 48. EN: «*The disease is said to have begun south of Egypt in Aethiopia; thence it descended into Egypt and Libya, and after spreading over the greater part of the Persian empire, suddenly fell upon Athens*» (English translation by Benjamin Jowett, 1881). Of note, in 'ἐς δὲ τὴν ᾿Αθηναίων πόλιν', the genitive of the periphrasis emphasizes the 'anticipation' of the death; in 'ἐξαπιναίως ἐσέπεσε', the alliteration between the adverb and predicate reflects the completely unexpected character of the circumstances.

Africa, Europe and West Asia (541–549 AD), and the ongoing global HIV/AIDS pandemic, which claimed approximately 40.1 million lives from 1981 to 2021 (Harbeck et al., 2013; Rodríguez-Frías et al., 2021; World Health Organization [WHO], 2022*a*).

Since 2020, Italy—like the rest of the world—has been experiencing one of the most severe pandemics in recent history, in which a devastating health crisis has been associated with vast detrimental effects on society, the economy and people's personal lives.

From a public health perspective, a broader understanding of COVID-19—including its wider impact on the management of other conditions as well as on the healthcare system's response and resilience—is crucial to take the most appropriate actions to contain disease transmission and deal with the consequences of the illness. Indeed, the implementation of public health and policy measures depends on the extent of COVID-19 cases and the associated healthcare burden. This work identified and collected research on the indirect impacts of SARS-CoV-2 infection and COVID-19 using population-based evidence from the epicentre of the Italian outbreak in 2020.

*Project objective and definition*

This work aimed to evaluate the changes in hospital care for non-COVID-19 diseases during the pandemic in the provinces of Bergamo and Brescia, two densely populated, large geographical areas in northern Italy.

The pandemic has had major impacts on health services and healthcare facilities. In early 2020, hospitals quickly became overwhelmed by the increasing number of patients requiring respiratory and intensive care. Hospital rearrangements were rapidly needed, and facilities and professionals became overloaded. Stay-at-home orders and the fear of contagion further inhibited people's access to healthcare facilities and services. Globally, the COVID-19-related reductions in health services have resulted in substantial disruptions in the provision of care for non-COVID-19 conditions (Ferrara and Albano, 2020).

Lombardy registered the highest COVID-19 burden in Italy and Europe in the first months of the pandemic in 2020. The first official case was confirmed on February 21, 2020. Some provinces, such as Bergamo, Brescia, Cremona, Lodi and the metropolitan area of Milan, were rapidly and severely hit by COVID-19. Among others, the areas of the Bassa Val Seriana, a valley in the province of Bergamo, and the municipalities of Montichiari and Orzinuovi in Brescia registered fast rises in SARS-CoV-2 infections and COVID-19 deaths. The sudden outbreaks occurring in

these areas and the respective provinces caught local healthcare services off guard and thus had major impacts on hospital activities.

This work describes the activities that were initiated in the first pandemic weeks. Obtaining information from the healthcare administrative databases maintained by the local Health Protection Agencies (HPAs) that serve the epicentre of the Italian and Lombard outbreak has been key to understanding the exact extent of the impact COVID-19 has had on health services. The findings of this study could be used to inform policies and action plans to improve service responses and resilience.

# Chapter 1

# Background on COVID-19

*1.1 Introduction*

At the close of 2019, a cluster of patients with pneumonia of unknown origin was linked to the Huanan Seafood Market, a live animal and seafood market in Wuhan, the capital of Hubei Province in Central China (Pekar et al., 2022; Worobey et al. 2022). The analyses of bronchoalveolar lavage fluid specimens from those patients revealed the presence of a novel coronavirus strain belonging to the family *Coronaviridae* that fell within the subgenus *Sarbecovirus* of the genus *Betacoronavirus* (Zhu et al., 2020). Initially named 2019-nCoV, the Coronaviridae Study Group of the International Committee on Taxonomy of Viruses recognized this virus as forming a sister clade to the prototype human and bat severe acute respiratory syndrome coronaviruses (SARS-CoVs) and thus designated it as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in early February 2020 (Coronaviridae Study Group of the International Committee on Taxonomy of Viruses, 2020). On February 11, 2020, the WHO announced the official names for both the virus and the disease associated with it, coronavirus disease 2019, abbreviated as COVID-19 (WHO, 2020*a*).

The coronavirus family comprises highly diverse enveloped positive-sense single-stranded RNA viruses and are distributed broadly among mammals (including humans) and avian species and which primarily cause respiratory and enteric diseases. The name '*coronavirus*' comes from Ancient Greek κορώνη (*korṓnē*, 'crown') owing to the characteristic appearance under electron microscopy of bulbous surface projections that resemble a solar corona (V'kovski et al., 2021).

Before December 31, 2019, six coronavirus species were recognized to cause disease in humans (Corman et al., 2018). Four human coronaviruses—HCoV-229E, -NL63, -OC43 and -HKU1—are ubiquitously and regularly responsible for upper and lower respiratory tract infections and are commonly associated with the common cold that can cause rhinorrhoea, nasal congestion, sore throat and other mild-to-moderate symptoms (Poutanen, 2012). More severe diseases have also been described, such as acute bronchiolitis, pneumonia, febrile seizures and croup (especially for HCoV-NL63) (McNamara and Van Doorn, 2014).The two other strains belonging to the

genus *Betacoronavirus* (of which HCoV-OC43 and -HKU1 are also part) are severe acute respiratory syndrome coronavirus (SARS-CoV-1) and Middle East respiratory syndrome coronavirus (MERS-CoV), which are linked to more severe and sometimes fatal illness; both represent the paradigm of emerging 21st-century epidemic-prone zoonotic viruses and have triggered numerous outbreaks and health crises (Cui et al., 2019). SARS-CoV-1 was first described as the causal agent of an outbreak of atypical pneumonia with severe acute respiratory syndrome originating in November 2002 in Guangdong Province, China that infected over 8,000 people and caused at least 774 deaths in 30 countries and territories worldwide (Centers for Disease Control and Prevention [CDC], 2017; Zhong, et al., 2003). MERS-CoV causes a severe respiratory disease that was first identified in Saudi Arabia in 2012; as of July 2022, more than 2,600 laboratory-confirmed cases of MERS and approximately 900 associated deaths (case–fatality ratio [CFR] of ~35%) were identified in 27 countries, the majority of which occurred in Saudi Arabia (European Centre for Disease Prevention and Control [ECDC], 2022).

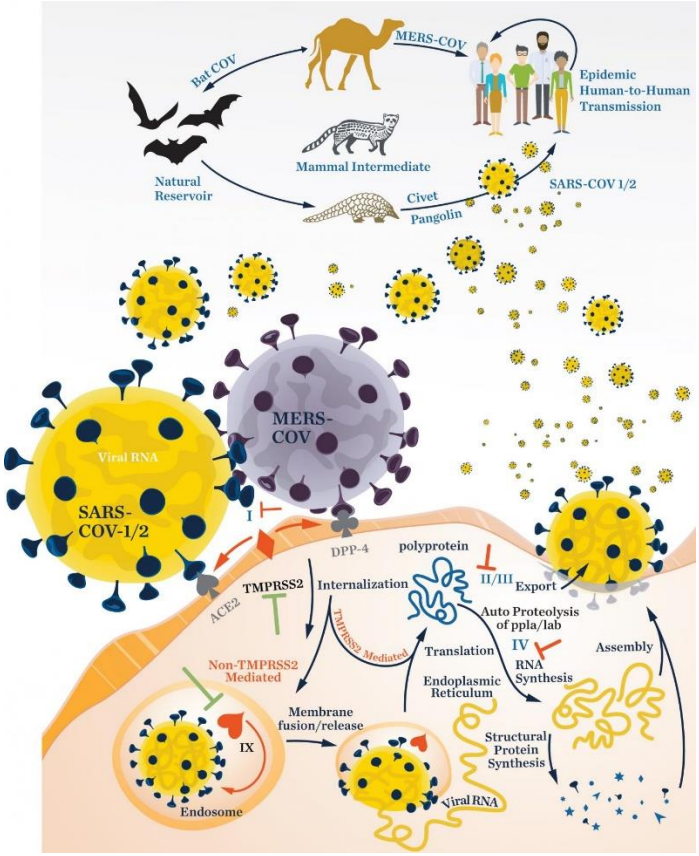


FIGURE 1.1: Coronavirus lifecycle as represented by SARS-CoV-1/2 and MERS-CoV. The Roman numerals in the figure represent host and viral proteins implicated in host cell recognition by SARS-CoV-2 and viral replication: I.

spike glycoprotein; II. main protease (Mpro/3CLpro); III. papain-like protease (PLpro); IV. RNA-dependent RNA polymerase (RdRp). V. NSP1; VI. NSP13; VII. Orf8b; VIII. TMPRSS2; IX. cathepsin L. Abbreviations: SARS-CoV-1/2, severe acute respiratory syndrome coronavirus ½; MERS-CoV, Middle East respiratory syndrome coronavirus; ACE-2, angiotensin-converting enzyme 2; TMPRSS2, type 2 transmembrane serine protease; DPP-4, dipeptidyl peptidase 4 receptor. Illustration: Jennifer Matthews/ Scripps Oceanography, 2021. Source: Coronavirus lifecycle (Image) - Available from: www.eurekalert.org/ multimedia/914192. This image is licensed under CC BY-SA 4.0, with no usage restrictions.

### *1.2 Aetiology of SARS-CoV-2 infection*

Bats are the natural reservoir for most severe acute respiratory syndrome-related coronaviruses (genus *Betacoronavirus*, subgenus *Sarbecovirus*). SARS-CoV-2 can be transmitted to humans through several pathways that exploit host receptors to enter cells and deliver viral RNA to the cytoplasm (Parasher, 2021). Person-to-person transmission is the main route by which people are infected with SARS-CoV-2, which occurs through exposure to respiratory droplets and aerosols. Exposure to respiratory fluids may occur through (1) direct inhalation of fine respiratory particles (produced from talking, breathing, coughing or sneezing); (2) contact with the mouth, nose or eyes through direct splashes and sprays; and (3) touching mucous membranes with hands that have previously contacted virus-containing respiratory fluids (which can also occur by touching contaminated inanimate surfaces and fomites) (CDC, 2021*a*).

Coronavirus lifecycle is presented in Figure 1.1. The envelope of coronaviruses is made up of four major structural proteins: the spike (S), nucleocapsid (N), membrane (M) and envelop (E) proteins (Schoeman and Fielding, 2019). The viral homotrimeric transmembrane glycoprotein S mediates the cellular attachment and penetration through its two subunits, S1 and S2. S1binds the host cell receptor through its receptor-binding domain (RBD), and S2 plays a role in the fusion of viral and host cell membranes and internalization (Parasher, 2021). The membrane protein angiotensin-converting enzyme 2 (ACE-2) expressed on pulmonary epithelial cells (and in other tissues) has been identified as the functional receptor for the RBD (Yan et al., 2020). Its presence on human cells thus regulates SARS.CoV-2 cellular tropism: respiratory tract and lung parenchyma are not the only tissues that express ACE-2,

being also expressed on vascular epithelia, gastrointestinal tract, kidney, pancreas, testicles and central nervous system (CNS), including on neurons and glial cells (Leven and Bösel, 2021).

Once engaged with ACE-2, the S protein undergoes activation via two-phase protease cleavage at the S1/S2 cleavage site, and the stimulation of conformational change leads to membrane fusion between the host cell and the virus (Belouzard et al., 2021). In infected cells, the RNA polymerase converts the viral genome into a negative-stranded RNA (transcription), which serves as a template for the production of new strands of positive mRNAs from which viral protein synthesis occurs (translation) (Lai and Cavanagh, 1997; Roberts et al., 2011).The viral RNA-synthesizing machinery integrates with modified endoplasmic reticulum membranes through the N and M proteins, and the newly formed viral particles are transported via exocytosis to the extracellular space, where they invade adjacent epithelial cells or are spread in respiratory droplets, resulting in community transmission (Cascella et al., 2022; Parasher, 2021). Unlike SARS-CoV-1 and MERS-CoV, SARS-CoV-2 can replicate in the upper respiratory tract, which likely explains its relatively easy transmissibility (Osuchowski et al., 2021; Rockx et al., 2020). It is also capable of infecting a wider range of cells, having shown tropism for respiratory epithelial and intestinal epithelial cells, alveolar macrophages, cardiocytes, olfactory sustentacular cells, bile duct cells and testicular Sertoli cells (along with abortive infection in haematopoietic components) (Osuchowski et al., 2021).

Similar to other viruses that use RNA as genetic material, SARS-CoV-2 is highly prone to genetic mutations, which has resulted in the progressive appearance of mutant variants with different characteristics than the ancestral strain. The WHO and other organizations have recognized specific variants of interest (VOIs) and variants of concern (VOCs) that have shown increased infectivity rates and pose an increased risk to global public health (Cascella et al., 2022). As of August 2022, five SARS-CoV-2 VOCs have been identified (Figure 1.2) (O'Toole et al., 2022; Rambaut et al., 2021; Rambaut et al., 2020).

An updated full list of epidemiological lineages can be found at: Cov-Lineages.org Lineage Report, available from: cov-lineages.org/lineage_list.html (O'Toole et al., 2022; Rambaut et al., 2021; Rambaut et al., 2020).

For a complete overview of SARS-CoV-2 features and associated evaluation, please refer to the specific references.

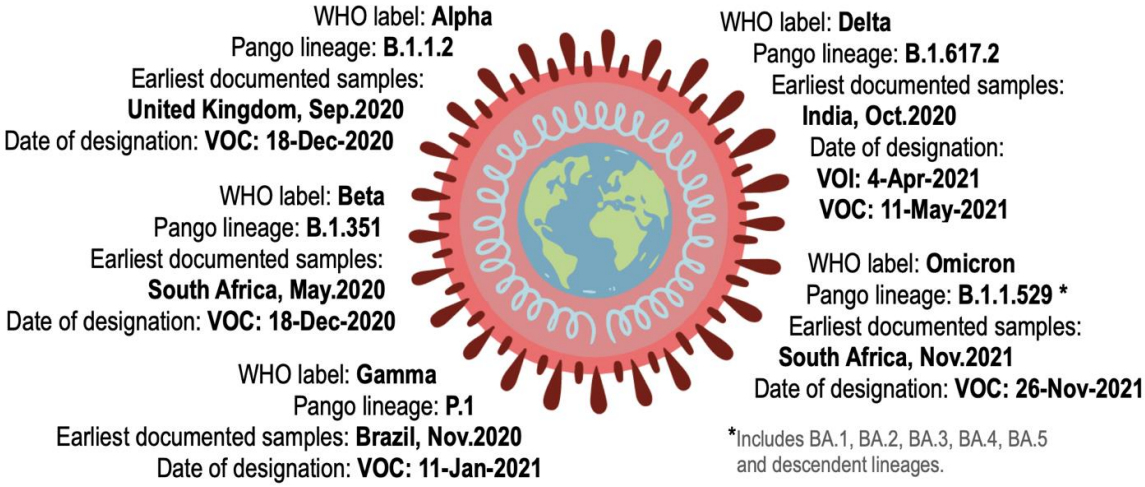


FIGURE 1.2: SARS-CoV-2 variants of concern (VOCs). Abbreviations: Pango, Phylogenetic assignment of named global outbreak lineages; WHO, World Health Organization. Adapted from an image by Philippa Steinberg for the Innovative Genomics Institute (Berkeley, CA, US). Available from: https://innovativegenomics.org/free-covid-19-illustrations/ This image is licensed under CC BY-NC-SA 4.0, with no usage restrictions.

### *1.3 Pathophysiology and clinical presentation of COVID-19*

COVID-19 exhibits diverse clinical manifestations, ranging from asymptomatic infection to severe respiratory manifestations, multiorgan failure and death (Balasco et al., 2021; Conti et al., 2020*a*; Ducherty et al., 2020). Patients commonly present with nonspecific flu-like symptoms, such as fever, cough, fatigue, headache, shortness of breath or difficulty breathing, anosmia/ageusia, diarrhoea, and others (CDC, 2022*a*).

Although sharing some clinical characteristics with other coronavirus infections, the disease associated with SARS-CoV-2 infection has been recognized as a novel disease entity with distinct pathophysiology and clinical features that set COVID-19 apart from SARS and MERS, influenza, and non-COVID-19-related acute respiratory distress syndrome (ARDS) (Grasselli et al., 2020; Osuchowski et al., 2021; Panwar et al., 2020).

Early in infection, SARS-CoV-2 spreads in the body via the mucus membranes and enters the blood. It primarily targets the respiratory tract cells (i.e., nasal and bronchial epithelial cells and pneumocytes), into which it gains access by binding ACE-2 receptors. Distinct from SARS-CoV-1 and MERS-CoV infections, the viral load

in the upper respiratory tract peaks during the late incubation period (mean incubation 6.38 days; range 2–18 days, with differences according to the VOC predominance [Elias et al., 2021; Lauer et al., 2020]) and the pre-symptomatic phase: simultaneously, viral transmission can start 1 or 2 days before symptoms begin (Benefield et al., 2020; Challenger et al., 2022). In host cells, the release of newly formed virions from SARS-CoV-2 replication causes cell death and tissue damage and dysfunction, contributing to disease onset and progression. Typical acute and severe manifestations of COVID-19 involve the upper and lower respiratory tracts, but extrapulmonary and systemic features have also been extensively reported (Ducherty et al., 2020; Gupta et al., 2020).

In the sections below, the main pathophysiological and clinical features of COVID-19 are described. For further information, please refer to the referenced studies.

### *1.3.1 Pathophysiological effects on the respiratory tract and lungs*

ACE-2 expression in human respiratory tract tissues correlates with the sites of SARS-CoV-2 infection. The high gradient of ACE-2 expression by cells of the upper airways (in addition to monocytes/macrophages, mast cells and vascular endothelial cells) facilitates the initial viral infection (Hou et al., 2020; Marik et al., 2021). Host target cells – particularly type II alveolar epithelial cells – express the type 2 transmembrane serine protease (TMPRSS2), a host membrane-anchored protein that promotes viral uptake by cleaving ACE-2 and activating the SARS-CoV-2 S proteins, which mediates coronavirus entrance. TMPRSS2 expression correlates with lung disease severity (Hoffmann et al., 2020; Marik et al., 2021). Indeed, this mechanism explains why alveolar type II cells of the lungs are particularly susceptible to immunity-mediated diffuse alveolar damage (DAD). The pathology of DAD involves hyaline membrane formation, microvascular thrombi and lymphocytic inflammation, which together lead to non-cardiogenic protein-rich pulmonary oedema and result in impaired gas exchange between the respiratory and circulatory systems (Brosnahan et al. 2020; Diamond et al., 2022*a*). DAD is the histological hallmark for the ARDS, a life-threatening syndrome of acute respiratory failure that develops as a stereotypic response to various aetiologies, most commonly in the setting of pneumonia (Diamond et al., 2022*a*; Grasselli et al., 2020).

A wide range of respiratory and systemic sequalae has been observed in non-COVID-19 and COVID-19 ARDS (Grasselli et al., 2020; Madotto et al., 2020; Panwar et al., 2020). Tissue hypoxia leads to cell death, organ failure, and is associated with significant mortality risk. The main causes of death in ARDS patients are sepsis and

multiorgan failure (Diamond et al., 2022*a*). In real-world clinical practice, ARDS mortality rates vary widely according to the setting, being on average as high as ~40%, and ARDS mortality is much higher in older patients and those with comorbidities (Auriemma et al., 2020; Rezoagli et al., 2021). In COVID-19 patients, respiratory failure is the primary cause of death (Grasselli et al., 2020; Zhang et al., 2020; Zhou et al., 2020).

COVID-19 also presents with upper respiratory tract symptoms such as throat dryness, soreness and redness, and cough and rhinorrhoea, etc (CDC, 2022*a*; Della Valle et al., 2021; Tomaselli et al., 2022).

### *1.3.2 Pathophysiological effects on the cardiovascular system*

One of the most critical pathophysiological effects ofSARS-CoV-2 is its ability to promote coagulation abnormalities that are key for the genesis of COVID-19-related organ damage. The pathophysiology of COVID-19-associated coagulopathy includes high levels of D-dimer and fibrinogen, mild thrombocytopenia, changes in the quantities and levels of platelet activation, and alterations of other coagulation parameters (Conway et al., 2022; Len et al., 2022). The evidence to date suggests that the high incidence of thrombotic complications in COVID-19 patients can be explained by the complex interplay between the local and systemic hyperinflammatory response, endotheliopathy, and the coagulation system (Leentjens et al., 2021; Lim et al., 2021). COVID-19-associated coagulopathy (CAC) displays a hypercoagulable state accompanied by frequent arterial and venous thrombosis and disseminated intravascular coagulation, with an increased risk of macro- and micro-vascular complications, progression to multiorgan failure and increased mortality (Conway et al., 2022; Grasselli et al., 2020; Lorini et al., 2021; Manolis et al., 2021). In particular, according to a recently published review on the mechanisms of coagulopathy in patients with severe COVID-19, the most common complication is pulmonary arterial thrombosis attributable to thrombotic occlusion of small- to mid-sized pulmonary arteries, which leads to infarction of the lung parenchyma (Manolis et al., 2021). Other clinical manifestations of CAC may include, among others, ischemic stroke, myocardial injury and acute myocardial infarction (MI), deep vein thrombosis, acute limb ischemia and systemic arterial thromboembolism (Bilaloglu et al., 2020; Conway et al., 2022; Manolis et al., 2021).

### *1.3.3 Other pathophysiological effects of SARS-CoV-2 infection*

Although the lung is the main affected organ in severe COVID-19, other body organs can also be harmed, including the gastrointestinal tract, where the endothelial

cells and enterocytes of the small intestine and the epithelial cells of the oesophagus and colon highly express ACE-2 receptors. Common gastrointestinal symptoms of COVID-19 include diarrhoea, nausea, vomiting and abdominal pain (CDC, 2022*a*; Troisi et al., 2021). Liver damage has also been reported in a large number of patients with COVID-19 who presented altered liver enzyme concentrations (e.g., elevated levels of aspartate transaminase, alanine aminotransferase and bilirubin) (Troisi et al., 2021).

Clinical studies have also identified kidney injury concurrent with COVID-19, with frequently observed proteinuria and haematuria, which increases the difficulty of treatment and care, particularly for those with pre-existing kidney conditions (Han and Ye, 2021).

COVID-19 patients can present neurological manifestations relating to CNS, peripheral nervous system and skeletal muscle injury, including anosmia, ageusia dizziness, agitation, inattention, disorientation and paraesthesia (Leven and Bösel, 2021; Zubair et al. 2020). There are many potential direct and indirect mechanisms by which SARS-CoV-2 invades nervous system tissues, such as the olfactory (through the cribriform plate), trans-synaptic (axonal transport of virus particles), leukocytic (migration of infected leukocytes), haematogenic (across the vascular endothelium) and gastrointestinal routes (Aghagoli et al., 2021; Leven and Bösel, 2021; Zubair et al. 2020).

### *1.3.4 Host response*

Together with hypercoagulability, hyperinflammation is the most important systemic complication of COVID-19. SARS-CoV-2 infection can hyperactivate the innate immune response, eliciting a proinflammatory cytokine storm also known as hypercytokinemia, which correlates with systemic inflammation (Osuchowski et al., 2021; Rabaan et al., 2021). This unmodulated inflammatory reaction can be reminiscent of that of SARS and MERS, in which hyperinflammation inhibits the adaptive immune response and is responsible for tissue damage, acute lung injury, ARDS, organ failure (particularly heart and kidney) and increased mortality (Tomerak et al., 2021). In severe COVID-19, interleukin 6 (IL-6), IL-10 and tumour necrosis factor-alpha (TNF-$\alpha$) production is upregulated, likely by the inflammasome in the cells implicated in cytokine storm inflammation (Mangalmurti and Hunter, 2020; Osuchowski et al., 2021; Tomerak et al., 2021). Some COVID-19 manifestations and outcomes have been linked to specific cytokines. For example, IL-6 and TNF are reported to cause fever and constitutional symptoms (Mangalmurti and Hunter, 2020). Furthermore, IL-6 is associated with vascular leakage and the activation of

complement and coagulation cascades (Tomerak et al., 2021); in this sense, some researchers speculate that COVID-19 patients with comorbid diabetes, cardiovascular diseases (CVD), or hypertension (as well as other conditions that impair the vascular system) are less tolerant of systemic cytokines and thus are more likely to suffer severe and lethal disease (Mangalmurti and Hunter, 2020; Tomerak et al., 2021). The overproduction of cytokines triggered by SARS-CoV-2 is also associated with lymphopenia, particularly in CD4+ (helper) and CD8+ (cytotoxic) T cells (but not in B lymphocytes), which may impair the production of anti-SARS-CoV-2 antibodies (Manjili et al., 2020).

Since the first weeks of the pandemic, severe inflammatory patterns have also been described in paediatric patients infected with SARS-CoV-2: multisystem inflammatory syndrome in children (MIS-C) results from an abnormal immune response to the virus in school-age populations weeks after the initial infection. Although a rare complication, MIS-C can lead to critical illness, with a high incidence of shock, myocardial involvement, respiratory failure and death (Son and Friedman, 2022). Rarely, some adults experience clinical manifestations similar to MIS-C; this condition is called multisystem inflammatory syndrome in adults (MIS-A). In both MIS-C and MIS-A, the signs and symptoms depend on the organs and tissues affected (which may include the heart, lungs, blood vessels, kidneys, digestive system, brain, skin and eyes) (CDC, 2021*b*).

### *1.3.5 Immune response and immunity to SARS-CoV-2*

The immune response associated with SARS-CoV-2 infection plays an important role in COVID-19 pathogenesis. Beyond hyperinflammation and hypercoagulability, severe outcomes in COVID-19 are also due to a dysregulated immune response (Boechat et al., 2021; Li et al., 2022).

The innate immune system, the first line of defence against pathogens entering the body, responds to SARS-CoV-2 by limiting viral entry, replication and assembly, helping to remove infected cells, and activating the adaptive immune system (Diamond et al., 2022*b*). As in many other viral infections, pattern recognition receptors, a class of proteins capable of recognizing specific molecular structures on a pathogen's surface, activate innate immune signalling pathways through Toll-like receptor signalling. This activates the transcription of pro-inflammatory cytokines (e.g., TNF, IL-6, IL-1, and interferons [IFNs]) and other sensors that recruit macrophages, neutrophils, and lymphocytes. Among others, IFNs (particularly IFN-$\gamma$) have an important antiviral mechanism and prime functions that enhance the immune response to SARS-CoV-2 (Lauro et al., 2021). IFN signalling also modulates

natural killer cells and T cells. For instance, people with reduced or ineffective IFN responses are at high risk of failing to control a primary SARS-CoV-2 infection and are more prone to severe COVID-19 outcomes (Bastard et al., 2021; Diamond et al., 2022*b*; Sette and Crotty, 2021). Ideally, innate immunity limit viral infection without promoting the activation of the adaptive immune system (Li et al., 2022).

As in other viral infections, the body's defence against SARS-CoV-2 involves host components of the adaptive immune system – B cells (the source of antibodies), CD4+ T cells and CD8+ T cells – which all have distinctive roles (Sette and Crotty, 2021). During primary infection, SARS-CoV-2 viral particles activate the adaptive immune response via antigen-presenting cells (mediated by surface major histocompatibility complex class II receptors) or through B cell receptors. The polyfunctional profile of CD4+ T helper cells also plays an important role in cytokine secretion, cell-to-cell contact and secondary signalling that involve other immune cells (e.g., helping the humoral response mature B cells, stimulating cellular response formation) (Lauro et al, 2021; Moss, 2022; Steiner et al., 2022). In infected patients, B cells secrete SARS-CoV-2 RBD-specific type A, M and G immunoglobulins (IgA, IgM and IgG), which inhibit viral activity and are crucial in the resolution of both infection and disease. More specifically, neutralizing antibody responses against SARS-CoV-2 N- and S-proteins are reported in the acute phase of infection, but N-specific antibodies rapidly wane in post-infection, whereas S-specific IgGs peak between weeks three and seven after symptom onset and persist over time with a slow decay (ECDC, 2021; Martin et al., 2022). Seroconversion has been described in more than 90% (range, 91-99) patients after primary infection (ECDC, 2021).

The duration and level of protection conferred by natural SARS-CoV-2 infection against reinfection and COVID-19 development remain important issues, particularly considering the number of people who are still unvaccinated and the increased immune escape of new SARS-CoV-2 VOCs. The available evidence suggests a contraction of SARS-CoV-2 IgG in the 3–6 months after the infection; however, T-cell and memory B-cell responses persist for up to 8 months, thus resulting in sustained protection against the disease during this time window, with differences according to individual characteristics (e.g., lower responses in older adults), disease severity (more pronounced following symptomatic infection), and the increased immune escape of new SARS-CoV-2 variants (ECDC, 2021; Michlmayr et al., 2022).

### *1.4 Diagnostic testing for SARS-CoV-2 infection and COVID-19 diagnosis*

The gold standard for identifying current SARS-CoV-2 infection is reverse transcription polymerase chain reaction (RT-PCR) for the detection of viral RNA from a nasopharyngeal swab sample. Other tests employ either nucleic acid amplification or antigen detection. Tests should be undertaken by people with symptoms consistent with COVID-19 and those with known risk exposures to SARS-CoV-2. Testing is also the standard strategy for screening and determining the length of a patient's isolation period (US National Institute of Health [NIH], 2022).

In COVID-19 patients, the clinical evaluation mainly includes chest imaging (e.g., X-ray, ultrasound or computed tomography scan), electrocardiogram and laboratory examinations, such as complete blood cell count with differential and metabolic profiling of liver and renal function indexes. Measurements of some inflammatory markers (e.g., D-dimer, C-reactive protein and ferritin) are also used for their prognostic value (NIH, 2022).

### *1.5 Current understanding of COVID-19 treatment*

A high proportion of SARS-CoV-2-infected individuals can be asymptomatic and do not require medical treatment. However, mild to moderate symptoms and critical illness necessitate increasing management levels. At times during the pandemic, the rapid increase in cases of COVID-19 and the emergence of new VOCs have led to a race for effective treatments (Ferrara and Albano, 2022; Massi and Emendi, 2021; NIH, 2022). In the absence of drugs with proven efficacy against SARS-CoV-2, the international and national medicines agencies have initiated clinical trials of molecules used to treat other diseases and have authorized compassionate or off-label use of specific drugs (Massi and Emendi, 2021).

Globally, numerous existing and novel molecules have been studied as possible COVID-19 treatments (Massi and Emendi, 2021; NIH, 2022). Here, the current guidelines for mild to moderate and severe COVID-19 treatment authorized by the Italian Medicines Agency (Agenzia Italiana del Farmaco, AIFA) are presented.

#### *1.5.1 At-home management of COVID-19 patients*

According to the AIFA's "Recommendations on medicines to be used for the home management of COVID-19 cases", paracetamol, non-steroidal anti-inflammatory drugs (NSAIDs) and other symptomatic medicines (based on clinical judgment) can be used as symptomatic therapy, for example to treat fever or joint or

muscle pain. The use of corticosteroids at home may be considered for patients who present risk factors for progression to severe disease, in the presence of worsening pulse oximetry parameters requiring oxygen therapy, and if hospitalization is not immediately possible. Low molecular weight heparins (LMWHs) can be used in COVID-19 patients with reduced mobility for the prophylaxis of thrombo-embolic events. However, the routine use of heparins is not recommended in non-hospitalized and non-bedridden patients. Three antivirals – remdesivir, nirmatrelvir plus ritonavir, and molnupiravir – are authorized for the treatment of COVID-19 in adults who do not require supplemental oxygen but who present risk factors associated with progression to severe disease, including cancer, chronic kidney insufficiency disease (CKD), chronic obstructive pulmonary disease (COPD) and/or other chronic respiratory diseases, uncompensated type 2 diabetes mellitus, primary or acquired immunodeficiency or obesity. These antivirals should be administered as soon as possible after the diagnosis of COVID-19 and within 5 (nirmatrelvir plus ritonavir and molnupiravir) or 7 days (remdesivir) after symptom onset. Bamlanivimab plus etesevimab, casirivimab plus imdevimab, and sotrovimab are the monoclonal antibodies authorized in Italy for patients who test positive for SARS-CoV-2 infection and are at high risk of progression to severe COVID-19 (AIFA, 2022*a*).

The AIFA living guidelines on COVID-19 therapeutics also state that the use of antibiotics, hydroxychloroquine, lopinavir plus ritonavir, darunavir plus ritonavir, and cobicistat are not recommended for the treatment of SARS-CoV-2 infection and COVID-19 (AIFA, 2022*a*; Ferrara and Albano, 2022).

### *1.5.2 Hospital management of COVID-19 patients*

AIFA considers the use of corticosteroids and LMWHs to be the standard of care for hospitalized COVID-19 patients. Dexamethasone (and other class molecules) has shown effectiveness for mortality reduction in patients requiring supplemental oxygen therapy (with or without mechanical ventilation). The use of LMWHs for the prophylaxis of thrombo-embolic events in patients with acute respiratory infection (who are bedridden or have reduced mobility) is recommended in the absence of contraindications. In select cases, patients may benefit from the use of casirivimab plus imdevimab (the effectiveness of which, as of all monoclonal antibodies, may be reduced against some viral variants) and remdesivir (within 10 days of symptom onset). Other possible treatments include tocilizumab (a monoclonal antibody authorized in adults with severe COVID-19 and/or with high levels of systemic immune-inflammation index [SII]), anakinra (an IL-1 receptor antagonist authorized for adults with moderate-to-severe COVID-19 pneumonia with $pO_2/FiO_2$>150mmHg

and who are not undergoing continuous-positive airway pressure [C-PAP] or mechanical ventilation), baricitinib (a JAK-inhibitor considered for adults with severe COVID-19, those who require high-flow oxygen therapy or noninvasive mechanical ventilation, and/or those with high SII), and sarilumab (an IL-6 inhibitor authorized for patients with severe COVID-19, high SII, and with a rapidly deteriorating clinical condition) (AIFA, 2022*b*).

In December 2021, the WHO warned against the use of convalescent plasma (administered as a transfusion of blood plasma from recovered COVID-19 patients) outside clinical trials for severe and critical illness because the evidence showed no reduction in the risk of respiratory damage or death and was not cost-effective (WHO, 2021*a*).

ARDS patients usually require mechanical ventilation, which can be vital to prevent secondary lung injury and improve patient outcomes (Madotto et al., 2020).

Similar to those for at-home management of the disease, the living guidelines for treating COVID-19 in a hospital setting recommend against the use of hydroxychloroquine, lopinavir plus ritonavir, darunavir plus ritonavir, cobicistat or routine antibiotics for the treatment of COVID-19 (AIFA, 2022*b*).

## *1.6 COVID-19 prevention*

### *1.6.1 Impact of community mitigation strategies*

Given that SARS-CoV-2 is primarily spread through respiratory droplets and aerosols, the respiratory tract and mouth are directly exposed to the viral particles. The primary preventive measures to reduce transmission rates are based on community mitigation strategies, also known as nonpharmaceutical interventions (NPIs). These include promoting and facilitating physical distancing, advising people to voluntarily self-isolate if experiencing COVID-19-related symptoms, limiting the size of public gatherings, promoting teleworking, closing selected businesses and schools, and promoting environmental measures (such as regular cleaning of frequently touched surfaces, regular ventilation of indoor spaces), hand hygiene, and the wearing of face masks. Wearing face masks, in particular, has been recommended and promoted in many countries as an effective physical intervention to prevent disease transmission (ECDC, 2020).

To mitigate the COVID-19-related health and social burden, various physical distancing strategies have been globally enforced during the constantly evolving epidemiological landscape of SARS-CoV-2 and its variants, ranging from compulsory

lockdowns to more limited measures. Growing evidence has shown that NPIs have played a critical role in limiting the impact of COVID-19, and some interventions – namely wearing face masks and the isolation of cases – will continue to be an effective tool to prevent SARS-CoV-2 transmission (Balasco et al., 2021; d'Alessandro et al., 2022; Della Valle et al., 2021; ECDC, 2020).

### *1.6.2 COVID-19 vaccines and vaccination strategies*

The spread of SARS-CoV-2 has highlighted the essential need for rapid research efforts towards the swift development of treatments and vaccines. COVID-19 vaccination has been fast-tracked worldwide, and timely immunization has meaningfully contributed to mitigating the pandemic, saving an estimated tens of millions of lives globally (Ferrara et al., 2022*a*; Watson et al., 2022).

As of August 2022, the WHO had listed 11 COVID-19 vaccines for emergency use through its Emergency Use Listing, a procedure by which the WHO assesses the quality, safety and efficacy of COVID-19 vaccines and details their risk management plans and programmatic suitability (e.g., cold chain requirements). With more than 12.3 billion vaccine doses administered, the real-world evidence on COVID-19 vaccination has supported the vaccines' safety and has validated their effectiveness in reducing the healthcare burden of hospitalizations and deaths associated with COVID-19 (Ferrara et al., 2022*a*; Ferrara et al., 2022*b*; WHO, 2020).

In Italy, five COVID-19 vaccines have been approved by AIFA after receiving marketing authorization from the European Medicines Agency (EMA): two mRNA vaccines, Pfizer-BioNTech mRNA BNT162b2 tozinameran (Comirnaty®) and Moderna mRNA-1273 (Spikevax®); two recombinant adenoviral vector vaccines, AstraZeneca-SKBioscience ChAdOx1-S (Vaxzevria®) and Johnson and Johnson Ad26.COV2.S (Jcovden®); and a recombinant, adjuvanted protein subunit vaccine, Novavax SARS-CoV-2 rS (Nuvaxovid®) (AIFA, 2022*c*).

The massive national vaccination campaign started on December 27, 2020, targeting healthcare workers as the first recipients to ensure their protection and safety at work and the sustainability of the healthcare system, which experienced excessive hospital overload, large shortages of healthcare resources, and high workloads (Ferrara and Albano, 2020; Ponticelli et al., 2022). Subsequently, doses were offered to other population groups in accordance with their risk of severe COVID-19 outcomes, starting with older adults and immunocompromised people. The booster administration of COVID-19 vaccines is ongoing in the country in accordance with data-driven vaccination policies and strategies to protect people as well as social and economic activities (Ferrara et al., 2022*a*; Ferrara et al., 2022*c*;

Ponticelli et al., 2021). Notably, the duration and amount of protective immunity conferred by COVID-19 vaccines is still unclear. For instance, different rates of breakthrough infections – defined as any SARS-CoV-2 infection diagnosed after the administration of a COVID-19 vaccine – have been widely reported in the literature. These differences are mostly owing to variability in the time-to-event, the setting, the populations enrolled, and the local vaccine types and policies (which might differ regarding the timing, mix-and-match of doses, and use of and changes in NPIs during the pandemic periods) (Ferrara et al., 2022*c*). Additionally, there is interindividual variability in vaccine responses, but it is quite difficult to predict (Ferrara et al., 2022*d*; Ferrara et al., 2022*e*; Lee et al., 2022; Sacco et al., 2022).

# Chapter 2

# Epidemiology of COVID-19

## *2.1 Introduction*

Over the past two-and-a-half years, the world has experienced one of the most devastating pandemics and health crises in contemporary history. A recent comprehensive geospatial analysis of the first COVID-19 cases showed that the epicentre clustered around the Huanan Seafood Market in Wuhan, China, further supporting early reports of the zoonotic origin of SARS-CoV-2 (Worobey et al., 2022).

Epidemiological analyses of influenza-like illness (ILI) and severe acute respiratory infection (SARI) surveillance, the latter of which was established in China after the 2003 SARS epidemic upon WHO recommendation, identified a marked increase in ILIs in children and adults at the end of 2019 in Wuhan, with no evidence of substantial SARS-CoV-2 transmission before December 2019 (WHO, 2021*b*).

The emergence of novel HCoVs has repeated with some frequency in recent decades owing to the wide distribution of coronaviruses, the recurrent recombination of their genomes, and increasing human–animal interactions that cause cross-species spillover (Santacroce et al., 2021; Zhu et al., 2020).

Compared with the coronaviruses that cause SARS and MERS, SARS-CoV-2 soon demonstrated much greater infectivity, resulting in a higher basic reproduction number ($R_0$ or 'R naught'), which is the average number of secondary infections per infectious case in a totally naïve population. The estimation of $R_0$ depends on the biological features of the pathogen, but it is also population-specific, reflecting the social aspects of adaptive human behaviours (Fenichel et al., 2011). The high contagiousness of SARS-CoV-2 is also owing to the broad viral tropism for ACE-2-expressing human cells, which enables the virus to infect more tissue types than other human respiratory viruses (Liu et al., 2020; Petersen et al., 2020).

The continuous evolution of SARS-CoV-2 variants—such as Delta and, more recently, Omicron BA.4 and BA.5, which achieved global predominance in the first half of 2022—leads to evidence of higher average effective reproduction number ($R_{eff}$), and perhaps, higher $R_0$ compared to the ancestral virus (Liu and Rocklöv, 2022; Liu and Rocklöv, 2021). Anecdotal evidence supports the hypothesis that BA.5 is the virus with the highest known $R_0$, reaching an $R_0$ of 18.6. This would make COVID-19 the

most infectious disease in human history, displacing measles, which has an $R_0$ of 18 (Esterman, 2022; Guerra et al., 2017). The 'growth advantage' of BA.5 (and other VOCs), however, does not reflect the claimed increased transmissibility compared with that of the VOCs it replaced. There are many mechanisms by which this (temporary) growth advantage is determined (even when $R_0$ is the same), and primarily include the variant's ability to evade infection-acquired or vaccine-induced immunity, which can also be associated with a shorter generation time (the average 'time interval between the infections of the infector and infectee in a transmission chain' [Lau et al., 2021]) and higher intrinsic transmissibility of the virus owing to biological changes that confer a competitive advantage, for example, by resulting in a higher viral load or better cell binding (Barut et al., 2022; Ferrara et al., 2022*c*; Shearer et al., 2022). These mechanisms might differentially affect $R_{eff}$, the average number of secondary cases generated by an infectious person in the presence of a particular set of public health measures and behavioural changes, and population immunity (i.e., in a population made up of both susceptible and non-susceptible hosts) (Annunziatio et al., 2020; Leung, 2021).

### *2.2 Overview of the global and European COVID-19 burden*

As of August 31, 2022, the WHO COVID-19 dashboard has registered more than 599 million confirmed cases of COVID-19 globally, including approximately 6.5 million deaths (WHO, 2020*b*) (Figure 2.1).


FIGURE 2.1: Map of COVID-19 Cases as of August 2022. Source: WHO COVID-19 Dashboard. Available online: https://covid19.who.int/ This image is licensed under CC BY-NC-SA 3.0, with no usage restrictions.

Dissimilarities in the incidence rates and the magnitude and timing of case surges over the two pandemic years are the effect of the different mitigation strategies implemented to contain the virus, including stay-at-home orders and the reduction of personal contacts, mask use, testing, isolation and contact tracing, and, more recently, vaccinations. Differences have also arisen owing to variability in the progressive appearance of VOCs and population characteristics (e.g., density and dynamics) (Institute for Health Metrics and Evaluation [IHME], 2020).

Such factors have contributed to shaping the global epidemiological curve, which peaked at the end of January 2022, when the surge in Omicron cases passed 4 million in a single day (WHO COVID-19 dashboard, 2020). Overall, two-fifths of the global cases have been registered in Europe (WHO COVID-19 dashboard, 2020), likely owing to the reasons listed above and, in particular, the extent of testing (Ritchie et al., 2020).

Epidemiological analyses have helped to determine risk factors that are potentially associated with SARS-CoV-2 infection, even if supportive evidence remains weak in some cases. The main risk factors associated with an increased odd of testing positive are an older age, male sex, a dense population, urban location, increased socioeconomic deprivation, belonging to an ethnic minority group, and professional exposure (e.g., healthcare workers). Current smoking status has been associated with a lower risk of testing positive. Autoimmune diseases, CKD and obesity are the most relevant clinical factors associated with infection (de Lusignan et al., 2020; Della Valle et al., 2021; Kompaniyets et al., 2021; Mehta et al., 2021; Tomaselli et al., 2022).

The risk of severe COVID-19 – proxied by the probability of hospitalization, intensive care unit (ICU) admission, intubation or mechanical ventilation, and death – is higher in older individuals, racial and ethnic minorities, those who face barriers to healthcare access, smokers (current and former), and patients with underlying medical conditions, including cancer, CKD, COPD, CVD, infection with human immunodeficiency virus (HIV) and acquired immunodeficiency syndrome (AIDS), neurocognitive disorders, obesity, primary immunodeficiencies, and the use of corticosteroids or other immunosuppressive medications (CDC, 2022*b*; Kompaniyets et al., 2021; Mehta et al., 2021; Pennington et al., 2020; Tomaselli et al., 2022). Figure 2.2 shows the COVID-19 mortality risk ratio (RR) for select age groups and comorbid conditions (panel A) and how it increases as the number of comorbid conditions increases (panel B).

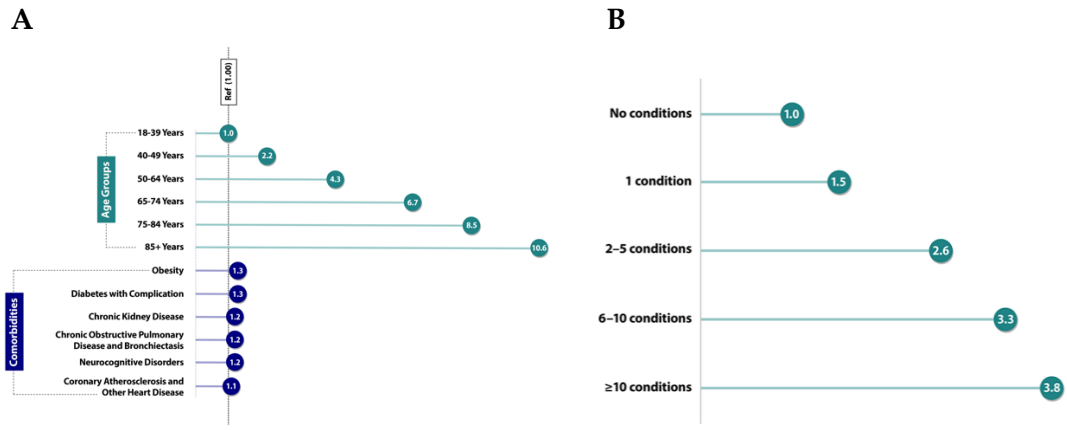


FIGURE 2.2: COVID-19 mortality Risk Ratios (RR). Panel A: COVID-19 mortality RR for selected age groups and comorbid conditions; Panel B: COVID-19 mortality RR increases with the number of comorbid conditions. Source: US Centers for Disease Control and Prevention, Underlying Medical Conditions Associated with Higher Risk for Severe COVID-19: Information for Healthcare Professionals [Updated 2022 Jun 15]. US Department of Health and Human Services; 2022 (CDC, 2022b). Available from: https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/underlyingconditions.html. This image is licensed under CC BY-SA 3.0, with no usage restrictions.

One of the most important epidemiological measures of the burden of COVID-19 is mortality. Reported CFRs have mirrored the variability seen in the incidence. This variability is mostly attributable to differences in reporting the incidence and mortality, as well as differences in population demographics and health status (e.g., the age structure of the population and the presence of pre-existing comorbidities), characteristics and availability of healthcare services, and vaccination campaigns and strategies (IHME, 2020). Indeed, the graphical distribution of the number of deaths is patterned after the curve of cases (Johns Hopkins University [JHU], 2020; Ritchie et al., 2020). As of August 2022, the five highest observed CFRs were registered in Yemen (18.1%), Sudan (7.9%), Syria (5.6%), Peru (5.3%) and Somalia (5.0%) (JHU, 2020; Ritchie et al., 2020). Considering the challenges in calculating the true numbers of cases and deaths and the large differences among populations and across pandemic periods, COVID-19-related CFRs warrant careful interpretation. Current evidence-based understanding is that the COVID-19 CFR is well below those estimated for SARS (~10%) and MERS (~34%) (Munster et al., 2020; Ritchie et al., 2020). The crude death rate can also be used to compare COVID-19 mortality across populations, times

and settings; it is reported to exceed 450 deaths per 100,000 inhabitants in Peru (653.0), Bulgaria (540.3), Hungary (487.4), Bosnia and Herzegovina (487.1), and North Macedonia (453.1) (JHU, 2020).

Similar to other health crises, the COVID-19 pandemic has had a large impact on overall all-cause mortality through direct and indirect effects, particularly during the first phase when surveillance systems were unable to determine the exact number of deaths due to COVID-19 and when overcrowded hospitals impacted the care of other clinical conditions. Excess death—calculated as the expected number of deaths for the same period based on previous years—provides a comprehensive measure of the total impact of the pandemic on mortality (Conti et al., 2020*a*; Conti et al., 2020*b*; Ritchie et al., 2020). The percentage difference between the observed and expected numbers of deaths enables comparability across settings, populations and groups. In the sections below, the mortality risk and excess mortality are described for Italy and Lombardy. For further evidence and cross-country comparisons, please refer to the referenced sources.

### *2.3 COVID-19 in Italy*

On the night of February 20, 2020, a 38-year-old otherwise healthy man was admitted to the Hospital of Codogno (a municipality in the province of Lodi, Lombardy) with mild pneumonia. This case was the first autochthonous COVID-19 case in Lombardy (and Italy). Although there was no direct evidence of SARS-CoV-2 transmission in the region before February 20, there has been some uncertainty about the potential presence of earlier undetected COVID-19 cases and clusters. A retrospective epidemiological investigation of the first official cases recorded in the regional COVID-19 integrated surveillance system suggested that SARS-CoV-2 was already circulating in approximately 15% of regional municipalities on the basis of its transmission dynamics (Cereda et al., 2021). After February 21, 2020, clusters of patients with COVID-19 were identified in Lombardy and Veneto (which borders Lombardy), and in the following weeks, COVID-19 spread to the rest of the country. On March 11, 2020, Italy became the first European country to impose a national lockdown to limit the spread of the virus (Conti et al., 2020*a*).

As of September 15, 2022, approximately 22.2 million cases and 175,000 deaths have been recorded in the COVID-19 Integrated Surveillance System established by the Italian National Institute of Health (Istituto Superiore di Sanità [ISS], 2020*a*).

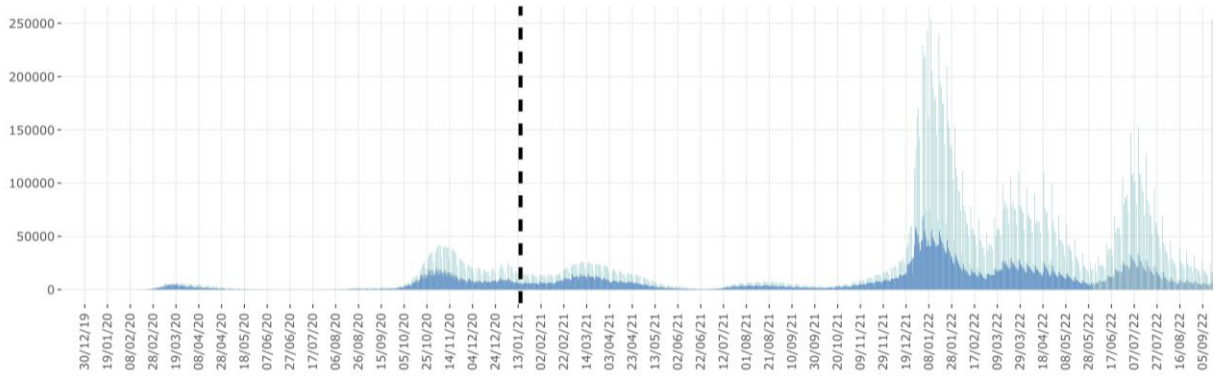


FIGURE 2.3: SARS-CoV-2 infections in Italy as of September 15, 2022. Cases are reported by date of sample/diagnosis (green) and by date of symptom onset (blue). Symptomatic cases are defined as individuals with a known date of symptom onset, excluding those reported as asymptomatic. From January 15, 2021 (dashed line), case numbers also included those who had a positive rapid antigen test, as per Ministry of Health instructions. Source: ISS–COVID-19 Integrated Surveillance Data. This image is freely available from: www.epicentro.iss.it/en/coronavirus/sars-cov-2-dashboard

Before the authorization of the first COVID-19 vaccines and the beginning of massive vaccination campaigns, the epidemic in Italy can be divided into three phases. The first phase corresponds to the detection of the first case until the end of May 2020 (the first wave). During this time there was a rapid increase in the number of cases and deaths, which were mainly concentrated in the north of the country. From June to mid-September 2020 was the so-called transition phase during which the number of cases dropped consistently in line with low viral circulation. Starting from the end of September 2020, the second wave developed with several outbreaks in the country, and a sustained exponential increase in cases occurred in October, which resulted in a new epidemic wave that peaked in November with more than 40,000 cases in a single day (ISS, 2020*a*). The second wave was characterized by an intricate evolution in the number of cases, with multiple increases and decreases in infections (d'Alessandro et al., 2021). These changes also reflected the time-varying magnitude of the stay-at-home orders that were enforced during the pandemic months (see *section* 3.1).

The differences in lockdown measures were also reflected in the modelled curves showing the number of deaths and excess mortality. A solid upward trend in overall mortality in the country was identified starting in late February 2020 (22–29

February), with a significant increase in the number of deaths compared with that expected based on previous years (2015–2019) (Conti et al., 2020*b*; ISS, 2020*a*). The ISS calculated that from March to May 2020, more than 50,000 excess deaths occurred in Italy compared with the average for the same period in 2015–2019. Over 45,000 of these excess deaths occurred in the north of the country, and the death toll in the northern regions reached +94.5% in March and +75.0% in April 2020 (ISS, 2020*a*).

During the transition phase, the overall mortality equalled that observed during the previous 5 years, but from mid-October 2020, the mortality increased again, with over 31,700 deaths in October and November, when overall mortality increased by +61.4% in the north of the country, +39.3% in the centre, and +34.7% in the south (ISS, 2020*a*).

The most recent updated ISS report 'Characteristics of SARS-CoV-2 patients dying in Italy' described the characteristics of 138,099 COVID-19 patients who died in Italy from the beginning of the pandemic until January 10, 2022. The patients were mostly men (56.4%) and had a median age of 82 years (range 0–109; interquartile range [IQR] 74–88), while the median age of patients who were infected was 43 years. Three-quarters of the deceased had three or more comorbidities, and the most common conditions were hypertension, ischemic heart disease and other CVDs, type 2 diabetes mellitus (T2DM), dementia and COPD, mirroring results from the global COVID-19 burden. Taken together, the data indicated that mortality in older patients was associated with the presence and number of pre-existing diseases, while in the younger populations it was more often associated with respiratory and non-respiratory complications of the infection, such as ARDS, acute renal injury (AKI), acute cardiac injury and other infections (ISS, 2020*b*).

According to the most recent available estimates (August 2022), the CFR in Italy is estimated to be 0.8%, and the crude death rate is 288.98 per 100,000 people (ISS, 2020*a*; JHU, 2020; Ritchie et al., 2020).

As a result of swift immunization efforts worldwide, COVID-19 vaccines have considerably changed the course of the pandemic in Italy (Ferrara et al., 2022*a*; Ferrara et al., 2022*e*). Indeed, despite case numbers rising to over 100,000 in a single day during the predominance of Omicron, the proportions of severe disease, hospitalization and mortality remained below levels that do not require strong restrictions as long as booster vaccination is conducted and masks are worn in specific contexts. A comparison of daily counts of COVID-19 deaths in Italy during the three pandemic years is presented in Figure 2.4.

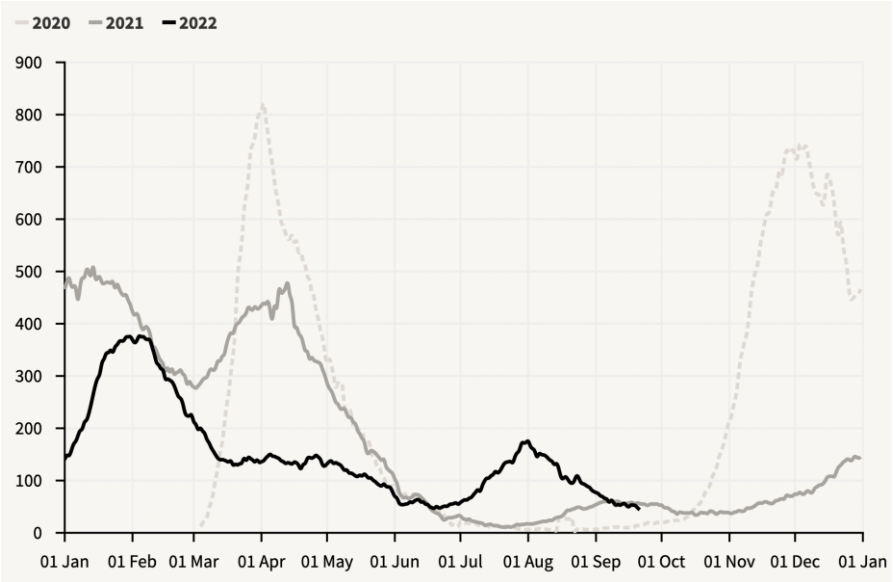


FIGURE 2.4: COVID-19 deaths in Italy as of September 15, 2022 in 2020 (dashed line), 2021 (grey line) and 2022 (black line). Source: Lab24. Coronavirus in Italia. Available from: https://lab24.ilsole24ore.com/coronavirus/. Data source: Presidenza del Consiglio dei Ministri-Dipartimento di Protezione Civile. Risorse dati su COVID-19. Available from: https://dati-covid.italia.it

*2.4 COVID-19 in the provinces of Bergamo and Brescia*

Images of Italian army trucks taking away coffins in Bergamo as morgues and cemeteries struggled to cope with the number of COVID-19 deaths spread around the world in March 2020. Indeed, Bergamo and Brescia were the two provinces hardest hit during the first wave of the Italian outbreak (Conti et al., 2020*a*).

According to the epidemiological analysis by Cereda et al., SARS-CoV-2 was already circulating in both provinces before February 20, 2020, with an estimated $R_0$ of 3 (95% confidence interval [95%CI] 2.5–3.5) in Bergamo and 3.3 (95%CI 2.9–3.7) in Brescia (Cereda et al., 2021).

During the emergency weeks in 2020, epidemiological surveillance missed a large proportion of cases. A nationwide sero-epidemiological study conducted by the Italian National Institute of Statistics (ISTAT) beginning in May 2020 found an overall anti-SARS-CoV-2 IgG prevalence of 2.5% in Italy, 7.5% in Lombardy and 24.1% in Bergamo (ISTAT, 2020).

The mortality and sero-epidemiological data describe the large COVID-19 burden in Italy, which was one of the largest COVID-19 epicentres in Europe (Cereda

et al., 2021; Conti et al., 2020*a*; Conti et al., 2020*b*; Della Valle et al., 2021). Figure 2.4 plots the percentage of daily deaths in relation to SARS-CoV-2 incidence (calculated as daily new positive swabs) and to the positive/total swabs ratio.

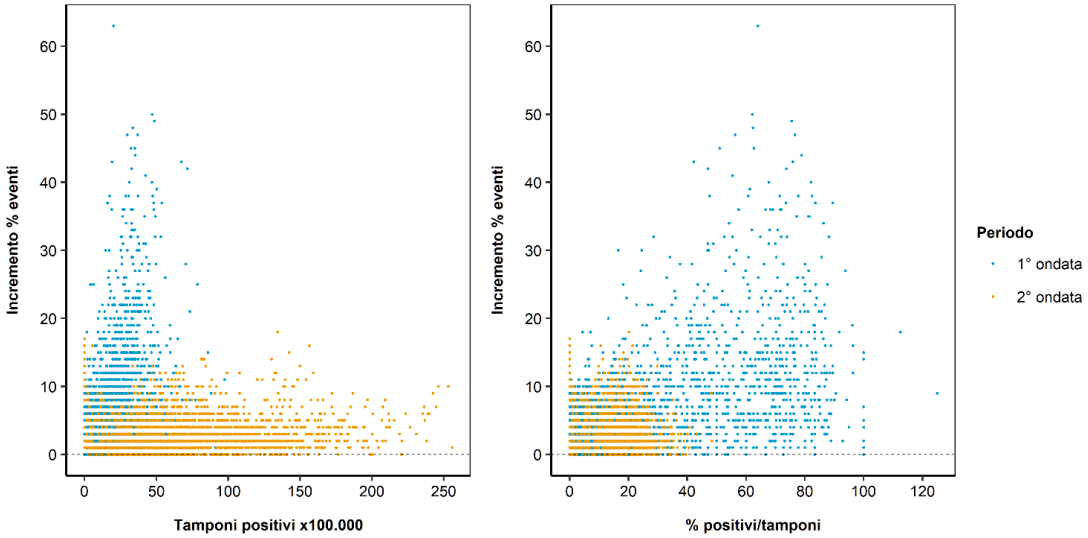


FIGURE 2.4: Scatterplot of the relationship between the daily deaths (percentage increase) and new positive swabs per 100,000 inhabitants (left panel), or the positive/total swabs ratio (right panel). Blue dots refer to the first wave and yellow dots to the second wave.

The background study for this dissertation analysed 104,849 deaths registered in the two HPAs up to June 30, 2021 (51,869 in Bergamo and 52,980 in Brescia) and found that the daily average number of deaths rose from 27.9 (standard deviation [SD] 6.4) in 2017–2019 to 38.9 (SD 45.1) during the pandemic period for the Bergamo HPA and from 29.2 (SD 6.8) to 38.3 (SD 28.0) in Brescia. The differential increases across age groups were similar in the two provinces, being higher in those aged 60 years or older and in subjects with chronic conditions. Changes in mortality predicted through regression analyses found a significant increase in overall deaths of 42.9% (95%CI 32.8–48.6) for the Bergamo area and 34.8% (95%CI 25.5–40.3) for Brescia (Figure 2.5).

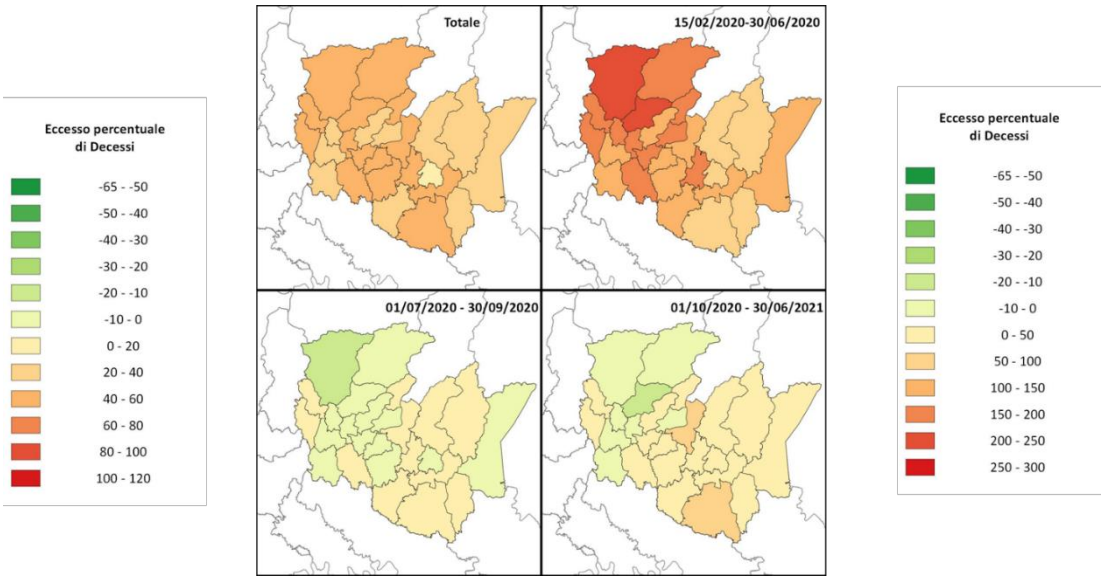


FIGURE 2.4: Geo-spatial distribution of percent excess death in the Bergamo and Brescia HPAs' districts during the first wave (15/02/2020-30/06/2020) and second wave (01/10/2020-30/06/2021), and the inter-wave period (01/07/2020-30/09/2020). Legend on the left refers to left panels and vice versa.

Excess mortality was concentrated in the first wave in 2020 (March–April), during which cumulative deaths increased by 1.66-fold (95%CI 1.35–1.85) for Bergamo and 1.04-fold (95%CI 0.79–1.18) for Brescia. Stratification by age showed that the increase in mortality was significant in age groups 70–79 and 80–89 years and, only for Bergamo, in men. An analysis of individuals without a positive SARS-CoV-2 test in the 21 days prior to death found an excess mortality of 94.1% (95%CI 66.3–115.2) in the Bergamo HPA and 49.7% (95%CI 27.8–67.1) in Brescia HPA (VICES-SMIRE Study Group, 2022).

# Chapter 3

# Impact of the COVID-19 pandemic on hospital admissions and emergency department visits

## *3.1 Introduction*

Lombardy rapidly became the first European area to be severely hit by COVID-19 (see sections 2.3 and 2.4). The emergency began with the detection of the first confirmed case on February 21, 2020—which was followed by strict stay-at-home measures in 11 municipalities in the Lombardy and Veneto regions—and culminated in regional and national lockdowns on March 7 and March 11, 2020, respectively (Conti et al., 2020*a*). The first national lockdown ended on May 4, 2020; however, the constantly evolving epidemiology of SARS-CoV-2 and the new surge in cases in autumn 2020 prompted the enforcement of new response actions to contain the pandemic. Unlike in the first wave, restrictions were upgraded using a system of region-based risk levels that included a set of indicators (e.g., number of cases and deaths, number of ICU admissions, percentage of occupied ICU beds, effective reproduction numbers—$R_t$, and $R_0$, etc.) that allowed the regional easing of restrictions to reduce the social and economic consequences of a protracted lockdown (d'Alessandro et al., 2021). Social-distancing restrictions were gradually eased from June 2021 and finally loosened in April 2022 as a consequence of broad COVID-19 vaccination in the population (Ferrara et al., 2022*a*; Ferrara et al., 2022*c*).

The COVID-19 pandemic impacted health services worldwide, overburdening hospitals and causing the rearrangement of facilities, while restrictive social-distancing measures and patients' fear of being infected created largescale disruptions in healthcare access (Caminiti et al., 2021; Ferrara and Albano, 2020; Nascimento et al., 2022; WHO, 2022*b*). Suddenly descending upon Lombardy, SARS-CoV-2 severely affected the provinces of Bergamo and Brescia (Cereda et al., 2021; Conti et al., 2020a), where it caught by surprise local healthcare services and particularly hospitals, which faced challenges in ensuring access to essential COVID-19 and non-COVID-19 care.

To understand the magnitude and time course of disruptions to hospital activity caused by the COVID-19 pandemic in these densely populated areas, a

longitudinal retrospective time series study was conducted on proxies of hospital access that were sourced from healthcare administrative databases (HADs), aiming at tracing important changes in overall hospital and emergency department (ED) admissions and providing data-driven responses to the burdens placed on local health services. In doing so, this research was designed to provide actionable approaches to better investigate COVID-19-related changes in healthcare utilization through 'new' strategies that could face methodological challenges underlined in previous literature (Corrao et al., 2022).

The analysis was divided into two phases: (*i*) a time series study on daily hospital admissions and ED visits during the pandemic period and (*ii*) a description of the spatial patterns of hospital and ED events that significantly increased owing to COVID-19, also exploring the effect of changing SARS-CoV-2 incidence in Bergamo and Brescia provinces (as measured by the number of daily cases registered in the COVID-19 integrated surveillance system).

### *3.2 Study population*

Italy has a tax-funded universal National Health Service (NHS) that is organised at three levels: national, regional and local. The Lombardy Regional Health Service (LHS) is served by eight Health Protection Agencies (HPAs) that cover mutually exclusive areas. Under the LHS, the 2015 Health and Social Care Reform (established on August 11, 2015, by law. no. 23 of the Lombardy Region) recognised HPAs as central purchasing bodies dedicated to drafting contracts between the Region and public and private health service providers (Garattini et al., 2022). HPAs are also primarily responsible for collecting population-level healthcare data including inpatient, outpatient, prescription, and mortality data (Regione Lombardia, 2019). The study population included all individuals covered by the HPAs of Brescia and Bergamo (Figure 3.1) from January 1, 2017 to June 30, 2021.

#### *3.2.1 The provinces of Bergamo and Brescia: demographics at a glance*

The province of Bergamo includes 243 municipalities; Bergamo is the capital and most populous city. As of the 2019 census (December 31), the province had a population of 1,108,126, establishing it as the third most populous province in Lombardy after Milan and Brescia. With Brescia as its capital city, the province of Brescia covers 203 municipalities and had a total of 1,255,437 inhabitants as of December 31, 2019. Both

provinces have the youngest age structure in Lombardy: the mean population age, the aging index, the old-age dependency ratio, and the structure index of the active population are the lowest in the region (ISTAT, 2021).

The Lombard population is considerably concentrated in the provinces of Milan (the capital of Lombardy), Brescia, and Bergamo, where more than half of the population lives in an area equal to 38% of the region (ISTAT, 2021). Selected 2019 demographic indicators for both provinces are listed in Table 3.1.

### *3.2.2 State of health in the provinces of Bergamo and Brescia*

The 2022 epidemiological update of ISS's non-communicable diseases (NCD) surveillance system indicated that more than 14 million people have at least one chronic condition, 3.5 million of which live in Lombardy, making up approximately one-third of the regional population (ISS, 2013).

The Lombardy Region activated the systematic surveillance of chronic diseases—termed 'Banca Dati Assistiti' (BDA)—a system based on automatic record linkages of databases on disease exemptions, treatments, hospital admissions, and outpatient visits (Lonati et al., 2008).

TABLE 3.1: 2019 Population statistics for Bergamo, Brescia, and the Lombardy Region

| Demographic indicators | Bergamo | Brescia | Lombardy |
|---|---|---|---|
| Mean age | 44.0 | 44.3 | 45.0 |
| Ageing index | 151.5 | 157.1 | 170.9 |
| Dependency ratio | 55.2 | 55.8 | 57.0 |
| Old-age dependency ratio | 33.3 | 34.1 | 35.9 |
| Structure index of the active population | 140.3 | 140.3 | 143.4 |

*Source:* Italian National Institute of Statistics
The *ageing index* measures the size of the older adult (aged 65 years and over) population per 100 persons younger than 15 years old. The *dependency ratio* refers to the number of dependents aged zero to 14 years and over the age of 65 years compared with the total population aged 15 to 64 years. The *old-age dependency ratio* is the ratio of the number of individuals aged 65 years and over to the number of people of working age (defined as those aged 20 to 64 years). The *structure index of the active population* defines the number of people in the 25 oldest generations (40–64-year-olds) over the 25 youngest ones (15–39-year-olds).

The OpenData website of the Lombardy Region presents information updated to 2017 on health and health systems in the eight HPAs. Data on patients with chronic or long-term illness in the LHS are grouped according to 62 conditions and are stratified by sex, age, area of residence, and level of complexity. The classification is based on three levels of complexity. The first, second, and third levels include patients

with more than three diseases, two or three diseases, and one chronic disease, respectively (Regione Lombardia, 2012).

In 2017, 350,193 and 384,946 patients with chronic or long-term disease were censused in the HPAs of Bergamo and Brescia, respectively. This translated to a prevalence of 11,163.29 and 11,480.54 per 100,000 inhabitants in Bergamo and Brescia, respectively. The distribution by level of complexity is displayed in Figure 3.2.

### *3.3 Data source*

To deliver the study objectives, HADs (detailed in Table 3.2) from the two HPAs were searched for data on hospital admissions, ED visits, and key population demographic and health characteristics.

TABLE 3.2: Data sources

| Healthcare administrative databases | Data retrieved |
|---|---|
| Registry of Lombardy Regional Health Service (LHS) customers | For each customer: age, sex, date of birth, date of death, district of residence, and LHS coverage period |
| Hospital discharge records (HDR) | For each admission: date, type (e.g., urgent or elective), diagnosis code (according to the 9th revision of the International Statistical Classification of Diseases – Clinical Modification [ICD-9-CM]), Diagnosis Related Group (DRG), and Major Diagnostic Category (MDC) |
| Emergency department visits | For each visit: date, colour-coded triage level (data from initial assessment upon arrival)[1], presenting complaint, and main diagnosis (ICD-9-CM code) |
| Banca Dati Assistiti (BDA), i.e., the registry of patients with chronic disease | For each patient: type and number of chronic and long-term illnesses |
| COVID-19 integrated surveillance | Daily number of SARS-CoV-2 swabs.[2] |

[1] The triage codes are: (i) *white* (minor trauma or complaints, evaluation in 240 min), (ii) *green* (non-urgent, evaluation in 120 min), (iii) *yellow* (urgent, evaluation in 15 min), (iv) *red* (emergent, resuscitation, or re-evaluation every 0 min), and (v) *black* (deceased).

[2] From January 15, 2021, the database further included cases diagnosed with rapid antigenic tests, as per the case definition updated by the Ministry of Health with Instruction no. 705-08/01/2021-DGPRE-DGPRE-P

For the regression analyses (see section 3.4.1), daily temperatures in the centroids of the two HPAs were sourced from the ERA5 reanalysis of the global climate produced by the Copernicus Climate Change Service at the European Centre for Medium-Range Weather Forecasts, which provides data on regular latitude–longitude grids at 0.25o x 0.25o resolution, with atmospheric parameters at 37 pressure levels (ECMWF, 2018).

### *3.4 Statistical analysis*

#### *3.4.1 First phase*

To model the variations in study outcomes (i.e., hospital admissions and ED visits) over the pandemic period, time series analyses of daily data were built for each event. Outcomes were assessed for both total and stratified data. For hospital admissions, stratification was performed by sex, age group (0–18, 19–59, 60–69, 70–79, 80–89, and ≥ 90 years), principal diagnosis (according to ICD-9-CM code), type of diagnosis-related group (DRG; medical or surgical), major diagnostic category (MDC), and chronic condition. A similar strategy was followed to investigate the time series of ED visits, which were sorted by sex, age group (0–18, 19–59, 60–69, 70–79, 80–89, and ≥ 90 years), triage code, presenting complaint, main diagnosis (ICD-9-CM code), and chronic condition.

The numbers of total and stratified daily hospital events during the pandemic period (2020–2021) were compared with those from the pre-pandemic (2017–2019) period using the Wilcoxon rank sum test. At the time of data sharing, the BDA and the ED visits database had collected data up to December 31, 2020 and 31 May 2021, respectively; therefore, comparisons were calibrated accordingly.

Next, to quantify the time-varying impact of the COVID-19 pandemic on the excesses or reductions of events, the data were fitted with quasi-Poisson generalized additive models with smooth spline functions for time variables and observed predictors (Bhaskaran et al., 2013) following the methodology described by Scortichini et al. (2020) with the inclusion of the following predictors:

- a linear term for the day date to explore long-term trends;
- a cyclic cubic B-spline with three equally spaced knots for the calendar date, to consider seasonality;
- indicators for weekdays to control for weekly variations and potential weekend effects;

- a constrained quadratic B-spline with 16 equally spaced knots (or 10 in the case of outcomes that stopped on December 31, 2020 in HADs) for the period from February 1, 2020 onwards (i.e., the pandemic period). This spline ensures the pandemic impact begins in February 2020 and then allows it to vary over the time-window considered;
- a cross-basis parameterization of the mean daily temperature at HPAs' centroids, modelling a distributed lag non-linear model over 0–21 lag days. This function accounts for possible differences in events attributable to non-optimal weather between the pre-pandemic and pandemic periods.

To ensure the consistency of the analysis, regression models were applied to events with a median daily number equal to or higher than five.

After dividing the pandemic period into three parts—roughly corresponding to the first wave (February 15 – June 30, 2020), the inter-wave (July 1 – September 30, 2020), and the second wave (October 1, 2020 – June 30, 2021)—cumulative variations were calculated as $\frac{RR-1}{RR} * n$, where $n$ is the number of events on a certain calendar date and RR the relative risk computed by comparing the pre-pandemic and pandemic periods. 95% CIs were estimated using simulation techniques (Scortichini et al., 2020).

Variations were expressed as percent variation in the cumulative number of hospital events using 2017–2019 cumulative data as a reference. Results are discussed separately for each hospital admissions and ED visits.

*3.4.2 Second phase*

For events that showed a significant COVID-19-attributable excess in the analyses described in 3.4.1, geospatial patterns were obtained by reiterating time series analyses stratified by the residential area of the corresponding LHS customers. Territorial units are based on existing HPA districts in the two provinces (Figure 3.1). This hierarchical system defines geographical areas for which a functional subdivision of HPA is empowered. This district-based analysis facilitates the collection and assessment of harmonised local statistics.

Subsequently, the association between the excess in outcomes and SARS-CoV-2 circulation was studied in two stages. First, scatter graphs of district-specific daily rates were plotted for positive SARS-CoV-2 swabs in the general population, the total number of SARS-CoV-2 swabs performed, and the ratio between positive and total swabs. Second, in order to model the temporal dependency between viral circulation and excesses in hospital events, generalized additive models were employed (following the building strategy described in section 3.4.1), in which the impact of

COVID-19 was assessed using a cross-basis parameterization of the daily SARS-CoV-2 incidence as positive swabs per 100,000 inhabitants for the pandemic periods and modelling a distributed lag non-linear model over 31 lag days with three degrees of freedom for the association with incidence. Such model allows non-linearity in bi- and three-dimensional exposure-lag response surface and thus offers a substantial advantage to traditional approaches (Smith et al., 2021). To quantify the direction and magnitude of the exposure–lag response, effects were expressed as the incidence rate ratio (IRR) of each hospital event associated with an increase of 1x100,000 in SARS-CoV-2 infections by time lag and reference level. IRR is the ratio of each hospital outcome rate in the "exposed" group ((i.e. specified increment in the incidence of SARS-CoV-2 infections compared to some reference level) to the outcomes rate in the 'non-exposed" group (i.e. SARS-CoV-2 incidence at the reference level) (Smith et al., 2021). Therefore, the IRR represents the effect that changing the proportion of cases in the population has on excess in hospital and ED admissions.

## *3.5 Results*

### *3.5.1 Hospital admissions*

Over the entire 2017–2021 study period, 1,067,484 hospitalizations were recorded in the two HPAs: 487,860 for Bergamo and 579,624 for Brescia. Overall, the COVID-19 outbreak caused a substantial reduction in the daily number of admissions (Table 3.3 and Figure 3.3). The average daily number of admissions in the Bergamo HPA dropped from 322.3 (SD 129.2) in the pre-outbreak period to 246.6 (SD 105.1) after the onset of COVID-19, and in the Brescia HPA from 382.3 (SD 140.5) pre-outbreak to 294.5 (SD 109.7) post-outbreak. The decreases were significant in both sexes and across all age groups.

Regression analyses showed a non-homogeneous impact across types of hospital admission. While the overall reduction reached −26.3% (95%CI −29.8% to −23.3%) and −24.1% (95%CI −27.7% to −20.9%) for Bergamo and Brescia, respectively, the decrease was larger for elective (−33.5% [95%CI −37.4% to −30.2%] and −33.0% [95%CI −36.9% to −29.4%]) than for urgent admissions (−11.5% [95%CI −16.0% to −8.1%] and −9.1% [95%CI −13.8% to −5.8%] (Tables 3.4a–c, Figures 3.4 and 3.5).

Focusing the analysis on urgent hospital admissions, excess events were estimated in the two provinces. In Bergamo, the excess during the first wave was 16.3% (95%CI 6.5% to 23.3%) in males and 39.0% (95%CI 31.0% to 45.1%) and 26.5% (95%CI 18.4 to 32.6%) in the 60–69-year and 70–79-year age groups, respectively.

Excess of more 20.9% (95%CI 14.1% to 26.4%) and 10.5% (95%CI 2.6% to 16.3%) in the 60–69-year and 70–79-year age groups, respectively, was also observed in Brescia (Tables 3.4b, Figures 3.4 and 3.5).

Table 3.4c details the changed in elective hospital admissions. Reductions persisted over the entire pandemic period (waves' distribution); however, the largest (−60.8%; 95%CI −68.6% to −51.2%) was registered during the first wave in the area of Bergamo for the older age groups in both HPAs.

Analyses based on the ICD-9-CM code of the primary diagnoses reported on the HDRs (Tables 3.5 and 3.6a–c) showed a significant excess of admissions for respiratory diseases (codes between 460 and 519) during the first wave, with 109.3% (95%CI 90.6% to 122.6%) and 60.0% (95%CI 45.4% to 70.3%) increases in the Bergamo and Brescia HPAs, respectively (Figures 3.6a and 3.7a). These increases were all attributable to the excess in urgent admissions, with more 229.7% (95%CI 169.5% to 286.4%) and 125.7% (95%CI 85.6% to 166.1%) admissions in the Bergamo and Brescia HPAs, respectively (Figures 3.6b and 3.7b). Reductions were described for all the other ICD-9-CM-based categories except elective admissions with diagnoses of complications of pregnancy, childbirth, and the puerperium (codes 630 to 677), for which a nonsignificant excess was observed (Figures 3.6c and 3.7c). Similarly, analyses stratified by MDC described a significant increase during the first wave for urgent admissions with diagnoses of the respiratory system (MDC 04) and a nonsignificant increase for elective admissions for pregnancy, childbirth, and the puerperium (MDC 14; Tables 3.7 and 3.8a–c, Figures 3.8a–c and 3.9a–c).

Results stratified by type of DRG (surgical or medical) are reported in Tables 3.9 and 3.10a–c, and Figures 10 and 11. Significant decreases were observed for both DRGs, with larger reductions in admissions with surgical DRGs during the first wave in both HPAs; the only exception was an increase of urgent admissions with medical DRGs in Bergamo during the first wave.

While significant reductions in hospital admissions were seen in chronic LHS patients censused in the BDA (Table 3.11, Figures 3.12a–c and 3.13a–c), no differences based on the type of comorbid condition were observed (Tables 3.12a–c).

### *3.5.2 Emergency department visits*

The ED database comprised 3,330,117 visits, of which 1,523,314 were associated with the Bergamo HPA and 1,806,803 were associated with the Brescia HPA.

The time series of the daily number of ED visits from 2017 is presented in Figure 3.14. Compared with those in the pre-pandemic period, ED visits decreased

over the entire study period because of COVID-19. The estimated overall reduction was −37.6%, (95%CI −38.68% to −36.76%) in Bergamo and −37.0% (95%CI −38.0% to −36.1%) in Brescia, being particularly marked (approximately −70%) for individuals aged 18 years or younger in both areas (Tables 3.13 and 3.14, Figures 3.15 and 3.16).

Analyses stratified by colour-coded triage level described reductions in all codes but red, which increased by 23.4% (95%CI 10.2% to 33.9%) and 22.4% (95% CI= 9.2% to 32.9%) in the provinces of Bergamo and Brescia, respectively, during the first wave (Tables 3.15 and 3.16, Figures 3.17 and 3.18).

Investigating the patterns of ED visits during the first wave according to the ICD-9-CM code of the main principal diagnosis (Table 3.17 and 3.18, Figures 3.19 and 3.20) and to the presenting complaint (Table 3.19 and 3.20, Figures 3.21 and 3.22), excesses of accesses of 37.3% (95%CI 5.7% to 75.5%) for diseases of the respiratory system (ICD-9-CM codes between 460 and 519) and 77.8% (95%CI 27.1% to 132.0%) for dyspnoea were registered in the Bergamo HPA.

Reductions in ED visits were observed in patients censused in the BDA (Table 3.21), with no differences based on the chronic conditions (Table 3.22, Figures 3.23 and 3.24).

### *3.5.3 Geospatial analyses*

As previously explained, geospatial analyses were limited to events that showed a significant excess (see sections 3.5.1 and 3.5.2). For urgent hospital admissions, these events were total admissions, admissions with ICD-9-CM for diseases of the respiratory systems, admissions with MDCs of the respiratory system, and admissions with medical DRGs. For ED visits, these included red-code and respiratory ICD-9-CM visits.

All described excesses in urgent hospital admissions followed a single geospatial pattern starting in the Val Seriana area—where the first cases were registered—and surrounding areas and were more intense in the first wave (Figure 3.25-27). Conversely, the second wave had a stronger impact on urgent admissions with a respiratory ICD-9-CM code (Figure 2.27) and MDC of the respiratory system (Figure 2.28) in the area of the Brescia HPA.

The excesses in red-code and respiratory ICD-9-CM code ED visits mirrored those in urgent hospital admissions, with the first events registered in Val Seriana and surrounding areas and higher intensity during the first wave (Figures 3.29 and 3.30). Red-code visits also registered a higher second-wave-impact in the province of Brescia.

Figures 3.31 to 3.36 allow the graphical study of the association between the listed events and the daily incidence of SARS-CoV-2, which was measured as the number of new positive swabs per 100,000 inhabitants—or the positive/total swabs ratio.

In the regression models built to investigate the association between the excess in hospital events and the SARS-CoV-2 circulation, results described a positive association—which was also stronger during the first wave—with the daily cases' incidence. The joint-effect of lag (days) and new positive SARS-CoV-2 swabs (per 100,000 inhabitants) on the predicted IRRs of each studied event was presented in Tables 3.23 to 3.34: there was a clear interaction effect between increments in viral circulation and lag on the IRR, whereby the response to changes in cases' incidence started immediately and continued over the following 7 days. The IRRs were not constant but increased with the increases in incidence (Figures 3.37–48).

### *3.6 Concluding remarks*

This research aimed to understand the indirect impact of the COVID-19 pandemic on hospital utilization in the epicentre of the Italian outbreak and, more in general, on the LHS. Measuring the unprecedented recent changes in hospital activity during COVID-19 is critical in addressing the resilience of health systems and their ability to optimize resource management in the post-pandemic (Corrao et al., 2022).

During the pandemic period, the number of patients admitted to hospitals and ED saw important reductions. Overall, the side effects of the COVID-19 pandemic were traced during the entire pandemic period and differences based on pandemic phases and type of hospital admission were observed. Moreover, the demographic characteristics across the two provinces may have contributed to HPA-related differences.

For most admissions, the COVID-19 impact was greater during the first months of the pandemic, when hospitals were overwhelmed with cases of the "novel" disease. Subsequently, a broader understanding of the disease course and management and the rapid development of management approaches including hospital reorganization and the building of space for beds softened the impact of COVID-19 on overall hospital activity. According to recently published hospital bed occupancy data (Ministry of Health, 2022), Lombardy registered the greatest proportion of ordinary hospital beds that were converted for COVID-19 patients (32.1% vs. the Italian mean of 20.5%); this compares with a pre-pandemic total hospital capacity of 352 and only four infectious disease beds per 100,000 population

(WHO Europe, 2020). The subsequent creation of COVID-19 hospitals, non-nosocomial facilities (i.e., COVID-10 hotels, where patients with mild disease could isolate with nursing support), and community-based and home services was crucial in responding to the surging demand for hospital care (Conti et al., 2020*a*; European Observatory on Health Systems and Policies [EOHSP], 2020; WHO, 2022*b*; WHO Europe, 2020).

The analyses found that only admissions related to COVID-19 increased significantly in 2020 and 2021 compared with those in the pre-pandemic period. The excess was observed in urgent hospital admissions and those with respiratory diagnoses while ED visits increased for only red-code and respiratory problems. In this sense, it is also worth mentioning that results are consistent with previous findings that highlighted the increase of hospital activity likely associated with COVID-19 patients, such as the surge in pre-MDC (i.e., MCD assignment based on extremely resource intensive procedure rather than principal diagnosis) that included mechanical ventilation DRGs (Kalanj et al., 2021).

The study of the geospatial distribution of excesses in these outcomes indicated a more-than-linear growth in exposure–response trends with an increment in positive SARS-CoV-2 swabs. The increase in magnitude of the response with greater cases' incidence is therefore consistent with a positive relationship between the viral circulation and admissions related to COVID-19.

Major reasons for the detrimental indirect impact of the COVID-19 pandemic on hospital activity are excessive organizational difficulties, hospital overload and the related substantial shortage of healthcare resources, the heavy workload of healthcare professionals and their task-shifting to ensure care for COVID-19 infections and acute life-threatening conditions, internal rearrangement of routine activities, and the closure of certain services, which resulted in a critical number of patients being deferred during the pandemic (Capuzzo et al., 2022; d'Alessandro et al., 2021; Ferrara et al., 2022*f*; Ferrara and Albano, 2020; Stirparo et al., 2022; Viganò et al., 2020; Voza et al., 2021). In addition, fear of contagion among healthcare users and patients, stay-at-home orders, recommendations to avoid unnecessary access to health services, and possible misinterpretation of the norm may have contributed to the reduced access to health services—particularly hospital and ED admission for non-life-threatening complaints (Bittleston et al., 2022; Mantica et al., 2020; Raucci et al., 2021; Spadea et al., 2021; Stirparo et al., 2022).

The analyses also described a notable change in ED utilization during the COVID-19 pandemic period. Previous research in other contexts has also observed a considerably greater reduction in the volume of non-hospitalized cases, suggesting a

decline in non-urgent or inappropriate ED visits mostly driven by the user avoidance effect (Stirparo et al. 2022; Wartelle et al., 2021).

Evidence from many countries and regions supports that COVID-19 caused substantial disruption in healthcare service delivery and utilization. The third round of the Global Pulse Survey on continuity of essential health services during the COVID-19 pandemic (Q3/2021) highlighted that 91% of the WHO countries reported disruption by the end of 2021 (WHO, 2022*b*), specifically in outpatient services and elective admissions and surgeries (Cedrone et al., 2022; Di Martino et al., 2022; Ferrara et al., 2022*f*; EOHSP, 2022; Robakowska et al., 2022; WHO, 2022*b*). To better understand the extent of disruptions in hospital utilization caused by the COVID-19 pandemic, this real-world analysis presents local findings from highly populated provinces in northern Italy using a robust methodology that considered the care that was expected to be provided during the pandemic based on population cohorts of the previous 5 years, corrected for relevant confounders such as seasonality in care provision, and adjusted for proxies of SARS-CoV-2 circulation. Therefore, this research is crucial in guiding future measures to address waiting lists/time and patient volumes and backlogs; such measures can deliver what are widely considered to be important unmet healthcare needs (EOHSP, 2022; WHO, 2022*b*). For instance, the backlog for elective surgery is estimated to have reached up to 33% in Europe, and 20% of waiting lists include people waiting for procedures (EOHSP, 2022; WHO, 2022*b*). Indeed, surgery systems worldwide were fragile to lockdowns, with a large number of patients—including those waiting for cancer surgery—not undergoing planned treatment and experiencing longer preoperative delays (COVIDSurg Collaborative, 2021; Ferrara et al., 2022*f*).

While Italy has begun planning for post-pandemic recovery with national and local plans for building longer-term health service resilience and preparedness, more research is needed to understand the precise extent of COVID-19's impact on the hospital functioning—also considering hospital bed management and occupancy, and possible supply-induced demand in pre-COVID-19 era—and on the efficiency in the management of clinical cases, as well as on the potential consequences to non-hospital and community care.

Similarly, population-based epidemiological analyses and health impact assessments should focus on the future course of the diseases whose management was paused during the pandemic.

To build a resilient healthcare system, research on health services should further propose strategies to address the prompt adaptation of services and the reorganization of hospital and community activities to minimize the impact of

COVID-19 (EOHSP, 2021; Ferrara et al., 2022*f*; Ferrara et al., 2022*g*; Ferrara and Albano, 2020).

### *3.7 Tables and Figures*

### *3.7.1 Tables*

TABLE 3.3: Difference in daily counts of total hospital admissions before (2017-2019) and during COVID-19 pandemic (2020-2021), stratified by sex and age

| | **Bergamo HPA** | | | **Brescia HPA** | | |
|---|---|---|---|---|---|---|
| | **Jan 2017 - Dec 2019** | **Jan 2020 - Jun 2021** | ***p*-value** | **Jan 2017 - Dec 2019** | **Jan 2020 - Jun 2021** | ***p*-value** |
| **Total** | | | | | | |
| Total | 352965 | 134895 | | 418561 | 161063 | |
| Daily events | | | | | | |
| Mean (±SD) | 322.34 (129.15) | 246.61 (105.08) | <0.001 | 382.25 (140.52) | 294.45 (109.71) | <0.001 |
| Median (IQR) | 379 (160-426) | 270 (133-326) | | 432 (217-495) | 319 (181-376) | |
| Min - max | 87-540 | 43-514 | | 130-635 | 53-584 | |
| **Sex** | | | | | | |
| **Female** | | | | | | |
| Total | 182069 | 68760 | | 218758 | 82971 | |
| Daily events | | | | | | |
| Mean (±SD) | 166.27 (63.73) | 125.7 (51.2) | <0.001 | 199.78 (71) | 151.68 (55.39) | <0.001 |
| Median (IQR) | 191 (90-217) | 135 (75-164) | | 222 (119-260) | 159 (99-192) | |
| Min - max | 48-291 | 24-265 | | 67-334 | 27-314 | |
| **Male** | | | | | | |
| Total | 170896 | 66135 | | 199803 | 78092 | |
| Daily events | | | | | | |
| Mean (±SD) | 156.07 (66.72) | 120.9 (55.93) | <0.001 | 182.47 (71.39) | 142.76 (56.36) | <0.001 |
| Median (IQR) | 183 (74-209) | 136 (61-165) | | 207 (99-237) | 151 (85-186) | |
| Min - max | 32-271 | 16-280 | | 47-325 | 18-290 | |
| **Age group** | | | | | | |
| **0-18 years** | | | | | | |
| Total | 28933 | 8721 | | 32192 | 8819 | |
| Daily events | | | | | | |
| Mean (±SD) | 26.42 (11.8) | 15.94 (8.78) | <0.001 | 29.4 (11.01) | 16.12 (8.61) | <0.001 |
| Median (IQR) | 29 (14-36) | 15 (8-22) | | 30 (20-38) | 15 (9-21) | |
| Min - max | 3-54 | 2-53 | | 5-59 | 1-51 | |
| **19-59 years** | | | | | | |
| Total | 145157 | 55351 | | 160872 | 61295 | |
| Daily events | | | | | | |

| | | | | | | |
|---|---|---|---|---|---|---|
| Mean (±SD) | 132.56 (56.99) | 101.19 (45.99) | <0.001 | 146.92 (60.98) | 112.06 (46.69) | <0.001 |
| Median (IQR) | 156 (62-176) | 109 (54-137) | | 172 (73-195) | 123 (64-148) | |
| Min - max | 19-251 | 21-209 | | 37-249 | 24-238 | |
| **60-69 years** | | | | | | |
| Total | 53792 | 21515 | | 59598 | 23941 | |
| Daily events | | | | | | |
| Mean (±SD) | 49.13 (23.79) | 39.33 (20.04) | <0.001 | 54.43 (24.95) | 43.77 (19.71) | <0.001 |
| Median (IQR) | 57 (22-68) | 43 (19-55) | | 61 (28-74) | 46 (26-59) | |
| Min - max | 4-98 | 4-89 | | 8-111 | 3-101 | |
| **70-79 years** | | | | | | |
| Total | 66020 | 26064 | | 80176 | 31675 | |
| Daily events | | | | | | |
| Mean (±SD) | 60.29 (25.9) | 47.65 (22.53) | <0.001 | 73.22 (29.51) | 57.91 (23.9) | <0.001 |
| Median (IQR) | 68 (32-82) | 49 (26-65) | | 80 (43-97) | 60 (36-76) | |
| Min - max | 13-107 | 1-113 | | 17-151 | 3-132 | |
| **80-89 years** | | | | | | |
| Total | 48219 | 19378 | | 67319 | 27648 | |
| Daily events | | | | | | |
| Mean (±SD) | 44.04 (14.51) | 35.43 (13.46) | <0.001 | 61.48 (17.82) | 50.54 (15.88) | <0.001 |
| Median (IQR) | 47 (30-55) | 36 (25-44) | | 64 (45-75) | 51 (38-61) | |
| Min - max | 12-82 | 4-79 | | 17-110 | 3-97 | |
| **90+ years** | | | | | | |
| Total | 10844 | 3866 | | 18404 | 7685 | |
| Daily events | | | | | | |
| Mean (±SD) | 9.9 (3.81) | 7.07 (3.44) | <0.001 | 16.81 (5.28) | 14.05 (5.2) | <0.001 |
| Median (IQR) | 9 (7-12) | 7 (5-9) | | 16 (13-20) | 14 (11-17) | |
| Min - max | 1-26 | 0-22 | | 3-34 | 0-32 | |

Abbreviations: HPA, Health Protection Agency; SD, standard deviation; IQR, interquartile range

TABLE 3.4a: Change in total hospital admissions during the pandemic period, stratified by sex and age

| | Bergamo HPA | | | Brescia HPA | | |
|---|---|---|---|---|---|---|
| | Total | Change (95%CI) | % Change (95%CI) | Total | Change (95%CI) | % Change (95%CI) |
| **Total** | | | | | | |
| All admissions from 15/02/2020 | 119970 | -42867 (-50800; -36353) | -26.33 (-29.75; -23.26) | 143319 | -45403 (-54763; -37921) | -24.06 (-27.65; -20.92) |
| 15/02/2020 - 30/06/2020 (1st wave) | 28894 | -17208 (-20855; -14440) | -37.33 (-41.92; -33.32) | 35099 | -18727 (-22971; -15671) | -34.79 (-39.56; -30.87) |
| 01/07/2020 - 30/09/2020 | 23532 | -3964 (-4906; -3111) | -14.42 (-17.25; -11.68) | 27481 | -4127 (-5186; -3145) | -13.06 (-15.88; -10.27) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 67544 | -21695 (-25619; -18221) | -24.31 (-27.50; -21.24) | 80739 | -22549 (-26972; -18457) | -21.83 (-25.04; -18.61) |
| **Sex** | | | | | | |
| **Female** | | | | | | |
| All admissions from 15/02/2020 | 61113 | -21948 (-26117; -18188) | -26.42 (-29.94; -22.94) | 73751 | -23308 (-28122; -19008) | -24.01 (-27.60; -20.49) |
| 15/02/2020 - 30/06/2020 (1st wave) | 14384 | -9092 (-10757; -7637) | -38.73 (-42.79; -34.68) | 17804 | -9937 (-11924; -8092) | -35.82 (-40.11; -31.25) |
| 01/07/2020 - 30/09/2020 | 12159 | -1984 (-2515; -1491) | -14.03 (-17.14; -10.93) | 14236 | -2045 (-2641; -1489) | -12.56 (-15.65; -9.47) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 34570 | -10872 (-13009; -8826) | -23.93 (-27.34; -20.34) | 41711 | -11326 (-13740; -9045) | -21.35 (-24.78; -17.82) |
| **Male** | | | | | | |
| All admissions from 15/02/2020 | 58857 | -20901 (-25114; -17615) | -26.21 (-29.91; -23.03) | 69568 | -22137 (-26947; -18373) | -24.14 (-27.92; -20.89) |
| 15/02/2020 - 30/06/2020 (1st wave) | 14510 | -8105 (-10193; -6659) | -35.84 (-41.26; -31.46) | 17295 | -8808 (-11271; -7075) | -33.74 (-39.45; -29.03) |
| 01/07/2020 - 30/09/2020 | 11373 | -1977 (-2483; -1530) | -14.81 (-17.92; -11.86) | 13245 | -2085 (-2616; -1544) | -13.60 (-16.49; -10.44) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 32974 | -10819 (-12779; -9023) | -24.70 (-27.93; -21.48) | 39028 | -11244 (-13626; -9264) | -22.37 (-25.88; -19.18) |
| **Age groups** | | | | | | |
| **0-18 years** | | | | | | |
| All admissions from 15/02/2020 | 7510 | -5418 (-6055; -4921) | -41.91 (-44.64; -39.58) | 7449 | -5702 (-6406; -5168) | -43.36 (-46.24; -40.96) |
| 15/02/2020 - 30/06/2020 (1st wave) | 1535 | -2173 (-2438; -1983) | -58.60 (-61.36; -56.36) | 1673 | -2125 (-2403; -1941) | -55.95 (-58.95; -53.70) |
| 01/07/2020 - 30/09/2020 | 1605 | -570 (-726; -419) | -26.20 (-31.14; -20.70) | 1610 | -478 (-634; -335) | -22.90 (-28.24; -17.21) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 4370 | -2675 (-3335; -2073) | -37.97 (-43.28; -32.18) | 4166 | -3099 (-3802; -2455) | -42.65 (-47.71; -37.08) |
| **19-59 years** | | | | | | |
| All admissions from 15/02/2020 | 49472 | -14945 (-16603; -13660) | -23.20 (-25.13; -21.64) | 54741 | -17474 (-19364; -16043) | -24.20 (-26.13; -22.66) |
| 15/02/2020 - 30/06/2020 (1st wave) | 11086 | -7270 (-8525; -6130) | -39.60 (-43.47; -35.61) | 12979 | -7595 (-8999; -6311) | -36.91 (-40.95; -32.72) |
| 01/07/2020 - 30/09/2020 | 9962 | -1028 (-1728; -438) | -9.35 (-14.78; -4.21) | 10660 | -1649 (-2451; -956) | -13.40 (-18.70; -8.23) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 28424 | -6647 (-7984; -5525) | -18.95 (-21.93; -16.27) | 31102 | -8230 (-9739; -6944) | -20.93 (-23.85; -18.25) |
| **60-69 years** | | | | | | |
| All admissions from 15/02/2020 | 19260 | -5905 (-7375; -4722) | -23.47 (-27.69; -19.69) | 21501 | -5806 (-7429; -4572) | -21.26 (-25.68; -17.53) |
| 15/02/2020 - 30/06/2020 (1st wave) | 4698 | -2394 (-2904; -1977) | -33.75 (-38.20; -29.62) | 5288 | -2536 (-3150; -2070) | -32.41 (-37.33; -28.13) |
| 01/07/2020 - 30/09/2020 | 3708 | -508 (-693; -340) | -12.04 (-15.76; -8.41) | 4004 | -542 (-757; -361) | -11.93 (-15.89; -8.26) |

| | | | | | | |
|---|---|---|---|---|---|---|
| 01/10/2020 - 30/06/2021 (2nd wave) | 10854 | -3003 (-3925; -2241) | -21.67 (-26.56; -17.12) | 12209 | -2728 (-3747; -1943) | -18.26 (-23.48; -13.73) |
| **70-79 years** | | | | | | |
| All admissions from 15/02/2020 | 23237 | -8126 (-10638; -6239) | -25.91 (-31.40; -21.17) | 28239 | -7912 (-10896; -5721) | -21.89 (-27.84; -16.85) |
| 15/02/2020 - 30/06/2020 (1st wave) | 5938 | -2881 (-3724; -2314) | -32.66 (-38.55; -28.04) | 7188 | -3183 (-4173; -2516) | -30.69 (-36.73; -25.93) |
| 01/07/2020 - 30/09/2020 | 4376 | -907 (-1334; -528) | -17.17 (-23.36; -10.78) | 5292 | -724 (-1219; -298) | -12.03 (-18.72; -5.33) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 12923 | -4339 (-5685; -3241) | -25.13 (-30.55; -20.05) | 15759 | -4005 (-5583; -2739) | -20.26 (-26.16; -14.80) |
| **80-89 years** | | | | | | |
| All admissions from 15/02/2020 | 17149 | -6653 (-9898; -4275) | -27.95 (-36.60; -19.96) | 24712 | -6258 (-10484; -3189) | -20.21 (-29.79; -11.43) |
| 15/02/2020 - 30/06/2020 (1st wave) | 4788 | -1872 (-2170; -1657) | -28.11 (-31.18; -25.71) | 6230 | -2491 (-2883; -2204) | -28.56 (-31.64; -26.13) |
| 01/07/2020 - 30/09/2020 | 3271 | -724 (-1189; -333) | -18.13 (-26.66; -9.25) | 4700 | -521 (-1121; -24) | -9.98 (-19.26; -0.51) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 9090 | -4057 (-6549; -2139) | -30.86 (-41.88; -19.05) | 13782 | -3246 (-6422; -763) | -19.06 (-31.78; -5.25) |
| **90+ years** | | | | | | |
| All admissions from 15/02/2020 | 3342 | -1908 (-3052; -1136) | -36.34 (-47.73; -25.38) | 6677 | -2296 (-4206; -1005) | -25.59 (-38.65; -13.08) |
| 15/02/2020 - 30/06/2020 (1st wave) | 849 | -629 (-997; -414) | -42.54 (-54.02; -32.76) | 1741 | -822 (-1470; -445) | -32.08 (-45.79; -20.36) |
| 01/07/2020 - 30/09/2020 | 610 | -232 (-402; -101) | -27.53 (-39.71; -14.16) | 1215 | -224 (-505; -9) | -15.54 (-29.38; -0.72) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 1883 | -1047 (-1641; -612) | -35.74 (-46.57; -24.54) | 3721 | -1251 (-2237; -523) | -25.15 (-37.55; -12.33) |

Abbreviations: HPA, Health Protection Agency; 95%CI, 95% confidence interval

TABLE 3.4b: Change in urgent hospital admissions during the pandemic period, stratified by sex and age

| | Bergamo HPA | | | Brescia HPA | | |
|---|---|---|---|---|---|---|
| | Total | Change (95%CI) | % Change (95%CI) | Total | Change (95%CI) | % Change (95%CI) |
| **Total** | | | | | | |
| All admissions from 15/02/2020 | 56249 | -7280 (-10744; -4938) | -11.46 (-16.04; -8.07) | 79979 | -8068 (-12749; -4917) | -9.16 (-13.75; -5.79) |
| 15/02/2020 - 30/06/2020 (1st wave) | 18052 | 596 (-737; 1601) | 3.42 (-3.92; 9.73) | 22752 | -1745 (-3633; -310) | -7.13 (-13.77; -1.35) |
| 01/07/2020 - 30/09/2020 | 9697 | -1488 (-2230; -816) | -13.31 (-18.70; -7.76) | 14185 | -1221 (-2259; -327) | -7.93 (-13.74; -2.25) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 28500 | -6388 (-9928; -3465) | -18.31 (-25.83; -10.84) | 43042 | -5101 (-10009; -1094) | -10.60 (-18.87; -2.48) |
| **Sex** | | | | | | |
| **Female** | | | | | | |
| All admissions from 15/02/2020 | 29384 | -5104 (-6671; -3888) | -14.80 (-18.50; -11.69) | 40889 | -5698 (-7739; -4092) | -12.23 (-15.91; -9.10) |
| 15/02/2020 - 30/06/2020 (1st wave) | 8651 | -735 (-1283; -252) | -7.83 (-12.91; -2.83) | 11174 | -1766 (-2535; -1123) | -13.65 (-18.49; -9.14) |
| 01/07/2020 - 30/09/2020 | 5436 | -761 (-1129; -430) | -12.28 (-17.20; -7.34) | 7552 | -641 (-1120; -227) | -7.83 (-12.91; -2.92) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 15297 | -3608 (-5211; -2297) | -19.08 (-25.41; -13.06) | 22163 | -3291 (-5463; -1499) | -12.93 (-19.78; -6.34) |
| **Male** | | | | | | |
| All admissions from 15/02/2020 | 26865 | -2181 (-4054; -964) | -7.51 (-13.11; -3.47) | 39090 | -2388 (-5071; -665) | -5.76 (-11.48; -1.67) |
| 15/02/2020 - 30/06/2020 (1st wave) | 9401 | 1315 (571; 1778) | 16.26 (6.47; 23.33) | 11578 | 12 (-1053; 691) | 0.10 (-8.34; 6.35) |
| 01/07/2020 - 30/09/2020 | 4261 | -724 (-1141; -365) | -14.52 (-21.12; -7.89) | 6633 | -582 (-1183; -50) | -8.06 (-15.13; -0.75) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 13203 | -2773 (-4656; -1274) | -17.36 (-26.07; -8.80) | 20879 | -1818 (-4516; 323) | -8.01 (-17.78; 1.57) |
| **Age groups** | | | | | | |
| **0-18 years** | | | | | | |
| All admissions from 15/02/2020 | 3518 | -2092 (-2807; -1536) | -37.29 (-44.38; -30.39) | 4035 | -2975 (-3879; -2277) | -42.44 (-49.02; -36.07) |
| 15/02/2020 - 30/06/2020 (1st wave) | 857 | -724 (-972; -563) | -45.79 (-53.13; -39.63) | 1027 | -998 (-1303; -793) | -49.28 (-55.92; -43.56) |
| 01/07/2020 - 30/09/2020 | 744 | -169 (-227; -114) | -18.48 (-23.42; -13.28) | 881 | -178 (-248; -115) | -16.78 (-21.99; -11.56) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 1917 | -1199 (-1675; -774) | -38.48 (-46.64; -28.77) | 2127 | -1799 (-2423; -1256) | -45.83 (-53.25; -37.13) |
| **19-59 years** | | | | | | |
| All admissions from 15/02/2020 | 20884 | -1085 (-1810; -421) | -4.94 (-7.97; -1.97) | 26260 | -2136 (-3089; -1291) | -7.52 (-10.53; -4.69) |
| 15/02/2020 - 30/06/2020 (1st wave) | 6057 | -16 (-500; 420) | -0.26 (-7.63; 7.45) | 7199 | -666 (-1315; -88) | -8.47 (-15.44; -1.21) |
| 01/07/2020 - 30/09/2020 | 3942 | -240 (-401; -95) | -5.74 (-9.22; -2.35) | 4923 | -399 (-596; -225) | -7.50 (-10.79; -4.37) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 10885 | -829 (-1118; -550) | -7.08 (-9.31; -4.81) | 14138 | -1071 (-1460; -701) | -7.04 (-9.36; -4.72) |
| **60-69 years** | | | | | | |
| All admissions from 15/02/2020 | 7409 | 287 (-469; 814) | 4.02 (-5.96; 12.34) | 10249 | 754 (-276; 1449) | 7.95 (-2.62; 16.47) |
| 15/02/2020 - 30/06/2020 (1st wave) | 2739 | 768 (648; 851) | 38.95 (30.97; 45.11) | 3184 | 551 (394; 666) | 20.93 (14.13; 26.43) |
| 01/07/2020 - 30/09/2020 | 1079 | -178 (-360; -26) | -14.14 (-25.04; -2.36) | 1660 | -61 (-319; 150) | -3.56 (-16.14; 9.93) |

| | | | | | | |
|---|---|---|---|---|---|---|
| 01/10/2020 - 30/06/2021 (2nd wave) | 3591 | -303 (-906; 159) | -7.79 (-20.14; 4.64) | 5405 | 265 (-497; 860) | 5.15 (-8.43; 18.93) |
| **70-79 years** | | | | | | |
| All admissions from 15/02/2020 | 10569 | -611 (-2047; 366) | -5.46 (-16.23; 3.59) | 15676 | 99 (-1869; 1424) | 0.63 (-10.65; 9.99) |
| 15/02/2020 - 30/06/2020 (1st wave) | 3852 | 808 (599; 948) | 26.53 (18.42; 32.64) | 4778 | 454 (119; 668) | 10.49 (2.57; 16.25) |
| 01/07/2020 - 30/09/2020 | 1620 | -297 (-537; -98) | -15.51 (-24.88; -5.72) | 2546 | -154 (-479; 131) | -5.69 (-15.84; 5.40) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 5097 | -1121 (-2383; -148) | -18.03 (-31.86; -2.83) | 8352 | -201 (-1942; 1161) | -2.35 (-18.87; 16.14) |
| **80-89 years** | | | | | | |
| All admissions from 15/02/2020 | 11037 | -2430 (-4451; -1099) | -18.04 (-28.74; -9.05) | 17932 | -2014 (-4980; -41) | -10.10 (-21.73; -0.23) |
| 15/02/2020 - 30/06/2020 (1st wave) | 3786 | 131 (-292; 437) | 3.58 (-7.15; 13.06) | 4984 | -531 (-1169; -75) | -9.62 (-19.00; -1.47) |
| 01/07/2020 - 30/09/2020 | 1824 | -393 (-679; -150) | -17.72 (-27.13; -7.58) | 3128 | -275 (-734; 95) | -8.08 (-19.01; 3.13) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 5427 | -2168 (-4224; -651) | -28.54 (-43.77; -10.72) | 9820 | -1209 (-4208; 982) | -10.96 (-30.00; 11.10) |
| **90+ years** | | | | | | |
| All admissions from 15/02/2020 | 2832 | -1435 (-2274; -872) | -33.63 (-44.54; -23.55) | 5827 | -1838 (-3274; -839) | -23.98 (-35.98; -12.59) |
| 15/02/2020 - 30/06/2020 (1st wave) | 761 | -409 (-631; -288) | -34.93 (-45.33; -27.44) | 1580 | -591 (-1003; -367) | -27.21 (-38.84; -18.85) |
| 01/07/2020 - 30/09/2020 | 488 | -185 (-347; -65) | -27.44 (-41.56; -11.71) | 1047 | -156 (-438; 51) | -12.98 (-29.51; 5.14) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 1583 | -842 (-1278; -507) | -34.72 (-44.67; -24.26) | 3200 | -1091 (-1867; -487) | -25.43 (-36.85; -13.21) |

Abbreviations: HPA, Health Protection Agency; 95%CI, 95% confidence interval

TABLE 3.4c: Change in elective hospital admissions during the pandemic period, stratified by sex and age

| | Bergamo HPA | | | Brescia HPA | | |
|---|---|---|---|---|---|---|
| | Total | Change (95%CI) | % Change (95%CI) | Total | Change (95%CI) | % Change (95%CI) |
| **Total** | | | | | | |
| All admissions from 15/02/2020 | 36348 | -18271 (-21722; -15743) | -33.45 (-37.41; -30.22) | 41239 | -20274 (-24086; -17198) | -32.96 (-36.87; -29.43) |
| 15/02/2020 - 30/06/2020 (1st wave) | 6333 | -9814 (-13862; -6645) | -60.78 (-68.64; -51.20) | 8339 | -9983 (-14569; -6330) | -54.49 (-63.60; -43.15) |
| 01/07/2020 - 30/09/2020 | 8124 | -1232 (-1663; -815) | -13.16 (-16.99; -9.12) | 8898 | -1452 (-1895; -980) | -14.03 (-17.56; -9.92) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 21891 | -7225 (-8825; -5941) | -24.81 (-28.73; -21.35) | 24002 | -8840 (-10631; -7316) | -26.92 (-30.70; -23.36) |
| **Sex** | | | | | | |
| **Female** | | | | | | |
| All admissions from 15/02/2020 | 17857 | -9057 (-11080; -7521) | -33.65 (-38.29; -29.64) | 21576 | -10266 (-12674; -8395) | -32.24 (-37.00; -28.01) |
| 15/02/2020 - 30/06/2020 (1st wave) | 3266 | -4689 (-6447; -3288) | -58.95 (-66.37; -50.17) | 4416 | -5078 (-7354; -3378) | -53.49 (-62.48; -43.34) |
| 01/07/2020 - 30/09/2020 | 3970 | -641 (-878; -437) | -13.91 (-18.11; -9.92) | 4583 | -760 (-1034; -510) | -14.22 (-18.40; -10.01) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 10621 | -3727 (-4290; -3198) | -25.97 (-28.77; -23.14) | 12577 | -4428 (-5103; -3819) | -26.04 (-28.86; -23.29) |
| **Male** | | | | | | |
| All admissions from 15/02/2020 | 18491 | -9186 (-10838; -8085) | -33.19 (-36.95; -30.42) | 19663 | -9970 (-11900; -8718) | -33.64 (-37.70; -30.72) |
| 15/02/2020 - 30/06/2020 (1st wave) | 3067 | -5098 (-7374; -3346) | -62.44 (-70.62; -52.17) | 3923 | -4869 (-7601; -3006) | -55.38 (-65.96; -43.38) |
| 01/07/2020 - 30/09/2020 | 4154 | -589 (-830; -332) | -12.42 (-16.65; -7.39) | 4315 | -690 (-954; -417) | -13.79 (-18.11; -8.82) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 11270 | -3499 (-4813; -2497) | -23.69 (-29.93; -18.14) | 11425 | -4411 (-5758; -3346) | -27.85 (-33.51; -22.65) |
| **Age groups** | | | | | | |
| **0-18 years** | | | | | | |
| All admissions from 15/02/2020 | 1489 | -671 (-965; -489) | -31.06 (-39.33; -24.73) | 1575 | -578 (-870; -397) | -26.84 (-35.59; -20.12) |
| 15/02/2020 - 30/06/2020 (1st wave) | 260 | -392 (-522; -312) | -60.12 (-66.76; -54.55) | 307 | -370 (-504; -274) | -54.67 (-62.15; -47.18) |
| 01/07/2020 - 30/09/2020 | 337 | -73 (-138; -24) | -17.84 (-29.02; -6.55) | 336 | -49 (-108; -3) | -12.69 (-24.31; -0.84) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 892 | -206 (-342; -110) | -18.74 (-27.70; -10.94) | 932 | -159 (-293; -63) | -14.55 (-23.94; -6.31) |
| **19-59 years** | | | | | | |
| All admissions from 15/02/2020 | 14014 | -5819 (-6998; -4990) | -29.34 (-33.30; -26.26) | 16303 | -6722 (-8071; -5772) | -29.19 (-33.11; -26.15) |
| 15/02/2020 - 30/06/2020 (1st wave) | 2508 | -3374 (-4824; -2159) | -57.36 (-65.79; -46.26) | 3461 | -3346 (-5103; -1917) | -49.16 (-59.59; -35.65) |
| 01/07/2020 - 30/09/2020 | 3038 | -314 (-498; -127) | -9.37 (-14.07; -4.03) | 3456 | -449 (-692; -227) | -11.49 (-16.68; -6.15) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 8468 | -2131 (-2881; -1516) | -20.11 (-25.38; -15.18) | 9386 | -2927 (-3830; -2228) | -23.77 (-28.98; -19.19) |
| **60-69 years** | | | | | | |
| All admissions from 15/02/2020 | 7621 | -3730 (-4426; -3161) | -32.86 (-36.74; -29.32) | 8138 | -4048 (-4816; -3446) | -33.22 (-37.18; -29.75) |
| 15/02/2020 - 30/06/2020 (1st wave) | 1324 | -2000 (-2717; -1454) | -60.17 (-67.24; -52.33) | 1588 | -2065 (-2831; -1459) | -56.52 (-64.06; -47.89) |
| 01/07/2020 - 30/09/2020 | 1698 | -195 (-315; -76) | -10.31 (-15.65; -4.27) | 1739 | -234 (-362; -108) | -11.87 (-17.22; -5.87) |

| | | | | | | |
|---|---|---|---|---|---|---|
| 01/10/2020 - 30/06/2021 (2nd wave) | 4599 | -1535 (-1881; -1215) | -25.02 (-29.03; -20.89) | 4811 | -1749 (-2124; -1431) | -26.67 (-30.63; -22.92) |
| **70-79 years** | | | | | | |
| All admissions from 15/02/2020 | 8719 | -4914 (-5702; -4305) | -36.04 (-39.54; -33.05) | 9543 | -5421 (-6333; -4759) | -36.23 (-39.89; -33.27) |
| 15/02/2020 - 30/06/2020 (1st wave) | 1478 | -2503 (-3442; -1727) | -62.87 (-69.96; -53.88) | 1902 | -2560 (-3623; -1688) | -57.38 (-65.57; -47.02) |
| 01/07/2020 - 30/09/2020 | 1935 | -398 (-527; -267) | -17.06 (-21.40; -12.13) | 2077 | -414 (-567; -279) | -16.63 (-21.44; -11.83) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 5306 | -2013 (-2612; -1580) | -27.50 (-32.99; -22.94) | 5564 | -2446 (-3096; -1939) | -30.54 (-35.75; -25.84) |
| **80-89 years** | | | | | | |
| All admissions from 15/02/2020 | 4183 | -2965 (-3925; -2359) | -41.48 (-48.41; -36.06) | 5114 | -3434 (-4551; -2734) | -40.17 (-47.09; -34.84) |
| 15/02/2020 - 30/06/2020 (1st wave) | 702 | -1401 (-2341; -835) | -66.62 (-76.93; -54.33) | 964 | -1532 (-2653; -862) | -61.39 (-73.35; -47.22) |
| 01/07/2020 - 30/09/2020 | 1031 | -243 (-325; -159) | -19.05 (-23.97; -13.37) | 1175 | -277 (-371; -181) | -19.08 (-23.99; -13.32) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 2450 | -1322 (-1548; -1130) | -35.05 (-38.72; -31.57) | 2975 | -1625 (-1912; -1387) | -35.32 (-39.12; -31.80) |
| **90+ years** | | | | | | |
| All admissions from 15/02/2020 | 322 | -399 (-886; -230) | -55.31 (-73.33; -41.66) | 566 | -471 (-1087; -238) | -45.44 (-65.76; -29.62) |
| 15/02/2020 - 30/06/2020 (1st wave) | 61 | -167 (-416; -71) | -73.20 (-87.22; -53.75) | 117 | -189 (-531; -61) | -61.81 (-81.93; -34.24) |
| 01/07/2020 - 30/09/2020 | 85 | -41 (-73; -19) | -32.74 (-46.32; -18.39) | 115 | -78 (-130; -44) | -40.50 (-53.05; -27.82) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 176 | -191 (-424; -97) | -51.99 (-70.66; -35.45) | 334 | -204 (-509; -73) | -37.89 (-60.39; -18.03) |

Abbreviations: HPA, Health Protection Agency; 95%CI, 95% confidence interval

TABLE 3.5: Difference in daily counts of total hospital admissions before (2017-2019) and during COVID-19 pandemic (2020-2021), stratified by main diagnosis

| | Bergamo HPA | | | Brescia HPA | | |
|---|---|---|---|---|---|---|
| Diagnostic Code Description (ICD-9-CM) | **Jan 2017 - Dec 2019** | **Jan 2020 - Jun 2021** | ***p*-value** | **Jan 2017 - Dec 2019** | **Jan 2020 - Jun 2021** | ***p*-value** |
| **Infection and Parasitic Diseases (001-139.9)** | | | | | | |
| Total | 6126 | 2109 | | 9374 | 3178 | |
| Daily events | | | | | | |
| Mean (±SD) | 5.59 (2.53) | 3.86 (2.22) | <0.001 | 8.56 (3.01) | 5.81 (2.95) | <0.001 |
| Median (IQR) | 5 (4-7) | 4 (2-5) | | 8 (7-11) | 6 (4-8) | |
| Min - max | 0-14 | 0-11 | | 2-21 | 0-17 | |
| **Neoplasms (140-239.9)** | | | | | | |
| Total | 39749 | 16087 | | 40379 | 16710 | |
| Daily events | | | | | | |
| Mean (±SD) | 36.3 (21.11) | 29.41 (18.53) | <0.001 | 36.88 (21.47) | 30.55 (19.01) | <0.001 |
| Median (IQR) | 41 (13-55) | 31 (11-45) | | 41 (15-54) | 33 (11-47) | |
| Min - max | 1-80 | 0-76 | | 0-83 | 0-84 | |
| **Endocrine, Nutritional and Metabolic Diseases and Immunity Disorders (240-279.9)** | | | | | | |
| Total | 6353 | 1844 | | 7930 | 2655 | |
| Daily events | | | | | | |
| Mean (±SD) | 5.8 (3.74) | 3.37 (2.64) | <0.001 | 7.24 (3.83) | 4.85 (3.33) | <0.001 |
| Median (IQR) | 5 (3-8) | 3 (1-5) | | 7 (4-10) | 4 (2-7) | |
| Min - max | 0-21 | 0-14 | | 0-21 | 0-18 | |
| **Diseases of Blood and Blood Forming Organs (280-289.9)** | | | | | | |
| Total | 2857 | 900 | | 4700 | 1941 | |
| Daily events | | | | | | |
| Mean (±SD) | 2.61 (1.81) | 1.65 (1.39) | <0.001 | 4.29 (2.38) | 3.55 (2.24) | <0.001 |
| Median (IQR) | 2 (1-4) | 1 (1-2) | | 4 (3-6) | 3 (2-5) | |
| Min - max | 0-9 | 0-7 | | 0-14 | 0-12 | |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Mental Disorders (290-319.9)** | | | | | | |
| Total | 7247 | 2567 | | 8181 | 3189 | |
| Daily events | | | | | | |
| Mean (±SD) | 6.62 (3.43) | 4.69 (2.7) | <0.001 | 7.47 (3.6) | 5.83 (3.25) | <0.001 |
| Median (IQR) | 6 (4-9) | 4 (3-7) | | 7 (5-10) | 5 (3-8) | |
| Min - max | 0-18 | 0-15 | | 0-18 | 0-15 | |
| **Diseases of Nervous System and Sense Organs (320-389.9)** | | | | | | |
| Total | 17844 | 6138 | | 20174 | 6187 | |
| Daily events | | | | | | |
| Mean (±SD) | 16.3 (10.19) | 11.22 (8.76) | <0.001 | 18.42 (10.57) | 11.31 (7.72) | <0.001 |
| Median (IQR) | 19 (5-24) | 11 (2-18) | | 20 (8-27) | 11 (4-17) | |
| Min - max | 0-46 | 0-36 | | 0-44 | 0-35 | |
| **Diseases of the Circulatory System (390-459.9)** | | | | | | |
| Total | 47014 | 17624 | | 59047 | 22724 | |
| Daily events | | | | | | |
| Mean (±SD) | 42.94 (14.36) | 32.22 (13.15) | <0.001 | 53.92 (17.94) | 41.54 (16.17) | <0.001 |
| Median (IQR) | 45 (31-54) | 32 (22-42) | | 57 (37-68) | 43 (29-53) | |
| Min - max | 10-80 | 4-72 | | 12-102 | 5-86 | |
| **Diseases of the Respiratory System (460-519.9)** | | | | | | |
| Total | 26788 | 15810 | | 40443 | 23834 | |
| Daily events | | | | | | |
| Mean (±SD) | 24.46 (10.69) | 28.9 (39.48) | <0.001 | 36.93 (14.34) | 43.57 (37.78) | 0.238 |
| Median (IQR) | 24 (16-32) | 18 (12-27) | | 36 (26-47) | 34 (22-50) | |
| Min - max | 1-60 | 1-254 | | 6-89 | 1-257 | |
| **Diseases of the Digestive System (520-579.9)** | | | | | | |
| Total | 37850 | 12878 | | 43246 | 14578 | |
| Daily events | | | | | | |
| Mean (±SD) | 34.57 (15.95) | 23.54 (13.89) | <0.001 | 39.49 (16.23) | 26.65 (12.98) | <0.001 |

| | | | | | | |
|---|---|---|---|---|---|---|
| Median (IQR) | 38 (17-48) | 23 (11-34) | | 42 (24-52) | 26 (16-36) | |
| Min - max | 4-72 | 1-64 | | 8-87 | 1-70 | |
| **Diseases of the Genitourinary System (580-629.9)** | | | | | | |
| Total | 31281 | 10186 | | 36425 | 12437 | |
| Daily events | | | | | | |
| Mean (±SD) | 28.57 (16.05) | 18.62 (12.53) | <0.001 | 33.26 (16.18) | 22.74 (13.07) | <0.001 |
| Median (IQR) | 32 (11-41) | 19 (6-28) | | 36 (16-46) | 22 (11-32) | |
| Min - max | 1-74 | 0-64 | | 4-71 | 0-67 | |
| **Complications of Pregnancy, Childbirth and the Puerperium (630-677.9)** | | | | | | |
| Total | 34382 | 14867 | | 36042 | 15393 | |
| Daily events | | | | | | |
| Mean (±SD) | 31.4 (9.12) | 27.18 (8.39) | <0.001 | 32.92 (9.97) | 28.14 (8.77) | <0.001 |
| Median (IQR) | 31 (24-38) | 27 (21-33) | | 33 (25-40) | 28 (22-34) | |
| Min - max | 6-60 | 2-50 | | 10-63 | 3-58 | |
| **Diseases of the Skin and Subcutaneous Tissue (680-709.9)** | | | | | | |
| Total | 3374 | 933 | | 3819 | 1035 | |
| Daily events | | | | | | |
| Mean (±SD) | 3.08 (2.48) | 1.71 (1.83) | <0.001 | 3.49 (2.45) | 1.89 (1.72) | <0.001 |
| Median (IQR) | 3 (1-5) | 1 (0-3) | | 3 (2-5) | 2 (1-3) | |
| Min - max | 0-12 | 0-9 | | 0-13 | 0-11 | |
| **Diseases of the Musculoskeletal System and Connective Tissue (710-739.9)** | | | | | | |
| Total | 28075 | 9520 | | 31928 | 10368 | |
| Daily events | | | | | | |
| Mean (±SD) | 25.64 (16.16) | 17.40 (13.98) | <0.001 | 29.16 (17.56) | 18.95 (14.76) | <0.001 |
| Median (IQR) | 28 (11-39) | 17 (4-28) | | 30 (15-43) | 18 (4-30) | |
| Min - max | 0-68 | 0-61 | | 0-74 | 0-74 | |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Congenital Anomalies (740-759.9)** | | | | | | |
| Total | 3847 | 1361 | | 3399 | 1298 | |
| Daily events | | | | | | |
| Mean (±SD) | 3.51 (3.19) | 2.49 (2.5) | <0.001 | 3.10 (2.67) | 2.37 (2.25) | <0.001 |
| Median (IQR) | 3 (1-6) | 2 (0-4) | | 3 (1-5) | 2 (0-4) | |
| Min - max | 0-21 | 0-13 | | 0-14 | 0-11 | |
| **Certain Conditions Originating in the Perinatal Period (760-779.9)** | | | | | | |
| Total | 547 | 217 | | 297 | 69 | |
| Daily events | | | | | | |
| Mean (±SD) | 0.50 (0.73) | 0.40 (0.66) | 0.003 | 0.27 (0.53) | 0.13 (0.36) | <0.001 |
| Median (IQR) | 0 (0-1) | 0 (0-1) | | 0 (0-0) | 0 (0-0) | |
| Min - max | 0-5 | 0-4 | | 0-3 | 0-2 | |
| **Symptoms, Signs and Ill-defined Conditions (780-799.9)** | | | | | | |
| Total | 8258 | 2422 | | 16781 | 4842 | |
| Daily events | | | | | | |
| Mean (±SD) | 7.54 (3.22) | 4.43 (2.61) | <0.001 | 15.33 (5.02) | 8.85 (4.22) | <0.001 |
| Median (IQR) | 7 (5-10) | 4 (2-6) | | 15 (12-19) | 8 (6-11) | |
| Min - max | 0-18 | 0-14 | | 3-33 | 0-27 | |
| **Injury and Poisoning (800-999.9)** | | | | | | |
| Total | 19036 | 7583 | | 24079 | 9638 | |
| Daily events | | | | | | |
| Mean (±SD) | 17.38 (5.11) | 13.86 (5.39) | <0.001 | 21.99 (6.23) | 17.62 (6.37) | <0.001 |
| Median (IQR) | 17 (14-21) | 14 (10-17) | | 22 (18-26) | 18 (13-22) | |
| Min - max | 4-39 | 1-29 | | 5-43 | 0-35 | |

Abbreviations: HPA, Health Protection Agency; ICD-9-CM, International Statistical Classification of Diseases, 9th revision, Clinical Modification; SD, standard deviation; IQR, interquartile range

TABLE 3.6a: Change in total hospital admissions during the pandemic period, stratified by main diagnosis

| | Bergamo HPA | | | Brescia HPA | | |
|---|---|---|---|---|---|---|
| Diagnostic Code Description (ICD-9-CM) | **Total** | **Change (95%CI)** | **% Change (95%CI)** | **Total** | **Change (95%CI)** | **% Change (95%CI)** |
| **Neoplasms (140-239.9)** | | | | | | |
| All admissions from 15/02/2020 | 14376 | -5506 (-7755; -3452) | -27.69 (-35.04; -19.36) | 15017 | -4265 (-6385; -2365) | -22.12 (-29.83; -13.61) |
| 15/02/2020 - 30/06/2020 (1st wave) | 2832 | -2737 (-3896; -1781) | -49.15 (-57.91; -38.61) | 3242 | -2304 (-3475; -1320) | -41.55 (-51.74; -28.94) |
| 01/07/2020 - 30/09/2020 | 2818 | -547 (-898; -225) | -16.26 (-24.16; -7.38) | 2920 | -292 (-615; 8) | -9.10 (-17.39; 0.27) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 8726 | -2222 (-3071; -1417) | -20.29 (-26.03; -13.97) | 8855 | -1669 (-2433; -951) | -15.86 (-21.55; -9.70) |
| **Diseases of Nervous System and Sense Organs (320-389.9)** | | | | | | |
| All admissions from 15/02/2020 | 5389 | -2750 (-3229; -2375) | -33.79 (-37.46; -30.59) | 5371 | -3033 (-3559; -2652) | -36.09 (-39.85; -33.05) |
| 15/02/2020 - 30/06/2020 (1st wave) | 913 | -1406 (-1864; -1094) | -60.62 (-67.12; -54.51) | 984 | -1510 (-2030; -1149) | -60.55 (-67.35; -53.87) |
| 01/07/2020 - 30/09/2020 | 1217 | -138 (-292; -19) | -10.15 (-19.35; -1.55) | 1158 | -210 (-368; -95) | -15.36 (-24.14; -7.61) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 3259 | -1207 (-1501; -949) | -27.02 (-31.54; -22.54) | 3229 | -1313 (-1633; -1055) | -28.91 (-33.59; -24.63) |
| **Diseases of the Circulatory System (390-459.9)** | | | | | | |
| All admissions from 15/02/2020 | 15582 | -6149 (-8299; -4472) | -28.30 (-34.75; -22.30) | 20166 | -5843 (-8388; -3853) | -22.46 (-29.38; -16.04) |
| 15/02/2020 - 30/06/2020 (1st wave) | 3246 | -2935 (-3770; -2254) | -47.48 (-53.73; -40.98) | 4373 | -3032 (-4008; -2220) | -40.94 (-47.82; -33.67) |
| 01/07/2020 - 30/09/2020 | 3070 | -445 (-698; -248) | -12.66 (-18.52; -7.48) | 3882 | -363 (-656; -134) | -8.55 (-14.45; -3.35) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 9266 | -2769 (-3900; -1894) | -23.01 (-29.62; -16.97) | 11911 | -2448 (-3801; -1423) | -17.05 (-24.19; -10.67) |
| **Diseases of the Respiratory System (460-519.9)** | | | | | | |
| All admissions from 15/02/2020 | 14449 | 1294 (-3239; 3612) | 9.83 (-18.31; 33.33) | 21699 | 3603 (-2724; 6817) | 19.91 (-11.15; 45.80) |
| 15/02/2020 - 30/06/2020 (1st wave) | 7685 | 4013 (3653; 4232) | 109.27 (90.58; 122.55) | 8162 | 3060 (2550; 3370) | 59.97 (45.43; 70.32) |
| 01/07/2020 - 30/09/2020 | 1295 | -578 (-875; -351) | -30.84 (-40.32; -21.32) | 2058 | -553 (-934; -250) | -21.19 (-31.22; -10.81) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 5469 | -2141 (-6545; 293) | -28.14 (-54.48; 5.66) | 11479 | 1096 (-5043; 4447) | 10.56 (-30.52; 63.24) |
| **Diseases of the Digestive System (520-579.9)** | | | | | | |
| All admissions from 15/02/2020 | 11343 | -6007 (-6711; -5490) | -34.62 (-37.17; -32.61) | 12790 | -7459 (-8281; -6869) | -36.84 (-39.30; -34.94) |
| 15/02/2020 - 30/06/2020 (1st wave) | 2004 | -2909 (-3841; -2160) | -59.21 (-65.71; -51.88) | 2666 | -3121 (-4248; -2215) | -53.93 (-61.44; -45.38) |
| 01/07/2020 - 30/09/2020 | 2572 | -458 (-610; -333) | -15.12 (-19.16; -11.47) | 2944 | -514 (-685; -373) | -14.87 (-18.89; -11.25) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 6767 | -2640 (-3782; -1821) | -28.06 (-35.85; -21.20) | 7180 | -3824 (-5155; -2866) | -34.75 (-41.79; -28.53) |
| **Diseases of the Genitourinary System (580-629.9)** | | | | | | |
| All admissions from 15/02/2020 | 8887 | -5307 (-7431; -4313) | -37.39 (-45.54; -32.67) | 10969 | -6183 (-8700; -5015) | -36.05 (-44.23; -31.37) |
| 15/02/2020 - 30/06/2020 (1st wave) | 1447 | -2684 (-5131; -1359) | -64.97 (-78.00; -48.43) | 2326 | -2659 (-5585; -1067) | -53.34 (-70.60; -31.45) |
| 01/07/2020 - 30/09/2020 | 1901 | -394 (-569; -249) | -17.18 (-23.03; -11.60) | 2268 | -589 (-805; -407) | -20.62 (-26.19; -15.21) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 5539 | -2229 (-2748; -1812) | -28.69 (-33.16; -24.65) | 6375 | -2935 (-3603; -2426) | -31.52 (-36.11; -27.57) |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Complications of Pregnancy, Childbirth and the Puerperium (630-677.9)** | | | | | | |
| All admissions from 15/02/2020 | 13547 | -785 (-1584; -112) | -5.48 (-10.47; -0.82) | 13990 | -1406 (-2251; -709) | -9.13 (-13.86; -4.82) |
| 15/02/2020 - 30/06/2020 (1st wave) | 3580 | -326 (-471; -204) | -8.36 (-11.63; -5.39) | 3846 | -336 (-495; -205) | -8.03 (-11.39; -5.06) |
| 01/07/2020 - 30/09/2020 | 2680 | -50 (-186; 61) | -1.85 (-6.50; 2.32) | 2796 | -103 (-229; 16) | -3.57 (-7.56; 0.57) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 7287 | -408 (-1096; 167) | -5.30 (-13.07; 2.34) | 7348 | -966 (-1688; -358) | -11.62 (-18.68; -4.64) |
| **Diseases of the Musculoskeletal System and Connective Tissue (710-739.9)** | | | | | | |
| All admissions from 15/02/2020 | 8282 | -5054 (-6025; -4446) | -37.90 (-42.11; -34.93) | 8920 | -6143 (-7330; -5517) | -40.78 (-45.11; -38.21) |
| 15/02/2020 - 30/06/2020 (1st wave) | 1161 | -2671 (-3908; -1774) | -69.70 (-77.09; -60.45) | 1548 | -2784 (-4128; -1815) | -64.26 (-72.73; -53.97) |
| 01/07/2020 - 30/09/2020 | 1926 | -84 (-331; 120) | -4.16 (-14.66; 6.67) | 2037 | -282 (-579; -33) | -12.17 (-22.12; -1.61) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 5195 | -2299 (-3716; -1558) | -30.68 (-41.70; -23.07) | 5335 | -3077 (-4717; -2174) | -36.58 (-46.93; -28.96) |
| **Symptoms, Signs and Ill-defined Conditions (780-799.9)** | | | | | | |
| All admissions from 15/02/2020 | 2077 | -1192 (-1388; -1053) | -36.46 (-40.06; -33.64) | 4204 | -2549 (-2960; -2245) | -37.75 (-41.32; -34.81) |
| 15/02/2020 - 30/06/2020 (1st wave) | 483 | -443 (-528; -379) | -47.86 (-52.21; -43.97) | 1004 | -894 (-1053; -765) | -47.11 (-51.20; -43.23) |
| 01/07/2020 - 30/09/2020 | 422 | -176 (-236; -124) | -29.40 (-35.86; -22.64) | 914 | -301 (-428; -184) | -24.77 (-31.92; -16.76) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 1172 | -573 (-771; -427) | -32.82 (-39.68; -26.72) | 2286 | -1354 (-1773; -1052) | -37.19 (-43.68; -31.52) |
| **Injury and Poisoning (800-999.9)** | | | | | | |
| All admissions from 15/02/2020 | 6791 | -1802 (-2174; -1506) | -20.97 (-24.25; -18.15) | 8694 | -2514 (-3011; -2124) | -22.43 (-25.73; -19.63) |
| 15/02/2020 - 30/06/2020 (1st wave) | 1563 | -822 (-944; -721) | -34.46 (-37.67; -31.55) | 2050 | -1034 (-1192; -894) | -33.54 (-36.77; -30.37) |
| 01/07/2020 - 30/09/2020 | 1486 | -125 (-215; -39) | -7.75 (-12.62; -2.57) | 1970 | -112 (-227; -4) | -5.39 (-10.33; -0.21) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 3742 | -855 (-1212; -574) | -18.60 (-24.46; -13.29) | 4674 | -1368 (-1828; -1000) | -22.64 (-28.11; -17.63) |

Abbreviations: HPA, Health Protection Agency; ICD-9-CM, International Statistical Classification of Diseases, 9th revision, Clinical Modification; 95%CI, 95% confidence interval

TABLE 3.6b: Change in urgent hospital admissions during the pandemic period, stratified by main diagnosis

| | Bergamo HPA | | | Brescia HPA | | |
|---|---|---|---|---|---|---|
| Diagnostic Code Description (ICD-9-CM) | **Total** | **Change (95%CI)** | **% Change (95%CI)** | **Total** | **Change (95%CI)** | **% Change (95%CI)** |
| **Neoplasms (140-239.9)** | | | | | | |
| All admissions from 15/02/2020 | 2692 | -316 (-549; -129) | -10.50 (-16.93; -4.58) | 2835 | -287 (-533; -94) | -9.18 (-15.82; -3.20) |
| 15/02/2020 - 30/06/2020 (1st wave) | 662 | -179 (-292; -76) | -21.24 (-30.62; -10.35) | 754 | -144 (-271; -33) | -16.07 (-26.47; -4.19) |
| 01/07/2020 - 30/09/2020 | 567 | 22 (-26; 64) | 4.01 (-4.39; 12.79) | 609 | 32 (-17; 81) | 5.48 (-2.78; 15.24) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 1463 | -159 (-281; -49) | -9.81 (-16.13; -3.24) | 1472 | -174 (-298; -63) | -10.56 (-16.84; -4.10) |
| **Diseases of Nervous System and Sense Organs (320-389.9)** | | | | | | |
| All admissions from 15/02/2020 | 855 | -640 (-1036; -385) | -42.83 (-54.79; -31.03) | 1987 | -903 (-1637; -424) | -31.25 (-45.17; -17.60) |
| 15/02/2020 - 30/06/2020 (1st wave) | 214 | -197 (-267; -142) | -47.94 (-55.51; -39.93) | 471 | -339 (-477; -237) | -41.88 (-50.32; -33.51) |
| 01/07/2020 - 30/09/2020 | 180 | -108 (-220; -49) | -37.57 (-54.98; -21.50) | 393 | -103 (-282; -3) | -20.76 (-41.74; -0.81) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 461 | -335 (-560; -181) | -42.09 (-54.85; -28.20) | 1123 | -461 (-909; -162) | -29.10 (-44.72; -12.58) |
| **Diseases of the Circulatory System (390-459.9)** | | | | | | |
| All admissions from 15/02/2020 | 9384 | -2892 (-4520; -1642) | -23.56 (-32.51; -14.89) | 13991 | -2315 (-4432; -721) | -14.20 (-24.06; -4.90) |
| 15/02/2020 - 30/06/2020 (1st wave) | 229 | -1073 (-1278; -921) | -31.91 (-35.82; -28.67) | 3273 | -1264 (-1540; -1052) | -27.86 (-31.99; -24.32) |
| 01/07/2020 - 30/09/2020 | 1623 | -283 (-562; -59) | -14.85 (-25.71; -3.52) | 2551 | -101 (-479; 207) | -3.82 (-15.80; 8.81) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 5471 | -1536 (-2694; -631) | -21.92 (-33.00; -10.35) | 8167 | -950 (-2439; 221) | -10.42 (-22.99; 2.78) |
| **Diseases of the Respiratory System (460-519.9)** | | | | | | |
| All admissions from 15/02/2020 | 12517 | 4249 (1625; 5363) | 51.38 (14.92; 74.96) | 18885 | 6456 (2487; 8114) | 51.94 (15.17; 75.34) |
| 15/02/2020 - 30/06/2020 (1st wave) | 7337 | 5112 (4615; 5438) | 229.73 (169.51; 286.42) | 7671 | 4273 (3537; 4789) | 125.74 (85.55; 166.13) |
| 01/07/2020 - 30/09/2020 | 802 | -310 (-464; -192) | -27.85 (-36.65; -19.31) | 1387 | -326 (-567; -140) | -19.05 (-29.00; -9.19) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 4378 | -554 (-3341; 923) | -11.23 (-43.28; 26.73) | 9827 | 2510 (-1726; 4749) | 34.30 (-14.94; 93.50) |
| **Diseases of the Digestive System (520-579.9)** | | | | | | |
| All admissions from 15/02/2020 | 5283 | -1419 (-1805; -1135) | -21.18 (-25.46; -17.69) | 8014 | -1883 (-2422; -1481) | -19.03 (-23.21; -15.59) |
| 15/02/2020 - 30/06/2020 (1st wave) | 1203 | -626 (-715; -545) | -34.23 (-37.28; -31.18) | 1864 | -945 (-1078; -823) | -33.65 (-36.65; -30.62) |
| 01/07/2020 - 30/09/2020 | 1129 | -120 (-264; 1) | -9.62 (-18.94; 0.10) | 1793 | -23 (-229; 152) | -1.25 (-11.35; 9.28) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 2951 | -673 (-884; -517) | -18.57 (-23.04; -14.91) | 4357 | -915 (-1196; -692) | -17.36 (-21.54; -13.70) |
| **Diseases of the Genitourinary System (580-629.9)** | | | | | | |
| All admissions from 15/02/2020 | 2239 | -608 (-1050; -297) | -21.34 (-31.91; -11.73) | 4673 | -1975 (-2998; -1229) | -29.71 (-39.08; -20.82) |
| 15/02/2020 - 30/06/2020 (1st wave) | 494 | -280 (-362; -220) | -36.16 (-42.30; -30.85) | 1107 | -694 (-883; -554) | -38.54 (-44.38; -33.34) |
| 01/07/2020 - 30/09/2020 | 488 | -69 (-107; -34) | -12.37 (-18.03; -6.53) | 1141 | -181 (-275; -100) | -13.70 (-19.43; -8.09) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 1257 | -259 (-612; 7) | -17.07 (-32.75; 0.53) | 2425 | -1100 (-1935; -487) | -31.21 (-44.38; -16.73) |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Complications of Pregnancy, Childbirth and the Puerperium (630-677.9)** | | | | | | |
| All admissions from 15/02/2020 | 8911 | -659 (-1041; -340) | -6.88 (-10.46; -3.68) | 8668 | -803 (-1171; -490) | -8.48 (-11.90; -5.35) |
| 15/02/2020 - 30/06/2020 (1st wave) | 238 | -210 (-342; -95) | -8.12 (-12.55; -3.84) | 2404 | -158 (-281; -47) | -6.17 (-10.45; -1.90) |
| 01/07/2020 - 30/09/2020 | 1803 | -60 (-154; 24) | -3.21 (-7.87; 1.34) | 1772 | -32 (-121; 47) | -1.79 (-6.37; 2.71) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 4728 | -389 (-751; -94) | -7.59 (-13.71; -1.94) | 4492 | -613 (-969; -317) | -12.00 (-17.74; -6.58) |
| **Diseases of the Musculoskeletal System and Connective Tissue (710-739.9)** | | | | | | |
| All admissions from 15/02/2020 | 425 | -240 (-348; -174) | -36.06 (-45.03; -29.01) | 589 | -289 (-432; -202) | -32.94 (-42.29; -25.58) |
| 15/02/2020 - 30/06/2020 (1st wave) | 120 | -71 (-141; -29) | -37.16 (-54.00; -19.46) | 147 | -130 (-228; -71) | -46.97 (-60.79; -32.67) |
| 01/07/2020 - 30/09/2020 | 84 | -22 (-56; 2) | -21.11 (-40.10; 2.63) | 131 | -9 (-55; 24) | -6.40 (-29.59; 21.89) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 221 | -146 (-220; -98) | -39.82 (-49.94; -30.76) | 311 | -150 (-232; -92) | -32.55 (-42.76; -22.79) |
| **Symptoms, Signs and Ill-defined Conditions (780-799.9)** | | | | | | |
| All admissions from 15/02/2020 | 1506 | -725 (-939; -569) | -32.50 (-38.41; -27.44) | 3233 | -1323 (-1729; -1011) | -29.04 (-34.85; -23.83) |
| 15/02/2020 - 30/06/2020 (1st wave) | 397 | -234 (-286; -188) | -37.04 (-41.89; -32.19) | 829 | -480 (-581; -382) | -36.67 (-41.19; -31.53) |
| 01/07/2020 - 30/09/2020 | 280 | -132 (-240; -58) | -32.08 (-46.18; -17.24) | 658 | -164 (-370; -24) | -19.96 (-36.01; -3.49) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 829 | -359 (-462; -280) | -30.25 (-35.79; -25.27) | 1746 | -679 (-865; -527) | -28.00 (-33.13; -23.17) |
| **Injury and Poisoning (800-999.9)** | | | | | | |
| All admissions from 15/02/2020 | 5163 | -1308 (-1778; -915) | -20.22 (-25.62; -15.06) | 6424 | -1269 (-1819; -809) | -16.49 (-22.07; -11.18) |
| 15/02/2020 - 30/06/2020 (1st wave) | 1277 | -532 (-708; -369) | -29.41 (-35.67; -22.43) | 1615 | -522 (-742; -327) | -24.44 (-31.49; -16.84) |
| 01/07/2020 - 30/09/2020 | 1126 | -105 (-207; -19) | -8.55 (-15.56; -1.65) | 1389 | -65 (-188; 37) | -4.50 (-11.92; 2.70) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 276 | -671 (-898; -480) | -19.56 (-24.54; -14.81) | 342 | -681 (-944; -455) | -16.60 (-21.63; -11.75) |

Abbreviations: HPA, Health Protection Agency; ICD-9-CM, International Statistical Classification of Diseases, 9th revision, Clinical Modification; 95%CI, 95% confidence interval

TABLE 3.6c: Change in elective hospital admissions during the pandemic period, stratified by main diagnosis

| | Bergamo HPA | | | Brescia HPA | | |
|---|---|---|---|---|---|---|
| Diagnostic Code Description (ICD-9-CM) | **Total** | **Change (95%CI)** | **% Change (95%CI)** | **Total** | **Change (95%CI)** | **% Change (95%CI)** |
| **Neoplasms (140-239.9)** | | | | | | |
| All admissions from 15/02/2020 | 7788 | -2935 (-4188; -1830) | -27.37 (-34.97; -19.03) | 8614 | -2339 (-3654; -1225) | -21.36 (-29.79; -12.45) |
| 15/02/2020 - 30/06/2020 (1st wave) | 158 | -1480 (-2062; -992) | -48.37 (-56.62; -38.57) | 1864 | -1306 (-1907; -810) | -41.21 (-50.57; -30.29) |
| 01/07/2020 - 30/09/2020 | 1476 | -388 (-638; -131) | -20.80 (-30.20; -8.14) | 1633 | -207 (-468; 27) | -11.26 (-22.27; 1.67) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 4732 | -1068 (-1567; -619) | -18.41 (-24.88; -11.57) | 5117 | -826 (-1306; -377) | -13.89 (-20.34; -6.86) |
| **Diseases of Nervous System and Sense Organs (320-389.9)** | | | | | | |
| All admissions from 15/02/2020 | 1611 | -799 (-1061; -645) | -33.15 (-39.72; -28.60) | 1353 | -746 (-1003; -600) | -35.55 (-42.56; -30.73) |
| 15/02/2020 - 30/06/2020 (1st wave) | 247 | -475 (-654; -370) | -65.80 (-72.59; -59.96) | 206 | -470 (-657; -370) | -69.53 (-76.14; -64.23) |
| 01/07/2020 - 30/09/2020 | 462 | 23 (-79; 100) | 5.20 (-14.54; 27.51) | 330 | -37 (-124; 24) | -10.20 (-27.35; 8.01) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 902 | -346 (-502; -228) | -27.75 (-35.77; -20.16) | 817 | -239 (-377; -139) | -22.61 (-31.56; -14.54) |
| **Diseases of the Circulatory System (390-459.9)** | | | | | | |
| All admissions from 15/02/2020 | 5224 | -2776 (-4671; -2005) | -34.70 (-47.21; -27.74) | 5698 | -2763 (-4614; -1976) | -32.65 (-44.74; -25.75) |
| 15/02/2020 - 30/06/2020 (1st wave) | 836 | -1506 (-3200; -797) | -64.30 (-79.28; -48.79) | 101 | -1453 (-3149; -731) | -58.99 (-75.71; -41.98) |
| 01/07/2020 - 30/09/2020 | 1225 | -145 (-241; -61) | -10.58 (-16.44; -4.72) | 1244 | -174 (-272; -87) | -12.28 (-17.94; -6.57) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 3163 | -1125 (-1379; -923) | -26.24 (-30.37; -22.59) | 3444 | -1136 (-1411; -918) | -24.80 (-29.07; -21.04) |
| **Diseases of the Respiratory System (460-519.9)** | | | | | | |
| All admissions from 15/02/2020 | 957 | -985 (-2240; -481) | -50.72 (-70.07; -33.47) | 132 | -767 (-2094; -238) | -36.74 (-61.34; -15.30) |
| 15/02/2020 - 30/06/2020 (1st wave) | 185 | -432 (-1131; -237) | -70.01 (-85.94; -56.12) | 225 | -444 (-1202; -228) | -66.39 (-84.23; -50.30) |
| 01/07/2020 - 30/09/2020 | 248 | -75 (-173; -10) | -23.11 (-41.06; -3.69) | 348 | -26 (-133; 44) | -7.05 (-27.69; 14.54) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 524 | -478 (-974; -214) | -47.73 (-65.02; -29.01) | 747 | -296 (-787; -31) | -28.38 (-51.32; -3.97) |
| **Diseases of the Digestive System (520-579.9)** | | | | | | |
| All admissions from 15/02/2020 | 2406 | -1898 (-2708; -1619) | -44.09 (-52.95; -40.22) | 2128 | -1895 (-2651; -1642) | -47.11 (-55.48; -43.56) |
| 15/02/2020 - 30/06/2020 (1st wave) | 338 | -993 (-2136; -440) | -74.60 (-86.34; -56.54) | 449 | -738 (-1848; -230) | -62.19 (-80.46; -33.91) |
| 01/07/2020 - 30/09/2020 | 576 | -140 (-252; -49) | -19.52 (-30.47; -7.87) | 501 | -192 (-299; -101) | -27.68 (-37.41; -16.74) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 1492 | -765 (-1319; -366) | -33.89 (-46.93; -19.71) | 1178 | -965 (-1517; -592) | -45.03 (-56.29; -33.46) |
| **Diseases of the Genitourinary System (580-629.9)** | | | | | | |
| All admissions from 15/02/2020 | 2652 | -2453 (-5947; -1702) | -48.05 (-69.16; -39.09) | 3209 | -2584 (-6839; -1678) | -44.60 (-68.06; -34.34) |
| 15/02/2020 - 30/06/2020 (1st wave) | 334 | -1078 (-4399; -385) | -76.35 (-92.94; -53.58) | 632 | -1091 (-5184; -214) | -63.33 (-89.13; -25.30) |
| 01/07/2020 - 30/09/2020 | 691 | -174 (-272; -94) | -20.07 (-28.28; -11.98) | 692 | -234 (-337; -151) | -25.24 (-32.74; -17.94) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 1627 | -1201 (-1491; -1019) | -42.47 (-47.81; -38.51) | 1885 | -1259 (-1576; -1063) | -40.04 (-45.54; -36.06) |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Complications of Pregnancy, Childbirth and the Puerperium (630-677.9)** | | | | | | |
| All admissions from 15/02/2020 | 1742 | 436 (-104; 803) | 33.38 (-5.64; 85.54) | 2894 | -124 (-1381; 733) | -4.12 (-32.31; 33.90) |
| 15/02/2020 - 30/06/2020 (1st wave) | 460 | 90 (-36; 179) | 24.37 (-7.22; 63.97) | 785 | -34 (-312; 168) | -4.20 (-28.46; 27.15) |
| 01/07/2020 - 30/09/2020 | 333 | 72 (-17; 143) | 27.71 (-4.90; 75.48) | 580 | -16 (-224; 144) | -2.75 (-27.90; 33.07) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 949 | 274 (-56; 493) | 40.50 (-5.62; 108.02) | 1529 | -74 (-863; 450) | -4.59 (-36.08; 41.68) |
| **Diseases of the Musculoskeletal System and Connective Tissue (710-739.9)** | | | | | | |
| All admissions from 15/02/2020 | 5599 | -2959 (-4026; -2511) | -34.57 (-41.83; -30.97) | 6614 | -3993 (-5274; -3487) | -37.64 (-44.36; -34.52) |
| 15/02/2020 - 30/06/2020 (1st wave) | 736 | -1755 (-3144; -1008) | -70.45 (-81.03; -57.80) | 114 | -1878 (-3270; -1033) | -62.22 (-74.15; -47.54) |
| 01/07/2020 - 30/09/2020 | 1303 | -43 (-188; 79) | -3.18 (-12.62; 6.46) | 1504 | -167 (-350; -10) | -9.97 (-18.89; -0.66) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 356 | -1161 (-2438; -583) | -24.59 (-40.64; -14.07) | 397 | -1949 (-3707; -1179) | -32.92 (-48.29; -22.89) |
| **Symptoms, Signs and Ill-defined Conditions (780-799.9)** | | | | | | |
| All admissions from 15/02/2020 | 412 | -247 (-784; -80) | -37.51 (-65.55; -16.30) | 830 | -1222 (-2940; -676) | -59.55 (-77.98; -44.87) |
| 15/02/2020 - 30/06/2020 (1st wave) | 65 | -124 (-185; -95) | -65.59 (-73.99; -59.49) | 148 | -392 (-571; -305) | -72.60 (-79.43; -67.35) |
| 01/07/2020 - 30/09/2020 | 110 | -14 (-79; 25) | -11.06 (-41.86; 28.78) | 236 | -139 (-328; -27) | -37.05 (-58.16; -10.24) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 237 | -110 (-527; 24) | -31.65 (-69.00; 11.08) | 446 | -691 (-2104; -236) | -60.78 (-82.51; -34.61) |
| **Injury and Poisoning (800-999.9)** | | | | | | |
| All admissions from 15/02/2020 | 1049 | -353 (-575; -264) | -25.20 (-35.42; -20.11) | 1492 | -471 (-824; -347) | -24.01 (-35.59; -18.85) |
| 15/02/2020 - 30/06/2020 (1st wave) | 194 | -185 (-335; -148) | -48.79 (-63.31; -43.30) | 285 | -270 (-558; -208) | -48.67 (-66.19; -42.15) |
| 01/07/2020 - 30/09/2020 | 212 | -55 (-174; 19) | -20.66 (-45.15; 9.69) | 394 | 23 (-133; 125) | 6.15 (-25.19; 46.32) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 643 | -113 (-222; -41) | -14.98 (-25.67; -5.95) | 813 | -224 (-375; -115) | -21.61 (-31.59; -12.35) |

Abbreviations: HPA, Health Protection Agency; ICD-9-CM, International Statistical Classification of Diseases, 9th revision, Clinical Modification; 95%CI, 95% confidence interval

TABLE 3.7: Difference in daily counts of total hospital admissions before (2017-2019) and during COVID-19 pandemic (2020-2021), stratified by Major Diagnostic Category (MDC)

| | Bergamo HPA | | | Brescia HPA | | |
|---|---|---|---|---|---|---|
| Major Diagnostic Category | **Jan 2017 - Dec 2019** | **Jan 2020 - Jun 2021** | ***p*-value** | **Jan 2017 - Dec 2019** | **Jan 2020 - Jun 2021** | ***p*-value** |
| **MDC 01 - Nervous System** | | | | | | |
| Total | 21314 | 7131 | | 24412 | 8579 | |
| Daily events | | | | | | |
| Mean (±SD) | 19.46 (8.01) | 13.04 (6.61) | <0.001 | 22.29 (8.38) | 15.68 (6.62) | <0.001 |
| Median (IQR) | 20 (12-25) | 12 (8-17) | | 23 (15-28) | 15 (10-20) | |
| Min - max | 2-45 | 1-40 | | 4-45 | 1-34 | |
| **MDC 02 - Eye** | | | | | | |
| Total | 5997 | 2239 | | 7297 | 2404 | |
| Daily events | | | | | | |
| Mean (±SD) | 5.48 (4.78) | 4.09 (3.88) | <0.001 | 6.66 (4.97) | 4.39 (3.63) | <0.001 |
| Median (IQR) | 5 (1-9) | 3 (0-7) | | 6 (2-10) | 4 (1-7) | |
| Min - max | 0-22 | 0-16 | | 0-24 | 0-17 | |
| **MDC 03 - Ear, Nose, Mouth, And Throat** | | | | | | |
| Total | 15848 | 3822 | | 21619 | 5553 | |
| Daily events | | | | | | |
| Mean (±SD) | 14.47 (10.06) | 6.99 (6.96) | <0.001 | 19.74 (12.1) | 10.15 (8.54) | <0.001 |
| Median (IQR) | 16 (3-22) | 5 (1-11) | | 21 (7-29) | 9 (3-15) | |
| Min - max | 0-42 | 0-44 | | 0-53 | 0-44 | |
| **MDC 04 - Respiratory System** | | | | | | |
| Total | 23817 | 16123 | | 33843 | 23119 | |
| Daily events | | | | | | |
| Mean (±SD) | 21.75 (7.48) | 29.48 (37.9) | 0.124 | 30.91 (9.96) | 42.27 (36.24) | <0.001 |
| Median (IQR) | 21 (16-27) | 20 (14-28) | | 30 (24-37) | 33 (22-47) | |
| Min - max | 5-58 | 1-246 | | 8-72 | 1-247 | |
| **MDC 05 - Circulatory System** | | | | | | |
| Total | 42306 | 16001 | | 54511 | 21027 | |

| | | | | | | |
|---|---|---|---|---|---|---|
| Daily events | | | | | | |
| Mean (±SD) | 38.64 (13.93) | 29.25 (13.18) | <0.001 | 49.78 (17.36) | 38.44 (16.4) | <0.001 |
| Median (IQR) | 41 (27-50) | 30 (18-40) | | 52 (34-64) | 40 (25-51) | |
| Min - max | 7-76 | 3-63 | | 11-97 | 3-82 | |
| **MDC 06 - Digestive System** | | | | | | |
| Total | 34972 | 11776 | | 42387 | 13758 | |
| Daily events | | | | | | |
| Mean (±SD) | 31.94 (13.99) | 21.53 (12.66) | <0.001 | 38.71 (14.83) | 25.15 (11.99) | <0.001 |
| Median (IQR) | 35 (17-43) | 21 (10-31) | | 41 (25-49) | 24 (16-33) | |
| Min - max | 5-64 | 1-56 | | 9-87 | 2-68 | |
| **MDC 07 - Hepatobiliary System and Pancreas** | | | | | | |
| Total | 13578 | 4881 | | 15347 | 5591 | |
| Daily events | | | | | | |
| Mean (±SD) | 12.4 (5.91) | 8.92 (4.84) | <0.001 | 14.02 (6.23) | 10.22 (5.21) | <0.001 |
| Median (IQR) | 13 (7-17) | 8 (5-12) | | 14 (9-18) | 10 (6-14) | |
| Min - max | 1-33 | 0-23 | | 1-34 | 0-28 | |
| **MDC 08 - Musculoskeletal System and Connective Tissue** | | | | | | |
| Total | 49764 | 18043 | | 59179 | 21129 | |
| Daily events | | | | | | |
| Mean (±SD) | 45.45 (22.32) | 32.99 (19.96) | <0.001 | 54.04 (24.86) | 38.63 (21.77) | <0.001 |
| Median (IQR) | 51 (23-63) | 34 (14-49) | | 59 (33-74) | 39 (17-56) | |
| Min - max | 3-97 | 2-85 | | 7-110 | 2-112 | |
| **MDC 09 - Skin, Subcutaneous Tissue, and Breast** | | | | | | |
| Total | 17510 | 6026 | | 16799 | 5942 | |
| Daily events | | | | | | |
| Mean (±SD) | 15.99 (11.25) | 11.02 (9.09) | <0.001 | 15.34 (9.94) | 10.86 (8.17) | <0.001 |
| Median (IQR) | 18 (3-25) | 11 (2-18) | | 17 (5-23) | 11 (3-17) | |
| Min - max | 0-49 | 0-36 | | 0-41 | 0-33 | |

| | | | | | | |
|---|---|---|---|---|---|---|
| **MDC 10 - Endocrine, Nutritional, and Metabolic System** | | | | | | |
| Total | 6236 | 1907 | | 7482 | 2619 | |
| Daily events | | | | | | |
| Mean (±SD) | 5.69 (3.79) | 3.49 (2.83) | <0.001 | 6.83 (3.92) | 4.79 (3.37) | <0.001 |
| Median (IQR) | 5 (3-8) | 3 (1-5) | | 7 (4-10) | 4 (2-7) | |
| Min - max | 0-20 | 0-13 | | 0-19 | 0-17 | |
| **MDC 11 - Kidney and Urinary Tract** | | | | | | |
| Total | 19255 | 7072 | | 27432 | 9790 | |
| Daily events | | | | | | |
| Mean (±SD) | 17.58 (9.63) | 12.93 (8.03) | <0.001 | 25.05 (11.4) | 17.9 (9.92) | <0.001 |
| Median (IQR) | 19 (7-25) | 13 (5-19) | | 27 (14-34) | 17 (10-26) | |
| Min - max | 0-42 | 0-37 | | 3-58 | 0-48 | |
| **MDC 12 - Male Reproductive System** | | | | | | |
| Total | 10765 | 3833 | | 10620 | 3463 | |
| Daily events | | | | | | |
| Mean (±SD) | 9.83 (7.7) | 7.01 (6.03) | <0.001 | 9.7 (7.13) | 6.33 (5.45) | <0.001 |
| Median (IQR) | 10 (2-16) | 6 (1-12) | | 10 (2-15) | 5 (2-10) | |
| Min - max | 0-33 | 0-25 | | 0-30 | 0-23 | |
| **MDC 13 - Female Reproductive System** | | | | | | |
| Total | 16956 | 5739 | | 16844 | 5740 | |
| Daily events | 15.48 (9.43) | 10.49 (7.73) | <0.001 | 15.38 (9.59) | 10.49 (7.69) | <0.001 |
| Mean (±SD) | 17 (6-23) | 9 (4-17) | | 17 (6-23) | 10 (3-16) | |
| Median (IQR) | 0-43 | 0-37 | | 0-45 | 0-30 | |
| Min - max | | | | | | |
| **MDC 14 - Pregnancy, Childbirth, and Puerperium** | | | | | | |
| Total | 34394 | 14883 | | 36058 | 15398 | |
| Daily events | | | | | | |
| Mean (±SD) | 31.41 (9.12) | 27.21 (8.4) | <0.001 | 32.93 (9.97) | 28.15 (8.77) | <0.001 |

| | | | | | | |
|---|---|---|---|---|---|---|
| Median (IQR) | 31 (24-38) | 27 (21-33) | | 33 (25-40) | 28 (22-34) | |
| Min - max | 6-60 | 2-50 | | 10-63 | 3-58 | |
| **MDC 15 - Newborn and Other Neonates (Perinatal Period)** | | | | | | |
| Total | 660 | 232 | | 428 | 121 | |
| Daily events | | | | | | |
| Mean (±SD) | 0.6 (0.8) | 0.42 (0.69) | <0.001 | 0.39 (0.65) | 0.22 (0.5) | <0.001 |
| Median (IQR) | 0 (0-1) | 0 (0-1) | | 0 (0-1) | 0 (0-0) | |
| Min - max | 0-5 | 0-4 | | 0-4 | 0-3 | |
| **MDC 16 - Blood and Blood Forming Organs and Immunological Disorders** | | | | | | |
| Total | 3287 | 1075 | | 5185 | 2117 | |
| Daily events | | | | | | |
| Mean (±SD) | 3 (1.97) | 1.97 (1.58) | <0.001 | 4.74 (2.54) | 3.87 (2.37) | <0.001 |
| Median (IQR) | 3 (2-4) | 2 (1-3) | | 5 (3-6) | 4 (2-5) | |
| Min - max | 0-10 | 0-9 | | 0-15 | 0-13 | |
| **MDC 17 - Myeloproliferative Diseases and Disorders (Poorly Differentiated Neoplasms)** | | | | | | |
| Total | 9272 | 3600 | | 8097 | 3208 | |
| Daily events | | | | | | |
| Mean (±SD) | 8.47 (5.6) | 6.58 (4.64) | <0.001 | 7.39 (4.92) | 5.86 (4.08) | <0.001 |
| Median (IQR) | 9 (3-12) | 6 (3-10) | | 8 (3-11) | 6 (2-9) | |
| Min - max | 0-27 | 0-23 | | 0-25 | 0-22 | |
| **MDC 18 - Infectious and Parasitic Diseases and Disorders** | | | | | | |
| Total | 4284 | 1588 | | 6230 | 2424 | |
| Daily events | | | | | | |
| Mean (±SD) | 3.91 (2.08) | 2.9 (1.87) | <0.001 | 5.69 (2.38) | 4.43 (2.45) | <0.001 |
| Median (IQR) | 4 (2-5) | 3 (1-4) | | 6 (4-7) | 4 (3-6) | |

| | | | | | | |
|---|---|---|---|---|---|---|
| Min - max | 0-13 | 0-10 | | 0-14 | 0-13 | |
| **MDC 19 - Mental Diseases and Disorders** | | | | | | |
| Total | 6475 | 2325 | | 7283 | 2889 | |
| Daily events | 5.91 (3.11) | 4.25 (2.52) | <0.001 | 6.65 (3.33) | 5.28 (3.03) | <0.001 |
| Mean (±SD) | 6 (4-8) | 4 (2-6) | | 7 (4-9) | 5 (3-8) | |
| Median (IQR) | 0-17 | 0-14 | | 0-17 | 0-14 | |
| Min - max | | | | | | |
| **MDC 20 - Alcohol/Drug Use or Induced Mental Disorders** | | | | | | |
| Total | 814 | 267 | | 966 | 323 | |
| Daily events | | | | | | |
| Mean (±SD) | 0.74 (0.91) | 0.49 (0.71) | <0.001 | 0.88 (0.96) | 0.59 (0.84) | <0.001 |
| Median (IQR) | 1 (0-1) | 0 (0-1) | | 1 (0-1) | 0 (0-1) | |
| Min - max | 0-5 | 0-3 | | 0-6 | 0-5 | |
| **MDC 21 - Injuries, Poison, and Toxic Effect of Drugs** | | | | | | |
| Total | 3535 | 1336 | | 2989 | 999 | |
| Daily events | | | | | | |
| Mean (±SD) | 3.23 (1.93) | 2.44 (1.66) | <0.001 | 2.73 (1.74) | 1.83 (1.43) | <0.001 |
| Median (IQR) | 3 (2-4) | 2 (1-3) | | 2 (1-4) | 2 (1-3) | |
| Min - max | 0-11 | 0-9 | | 0-11 | 0-9 | |
| **MDC 22 - Burns** | | | | | | |
| Total | 77 | 26 | | 182 | 75 | |
| Daily events | | | | | | |
| Mean (±SD) | 0.07 (0.26) | 0.05 (0.21) | 0.083 | 0.17 (0.4) | 0.14 (0.38) | 0.090 |
| Median (IQR) | 0 (0-0) | 0 (0-0) | | 0 (0-0) | 0 (0-0) | |
| Min - max | 0-2 | 0-1 | | 0-2 | 0-3 | |
| **MDC 23 - Factors Influencing Health Status** | | | | | | |
| Total | 9785 | 3863 | | 11122 | 3445 | |

| | | | | | | |
|---|---|---|---|---|---|---|
| Daily events | | | | | | |
| Mean (±SD) | 8.94 (5.53) | 7.06 (5.48) | <0.001 | 10.16 (6.13) | 6.3 (4.8) | <0.001 |
| Median (IQR) | 10 (3-13) | 6 (2-11) | | 11 (4-15) | 5 (2-9) | |
| Min - max | 0-25 | 0-25 | | 0-35 | 0-24 | |
| **MDC 24 - Multiple Significant Trauma** | | | | | | |
| Total | 427 | 132 | | 332 | 154 | |
| Daily events | | | | | | |
| Mean (±SD) | 0.39 (0.66) | 0.24 (0.51) | <0.001 | 0.3 (0.57) | 0.28 (0.56) | 0.438 |
| Median (IQR) | 0 (0-1) | 0 (0-0) | | 0 (0-1) | 0 (0-0) | |
| Min - max | 0-4 | 0-3 | | 0-3 | 0-3 | |
| **MDC 25 - HIV Infection** | | | | | | |
| Total | 118 | 43 | | 105 | 37 | |
| Daily events | | | | | | |
| Mean (±SD) | 0.11 (0.33) | 0.08 (0.29) | 0.063 | 0.1 (0.3) | 0.07 (0.27) | 0.040 |
| Median (IQR) | 0 (0-0) | 0 (0-0) | | 0 (0-0) | 0 (0-0) | |
| Min - max | 0-2 | 0-2 | | 0-2 | 0-2 | |
| **MDC 0 - Ungroupable** | | | | | | |
| Total | 322 | 136 | | 105 | 26 | |
| Daily events | | | | | | |
| Mean (±SD) | 0.29 (0.58) | 0.25 (0.53) | 0.178 | 0.1 (0.32) | 0.05 (0.23) | 0.001 |
| Median (IQR) | 0 (0-0) | 0 (0-0) | | 0 (0-0) | 0 (0-0) | |
| Min - max | 0-4 | 0-4 | | 0-2 | 0-2 | |

Abbreviations: HPA, Health Protection Agency; SD, standard deviation; IQR, interquartile range; HIV, Human Immunodeficiency Virus

TABLE 3.8a: Change in total hospital admissions during the pandemic period, stratified by Major Diagnostic Category (MDC)

| | Bergamo HPA | | | Brescia HPA | | |
|---|---|---|---|---|---|---|
| Major Diagnostic Category | **Total** | **Change (95%CI)** | **% Change (95%CI)** | **Total** | **Change (95%CI)** | **% Change (95%CI)** |
| **MDC 01 - Nervous System** | | | | | | |
| All admissions from 15/02/2020 | 6272 | -3066 (-4296; -1999) | -32.83 (-40.65; -24.17) | 7619 | -2665 (-3970; -1491) | -25.91 (-34.26; -16.36) |
| 15/02/2020 - 30/06/2020 (1st wave) | 1365 | -1301 (-1800; -888) | -48.80 (-56.87; -39.43) | 1692 | -1204 (-1730; -749) | -41.57 (-50.56; -30.68) |
| 01/07/2020 - 30/09/2020 | 1398 | -229 (-326; -141) | -14.08 (-18.93; -9.17) | 1621 | -224 (-325; -127) | -12.16 (-16.71; -7.28) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 3509 | -1535 (-2228; -920) | -30.44 (-38.84; -20.77) | 4306 | -1236 (-1979; -564) | -22.31 (-31.49; -11.58) |
| **MDC 03 - Ear, Nose, Mouth, And Throat** | | | | | | |
| All admissions from 15/02/2020 | 3177 | -4116 (-5899; -2798) | -56.44 (-64.99; -46.83) | 4649 | -4494 (-6699; -2856) | -49.15 (-59.03; -38.06) |
| 15/02/2020 - 30/06/2020 (1st wave) | 583 | -1535 (-2286; -1030) | -72.48 (-79.68; -63.85) | 881 | -1827 (-2800; -1202) | -67.46 (-76.07; -57.70) |
| 01/07/2020 - 30/09/2020 | 733 | -436 (-671; -231) | -37.28 (-47.79; -23.93) | 1053 | -389 (-665; -145) | -27.00 (-38.72; -12.07) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 1861 | -2145 (-3029; -1491) | -53.55 (-61.94; -44.49) | 2715 | -2278 (-3340; -1484) | -45.62 (-55.16; -35.34) |
| **MDC 04 - Respiratory System** | | | | | | |
| All admissions from 15/02/2020 | 14901 | -6149 (-8299; -4472) | -28.30 (-34.75; -22.30) | 20166 | -5843 (-8388; -3853) | -22.46 (-29.38; -16.04) |
| 15/02/2020 - 30/06/2020 (1st wave) | 3246 | -2935 (-3770; -2254) | -47.48 (-53.73; -40.98) | 4373 | -3032 (-4008; -2220) | -40.94 (-47.82; -33.67) |
| 01/07/2020 - 30/09/2020 | 3070 | -445 (-698; -248) | -12.66 (-18.52; -7.48) | 3882 | -363 (-656; -134) | -8.55 (-14.45; -3.35) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 9266 | -2769 (-3900; -1894) | -23.01 (-29.62; -16.97) | 11911 | -2448 (-3801; -1423) | -17.05 (-24.19; -10.67) |
| **MDC 05 - Circulatory System** | | | | | | |
| All admissions from 15/02/2020 | 14146 | -5356 (-6956; -3897) | -27.46 (-32.96; -21.60) | 18670 | -5471 (-7411; -3696) | -22.66 (-28.42; -16.53) |
| 15/02/2020 - 30/06/2020 (1st wave) | 2830 | -2707 (-3496; -1987) | -48.88 (-55.26; -41.25) | 3952 | -2877 (-3838; -1999) | -42.13 (-49.27; -33.59) |
| 01/07/2020 - 30/09/2020 | 2850 | -351 (-491; -219) | -10.95 (-14.71; -7.15) | 3563 | -362 (-534; -203) | -9.22 (-13.03; -5.39) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 8466 | -2299 (-3042; -1609) | -21.35 (-26.43; -15.97) | 11155 | -2232 (-3131; -1388) | -16.67 (-21.92; -11.07) |
| **MDC 06 - Digestive System** | | | | | | |
| All admissions from 15/02/2020 | 10320 | -5825 (-6514; -5295) | -36.08 (-38.69; -33.91) | 12044 | -6897 (-7728; -6272) | -36.41 (-39.09; -34.24) |
| 15/02/2020 - 30/06/2020 (1st wave) | 1894 | -2659 (-3417; -2028) | -58.40 (-64.34; -51.70) | 2510 | -2970 (-3889; -2205) | -54.20 (-60.78; -46.77) |
| 01/07/2020 - 30/09/2020 | 2294 | -492 (-685; -315) | -17.67 (-23.00; -12.08) | 2781 | -453 (-677; -250) | -14.02 (-19.57; -8.26) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 6132 | -2674 (-3424; -2151) | -30.36 (-35.83; -25.97) | 6753 | -3473 (-4338; -2870) | -33.96 (-39.11; -29.82) |
| **MDC 07 - Hepatobiliary System and Pancreas** | | | | | | |
| All admissions from 15/02/2020 | 4358 | -1544 (-1881; -1290) | -26.16 (-30.15; -22.84) | 4986 | -1788 (-2143; -1512) | -26.39 (-30.06; -23.27) |
| 15/02/2020 - 30/06/2020 (1st wave) | 879 | -818 (-1153; -550) | -48.21 (-56.74; -38.51) | 1153 | -776 (-1152; -482) | -40.23 (-49.99; -29.48) |
| 01/07/2020 - 30/09/2020 | 983 | -97 (-181; -23) | -8.94 (-15.58; -2.31) | 1126 | -74 (-166; 7) | -6.17 (-12.85; 0.64) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 2496 | -629 (-937; -405) | -20.13 (-27.29; -13.97) | 2707 | -938 (-1330; -663) | -25.73 (-32.94; -19.67) |
| **MDC 08 - Musculoskeletal System and Connective Tissue** | | | | | | |
| All admissions from 15/02/2020 | 15859 | -7407 (-8710; -6492) | -31.84 (-35.45; -29.05) | 18575 | -10014 (-11584; -8880) | -35.03 (-38.41; -32.34) |
| 15/02/2020 - 30/06/2020 (1st wave) | 2702 | -3944 (-4822; -3209) | -59.34 (-64.09; -54.29) | 3667 | -4566 (-5669; -3634) | -55.46 (-60.72; -49.77) |

| | | | | | | |
|---|---|---|---|---|---|---|
| 01/07/2020 - 30/09/2020 | 3569 | -232 (-496; -3) | -6.11 (-12.19; -0.07) | 4168 | -489 (-823; -197) | -10.50 (-16.49; -4.52) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 9588 | -3231 (-4810; -2026) | -25.20 (-33.41; -17.45) | 10740 | -4959 (-6850; -3495) | -31.59 (-38.94; -24.55) |
| **MDC 09 - Skin, Subcutaneous Tissue, and Breast** | | | | | | |
| All admissions from 15/02/2020 | 5267 | -3150 (-5012; -1684) | -37.43 (-48.76; -24.23) | 5253 | -2008 (-3633; -740) | -27.65 (-40.88; -12.35) |
| 15/02/2020 - 30/06/2020 (1st wave) | 906 | -1476 (-2381; -835) | -61.97 (-72.44; -47.96) | 1025 | -1119 (-1939; -544) | -52.20 (-65.42; -34.66) |
| 01/07/2020 - 30/09/2020 | 1048 | -351 (-702; -80) | -25.11 (-40.13; -7.11) | 1081 | -98 (-389; 124) | -8.32 (-26.44; 12.99) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 3313 | -1243 (-1632; -802) | -28.53 (-37.48; -18.41) | 3147 | -790 (-1343; -297) | -20.07 (-29.91; -8.63) |
| **MDC 11 - Kidney and Urinary Tract** | | | | | | |
| All admissions from 15/02/2020 | 6242 | -3465 (-4947; -2414) | -35.69 (-44.21; -27.89) | 8672 | -3340 (-5195; -2038) | -27.81 (-37.46; -19.03) |
| 15/02/2020 - 30/06/2020 (1st wave) | 1271 | -1382 (-2032; -942) | -52.10 (-61.52; -42.56) | 1956 | -1437 (-2278; -878) | -42.36 (-53.81; -30.99) |
| 01/07/2020 - 30/09/2020 | 1397 | -301 (-489; -150) | -17.70 (-25.93; -9.72) | 1996 | -240 (-480; -34) | -10.73 (-19.38; -1.67) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 3574 | -1782 (-2496; -1285) | -33.27 (-41.12; -26.44) | 4720 | -1663 (-2484; -1098) | -26.05 (-34.48; -18.88) |
| **MDC 12 - Male Reproductive System** | | | | | | |
| All admissions from 15/02/2020 | 3387 | -1597 (-2243; -1301) | -32.05 (-39.84; -27.75) | 3020 | -2134 (-2859; -1798) | -41.40 (-48.63; -37.32) |
| 15/02/2020 - 30/06/2020 (1st wave) | 453 | -1064 (-1949; -639) | -70.13 (-81.14; -58.52) | 566 | -919 (-1758; -518) | -61.90 (-75.64; -47.80) |
| 01/07/2020 - 30/09/2020 | 733 | -51 (-342; 180) | -6.49 (-31.82; 32.50) | 561 | -248 (-549; -10) | -30.69 (-49.44; -1.71) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 2201 | -483 (-1155; 82) | -17.99 (-34.42; 3.87) | 1893 | -966 (-1690; -361) | -33.79 (-47.17; -16.03) |
| **MDC 13 - Female Reproductive System** | | | | | | |
| All admissions from 15/02/2020 | 5059 | -2637 (-3235; -2279) | -34.27 (-39.00; -31.06) | 5074 | -3042 (-3685; -2627) | -37.48 (-42.07; -34.11) |
| 15/02/2020 - 30/06/2020 (1st wave) | 834 | -1483 (-2390; -913) | -64.01 (-74.13; -52.27) | 1043 | -1457 (-2439; -845) | -58.28 (-70.05; -44.77) |
| 01/07/2020 - 30/09/2020 | 944 | -192 (-469; -1) | -16.92 (-33.20; -0.14) | 797 | -369 (-664; -161) | -31.62 (-45.46; -16.84) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 3281 | -961 (-1358; -653) | -22.66 (-29.27; -16.59) | 3234 | -1216 (-1647; -866) | -27.33 (-33.75; -21.13) |
| **MDC 14 - Pregnancy, Childbirth, and Puerperium** | | | | | | |
| All admissions from 15/02/2020 | 13562 | -777 (-1599; -117) | -5.42 (-10.55; -0.86) | 13994 | -1406 (-2298; -672) | -9.13 (-14.10; -4.58) |
| 15/02/2020 - 30/06/2020 (1st wave) | 3582 | -327 (-472; -200) | -8.36 (-11.64; -5.30) | 3848 | -334 (-483; -191) | -7.99 (-11.16; -4.73) |
| 01/07/2020 - 30/09/2020 | 2681 | -50 (-174; 66) | -1.84 (-6.10; 2.51) | 2797 | -105 (-244; 8) | -3.61 (-8.02; 0.29) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 7299 | -401 (-1097; 185) | -5.20 (-13.06; 2.60) | 7349 | -967 (-1724; -346) | -11.63 (-19.00; -4.50) |
| **MDC 17 - Myeloproliferative Diseases and Disorders (Poorly Differentiated Neoplasms)** | | | | | | |
| All admissions from 15/02/2020 | 3230 | -934 (-1713; -354) | -22.42 (-34.66; -9.87) | 2859 | -383 (-1002; 73) | -11.83 (-25.94; 2.64) |
| 15/02/2020 - 30/06/2020 (1st wave) | 768 | -402 (-805; -116) | -34.37 (-51.18; -13.11) | 767 | -161 (-496; 74) | -17.38 (-39.25; 10.63) |
| 01/07/2020 - 30/09/2020 | 620 | -137 (-221; -60) | -18.06 (-26.31; -8.88) | 500 | -71 (-135; -14) | -12.47 (-21.30; -2.67) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 1842 | -395 (-722; -161) | -17.65 (-28.17; -8.06) | 1592 | -151 (-401; 27) | -8.66 (-20.14; 1.73) |
| **MDC 19 - Mental Diseases and Disorders** | | | | | | |
| All admissions from 15/02/2020 | 2076 | -436 (-596; -312) | -17.37 (-22.31; -13.07) | 2600 | -560 (-772; -406) | -17.73 (-22.91; -13.49) |
| 15/02/2020 - 30/06/2020 (1st wave) | 497 | -222 (-345; -126) | -30.87 (-41.00; -20.24) | 698 | -199 (-355; -83) | -22.16 (-33.71; -10.62) |
| 01/07/2020 - 30/09/2020 | 412 | -36 (-82; -1) | -8.04 (-16.58; -0.13) | 530 | -29 (-87; 15) | -5.22 (-14.11; 2.91) |

| | | | | | | |
|---|---|---|---|---|---|---|
| 01/10/2020 - 30/06/2021 (2nd wave) | 1167 | -178 (-345; -44) | -13.27 (-22.83; -3.67) | 1372 | -332 (-541; -165) | -19.50 (-28.28; -10.72) |
| **MDC 23 - Factors Influencing Health Status** | | | | | | |
| All admissions from 15/02/2020 | 3420 | -1399 (-2916; -421) | -29.03 (-46.02; -10.97) | 2956 | -2310 (-4000; -1235) | -43.87 (-57.50; -29.48) |
| 15/02/2020 - 30/06/2020 (1st wave) | 667 | -656 (-894; -475) | -49.59 (-57.27; -41.62) | 668 | -849 (-1113; -649) | -55.97 (-62.50; -49.27) |
| 01/07/2020 - 30/09/2020 | 684 | -157 (-283; -54) | -18.62 (-29.25; -7.31) | 638 | -230 (-367; -124) | -26.49 (-36.52; -16.23) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 2069 | -586 (-1780; 167) | -22.07 (-46.25; 8.76) | 1650 | -1231 (-2539; -436) | -42.73 (-60.61; -20.90) |

Abbreviations: HPA, Health Protection Agency; 95%CI, 95% confidence interval

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TABLE 3.8b: Change in urgent hospital admissions during the pandemic period, stratified by Major Diagnostic Category (MDC)

| | Bergamo HPA | | | Brescia HPA | | |
|---|---|---|---|---|---|---|
| Major Diagnostic Category | **Total** | **Change (95%CI)** | **% Change (95%CI)** | **Total** | **Change (95%CI)** | **% Change (95%CI)** |
| **MDC 01 - Nervous System** | | | | | | |
| All admissions from 15/02/2020 | 3478 | -1382 (-2259; -650) | -28.44 (-39.38; -15.74) | 5288 | -1081 (-2228; -134) | -16.98 (-29.64; -2.48) |
| 15/02/2020 - 30/06/2020 (1st wave) | 936 | -400 (-518; -299) | -29.94 (-35.60; -24.19) | 1317 | -457 (-609; -323) | -25.75 (-31.60; -19.70) |
| 01/07/2020 - 30/09/2020 | 649 | -220 (-411; -56) | -25.36 (-38.79; -7.97) | 1021 | -116 (-353; 101) | -10.24 (-25.70; 10.98) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 1893 | -762 (-1370; -275) | -28.70 (-41.99; -12.69) | 295 | -508 (-1298; 113) | -14.69 (-30.56; 4.00) |
| **MDC 03 - Ear, Nose, Mouth, And Throat** | | | | | | |
| All admissions from 15/02/2020 | 478 | -582 (-765; -467) | -54.89 (-61.53; -49.40) | 115 | -1228 (-1616; -981) | -51.64 (-58.42; -46.03) |
| 15/02/2020 - 30/06/2020 (1st wave) | 135 | -156 (-206; -119) | -53.57 (-60.45; -46.85) | 294 | -385 (-493; -297) | -56.73 (-62.63; -50.25) |
| 01/07/2020 - 30/09/2020 | 100 | -88 (-128; -55) | -46.72 (-56.21; -35.30) | 233 | -149 (-235; -81) | -38.93 (-50.26; -25.90) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 243 | -338 (-498; -243) | -58.18 (-67.20; -50.03) | 623 | -694 (-1035; -480) | -52.70 (-62.43; -43.53) |
| **MDC 04 - Respiratory System** | | | | | | |
| All admissions from 15/02/2020 | 13605 | 3718 (248; 5377) | 37.60 (1.86; 65.35) | 19789 | 6565 (1912; 8789) | 49.65 (10.70; 79.90) |
| 15/02/2020 - 30/06/2020 (1st wave) | 7467 | 4844 (4486; 5060) | 184.65 (150.52; 210.26) | 776 | 4167 (3689; 4474) | 115.97 (90.62; 136.12) |
| 01/07/2020 - 30/09/2020 | 108 | -325 (-522; -168) | -23.11 (-32.60; -13.46) | 1659 | -242 (-507; -29) | -12.75 (-23.42; -1.70) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 5058 | -801 (-4225; 1059) | -13.68 (-45.52; 26.47) | 1037 | 2641 (-1982; 5134) | 34.17 (-16.04; 98.06) |
| **MDC 05 - Circulatory System** | | | | | | |
| All admissions from 15/02/2020 | 7361 | -2391 (-3596; -1485) | -24.52 (-32.82; -16.79) | 11388 | -2110 (-3736; -863) | -15.63 (-24.70; -7.05) |
| 15/02/2020 - 30/06/2020 (1st wave) | 1717 | -997 (-1257; -810) | -36.75 (-42.26; -32.05) | 2619 | -1133 (-1487; -872) | -30.20 (-36.21; -24.97) |
| 01/07/2020 - 30/09/2020 | 1301 | -205 (-374; -64) | -13.59 (-22.33; -4.71) | 2045 | -124 (-364; 73) | -5.72 (-15.11; 3.70) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 4343 | -1189 (-1993; -569) | -21.50 (-31.45; -11.59) | 6724 | -853 (-1906; 5) | -11.25 (-22.09; 0.08) |
| **MDC 06 - Digestive System** | | | | | | |
| All admissions from 15/02/2020 | 4666 | -1569 (-1870; -1298) | -25.17 (-28.61; -21.76) | 7206 | -2187 (-2645; -1793) | -23.28 (-26.85; -19.92) |
| 15/02/2020 - 30/06/2020 (1st wave) | 109 | -646 (-733; -567) | -37.22 (-40.21; -34.21) | 1706 | -1012 (-1150; -884) | -37.24 (-40.27; -34.13) |
| 01/07/2020 - 30/09/2020 | 979 | -146 (-295; -20) | -13.01 (-23.15; -2.05) | 1663 | -50 (-291; 143) | -2.89 (-14.91; 9.43) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 2597 | -777 (-939; -635) | -23.02 (-26.55; -19.64) | 3837 | -1126 (-1364; -918) | -22.68 (-26.23; -19.30) |
| **MDC 07 - Hepatobiliary System and Pancreas** | | | | | | |
| All admissions from 15/02/2020 | 2445 | -328 (-558; -159) | -11.81 (-18.58; -6.10) | 3217 | -338 (-613; -139) | -9.51 (-16.01; -4.14) |
| 15/02/2020 - 30/06/2020 (1st wave) | 552 | -220 (-308; -149) | -28.46 (-35.82; -21.26) | 759 | -245 (-361; -163) | -24.43 (-32.23; -17.66) |
| 01/07/2020 - 30/09/2020 | 540 | 3 (-69; 57) | 0.61 (-11.32; 11.75) | 731 | 54 (-33; 119) | 7.90 (-4.38; 19.48) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 1353 | -111 (-227; -22) | -7.60 (-14.34; -1.58) | 1727 | -146 (-286; -30) | -7.81 (-14.19; -1.72) |
| **MDC 08 - Musculoskeletal System and Connective Tissue** | | | | | | |
| All admissions from 15/02/2020 | 4639 | -1057 (-1318; -841) | -18.55 (-22.13; -15.34) | 5764 | -1291 (-1617; -1021) | -18.30 (-21.91; -15.05) |
| 15/02/2020 - 30/06/2020 (1st wave) | 1142 | -455 (-566; -356) | -28.50 (-33.14; -23.78) | 1482 | -510 (-646; -383) | -25.59 (-30.35; -20.53) |

| | | | | | | |
|---|---|---|---|---|---|---|
| 01/07/2020 - 30/09/2020 | 977 | -66 (-130; -12) | -6.29 (-11.71; -1.19) | 1206 | -77 (-157; -11) | -6.01 (-11.50; -0.87) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 252 | -536 (-731; -390) | -17.54 (-22.49; -13.41) | 3076 | -705 (-950; -517) | -18.64 (-23.59; -14.39) |
| **MDC 09 - Skin, Subcutaneous Tissue, and Breast** | | | | | | |
| All admissions from 15/02/2020 | 415 | -220 (-298; -163) | -34.67 (-41.78; -28.15) | 908 | -465 (-629; -345) | -33.88 (-40.91; -27.55) |
| 15/02/2020 - 30/06/2020 (1st wave) | 108 | -76 (-115; -50) | -41.16 (-51.46; -31.56) | 251 | -153 (-226; -97) | -37.88 (-47.33; -27.88) |
| 01/07/2020 - 30/09/2020 | 105 | -21 (-42; -5) | -16.71 (-28.44; -4.64) | 211 | -44 (-84; -11) | -17.31 (-28.59; -4.77) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 202 | -124 (-173; -87) | -37.96 (-46.12; -30.06) | 446 | -268 (-381; -185) | -37.54 (-46.10; -29.33) |
| **MDC 11 - Kidney and Urinary Tract** | | | | | | |
| All admissions from 15/02/2020 | 2257 | -445 (-825; -162) | -16.47 (-26.78; -6.70) | 4472 | -1472 (-2299; -847) | -24.77 (-33.96; -15.92) |
| 15/02/2020 - 30/06/2020 (1st wave) | 510 | -228 (-305; -169) | -30.88 (-37.42; -24.84) | 1061 | -572 (-741; -436) | -35.04 (-41.12; -29.13) |
| 01/07/2020 - 30/09/2020 | 518 | -20 (-63; 15) | -3.78 (-10.77; 2.93) | 1099 | -80 (-175; -3) | -6.79 (-13.72; -0.26) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 1229 | -197 (-488; 21) | -13.80 (-28.44; 1.76) | 2312 | -820 (-1463; -340) | -26.18 (-38.75; -12.84) |
| **MDC 12 - Male Reproductive System** | | | | | | |
| All admissions from 15/02/2020 | 280 | 38 (-340; 160) | 15.78 (-54.87; 134.14) | 395 | -304 (-1252; 34) | -43.47 (-76.01; 9.51) |
| 15/02/2020 - 30/06/2020 (1st wave) | 59 | -6 (-121; 28) | -9.50 (-67.31; 89.97) | 84 | -109 (-409; -10) | -56.57 (-82.96; -10.29) |
| 01/07/2020 - 30/09/2020 | 42 | -3 (-25; 12) | -5.85 (-36.89; 38.89) | 92 | -39 (-104; 4) | -29.60 (-52.95; 4.89) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 179 | 47 (-182; 122) | 35.58 (-50.44; 212.83) | 219 | -156 (-744; 54) | -41.54 (-77.26; 32.71) |
| **MDC 13 - Female Reproductive System** | | | | | | |
| All admissions from 15/02/2020 | 352 | -86 (-235; 3) | -19.71 (-40.03; 0.72) | 602 | -325 (-639; -132) | -35.03 (-51.50; -17.93) |
| 15/02/2020 - 30/06/2020 (1st wave) | 87 | -41 (-70; -17) | -32.07 (-44.43; -16.68) | 151 | -108 (-177; -60) | -41.63 (-54.02; -28.38) |
| 01/07/2020 - 30/09/2020 | 71 | -5 (-65; 24) | -6.06 (-47.69; 52.08) | 108 | -67 (-189; -4) | -38.36 (-63.65; -3.32) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 194 | -41 (-113; 7) | -17.37 (-36.89; 3.82) | 343 | -150 (-294; -51) | -30.39 (-46.14; -12.88) |
| **MDC 14 - Pregnancy, Childbirth, and Puerperium** | | | | | | |
| All admissions from 15/02/2020 | 8925 | -654 (-1036; -316) | -6.83 (-10.40; -3.42) | 8673 | -801 (-1182; -461) | -8.46 (-12.00; -5.05) |
| 15/02/2020 - 30/06/2020 (1st wave) | 2382 | -211 (-336; -101) | -8.13 (-12.38; -4.05) | 2406 | -156 (-285; -45) | -6.09 (-10.58; -1.83) |
| 01/07/2020 - 30/09/2020 | 1804 | -60 (-148; 19) | -3.22 (-7.60; 1.07) | 1773 | -33 (-122; 46) | -1.84 (-6.46; 2.67) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 4739 | -383 (-757; -70) | -7.48 (-13.77; -1.45) | 4494 | -612 (-994; -299) | -11.98 (-18.11; -6.23) |
| **MDC 17 - Myeloproliferative Diseases and Disorders (Poorly Differentiated Neoplasms)** | | | | | | |
| All admissions from 15/02/2020 | 398 | -56 (-148; -6) | -12.40 (-27.13; -1.44) | 540 | -49 (-165; 15) | -8.37 (-23.36; 2.86) |
| 15/02/2020 - 30/06/2020 (1st wave) | 113 | -26 (-81; 12) | -18.60 (-41.77; 11.59) | 169 | 8 (-58; 51) | 4.93 (-25.59; 42.93) |
| 01/07/2020 - 30/09/2020 | 81 | -6 (-26; 10) | -6.60 (-24.49; 13.38) | 107 | -3 (-28; 16) | -2.45 (-20.54; 17.78) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 204 | -25 (-94; 8) | -10.83 (-31.53; 4.15) | 264 | -55 (-153; -7) | -17.14 (-36.75; -2.49) |
| **MDC 19 - Mental Diseases and Disorders** | | | | | | |
| All admissions from 15/02/2020 | 1531 | 75 (-344; 369) | 5.18 (-18.35; 31.74) | 219 | -398 (-1135; 139) | -15.38 (-34.14; 6.76) |
| 15/02/2020 - 30/06/2020 (1st wave) | 370 | -52 (-118; -1) | -12.24 (-24.18; -0.28) | 578 | -140 (-253; -55) | -19.54 (-30.45; -8.69) |
| 01/07/2020 - 30/09/2020 | 296 | 32 (-17; 75) | 12.25 (-5.50; 33.68) | 440 | -13 (-99; 61) | -2.94 (-18.42; 16.01) |

| | | | | | | |
|---|---|---|---|---|---|---|
| 01/10/2020 - 30/06/2021 (2nd wave) | 865 | 95 (-214; 306) | 12.30 (-19.83; 54.80) | 1172 | -244 (-805; 160) | -17.25 (-40.72; 15.81) |
| **MDC 23 - Factors Influencing Health Status** | | | | | | |
| All admissions from 15/02/2020 | 586 | -350 (-573; -221) | -37.38 (-49.44; -27.41) | 979 | -426 (-729; -248) | -30.34 (-42.67; -20.22) |
| 15/02/2020 - 30/06/2020 (1st wave) | 167 | -73 (-121; -43) | -30.39 (-41.98; -20.34) | 237 | -153 (-226; -107) | -39.30 (-48.77; -31.08) |
| 01/07/2020 - 30/09/2020 | 122 | -61 (-139; -14) | -33.24 (-53.28; -10.59) | 223 | -36 (-134; 24) | -13.77 (-37.57; 11.97) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 297 | -216 (-368; -119) | -42.13 (-55.34; -28.64) | 519 | -237 (-450; -103) | -31.39 (-46.43; -16.60) |

Abbreviations: HPA, Health Protection Agency; 95%CI, 95% confidence interval

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TABLE 3.8c: Change in elective hospital admissions during the pandemic period, stratified by Major Diagnostic Category (MDC)

| | Bergamo HPA | | | Brescia HPA | | |
|---|---|---|---|---|---|---|
| Major Diagnostic Category | **Total** | **Change (95%CI)** | **% Change (95%CI)** | **Total** | **Change (95%CI)** | **% Change (95%CI)** |
| **MDC 01 - Nervous System** | | | | | | |
| All admissions from 15/02/2020 | 22 | -1364 (-1702; -1170) | -38.26 (-43.62; -34.73) | 1913 | -1297 (-1612; -1112) | -40.40 (-45.73; -36.77) |
| 15/02/2020 - 30/06/2020 (1st wave) | 332 | -714 (-1119; -510) | -68.27 (-77.12; -60.57) | 319 | -591 (-977; -397) | -64.94 (-75.39; -55.44) |
| 01/07/2020 - 30/09/2020 | 614 | -11 (-133; 91) | -1.76 (-17.82; 17.30) | 513 | -90 (-200; 6) | -14.87 (-28.02; 1.12) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 1254 | -638 (-845; -485) | -33.73 (-40.26; -27.87) | 1081 | -616 (-791; -486) | -36.31 (-42.27; -31.03) |
| **MDC 03 - Ear, Nose, Mouth, And Throat** | | | | | | |
| All admissions from 15/02/2020 | 1123 | -887 (-1488; -539) | -44.12 (-56.99; -32.44) | 1523 | -746 (-1470; -347) | -32.87 (-49.11; -18.54) |
| 15/02/2020 - 30/06/2020 (1st wave) | 202 | -450 (-699; -313) | -69.00 (-77.58; -60.81) | 250 | -458 (-759; -304) | -64.67 (-75.22; -54.91) |
| 01/07/2020 - 30/09/2020 | 275 | -61 (-159; 14) | -18.13 (-36.62; 5.34) | 411 | 1 (-114; 89) | 0.19 (-21.69; 27.60) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 646 | -376 (-708; -202) | -36.79 (-52.27; -23.80) | 862 | -289 (-664; -90) | -25.10 (-43.50; -9.43) |
| **MDC 04 - Respiratory System** | | | | | | |
| All admissions from 15/02/2020 | 1051 | -658 (-913; -495) | -38.49 (-46.49; -32.04) | 938 | -487 (-692; -337) | -34.18 (-42.46; -26.45) |
| 15/02/2020 - 30/06/2020 (1st wave) | 227 | -253 (-362; -173) | -52.68 (-61.43; -43.26) | 229 | -206 (-307; -134) | -47.35 (-57.25; -36.99) |
| 01/07/2020 - 30/09/2020 | 223 | -69 (-108; -34) | -23.58 (-32.71; -13.36) | 190 | -60 (-95; -30) | -24.06 (-33.40; -13.74) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 601 | -336 (-487; -239) | -35.88 (-44.75; -28.48) | 519 | -221 (-331; -142) | -29.85 (-38.94; -21.45) |
| **MDC 05 - Circulatory System** | | | | | | |
| All admissions from 15/02/2020 | 5727 | -2603 (-3357; -2240) | -31.25 (-36.96; -28.12) | 6602 | -3259 (-4089; -2825) | -33.05 (-38.25; -29.97) |
| 15/02/2020 - 30/06/2020 (1st wave) | 939 | -1474 (-2420; -936) | -61.09 (-72.04; -49.91) | 1208 | -1624 (-2691; -1008) | -57.34 (-69.01; -45.49) |
| 01/07/2020 - 30/09/2020 | 1301 | -152 (-277; -38) | -10.49 (-17.54; -2.80) | 1396 | -254 (-394; -133) | -15.39 (-22.02; -8.71) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 3487 | -977 (-1372; -703) | -21.88 (-28.23; -16.78) | 3998 | -1382 (-1844; -1046) | -25.68 (-31.57; -20.74) |
| **MDC 06 - Digestive System** | | | | | | |
| All admissions from 15/02/2020 | 2065 | -1403 (-2331; -931) | -40.46 (-53.03; -31.07) | 2151 | -1050 (-1894; -611) | -32.80 (-46.83; -22.12) |
| 15/02/2020 - 30/06/2020 (1st wave) | 361 | -692 (-1264; -382) | -65.72 (-77.79; -51.44) | 434 | -539 (-1088; -256) | -55.41 (-71.48; -37.06) |
| 01/07/2020 - 30/09/2020 | 452 | -129 (-218; -64) | -22.17 (-32.51; -12.36) | 471 | -98 (-184; -38) | -17.26 (-28.13; -7.50) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 1252 | -582 (-880; -421) | -31.74 (-41.28; -25.17) | 1246 | -412 (-681; -265) | -24.86 (-35.32; -17.53) |
| **MDC 07 - Hepatobiliary System and Pancreas** | | | | | | |
| All admissions from 15/02/2020 | 1793 | -1158 (-1519; -942) | -39.23 (-45.86; -34.44) | 1726 | -1439 (-1862; -1187) | -45.46 (-51.90; -40.75) |
| 15/02/2020 - 30/06/2020 (1st wave) | 296 | -581 (-956; -349) | -66.23 (-76.36; -54.14) | 390 | -525 (-892; -294) | -57.37 (-69.58; -43.00) |
| 01/07/2020 - 30/09/2020 | 418 | -97 (-165; -35) | -18.86 (-28.30; -7.73) | 381 | -125 (-191; -67) | -24.74 (-33.45; -14.91) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 1079 | -480 (-958; -151) | -30.79 (-47.02; -12.30) | 955 | -789 (-1340; -405) | -45.23 (-58.39; -29.75) |
| **MDC 08 - Musculoskeletal System and Connective Tissue** | | | | | | |
| All admissions from 15/02/2020 | 7349 | -3596 (-4574; -3088) | -32.85 (-38.36; -29.58) | 9098 | -4869 (-6097; -4249) | -34.86 (-40.12; -31.84) |
| 15/02/2020 - 30/06/2020 (1st wave) | 1036 | -2132 (-2751; -1740) | -67.30 (-72.64; -62.68) | 1576 | -2513 (-3366; -2001) | -61.45 (-68.11; -55.95) |

| | | | | | | |
|---|---|---|---|---|---|---|
| 01/07/2020 - 30/09/2020 | 1662 | -135 (-254; -34) | -7.50 (-13.26; -2.01) | 2112 | -161 (-310; -34) | -7.06 (-12.80; -1.59) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 4651 | -1329 (-2401; -710) | -22.22 (-34.05; -13.25) | 541 | -2196 (-3702; -1362) | -28.87 (-40.63; -20.11) |
| **MDC 09 - Skin, Subcutaneous Tissue, and Breast** | | | | | | |
| All admissions from 15/02/2020 | 2078 | -906 (-1610; -403) | -30.37 (-43.65; -16.23) | 2282 | -537 (-1183; -64) | -19.03 (-34.15; -2.73) |
| 15/02/2020 - 30/06/2020 (1st wave) | 378 | -507 (-789; -311) | -57.31 (-67.60; -45.15) | 433 | -404 (-668; -214) | -48.29 (-60.68; -33.07) |
| 01/07/2020 - 30/09/2020 | 373 | -144 (-340; 0) | -27.81 (-47.66; 0.06) | 447 | -15 (-177; 107) | -3.29 (-28.32; 31.36) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 1327 | -255 (-510; -68) | -16.14 (-27.75; -4.89) | 1402 | -117 (-350; 58) | -7.70 (-19.98; 4.29) |
| **MDC 11 - Kidney and Urinary Tract** | | | | | | |
| All admissions from 15/02/2020 | 2972 | -1822 (-2451; -1473) | -38.00 (-45.20; -33.14) | 369 | -2046 (-2799; -1627) | -35.67 (-43.14; -30.60) |
| 15/02/2020 - 30/06/2020 (1st wave) | 495 | -789 (-1333; -478) | -61.46 (-72.93; -49.13) | 801 | -821 (-1473; -435) | -50.62 (-64.77; -35.21) |
| 01/07/2020 - 30/09/2020 | 680 | -135 (-220; -62) | -16.58 (-24.46; -8.39) | 785 | -202 (-308; -107) | -20.48 (-28.20; -12.01) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 1797 | -897 (-1111; -733) | -33.30 (-38.21; -28.97) | 2104 | -1022 (-1270; -832) | -32.70 (-37.64; -28.33) |
| **MDC 12 - Male Reproductive System** | | | | | | |
| All admissions from 15/02/2020 | 133 | -841 (-1195; -682) | -38.73 (-47.32; -33.89) | 981 | -800 (-1119; -658) | -44.93 (-53.28; -40.13) |
| 15/02/2020 - 30/06/2020 (1st wave) | 175 | -485 (-978; -233) | -73.49 (-84.82; -57.06) | 184 | -362 (-807; -139) | -66.31 (-81.43; -42.99) |
| 01/07/2020 - 30/09/2020 | 317 | -27 (-148; 53) | -7.79 (-31.87; 20.07) | 188 | -76 (-171; -11) | -28.79 (-47.69; -5.47) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 838 | -329 (-561; -167) | -28.19 (-40.12; -16.62) | 609 | -362 (-559; -233) | -37.29 (-47.84; -27.70) |
| **MDC 13 - Female Reproductive System** | | | | | | |
| All admissions from 15/02/2020 | 1617 | -1265 (-1714; -993) | -43.90 (-51.46; -38.04) | 1955 | -1368 (-1890; -1064) | -41.17 (-49.15; -35.24) |
| 15/02/2020 - 30/06/2020 (1st wave) | 278 | -576 (-865; -395) | -67.46 (-75.68; -58.71) | 397 | -622 (-981; -401) | -61.04 (-71.19; -50.27) |
| 01/07/2020 - 30/09/2020 | 357 | -110 (-165; -70) | -23.48 (-31.64; -16.35) | 369 | -149 (-222; -103) | -28.76 (-37.56; -21.84) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 982 | -579 (-755; -444) | -37.11 (-43.45; -31.14) | 1189 | -597 (-812; -452) | -33.43 (-40.58; -27.53) |
| **MDC 14 - Pregnancy, Childbirth, and Puerperium** | | | | | | |
| All admissions from 15/02/2020 | 1743 | 437 (-101; 803) | 33.45 (-5.49; 85.51) | 2893 | -126 (-1407; 734) | -4.18 (-32.73; 34.00) |
| 15/02/2020 - 30/06/2020 (1st wave) | 460 | 90 (-32; 180) | 24.37 (-6.50; 64.42) | 785 | -35 (-314; 166) | -4.24 (-28.56; 26.88) |
| 01/07/2020 - 30/09/2020 | 333 | 72 (-16; 139) | 27.70 (-4.61; 71.57) | 580 | -17 (-223; 143) | -2.79 (-27.78; 32.68) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 950 | 275 (-55; 494) | 40.65 (-5.48; 108.51) | 1528 | -75 (-873; 450) | -4.67 (-36.37; 41.73) |
| **MDC 17 - Myeloproliferative Diseases and Disorders (Poorly Differentiated Neoplasms)** | | | | | | |
| All admissions from 15/02/2020 | 1987 | -681 (-1241; -274) | -25.52 (-38.45; -12.12) | 1973 | -303 (-787; 38) | -13.33 (-28.51; 1.94) |
| 15/02/2020 - 30/06/2020 (1st wave) | 504 | -224 (-400; -99) | -30.74 (-44.22; -16.41) | 527 | -124 (-290; -11) | -19.08 (-35.46; -2.11) |
| 01/07/2020 - 30/09/2020 | 367 | -139 (-224; -62) | -27.46 (-37.93; -14.53) | 331 | -77 (-148; -14) | -18.87 (-30.87; -4.13) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 1116 | -318 (-632; -91) | -22.19 (-36.15; -7.54) | 1115 | -102 (-366; 86) | -8.39 (-24.73; 8.37) |
| **MDC 19 - Mental Diseases and Disorders** | | | | | | |
| All admissions from 15/02/2020 | 291 | -226 (-410; -144) | -43.76 (-58.50; -33.13) | 294 | -179 (-337; -104) | -37.84 (-53.43; -26.10) |
| 15/02/2020 - 30/06/2020 (1st wave) | 66 | -83 (-218; -31) | -55.61 (-76.78; -32.10) | 87 | -55 (-161; -7) | -38.62 (-64.87; -7.45) |
| 01/07/2020 - 30/09/2020 | 66 | -29 (-62; -7) | -30.76 (-48.50; -9.65) | 63 | -19 (-47; -2) | -23.48 (-42.70; -2.78) |

| | | | | | | |
|---|---|---|---|---|---|---|
| 01/10/2020 - 30/06/2021 (2nd wave) | 159 | -114 (-185; -73) | -41.85 (-53.72; -31.57) | 144 | -105 (-168; -68) | -42.14 (-53.83; -32.11) |
| **MDC 23 - Factors Influencing Health Status** | | | | | | |
| All admissions from 15/02/2020 | 1075 | -628 (-1168; -334) | -36.88 (-52.07; -23.70) | 927 | -897 (-1484; -585) | -49.18 (-61.56; -38.68) |
| 15/02/2020 - 30/06/2020 (1st wave) | 216 | -275 (-348; -219) | -56.03 (-61.70; -50.31) | 240 | -314 (-399; -249) | -56.69 (-62.47; -50.91) |
| 01/07/2020 - 30/09/2020 | 234 | -76 (-144; -21) | -24.47 (-38.15; -8.22) | 194 | -101 (-165; -50) | -34.17 (-45.98; -20.60) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 625 | -277 (-754; -15) | -30.71 (-54.66; -2.36) | 493 | -482 (-1006; -198) | -49.45 (-67.11; -28.63) |

Abbreviations: HPA, Health Protection Agency; 95%CI, 95% confidence interval

TABLE 3.9: Difference in daily counts of total hospital admissions before (2017-2019) and during COVID-19 pandemic (2020-2021), stratified by Diagnosis Related Group

| Diagnosis Related Group (DRG) type | Bergamo HPA | | | Brescia HPA | | |
|---|---|---|---|---|---|---|
| | **Jan 2017 - Dec 2019** | **Jan 2020 - Jun 2021** | ***p*-value** | **Jan 2017 - Dec 2019** | **Jan 2020 - Jun 2021** | ***p*-value** |
| **DRG for surgical procedures** | | | | | | |
| Total | 188425 | 70254 | | 203362 | 75244 | |
| Daily events | | | | | | |
| Mean (±SD) | 172.08 (89.82) | 128.44 (77.8) | <0.001 | 185.72 (97.85) | 137.56 (78.89) | <0.001 |
| Median (IQR) | 207 (66-246) | 141 (50-192) | | 218 (79-267) | 150 (58-202) | |
| Min - max | 18-318 | 15-315 | | 22-369 | 16-348 | |
| **Medical DRG** | | | | | | |
| Total | 164510 | 64641 | | 215167 | 85818 | |
| Daily events | | | | | | |
| Mean (±SD) | 150.24 (41.72) | 118.17 (42.84) | <0.001 | 196.5 (45.96) | 156.89 (43.49) | <0.001 |
| Median (IQR) | 165 (102-183) | 120 (86-136) | | 211 (149-232) | 159 (125-179) | |
| Min - max | 66-242 | 19-285 | | 94-299 | 18-307 | |

Abbreviations: HPA, Health Protection Agency; SD, standard deviation; IQR, interquartile range

TABLE 3.10a: Change in total hospital admissions during the pandemic period, stratified by Diagnosis Related Group (DRG) type

| | Bergamo HPA | | | Brescia HPA | | |
|---|---|---|---|---|---|---|
| DRG type | **Total** | **Change (95%CI)** | **% Change (95%CI)** | **Total** | **Change (95%CI)** | **% Change (95%CI)** |
| **DRG for surgical procedures** | | | | | | |
| All admissions from 15/02/2020 | 62173 | -27735 (-30580; -25272) | -30.85 (-32.97; -28.90) | 66510 | -30776 (-33880; -28088) | -31.63 (-33.75; -29.69) |
| 15/02/2020 - 30/06/2020 (1st wave) | 11260 | -14567 (-18429; -11194) | -56.40 (-62.07; -49.85) | 13647 | -14601 (-18822; -10863) | -51.69 (-57.97; -44.32) |
| 01/07/2020 - 30/09/2020 | 13256 | -1513 (-2254; -848) | -10.24 (-14.53; -6.01) | 13684 | -1968 (-2763; -1233) | -12.57 (-16.80; -8.26) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 37657 | -11656 (-14402; -9253) | -23.64 (-27.67; -19.73) | 39179 | -14207 (-17210; -11563) | -26.61 (-30.52; -22.79) |
| **Medical DRG** | | | | | | |
| All admissions from 15/02/2020 | 57797 | -15114 (-21083; -10543) | -20.73 (-26.73; -15.43) | 76808 | -14805 (-22262; -9103) | -16.16 (-22.47; -10.60) |
| 15/02/2020 - 30/06/2020 (1st wave) | 17634 | -2737 (-3252; -2399) | -13.44 (-15.57; -11.97) | 21452 | -4308 (-4958; -3876) | -16.72 (-18.77; -15.30) |
| 01/07/2020 - 30/09/2020 | 10276 | -2418 (-3440; -1589) | -19.05 (-25.08; -13.39) | 13797 | -2139 (-3411; -1113) | -13.42 (-19.82; -7.47) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 29887 | -9959 (-14708; -6166) | -24.99 (-32.98; -17.10) | 41559 | -8358 (-14296; -3613) | -16.74 (-25.60; -8.00) |

Abbreviations: HPA, Health Protection Agency; 95%CI, 95% confidence interval

TABLE 3.10b: Change in urgent hospital admissions during the pandemic period, stratified by Diagnosis Related Group (DRG) type

| | Bergamo HPA | | | Brescia HPA | | |
|---|---|---|---|---|---|---|
| DRG type | **Total** | **Change (95%CI)** | **% Change (95%CI)** | **Total** | **Change (95%CI)** | **% Change (95%CI)** |
| **DRG for surgical procedures** | | | | | | |
| All admissions from 15/02/2020 | 13883 | -1312 (-1845; -843) | -8.63 (-11.73; -5.73) | 17257 | -1292 (-1921; -730) | -6.97 (-10.01; -4.06) |
| 15/02/2020 - 30/06/2020 (1st wave) | 3503 | -732 (-949; -540) | -17.29 (-21.32; -13.35) | 4395 | -735 (-995; -504) | -14.33 (-18.47; -10.28) |
| 01/07/2020 - 30/09/2020 | 2747 | 19 (-85; 118) | 0.68 (-2.99; 4.47) | 3331 | -19 (-145; 103) | -0.56 (-4.16; 3.17) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 7633 | -598 (-929; -296) | -7.27 (-10.85; -3.73) | 9531 | -538 (-929; -173) | -5.34 (-8.88; -1.79) |
| **Medical DRG** | | | | | | |
| All admissions from 15/02/2020 | 42366 | -5958 (-9287; -3716) | -12.33 (-17.98; -8.06) | 62722 | -6790 (-11540; -3698) | -9.77 (-15.54; -5.57) |
| 15/02/2020 - 30/06/2020 (1st wave) | 14549 | 1326 (-3; 2249) | 10.03 (-0.02; 18.28) | 18357 | -1014 (-3029; 393) | -5.24 (-14.16; 2.19) |
| 01/07/2020 - 30/09/2020 | 695 | -1506 (-2357; -789) | -17.81 (-25.32; -10.20) | 10854 | -1209 (-2438; -169) | -10.02 (-18.34; -1.54) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 20867 | -5779 (-9175; -3062) | -21.69 (-30.54; -12.79) | 33511 | -4568 (-9424; -587) | -12.00 (-21.95; -1.72) |

Abbreviations: HPA, Health Protection Agency; 95%CI, 95% confidence interval

TABLE 3.10c: Change in elective hospital admissions during the pandemic period, stratified by Diagnosis Related Group (DRG) type

| | Bergamo HPA | | | Brescia HPA | | |
|---|---|---|---|---|---|---|
| DRG type | **Total** | **Change (95%CI)** | **% Change (95%CI)** | **Total** | **Change (95%CI)** | **% Change (95%CI)** |
| **DRG for surgical procedures** | | | | | | |
| All admissions from 15/02/2020 | 27512 | -12598 (-15796; -10274) | -31.41 (-36.47; -27.19) | 31039 | -13510 (-17183; -10860) | -30.33 (-35.63; -25.92) |
| 15/02/2020 - 30/06/2020 (1st wave) | 4533 | -7371 (-10581; -4802) | -61.92 (-70.01; -51.44) | 5982 | -7432 (-10938; -4512) | -55.40 (-64.65; -43.00) |
| 01/07/2020 - 30/09/2020 | 6058 | -670 (-1010; -341) | -9.96 (-14.29; -5.33) | 668 | -658 (-1008; -313) | -8.96 (-13.11; -4.47) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 16921 | -4557 (-5651; -3633) | -21.22 (-25.04; -17.68) | 18377 | -5420 (-6677; -4348) | -22.78 (-26.65; -19.13) |
| **Medical DRG** | | | | | | |
| All admissions from 15/02/2020 | 8836 | -5631 (-6269; -5112) | -38.92 (-41.50; -36.65) | 10199 | -6756 (-7538; -6209) | -39.85 (-42.50; -37.84) |
| 15/02/2020 - 30/06/2020 (1st wave) | 18 | -2419 (-3185; -1787) | -57.34 (-63.89; -49.82) | 2357 | -2544 (-3497; -1773) | -51.91 (-59.73; -42.92) |
| 01/07/2020 - 30/09/2020 | 2066 | -557 (-820; -334) | -21.24 (-28.41; -13.90) | 2218 | -802 (-1125; -546) | -26.56 (-33.65; -19.76) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 497 | -2655 (-3245; -2247) | -34.82 (-39.50; -31.14) | 5624 | -3410 (-4066; -2917) | -37.74 (-41.96; -34.15) |

Abbreviations: HPA, Health Protection Agency; 95%CI, 95% confidence interval

TABLE 3.11: Difference in daily counts of total hospital admissions before (2017-2019) and during COVID-19 pandemic (2020-2021) in individuals with chronic conditions

| | Bergamo HPA | | | Brescia HPA | | |
|---|---|---|---|---|---|---|
| | **Jan 2017 - Dec 2019** | **Jan - Dec 2020** | ***p*-value** | **Jan 2017 - Dec 2019** | **Jan - Dec 2020** | ***p*-value** |
| **Total** | | | | | | |
| Total | 120951 | 46478 | | 150898 | 62110 | |
| Daily events | | | | | | |
| Mean (±SD) | 110.46 (96.76) | 84.97 (76.5) | <0.001 | 137.81 (117.01) | 113.55 (96.42) | <0.001 |
| Median (IQR) | 86 (0-207) | 70 (0-150) | | 121 (0-251) | 108 (0-199) | |
| Min - max | 0-278 | 0-283 | | 0-364 | 0-335 | |
| **Condition** | | | | | | |
| **Organ Transplant** | | | | | | |
| Total | 1770 | 589 | | 1478 | 702 | |
| Daily events | | | | | | |
| Mean (±SD) | 2.42 (1.98) | 1.61 (1.55) | <0.001 | 2.02 (1.57) | 1.92 (1.55) | 0.210 |
| Median (IQR) | 2 (1-4) | 1 (0-3) | | 2 (1-3) | 2 (1-3) | |
| Min - max | 0-12 | 0-8 | | 0-10 | 0-8 | |
| **Chronic Kidney Disease** | | | | | | |
| Total | 7618 | 2945 | | 11794 | 4902 | |
| Daily events | | | | | | |
| Mean (±SD) | 10.44 (5.23) | 8.05 (4.48) | <0.001 | 16.16 (6.61) | 13.39 (5.81) | <0.001 |
| Median (IQR) | 10 (6-14) | 7 (5-11) | | 16 (11-21) | 13 (9-18) | |
| Min - max | 0-25 | 0-25 | | 2-36 | 2-28 | |
| **HIV Infection** | | | | | | |
| Total | 905 | 1 | | 1.234 | 692 | |
| Daily events | | | | | | |
| Mean (±SD) | 1.24 (1.2) | 0 (0.05) | <0.001 | 1.69 (1.47) | 1.89 (1.58) | 0.066 |
| Median (IQR) | 1 (0-2) | 0 (0-0) | | 1 (1-3) | 2 (1-3) | |
| Min - max | 0-6 | 0-1 | | 0-10 | 0-9 | |
| **Neoplasm** | | | | | | |

| | | | | | | |
|---|---|---|---|---|---|---|
| Total | 33959 | 13195 | | 38842 | 16263 | |
| Daily events | | | | | | |
| Mean (±SD) | 46.52 (22.24) | 36.05 (18.72) | <0.001 | 53.21 (23.45) | 44.43 (19.86) | <0.001 |
| Median (IQR) | 52 (23-64) | 35 (19-50) | | 57.5 (30-71) | 45 (26-60) | |
| Min - max | 6-102 | 4-93 | | 10-110 | 10-99 | |
| **Type 1 Diabetes Mellitus** | | | | | | |
| Total | 548 | 165 | | 618 | 236 | |
| Daily events | | | | | | |
| Mean (±SD) | 0.75 (0.91) | 0.45 (0.68) | <0.001 | 0.85 (0.92) | 0.64 (0.8) | 0.001 |
| Median (IQR) | 1 (0-1) | 0 (0-1) | | 1 (0-1) | 0 (0-1) | |
| Min - max | 0-5 | 0-4 | | 0-4 | 0-4 | |
| **Type 2 Diabetes Mellitus** | | | | | | |
| Total | 24324 | 9342 | | 34080 | 14489 | |
| Daily events | | | | | | |
| Mean (±SD) | 33.32 (13.82) | 25.52 (11.21) | <0.001 | 46.68 (17.81) | 39.59 (15.13) | <0.001 |
| Median (IQR) | 35.5 (20-45) | 25 (16-34) | | 49 (30-60) | 39 (26-51) | |
| Min - max | 6-65 | 4-56 | | 12-93 | 11-82 | |
| **Cardio-Cerebrovascular Disease** | | | | | | |
| Total | 86699 | 33326 | | 113849 | 47080 | |
| Daily events | | | | | | |
| Mean (±SD) | 118.77 (48.21) | 91.05 (40.44) | <0.001 | 155.96 (57.77) | 128.63 (48.37) | <0.001 |
| Median (IQR) | 133 (66-160) | 93 (52-122) | | 173 (95-203) | 133 (83-167) | |
| Min - max | 26-203 | 25-183 | | 45-276 | 39-245 | |
| **Respiratory Disease** | | | | | | |
| Total | 13800 | 5012 | | 18915 | 7336 | |
| Daily events | | | | | | |
| Mean (±SD) | 18.9 (8.23) | 13.69 (6.75) | <0.001 | 25.91 (10.11) | 20.04 (8.8) | <0.001 |
| Median (IQR) | 20 (12-25) | 12 (8-18) | | 27 (17-34) | 19 (13-26) | |
| Min - max | 1-48 | 1-34 | | 5-58 | 2-60 | |
| **Digestive and Liver Disease** | | | | | | |
| Total | 8220 | 3170 | | 10058 | 4089 | |

| | | | | | | |
|---|---|---|---|---|---|---|
| Daily events | | | | | | |
| Mean (±SD) | 11.26 (5.95) | 8.66 (4.74) | <0.001 | 13.78 (6.23) | 11.17 (5.19) | <0.001 |
| Median (IQR) | 12 (6-16) | 8 (5-12) | | 14 (9-18) | 11 (7-15) | |
| Min - max | 0-30 | 0-24 | | 1-33 | 2-26 | |
| **Neuropathy** | | | | | | |
| Total | 7696 | 2783 | | 10376 | 4364 | |
| Daily events | | | | | | |
| Mean (±SD) | 10.54 (5.14) | 7.6 (4.43) | <0.001 | 14.21 (5.73) | 11.92 (5.07) | <0.001 |
| Median (IQR) | 11 (6-14) | 7 (4-10) | | 14 (10-18) | 11 (8-15) | |
| Min - max | 0-25 | 0-24 | | 2-35 | 1-29 | |
| **Autoimmune Disorder** | | | | | | |
| Total | 6636 | 2651 | | 6483 | 2591 | |
| Daily events | | | | | | |
| Mean (±SD) | 9.09 (4.96) | 7.24 (4.46) | <0.001 | 8.88 (4.62) | 7.08 (3.95) | <0.001 |
| Median (IQR) | 9 (5-13) | 7 (4-10) | | 9 (5-12) | 7 (4-10) | |
| Min - max | 0-24 | 0-23 | | 0-25 | 0-20 | |
| **Endocrine Disorder** | | | | | | |
| Total | 37401 | 14549 | | 49417 | 20693 | |
| Daily events | 51.23 (22.32) | 39.75 (18.56) | <0.001 | 67.69 (26.6) | 56.54 (22.37) | <0.001 |
| Mean (±SD) | 57 (28-70) | 39 (23-55) | | 72 (41-89) | 56 (37-73) | |
| Median (IQR) | 10-101 | 8-88 | | 15-130 | 14-115 | |
| Min - max | | | | | | |
| **Others** | | | | | | |
| Total | 3980 | 1570 | | 4850 | 2091 | |
| Daily events | | | | | | |
| Mean (±SD) | 5.45 (3.51) | 4.29 (3.07) | <0.001 | 6.64 (3.86) | 5.71 (3.25) | <0.001 |
| Median (IQR) | 5 (3-8) | 4 (2-6) | | 6 (4-9) | 5 (3-8) | |
| Min - max | 0-17 | 0-14 | | 0-21 | 0-16 | |

Abbreviations: HPA, Health Protection Agency; SD, standard deviation; IQR, interquartile range; HIV, human immunodeficiency virus

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TABLE 3.12a: Change in total hospital admissions of patient with chronic conditions during the pandemic period, stratified by comorbidity

| | Bergamo HPA | | | Brescia HPA | | |
|---|---|---|---|---|---|---|
| | Total | Change (95%CI) | % Change (95%CI) | Total | Change (95%CI) | % Change (95%CI) |
| **Total** | | | | | | |
| All admissions from 15/02/2020 | 38999 | -24039 (-28515; -20690) | -38.13 (-42.24; -34.66) | 52376 | -29138 (-34717; -24726) | -35.75 (-39.86; -32.07) |
| 15/02/2020 - 30/06/2020 (1st wave) | 13842 | -14186 (-17677; -11594) | -50.61 (-56.08; -45.58) | 19344 | -16793 (-21269; -13332) | -46.47 (-52.37; -40.80) |
| 01/07/2020 - 30/09/2020 | 1295 | -3647 (-4324; -2999) | -21.97 (-25.03; -18.80) | 16848 | -4498 (-5351; -3652) | -21.07 (-24.10; -17.81) |
| 01/10/2020 - 31/12/2020 | 12207 | -6206 (-7033; -5528) | -33.71 (-36.56; -31.17) | 16184 | -7847 (-8868; -6926) | -32.65 (-35.40; -29.97) |
| **Condition** | | | | | | |
| **Chronic Kidney Disease** | | | | | | |
| All admissions from 15/02/2020 | 2671 | -2169 (-2759; -1683) | -44.81 (-50.81; -38.66) | 4346 | -2959 (-3779; -2284) | -40.50 (-46.51; -34.45) |
| 15/02/2020 - 30/06/2020 (1st wave) | 977 | -1216 (-1635; -874) | -55.45 (-62.59; -47.21) | 1563 | -1550 (-2136; -1077) | -49.79 (-57.75; -40.80) |
| 01/07/2020 - 30/09/2020 | 857 | -398 (-499; -311) | -31.72 (-36.81; -26.62) | 1402 | -592 (-759; -446) | -29.68 (-35.11; -24.13) |
| 01/10/2020 - 31/12/2020 | 837 | -555 (-693; -434) | -39.85 (-45.28; -34.13) | 1381 | -817 (-1013; -653) | -37.17 (-42.31; -32.12) |
| **Neoplasm** | | | | | | |
| All admissions from 15/02/2020 | 10947 | -7807 (-9248; -6676) | -41.63 (-45.79; -37.88) | 13659 | -8837 (-10528; -7497) | -39.28 (-43.53; -35.44) |
| 15/02/2020 - 30/06/2020 (1st wave) | 3926 | -4530 (-5802; -3530) | -53.57 (-59.64; -47.34) | 5225 | -4869 (-6432; -3732) | -48.24 (-55.18; -41.67) |
| 01/07/2020 - 30/09/2020 | 3658 | -1281 (-1529; -1073) | -25.94 (-29.48; -22.69) | 4352 | -1535 (-1823; -1271) | -26.08 (-29.53; -22.61) |
| 01/10/2020 - 31/12/2020 | 3363 | -1996 (-2256; -1733) | -37.25 (-40.15; -34.00) | 4082 | -2433 (-2748; -2123) | -37.34 (-40.23; -34.21) |
| **Type 2 Diabetes Mellitus** | | | | | | |
| All admissions from 15/02/2020 | 7903 | -5147 (-6435; -4220) | -39.44 (-44.88; -34.81) | 12276 | -6771 (-8662; -5415) | -35.55 (-41.37; -30.61) |
| 15/02/2020 - 30/06/2020 (1st wave) | 2861 | -2898 (-3811; -2251) | -50.32 (-57.12; -44.04) | 4588 | -3758 (-5078; -2839) | -45.03 (-52.53; -38.23) |
| 01/07/2020 - 30/09/2020 | 2571 | -910 (-1158; -703) | -26.14 (-31.05; -21.48) | 3892 | -1169 (-1524; -876) | -23.10 (-28.14; -18.37) |
| 01/10/2020 - 31/12/2020 | 2471 | -1339 (-1596; -1114) | -35.14 (-39.24; -31.06) | 3796 | -1844 (-2233; -1497) | -32.69 (-37.04; -28.29) |
| **Cardio-Cerebrovascular Disease** | | | | | | |
| All admissions from 15/02/2020 | 28087 | -17665 (-21403; -14750) | -38.61 (-43.25; -34.43) | 39953 | -21823 (-26859; -17889) | -35.33 (-40.20; -30.93) |
| 15/02/2020 - 30/06/2020 (1st wave) | 9895 | -10426 (-13132; -8280) | -51.31 (-57.03; -45.56) | 14586 | -12651 (-16306; -9743) | -46.45 (-52.78; -40.05) |
| 01/07/2020 - 30/09/2020 | 9296 | -2777 (-3422; -2207) | -23.00 (-26.91; -19.19) | 129 | -3375 (-4234; -2619) | -20.74 (-24.71; -16.88) |
| 01/10/2020 - 31/12/2020 | 8896 | -4462 (-5123; -3894) | -33.40 (-36.54; -30.45) | 12467 | -5796 (-6701; -5023) | -31.74 (-34.96; -28.72) |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Respiratory Disease** | | | | | | |
| All admissions from 15/02/2020 | 413 | -3519 (-4099; -3005) | -46.01 (-49.81; -42.12) | 6064 | -4553 (-5369; -3851) | -42.88 (-46.96; -38.84) |
| 15/02/2020 - 30/06/2020 (1st wave) | 1483 | -1853 (-2125; -1637) | -55.54 (-58.90; -52.47) | 2222 | -2486 (-2881; -2194) | -52.81 (-56.46; -49.68) |
| 01/07/2020 - 30/09/2020 | 1343 | -643 (-812; -478) | -32.36 (-37.69; -26.26) | 1986 | -784 (-1024; -550) | -28.31 (-34.02; -21.69) |
| 01/10/2020 - 31/12/2020 | 1304 | -1024 (-1232; -829) | -43.98 (-48.59; -38.86) | 1856 | -1282 (-1555; -1022) | -40.86 (-45.58; -35.51) |
| **Digestive and Liver Disease** | | | | | | |
| All admissions from 15/02/2020 | 2694 | -1664 (-1961; -1457) | -38.18 (-42.13; -35.10) | 3459 | -2144 (-2527; -1840) | -38.27 (-42.22; -34.72) |
| 15/02/2020 - 30/06/2020 (1st wave) | 924 | -970 (-1217; -801) | -51.21 (-56.83; -46.42) | 1269 | -1176 (-1487; -946) | -48.09 (-53.96; -42.70) |
| 01/07/2020 - 30/09/2020 | 886 | -322 (-457; -226) | -26.67 (-34.02; -20.35) | 116 | -339 (-488; -211) | -22.63 (-29.59; -15.42) |
| 01/10/2020 - 31/12/2020 | 884 | -372 (-584; -189) | -29.60 (-39.78; -17.60) | 103 | -629 (-896; -380) | -37.92 (-46.52; -26.95) |
| **Neuropathy** | | | | | | |
| All admissions from 15/02/2020 | 2332 | -1817 (-2528; -1280) | -43.79 (-52.01; -35.44) | 3726 | -2176 (-3198; -1440) | -36.87 (-46.19; -27.87) |
| 15/02/2020 - 30/06/2020 (1st wave) | 789 | -1058 (-1537; -732) | -57.28 (-66.08; -48.13) | 1294 | -1223 (-1901; -767) | -48.58 (-59.50; -37.21) |
| 01/07/2020 - 30/09/2020 | 870 | -268 (-363; -183) | -23.56 (-29.42; -17.41) | 1291 | -345 (-475; -222) | -21.07 (-26.88; -14.65) |
| 01/10/2020 - 31/12/2020 | 673 | -491 (-699; -324) | -42.17 (-50.93; -32.51) | 1141 | -609 (-907; -371) | -34.80 (-44.30; -24.53) |
| **Autoimmune Disorder** | | | | | | |
| All admissions from 15/02/2020 | 2189 | -1356 (-1828; -1012) | -38.26 (-45.50; -31.60) | 2178 | -1100 (-1551; -763) | -33.56 (-41.59; -25.94) |
| 15/02/2020 - 30/06/2020 (1st wave) | 805 | -773 (-1055; -565) | -48.99 (-56.71; -41.24) | 794 | -621 (-880; -437) | -43.88 (-52.56; -35.50) |
| 01/07/2020 - 30/09/2020 | 699 | -199 (-301; -116) | -22.12 (-30.11; -14.28) | 705 | -160 (-252; -76) | -18.48 (-26.34; -9.73) |
| 01/10/2020 - 31/12/2020 | 685 | -385 (-533; -272) | -35.97 (-43.77; -28.42) | 679 | -319 (-463; -215) | -31.97 (-40.53; -24.07) |
| **Endocrine Disorder** | | | | | | |
| All admissions from 15/02/2020 | 12212 | -7284 (-9027; -5835) | -37.36 (-42.50; -32.33) | 17458 | -8856 (-11340; -6918) | -33.65 (-39.38; -28.38) |
| 15/02/2020 - 30/06/2020 (1st wave) | 438 | -4175 (-5173; -3394) | -48.80 (-54.15; -43.66) | 6404 | -5249 (-6638; -4193) | -45.04 (-50.90; -39.57) |
| 01/07/2020 - 30/09/2020 | 4013 | -1164 (-1572; -789) | -22.48 (-28.14; -16.43) | 5648 | -1248 (-1811; -760) | -18.10 (-24.28; -11.85) |
| 01/10/2020 - 31/12/2020 | 3819 | -1945 (-2402; -1570) | -33.75 (-38.61; -29.13) | 5406 | -2359 (-2947; -1857) | -30.38 (-35.28; -25.57) |

Abbreviations: HPA, Health Protection Agency; 95%CI, 95% confidence interval

TABLE 3.12b: Change in urgent hospital admissions of patient with chronic conditions during the pandemic period, stratified by comorbidity

| | Bergamo HPA | | | Brescia HPA | | |
|---|---|---|---|---|---|---|
| | Total | Change (95%CI) | % Change (95%CI) | Total | Change (95%CI) | % Change (95%CI) |
| **Total** | | | | | | |
| All admissions from 15/02/2020 | 1873 | -8075 (-10669; -6289) | -30.12 (-36.29; -25.14) | 30973 | -10692 (-14677; -8021) | -25.66 (-32.15; -20.57) |
| 15/02/2020 - 30/06/2020 (1st wave) | 8036 | -3185 (-3671; -2903) | -28.39 (-31.36; -26.54) | 124 | -5234 (-5961; -4817) | -29.68 (-32.46; -27.98) |
| 01/07/2020 - 30/09/2020 | 525 | -2113 (-3110; -1273) | -28.70 (-37.20; -19.52) | 9087 | -2248 (-3770; -963) | -19.83 (-29.32; -9.58) |
| 01/10/2020 - 31/12/2020 | 5444 | -2777 (-3937; -1860) | -33.78 (-41.97; -25.47) | 9486 | -3211 (-4995; -1807) | -25.29 (-34.49; -16.00) |
| **Condition** | | | | | | |
| **Chronic Kidney Disease** | | | | | | |
| All admissions from 15/02/2020 | 1463 | -1032 (-1248; -861) | -41.36 (-46.03; -37.06) | 309 | -2004 (-2437; -1669) | -39.34 (-44.09; -35.07) |
| 15/02/2020 - 30/06/2020 (1st wave) | 577 | -498 (-605; -412) | -46.31 (-51.20; -41.68) | 1188 | -941 (-1161; -783) | -44.21 (-49.42; -39.73) |
| 01/07/2020 - 30/09/2020 | 432 | -221 (-287; -161) | -33.87 (-39.88; -27.21) | 938 | -436 (-570; -311) | -31.75 (-37.80; -24.91) |
| 01/10/2020 - 31/12/2020 | 454 | -313 (-386; -252) | -40.80 (-45.93; -35.68) | 964 | -626 (-775; -501) | -39.38 (-44.56; -34.19) |
| **Neoplasm** | | | | | | |
| All admissions from 15/02/2020 | 4577 | -3091 (-3875; -2508) | -40.31 (-45.85; -35.40) | 7104 | -4018 (-5132; -3174) | -36.13 (-41.94; -30.88) |
| 15/02/2020 - 30/06/2020 (1st wave) | 1891 | -1363 (-1672; -1165) | -41.89 (-46.92; -38.13) | 2796 | -1868 (-2285; -1588) | -40.05 (-44.98; -36.23) |
| 01/07/2020 - 30/09/2020 | 1326 | -782 (-1078; -531) | -37.08 (-44.83; -28.60) | 2153 | -927 (-1333; -581) | -30.10 (-38.24; -21.26) |
| 01/10/2020 - 31/12/2020 | 136 | -946 (-1191; -742) | -41.03 (-46.69; -35.30) | 2155 | -1223 (-1579; -918) | -36.21 (-42.29; -29.88) |
| **Type 2 Diabetes Mellitus** | | | | | | |
| All admissions from 15/02/2020 | 4492 | -2201 (-3315; -1547) | -32.89 (-42.46; -25.62) | 7962 | -2800 (-4531; -1796) | -26.02 (-36.27; -18.40) |
| 15/02/2020 - 30/06/2020 (1st wave) | 1866 | -926 (-1372; -708) | -33.17 (-42.37; -27.52) | 3167 | -1343 (-2018; -1009) | -29.77 (-38.92; -24.16) |
| 01/07/2020 - 30/09/2020 | 1249 | -555 (-837; -329) | -30.77 (-40.13; -20.84) | 2284 | -645 (-1098; -288) | -22.02 (-32.47; -11.21) |
| 01/10/2020 - 31/12/2020 | 1377 | -720 (-1121; -444) | -34.33 (-44.87; -24.39) | 2511 | -812 (-1426; -386) | -24.44 (-36.23; -13.31) |
| **Cardio-Cerebrovascular Disease** | | | | | | |
| All admissions from 15/02/2020 | 14296 | -6702 (-9011; -5106) | -31.92 (-38.66; -26.32) | 24759 | -8905 (-12561; -6396) | -26.45 (-33.66; -20.53) |
| 15/02/2020 - 30/06/2020 (1st wave) | 609 | -2698 (-3164; -2425) | -30.70 (-34.19; -28.48) | 9814 | -4416 (-5136; -3979) | -31.03 (-34.35; -28.85) |
| 01/07/2020 - 30/09/2020 | 3971 | -1728 (-2640; -998) | -30.33 (-39.93; -20.09) | 7269 | -1860 (-3343; -718) | -20.37 (-31.50; -8.99) |
| 01/10/2020 - 31/12/2020 | 4235 | -2276 (-3319; -1448) | -34.96 (-43.93; -25.48) | 7676 | -2629 (-4281; -1299) | -25.51 (-35.80; -14.48) |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Respiratory Disease** | | | | | | |
| All admissions from 15/02/2020 | 2261 | -1779 (-2517; -1319) | -44.03 (-52.68; -36.85) | 394 | -2254 (-3341; -1583) | -36.39 (-45.89; -28.66) |
| 15/02/2020 - 30/06/2020 (1st wave) | 999 | -714 (-850; -611) | -41.69 (-45.97; -37.95) | 1546 | -1124 (-1332; -959) | -42.09 (-46.27; -38.28) |
| 01/07/2020 - 30/09/2020 | 628 | -434 (-722; -222) | -40.89 (-53.48; -26.14) | 1189 | -424 (-856; -105) | -26.30 (-41.85; -8.13) |
| 01/10/2020 - 31/12/2020 | 634 | -630 (-1017; -357) | -49.84 (-61.59; -36.02) | 1205 | -706 (-1287; -297) | -36.95 (-51.65; -19.75) |
| **Digestive and Liver Disease** | | | | | | |
| All admissions from 15/02/2020 | 1284 | -344 (-686; -103) | -21.11 (-34.84; -7.40) | 2177 | -1082 (-1769; -607) | -33.20 (-44.83; -21.80) |
| 15/02/2020 - 30/06/2020 (1st wave) | 499 | -171 (-333; -69) | -25.49 (-40.05; -12.16) | 832 | -532 (-868; -327) | -39.00 (-51.07; -28.21) |
| 01/07/2020 - 30/09/2020 | 381 | -101 (-170; -40) | -20.96 (-30.87; -9.49) | 691 | -268 (-407; -147) | -27.91 (-37.07; -17.57) |
| 01/10/2020 - 31/12/2020 | 404 | -72 (-196; 24) | -15.10 (-32.67; 6.35) | 654 | -282 (-522; -93) | -30.16 (-44.37; -12.43) |
| **Neuropathy** | | | | | | |
| All admissions from 15/02/2020 | 1295 | -838 (-1240; -570) | -39.30 (-48.91; -30.57) | 2752 | -1236 (-1974; -766) | -30.99 (-41.76; -21.78) |
| 15/02/2020 - 30/06/2020 (1st wave) | 503 | -406 (-566; -315) | -44.65 (-52.93; -38.52) | 1005 | -617 (-902; -451) | -38.05 (-47.29; -31.00) |
| 01/07/2020 - 30/09/2020 | 423 | -171 (-265; -89) | -28.78 (-38.56; -17.43) | 885 | -240 (-413; -91) | -21.33 (-31.82; -9.33) |
| 01/10/2020 - 31/12/2020 | 369 | -262 (-425; -150) | -41.50 (-53.52; -28.91) | 862 | -378 (-692; -165) | -30.51 (-44.52; -16.08) |
| **Autoimmune Disorder** | | | | | | |
| All admissions from 15/02/2020 | 964 | -225 (-397; -115) | -18.93 (-29.18; -10.65) | 1177 | -270 (-466; -145) | -18.69 (-28.35; -10.99) |
| 15/02/2020 - 30/06/2020 (1st wave) | 455 | -42 (-135; 20) | -8.54 (-22.82; 4.58) | 476 | -131 (-248; -56) | -21.62 (-34.25; -10.59) |
| 01/07/2020 - 30/09/2020 | 243 | -73 (-150; -24) | -23.19 (-38.22; -9.03) | 342 | -59 (-141; -5) | -14.76 (-29.25; -1.37) |
| 01/10/2020 - 31/12/2020 | 266 | -109 (-202; -51) | -29.11 (-43.12; -16.00) | 359 | -80 (-185; -11) | -18.22 (-33.96; -2.98) |
| **Endocrine Disorder** | | | | | | |
| All admissions from 15/02/2020 | 5942 | -2401 (-3543; -1648) | -28.78 (-37.35; -21.72) | 10319 | -3003 (-4734; -1828) | -22.54 (-31.45; -15.05) |
| 15/02/2020 - 30/06/2020 (1st wave) | 2624 | -788 (-965; -666) | -23.10 (-26.88; -20.25) | 4142 | -1486 (-1780; -1266) | -26.41 (-30.06; -23.41) |
| 01/07/2020 - 30/09/2020 | 1599 | -668 (-1134; -295) | -29.48 (-41.50; -15.59) | 3019 | -558 (-1299; 36) | -15.60 (-30.08; 1.21) |
| 01/10/2020 - 31/12/2020 | 1719 | -945 (-1525; -504) | -35.47 (-47.00; -22.68) | 3158 | -958 (-1854; -283) | -23.28 (-36.99; -8.23) |

Abbreviations: HPA, Health Protection Agency; 95%CI, 95% confidence interval

TABLE 3.12c: Change in elective hospital admissions of patient with chronic conditions during the pandemic period, stratified by comorbidity

| | Bergamo HPA | | | Brescia HPA | | |
|---|---|---|---|---|---|---|
| | Total | Change (95%CI) | % Change (95%CI) | Total | Change (95%CI) | % Change (95%CI) |
| **Total** | | | | | | |
| All admissions from 15/02/2020 | 13305 | -9724 (-11660; -8294) | -42.23 (-46.71; -38.40) | 1589 | -11779 (-14151; -10046) | -42.57 (-47.11; -38.73) |
| 15/02/2020 - 30/06/2020 (1st wave) | 3883 | -6795 (-9545; -4600) | -63.64 (-71.08; -54.23) | 5284 | -7492 (-10839; -4838) | -58.64 (-67.23; -47.80) |
| 01/07/2020 - 30/09/2020 | 513 | -863 (-1358; -385) | -14.40 (-20.93; -6.99) | 5753 | -1367 (-1957; -802) | -19.20 (-25.38; -12.23) |
| 01/10/2020 - 31/12/2020 | 4292 | -2066 (-2822; -1472) | -32.49 (-39.66; -25.54) | 4853 | -2920 (-3839; -2197) | -37.56 (-44.17; -31.17) |
| **Condition** | | | | | | |
| **Chronic Kidney Disease** | | | | | | |
| All admissions from 15/02/2020 | 762 | -657 (-1071; -474) | -46.31 (-58.42; -38.34) | 969 | -751 (-1160; -544) | -43.68 (-54.49; -35.97) |
| 15/02/2020 - 30/06/2020 (1st wave) | 228 | -449 (-858; -247) | -66.34 (-79.01; -51.99) | 295 | -454 (-871; -246) | -60.62 (-74.69; -45.49) |
| 01/07/2020 - 30/09/2020 | 289 | -85 (-145; -41) | -22.64 (-33.48; -12.49) | 371 | -137 (-220; -74) | -26.98 (-37.21; -16.62) |
| 01/10/2020 - 31/12/2020 | 245 | -123 (-187; -82) | -33.46 (-43.29; -24.99) | 303 | -160 (-235; -110) | -34.61 (-43.67; -26.71) |
| **Neoplasm** | | | | | | |
| All admissions from 15/02/2020 | 4287 | -3100 (-4026; -2349) | -41.96 (-48.43; -35.40) | 5043 | -3208 (-4242; -2369) | -38.88 (-45.69; -31.96) |
| 15/02/2020 - 30/06/2020 (1st wave) | 1451 | -2030 (-2950; -1277) | -58.32 (-67.03; -46.80) | 1933 | -1984 (-3023; -1131) | -50.65 (-61.00; -36.91) |
| 01/07/2020 - 30/09/2020 | 1547 | -361 (-507; -235) | -18.92 (-24.67; -13.20) | 1672 | -415 (-573; -277) | -19.88 (-25.51; -14.23) |
| 01/10/2020 - 31/12/2020 | 1289 | -708 (-874; -560) | -35.46 (-40.41; -30.29) | 1438 | -809 (-990; -643) | -35.99 (-40.78; -30.88) |
| **Type 2 Diabetes Mellitus** | | | | | | |
| All admissions from 15/02/2020 | 2434 | -1884 (-2432; -1571) | -43.64 (-49.98; -39.23) | 3386 | -2752 (-3545; -2297) | -44.84 (-51.15; -40.42) |
| 15/02/2020 - 30/06/2020 (1st wave) | 712 | -1284 (-1987; -824) | -64.33 (-73.62; -53.64) | 114 | -1675 (-2686; -1011) | -59.51 (-70.20; -47.00) |
| 01/07/2020 - 30/09/2020 | 982 | -158 (-326; -24) | -13.83 (-24.90; -2.42) | 1246 | -362 (-598; -167) | -22.53 (-32.44; -11.82) |
| 01/10/2020 - 31/12/2020 | 740 | -443 (-606; -320) | -37.42 (-45.03; -30.18) | 1 | -715 (-946; -538) | -41.68 (-48.62; -34.99) |
| **Cardio-Cerebrovascular Disease** | | | | | | |
| All admissions from 15/02/2020 | 9398 | -6832 (-8590; -5832) | -42.10 (-47.75; -38.29) | 11556 | -8763 (-10879; -7515) | -43.13 (-48.49; -39.40) |
| 15/02/2020 - 30/06/2020 (1st wave) | 2642 | -4937 (-7414; -3211) | -65.14 (-73.73; -54.86) | 3719 | -5592 (-8555; -3435) | -60.06 (-69.70; -48.02) |
| 01/07/2020 - 30/09/2020 | 3671 | -569 (-946; -239) | -13.41 (-20.48; -6.12) | 4296 | -989 (-1462; -577) | -18.72 (-25.38; -11.85) |
| 01/10/2020 - 31/12/2020 | 3085 | -1326 (-2072; -719) | -30.07 (-40.18; -18.90) | 3541 | -2182 (-3134; -1448) | -38.12 (-46.95; -29.02) |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Respiratory Disease** | | | | | | |
| All admissions from 15/02/2020 | 1181 | -1126 (-1571; -878) | -48.80 (-57.08; -42.66) | 1567 | -1487 (-2085; -1152) | -48.68 (-57.10; -42.37) |
| 15/02/2020 - 30/06/2020 (1st wave) | 326 | -699 (-1167; -426) | -68.20 (-78.17; -56.63) | 511 | -876 (-1505; -496) | -63.17 (-74.66; -49.23) |
| 01/07/2020 - 30/09/2020 | 463 | -148 (-227; -81) | -24.18 (-32.86; -14.86) | 584 | -228 (-333; -144) | -28.06 (-36.33; -19.79) |
| 01/10/2020 - 31/12/2020 | 392 | -279 (-381; -199) | -41.57 (-49.31; -33.64) | 472 | -382 (-504; -290) | -44.76 (-51.62; -38.06) |
| **Digestive and Liver Disease** | | | | | | |
| All admissions from 15/02/2020 | 972 | -710 (-943; -568) | -42.22 (-49.24; -36.88) | 953 | -720 (-956; -571) | -43.04 (-50.07; -37.48) |
| 15/02/2020 - 30/06/2020 (1st wave) | 294 | -446 (-636; -316) | -60.26 (-68.37; -51.81) | 324 | -444 (-645; -309) | -57.83 (-66.58; -48.84) |
| 01/07/2020 - 30/09/2020 | 360 | -114 (-204; -40) | -24.05 (-36.16; -10.09) | 343 | -62 (-136; -3) | -15.34 (-28.33; -0.79) |
| 01/10/2020 - 31/12/2020 | 318 | -150 (-311; -61) | -32.10 (-49.44; -16.08) | 286 | -214 (-398; -118) | -42.76 (-58.16; -29.29) |
| **Neuropathy** | | | | | | |
| All admissions from 15/02/2020 | 735 | -725 (-3002; -496) | -49.67 (-80.33; -40.29) | 720 | -687 (-2677; -465) | -48.82 (-78.80; -39.24) |
| 15/02/2020 - 30/06/2020 (1st wave) | 184 | -472 (-2716; -222) | -71.94 (-93.66; -54.70) | 218 | -422 (-2411; -174) | -65.92 (-91.71; -44.40) |
| 01/07/2020 - 30/09/2020 | 337 | -63 (-134; -7) | -15.70 (-28.47; -1.98) | 303 | -88 (-153; -37) | -22.51 (-33.55; -10.77) |
| 01/10/2020 - 31/12/2020 | 214 | -191 (-271; -140) | -47.14 (-55.87; -39.58) | 199 | -177 (-249; -132) | -47.10 (-55.59; -39.95) |
| **Autoimmune Disorder** | | | | | | |
| All admissions from 15/02/2020 | 744 | -730 (-1316; -364) | -49.53 (-63.88; -32.82) | 710 | -453 (-918; -162) | -38.94 (-56.40; -18.54) |
| 15/02/2020 - 30/06/2020 (1st wave) | 220 | -447 (-886; -184) | -67.01 (-80.11; -45.52) | 243 | -272 (-610; -67) | -52.83 (-71.52; -21.63) |
| 01/07/2020 - 30/09/2020 | 286 | -80 (-158; -21) | -21.84 (-35.57; -6.94) | 257 | -40 (-104; 8) | -13.54 (-28.88; 3.09) |
| 01/10/2020 - 31/12/2020 | 238 | -203 (-303; -134) | -46.08 (-55.98; -35.95) | 210 | -140 (-219; -83) | -40.05 (-51.01; -28.32) |
| **Endocrine Disorder** | | | | | | |
| All admissions from 15/02/2020 | 4216 | -2960 (-3693; -2473) | -41.25 (-46.69; -36.97) | 547 | -3891 (-4830; -3286) | -41.56 (-46.89; -37.53) |
| 15/02/2020 - 30/06/2020 (1st wave) | 1198 | -2126 (-3052; -1441) | -63.96 (-71.81; -54.60) | 1769 | -2557 (-3728; -1677) | -59.11 (-67.82; -48.66) |
| 01/07/2020 - 30/09/2020 | 1663 | -219 (-438; -50) | -11.62 (-20.85; -2.90) | 2023 | -419 (-681; -215) | -17.15 (-25.17; -9.62) |
| 01/10/2020 - 31/12/2020 | 1355 | -616 (-866; -428) | -31.24 (-39.00; -24.01) | 1678 | -915 (-1237; -662) | -35.28 (-42.43; -28.28) |

Abbreviations: HPA, Health Protection Agency; 95%CI, 95% confidence interval

TABLE 3.13: Difference in daily counts of ED visits before (2017-2019) and during COVID-19 pandemic (2020-2021), stratified by sex and age

| | Bergamo HPA | | | Brescia HPA | | |
|---|---|---|---|---|---|---|
| | **Jan 2017 - Dec 2019** | **Jan 2020 - Jun 2021** | ***p*-value** | **Jan 2017 - Dec 2019** | **Jan 2020 - Jun 2021** | ***p*-value** |
| **Total** | | | | | | |
| Total | 1165401 | 357913 | | 1369296 | 437507 | |
| Daily events | | | | | | |
| Mean (±SD) | 1064.29 (80.05) | 692.29 (186.15) | <0.001 | 1250.5 (103.31) | 846.24 (204.8) | <0.001 |
| Median (IQR) | 1058 (1012 -1109) | 680 (578 -777) | | 1241 (1183 -1305) | 843 (717 -966) | |
| Min - max | 800 -1350 | 267 -1251 | | 939 -1634 | 345 -1606 | |
| **Sex** | | | | | | |
| **Female** | | | | | | |
| Total | 586357 | 177209 | | 689391 | 215867 | |
| Daily events | | | | | | |
| Mean (±SD) | 535.49 (42.04) | 342.76 (94.6) | <0.001 | 629.58 (53.88) | 417.54 (103.81) | <0.001 |
| Median (IQR) | 533 (509 -559) | 339 (288 -384) | | 626 (595 -658) | 413 (353 -472) | |
| Min - max | 417 -691 | 112 -630 | | 467 -857 | 176 -796 | |
| **Male** | | | | | | |
| Total | 579044 | 180704 | | 679905 | 221640 | |
| Daily events | | | | | | |
| Mean (±SD) | 528.81 (47.39) | 349.52 (95.34) | <0.001 | 620.92 (57.28) | 428.7 (104.18) | <0.001 |
| Median (IQR) | 528 (496 -556) | 346 (290 -395) | | 616 (584 -653) | 428 (362 -493) | |
| Min - max | 381 -684 | 127 -646 | | 435 -829 | 164 -810 | |
| **Age group** | | | | | | |
| **0-18 years** | | | | | | |
| Total | 256574 | 54166 | | 290035 | 64211 | |
| Daily events | | | | | | |
| Mean (±SD) | 234.31 (48.82) | 104.77 (65.07) | <0.001 | 264.87 (51.08) | 124.2 (66.14) | <0.001 |
| Median (IQR) | 230 (202 -263) | 92 (71 -119) | | 263 (232 -296) | 114 (86 -142) | |
| Min - max | 113 -468 | 12 -399 | | 141 -452 | 16 -435 | |
| **19-59 years** | | | | | | |
| Total | 555792 | 176091 | | 640805 | 211423 | |
| Daily events | | | | | | |
| Mean (±SD) | 507.57 (46.24) | 340.6 (87.61) | <0.001 | 585.21 (60.51) | 408.94 (97.26) | <0.001 |
| Median (IQR) | 504 (476 -535) | 343 (289 -392) | | 579 (543 -620) | 411 (352 -474) | |
| Min - max | 346 -694 | 108 -573 | | 403 -800 | 141 -752 | |

| | | | | | | |
|---|---|---|---|---|---|---|
| **60-69 years** | | | | | | |
| Total | 109858 | 39954 | | 126531 | 47061 | |
| Daily events | | | | | | |
| Mean (±SD) | 100.33 (13.41) | 77.28 (18.19) | <0.001 | 115.55 (15.74) | 91.03 (19.83) | <0.001 |
| Median (IQR) | 100 (91 -109) | 77 (65 -89) | | 115 (105 -126) | 92 (77 -104) | |
| Min - max | 56 -139 | 27 -140 | | 75 -177 | 28 -176 | |
| **70-79 years** | | | | | | |
| Total | 119289 | 42361 | | 146616 | 53091 | |
| Daily events | | | | | | |
| Mean (±SD) | 108.94 (14.18) | 81.94 (20.16) | <0.001 | 133.9 (18.79) | 102.69 (21.71) | <0.001 |
| Median (IQR) | 109 (99 -118) | 81 (67 -95) | | 133 (121 -146) | 103 (87 -117) | |
| Min - max | 64 -168 | 29 -143 | | 80 -203 | 33 -156 | |
| **80-89 years** | | | | | | |
| Total | 99731 | 36722 | | 129517 | 48229 | |
| Daily events | | | | | | |
| Mean (±SD) | 91.08 (13.02) | 71.03 (16.59) | <0.001 | 118.28 (16.6) | 93.29 (20.22) | <0.001 |
| Median (IQR) | 91 (82 -99) | 70 (61 -80) | | 117 (107 -129) | 92 (80 -106) | |
| Min - max | 56 -141 | 32 -127 | | 76 -182 | 39 -167 | |
| **90+ years** | | | | | | |
| Total | 24157 | 8619 | | 35792 | 13492 | |
| Daily events | | | | | | |
| Mean (±SD) | 22.06 (5.48) | 16.67 (6.26) | <0.001 | 32.69 (7.6) | 26.1 (8.16) | <0.001 |
| Median (IQR) | 22 (18 -25) | 16 (12 -20) | | 32 (27 -37) | 26 (21 -30) | |
| Min - max | 7 -44 | 4 -39 | | 16 -62 | 9 -59 | |

Abbreviations: ED, Emergency Department; HPA, Health Protection Agency; SD, standard deviation; IQR, interquartile range

TABLE 3.14: Change in ED visits during the pandemic period, stratified by sex and age

| | Bergamo HPA | | | Brescia HPA | | |
|---|---|---|---|---|---|---|
| | Total | Change (95%CI) | % Change (95%CI) | Total | Change (95%CI) | % Change (95%CI) |
| **Total** | | | | | | |
| All visits from 15/02/2020 | 308719 | -186315 (-194772; -179475) | -37.64 (-38.68; -36.76) | 383640 | -225138 (-234940; -216626) | -36.98 (-37.98; -36.09) |
| 15/02/2020 - 30/06/2020 (1st wave) | 81425 | -67495 (-69934; -65308) | -45.32 (-46.20; -44.51) | 99261 | -81460 (-84465; -78714) | -45.08 (-45.97; -44.23) |
| 01/07/2020 - 30/09/2020 | 71078 | -22838 (-24301; -21538) | -24.32 (-25.48; -23.26) | 88428 | -27370 (-29121; -25625) | -23.64 (-24.77; -22.47) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 156216 | -95982 (-101105; -91798) | -38.06 (-39.29; -37.01) | 195951 | -116308 (-122217; -111287) | -37.25 (-38.41; -36.22) |
| **Sex** | | | | | | |
| **Female** | | | | | | |
| All visits from 15/02/2020 | 152477 | -95653 (-99323; -92494) | -38.55 (-39.45; -37.76) | 188593 | -115778 (-120254; -111940) | -38.04 (-38.94; -37.25) |
| 15/02/2020 - 30/06/2020 (1st wave) | 39383 | -34575 (-36019; -33279) | -46.75 (-47.77; -45.80) | 48155 | -41734 (-43473; -40255) | -46.43 (-47.45; -45.53) |
| 01/07/2020 - 30/09/2020 | 34785 | -12021 (-12833; -11300) | -25.68 (-26.95; -24.52) | 43175 | -14360 (-15331; -13455) | -24.96 (-26.20; -23.76) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 78309 | -49056 (-50936; -47368) | -38.52 (-39.41; -37.69) | 97263 | -59684 (-62041; -57720) | -38.03 (-38.95; -37.24) |
| **Male** | | | | | | |
| All visits from 15/02/2020 | 156242 | -90666 (-95630; -86626) | -36.72 (-37.97; -35.67) | 195047 | -109344 (-115487; -104597) | -35.92 (-37.19; -34.91) |
| 15/02/2020 - 30/06/2020 (1st wave) | 42042 | -32914 (-34290; -31658) | -43.91 (-44.92; -42.96) | 51106 | -39719 (-41535; -38255) | -43.73 (-44.83; -42.81) |
| 01/07/2020 - 30/09/2020 | 36293 | -10820 (-11599; -10060) | -22.97 (-24.22; -21.70) | 45253 | -13016 (-14027; -12127) | -22.34 (-23.66; -21.13) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 77907 | -46931 (-50189; -44232) | -37.59 (-39.18; -36.21) | 98688 | -56608 (-60598; -53448) | -36.45 (-38.04; -35.13) |
| **Age groups** | | | | | | |
| **0-18 years** | | | | | | |
| All visits from 15/02/2020 | 42340 | -61033 (-65543; -57416) | -59.04 (-60.75; -57.56) | 51883 | -73966 (-79379; -69584) | -58.77 (-60.47; -57.29) |
| 15/02/2020 - 30/06/2020 (1st wave) | 9594 | -22883 (-27542; -18864) | -70.46 (-74.17; -66.29) | 12118 | -26973 (-32599; -22217) | -69.00 (-72.90; -64.71) |
| 01/07/2020 - 30/09/2020 | 10545 | -6062 (-6490; -5670) | -36.50 (-38.10; -34.97) | 12614 | -7304 (-7806; -6791) | -36.67 (-38.23; -34.99) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 22201 | -32088 (-33321; -30910) | -59.11 (-60.01; -58.20) | 27151 | -39689 (-41139; -38343) | -59.38 (-60.24; -58.54) |
| **19-59 years** | | | | | | |
| All visits from 15/02/2020 | 153852 | -79747 (-82068; -77285) | -34.14 (-34.79; -33.44) | 187418 | -96521 (-99505; -93652) | -33.99 (-34.68; -33.32) |
| 15/02/2020 - 30/06/2020 (1st wave) | 39171 | -30964 (-32552; -29264) | -44.15 (-45.39; -42.76) | 47656 | -36481 (-38601; -34481) | -43.36 (-44.75; -41.98) |
| 01/07/2020 - 30/09/2020 | 36456 | -10455 (-11045; -9822) | -22.29 (-23.25; -21.22) | 44576 | -12496 (-13325; -11701) | -21.90 (-23.01; -20.79) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 78225 | -38327 (-39790; -36925) | -32.88 (-33.72; -32.07) | 95186 | -47545 (-49467; -45842) | -33.31 (-34.20; -32.51) |
| **60-69 years** | | | | | | |
| All visits from 15/02/2020 | 35409 | -12233 (-13579; -11096) | -25.68 (-27.72; -23.86) | 42311 | -13692 (-15250; -12341) | -24.45 (-26.49; -22.58) |
| 15/02/2020 - 30/06/2020 (1st wave) | 10140 | -3904 (-4209; -3617) | -27.80 (-29.33; -26.29) | 11649 | -4585 (-4933; -4241) | -28.24 (-29.75; -26.69) |
| 01/07/2020 - 30/09/2020 | 7772 | -1796 (-2044; -1586) | -18.77 (-20.83; -16.95) | 9434 | -2077 (-2366; -1819) | -18.05 (-20.05; -16.17) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 17497 | -6533 (-7532; -5654) | -27.19 (-30.09; -24.42) | 21228 | -7030 (-8187; -6022) | -24.88 (-27.83; -22.10) |

| | | | | | | |
|---|---|---|---|---|---|---|
| **70-79 years** | | | | | | |
| All visits from 15/02/2020 | 37497 | -14724 (-16643; -13197) | -28.20 (-30.74; -26.03) | 47506 | -17293 (-19663; -15416) | -26.69 (-29.27; -24.50) |
| 15/02/2020 - 30/06/2020 (1st wave) | 11105 | -4049 (-4561; -3616) | -26.72 (-29.12; -24.56) | 13143 | -5515 (-6153; -4947) | -29.56 (-31.89; -27.35) |
| 01/07/2020 - 30/09/2020 | 8140 | -2038 (-2277; -1816) | -20.02 (-21.86; -18.24) | 10298 | -2488 (-2802; -2208) | -19.46 (-21.39; -17.66) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 18252 | -8636 (-10584; -6917) | -32.12 (-36.70; -27.48) | 24065 | -9289 (-11793; -7194) | -27.85 (-32.89; -23.01) |
| **80-89 years** | | | | | | |
| All visits from 15/02/2020 | 32256 | -14030 (-15757; -12835) | -30.31 (-32.82; -28.47) | 42864 | -17198 (-19272; -15634) | -28.63 (-31.02; -26.73) |
| 15/02/2020 - 30/06/2020 (1st wave) | 9417 | -4015 (-4688; -3456) | -29.89 (-33.24; -26.85) | 11537 | -5713 (-6607; -4990) | -33.12 (-36.42; -30.19) |
| 01/07/2020 - 30/09/2020 | 6704 | -2019 (-2392; -1691) | -23.14 (-26.30; -20.14) | 9092 | -2385 (-2838; -1962) | -20.78 (-23.79; -17.75) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 16135 | -7995 (-9791; -6597) | -33.13 (-37.76; -29.02) | 22235 | -9100 (-11317; -7263) | -29.04 (-33.73; -24.62) |
| **90+ years** | | | | | | |
| All visits from 15/02/2020 | 7365 | -4278 (-5060; -3729) | -36.74 (-40.73; -33.61) | 11658 | -6040 (-7186; -5234) | -34.13 (-38.13; -30.99) |
| 15/02/2020 - 30/06/2020 (1st wave) | 1998 | -1431 (-1727; -1231) | -41.73 (-46.36; -38.12) | 3158 | -2031 (-2461; -1733) | -39.14 (-43.80; -35.44) |
| 01/07/2020 - 30/09/2020 | 1461 | -612 (-878; -416) | -29.51 (-37.54; -22.18) | 2414 | -699 (-1093; -412) | -22.45 (-31.17; -14.59) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 3906 | -2236 (-2522; -1998) | -36.40 (-39.24; -33.84) | 6086 | -3311 (-3731; -2967) | -35.23 (-38.00; -32.77) |

Abbreviations: ED, Emergency Department; HPA, Health Protection Agency; 95%CI, 95% confidence interval

TABLE 3.15: Difference in daily counts of ED visits before (2017-2019) and during COVID-19 pandemic (2020-2021), stratified by triage code

| | Bergamo HPA | | | Brescia HPA | | |
|---|---|---|---|---|---|---|
| **Triage code** | **Jan 2017 - Dec 2019** | **Jan 2020 - Jun 2021** | ***p*-value** | **Jan 2017 - Dec 2019** | **Jan 2020 - Jun 2021** | ***p*-value** |
| **White** | 47683 | 13476 | | 86843 | 25539 | |
| Total | | | | | | |
| Daily events | | | | | | |
| Mean (±SD) | 43.55 (10.72) | 26.07 (12.92) | <0.001 | 79.31 (19.23) | 49.4 (19.56) | <0.001 |
| Median (IQR) | 43 (36 -50) | 25 (18 -33) | | 78 (66 -91) | 48 (37 -62) | |
| Min - max | 16 -83 | 0 -150 | | 27 -168 | 1 -111 | |
| **Green** | | | | | | |
| Total | 839553 | 243408 | | 988258 | 298325 | |
| Daily events | | | | | | |
| Mean (±SD) | 766.72 (63.73) | 470.81 (154.85) | <0.001 | 902.52 (79.9) | 577.03 (164.31) | <0.001 |
| Median (IQR) | 762 (724 -808) | 464 (381 -542) | | 892 (852 -947) | 567 (475 -665) | |
| Min - max | 555 -963 | 110 -932 | | 653 -1199 | 167 -1177 | |
| **Yellow** | | | | | | |
| Total | 235145 | 84017 | | 274092 | 102343 | |
| Daily events | | | | | | |
| Mean (±SD) | 214.74 (25.67) | 162.51 (34.47) | <0.001 | 250.31 (29.1) | 197.96 (35.07) | <0.001 |
| Median (IQR) | 214 (198 -231) | 159 (141 -178) | | 250 (231 -269) | 198 (174 -221) | |
| Min - max | 138 -296 | 74 -290 | | 164 -361 | 80 -315 | |
| **Red** | | | | | | |
| Total | 16640 | 9988 | | 19915 | 9889 | |
| Daily events | | | | | | |
| Mean (±SD) | 15.2 (5.08) | 19.32 (12.94) | <0.001 | 18.19 (4.61) | 19.13 (8.83) | 0.450 |
| Median (IQR) | 15 (11 -19) | 17 (14 -21) | | 18 (15 -21) | 18 (14 -21) | |
| Min - max | 2 -35 | 4 -102 | | 6 -34 | 6 -83 | |
| **Black** | | | | | | |
| Total | 264 | 350 | | 34 | 12 | |

| | | | | | | |
|---|---|---|---|---|---|---|
| Daily events | | | | | | |
| Mean (±SD) | 0.24 (0.5) | 0.68 (1.98) | 0.017 | 0.03 (0.18) | 0.02 (0.15) | 0.430 |
| Median (IQR) | 0 (0-0) | 0 (0-1) | | 0 (0-0) | 0 (0-0) | |
| Min - max | 0 -3 | 0 -15 | | 0 -2 | 0 -1 | |
| **Other** | | | | | | |
| Total | 26101 | 6667 | | 154 | 1399 | |
| Daily events | | | | | | |
| Mean (±SD) | 23.84 (12.68) | 12.90 (6.39) | <0.001 | 0.14 (0.37) | 2.71 (2.4) | <0.001 |
| Median (IQR) | 22 (18 -27) | 13 (9 -17) | | 0 (0-0) | 2 (1 -4) | |
| Min - max | 6 -133 | 0 -39 | | 0 -2 | 0 -11 | |

Abbreviations: ED, Emergency Department; HPA, Health Protection Agency; SD, standard deviation; IQR, interquartile range

TABLE 3.16: Change in ED visits during the pandemic period, stratified by triage code

| | Bergamo HPA | | | Brescia HPA | | |
|---|---|---|---|---|---|---|
| | **Total** | **Change (95%CI)** | **% Change (95%CI)** | **Total** | **Change (95%CI)** | **% Change (95%CI)** |
| **Triage code** | | | | | | |
| **White** | | | | | | |
| All visits from 15/02/2020 | 11779 | -5095 (-6803; -3712) | -30.20 (-36.61; -23.96) | 22548 | -7781 (-10743; -5370) | -25.65 (-32.27; -19.23) |
| 15/02/2020 - 30/06/2020 (1st wave) | 2642 | -2302 (-2674; -2001) | -46.56 (-50.30; -43.09) | 5098 | -4167 (-4891; -3562) | -44.98 (-48.96; -41.13) |
| 01/07/2020 - 30/09/2020 | 3575 | -326 (-500; -182) | -8.36 (-12.26; -4.84) | 6135 | -645 (-937; -390) | -9.52 (-13.25; -5.97) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 5562 | -2467 (-3864; -1364) | -30.73 (-40.99; -19.70) | 11315 | -2968 (-5384; -1023) | -20.78 (-32.24; -8.29) |
| **Green** | | | | | | |
| All visits from 15/02/2020 | 207407 | -151978 (-161198; -143465) | -42.29 (-43.73; -40.89) | 259332 | -184472 (-196028; -174683) | -41.57 (-43.05; -40.25) |
| 15/02/2020 - 30/06/2020 (1st wave) | 51475 | -57022 (-66709; -48300) | -52.56 (-56.44; -48.41) | 66132 | -65910 (-78154; -55168) | -49.92 (-54.17; -45.48) |
| 01/07/2020 - 30/09/2020 | 49664 | -18225 (-19177; -17245) | -26.85 (-27.86; -25.77) | 61942 | -22221 (-23418; -21065) | -26.40 (-27.43; -25.38) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 106268 | -76731 (-79080; -74502) | -41.93 (-42.67; -41.21) | 131258 | -96341 (-99354; -93614) | -42.33 (-43.08; -41.63) |
| **Yellow** | | | | | | |
| All visits from 15/02/2020 | 74357 | -23977 (-29004; -19747) | -24.38 (-28.06; -20.98) | 91301 | -35594 (-41951; -30051) | -28.05 (-31.48; -24.76) |
| 15/02/2020 - 30/06/2020 (1st wave) | 22133 | -7225 (-10204; -4841) | -24.61 (-31.55; -17.95) | 24960 | -11873 (-15810; -8811) | -32.23 (-38.78; -26.09) |
| 01/07/2020 - 30/09/2020 | 14982 | -3611 (-4071; -3148) | -19.42 (-21.37; -17.36) | 18495 | -4819 (-5388; -4232) | -20.67 (-22.56; -18.62) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 37242 | -13141 (-14973; -11486) | -26.08 (-28.68; -23.57) | 47846 | -18902 (-21266; -16645) | -28.32 (-30.77; -25.81) |
| **Red** | | | | | | |
| All visits from 15/02/2020 | 9058 | -1983 (-7998; 1166) | -17.96 (-46.89; 14.77) | 9087 | 1033 (-3119; 3246) | 12.83 (-25.56; 55.58) |
| 15/02/2020 - 30/06/2020 (1st wave) | 3684 | 699 (342; 932) | 23.43 (10.24; 33.85) | 2897 | 530 (243; 717) | 22.37 (9.16; 32.89) |
| 01/07/2020 - 30/09/2020 | 1363 | -456 (-1148; 12) | -25.07 (-45.72; 0.88) | 1440 | 17 (-539; 384) | 1.17 (-27.25; 36.40) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 4011 | -2226 (-7292; 301) | -35.69 (-64.51; 8.11) | 4750 | 487 (-2896; 2203) | 11.42 (-37.87; 86.51) |

Abbreviations: ED, Emergency Department; HPA, Health Protection Agency; 95%CI, 95% confidence interval

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TABLE 3.17: Difference in daily counts of ED visits before (2017-2019) and during COVID-19 pandemic (2020-2021), stratified by main diagnosis

| | Bergamo HPA | | | ATS Brescia HPA | | |
|---|---|---|---|---|---|---|
| Diagnostic Code Description (ICD-9-CM) | **Jan 2017 - Dec 2019** | **Jan 2020 - Jun 2021** | ***p*-value** | **Jan 2017 - Dec 2019** | **Jan 2020 - Jun 2021** | ***p*-value** |
| **Infection and Parasitic Diseases (001-139.9)** | | | | | | |
| Total | 27230 | 5997 | | 58944 | 13901 | |
| Daily events | | | | | | |
| Mean (±SD) | 24.87 (7.63) | 11.6 (6.15) | <0.001 | 53.83 (16.84) | 26.89 (12.09) | <0.001 |
| Median (IQR) | 24 (20 -29) | 10 (8 -14) | | 50 (42 -62) | 24 (19 -32) | |
| Min - max | 7 -58 | 1 -56 | | 21 -147 | 5 -96 | |
| **Neoplasms (140-239.9)** | | | | | | |
| Total | 3307 | 1431 | | 2946 | 1360 | |
| Daily events | | | | | | |
| Mean (±SD) | 3.02 (1.88) | 2.77 (1.89) | 0.005 | 2.69 (1.78) | 2.63 (1.81) | 0.416 |
| Median (IQR) | 3 (2 -4) | 3 (1 -4) | | 2 (1 -4) | 2 (1 -4) | |
| Min - max | 0 -10 | 0 -9 | | 0 -12 | 0 -11 | |
| **Endocrine. Nutritional and Metabolic Diseases and Immunity Disorders (240-279.9)** | | | | | | |
| Total | 5752 | 1900 | | 5753 | 2021 | 5752 |
| Daily events | | | | | | |
| Mean (±SD) | 5.25 (2.42) | 3.68 (2.07) | <0.001 | 5.25 (2.39) | 3.91 (2.21) | <0.001 |
| Median (IQR) | 5 (3 -7) | 3 (2 -5) | | 5 (3 -7) | 4 (2 -5) | |
| Min - max | 0 -17 | 0 -12 | | 0 -16 | 0 -11 | |
| **Diseases of Blood and Blood Forming Organs (280-289.9)** | | | | | | |
| Total | 6022 | 2589 | | 7026 | 2974 | |
| Daily events | | | | | | |
| Mean (±SD) | 5.5 (2.84) | 5.01 (2.92) | 0.001 | 6.42 (3.18) | 5.75 (3.37) | <0.001 |
| Median (IQR) | 5 (3 -7) | 5 (3 -7) | | 6 (4 -8) | 5 (3 -8) | |
| Min - max | 0 -16 | 0 -14 | | 0 -18 | 0 -17 | |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Mental Disorders (290-319.9)** | | | | | | |
| Total | 34098 | 13874 | | 29018 | 10726 | |
| Daily events | | | | | | |
| Mean (±SD) | 31.14 (7.62) | 26.84 (10.48) | <0.001 | 26.5 (7.85) | 20.75 (8.27) | <0.001 |
| Median (IQR) | 31 (26 -36) | 26 (21 -33) | | 26 (21 -31) | 20 (15 -25) | |
| Min - max | 11 -67 | 2 -68 | | 7 -70 | 1 -50 | |
| **Diseases of Nervous System and Sense Organs (320-389.9)** | | | | | | |
| Total | 75558 | 19058 | | 144492 | 51430 | |
| Daily events | | | | | | |
| Mean (±SD) | 69 (12.82) | 36.86 (15.63) | <0.001 | 131.96 (22.08) | 99.48 (33.6) | <0.001 |
| Median (IQR) | 68 (60 -77) | 37 (27 -47) | | 129 (116 -146) | 101 (81 -124) | |
| Min - max | 37 -122 | 2 -91 | | 72 -209 | 6 -194 | |
| **Diseases of the Circulatory System (390-459.9)** | | | | | | |
| Total | 50787 | 18824 | | 62820 | 22391 | |
| Daily events | | | | | | |
| Mean (±SD) | 46.38 (8.77) | 36.41 (10.12) | <0.001 | 57.37 (11.55) | 43.31 (12.42) | <0.001 |
| Median (IQR) | 46 (40 -52) | 36 (30 -44) | | 57 (49 -65) | 43 (35 -51) | |
| Min - max | 16 -76 | 10 -66 | | 29 -100 | 9 -88 | |
| **Diseases of the Respiratory System (460-519.9)** | | | | | | |
| Total | 74027 | 27631 | | 86459 | 31789 | 74027 |
| Daily events | | | | | | |
| Mean (±SD) | 67.6 (30.39) | 53.44 (58.23) | <0.001 | 78.96 (34.88) | 61.49 (49.21) | <0.001 |
| Median (IQR) | 60 (47 -81) | 32 (25 -47) | | 71 (55 -94) | 44 (32 -74) | |
| Min - max | 21 -261 | 12 -356 | | 22 -249 | 11 -343 | |
| **Diseases of the Digestive System (520-579.9)** | | | | | | |
| Total | 48876 | 15789 | | 45128 | 15197 | |
| Daily events | | | | | | |
| Mean (±SD) | 44.64 (8.66) | 30.54 (10.09) | <0.001 | 41.21 (7.14) | 29.39 (9.24) | <0.001 |

| | | | | | | |
|---|---|---|---|---|---|---|
| Median (IQR) | 44 (39 -50) | 31 (24 -37) | | 41 (36 -46) | 29 (23 -35) | |
| Min - max | 23 -79 | 4 -61 | | 22 -62 | 4 -57 | |
| **Diseases of the Genitourinary System (580-629.9)** | | | | | | |
| Total | 37898 | 11595 | | 41032 | 12774 | |
| Daily events | | | | | | |
| Mean (±SD) | 34.61 (6.58) | 22.43 (8) | <0.001 | 37.47 (6.81) | 24.71 (8.13) | <0.001 |
| Median (IQR) | 34 (30 -39) | 22 (18 -27) | | 37 (33 -42) | 25 (20 -30) | |
| Min - max | 13 -55 | 2 -43 | | 20 -65 | 2 -51 | |
| **Complications of Pregnancy, Childbirth and the Puerperium (630-677.9)** | | | | | | |
| Total | 36042 | 14133 | | 46403 | 16999 | |
| Daily events | | | | | | |
| Mean (±SD) | 32.92 (6.71) | 27.34 (6.5) | <0.001 | 42.38 (7.18) | 32.88 (6.98) | <0.001 |
| Median (IQR) | 33 (28 -37) | 27 (23 -32) | | 42 (37 -47) | 32 (28 -38) | |
| Min - max | 13 -55 | 9 -45 | | 18 -64 | 12 -56 | |
| **Diseases of the Skin and Subcutaneous Tissue (680-709.9)** | | | | | | |
| Total | 20216 | 4420 | | 27791 | 6596 | |
| Daily events | | | | | | |
| Mean (±SD) | 18.46 (4.91) | 8.55 (4.77) | <0.001 | 25.38 (6.96) | 12.76 (6.55) | <0.001 |
| Median (IQR) | 18 (15 -21) | 8 (5 -11) | | 25 (20 -30) | 12 (8 -17) | |
| Min - max | 6 -37 | 0 -26 | | 8 -54 | 0 -33 | |
| **Diseases of the Musculoskeletal System and Connective Tissue (710-739.9)** | | | | | | |
| Total | 69184 | 18668 | | 78815 | 21166 | |
| Daily events | | | | | | |
| Mean (±SD) | 63.18 (10.8) | 36.11 (15.83) | <0.001 | 71.98 (12.47) | 40.94 (18.83) | <0.001 |
| Median (IQR) | 62 (56 -70) | 36 (27 -46) | | 71 (63 -79) | 39 (29 -52) | |
| Min - max | 26 -110 | 0 -82 | | 33 -120 | 2 -118 | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Congenital Anomalies (740-759.9)** | | | | | | | |
| Total | 90459 | 24865 | | 11191 | 3651 | 90459 | |
| Daily events | | | | | | | |
| Mean (±SD) | 82.61 (21.06) | 48.09 (24.65) | <0.001 | 10.22 (5.62) | 7.06 (4.39) | | <0.001 |
| Median (IQR) | 84 (70 -97) | 42 (30 -65) | | 9 (6 -13) | 6 (4 -9) | | |
| Min - max | 20 -139 | 4 -136 | | 0 -42 | 0 -36 | | |
| **Certain Conditions Originating in the Perinatal Period (760-779.9)** | | | | | | | |
| Total | 997 | 368 | | 1271 | 337 | 997 | |
| Daily events | | | | | | | |
| Mean (±SD) | 0.91 (0.95) | 0.71 (0.91) | <0.001 | 1.16 (1.11) | 0.65 (0.8) | | |
| Median (IQR) | 1 (0 -1) | 0 (0-1) | | 1 (0 -2) | 0 (0-1) | | |
| Min - max | 0 -5 | 0 -5 | | 0 -7 | 0 -4 | | |
| **Symptoms, Signs and Ill-defined Conditions (780-799.9)** | | | | | | | |
| Total | 199953 | 59488 | | 234973 | 74838 | | 199953 |
| Daily events | | | | | | | |
| Mean (±SD) | 182.61 (21.35) | 115.06 (35.33) | <0.001 | 214.59 (25.16) | 144.75 (38.77) | | <0.001 |
| Median (IQR) | 182 (168 -196) | 113 (97 -129) | | 213 (198 -229) | 141 (122 -164) | | |
| Min - max | 113 -280 | 17 -246 | | 147 -305 | 43 -280 | | |
| **Injury and Poisoning (800-999.9)** | | | | | | | |
| Total | 142329 | 44464 | | 154605 | 45017 | | |
| Daily events | | | | | | | |
| Mean (±SD) | 129.98 (21.43) | 86 (30.2) | <0.001 | 141.19 (22.54) | 87.07 (30.23) | | <0.001 |
| Median (IQR) | 128 (116 -145) | 86 (69 -107) | | 140 (125 -155) | 87 (66 -109) | | |
| Min - max | 61 -245 | 9 -159 | | 76 -231 | 14 -169 | | |

Abbreviations: ED, Emergency Department; HPA, Health Protection Agency; ICD-9-CM, International Statistical Classification of Diseases, 9th revision, Clinical Modification; SD, standard deviation; IQR, interquartile range

TABLE 3.18: Change in ED visits during the pandemic period, stratified by main diagnosis

| Diagnostic Code Description (ICD-9-CM) | Bergamo HPA Total | Bergamo HPA Change (95%CI) | Bergamo HPA % Change (95%CI) | Brescia HPA Total | Brescia HPA Change (95%CI) | Brescia HPA % Change (95%CI) |
|---|---|---|---|---|---|---|
| **Infection and Parasitic Diseases (001-139.9)** | | | | | | |
| All visits from 15/02/2020 | 4917 | -5152 (-6986; -3777) | -51.17 (-58.69; -43.45) | 11928 | -9342 (-13085; -6519) | -43.92 (-52.31; -35.34) |
| 15/02/2020 - 30/06/2020 (1st wave) | 1209 | -1972 (-2577; -1530) | -61.99 (-68.07; -55.85) | 2762 | -3746 (-4957; -2830) | -57.56 (-64.22; -50.61) |
| 01/07/2020 - 30/09/2020 | 1077 | -592 (-761; -461) | -35.48 (-41.39; -29.98) | 2191 | -1430 (-1785; -1123) | -39.49 (-44.89; -33.88) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 2631 | -2588 (-3948; -1512) | -49.59 (-60.01; -36.50) | 6975 | -4166 (-6925; -1954) | -37.39 (-49.82; -21.88) |
| **Mental Disorders (290-319.9)** | | | | | | |
| All visits from 15/02/2020 | 12500 | -1609 (-9980; 3330) | -11.41 (-44.40; 36.31) | 9418 | -7419 (-17927; -1349) | -44.06 (-65.56; -12.53) |
| 15/02/2020 - 30/06/2020 (1st wave) | 2650 | -1510 (-2562; -660) | -36.30 (-49.15; -19.93) | 2446 | -2257 (-3553; -1283) | -47.99 (-59.22; -34.41) |
| 01/07/2020 - 30/09/2020 | 2562 | -359 (-1097; 238) | -12.30 (-29.99; 10.22) | 2237 | -924 (-1711; -291) | -29.24 (-43.34; -11.52) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 7288 | 260 (-6350; 3728) | 3.70 (-46.56; 104.70) | 4735 | -4238 (-12833; 245) | -47.23 (-73.05; 5.45) |
| **Diseases of Nervous System and Sense Organs (320-389.9)** | | | | | | |
| All visits from 15/02/2020 | 16263 | -15761 (-27438; -6973) | -49.22 (-62.79; -30.01) | 46976 | -22348 (-47376; -3369) | -32.24 (-50.21; -6.69) |
| 15/02/2020 - 30/06/2020 (1st wave) | 3459 | -6197 (-11108; -2926) | -64.18 (-76.26; -45.82) | 10277 | -9859 (-19997; -2969) | -48.96 (-66.05; -22.42) |
| 01/07/2020 - 30/09/2020 | 4255 | -1898 (-3449; -585) | -30.85 (-44.77; -12.08) | 11472 | -1846 (-5146; 894) | -13.86 (-30.97; 8.46) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 8549 | -7666 (-13000; -3486) | -47.28 (-60.33; -28.97) | 25227 | -10643 (-22445; -1519) | -29.67 (-47.08; -5.68) |
| **Diseases of the Circulatory System (390-459.9)** | | | | | | |
| All visits from 15/02/2020 | 16669 | -5990 (-7021; -5034) | -26.44 (-29.64; -23.19) | 19813 | -6275 (-7460; -5203) | -24.05 (-27.35; -20.80) |
| 15/02/2020 - 30/06/2020 (1st wave) | 4093 | -2455 (-2760; -2207) | -37.49 (-40.27; -35.03) | 4874 | -2759 (-3134; -2460) | -36.14 (-39.14; -33.54) |
| 01/07/2020 - 30/09/2020 | 3227 | -834 (-1208; -470) | -20.53 (-27.24; -12.72) | 3952 | -659 (-1071; -250) | -14.30 (-21.33; -5.94) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 9349 | -2702 (-3173; -2277) | -22.42 (-25.34; -19.58) | 10987 | -2858 (-3385; -2375) | -20.64 (-23.55; -17.77) |
| **Diseases of the Respiratory System (460-519.9)** | | | | | | |
| All visits from 15/02/2020 | 22782 | -8766 (-12679; -7302) | -27.79 (-35.76; -24.27) | 26804 | -12393 (-17405; -10434) | -31.62 (-39.37; -28.02) |
| 15/02/2020 - 30/06/2020 (1st wave) | 12490 | 3394 (678; 5374) | 37.32 (5.74; 75.52) | 11279 | -49 (-3451; 2375) | -0.43 (-23.43; 26.67) |
| 01/07/2020 - 30/09/2020 | 2278 | -1806 (-2043; -1578) | -44.22 (-47.29; -40.93) | 2780 | -2215 (-2500; -1954) | -44.34 (-47.35; -41.28) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 8014 | -10354 (-16214; -6636) | -56.37 (-66.92; -45.30) | 12745 | -10130 (-17420; -5434) | -44.28 (-57.75; -29.89) |
| **Diseases of the Digestive System (520-579.9)** | | | | | | |
| All visits from 15/02/2020 | 13768 | -7689 (-9594; -6152) | -35.84 (-41.07; -30.88) | 13304 | -6161 (-7833; -4703) | -31.65 (-37.06; -26.12) |
| 15/02/2020 - 30/06/2020 (1st wave) | 3344 | -3027 (-4173; -2134) | -47.51 (-55.52; -38.96) | 3351 | -2332 (-3278; -1443) | -41.03 (-49.45; -30.10) |
| 01/07/2020 - 30/09/2020 | 3094 | -1091 (-1792; -543) | -26.07 (-36.68; -14.94) | 3179 | -559 (-1146; -36) | -14.96 (-26.50; -1.13) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 7330 | -3571 (-3934; -3256) | -32.76 (-34.92; -30.76) | 6774 | -3270 (-3612; -2966) | -32.56 (-34.78; -30.45) |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Diseases of the Genitourinary System (580-629.9)** | | | | | | |
| All visits from 15/02/2020 | 10135 | -5087 (-6252; -4283) | -33.42 (-38.15; -29.71) | 11257 | -6853 (-8278; -5862) | -37.84 (-42.38; -34.24) |
| 15/02/2020 - 30/06/2020 (1st wave) | 2269 | -2204 (-2463; -1975) | -49.28 (-52.05; -46.53) | 2735 | -2584 (-2891; -2322) | -48.58 (-51.39; -45.92) |
| 01/07/2020 - 30/09/2020 | 2385 | -793 (-922; -671) | -24.95 (-27.88; -21.97) | 2779 | -874 (-1021; -738) | -23.92 (-26.87; -20.99) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 5481 | -2090 (-3433; -1067) | -27.60 (-38.51; -16.29) | 5743 | -3395 (-5014; -2184) | -37.15 (-46.61; -27.55) |
| **Complications of Pregnancy, Childbirth and the Puerperium (630-677.9)** | | | | | | |
| All visits from 15/02/2020 | 12809 | -1335 (-2300; -491) | -9.44 (-15.22; -3.69) | 15450 | -2564 (-3760; -1464) | -14.23 (-19.57; -8.65) |
| 15/02/2020 - 30/06/2020 (1st wave) | 3371 | -825 (-985; -672) | -19.67 (-22.62; -16.62) | 4175 | -1107 (-1319; -919) | -20.95 (-24.01; -18.03) |
| 01/07/2020 - 30/09/2020 | 2734 | -41 (-188; 96) | -1.48 (-6.44; 3.63) | 3383 | -175 (-362; 6) | -4.93 (-9.66; 0.18) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 6704 | -469 (-1170; 173) | -6.54 (-14.86; 2.65) | 7892 | -1282 (-2187; -449) | -13.98 (-21.70; -5.39) |
| **Diseases of the Musculoskeletal System and Connective Tissue (710-739.9)** | | | | | | |
| All visits from 15/02/2020 | 15822 | -14092 (-15611; -13208) | -47.11 (-49.66; -45.50) | 17932 | -17496 (-19379; -16435) | -49.39 (-51.94; -47.82) |
| 15/02/2020 - 30/06/2020 (1st wave) | 3369 | -5481 (-6346; -4787) | -61.93 (-65.32; -58.69) | 4165 | -6385 (-7512; -5522) | -60.52 (-64.33; -57.00) |
| 01/07/2020 - 30/09/2020 | 3978 | -2008 (-2325; -1705) | -33.54 (-36.89; -30.00) | 4719 | -2105 (-2480; -1753) | -30.84 (-34.45; -27.08) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 8475 | -6603 (-8946; -4993) | -43.79 (-51.35; -37.08) | 9048 | -9007 (-11854; -7016) | -49.89 (-56.71; -43.67) |
| **Congenital Anomalies (740-759.9)** | | | | | | |
| All visits from 15/02/2020 | 21328 | -16553 (-28852; -12167) | -43.70 (-57.50; -36.32) | 3260 | -1628 (-3037; -1161) | -33.31 (-48.23; -26.26) |
| 15/02/2020 - 30/06/2020 (1st wave) | 6335 | -5408 (-7074; -4341) | -46.05 (-52.75; -40.66) | 674 | -743 (-958; -607) | -52.43 (-58.71; -47.38) |
| 01/07/2020 - 30/09/2020 | 6545 | -240 (-2801; 1446) | -3.53 (-29.97; 28.36) | 750 | -307 (-704; -48) | -29.02 (-48.42; -6.04) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 8448 | -10905 (-25157; -2910) | -56.35 (-74.86; -25.62) | 1836 | -578 (-2320; 395) | -23.96 (-55.82; 27.41) |
| **Symptoms, Signs and Ill-defined Conditions (780-799.9)** | | | | | | |
| All visits from 15/02/2020 | 50916 | -32346 (-35126; -30455) | -38.85 (-40.82; -37.43) | 64750 | -39863 (-43209; -37518) | -38.11 (-40.02; -36.69) |
| 15/02/2020 - 30/06/2020 (1st wave) | 13129 | -11470 (-14659; -8797) | -46.63 (-52.75; -40.12) | 17564 | -12730 (-16707; -9484) | -42.02 (-48.75; -35.06) |
| 01/07/2020 - 30/09/2020 | 11033 | -4406 (-4861; -4015) | -28.54 (-30.58; -26.68) | 14241 | -5388 (-5927; -4899) | -27.45 (-29.39; -25.59) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 26754 | -16470 (-18107; -15245) | -38.10 (-40.36; -36.30) | 32945 | -21745 (-23856; -20151) | -39.76 (-42.00; -37.95) |
| **Injury and Poisoning (800-999.9)** | | | | | | |
| All visits from 15/02/2020 | 38829 | -17525 (-25665; -11193) | -31.10 (-39.79; -22.38) | 39458 | -26141 (-35798; -18774) | -39.85 (-47.57; -32.24) |
| 15/02/2020 - 30/06/2020 (1st wave) | 8928 | -8647 (-9493; -7935) | -49.20 (-51.53; -47.06) | 9533 | -10610 (-11569; -9790) | -52.67 (-54.82; -50.66) |
| 01/07/2020 - 30/09/2020 | 9870 | -1611 (-2699; -681) | -14.03 (-21.47; -6.46) | 10307 | -2733 (-3953; -1700) | -20.96 (-27.72; -14.16) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 20031 | -7267 (-13610; -2469) | -26.62 (-40.46; -10.97) | 19618 | -12797 (-20519; -7166) | -39.48 (-51.12; -26.75) |

Abbreviations: ED, Emergency Department; HPA, Health Protection Agency; ICD-9-CM, International Statistical Classification of Diseases, 9th revision, Clinical Modification; 95%CI, 95% confidence interval

TABLE 3.19: Difference in daily counts of ED visits before (2017-2019) and during COVID-19 pandemic (2020-2021), stratified by presenting complaint

| | Bergamo HPA | | | Brescia HPA | | |
|---|---|---|---|---|---|---|
| | **Jan 2017 - Dec 2019** | **Jan 2020 - Jun 2021** | ***p*-value** | **Jan 2017 - Dec 2019** | **Jan 2020 - Jun 2021** | ***p*-value** |
| **Coma** | | | | | | |
| Total | 365 | 162 | | 836 | 337 | |
| Daily events | | | | | | |
| Mean (±SD) | 0.33 (0.58) | 0.31 (0.57) | 0.434 | 0.76 (0.89) | 0.65 (0.82) | 0.021 |
| Median (IQR) | 0 (0-1) | 0 (0-1) | | 1 (0-1) | 0 (0-1) | |
| Min - max | 0-4 | 0-3 | | 0-4 | 0-4 | |
| **Acute neurological problems** | | | | | | |
| Total | 2792 | 1261 | | 6199 | 2539 | 2792 |
| Daily events | | | | | | |
| Mean (±SD) | 2.55 (1.74) | 2.44 (1.61) | 0.442 | 5.66 (2.91) | 4.91 (2.57) | <0.001 |
| Median (IQR) | 2 (1-3) | 2 (1-3) | | 5 (4-7) | 5 (3-6) | |
| Min - max | 0-10 | 0-10 | | 0-18 | 0-15 | |
| **Other neurological symptoms** | | | | | | |
| Total | 16002 | 5620 | | 31846 | 11005 | 16002 |
| Daily events | | | | | | |
| Mean (±SD) | 14.61 (5.38) | 10.87 (4.81) | <0.001 | 29.08 (8.15) | 21.29 (7.77) | <0.001 |
| Median (IQR) | 14 (11-18) | 10 (7-14) | | 29 (23-34) | 21 (16-26) | |
| Min - max | 1-35 | 1-28 | | 10-66 | 4-46 | |
| **Abdominal pain** | | | | | | |
| Total | 48510 | 14970 | | 79976 | 24300 | |
| Daily events | | | | | | |
| Mean (±SD) | 44.3 (8.34) | 28.96 (10.84) | <0.001 | 73.04 (10.55) | 47 (15.11) | <0.001 |
| Median (IQR) | 44 (38-50) | 28 (22-35) | | 73 (66-80) | 48 (38-57) | |
| Min - max | 22-74 | 2-63 | | 47-111 | 6-95 | |
| **Thoracic pain** | | | | | | |
| Total | 22808 | 8667 | | 38712 | 13206 | |
| Daily events | | | | | | |
| Mean (±SD) | 20.83 (5.74) | 16.76 (5.73) | <0.001 | 35.35 (8.22) | 25.54 (7.86) | <0.001 |

| | | | | | | |
|---|---|---|---|---|---|---|
| Median (IQR) | 20 (17-24) | 16 (13-20) | | 35 (29-40) | 25 (21-30) | |
| Min - max | 7-45 | 2-35 | | 15-67 | 5-53 | |
| **Dyspnoea** | | | | | | |
| Total | 20982 | 11234 | | 34636 | 16052 | |
| Daily events | | | | | | |
| Mean (±SD) | 19.16 (6.96) | 21.73 (22.43) | <0.001 | 31.63 (10.16) | 31.05 (16.89) | <0.001 |
| Median (IQR) | 18 (14-23) | 16 (12-22) | | 30 (25-38) | 28 (20-36) | |
| Min - max | 3-54 | 4-155 | | 8-73 | 9-127 | |
| **Precordial pain** | | | | | | |
| Total | 2309 | 757 | | 3649 | 1191 | |
| Daily events | | | | | | |
| Mean (±SD) | 2.11 (1.66) | 1.46 (1.35) | <0.001 | 3.33 (2.2) | 2.3 (1.72) | <0.001 |
| Median (IQR) | 2 (1-3) | 1 (0-2) | | 3 (2-5) | 2 (1-3) | |
| Min - max | 0-11 | 0-9 | | 0-12 | 0-8 | |
| **Shock** | | | | | | |
| Total | 136 | 103 | | 121 | 53 | |
| Daily events | | | | | | |
| Mean (±SD) | 0.12 (0.38) | 0.2 (0.49) | 0.002 | 0.11 (0.33) | 0.1 (0.33) | 0.439 |
| Median (IQR) | 0 (0-0) | 0 (0-0) | | 0 (0-0) | 0 (0-0) | |
| Min - max | 0 -2 | 0 -3 | | 0 -2 | 0 -2 | |
| **Hemorrhage** | | | | | | |
| Total | 3072 | 975 | | 7202 | 2448 | |
| Daily events | | | | | | |
| Mean (±SD) | 2.81 (1.79) | 1.89 (1.61) | <0.001 | 6.58 (2.86) | 4.74 (2.45) | <0.001 |
| Median (IQR) | 3 (1-4) | 2 (1-3) | | 6 (4-8) | 4 (3-6) | |
| Min - max | 0-11 | 0-8 | | 0-18 | 0-14 | |
| **Trauma** | | | | | | |
| Total | 253791 | 76996 | | 324558 | 95711 | |
| Daily events | | | | | | |
| Mean (±SD) | 231.77 (35.44) | 148.93 (56.54) | <0.001 | 296.4 (44.54) | 185.13 (65.85) | <0.001 |

| | | | | | | |
|---|---|---|---|---|---|---|
| Median (IQR) | 232 (208-256) | 153 (117-192) | | 295 (268-324) | 186 (145-234) | |
| Min - max | 113-383 | 8-305 | | 157-454 | 23-388 | |
| **Intoxication** | | | | | | |
| Total | 1386 | 577 | | 2647 | 903 | |
| Daily events | | | | | | |
| Mean (±SD) | 1.27 (1.31) | 1.12 (1.35) | 0.006 | 2.42 (1.99) | 1.75 (1.65) | <0.001 |
| Median (IQR) | 1 (0-2) | 1 (0-2) | | 2 (1-3) | 1 (1-2) | |
| Min - max | 0-12 | 0-11 | | 0-19 | 0-16 | |
| **Fever** | | | | | | |
| Total | 32777 | 11879 | | 57353 | 21009 | |
| Daily events | | | | | | |
| Mean (±SD) | 29.93 (16.12) | 22.98 (20.25) | <0.001 | 52.38 (26.01) | 40.64 (28.16) | <0.001 |
| Median (IQR) | 25 (20-36) | 16 (12-23) | | 45 (35-61) | 31 (24-45) | |
| Min - max | 6-136 | 3-117 | | 14-201 | 12-175 | |
| **Allergic reaction** | | | | | | |
| Total | 4464 | 1060 | | 5622 | 1381 | |
| Daily events | | | | | | |
| Mean (±SD) | 4.08 (2.66) | 2.05 (1.92) | <0.001 | 5.13 (2.78) | 2.67 (2.14) | <0.001 |
| Median (IQR) | 4 (2-5) | 2 (1-3) | | 5 (3-7) | 2 (1-4) | |
| Min - max | 0-18 | 0-13 | | 0-16 | 0-11 | |
| **Heart rhythm problems** | | | | | | |
| Total | 9542 | 3706 | | 14217 | 5146 | |
| Daily events | | | | | | |
| Mean (±SD) | 8.71 (3.43) | 7.17 (3.33) | <0.001 | 12.98 (4.26) | 9.95 (3.96) | <0.001 |
| Median (IQR) | 8 (6-11) | 7 (5-9) | | 13 (10-16) | 10 (7-12) | |
| Min - max | 1-24 | 0-19 | | 2-27 | 1-24 | |
| **Arterial hypertension** | | | | | | |
| Total | 2062 | 779 | | 4387 | 1652 | |
| Daily events | | | | | | |

| | | | | | | |
|---|---|---|---|---|---|---|
| Mean (±SD) | 1.88 (1.53) | 1.51 (1.35) | <0.001 | 4.01 (2.33) | 3.2 (2.15) | <0.001 |
| Median (IQR) | 2 (1-3) | 1 (0-2) | | 4 (2-5) | 3 (2-4) | |
| Min - max | 0-7 | 0-7 | | 0-14 | 0-10 | |
| **Psychomotor agitation** | | | | | | |
| Total | 3456 | 1614 | | 3133 | 1539 | |
| Daily events | | | | | | |
| Mean (±SD) | 3.16 (2.06) | 3.12 (2.01) | 0.821 | 2.86 (1.89) | 2.98 (1.98) | 0.337 |
| Median (IQR) | 3 (2-4) | 3 (2-4) | | 3 (1-4) | 3 (1-4) | |
| Min - max | 0-13 | 0-13 | | 0-13 | 0-10 | |
| **Ophthalmic problems** | | | | | | |
| Total | 34073 | 10183 | | 54563 | 16150 | |
| Daily events | | | | | | |
| Mean (±SD) | 31.12 (8.16) | 19.7 (8.73) | <0.001 | 49.83 (11.28) | 31.24 (12.25) | <0.001 |
| Median (IQR) | 31 (26-37) | 20 (14-26) | | 50 (42-57) | 31 (23-40) | |
| Min - max | 8-61 | 0-41 | | 15-85 | 2-69 | |
| **Otolaryngologic problems** | | | | | | |
| Total | 20156 | 5259 | | 43954 | 10678 | |
| Daily events | | | | | | |
| Mean (±SD) | 18.41 (5.57) | 10.17 (6.07) | <0.001 | 40.14 (9.01) | 20.65 (10.94) | <0.001 |
| Median (IQR) | 18 (15-22) | 9 (6-13) | | 39 (34-45) | 19 (13-26) | |
| Min - max | 4-49 | 0-31 | | 18-89 | 0-68 | |
| **Obstetrical-gynecological problems** | | | | | | |
| Total | 85075 | 29153 | | 76708 | 26817 | |
| Daily events | | | | | | |
| Mean (±SD) | 77.69 (10.66) | 56.39 (12.51) | <0.001 | 70.05 (9.96) | 51.87 (10.99) | <0.001 |
| Median (IQR) | 78 (71-85) | 57 (48-64) | | 70 (63-77) | 52 (44-59) | |
| Min - max | 43-119 | 19-97 | | 43-104 | 15-83 | |
| **Dermatological problems** | | | | | | |

| | | | | | | |
|---|---|---|---|---|---|---|
| Total | 9216 | 1737 | | 20243 | 4141 | |
| Daily events | | | | | | |
| Mean (±SD) | 8.42 (3.73) | 3.36 (2.62) | <0.001 | 18.49 (6.56) | 8.01 (4.91) | <0.001 |
| Median (IQR) | 8 (6-11) | 3 (1-5) | | 18 (14-23) | 7 (4-11) | |
| Min - max | 0-24 | 0-15 | | 4-44 | 0-27 | |
| **Odontostomatological problems** | | | | | | |
| Total | 2798 | 662 | | 2116 | 554 | |
| Daily events | | | | | | |
| Mean (±SD) | 2.56 (1.72) | 1.28 (1.37) | <0.001 | 1.93 (1.45) | 1.07 (1.17) | <0.001 |
| Median (IQR) | 2 (1-3) | 1 (0-2) | | 2 (1-3) | 1 (0-2) | |
| Min - max | 0-10 | 0-8 | | 0-10 | 0-7 | |
| **Urological problems** | | | | | | |
| Total | 21557 | 8047 | | 40354 | 13409 | |
| Daily events | | | | | | |
| Mean (±SD) | 19.69 (5.66) | 15.56 (6.34) | <0.001 | 36.85 (6.92) | 25.94 (8.73) | <0.001 |
| Median (IQR) | 19 (16-23) | 15 (11-20) | | 37 (32-41) | 26 (20-32) | |
| Min - max | 5-40 | 1-38 | | 18-63 | 3-51 | |
| **Other symptoms or disorders** | | | | | | |
| Total | 542121 | 157492 | | 498027 | 159686 | |
| Daily events | | | | | | |
| Mean (±SD) | 495.09 (53.4) | 304.63 (91) | <0.001 | 454.82 (49.55) | 308.87 (84.36) | <0.001 |
| Median (IQR) | 491 (459-525) | 295 (249-342) | | 450 (422-482) | 306 (260-347) | |
| Min - max | 329-729 | 98-608 | | 310-645 | 116-629 | |
| **Medico-legal examinations** | | | | | | |
| Total | 332 | 92 | | 499 | 166 | |
| Daily events | | | | | | |
| Mean (±SD) | 0.3 (0.54) | 0.18 (0.66) | <0.001 | 0.46 (0.68) | 0.32 (0.56) | <0.001 |
| Median (IQR) | 0 (0-1) | 0 (0-0) | | 0 (0-1) | 0 (0-1) | |

| | | | | | | |
|---|---|---|---|---|---|---|
| Min - max | 0-3 | 0-12 | | 0-4 | 0-3 | |
| **Social problems** | | | | | | |
| Total | 273 | 108 | | 347 | 105 | |
| Daily events | | | | | | |
| Mean (±SD) | 0.25 (0.53) | 0.21 (0.45) | 0.327 | 0.32 (0.56) | 0.2 (0.52) | <0.001 |
| Median (IQR) | 0 (0-0) | 0 (0-0) | | 0 (0-1) | 0 (0-0) | |
| Min - max | 0-4 | 0-2 | | 0-3 | 0-5 | |
| **Fall** | | | | | | |
| Total | 7559 | 1246 | | 4371 | 1294 | |
| Daily events | | | | | | |
| Mean (±SD) | 6.9 (8.44) | 2.41 (1.79) | <0.001 | 3.99 (3.06) | 2.5 (2.23) | <0.001 |
| Median (IQR) | 3 (1-10) | 2 (1-3) | | 4 (2-6) | 2 (1-4) | |
| Min - max | 0-42 | 0-10 | | 0-18 | 0-16 | |
| **Burn** | | | | | | |
| Total | 1123 | 326 | | 1544 | 438 | |
| Daily events | | | | | | |
| Mean (±SD) | 1.03 (1.04) | 0.63 (0.87) | <0.001 | 1.41 (1.21) | 0.85 (1) | <0.001 |
| Median (IQR) | 1 (0-2) | 0 (0-1) | | 1 (1-2) | 1 (0-1) | |
| Min - max | 0-5 | 0-5 | | 0-7 | 0-7 | |
| **Psychiatric problems** | | | | | | |
| Total | 4984 | 1986 | | 4760 | 1987 | |
| Daily events | | | | | | |
| Mean (±SD) | 4.55 (2.41) | 3.84 (2.21) | <0.001 | 4.35 (2.38) | 3.84 (2.35) | <0.001 |
| Median (IQR) | 4 (3-6) | 4 (2-5) | | 4 (3-6) | 4 (2-5) | |
| Min - max | 0-16 | 0-14 | | 0-13 | 0-12 | |
| **Pneumological/Respiratory problems** | | | | | | |
| Total | 1140 | 528 | | 3213 | 2390 | |
| Daily events | | | | | | |

| | | | | | | |
|---|---|---|---|---|---|---|
| Mean (±SD) | 1.04 (1.36) | 1.02 (2.21) | <0.001 | 2.93 (2.56) | 4.62 (4.81) | <0.001 |
| Median (IQR) | 1 (0-2) | 0 (0-1) | | 2 (1-4) | 3 (2-6) | |
| Min - max | 0-10 | 0-23 | | 0-18 | 0-37 | |
| **Interpersonal violence** | | | | | | |
| Total | 2218 | 658 | | 3033 | 1047 | |
| Daily events | | | | | | |
| Mean (±SD) | 2.03 (1.65) | 1.27 (1.28) | <0.001 | 2.77 (1.83) | 2.03 (1.79) | <0.001 |
| Median (IQR) | 2 (1-3) | 1 (0-2) | | 3 (1-4) | 2 (1-3) | |
| Min - max | 0-9 | 0-8 | | 0-12 | 0-10 | |
| **Self-harm** | | | | | | |
| Total | 144 | 49 | | 394 | 159 | |
| Daily events | | | | | | |
| Mean (±SD) | 0.13 (0.37) | 0.09 (0.32) | 0.035 | 0.36 (0.65) | 0.31 (0.56) | 0.224 |
| Median (IQR) | 0 (0-0) | 0 (0-0) | | 0 (0-1) | 0 (0-1) | |
| Min - max | 0-2 | 0-2 | | 0-5 | 0-3 | |

Abbreviations: ED, Emergency Department; HPA, Health Protection Agency; SD, standard deviation; IQR, interquartile range

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TABLE 3.20: Change in ED visits during the pandemic period, stratified by presenting complaint

| | Bergamo HPA | | | Bergamo HPA | | |
|---|---|---|---|---|---|---|
| | Total | Change (95%CI) | % Change (95%CI) | Total | Change (95%CI) | % Change (95%CI) |
| **Neurological symptoms** | | | | | | |
| All visits from 15/02/2020 | 4875 | -3744 (-5532; -2333) | -43.44 (-53.16; -32.36) | 9820 | -4793 (-7692; -2488) | -32.80 (-43.92; -20.22) |
| 15/02/2020 - 30/06/2020 (1st wave) | 1244 | -1185 (-1459; -954) | -48.80 (-53.98; -43.41) | 2328 | -1847 (-2336; -1465) | -44.24 (-50.09; -38.62) |
| 01/07/2020 - 30/09/2020 | 991 | -534 (-865; -273) | -35.00 (-46.62; -21.59) | 2152 | -650 (-1214; -174) | -23.19 (-36.06; -7.48) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 2640 | -2025 (-3213; -1084) | -43.40 (-54.89; -29.10) | 5340 | -2296 (-4212; -807) | -30.07 (-44.10; -13.13) |
| **Abdominal pain** | | | | | | |
| All visits from 15/02/2020 | 12879 | -9519 (-10699; -8467) | -42.50 (-45.38; -39.67) | 21477 | -14308 (-16154; -12687) | -39.98 (-42.93; -37.14) |
| 15/02/2020 - 30/06/2020 (1st wave) | 3116 | -3472 (-4012; -2973) | -52.70 (-56.28; -48.83) | 5261 | -5134 (-5942; -4400) | -49.39 (-53.04; -45.55) |
| 01/07/2020 - 30/09/2020 | 3040 | -1282 (-1705; -882) | -29.66 (-35.94; -22.48) | 5209 | -1609 (-2258; -987) | -23.60 (-30.24; -15.93) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 6723 | -4766 (-5110; -4468) | -41.48 (-43.19; -39.93) | 11007 | -7564 (-8136; -7080) | -40.73 (-42.50; -39.14) |
| **Thoracic Pain** | | | | | | |
| All visits from 15/02/2020 | 7562 | -3957 (-5015; -3237) | -34.35 (-39.87; -29.97) | 11588 | -4971 (-6419; -4004) | -30.02 (-35.65; -25.68) |
| 15/02/2020 - 30/06/2020 (1st wave) | 2172 | -1096 (-1404; -878) | -33.55 (-39.26; -28.78) | 3006 | -1880 (-2367; -1528) | -38.48 (-44.06; -33.71) |
| 01/07/2020 - 30/09/2020 | 1398 | -544 (-841; -301) | -28.01 (-37.56; -17.73) | 2289 | -510 (-937; -170) | -18.22 (-29.05; -6.90) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 3992 | -2316 (-3247; -1614) | -36.72 (-44.85; -28.79) | 6293 | -2581 (-3864; -1610) | -29.09 (-38.04; -20.37) |
| **Dyspnoea** | | | | | | |
| All visits from 15/02/2020 | 10144 | 1 (-777; 302) | 0.01 (-7.12; 3.07) | 14481 | -1799 (-3058; -1329) | -11.05 (-17.44; -8.41) |
| 15/02/2020 - 30/06/2020 (1st wave) | 5197 | 2275 (1106; 2957) | 77.84 (27.05; 131.98) | 5217 | 491 (-1469; 1592) | 10.38 (-21.97; 43.92) |
| 01/07/2020 - 30/09/2020 | 1061 | -444 (-560; -335) | -29.51 (-34.54; -24.01) | 1582 | -767 (-956; -602) | -32.66 (-37.68; -27.56) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 3886 | -1829 (-3219; -918) | -32.01 (-45.30; -19.11) | 7682 | -1522 (-3799; -63) | -16.54 (-33.09; -0.81) |
| **Trauma** | | | | | | |
| All visits from 15/02/2020 | 67139 | -45210 (-49460; -41735) | -40.24 (-42.42; -38.33) | 84546 | -55844 (-61089; -51631) | -39.78 (-41.95; -37.91) |
| 15/02/2020 - 30/06/2020 (1st wave) | 14587 | -19817 (-24372; -15599) | -57.60 (-62.56; -51.68) | 19516 | -23671 (-29508; -18287) | -54.81 (-60.19; -48.37) |
| 01/07/2020 - 30/09/2020 | 17565 | -4553 (-5028; -4096) | -20.58 (-22.25; -18.91) | 22167 | -5702 (-6297; -5101) | -20.46 (-22.12; -18.71) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 34987 | -20841 (-22390; -19669) | -37.33 (-39.02; -35.99) | 42863 | -26470 (-28518; -24917) | -38.18 (-39.95; -36.76) |
| **Fever** | | | | | | |
| All visits from 15/02/2020 | 9354 | -5158 (-7547; -3518) | -35.54 (-44.65; -27.33) | 17463 | -7927 (-11800; -5314) | -31.22 (-40.32; -23.33) |
| 15/02/2020 - 30/06/2020 (1st wave) | 4201 | -22 (-511; 257) | -0.52 (-10.85; 6.52) | 7217 | -144 (-989; 314) | -1.96 (-12.05; 4.55) |
| 01/07/2020 - 30/09/2020 | 1534 | -714 (-871; -564) | -31.76 (-36.22; -26.87) | 2812 | -1177 (-1447; -910) | -29.51 (-33.97; -24.45) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 3619 | -4422 (-6259; -3062) | -54.99 (-63.36; -45.83) | 7434 | -6606 (-9577; -4335) | -47.05 (-56.30; -36.83) |
| **Heart rhythm problems** | | | | | | |
| All visits from 15/02/2020 | 3282 | -1629 (-2298; -1102) | -33.16 (-41.19; -25.14) | 4605 | -1633 (-2526; -985) | -26.18 (-35.42; -17.62) |
| 15/02/2020 - 30/06/2020 (1st wave) | 837 | -550 (-721; -415) | -39.67 (-46.27; -33.16) | 1189 | -637 (-850; -460) | -34.88 (-41.68; -27.91) |

| | | | | | | |
|---|---|---|---|---|---|---|
| 01/07/2020 - 30/09/2020 | 643 | -217 (-398; -81) | -25.20 (-38.25; -11.15) | 945 | -145 (-371; 28) | -13.29 (-28.21; 3.01) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 1802 | -862 (-1203; -589) | -32.34 (-40.03; -24.64) | 2471 | -851 (-1291; -512) | -25.63 (-34.32; -17.16) |
| **Ophthalmic problems** | | | | | | |
| All visits from 15/02/2020 | 8910 | -6184 (-6752; -5754) | -40.97 (-43.11; -39.24) | 14389 | -10887 (-11844; -10167) | -43.07 (-45.15; -41.40) |
| 15/02/2020 - 30/06/2020 (1st wave) | 1845 | -2647 (-3226; -2204) | -58.93 (-63.62; -54.43) | 3267 | -4219 (-5139; -3502) | -56.36 (-61.14; -51.73) |
| 01/07/2020 - 30/09/2020 | 2202 | -820 (-951; -697) | -27.13 (-30.16; -24.03) | 3629 | -1427 (-1643; -1228) | -28.22 (-31.17; -25.29) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 4863 | -2717 (-3465; -2037) | -35.85 (-41.61; -29.53) | 7493 | -5241 (-6497; -4133) | -41.16 (-46.44; -35.55) |
| **Otolaryngologic problems** | | | | | | |
| All visits from 15/02/2020 | 4295 | -4921 (-5561; -4586) | -53.40 (-56.42; -51.64) | 8898 | -11083 (-12464; -10350) | -55.47 (-58.35; -53.77) |
| 15/02/2020 - 30/06/2020 (1st wave) | 933 | -1675 (-2076; -1343) | -64.23 (-69.00; -59.00) | 2187 | -3590 (-4488; -2846) | -62.14 (-67.23; -56.55) |
| 01/07/2020 - 30/09/2020 | 1142 | -685 (-822; -554) | -37.51 (-41.86; -32.66) | 2594 | -1344 (-1639; -1079) | -34.12 (-38.72; -29.37) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 2220 | -2560 (-3552; -1927) | -53.56 (-61.54; -46.47) | 4117 | -6150 (-8211; -4806) | -59.90 (-66.61; -53.86) |
| **Obstetrical-gynecological problems** | | | | | | |
| All visits from 15/02/2020 | 25985 | -8531 (-9381; -7748) | -24.72 (-26.52; -22.97) | 24038 | -7510 (-8214; -6824) | -23.80 (-25.47; -22.11) |
| 15/02/2020 - 30/06/2020 (1st wave) | 6599 | -3552 (-4072; -3030) | -34.99 (-38.16; -31.47) | 6244 | -3014 (-3481; -2556) | -32.55 (-35.79; -29.05) |
| 01/07/2020 - 30/09/2020 | 5650 | -1215 (-1722; -701) | -17.70 (-23.36; -11.04) | 5445 | -750 (-1208; -295) | -12.11 (-18.16; -5.13) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 13736 | -3764 (-4364; -3225) | -21.51 (-24.11; -19.02) | 12349 | -3746 (-4310; -3246) | -23.27 (-25.87; -20.82) |
| **Dermatological problems** | | | | | | |
| All visits from 15/02/2020 | 1459 | -2600 (-3426; -2156) | -64.06 (-70.13; -59.64) | 3545 | -5630 (-7443; -4685) | -61.36 (-67.74; -56.93) |
| 15/02/2020 - 30/06/2020 (1st wave) | 321 | -861 (-1461; -530) | -72.85 (-81.99; -62.28) | 917 | -1754 (-3090; -1021) | -65.67 (-77.12; -52.68) |
| 01/07/2020 - 30/09/2020 | 495 | -476 (-587; -379) | -49.02 (-54.26; -43.38) | 1046 | -1173 (-1418; -950) | -52.86 (-57.54; -47.61) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 643 | -1263 (-1556; -1073) | -66.27 (-70.76; -62.52) | 1582 | -2703 (-3344; -2288) | -63.08 (-67.89; -59.13) |
| **Urological problems** | | | | | | |
| All visits from 15/02/2020 | 7075 | -3463 (-4018; -3030) | -32.86 (-36.22; -29.99) | 12092 | -5496 (-6420; -4761) | -31.25 (-34.68; -28.25) |
| 15/02/2020 - 30/06/2020 (1st wave) | 1612 | -1369 (-1729; -1086) | -45.93 (-51.76; -40.26) | 2937 | -2172 (-2770; -1673) | -42.52 (-48.53; -36.29) |
| 01/07/2020 - 30/09/2020 | 1815 | -380 (-533; -241) | -17.31 (-22.69; -11.70) | 3160 | -486 (-723; -270) | -13.33 (-18.62; -7.88) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 3648 | -1714 (-1948; -1525) | -31.96 (-34.81; -29.48) | 5995 | -2838 (-3204; -2534) | -32.13 (-34.83; -29.71) |
| **Other symptoms or disorders** | | | | | | |
| All visits from 15/02/2020 | 134468 | -89441 (-97337; -82696) | -39.95 (-41.99; -38.08) | 138603 | -85667 (-93672; -79006) | -38.20 (-40.33; -36.31) |
| 15/02/2020 - 30/06/2020 (1st wave) | 35834 | -31766 (-33066; -30502) | -46.99 (-47.99; -45.98) | 35347 | -30510 (-31767; -29267) | -46.33 (-47.33; -45.30) |
| 01/07/2020 - 30/09/2020 | 30983 | -10619 (-11408; -9840) | -25.53 (-26.91; -24.10) | 31572 | -10590 (-11358; -9793) | -25.12 (-26.46; -23.67) |
| 01/10/2020 - 30/06/2021 (2nd wave) | 67651 | -47056 (-53675; -41290) | -41.02 (-44.24; -37.90) | 71684 | -44567 (-51231; -39022) | -38.34 (-41.68; -35.25) |

Abbreviations: ED, Emergency Department; HPA, Health Protection Agency; 95%CI, 95% confidence interval

TABLE 3.21: Difference in daily counts of ED visits before (2017-2019) and during COVID-19 pandemic (2020-2021) in individuals with chronic conditions

| | Bergamo HPA | | | Brescia HPA | | |
|---|---|---|---|---|---|---|
| | **Jan 2017 - Dec 2019** | **Jan -Dec 2020** | ***p*-value** | **Jan 2017 - Dec 2019** | **Jan -Dec 2020** | ***p*-value** |
| **Total** | | | | | | |
| Total | 272163 | 98488 | | 346978 | 131968 | |
| Daily events | | | | | | |
| Mean (±SD) | 372.83 (41.74) | 269.09 (66.77) | <0.001 | 475.31 (57.07) | 360.57 (84.66) | <0.001 |
| Median (IQR) | 369 (344-400) | 269 (222-321) | | 470 (433-514) | 363 (308-424) | |
| Min - max | 264-508 | 94-426 | | 332-702 | 132-603 | |
| **Condition** | | | | | | |
| **Organ Transplant** | | | | | | |
| Total | 1906 | 713 | | 2083 | 931 | |
| Daily events | | | | | | |
| Mean (±SD) | 2.61 (1.68) | 1.95 (1.49) | <0.001 | 2.85 (1.71) | 2.54 (1.62) | 0.010 |
| Median (IQR) | 2 (1-4) | 2 (1-3) | | 3 (2-4) | 2 (1-4) | |
| Min - max | 0-10 | 0-8 | | 0-9 | 0-8 | |
| **Chronic Kidney Disease** | | | | | | |
| Total | 11131 | 4084 | | 18050 | 7382 | |
| Daily events | | | | | | |
| Mean (±SD) | 15.25 (4.87) | 11.16 (3.99) | <0.001 | 24.73 (6.45) | 20.17 (6.25) | <0.001 |
| Median (IQR) | 15 (12-18) | 11 (8-14) | | 24 (20-29) | 20 (16-25) | |
| Min - max | 3-36 | 3-22 | | 6-44 | 5-41 | |
| **HIV Infection** | | | | | | |
| Total | 2643 | 2 | | 3550 | 1558 | |
| Daily events | | | | | | |
| Mean (±SD) | 3.62 (1.97) | 0.01 (0.07) | <0.001 | 4.86 (2.39) | 4.26 (2.39) | <0.001 |
| Median (IQR) | 3 (2-5) | 0 (0-0) | | 5 (3-6) | 4 (2-6) | |
| Min - max | 0-10 | 0-1 | | 0-13 | 0-12 | |
| **Neoplasm** | | | | | | |
| Total | 58150 | 20857 | | 68054 | 26203 | |

| | | | | | | |
|---|---|---|---|---|---|---|
| Daily events | | | | | | |
| Mean (±SD) | 79.66 (13.54) | 56.99 (15.62) | <0.001 | 93.22 (15.9) | 71.59 (18.74) | <0.001 |
| Median (IQR) | 79 (70-89) | 56 (47-69) | | 93 (82-103) | 73 (59-85) | |
| Min - max | 44-124 | 14-99 | | 52-150 | 22-121 | |
| **Type 1 Diabetes Mellitus** | | | | | | |
| Total | 1564 | 550 | | 1884 | 683 | |
| Daily events | | | | | | |
| Mean (±SD) | 2.14 (1.55) | 1.5 (1.29) | <0.001 | 2.58 (1.67) | 1.87 (1.41) | <0.001 |
| Median (IQR) | 2 (1-3) | 1 (1-2) | | 2 (1-4) | 2 (1-3) | |
| Min - max | 0-9 | 0-7 | | 0-10 | 0-7 | |
| **Type 2 Diabetes Mellitus** | | | | | | |
| Total | 47876 | 18184 | | 67312 | 27018 | |
| Daily events | | | | | | |
| Mean (±SD) | 65.58 (11.8) | 49.68 (12.72) | <0.001 | 92.21 (15.17) | 73.82 (17.95) | <0.001 |
| Median (IQR) | 65 (58-73) | 50 (40-58) | | 92 (81-103) | 74 (62-87) | |
| Min - max | 37-109 | 18-86 | | 57-143 | 26-119 | |
| **Cardio-Cerebrovascular Disease** | | | | | | |
| Total | 183467 | 67573 | | 243185 | 93898 | |
| Daily events | | | | | | |
| Mean (±SD) | 251.32 (31.8) | 184.63 (44.36) | <0.001 | 333.13 (44.22) | 256.55 (59.16) | <0.001 |
| Median (IQR) | 249 (230-272) | 185 (156-218) | | 330.5 (302-362) | 257 (219-301) | |
| Min - max | 169-373 | 74-282 | | 231-522 | 102-416 | |
| **Respiratory Disease** | | | | | | |
| Total | 34420 | 11796 | | 45603 | 16168 | |
| Daily events | | | | | | |
| Mean (±SD) | 47.15 (9.18) | 32.23 (10.91) | <0.001 | 62.47 (10.61) | 44.17 (14.07) | <0.001 |
| Median (IQR) | 47 (41-53) | 31 (25-39) | | 62 (55-70) | 44 (34-53) | |
| Min - max | 22-82 | 8-61 | | 32-106 | 12-81 | |
| **Digestive and Liver Disease** | | | | | | |
| Total | 18953 | 6991 | | 22524 | 8685 | |
| Daily events | | | | | | |

| | | | | | | |
|---|---|---|---|---|---|---|
| Mean (±SD) | 25.96 (5.85) | 19.1 (6.34) | <0.001 | 30.85 (6.99) | 23.73 (7.08) | <0.001 |
| Median (IQR) | 26 (22-30) | 19 (14-24) | | 30 (26-35) | 24 (18-29) | |
| Min - max | 10-54 | 2-39 | | 15-61 | 7-48 | |
| **Neuropathy** | | | | | | |
| Total | 17326 | 6421 | | 23425 | 9304 | |
| Daily events | | | | | | |
| Mean (±SD) | 23.73 (5.85) | 17.54 (5.95) | <0.001 | 32.09 (7.22) | 25.42 (8.16) | <0.001 |
| Median (IQR) | 23 (20-28) | 18 (13-22) | | 32 (27-37) | 25 (21-31) | |
| Min - max | 9-43 | 4-38 | | 14-58 | 2-56 | |
| **Autoimmune Disorder** | | | | | | |
| Total | 17122 | 6319 | | 16575 | 6302 | |
| Daily events | | | | | | |
| Mean (±SD) | 23.45 (5.43) | 17.27 (5.97) | <0.001 | 22.71 (5.42) | 17.22 (6.07) | <0.001 |
| Median (IQR) | 23 (20-27) | 17 (13-21) | | 22 (19-26) | 17 (13-21) | |
| Min - max | 8-44 | 3-38 | | 10-44 | 4-38 | |
| **Endocrine Disorder** | | | | | | |
| Total | 79948 | 29664 | | 106581 | 41535 | |
| Daily events | | | | | | |
| Mean (±SD) | 109.52 (15.44) | 81.05 (20.73) | <0.001 | 146 (21.46) | 113.48 (26.7) | <0.001 |
| Median (IQR) | 109 (98 -120) | 81 (66-96) | | 145 (132-160) | 113 (93-132) | |
| Min - max | 68-157 | 34-132 | | 90-218 | 40-183 | |
| **Others** | | | | | | |
| Total | 10136 | 3661 | | 13384 | 5279 | |
| Daily events | | | | | | |
| Mean (±SD) | 13.88 (4.04) | 10 (4.58) | <0.001 | 18.33 (4.8) | 14.42 (5.37) | <0.001 |
| Median (IQR) | 14 (11-17) | 10 (6-13) | | 18 (15-21) | 14 (11-18) | |
| Min - max | 3-29 | 1-27 | | 7-36 | 2-30 | |

Abbreviations: ED, Emergency Department; HPA, Health Protection Agency; SD, standard deviation; IQR, interquartile range; HIV, human immunodeficiency virus

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TABLE 3.22: Change in ED visits during the pandemic period, stratified by chronic condition

| | Bergamo HPA | | | Brescia HPA | | |
|---|---|---|---|---|---|---|
| | Total | Change (95%CI) | % Change (95%CI) | Total | Change (95%CI) | % Change (95%CI) |
| **Total** | | | | | | |
| All visits from 15/02/2020 | 82210 | -53435 (-63167; -44616) | -39.39 (-43.45; -35.18) | 111984 | -61857 (-74215; -50673) | -35.58 (-39.86; -31.15) |
| 15/02/2020 - 30/06/2020 (1st wave) | 31967 | -26765 (-31332; -22693) | -45.57 (-49.50; -41.52) | 43171 | -31111 (-36929; -25877) | -41.88 (-46.10; -37.48) |
| 01/07/2020 - 30/09/2020 | 28076 | -10953 (-13088; -9060) | -28.06 (-31.79; -24.40) | 38050 | -12527 (-15254; -10091) | -24.77 (-28.62; -20.96) |
| 01/10/2020 - 31/12/2020 | 22167 | -15716 (-19006; -12961) | -41.49 (-46.16; -36.90) | 30763 | -18219 (-22368; -14482) | -37.20 (-42.10; -32.01) |
| **Condition** | | | | | | |
| **Chronic Kidney Disease** | | | | | | |
| All visits from 15/02/2020 | 3485 | -3423 (-4637; -2361) | -49.55 (-57.09; -40.38) | 6286 | -4507 (-6332; -2902) | -41.76 (-50.18; -31.59) |
| 15/02/2020 - 30/06/2020 (1st wave) | 39383 | -1654 (-2406; -1029) | -55.53 (-64.50; -43.73) | 2428 | -2055 (-3168; -1126) | -45.84 (-56.61; -31.69) |
| 01/07/2020 - 30/09/2020 | 34785 | -785 (-1022; -560) | -40.47 (-46.94; -32.65) | 2099 | -1091 (-1480; -718) | -34.21 (-41.36; -25.50) |
| 01/10/2020 - 31/12/2020 | 78309 | -984 (-1258; -730) | -49.46 (-55.56; -42.04) | 1759 | -1361 (-1786; -980) | -43.62 (-50.38; -35.77) |
| **Neoplasm** | | | | | | |
| All visits from 15/02/2020 | 17546 | -13862 (-16877; -11067) | -44.14 (-49.03; -38.68) | 22441 | -14579 (-18105; -11321) | -39.38 (-44.65; -33.53) |
| 15/02/2020 - 30/06/2020 (1st wave) | 6819 | -6729 (-8196; -5352) | -49.67 (-54.59; -43.97) | 8591 | -6977 (-8655; -5405) | -44.82 (-50.19; -38.62) |
| 01/07/2020 - 30/09/2020 | 5926 | -10820 (-11599; -10060) | -34.74 (-40.44; -28.71) | 7673 | -3219 (-4261; -2296) | -29.55 (-35.71; -23.03) |
| 01/10/2020 - 31/12/2020 | 4801 | -3155 (-4024; -2387) | -45.32 (-49.37; -40.69) | 6177 | -4384 (-5220; -3565) | -41.51 (-45.80; -36.59) |
| **Type 2 Diabetes Mellitus** | | | | | | |
| All visits from 15/02/2020 | 15409 | -9961 (-11661; -8540) | -39.26 (-43.08; -35.66) | 23065 | -12932 (-15248; -10973) | -35.93 (-39.80; -32.24) |
| 15/02/2020 - 30/06/2020 (1st wave) | 5987 | -4928 (-5772; -4256) | -45.15 (-49.09; -41.55) | 8857 | -6351 (-7435; -5432) | -41.76 (-45.64; -38.02) |
| 01/07/2020 - 30/09/2020 | 5103 | -2176 (-2596; -1817) | -29.89 (-33.72; -26.25) | 7685 | -2827 (-3425; -2315) | -26.89 (-30.83; -23.15) |
| 01/10/2020 - 31/12/2020 | 4319 | -2857 (-3390; -2377) | -39.81 (-43.97; -35.50) | 6523 | -3754 (-4532; -3096) | -36.53 (-41.00; -32.19) |
| **Cardio-Cerebrovascular Disease** | | | | | | |
| All visits from 15/02/2020 | 56743 | -37129 (-43853; -31158) | -39.55 (-43.59; -35.45) | 79951 | -44497 (-53344; -36635) | -35.76 (-40.02; -31.42) |
| 15/02/2020 - 30/06/2020 (1st wave) | 22057 | -18386 (-21604; -15599) | -45.46 (-49.48; -41.43) | 30811 | -22030 (-26210; -18406) | -41.69 (-45.97; -37.40) |
| 01/07/2020 - 30/09/2020 | 19259 | -7788 (-9184; -6512) | -28.79 (-32.29; -25.27) | 26872 | -9334 (-11196; -7630) | -25.78 (-29.41; -22.11) |
| 01/10/2020 - 31/12/2020 | 15427 | -10955 (-13318; -8967) | -41.52 (-46.33; -36.76) | 22268 | -13133 (-16280; -10487) | -37.10 (-42.23; -32.02) |
| **Respiratory Disease** | | | | | | |
| All visits from 15/02/2020 | 9595 | -8160 (-9977; -6654) | -45.96 (-50.97; -40.95) | 13448 | -9289 (-11626; -7387) | -40.85 (-46.37; -35.45) |
| 15/02/2020 - 30/06/2020 (1st wave) | 3764 | -4048 (-4493; -3683) | -51.82 (-54.42; -49.46) | 5003 | -4960 (-5517; -4501) | -49.79 (-52.44; -47.36) |
| 01/07/2020 - 30/09/2020 | 3259 | -1692 (-2465; -1078) | -34.18 (-43.07; -24.85) | 4722 | -1604 (-2579; -795) | -25.36 (-35.32; -14.41) |
| 01/10/2020 - 31/12/2020 | 2572 | -2420 (-3170; -1818) | -48.47 (-55.21; -41.41) | 3723 | -2724 (-3649; -1925) | -42.25 (-49.50; -34.08) |
| **Digestive and Liver Disease** | | | | | | |
| All visits from 15/02/2020 | 5857 | -3235 (-3597; -2918) | -35.58 (-38.05; -33.26) | 7420 | -4155 (-4611; -3771) | -35.90 (-38.33; -33.69) |

| | | | | | | |
|---|---|---|---|---|---|---|
| 15/02/2020 - 30/06/2020 (1st wave) | 2161 | -1684 (-1948; -1454) | -43.80 (-47.40; -40.22) | 2904 | -2060 (-2394; -1753) | -41.50 (-45.19; -37.64) |
| 01/07/2020 - 30/09/2020 | 2008 | -712 (-846; -585) | -26.18 (-29.64; -22.57) | 2551 | -930 (-1104; -771) | -26.71 (-30.21; -23.22) |
| 01/10/2020 - 31/12/2020 | 1688 | -838 (-1071; -655) | -33.19 (-38.82; -27.97) | 1965 | -1165 (-1431; -939) | -37.23 (-42.14; -32.34) |
| **Neuropathy** | | | | | | |
| All visits from 15/02/2020 | 5322 | -4032 (-4867; -3353) | -43.10 (-47.77; -38.65) | 7865 | -5009 (-6154; -4076) | -38.91 (-43.90; -34.13) |
| 15/02/2020 - 30/06/2020 (1st wave) | 2070 | -1945 (-2222; -1712) | -48.44 (-51.77; -45.26) | 2966 | -2463 (-2833; -2154) | -45.36 (-48.86; -42.08) |
| 01/07/2020 - 30/09/2020 | 1820 | -853 (-1053; -673) | -31.91 (-36.65; -27.00) | 2630 | -1060 (-1337; -811) | -28.72 (-33.71; -23.57) |
| 01/10/2020 - 31/12/2020 | 1432 | -1234 (-1669; -904) | -46.29 (-53.83; -38.70) | 2269 | -1487 (-2093; -1027) | -39.59 (-47.99; -31.15) |
| **Autoimmune Disorder** | | | | | | |
| All visits from 15/02/2020 | 5246 | -2594 (-2933; -2295) | -33.09 (-35.86; -30.44) | 5282 | -2683 (-3031; -2380) | -33.68 (-36.46; -31.06) |
| 15/02/2020 - 30/06/2020 (1st wave) | 2152 | -1270 (-1535; -1010) | -37.10 (-41.64; -31.93) | 2042 | -1394 (-1655; -1141) | -40.57 (-44.77; -35.84) |
| 01/07/2020 - 30/09/2020 | 1759 | -474 (-611; -338) | -21.22 (-25.80; -16.11) | 1836 | -557 (-701; -412) | -23.29 (-27.65; -18.34) |
| 01/10/2020 - 31/12/2020 | 1335 | -851 (-1118; -642) | -38.92 (-45.59; -32.48) | 1404 | -731 (-975; -529) | -34.24 (-40.99; -27.35) |
| **Endocrine Disorder** | | | | | | |
| All visits from 15/02/2020 | 24872 | -15861 (-19222; -12880) | -38.94 (-43.59; -34.12) | 35396 | -18870 (-23308; -14929) | -34.77 (-39.70; -29.67) |
| 15/02/2020 - 30/06/2020 (1st wave) | 9678 | -7777 (-9624; -6186) | -44.56 (-49.86; -38.99) | 13854 | -9140 (-11570; -7046) | -39.75 (-45.51; -33.71) |
| 01/07/2020 - 30/09/2020 | 8505 | -3261 (-3855; -2712) | -27.72 (-31.19; -24.18) | 11881 | -3942 (-4740; -3206) | -24.91 (-28.52; -21.25) |
| 01/10/2020 - 31/12/2020 | 6689 | -4822 (-5899; -3935) | -41.89 (-46.86; -37.04) | 9661 | -5788 (-7208; -4609) | -37.47 (-42.73; -32.30) |
| **Other** | | | | | | |
| All visits from 15/02/2020 | 2933 | -2218 (-2718; -1834) | -43.06 (-48.10; -38.47) | 4373 | -2902 (-3598; -2405) | -39.89 (-45.14; -35.48) |
| 15/02/2020 - 30/06/2020 (1st wave) | 1134 | -1132 (-1386; -933) | -49.96 (-55.00; -45.14) | 1710 | -1529 (-1886; -1244) | -47.21 (-52.45; -42.11) |
| 01/07/2020 - 30/09/2020 | 1021 | -422 (-589; -299) | -29.25 (-36.59; -22.67) | 1505 | -479 (-688; -320) | -24.15 (-31.39; -17.54) |
| 01/10/2020 - 31/12/2020 | 778 | -664 (-797; -562) | -46.05 (-50.60; -41.94) | 1158 | -894 (-1073; -757) | -43.56 (-48.10; -39.53) |

Abbreviations: ED, Emergency Department; HPA, Health Protection Agency; 95%CI, 95% confidence interval

TABLE 3.23: Joint effect of lag (days) and new positive SARS-CoV-2 swabs per 100,000 inhabitants on predicted incidence rate ratio (IRR) of urgent hospital admission during the first wave

| | IRR | | | | | | |
|---|---|---|---|---|---|---|---|
| **Lag (days)** | **Reference level*: 5x100000** | **Reference level*: 10x100000** | **Reference level*: 15x100000** | **Reference level*: 20x100000** | **Reference level*: 30x100000** | **Reference level*: 50x100000** | **Reference level*: 75x100000** |
| 0 | 1.014 (1.010 - 1.017) | 1.031 (1.023 - 1.038) | 1.047 (1.037 - 1.057) | 1.063 (1.050 - 1.076) | 1.095 (1.078 - 1.112) | 1.154 (1.130 - 1.178) | 1.221 (1.189 - 1.254) |
| 1 | 1.010 (1.008 - 1.013) | 1.023 (1.018 - 1.028) | 1.036 (1.029 - 1.043) | 1.048 (1.039 - 1.057) | 1.073 (1.061 - 1.085) | 1.120 (1.105 - 1.136) | 1.175 (1.153 - 1.197) |
| 2 | 1.007 (1.006 - 1.009) | 1.017 (1.013 - 1.020) | 1.026 (1.021 - 1.031) | 1.036 (1.030 - 1.042) | 1.055 (1.047 - 1.062) | 1.092 (1.082 - 1.102) | 1.136 (1.123 - 1.150) |
| 3 | 1.005 (1.004 - 1.006) | 1.011 (1.009 - 1.014) | 1.018 (1.014 - 1.022) | 1.025 (1.020 - 1.029) | 1.039 (1.033 - 1.044) | 1.068 (1.062 - 1.074) | 1.103 (1.095 - 1.112) |
| 4 | 1.003 (1.002 - 1.004) | 1.007 (1.004 - 1.009) | 1.011 (1.008 - 1.014) | 1.016 (1.012 - 1.020) | 1.025 (1.021 - 1.030) | 1.047 (1.042 - 1.053) | 1.076 (1.069 - 1.083) |
| 5 | 1.001 (1.000 - 1.002) | 1.003 (1.000 - 1.006) | 1.005 (1.002 - 1.009) | 1.008 (1.003 - 1.012) | 1.014 (1.009 - 1.020) | 1.030 (1.024 - 1.037) | 1.053 (1.045 - 1.061) |
| 6 | 1.000 (0.998 - 1.001) | 1.000 (0.997 - 1.003) | 1.000 (0.996 - 1.005) | 1.002 (0.996 - 1.007) | 1.005 (0.999 - 1.012) | 1.017 (1.009 - 1.025) | 1.035 (1.025 - 1.044) |
| 7 | 0.999 (0.997 - 1.000) | 0.997 (0.994 - 1.001) | 0.997 (0.992 - 1.001) | 0.997 (0.991 - 1.002) | 0.998 (0.991 - 1.005) | 1.006 (0.997 - 1.014) | 1.020 (1.009 - 1.030) |
| 8 | 0.998 (0.996 - 0.999) | 0.995 (0.992 - 0.999) | 0.994 (0.989 - 0.999) | 0.993 (0.987 - 0.999) | 0.992 (0.985 - 1.000) | 0.997 (0.988 - 1.006) | 1.008 (0.997 - 1.019) |
| 9 | 0.997 (0.995 - 0.999) | 0.994 (0.991 - 0.997) | 0.992 (0.987 - 0.996) | 0.990 (0.984 - 0.996) | 0.988 (0.981 - 0.996) | 0.990 (0.981 - 1.000) | 0.999 (0.988 - 1.010) |
| 10 | 0.997 (0.995 - 0.998) | 0.993 (0.990 - 0.996) | 0.990 (0.986 - 0.995) | 0.988 (0.982 - 0.994) | 0.985 (0.978 - 0.993) | 0.985 (0.976 - 0.995) | 0.992 (0.981 - 1.003) |
| 11 | 0.996 (0.995 - 0.998) | 0.993 (0.989 - 0.996) | 0.989 (0.985 - 0.994) | 0.987 (0.981 - 0.992) | 0.984 (0.977 - 0.991) | 0.982 (0.974 - 0.991) | 0.987 (0.977 - 0.997) |
| 12 | 0.996 (0.995 - 0.998) | 0.992 (0.989 - 0.995) | 0.989 (0.985 - 0.993) | 0.986 (0.981 - 0.992) | 0.983 (0.976 - 0.989) | 0.981 (0.973 - 0.988) | 0.984 (0.975 - 0.993) |
| 13 | 0.996 (0.995 - 0.998) | 0.993 (0.990 - 0.995) | 0.989 (0.985 - 0.993) | 0.987 (0.982 - 0.991) | 0.983 (0.977 - 0.989) | 0.980 (0.973 - 0.987) | 0.983 (0.975 - 0.990) |
| 14 | 0.997 (0.995 - 0.998) | 0.993 (0.990 - 0.996) | 0.990 (0.986 - 0.994) | 0.987 (0.983 - 0.992) | 0.983 (0.978 - 0.989) | 0.980 (0.974 - 0.986) | 0.982 (0.975 - 0.989) |
| 15 | 0.997 (0.996 - 0.998) | 0.994 (0.991 - 0.996) | 0.991 (0.987 - 0.994) | 0.988 (0.984 - 0.993) | 0.985 (0.979 - 0.990) | 0.981 (0.975 - 0.987) | 0.982 (0.976 - 0.989) |

*Effects are relative to a unit increase in reference level

TABLE 3.24: Joint effect of lag (days) and new positive swabs per 100,000 inhabitants on predicted incidence rate ratio (IRR) of urgent hospital admission during the second wave

| | IRR | | | | | | |
|---|---|---|---|---|---|---|---|
| **Lag (days)** | **Reference level*: 5x100000** | **Reference level*: 10x100000** | **Reference level*: 15x100000** | **Reference level*: 20x100000** | **Reference level*: 50x100000** | **Reference level*: 100x100000** | **Reference level*: 200x100000** |
| 0 | 1.002 (1.000 - 1.004) | 1.004 (1.000 - 1.008) | 1.006 (1.001 - 1.012) | 1.009 (1.001 - 1.016) | 1.023 (1.007 - 1.040) | 1.049 (1.023 - 1.076) | 1.104 (1.069 - 1.141) |
| 1 | 1.001 (1.000 - 1.002) | 1.003 (1.000 - 1.005) | 1.004 (1.000 - 1.008) | 1.006 (1.000 - 1.011) | 1.016 (1.004 - 1.028) | 1.035 (1.017 - 1.053) | 1.079 (1.055 - 1.104) |
| 2 | 1.001 (1.000 - 1.001) | 1.001 (1.000 - 1.003) | 1.002 (1.000 - 1.005) | 1.003 (1.000 - 1.007) | 1.009 (1.002 - 1.017) | 1.023 (1.011 - 1.035) | 1.057 (1.042 - 1.073) |
| 3 | 1.000 (1.000 - 1.001) | 1.000 (0.999 - 1.002) | 1.001 (0.999 - 1.002) | 1.001 (0.999 - 1.003) | 1.004 (0.999 - 1.009) | 1.013 (1.005 - 1.021) | 1.039 (1.029 - 1.049) |
| 4 | 1.000 (0.999 - 1.000) | 1.000 (0.999 - 1.001) | 0.999 (0.998 - 1.001) | 0.999 (0.997 - 1.001) | 1.000 (0.995 - 1.004) | 1.004 (0.998 - 1.011) | 1.023 (1.015 - 1.032) |
| 5 | 0.999 (0.999 - 1.000) | 0.999 (0.998 - 1.000) | 0.998 (0.997 - 1.000) | 0.998 (0.996 - 1.000) | 0.996 (0.991 - 1.001) | 0.997 (0.990 - 1.005) | 1.010 (1.000 - 1.020) |
| 6 | 0.999 (0.999 - 1.000) | 0.998 (0.997 - 1.000) | 0.998 (0.996 - 1.000) | 0.997 (0.994 - 1.000) | 0.994 (0.988 - 0.999) | 0.992 (0.983 - 1.001) | 0.999 (0.988 - 1.011) |
| 7 | 0.999 (0.998 - 1.000) | 0.998 (0.997 - 1.000) | 0.997 (0.995 - 0.999) | 0.996 (0.993 - 0.999) | 0.992 (0.985 - 0.998) | 0.988 (0.978 - 0.998) | 0.991 (0.978 - 1.004) |
| 8 | 0.999 (0.998 - 1.000) | 0.998 (0.996 - 1.000) | 0.997 (0.994 - 0.999) | 0.996 (0.993 - 0.999) | 0.991 (0.984 - 0.998) | 0.985 (0.975 - 0.996) | 0.984 (0.970 - 0.998) |
| 9 | 0.999 (0.998 - 1.000) | 0.998 (0.996 - 0.999) | 0.997 (0.994 - 0.999) | 0.996 (0.992 - 0.999) | 0.990 (0.983 - 0.997) | 0.984 (0.973 - 0.995) | 0.979 (0.965 - 0.994) |
| 10 | 0.999 (0.998 - 1.000) | 0.998 (0.996 - 0.999) | 0.997 (0.994 - 0.999) | 0.996 (0.992 - 0.999) | 0.990 (0.983 - 0.997) | 0.983 (0.972 - 0.994) | 0.976 (0.962 - 0.990) |
| 11 | 0.999 (0.998 - 1.000) | 0.998 (0.996 - 0.999) | 0.997 (0.994 - 0.999) | 0.996 (0.993 - 0.999) | 0.990 (0.983 - 0.997) | 0.983 (0.972 - 0.993) | 0.974 (0.961 - 0.988) |
| 12 | 0.999 (0.998 - 1.000) | 0.998 (0.997 - 1.000) | 0.997 (0.995 - 0.999) | 0.996 (0.993 - 0.999) | 0.991 (0.984 - 0.997) | 0.983 (0.974 - 0.993) | 0.974 (0.962 - 0.986) |
| 13 | 0.999 (0.999 - 1.000) | 0.998 (0.997 - 1.000) | 0.997 (0.995 - 0.999) | 0.997 (0.994 - 0.999) | 0.992 (0.986 - 0.997) | 0.985 (0.976 - 0.994) | 0.975 (0.963 - 0.986) |
| 14 | 0.999 (0.999 - 1.000) | 0.999 (0.997 - 1.000) | 0.998 (0.996 - 1.000) | 0.997 (0.995 - 1.000) | 0.993 (0.987 - 0.998) | 0.987 (0.978 - 0.995) | 0.976 (0.966 - 0.986) |
| 15 | 1.000 (0.999 - 1.000) | 0.999 (0.998 - 1.000) | 0.998 (0.997 - 1.000) | 0.998 (0.995 - 1.000) | 0.994 (0.989 - 0.999) | 0.989 (0.981 - 0.996) | 0.979 (0.969 - 0.988) |

*Effects are relative to a unit increase in reference level

TABLE 3.25: Joint effect of lag (days) and new positive SARS-CoV-2 swabs per 100,000 inhabitants on predicted incidence rate ratio (IRR) of urgent hospital admission with medical DRG during the first wave

| | IRR | | | | | | |
|---|---|---|---|---|---|---|---|
| **Lag (days)** | **Reference level*: 5x100000** | **Reference level*: 10x100000** | **Reference level*: 15x100000** | **Reference level*: 20x100000** | **Reference level*: 30x100000** | **Reference level*: 50x100000** | **Reference level*: 75x100000** |
| 0 | 1.020 (1.016 - 1.023) | 1.043 (1.035 - 1.051) | 1.066 (1.055 - 1.078) | 1.089 (1.074 - 1.104) | 1.131 (1.111 - 1.151) | 1.205 (1.178 - 1.233) | 1.282 (1.244 - 1.321) |
| 1 | 1.015 (1.012 - 1.018) | 1.033 (1.028 - 1.039) | 1.051 (1.043 - 1.059) | 1.068 (1.058 - 1.078) | 1.101 (1.088 - 1.114) | 1.160 (1.142 - 1.178) | 1.222 (1.197 - 1.247) |
| 2 | 1.011 (1.009 - 1.013) | 1.024 (1.021 - 1.028) | 1.038 (1.032 - 1.043) | 1.050 (1.044 - 1.057) | 1.075 (1.067 - 1.084) | 1.121 (1.110 - 1.133) | 1.171 (1.156 - 1.187) |
| 3 | 1.007 (1.006 - 1.009) | 1.017 (1.014 - 1.020) | 1.026 (1.022 - 1.030) | 1.035 (1.031 - 1.040) | 1.054 (1.048 - 1.060) | 1.089 (1.082 - 1.096) | 1.130 (1.120 - 1.139) |
| 4 | 1.005 (1.003 - 1.006) | 1.010 (1.008 - 1.013) | 1.017 (1.013 - 1.020) | 1.023 (1.018 - 1.027) | 1.036 (1.030 - 1.041) | 1.063 (1.056 - 1.069) | 1.095 (1.087 - 1.103) |
| 5 | 1.002 (1.001 - 1.004) | 1.005 (1.002 - 1.008) | 1.008 (1.004 - 1.013) | 1.012 (1.007 - 1.017) | 1.021 (1.014 - 1.027) | 1.041 (1.033 - 1.048) | 1.067 (1.058 - 1.076) |
| 6 | 1.000 (0.998 - 1.002) | 1.001 (0.997 - 1.004) | 1.002 (0.997 - 1.007) | 1.004 (0.998 - 1.010) | 1.009 (1.001 - 1.016) | 1.023 (1.014 - 1.032) | 1.044 (1.033 - 1.055) |
| 7 | 0.998 (0.997 - 1.000) | 0.997 (0.994 - 1.001) | 0.997 (0.992 - 1.002) | 0.997 (0.990 - 1.003) | 0.999 (0.991 - 1.007) | 1.009 (0.999 - 1.019) | 1.026 (1.014 - 1.038) |
| 8 | 0.997 (0.995 - 0.999) | 0.994 (0.991 - 0.998) | 0.993 (0.987 - 0.998) | 0.992 (0.985 - 0.998) | 0.991 (0.983 - 1.000) | 0.997 (0.987 - 1.008) | 1.011 (0.999 - 1.024) |
| 9 | 0.996 (0.994 - 0.998) | 0.993 (0.989 - 0.996) | 0.990 (0.984 - 0.995) | 0.988 (0.981 - 0.994) | 0.986 (0.977 - 0.994) | 0.989 (0.979 - 1.000) | 1.001 (0.988 - 1.014) |
| 10 | 0.996 (0.994 - 0.997) | 0.991 (0.987 - 0.995) | 0.988 (0.982 - 0.993) | 0.985 (0.979 - 0.991) | 0.982 (0.974 - 0.990) | 0.983 (0.973 - 0.994) | 0.993 (0.981 - 1.005) |
| 11 | 0.995 (0.994 - 0.997) | 0.990 (0.987 - 0.994) | 0.986 (0.981 - 0.991) | 0.983 (0.977 - 0.990) | 0.980 (0.972 - 0.987) | 0.980 (0.970 - 0.989) | 0.988 (0.977 - 0.999) |
| 12 | 0.995 (0.994 - 0.997) | 0.990 (0.987 - 0.993) | 0.986 (0.981 - 0.991) | 0.983 (0.977 - 0.988) | 0.979 (0.971 - 0.986) | 0.978 (0.969 - 0.986) | 0.985 (0.975 - 0.995) |
| 13 | 0.995 (0.994 - 0.997) | 0.990 (0.987 - 0.993) | 0.986 (0.982 - 0.990) | 0.983 (0.978 - 0.988) | 0.979 (0.972 - 0.985) | 0.977 (0.970 - 0.985) | 0.984 (0.975 - 0.993) |
| 14 | 0.996 (0.994 - 0.997) | 0.991 (0.988 - 0.994) | 0.987 (0.983 - 0.991) | 0.984 (0.979 - 0.989) | 0.979 (0.973 - 0.986) | 0.978 (0.971 - 0.985) | 0.984 (0.977 - 0.992) |
| 15 | 0.996 (0.994 - 0.997) | 0.991 (0.989 - 0.994) | 0.988 (0.984 - 0.992) | 0.985 (0.980 - 0.990) | 0.981 (0.975 - 0.987) | 0.980 (0.973 - 0.986) | 0.985 (0.979 - 0.992) |

*Effects are relative to a unit increase in reference level

TABLE 3.26: Joint effect of lag (days) and new positive SARS-CoV-2 swabs per 100,000 inhabitants on predicted incidence rate ratio (IRR) of urgent hospital admission with medical DRG during the second wave

| | IRR | | | | | | |
|---|---|---|---|---|---|---|---|
| **Lag (days)** | **Reference level*: 5x100000** | **Reference level*: 10x100000** | **Reference level*: 15x100000** | **Reference level*: 20x100000** | **Reference level*: 50x100000** | **Reference level*: 100x100000** | **Reference level*: 200x100000** |
| 0 | 1.002 (1.000 - 1.004) | 1.005 (1.000 - 1.009) | 1.007 (1.001 - 1.014) | 1.010 (1.001 - 1.019) | 1.026 (1.007 - 1.046) | 1.055 (1.025 - 1.086) | 1.117 (1.076 - 1.159) |
| 1 | 1.001 (1.000 - 1.003) | 1.003 (1.000 - 1.006) | 1.005 (1.000 - 1.010) | 1.007 (1.001 - 1.013) | 1.019 (1.005 - 1.032) | 1.041 (1.020 - 1.062) | 1.091 (1.064 - 1.120) |
| 2 | 1.001 (1.000 - 1.002) | 1.002 (1.000 - 1.004) | 1.003 (1.000 - 1.006) | 1.004 (1.000 - 1.008) | 1.012 (1.003 - 1.021) | 1.028 (1.015 - 1.042) | 1.069 (1.051 - 1.087) |
| 3 | 1.000 (1.000 - 1.001) | 1.001 (0.999 - 1.002) | 1.001 (0.999 - 1.003) | 1.002 (0.999 - 1.005) | 1.007 (1.001 - 1.012) | 1.018 (1.009 - 1.027) | 1.050 (1.038 - 1.062) |
| 4 | 1.000 (0.999 - 1.000) | 1.000 (0.999 - 1.001) | 1.000 (0.998 - 1.002) | 1.000 (0.998 - 1.002) | 1.002 (0.997 - 1.007) | 1.009 (1.002 - 1.017) | 1.033 (1.023 - 1.043) |
| 5 | 1.000 (0.999 - 1.000) | 0.999 (0.998 - 1.001) | 0.999 (0.997 - 1.001) | 0.999 (0.996 - 1.001) | 0.998 (0.993 - 1.004) | 1.002 (0.993 - 1.010) | 1.019 (1.008 - 1.030) |
| 6 | 0.999 (0.999 - 1.000) | 0.999 (0.997 - 1.000) | 0.998 (0.996 - 1.000) | 0.998 (0.995 - 1.001) | 0.995 (0.989 - 1.002) | 0.996 (0.986 - 1.006) | 1.007 (0.994 - 1.021) |
| 7 | 0.999 (0.998 - 1.000) | 0.998 (0.997 - 1.000) | 0.997 (0.995 - 1.000) | 0.997 (0.993 - 1.000) | 0.993 (0.986 - 1.001) | 0.991 (0.980 - 1.003) | 0.998 (0.983 - 1.013) |
| 8 | 0.999 (0.998 - 1.000) | 0.998 (0.996 - 1.000) | 0.997 (0.994 - 1.000) | 0.996 (0.992 - 1.000) | 0.992 (0.984 - 1.000) | 0.988 (0.975 - 1.000) | 0.990 (0.974 - 1.006) |
| 9 | 0.999 (0.998 - 1.000) | 0.998 (0.996 - 1.000) | 0.997 (0.994 - 1.000) | 0.996 (0.992 - 1.000) | 0.991 (0.982 - 0.999) | 0.985 (0.973 - 0.998) | 0.984 (0.968 - 1.000) |
| 10 | 0.999 (0.998 - 1.000) | 0.998 (0.996 - 1.000) | 0.997 (0.994 - 1.000) | 0.996 (0.992 - 0.999) | 0.990 (0.982 - 0.998) | 0.984 (0.971 - 0.996) | 0.979 (0.963 - 0.995) |
| 11 | 0.999 (0.998 - 1.000) | 0.998 (0.996 - 1.000) | 0.997 (0.994 - 0.999) | 0.996 (0.992 - 0.999) | 0.990 (0.982 - 0.998) | 0.983 (0.971 - 0.995) | 0.976 (0.961 - 0.991) |
| 12 | 0.999 (0.998 - 1.000) | 0.998 (0.996 - 1.000) | 0.997 (0.994 - 0.999) | 0.996 (0.993 - 0.999) | 0.990 (0.983 - 0.998) | 0.983 (0.972 - 0.994) | 0.974 (0.960 - 0.988) |
| 13 | 0.999 (0.998 - 1.000) | 0.998 (0.997 - 1.000) | 0.997 (0.995 - 0.999) | 0.996 (0.993 - 0.999) | 0.991 (0.984 - 0.997) | 0.983 (0.973 - 0.994) | 0.974 (0.961 - 0.986) |
| 14 | 0.999 (0.999 - 1.000) | 0.998 (0.997 - 1.000) | 0.997 (0.995 - 1.000) | 0.997 (0.994 - 0.999) | 0.992 (0.985 - 0.998) | 0.985 (0.975 - 0.994) | 0.974 (0.962 - 0.986) |
| 15 | 0.999 (0.999 - 1.000) | 0.999 (0.997 - 1.000) | 0.998 (0.996 - 1.000) | 0.997 (0.994 - 1.000) | 0.993 (0.987 - 0.998) | 0.986 (0.977 - 0.995) | 0.975 (0.964 - 0.986) |

*Effects are relative to a unit increase in reference level

TABLE 3.27: Joint effect of lag (days) and new positive SARS-CoV-2 swabs per 100,000 inhabitants on predicted incidence rate ratio (IRR) of urgent hospital admission with respiratory diagnosis during the first wave

| | IRR | | | | | | |
|---|---|---|---|---|---|---|---|
| **Lag (days)** | **Reference level*: 5x100000** | **Reference level*: 10x100000** | **Reference level*: 15x100000** | **Reference level*: 20x100000** | **Reference level*: 30x100000** | **Reference level*: 50x100000** | **Reference level*: 75x100000** |
| 0 | 1.090 (1.085 - 1.096) | 1.202 (1.190 - 1.215) | 1.312 (1.292 - 1.332) | 1.416 (1.389 - 1.443) | 1.605 (1.565 - 1.646) | 1.876 (1.815 - 1.940) | 2.011 (1.928 - 2.098) |
| 1 | 1.071 (1.067 - 1.075) | 1.158 (1.149 - 1.166) | 1.241 (1.228 - 1.254) | 1.319 (1.302 - 1.336) | 1.458 (1.433 - 1.483) | 1.652 (1.616 - 1.689) | 1.748 (1.699 - 1.799) |
| 2 | 1.055 (1.052 - 1.057) | 1.120 (1.114 - 1.125) | 1.182 (1.173 - 1.190) | 1.239 (1.229 - 1.250) | 1.340 (1.325 - 1.355) | 1.479 (1.459 - 1.499) | 1.549 (1.521 - 1.577) |
| 3 | 1.040 (1.038 - 1.042) | 1.088 (1.084 - 1.092) | 1.133 (1.127 - 1.139) | 1.174 (1.167 - 1.181) | 1.246 (1.236 - 1.255) | 1.344 (1.332 - 1.356) | 1.395 (1.379 - 1.412) |
| 4 | 1.028 (1.026 - 1.030) | 1.062 (1.058 - 1.065) | 1.092 (1.087 - 1.098) | 1.121 (1.114 - 1.128) | 1.170 (1.161 - 1.179) | 1.239 (1.228 - 1.250) | 1.278 (1.265 - 1.291) |
| 5 | 1.018 (1.016 - 1.020) | 1.040 (1.035 - 1.044) | 1.060 (1.053 - 1.066) | 1.078 (1.070 - 1.086) | 1.110 (1.100 - 1.121) | 1.157 (1.145 - 1.170) | 1.188 (1.172 - 1.203) |
| 6 | 1.010 (1.008 - 1.012) | 1.022 (1.017 - 1.027) | 1.033 (1.026 - 1.040) | 1.044 (1.035 - 1.053) | 1.063 (1.052 - 1.075) | 1.094 (1.080 - 1.109) | 1.119 (1.102 - 1.137) |
| 7 | 1.003 (1.001 - 1.006) | 1.007 (1.002 - 1.013) | 1.012 (1.004 - 1.019) | 1.017 (1.007 - 1.026) | 1.026 (1.014 - 1.039) | 1.047 (1.031 - 1.062) | 1.068 (1.049 - 1.087) |
| 8 | 0.998 (0.995 - 1.000) | 0.996 (0.991 - 1.002) | 0.996 (0.988 - 1.003) | 0.996 (0.986 - 1.006) | 0.999 (0.986 - 1.011) | 1.011 (0.995 - 1.027) | 1.031 (1.011 - 1.050) |
| 9 | 0.994 (0.991 - 0.996) | 0.988 (0.983 - 0.993) | 0.983 (0.976 - 0.991) | 0.980 (0.971 - 0.990) | 0.978 (0.966 - 0.991) | 0.985 (0.970 - 1.001) | 1.005 (0.986 - 1.024) |
| 10 | 0.991 (0.989 - 0.994) | 0.982 (0.977 - 0.987) | 0.975 (0.968 - 0.982) | 0.970 (0.961 - 0.979) | 0.964 (0.953 - 0.976) | 0.968 (0.954 - 0.983) | 0.988 (0.971 - 1.006) |
| 11 | 0.989 (0.987 - 0.992) | 0.978 (0.973 - 0.983) | 0.969 (0.963 - 0.976) | 0.963 (0.955 - 0.971) | 0.956 (0.945 - 0.966) | 0.958 (0.945 - 0.972) | 0.979 (0.964 - 0.995) |
| 12 | 0.988 (0.986 - 0.990) | 0.976 (0.971 - 0.980) | 0.966 (0.960 - 0.973) | 0.959 (0.952 - 0.967) | 0.951 (0.942 - 0.961) | 0.954 (0.943 - 0.966) | 0.977 (0.963 - 0.991) |
| 13 | 0.988 (0.986 - 0.990) | 0.975 (0.971 - 0.980) | 0.966 (0.960 - 0.972) | 0.959 (0.952 - 0.966) | 0.951 (0.942 - 0.960) | 0.955 (0.945 - 0.965) | 0.980 (0.968 - 0.992) |
| 14 | 0.988 (0.986 - 0.990) | 0.976 (0.972 - 0.980) | 0.967 (0.961 - 0.973) | 0.960 (0.953 - 0.967) | 0.953 (0.945 - 0.962) | 0.959 (0.950 - 0.969) | 0.987 (0.976 - 0.997) |
| 15 | 0.989 (0.987 - 0.991) | 0.978 (0.974 - 0.982) | 0.969 (0.964 - 0.975) | 0.964 (0.957 - 0.971) | 0.958 (0.950 - 0.967) | 0.967 (0.957 - 0.976) | 0.997 (0.987 - 1.007) |

*Effects are relative to a unit increase in reference level

TABLE 3.28: Joint effect of lag (days) and new positive SARS-CoV-2 swabs per 100,000 inhabitants on predicted incidence rate ratio (IRR) of urgent hospital admission with respiratory diagnosis during the second wave

| | IRR | | | | | | |
|---|---|---|---|---|---|---|---|
| **Lag (days)** | **Reference level*: 5x100000** | **Reference level*: 10x100000** | **Reference level*: 15x100000** | **Reference level*: 20x100000** | **Reference level*: 50x100000** | **Reference level*: 100x100000** | **Reference level*: 200x100000** |
| 0 | 1.009 (1.005 - 1.012) | 1.019 (1.011 - 1.027) | 1.030 (1.018 - 1.042) | 1.040 (1.024 - 1.056) | 1.101 (1.064 - 1.139) | 1.195 (1.133 - 1.260) | 1.354 (1.267 - 1.446) |
| 1 | 1.007 (1.005 - 1.010) | 1.016 (1.011 - 1.022) | 1.026 (1.017 - 1.034) | 1.035 (1.023 - 1.046) | 1.087 (1.061 - 1.114) | 1.168 (1.126 - 1.213) | 1.306 (1.247 - 1.368) |
| 2 | 1.006 (1.005 - 1.008) | 1.014 (1.010 - 1.018) | 1.022 (1.016 - 1.027) | 1.030 (1.022 - 1.037) | 1.074 (1.057 - 1.092) | 1.144 (1.116 - 1.173) | 1.262 (1.224 - 1.301) |
| 3 | 1.005 (1.004 - 1.006) | 1.012 (1.010 - 1.014) | 1.018 (1.015 - 1.022) | 1.025 (1.020 - 1.030) | 1.063 (1.052 - 1.074) | 1.122 (1.104 - 1.140) | 1.222 (1.198 - 1.247) |
| 4 | 1.004 (1.004 - 1.005) | 1.010 (1.008 - 1.012) | 1.015 (1.012 - 1.018) | 1.021 (1.017 - 1.025) | 1.052 (1.043 - 1.062) | 1.102 (1.087 - 1.116) | 1.186 (1.166 - 1.206) |
| 5 | 1.004 (1.003 - 1.005) | 1.008 (1.006 - 1.010) | 1.013 (1.009 - 1.016) | 1.017 (1.012 - 1.022) | 1.043 (1.032 - 1.053) | 1.083 (1.066 - 1.100) | 1.152 (1.130 - 1.175) |
| 6 | 1.003 (1.002 - 1.004) | 1.006 (1.004 - 1.009) | 1.010 (1.006 - 1.014) | 1.013 (1.008 - 1.019) | 1.034 (1.022 - 1.046) | 1.066 (1.046 - 1.086) | 1.122 (1.096 - 1.148) |
| 7 | 1.002 (1.001 - 1.004) | 1.005 (1.002 - 1.008) | 1.008 (1.003 - 1.012) | 1.010 (1.004 - 1.017) | 1.026 (1.012 - 1.040) | 1.051 (1.029 - 1.073) | 1.094 (1.065 - 1.123) |
| 8 | 1.002 (1.000 - 1.003) | 1.004 (1.000 - 1.007) | 1.005 (1.000 - 1.011) | 1.007 (1.001 - 1.014) | 1.019 (1.004 - 1.034) | 1.037 (1.013 - 1.061) | 1.069 (1.039 - 1.100) |
| 9 | 1.001 (0.999 - 1.003) | 1.002 (0.999 - 1.006) | 1.004 (0.998 - 1.009) | 1.005 (0.998 - 1.012) | 1.012 (0.997 - 1.028) | 1.024 (1.001 - 1.049) | 1.046 (1.016 - 1.077) |
| 10 | 1.001 (0.999 - 1.002) | 1.001 (0.998 - 1.005) | 1.002 (0.997 - 1.007) | 1.003 (0.996 - 1.009) | 1.007 (0.992 - 1.022) | 1.013 (0.990 - 1.037) | 1.026 (0.997 - 1.056) |
| 11 | 1.000 (0.999 - 1.002) | 1.000 (0.997 - 1.003) | 1.000 (0.996 - 1.005) | 1.000 (0.994 - 1.007) | 1.001 (0.987 - 1.016) | 1.003 (0.981 - 1.026) | 1.008 (0.980 - 1.036) |
| 12 | 1.000 (0.998 - 1.001) | 0.999 (0.996 - 1.002) | 0.999 (0.995 - 1.004) | 0.999 (0.993 - 1.005) | 0.997 (0.984 - 1.010) | 0.994 (0.974 - 1.015) | 0.992 (0.967 - 1.017) |
| 13 | 0.999 (0.998 - 1.001) | 0.999 (0.996 - 1.001) | 0.998 (0.994 - 1.002) | 0.997 (0.992 - 1.003) | 0.993 (0.981 - 1.005) | 0.987 (0.968 - 1.005) | 0.978 (0.955 - 1.001) |
| 14 | 0.999 (0.998 - 1.000) | 0.998 (0.995 - 1.000) | 0.997 (0.993 - 1.001) | 0.996 (0.991 - 1.001) | 0.989 (0.978 - 1.000) | 0.980 (0.963 - 0.997) | 0.966 (0.945 - 0.986) |
| 15 | 0.999 (0.998 - 1.000) | 0.997 (0.995 - 1.000) | 0.996 (0.992 - 0.999) | 0.994 (0.990 - 0.999) | 0.986 (0.976 - 0.997) | 0.974 (0.958 - 0.990) | 0.956 (0.937 - 0.975) |

*Effects are relative to a unit increase in reference level

TABLE 3.29: Joint effect of lag (days) and new positive SARS-CoV-2 swabs per 100,000 inhabitants on predicted incidence rate ratio (IRR) of urgent hospital admission with respiratory system MDC during the first wave

| | IRR | | | | | | |
|---|---|---|---|---|---|---|---|
| **Lag (days)** | **Reference level*: 5x100000** | **Reference level*: 10x100000** | **Reference level*: 15x100000** | **Reference level*: 20x100000** | **Reference level*: 30x100000** | **Reference level*: 50x100000** | **Reference level*: 75x100000** |
| 0 | 1.083 (1.077 - 1.088) | 1.184 (1.172 - 1.197) | 1.283 (1.264 - 1.302) | 1.377 (1.352 - 1.403) | 1.547 (1.509 - 1.585) | 1.789 (1.732 - 1.848) | 1.914 (1.836 - 1.994) |
| 1 | 1.065 (1.062 - 1.069) | 1.145 (1.136 - 1.153) | 1.220 (1.208 - 1.233) | 1.291 (1.275 - 1.308) | 1.417 (1.394 - 1.441) | 1.594 (1.560 - 1.629) | 1.685 (1.638 - 1.733) |
| 2 | 1.050 (1.048 - 1.053) | 1.111 (1.105 - 1.116) | 1.167 (1.159 - 1.175) | 1.220 (1.210 - 1.231) | 1.312 (1.298 - 1.327) | 1.441 (1.422 - 1.461) | 1.509 (1.482 - 1.536) |
| 3 | 1.037 (1.036 - 1.039) | 1.082 (1.078 - 1.086) | 1.123 (1.118 - 1.129) | 1.162 (1.154 - 1.169) | 1.228 (1.219 - 1.237) | 1.321 (1.309 - 1.332) | 1.372 (1.356 - 1.387) |
| 4 | 1.027 (1.025 - 1.028) | 1.058 (1.054 - 1.062) | 1.087 (1.081 - 1.092) | 1.113 (1.107 - 1.120) | 1.160 (1.151 - 1.169) | 1.226 (1.216 - 1.236) | 1.265 (1.252 - 1.278) |
| 5 | 1.017 (1.015 - 1.019) | 1.038 (1.034 - 1.042) | 1.057 (1.051 - 1.063) | 1.074 (1.067 - 1.082) | 1.105 (1.096 - 1.115) | 1.151 (1.139 - 1.163) | 1.182 (1.167 - 1.197) |
| 6 | 1.010 (1.007 - 1.012) | 1.021 (1.017 - 1.026) | 1.032 (1.026 - 1.039) | 1.043 (1.034 - 1.051) | 1.062 (1.051 - 1.073) | 1.093 (1.079 - 1.107) | 1.119 (1.101 - 1.136) |
| 7 | 1.004 (1.001 - 1.006) | 1.008 (1.003 - 1.013) | 1.013 (1.006 - 1.020) | 1.018 (1.009 - 1.027) | 1.028 (1.016 - 1.040) | 1.048 (1.033 - 1.064) | 1.070 (1.052 - 1.089) |
| 8 | 0.999 (0.996 - 1.001) | 0.998 (0.992 - 1.003) | 0.998 (0.990 - 1.005) | 0.998 (0.989 - 1.008) | 1.002 (0.990 - 1.014) | 1.015 (0.999 - 1.030) | 1.034 (1.016 - 1.053) |
| 9 | 0.995 (0.992 - 0.997) | 0.990 (0.985 - 0.995) | 0.986 (0.979 - 0.994) | 0.984 (0.975 - 0.993) | 0.983 (0.971 - 0.995) | 0.990 (0.975 - 1.005) | 1.009 (0.991 - 1.027) |
| 10 | 0.992 (0.990 - 0.995) | 0.984 (0.979 - 0.989) | 0.978 (0.971 - 0.985) | 0.974 (0.965 - 0.982) | 0.969 (0.958 - 0.980) | 0.973 (0.959 - 0.987) | 0.992 (0.975 - 1.009) |
| 11 | 0.990 (0.988 - 0.993) | 0.980 (0.976 - 0.985) | 0.973 (0.966 - 0.979) | 0.967 (0.959 - 0.975) | 0.960 (0.950 - 0.971) | 0.963 (0.950 - 0.976) | 0.982 (0.967 - 0.998) |
| 12 | 0.989 (0.987 - 0.991) | 0.978 (0.974 - 0.983) | 0.970 (0.964 - 0.976) | 0.963 (0.956 - 0.971) | 0.956 (0.946 - 0.965) | 0.958 (0.946 - 0.969) | 0.978 (0.965 - 0.992) |
| 13 | 0.989 (0.987 - 0.991) | 0.978 (0.974 - 0.982) | 0.969 (0.963 - 0.975) | 0.962 (0.955 - 0.969) | 0.955 (0.946 - 0.963) | 0.957 (0.947 - 0.967) | 0.979 (0.967 - 0.991) |
| 14 | 0.989 (0.987 - 0.991) | 0.978 (0.974 - 0.982) | 0.969 (0.964 - 0.975) | 0.963 (0.956 - 0.970) | 0.956 (0.948 - 0.964) | 0.960 (0.951 - 0.969) | 0.984 (0.973 - 0.994) |
| 15 | 0.990 (0.988 - 0.992) | 0.979 (0.975 - 0.983) | 0.971 (0.966 - 0.977) | 0.966 (0.959 - 0.973) | 0.960 (0.952 - 0.968) | 0.966 (0.956 - 0.975) | 0.991 (0.981 - 1.001) |

*Effects are relative to a unit increase in reference level

TABLE 3.30: Joint effect of lag (days) and new positive SARS-CoV-2 swabs per 100,000 inhabitants on predicted incidence rate ratio (IRR) of urgent hospital admission with respiratory system MDC during the second wave

| | IRR | | | | | | |
|---|---|---|---|---|---|---|---|
| **Lag (days)** | **Reference level*: 5x100000** | **Reference level*: 10x100000** | **Reference level*: 15x100000** | **Reference level*: 20x100000** | **Reference level*: 50x100000** | **Reference level*: 100x100000** | **Reference level*: 200x100000** |
| 0 | 1.007 (1.004 - 1.010) | 1.015 (1.008 - 1.023) | 1.024 (1.013 - 1.036) | 1.033 (1.017 - 1.048) | 1.083 (1.048 - 1.119) | 1.162 (1.104 - 1.222) | 1.301 (1.221 - 1.386) |
| 1 | 1.006 (1.004 - 1.008) | 1.013 (1.008 - 1.019) | 1.021 (1.013 - 1.029) | 1.028 (1.018 - 1.039) | 1.072 (1.047 - 1.097) | 1.140 (1.100 - 1.182) | 1.261 (1.207 - 1.319) |
| 2 | 1.005 (1.004 - 1.007) | 1.012 (1.008 - 1.015) | 1.018 (1.013 - 1.023) | 1.024 (1.017 - 1.031) | 1.061 (1.045 - 1.078) | 1.121 (1.094 - 1.147) | 1.225 (1.190 - 1.261) |
| 3 | 1.004 (1.003 - 1.005) | 1.010 (1.007 - 1.012) | 1.015 (1.012 - 1.019) | 1.021 (1.016 - 1.025) | 1.052 (1.042 - 1.063) | 1.102 (1.085 - 1.119) | 1.191 (1.169 - 1.214) |
| 4 | 1.004 (1.003 - 1.004) | 1.008 (1.006 - 1.010) | 1.013 (1.010 - 1.016) | 1.017 (1.013 - 1.021) | 1.043 (1.035 - 1.052) | 1.085 (1.071 - 1.099) | 1.160 (1.142 - 1.179) |
| 5 | 1.003 (1.002 - 1.004) | 1.007 (1.004 - 1.009) | 1.010 (1.007 - 1.014) | 1.014 (1.010 - 1.018) | 1.035 (1.026 - 1.045) | 1.070 (1.054 - 1.086) | 1.132 (1.111 - 1.153) |
| 6 | 1.002 (1.001 - 1.004) | 1.005 (1.003 - 1.008) | 1.008 (1.004 - 1.012) | 1.011 (1.006 - 1.016) | 1.028 (1.016 - 1.040) | 1.055 (1.037 - 1.074) | 1.105 (1.081 - 1.130) |
| 7 | 1.002 (1.000 - 1.003) | 1.004 (1.001 - 1.007) | 1.006 (1.002 - 1.011) | 1.008 (1.002 - 1.014) | 1.021 (1.008 - 1.035) | 1.042 (1.021 - 1.064) | 1.081 (1.054 - 1.109) |
| 8 | 1.001 (1.000 - 1.003) | 1.003 (1.000 - 1.006) | 1.004 (1.000 - 1.009) | 1.006 (1.000 - 1.012) | 1.015 (1.001 - 1.030) | 1.030 (1.008 - 1.053) | 1.059 (1.030 - 1.089) |
| 9 | 1.001 (0.999 - 1.002) | 1.002 (0.999 - 1.005) | 1.003 (0.998 - 1.008) | 1.004 (0.997 - 1.010) | 1.010 (0.995 - 1.024) | 1.020 (0.997 - 1.043) | 1.039 (1.010 - 1.069) |
| 10 | 1.000 (0.999 - 1.002) | 1.001 (0.998 - 1.004) | 1.001 (0.996 - 1.006) | 1.002 (0.995 - 1.008) | 1.005 (0.990 - 1.019) | 1.010 (0.988 - 1.032) | 1.021 (0.993 - 1.050) |
| 11 | 1.000 (0.999 - 1.001) | 1.000 (0.997 - 1.003) | 1.000 (0.995 - 1.005) | 1.000 (0.994 - 1.006) | 1.000 (0.987 - 1.014) | 1.001 (0.980 - 1.022) | 1.005 (0.979 - 1.032) |
| 12 | 1.000 (0.998 - 1.001) | 0.999 (0.996 - 1.002) | 0.999 (0.995 - 1.003) | 0.998 (0.993 - 1.004) | 0.996 (0.984 - 1.009) | 0.993 (0.974 - 1.013) | 0.991 (0.967 - 1.015) |
| 13 | 0.999 (0.998 - 1.001) | 0.999 (0.996 - 1.001) | 0.998 (0.994 - 1.002) | 0.997 (0.992 - 1.002) | 0.993 (0.981 - 1.004) | 0.986 (0.969 - 1.004) | 0.978 (0.957 - 1.000) |
| 14 | 0.999 (0.998 - 1.000) | 0.998 (0.996 - 1.000) | 0.997 (0.993 - 1.000) | 0.996 (0.991 - 1.001) | 0.989 (0.979 - 1.000) | 0.980 (0.964 - 0.997) | 0.967 (0.948 - 0.987) |
| 15 | 0.999 (0.998 - 1.000) | 0.997 (0.995 - 1.000) | 0.996 (0.993 - 0.999) | 0.995 (0.990 - 0.999) | 0.987 (0.977 - 0.997) | 0.975 (0.960 - 0.991) | 0.958 (0.940 - 0.977) |

*Effects are relative to a unit increase in reference level

TABLE 3.31: Joint effect of lag (days) and new positive SARS-CoV-2 swabs per 100,000 inhabitants on predicted incidence rate ratio (IRR) of red-code ED visit during the first wave

| | IRR | | | | | | |
|---|---|---|---|---|---|---|---|
| **Lag (days)** | **Reference level*: 5x100000** | **Reference level*: 10x100000** | **Reference level*: 15x100000** | **Reference level*: 20x100000** | **Reference level*: 30x100000** | **Reference level*: 50x100000** | **Reference level*: 75x100000** |
| 0 | 1.017 (1.009 - 1.025) | 1.040 (1.024 - 1.057) | 1.066 (1.042 - 1.090) | 1.094 (1.063 - 1.126) | 1.158 (1.116 - 1.201) | 1.311 (1.249 - 1.375) | 1.537 (1.447 - 1.632) |
| 1 | 1.013 (1.007 - 1.018) | 1.031 (1.019 - 1.042) | 1.051 (1.034 - 1.068) | 1.074 (1.052 - 1.095) | 1.125 (1.096 - 1.154) | 1.249 (1.209 - 1.290) | 1.431 (1.373 - 1.491) |
| 2 | 1.009 (1.005 - 1.013) | 1.023 (1.015 - 1.030) | 1.038 (1.027 - 1.049) | 1.056 (1.042 - 1.070) | 1.096 (1.078 - 1.115) | 1.196 (1.171 - 1.221) | 1.341 (1.306 - 1.377) |
| 3 | 1.006 (1.003 - 1.009) | 1.015 (1.010 - 1.021) | 1.027 (1.019 - 1.035) | 1.040 (1.030 - 1.050) | 1.071 (1.059 - 1.084) | 1.150 (1.135 - 1.165) | 1.266 (1.244 - 1.287) |
| 4 | 1.003 (1.001 - 1.006) | 1.009 (1.004 - 1.015) | 1.017 (1.009 - 1.025) | 1.026 (1.017 - 1.036) | 1.050 (1.038 - 1.061) | 1.111 (1.098 - 1.124) | 1.202 (1.185 - 1.219) |
| 5 | 1.001 (0.998 - 1.004) | 1.004 (0.998 - 1.010) | 1.009 (1.000 - 1.017) | 1.015 (1.004 - 1.025) | 1.032 (1.018 - 1.045) | 1.078 (1.062 - 1.094) | 1.148 (1.128 - 1.168) |
| 6 | 0.999 (0.996 - 1.002) | 1.000 (0.993 - 1.006) | 1.002 (0.992 - 1.011) | 1.005 (0.993 - 1.017) | 1.016 (1.001 - 1.031) | 1.050 (1.031 - 1.069) | 1.103 (1.080 - 1.127) |
| 7 | 0.997 (0.994 - 1.001) | 0.996 (0.988 - 1.003) | 0.996 (0.985 - 1.006) | 0.997 (0.984 - 1.010) | 1.003 (0.986 - 1.020) | 1.026 (1.005 - 1.047) | 1.065 (1.040 - 1.091) |
| 8 | 0.996 (0.992 - 1.000) | 0.993 (0.985 - 1.001) | 0.991 (0.980 - 1.002) | 0.990 (0.976 - 1.004) | 0.992 (0.975 - 1.010) | 1.006 (0.984 - 1.028) | 1.034 (1.008 - 1.061) |
| 9 | 0.995 (0.991 - 0.999) | 0.990 (0.983 - 0.998) | 0.987 (0.976 - 0.998) | 0.985 (0.971 - 0.998) | 0.983 (0.966 - 1.001) | 0.990 (0.968 - 1.012) | 1.008 (0.983 - 1.034) |
| 10 | 0.994 (0.991 - 0.998) | 0.989 (0.981 - 0.996) | 0.984 (0.973 - 0.995) | 0.980 (0.967 - 0.994) | 0.976 (0.959 - 0.993) | 0.977 (0.956 - 0.998) | 0.987 (0.963 - 1.012) |
| 11 | 0.994 (0.990 - 0.997) | 0.987 (0.980 - 0.995) | 0.982 (0.972 - 0.992) | 0.977 (0.965 - 0.990) | 0.971 (0.955 - 0.987) | 0.966 (0.947 - 0.986) | 0.971 (0.949 - 0.993) |
| 12 | 0.994 (0.990 - 0.997) | 0.987 (0.980 - 0.993) | 0.980 (0.971 - 0.990) | 0.975 (0.964 - 0.987) | 0.967 (0.952 - 0.982) | 0.958 (0.941 - 0.976) | 0.958 (0.938 - 0.977) |
| 13 | 0.994 (0.990 - 0.997) | 0.986 (0.980 - 0.993) | 0.980 (0.971 - 0.989) | 0.974 (0.963 - 0.985) | 0.964 (0.951 - 0.978) | 0.953 (0.937 - 0.968) | 0.948 (0.931 - 0.965) |
| 14 | 0.994 (0.991 - 0.997) | 0.986 (0.980 - 0.992) | 0.979 (0.971 - 0.988) | 0.973 (0.963 - 0.984) | 0.963 (0.951 - 0.976) | 0.949 (0.935 - 0.963) | 0.941 (0.926 - 0.956) |
| 15 | 0.994 (0.991 - 0.997) | 0.986 (0.981 - 0.992) | 0.980 (0.972 - 0.988) | 0.974 (0.964 - 0.984) | 0.963 (0.950 - 0.975) | 0.947 (0.933 - 0.960) | 0.936 (0.923 - 0.950) |

*Effects are relative to a unit increase in reference level

TABLE 3.32: Joint effect of lag (days) and new positive SARS-CoV-2 swabs per 100,000 inhabitants on predicted incidence rate ratio (IRR) of red-code ED visit during the second wave

| | IRR | | | | | | |
|---|---|---|---|---|---|---|---|
| **Lag (days)** | **Reference level*: 5x100000** | **Reference level*: 10x100000** | **Reference level*: 15x100000** | **Reference level*: 20x100000** | **Reference level*: 50x100000** | **Reference level*: 100x100000** | **Reference level*: 200x100000** |
| 0 | 0.998 (0.993 - 1.002) | 0.995 (0.985 - 1.005) | 0.992 (0.978 - 1.007) | 0.990 (0.971 - 1.010) | 0.980 (0.939 - 1.023) | 0.977 (0.915 - 1.043) | 1.011 (0.930 - 1.100) |
| 1 | 0.998 (0.995 - 1.001) | 0.995 (0.989 - 1.002) | 0.993 (0.983 - 1.003) | 0.991 (0.978 - 1.005) | 0.982 (0.953 - 1.012) | 0.979 (0.936 - 1.025) | 1.011 (0.953 - 1.072) |
| 2 | 0.998 (0.996 - 1.000) | 0.996 (0.991 - 1.000) | 0.994 (0.987 - 1.001) | 0.992 (0.983 - 1.001) | 0.984 (0.965 - 1.004) | 0.982 (0.952 - 1.012) | 1.010 (0.972 - 1.050) |
| 3 | 0.998 (0.997 - 1.000) | 0.996 (0.993 - 0.999) | 0.994 (0.990 - 0.999) | 0.993 (0.987 - 0.999) | 0.985 (0.972 - 0.999) | 0.983 (0.963 - 1.004) | 1.009 (0.983 - 1.035) |
| 4 | 0.998 (0.997 - 1.000) | 0.997 (0.994 - 0.999) | 0.995 (0.991 - 0.999) | 0.993 (0.988 - 0.999) | 0.987 (0.976 - 0.998) | 0.985 (0.968 - 1.002) | 1.007 (0.985 - 1.030) |
| 5 | 0.999 (0.997 - 1.000) | 0.997 (0.994 - 1.000) | 0.995 (0.991 - 1.000) | 0.994 (0.988 - 1.000) | 0.988 (0.975 - 1.001) | 0.986 (0.967 - 1.006) | 1.005 (0.980 - 1.031) |
| 6 | 0.999 (0.997 - 1.000) | 0.997 (0.994 - 1.001) | 0.996 (0.991 - 1.001) | 0.995 (0.988 - 1.002) | 0.989 (0.974 - 1.004) | 0.987 (0.964 - 1.011) | 1.003 (0.974 - 1.034) |
| 7 | 0.999 (0.997 - 1.001) | 0.997 (0.994 - 1.001) | 0.996 (0.990 - 1.002) | 0.995 (0.987 - 1.003) | 0.990 (0.973 - 1.007) | 0.988 (0.962 - 1.015) | 1.001 (0.967 - 1.036) |
| 8 | 0.999 (0.997 - 1.001) | 0.998 (0.993 - 1.002) | 0.997 (0.990 - 1.003) | 0.995 (0.987 - 1.004) | 0.991 (0.972 - 1.009) | 0.988 (0.961 - 1.017) | 0.999 (0.963 - 1.036) |
| 9 | 0.999 (0.997 - 1.001) | 0.998 (0.994 - 1.002) | 0.997 (0.990 - 1.003) | 0.996 (0.987 - 1.004) | 0.991 (0.973 - 1.010) | 0.989 (0.960 - 1.018) | 0.997 (0.960 - 1.035) |
| 10 | 0.999 (0.997 - 1.001) | 0.998 (0.994 - 1.002) | 0.997 (0.991 - 1.003) | 0.996 (0.988 - 1.005) | 0.992 (0.974 - 1.011) | 0.989 (0.961 - 1.018) | 0.994 (0.958 - 1.032) |
| 11 | 0.999 (0.997 - 1.001) | 0.998 (0.994 - 1.002) | 0.997 (0.991 - 1.003) | 0.996 (0.988 - 1.004) | 0.992 (0.975 - 1.010) | 0.989 (0.963 - 1.017) | 0.992 (0.958 - 1.028) |
| 12 | 0.999 (0.998 - 1.001) | 0.998 (0.995 - 1.002) | 0.997 (0.992 - 1.003) | 0.997 (0.989 - 1.004) | 0.993 (0.976 - 1.009) | 0.990 (0.965 - 1.015) | 0.990 (0.958 - 1.023) |
| 13 | 0.999 (0.998 - 1.001) | 0.998 (0.995 - 1.002) | 0.998 (0.992 - 1.003) | 0.997 (0.990 - 1.004) | 0.993 (0.978 - 1.008) | 0.990 (0.967 - 1.013) | 0.988 (0.959 - 1.018) |
| 14 | 0.999 (0.998 - 1.001) | 0.998 (0.995 - 1.002) | 0.998 (0.993 - 1.003) | 0.997 (0.991 - 1.003) | 0.993 (0.980 - 1.008) | 0.990 (0.969 - 1.012) | 0.986 (0.960 - 1.014) |
| 15 | 0.999 (0.998 - 1.001) | 0.999 (0.996 - 1.002) | 0.998 (0.993 - 1.002) | 0.997 (0.991 - 1.003) | 0.994 (0.981 - 1.007) | 0.990 (0.970 - 1.011) | 0.985 (0.960 - 1.011) |

*Effects are relative to a unit increase in reference level

TABLE 3.33: Joint effect of lag (days) and new positive SARS-CoV-2 swabs per 100,000 inhabitants on predicted incidence rate ratio (IRR) of ED visit with respiratory diagnosis during the first wave

| | IRR | | | | | | |
|---|---|---|---|---|---|---|---|
| **Lag (days)** | **Reference level*: 5x100000** | **Reference level*: 10x100000** | **Reference level*: 15x100000** | **Reference level*: 20x100000** | **Reference level*: 30x100000** | **Reference level*: 50x100000** | **Reference level*: 75x100000** |
| 0 | 1.043 (1.038 - 1.048) | 1.097 (1.086 - 1.107) | 1.150 (1.135 - 1.166) | 1.203 (1.182 - 1.223) | 1.305 (1.277 - 1.335) | 1.496 (1.453 - 1.541) | 1.698 (1.635 - 1.764) |
| 1 | 1.033 (1.029 - 1.036) | 1.073 (1.066 - 1.080) | 1.113 (1.102 - 1.123) | 1.152 (1.138 - 1.165) | 1.227 (1.209 - 1.246) | 1.365 (1.339 - 1.392) | 1.509 (1.471 - 1.549) |
| 2 | 1.024 (1.021 - 1.026) | 1.053 (1.048 - 1.057) | 1.081 (1.075 - 1.088) | 1.109 (1.101 - 1.118) | 1.163 (1.152 - 1.174) | 1.262 (1.246 - 1.277) | 1.365 (1.342 - 1.387) |
| 3 | 1.016 (1.014 - 1.018) | 1.036 (1.032 - 1.039) | 1.055 (1.050 - 1.060) | 1.074 (1.068 - 1.080) | 1.111 (1.104 - 1.119) | 1.180 (1.171 - 1.189) | 1.253 (1.240 - 1.266) |
| 4 | 1.010 (1.008 - 1.011) | 1.021 (1.018 - 1.025) | 1.033 (1.029 - 1.038) | 1.046 (1.040 - 1.051) | 1.069 (1.062 - 1.077) | 1.116 (1.107 - 1.125) | 1.167 (1.156 - 1.179) |
| 5 | 1.004 (1.002 - 1.006) | 1.010 (1.006 - 1.014) | 1.016 (1.010 - 1.021) | 1.022 (1.016 - 1.029) | 1.036 (1.028 - 1.045) | 1.066 (1.056 - 1.077) | 1.102 (1.089 - 1.115) |
| 6 | 1.000 (0.998 - 1.002) | 1.000 (0.996 - 1.005) | 1.002 (0.996 - 1.008) | 1.004 (0.996 - 1.012) | 1.010 (1.000 - 1.020) | 1.028 (1.016 - 1.041) | 1.053 (1.038 - 1.069) |
| 7 | 0.996 (0.994 - 0.999) | 0.993 (0.988 - 0.998) | 0.991 (0.984 - 0.998) | 0.990 (0.982 - 0.998) | 0.991 (0.980 - 1.001) | 1.000 (0.987 - 1.013) | 1.018 (1.002 - 1.035) |
| 8 | 0.994 (0.991 - 0.996) | 0.988 (0.983 - 0.992) | 0.983 (0.976 - 0.990) | 0.979 (0.971 - 0.988) | 0.976 (0.965 - 0.987) | 0.980 (0.966 - 0.994) | 0.994 (0.977 - 1.011) |
| 9 | 0.992 (0.990 - 0.994) | 0.983 (0.979 - 0.988) | 0.977 (0.970 - 0.984) | 0.972 (0.963 - 0.980) | 0.966 (0.955 - 0.977) | 0.967 (0.953 - 0.980) | 0.979 (0.963 - 0.996) |
| 10 | 0.991 (0.988 - 0.993) | 0.981 (0.976 - 0.985) | 0.973 (0.966 - 0.980) | 0.967 (0.959 - 0.975) | 0.960 (0.950 - 0.970) | 0.959 (0.947 - 0.972) | 0.972 (0.956 - 0.987) |
| 11 | 0.990 (0.988 - 0.992) | 0.979 (0.975 - 0.984) | 0.971 (0.965 - 0.977) | 0.965 (0.957 - 0.972) | 0.957 (0.947 - 0.967) | 0.957 (0.945 - 0.969) | 0.971 (0.957 - 0.985) |
| 12 | 0.989 (0.987 - 0.991) | 0.979 (0.974 - 0.983) | 0.970 (0.964 - 0.976) | 0.964 (0.957 - 0.971) | 0.957 (0.948 - 0.966) | 0.959 (0.948 - 0.969) | 0.975 (0.963 - 0.988) |
| 13 | 0.989 (0.988 - 0.991) | 0.979 (0.975 - 0.983) | 0.971 (0.965 - 0.976) | 0.965 (0.958 - 0.971) | 0.959 (0.950 - 0.967) | 0.963 (0.954 - 0.973) | 0.984 (0.973 - 0.995) |
| 14 | 0.990 (0.988 - 0.992) | 0.979 (0.976 - 0.983) | 0.972 (0.967 - 0.977) | 0.967 (0.960 - 0.973) | 0.962 (0.954 - 0.970) | 0.970 (0.962 - 0.979) | 0.996 (0.987 - 1.006) |
| 15 | 0.990 (0.988 - 0.992) | 0.981 (0.977 - 0.984) | 0.974 (0.968 - 0.979) | 0.969 (0.963 - 0.976) | 0.966 (0.958 - 0.974) | 0.979 (0.970 - 0.988) | 1.011 (1.001 - 1.020) |

*Effects are relative to a unit increase in reference level

TABLE 3.34: Joint effect of lag (days) and new positive SARS-CoV-2 swabs per 100,000 inhabitants on predicted incidence rate ratio (IRR) of ED visit with respiratory diagnosis during the second wave

| | IRR | | | | | | |
|---|---|---|---|---|---|---|---|
| **Lag (days)** | **Reference level*: 5x100000** | **Reference level*: 10x100000** | **Reference level*: 15x100000** | **Reference level*: 20x100000** | **Reference level*: 50x100000** | **Reference level*: 100x100000** | **Reference level*: 200x100000** |
| 0 | 0.999 (0.995 - 1.002) | 0.997 (0.990 - 1.004) | 0.996 (0.986 - 1.007) | 0.996 (0.982 - 1.010) | 1.005 (0.974 - 1.036) | 1.054 (1.005 - 1.105) | 1.258 (1.185 - 1.336) |
| 1 | 0.998 (0.996 - 1.000) | 0.996 (0.991 - 1.001) | 0.995 (0.987 - 1.002) | 0.994 (0.984 - 1.004) | 0.998 (0.976 - 1.019) | 1.035 (1.001 - 1.070) | 1.199 (1.150 - 1.251) |
| 2 | 0.998 (0.996 - 0.999) | 0.996 (0.992 - 0.999) | 0.994 (0.989 - 0.999) | 0.992 (0.986 - 0.999) | 0.992 (0.978 - 1.006) | 1.019 (0.997 - 1.042) | 1.150 (1.119 - 1.182) |
| 3 | 0.998 (0.997 - 0.999) | 0.995 (0.993 - 0.997) | 0.993 (0.990 - 0.996) | 0.991 (0.987 - 0.996) | 0.988 (0.979 - 0.997) | 1.006 (0.992 - 1.021) | 1.108 (1.088 - 1.128) |
| 4 | 0.998 (0.997 - 0.998) | 0.995 (0.993 - 0.997) | 0.993 (0.990 - 0.995) | 0.991 (0.987 - 0.994) | 0.985 (0.977 - 0.993) | 0.996 (0.984 - 1.008) | 1.073 (1.057 - 1.090) |
| 5 | 0.998 (0.997 - 0.999) | 0.995 (0.993 - 0.997) | 0.992 (0.989 - 0.996) | 0.990 (0.986 - 0.994) | 0.983 (0.974 - 0.992) | 0.988 (0.974 - 1.002) | 1.044 (1.025 - 1.063) |
| 6 | 0.998 (0.997 - 0.999) | 0.995 (0.993 - 0.997) | 0.993 (0.989 - 0.996) | 0.990 (0.985 - 0.995) | 0.982 (0.971 - 0.992) | 0.982 (0.965 - 0.998) | 1.020 (0.998 - 1.042) |
| 7 | 0.998 (0.997 - 0.999) | 0.995 (0.992 - 0.998) | 0.993 (0.989 - 0.997) | 0.991 (0.985 - 0.996) | 0.981 (0.969 - 0.994) | 0.977 (0.959 - 0.996) | 1.001 (0.976 - 1.026) |
| 8 | 0.998 (0.997 - 0.999) | 0.996 (0.993 - 0.999) | 0.993 (0.989 - 0.998) | 0.991 (0.985 - 0.997) | 0.981 (0.968 - 0.995) | 0.975 (0.955 - 0.995) | 0.985 (0.959 - 1.011) |
| 9 | 0.998 (0.997 - 1.000) | 0.996 (0.993 - 0.999) | 0.994 (0.989 - 0.999) | 0.992 (0.986 - 0.998) | 0.982 (0.969 - 0.996) | 0.973 (0.953 - 0.994) | 0.973 (0.947 - 0.999) |
| 10 | 0.998 (0.997 - 1.000) | 0.996 (0.993 - 1.000) | 0.995 (0.990 - 0.999) | 0.993 (0.987 - 0.999) | 0.983 (0.970 - 0.997) | 0.973 (0.953 - 0.993) | 0.964 (0.939 - 0.990) |
| 11 | 0.999 (0.997 - 1.000) | 0.997 (0.994 - 1.000) | 0.995 (0.991 - 1.000) | 0.994 (0.988 - 1.000) | 0.985 (0.972 - 0.998) | 0.973 (0.954 - 0.992) | 0.957 (0.934 - 0.982) |
| 12 | 0.999 (0.998 - 1.000) | 0.997 (0.995 - 1.000) | 0.996 (0.992 - 1.000) | 0.995 (0.989 - 1.000) | 0.987 (0.975 - 0.998) | 0.974 (0.956 - 0.992) | 0.953 (0.931 - 0.976) |
| 13 | 0.999 (0.998 - 1.000) | 0.998 (0.995 - 1.000) | 0.997 (0.993 - 1.001) | 0.996 (0.991 - 1.001) | 0.988 (0.978 - 0.999) | 0.976 (0.959 - 0.992) | 0.951 (0.931 - 0.971) |
| 14 | 0.999 (0.998 - 1.000) | 0.998 (0.996 - 1.001) | 0.997 (0.994 - 1.001) | 0.996 (0.992 - 1.001) | 0.990 (0.980 - 1.000) | 0.978 (0.963 - 0.993) | 0.950 (0.932 - 0.969) |
| 15 | 0.999 (0.998 - 1.000) | 0.999 (0.997 - 1.001) | 0.998 (0.995 - 1.001) | 0.997 (0.993 - 1.002) | 0.992 (0.982 - 1.001) | 0.980 (0.965 - 0.994) | 0.951 (0.934 - 0.969) |

*Effects are relative to a unit increase in reference level

### *3.7.2 Figures*


FIGURE 3.1: Areas served by the Health Protection Agencies (HPA, IT: Agenzie di Tutela della Salute) of Bergamo and Brescia. Each HPA is subdivided into districts.

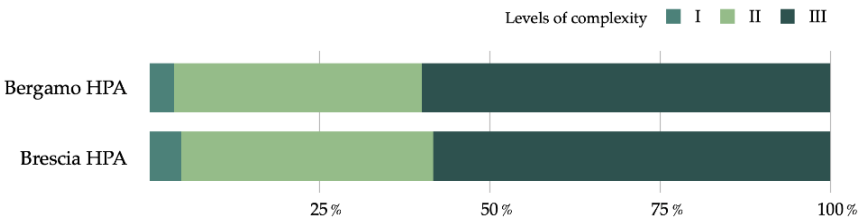


FIGURE 3.2: Proportion of patients with chronic or long-term conditions by the level of complexity. Source: OpenData website of Lombardy Region (2012). HPA, Health Protection Agency

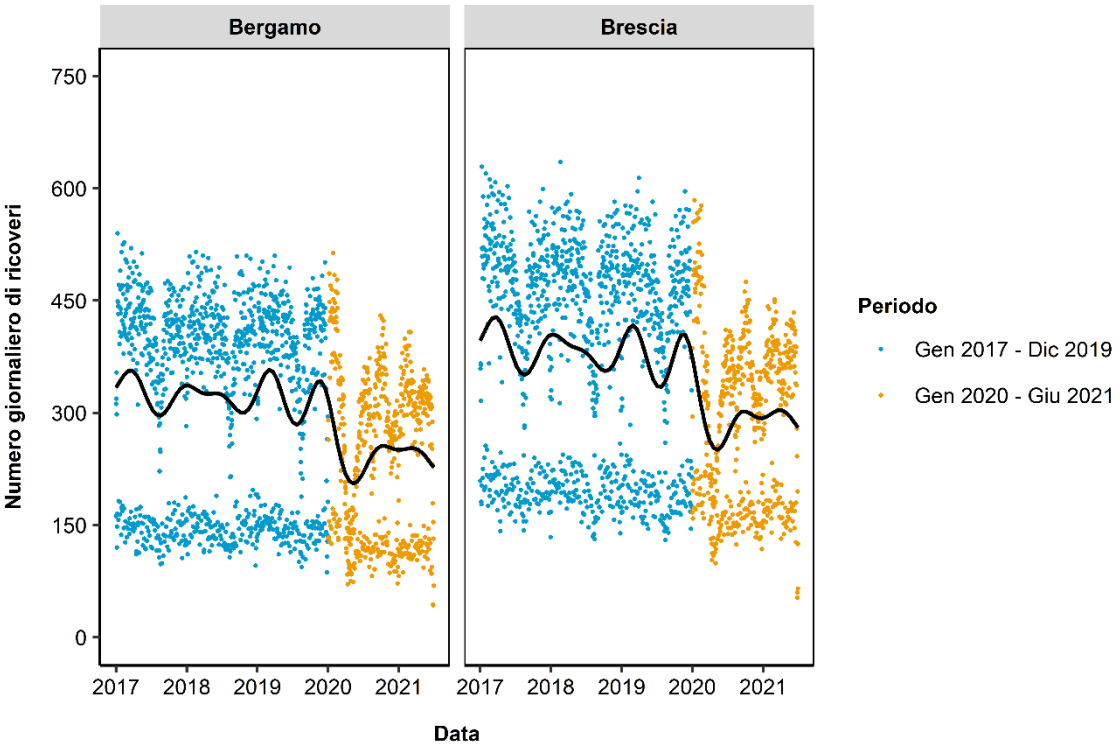


FIGURE 3.3: Time series of the daily number of hospital admissions in the general population of the two HPAs

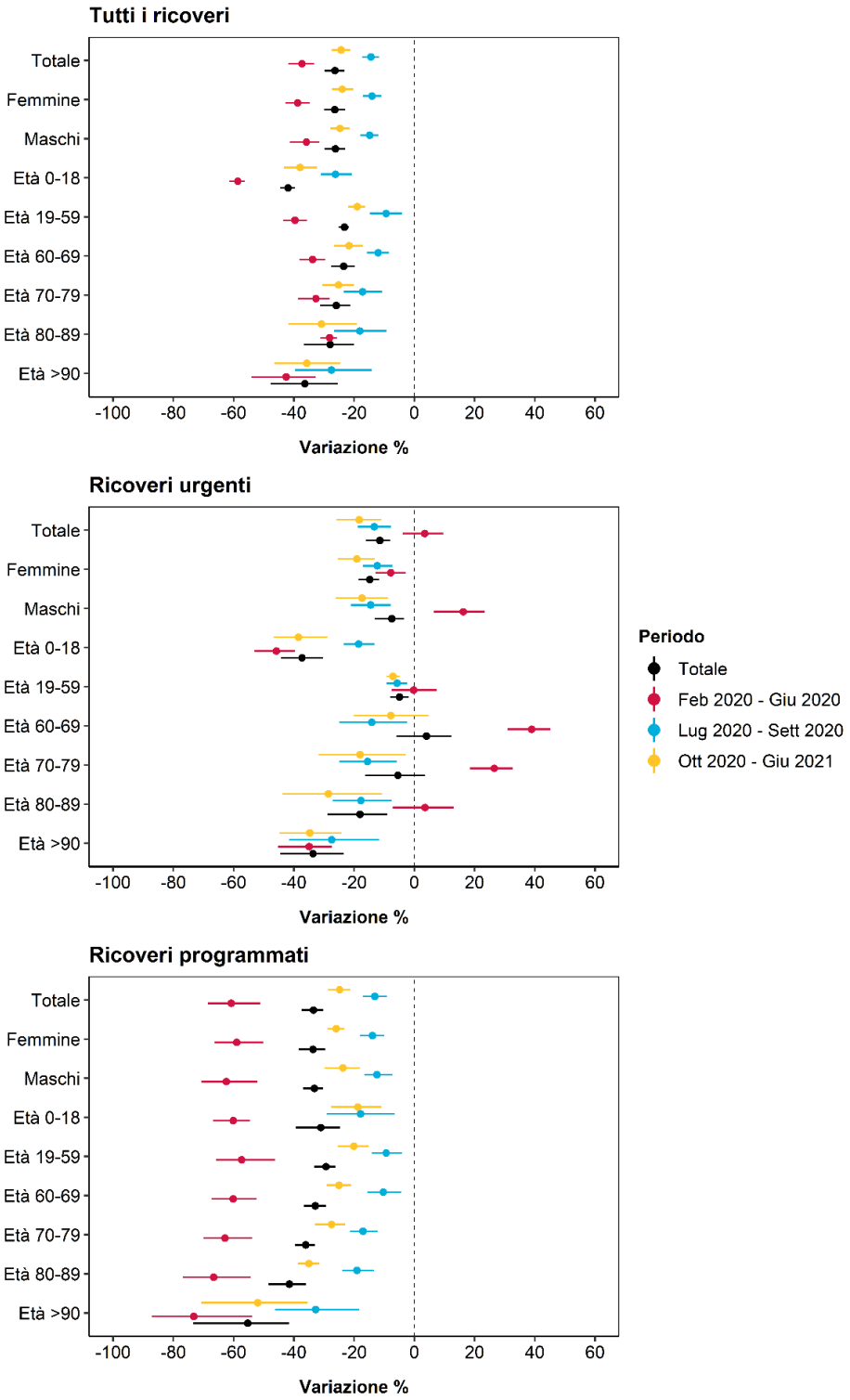


FIGURE 3.4: Estimated variation of hospital admissions in Bergamo HPA, stratified by type of admission (total, urgent and elective), and sex and age

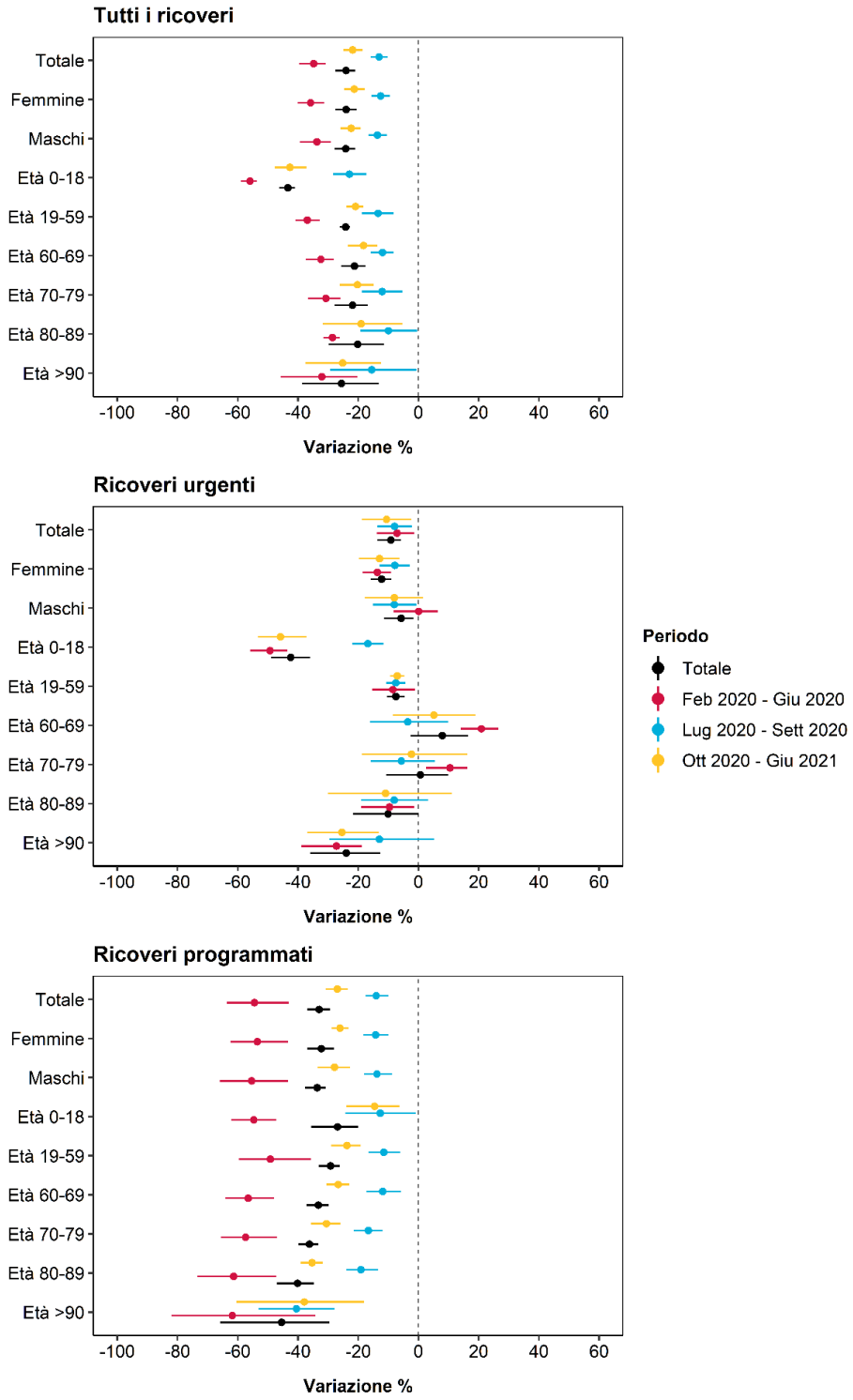


FIGURE 3.5: Estimated variation of hospital admissions in Brescia HPA, stratified by type of admission (total, urgent and elective), and sex and age

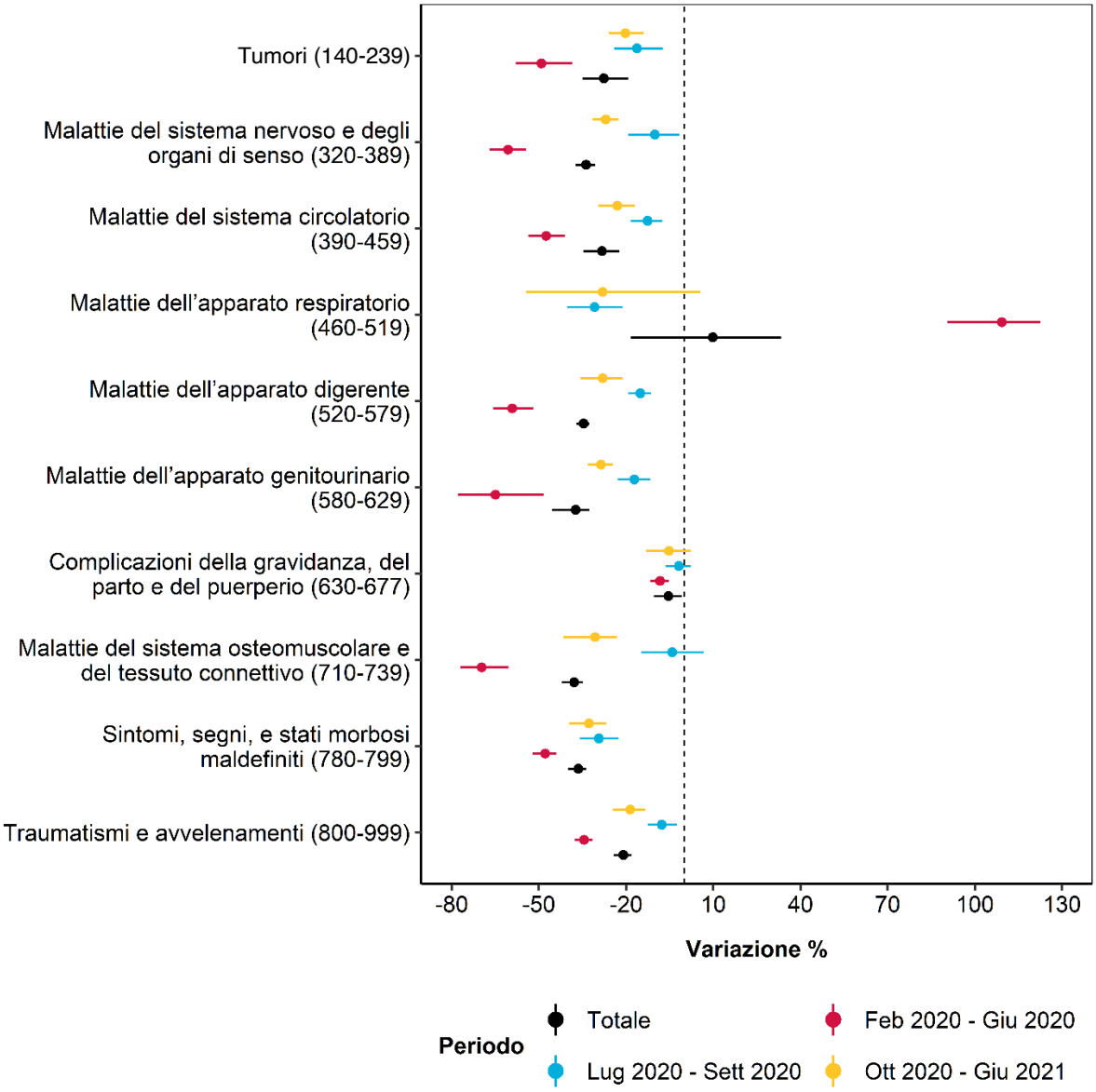


FIGURE 3.6a: Estimated variation of total hospital admissions in Bergamo HPA, stratified by main diagnosis (based on ICD-9-CM codes)

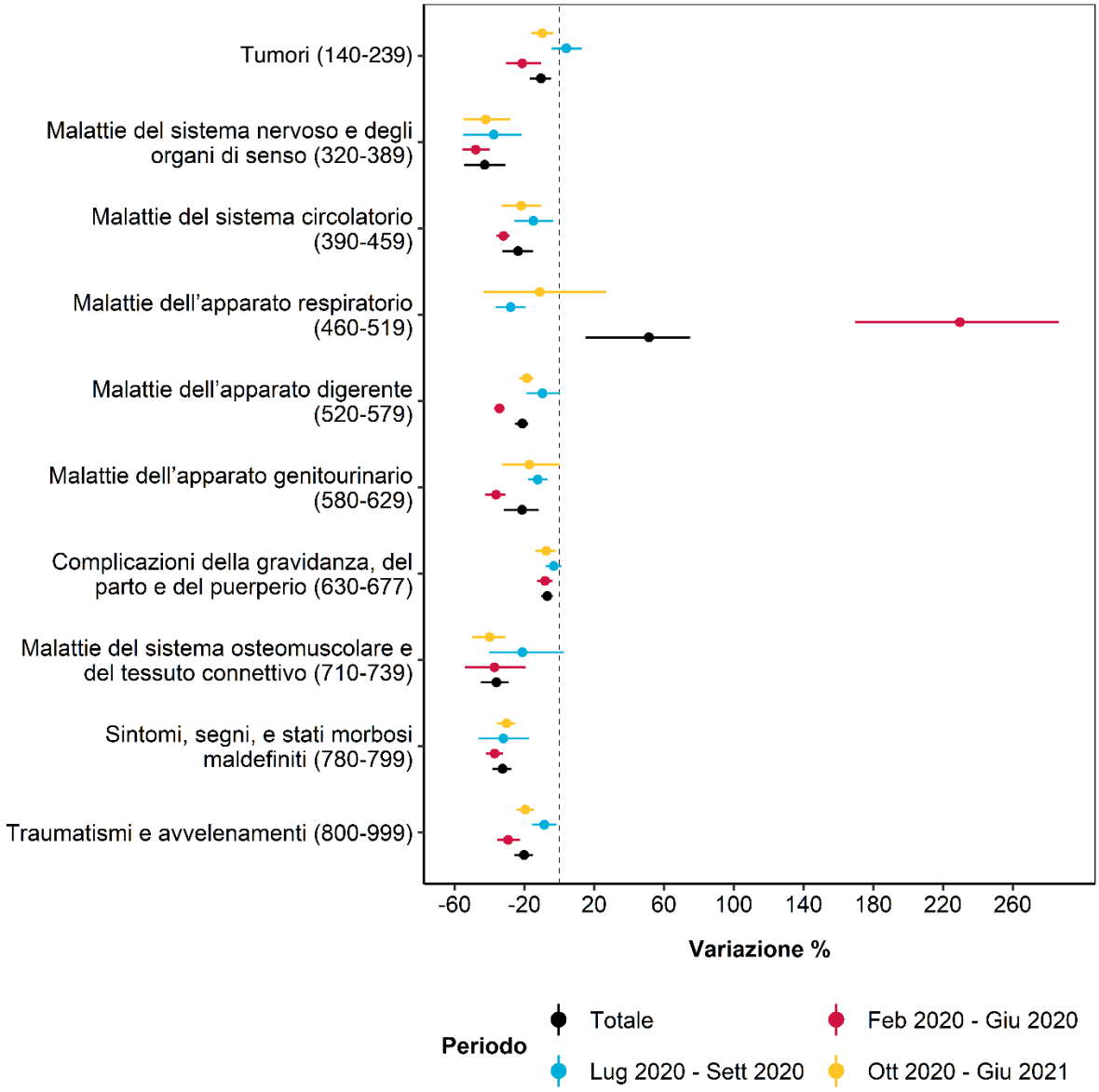


FIGURE 3.6b: Estimated variation of urgent hospital admissions in Bergamo HPA, stratified by main diagnosis (based on ICD-9-CM codes)

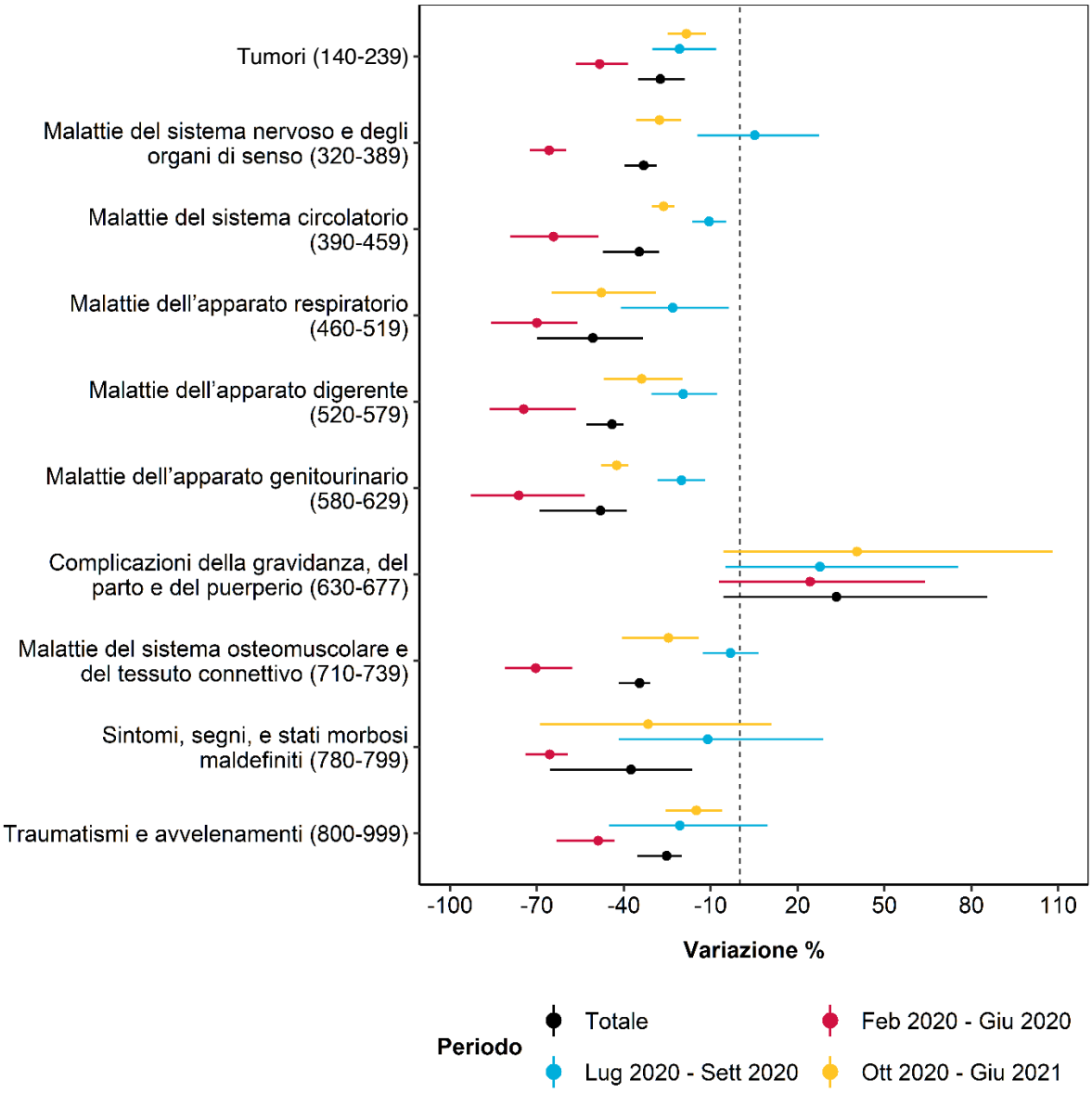


FIGURE 3.6c: Estimated variation of elective hospital admissions in Bergamo HPA, stratified by main diagnosis (based on ICD-9-CM codes)

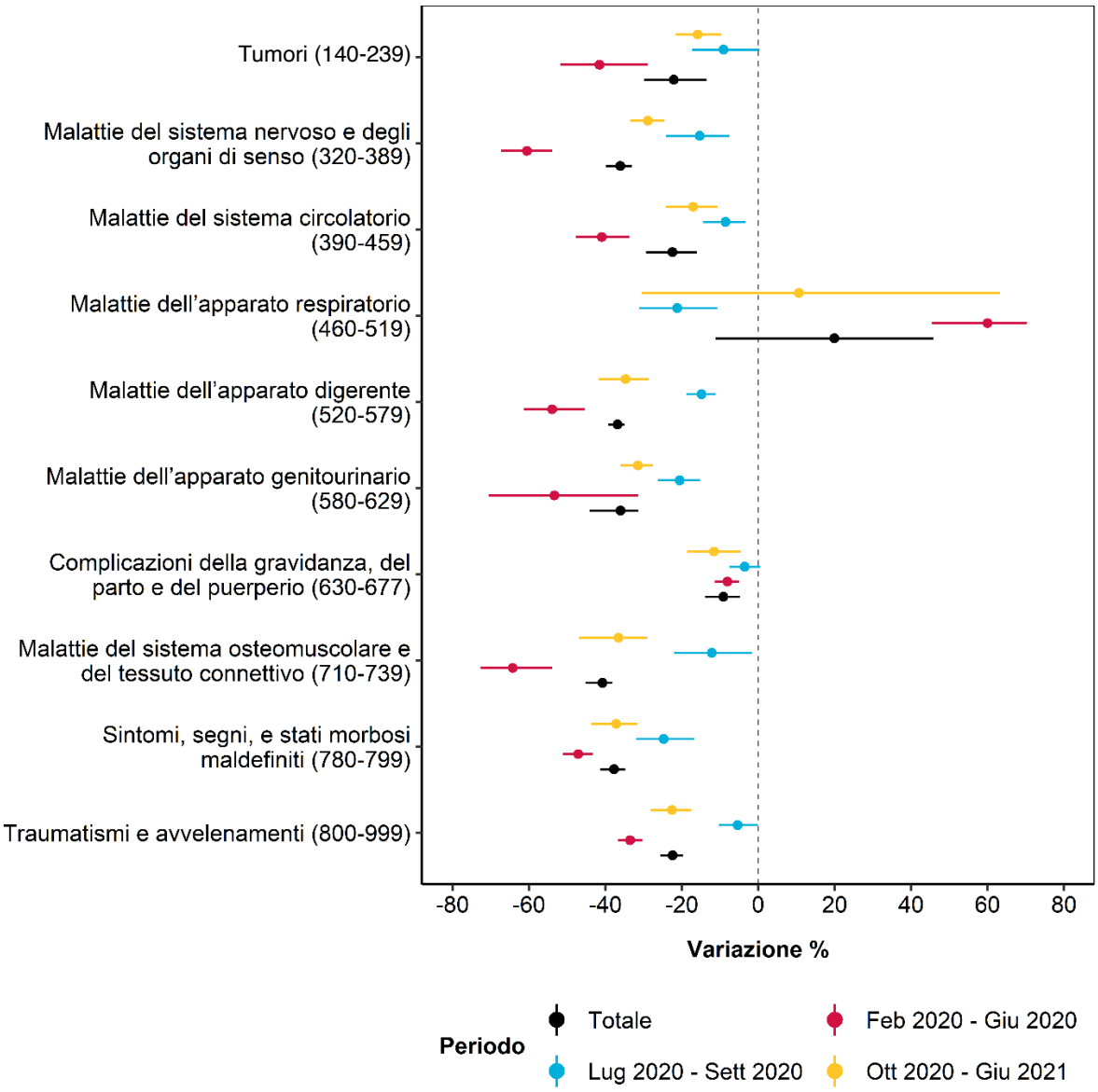


FIGURE 3.7a: Estimated variation of total hospital admissions in Brescia HPA, stratified by main diagnosis (based on ICD-9-CM codes)

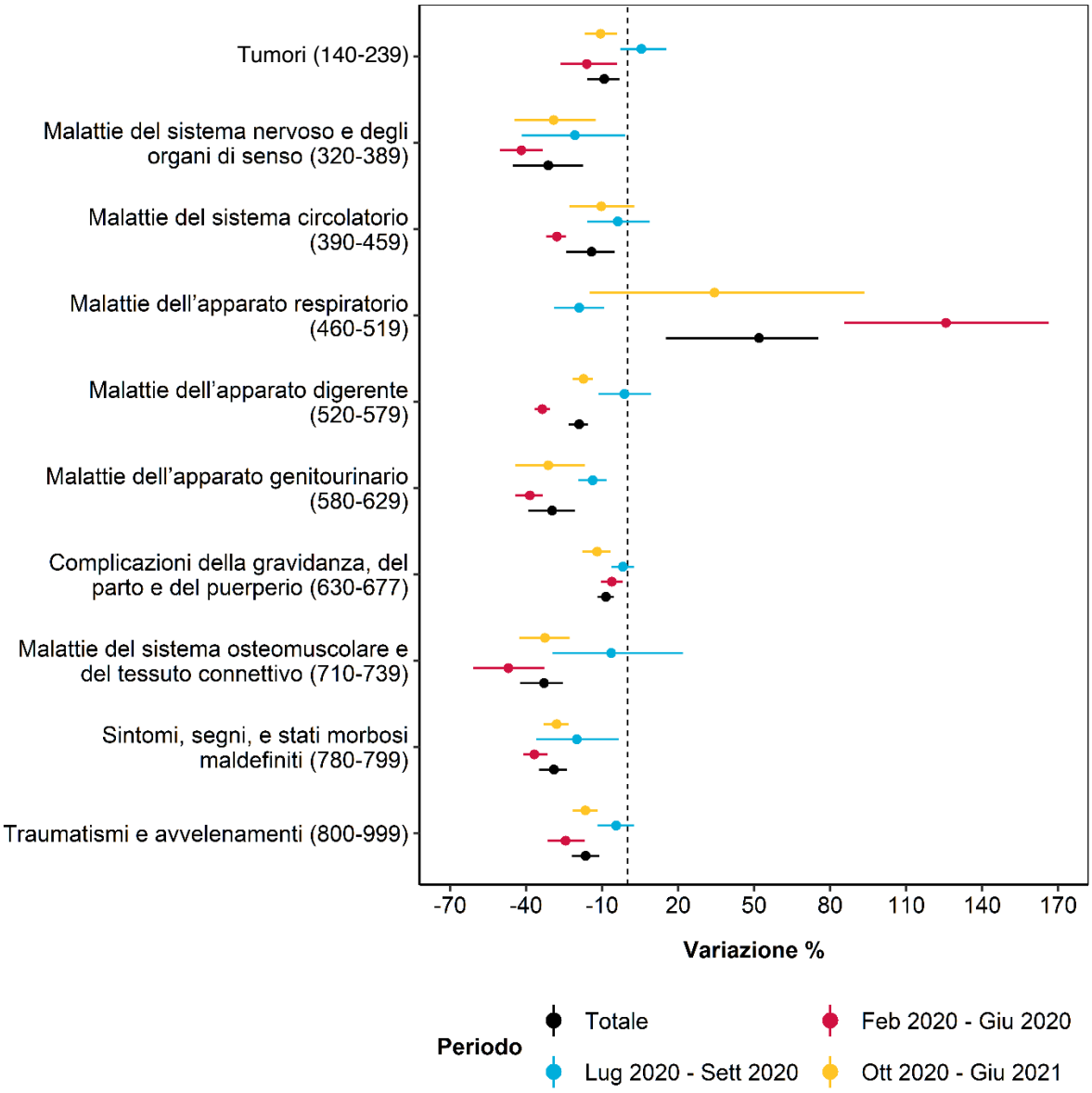


FIGURE 3.7b: Estimated variation of urgent hospital admissions in Brescia HPA, stratified by main diagnosis (based on ICD-9-CM codes)

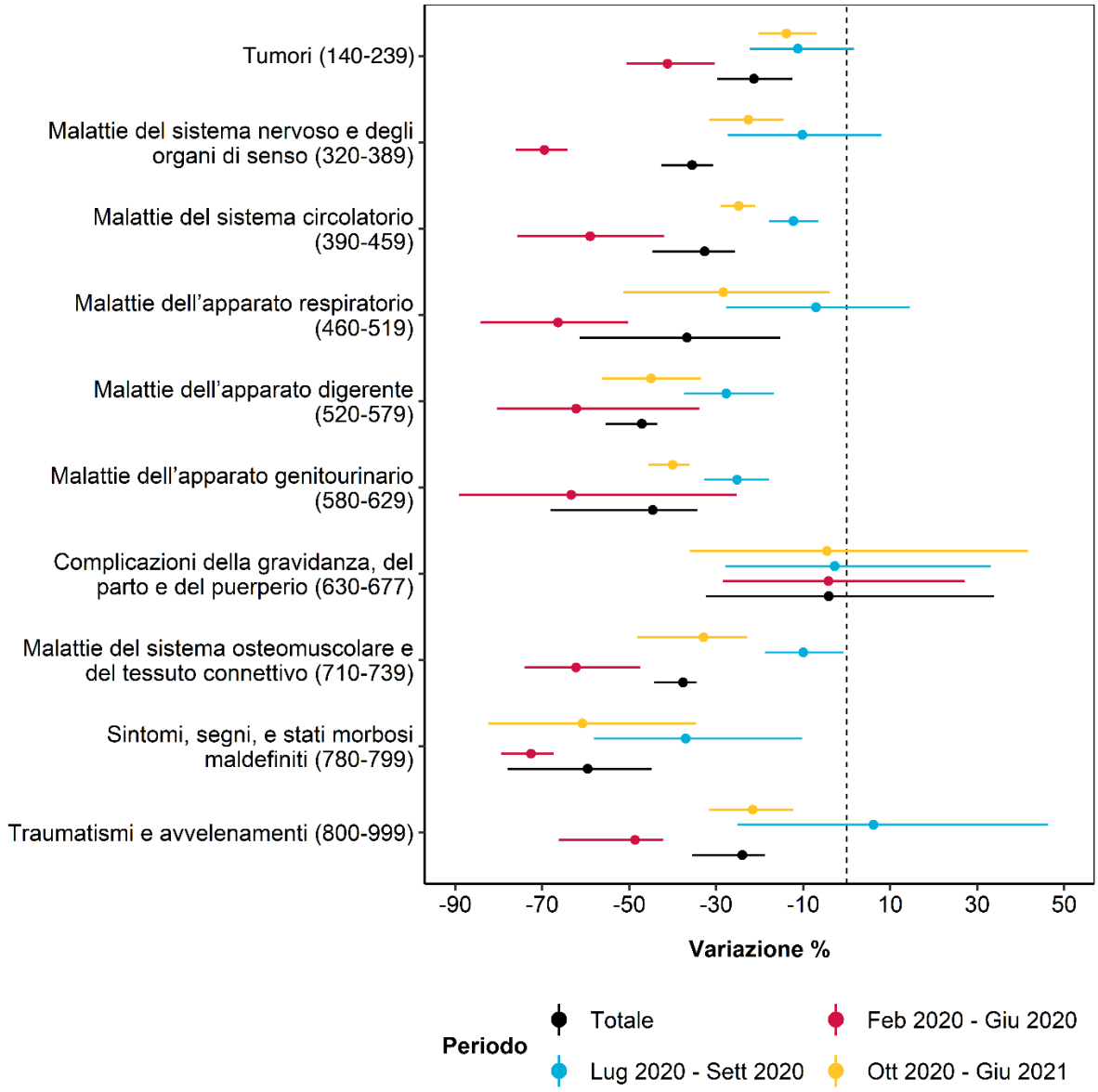


FIGURE 3.7c: Estimated variation of elective hospital admissions in Brescia HPA, stratified by main diagnosis (based on ICD-9-CM codes)

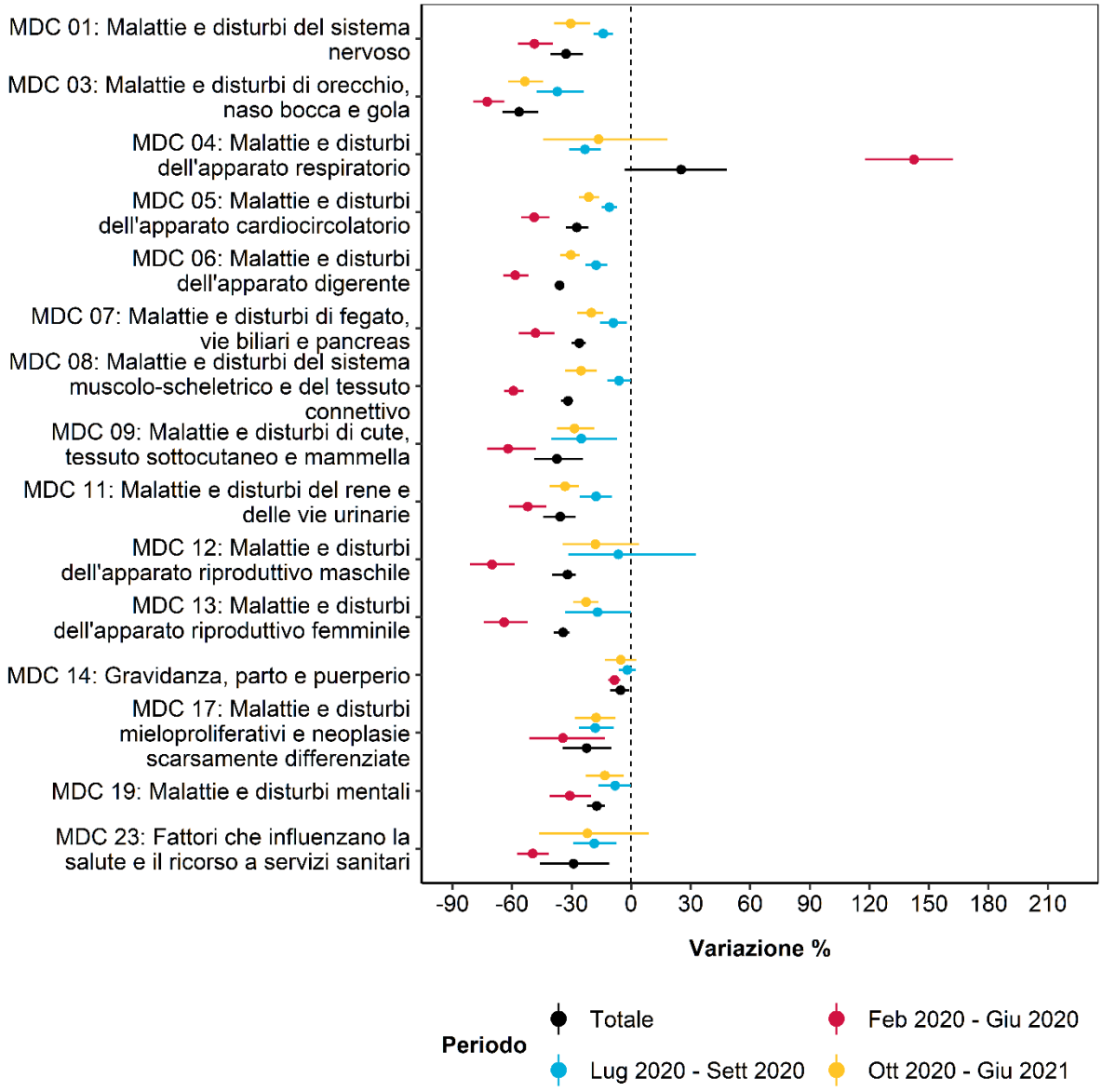


FIGURE 3.8: Estimated variation of total hospital admissions in Bergamo HPA, stratified by Major Diagnostic Category (MDC)

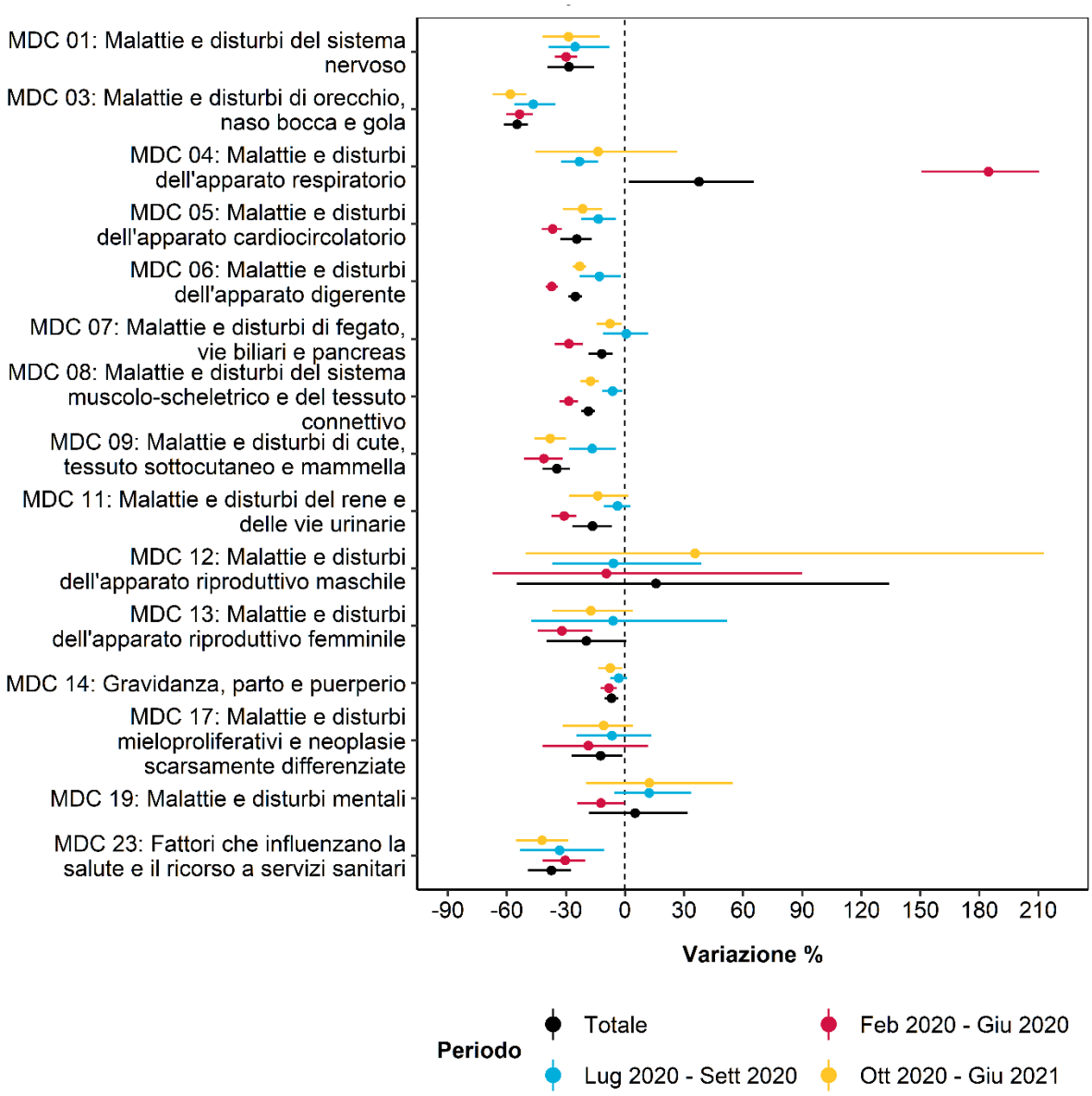


FIGURE 3.8b: Estimated variation of urgent hospital admissions in Bergamo HPA, stratified by Major Diagnostic Category (MDC)

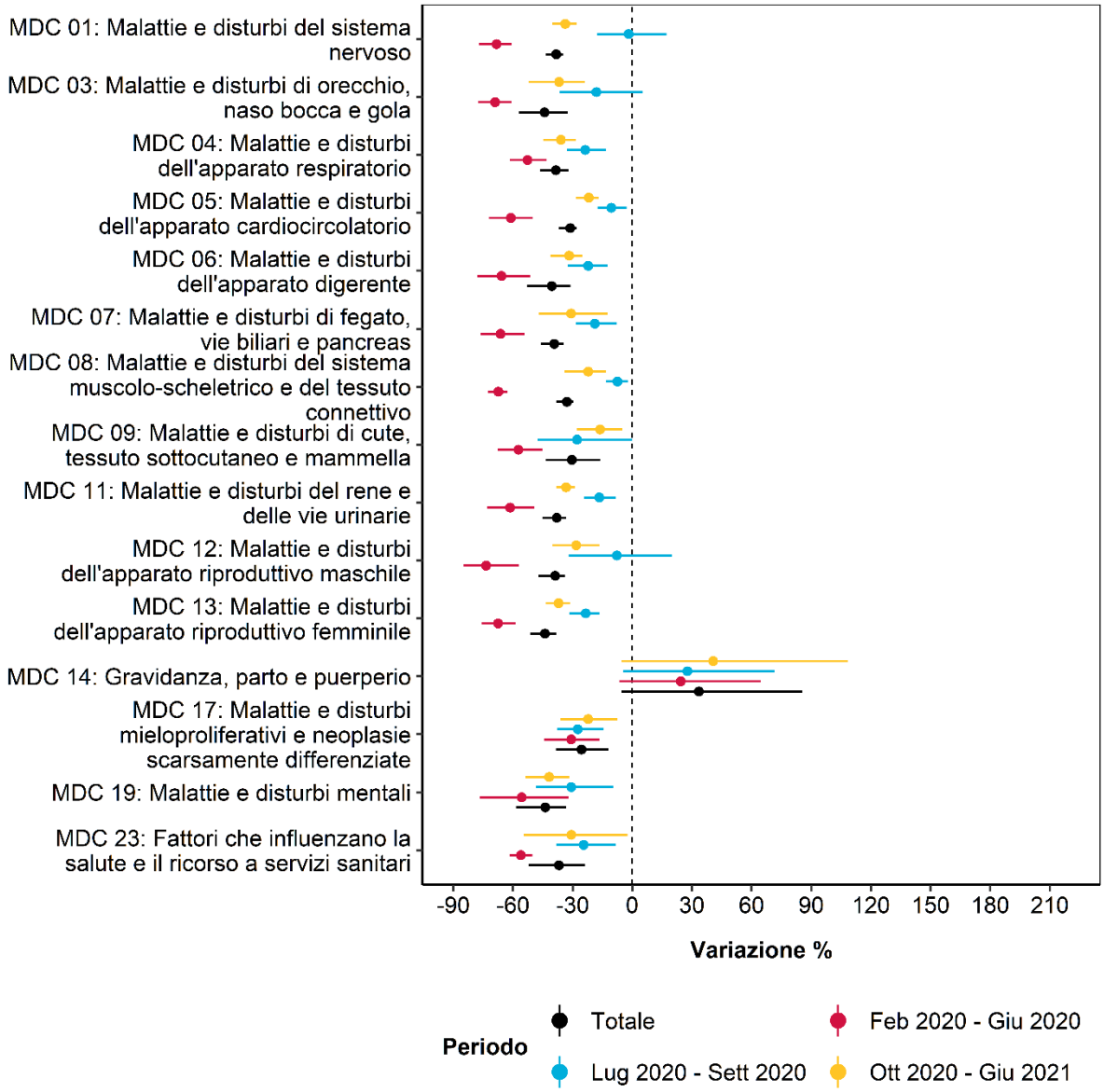


FIGURE 3.8c: Estimated variation of elective hospital admissions in Bergamo HPA, stratified by Major Diagnostic Category (MDC)

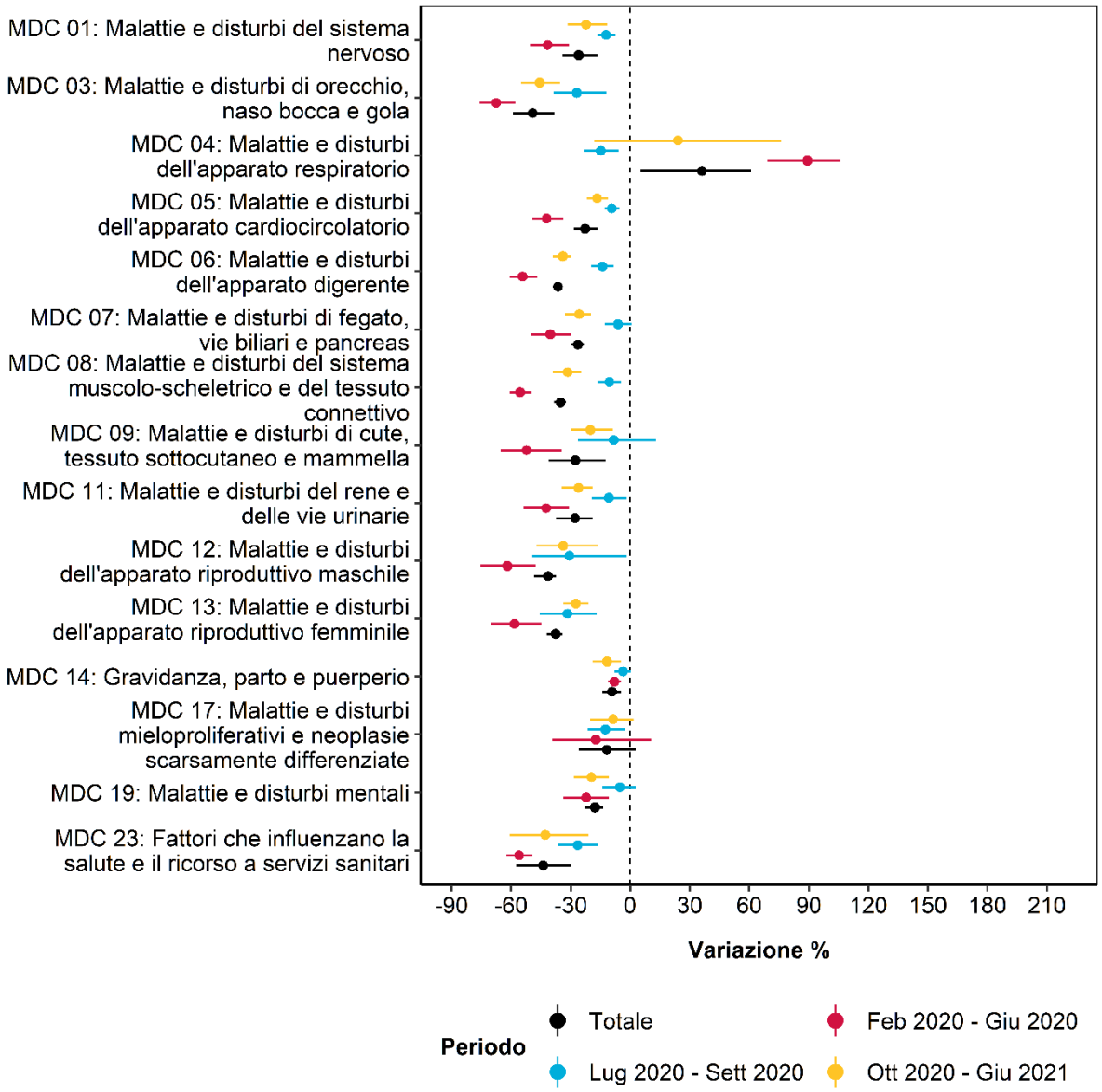


FIGURE 3.9a: Estimated variation of total hospital admissions in Brescia HPA, stratified by Major Diagnostic Category (MDC)

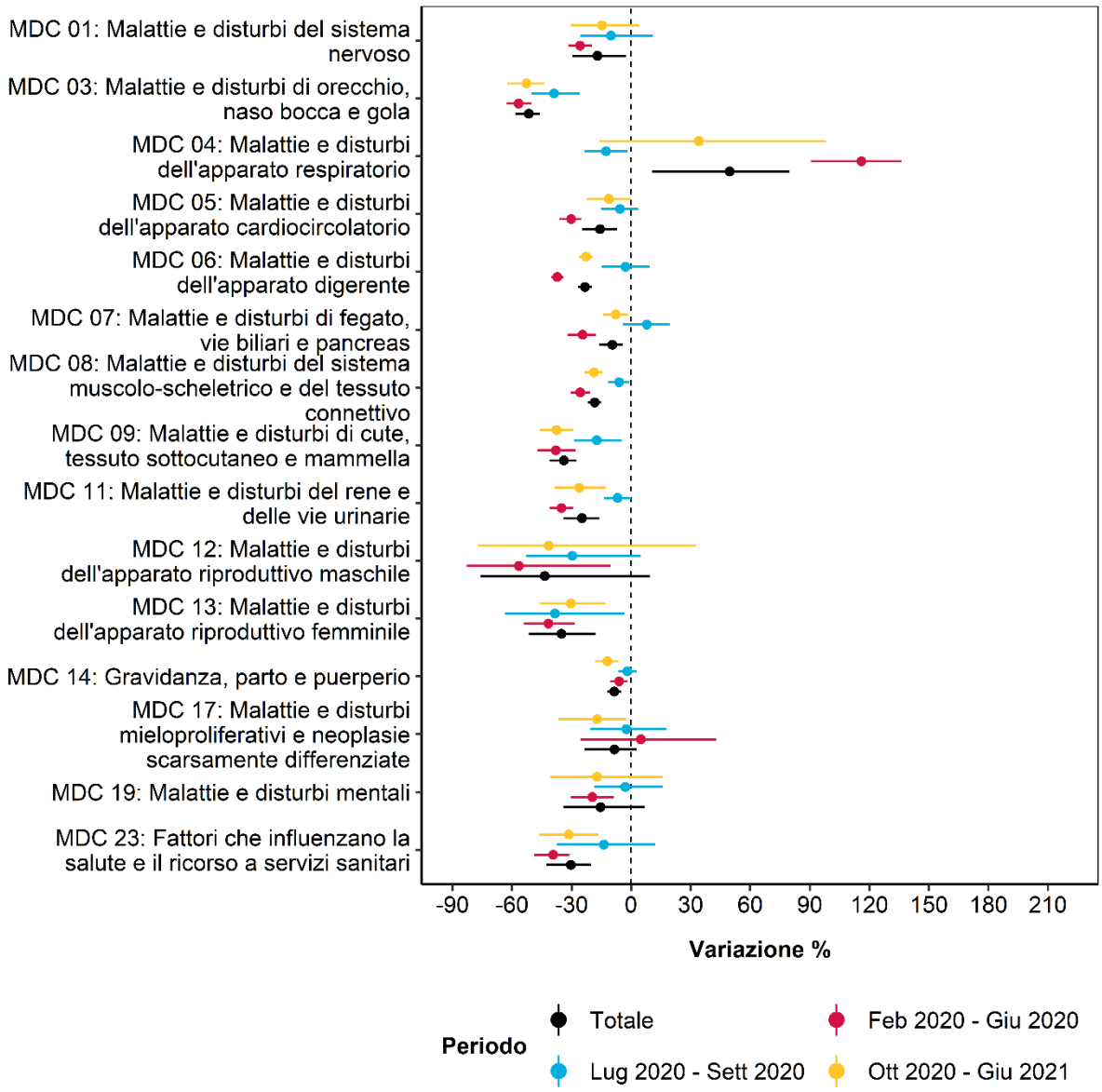


FIGURE 3.9b: Estimated variation of urgent hospital admissions in Brescia HPA, stratified by Major Diagnostic Category (MDC)

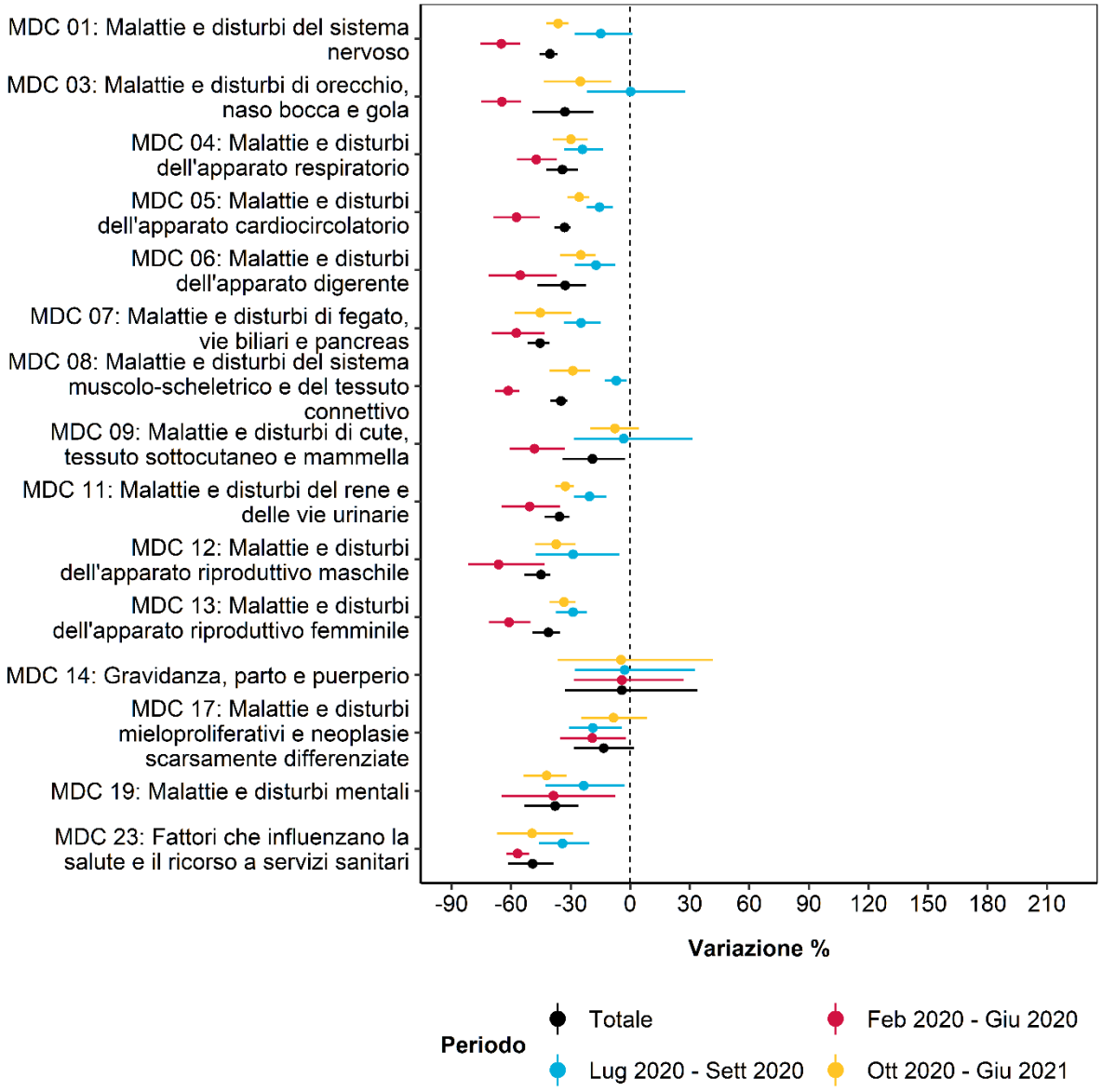


FIGURE 3.9c: Estimated variation of elective hospital admissions in Brescia HPA, stratified by Major Diagnostic Category (MDC)

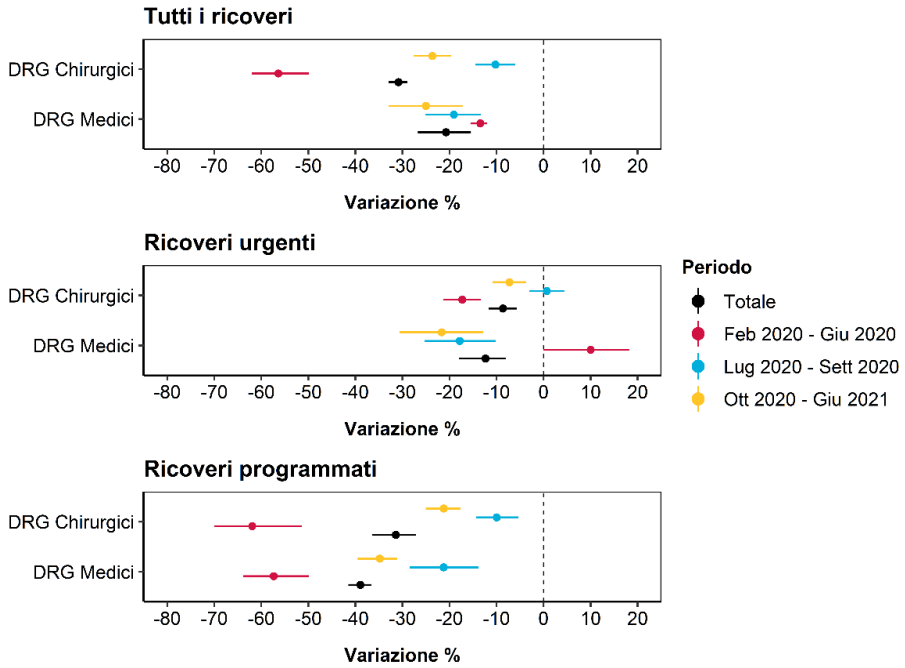


FIGURE 3.10: Estimated variation of hospital admissions in Bergamo HPA, stratified by type of admission (total, urgent and elective) and Diagnosis Related Group (DRG)

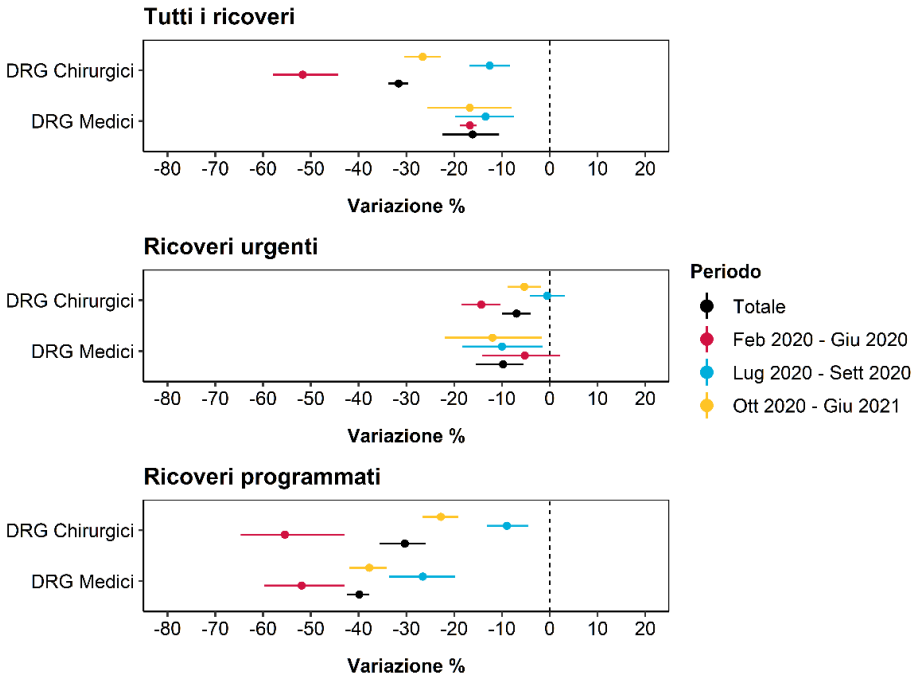


FIGURE 3.11: Estimated variation of hospital admissions in Brescia HPA, stratified by type of admission (total,

urgent and elective) and Diagnosis Related Group (DRG)

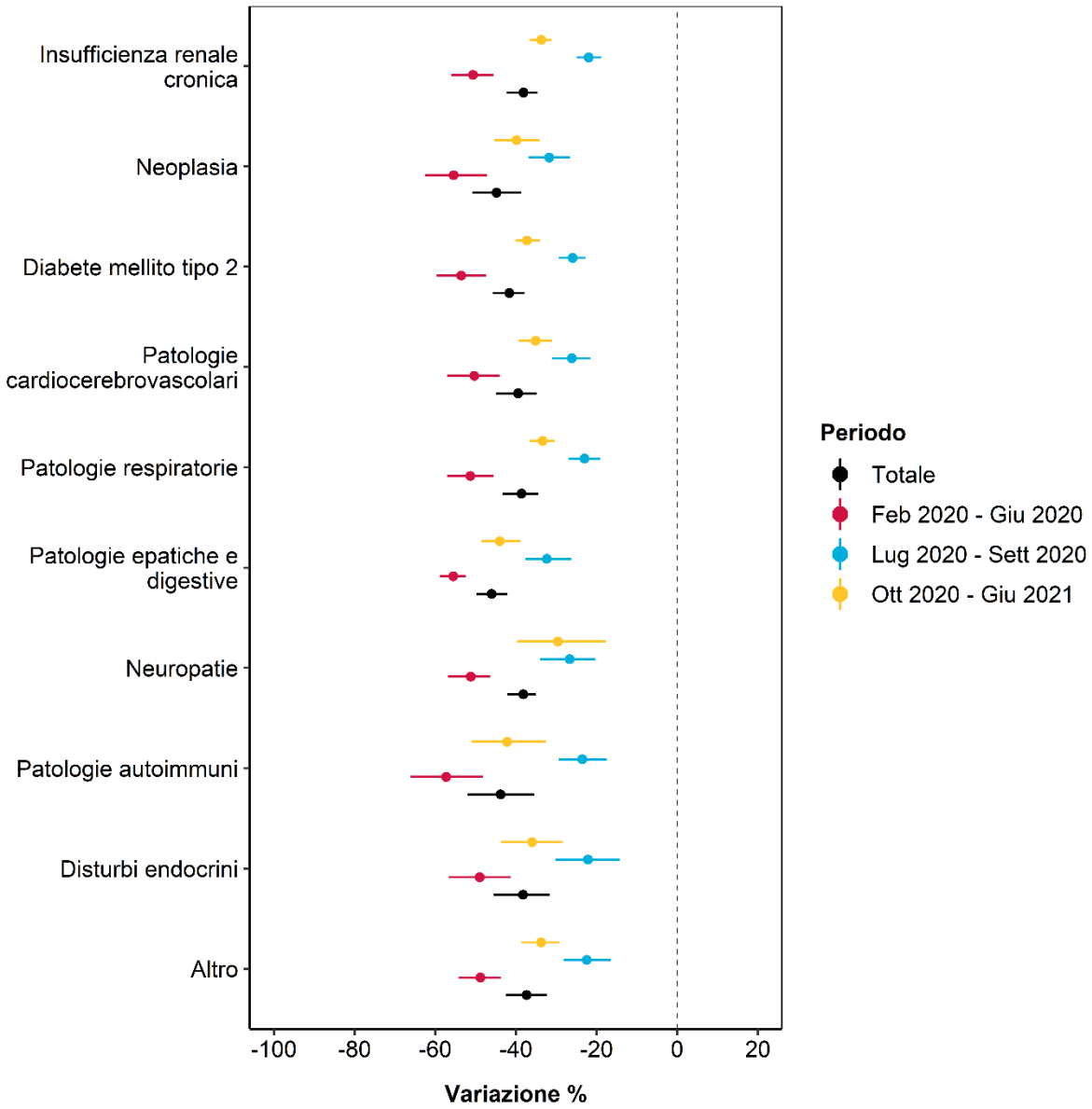


FIGURE 3.12a: Estimated variation of total hospital admissions in patients with chronic condition of Bergamo HPA, stratified by comorbidity

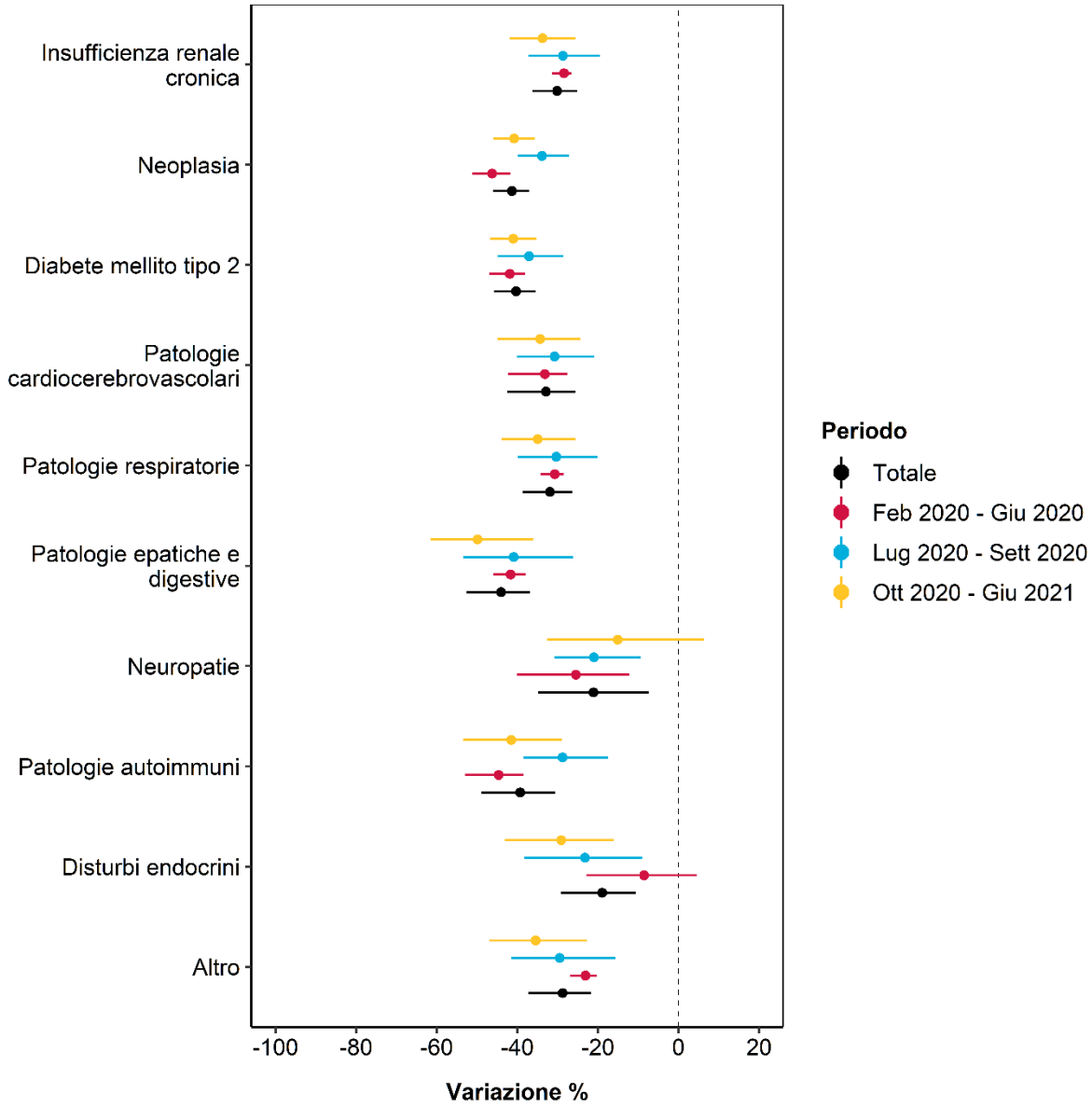


FIGURE 3.12b: Estimated variation of urgent hospital admissions in patients with chronic condition of Bergamo HPA, stratified by comorbidity

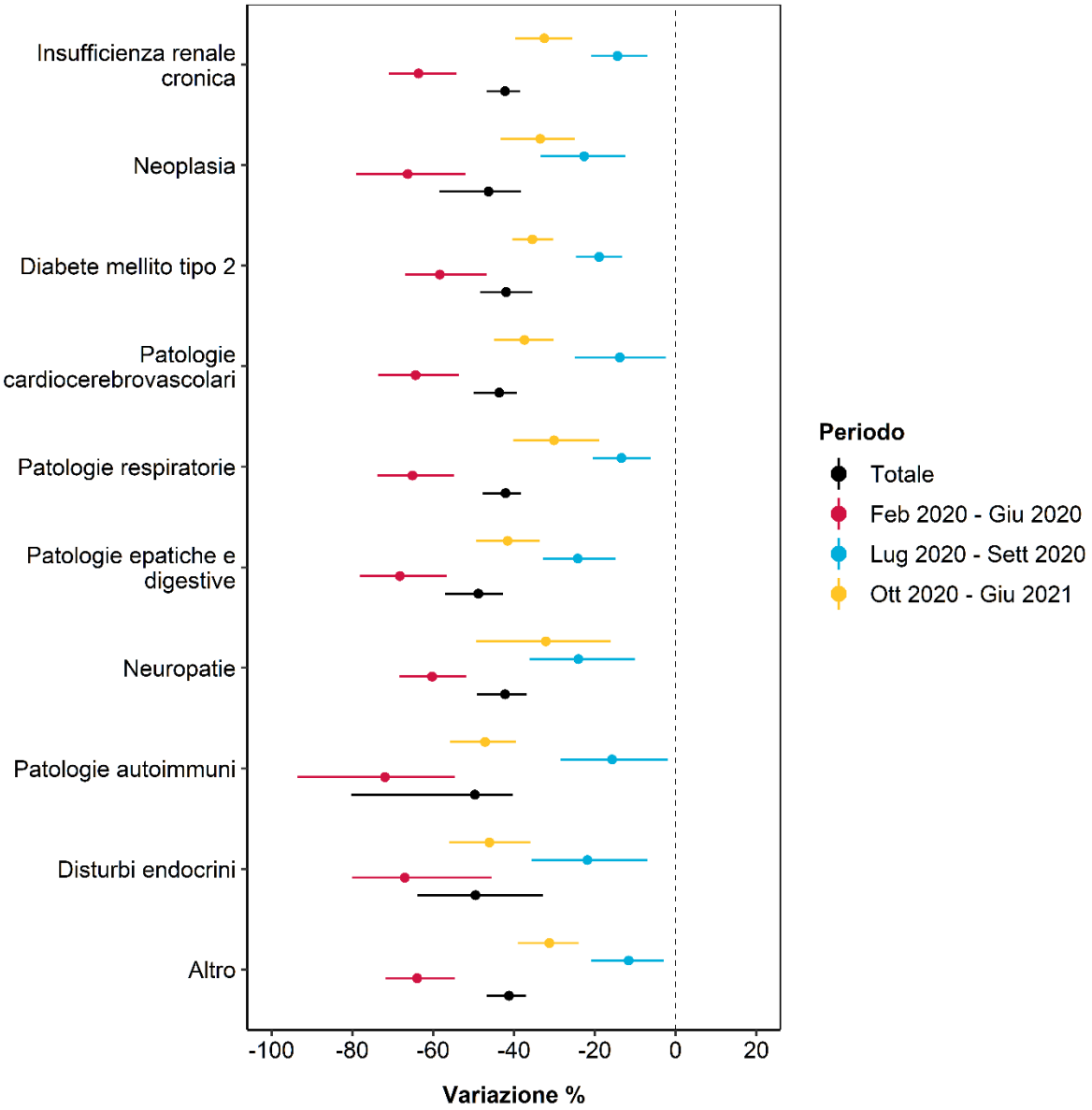


FIGURE 3.12c: Estimated variation of elective hospital admissions in patients with chronic condition of Bergamo HPA, stratified by comorbidity

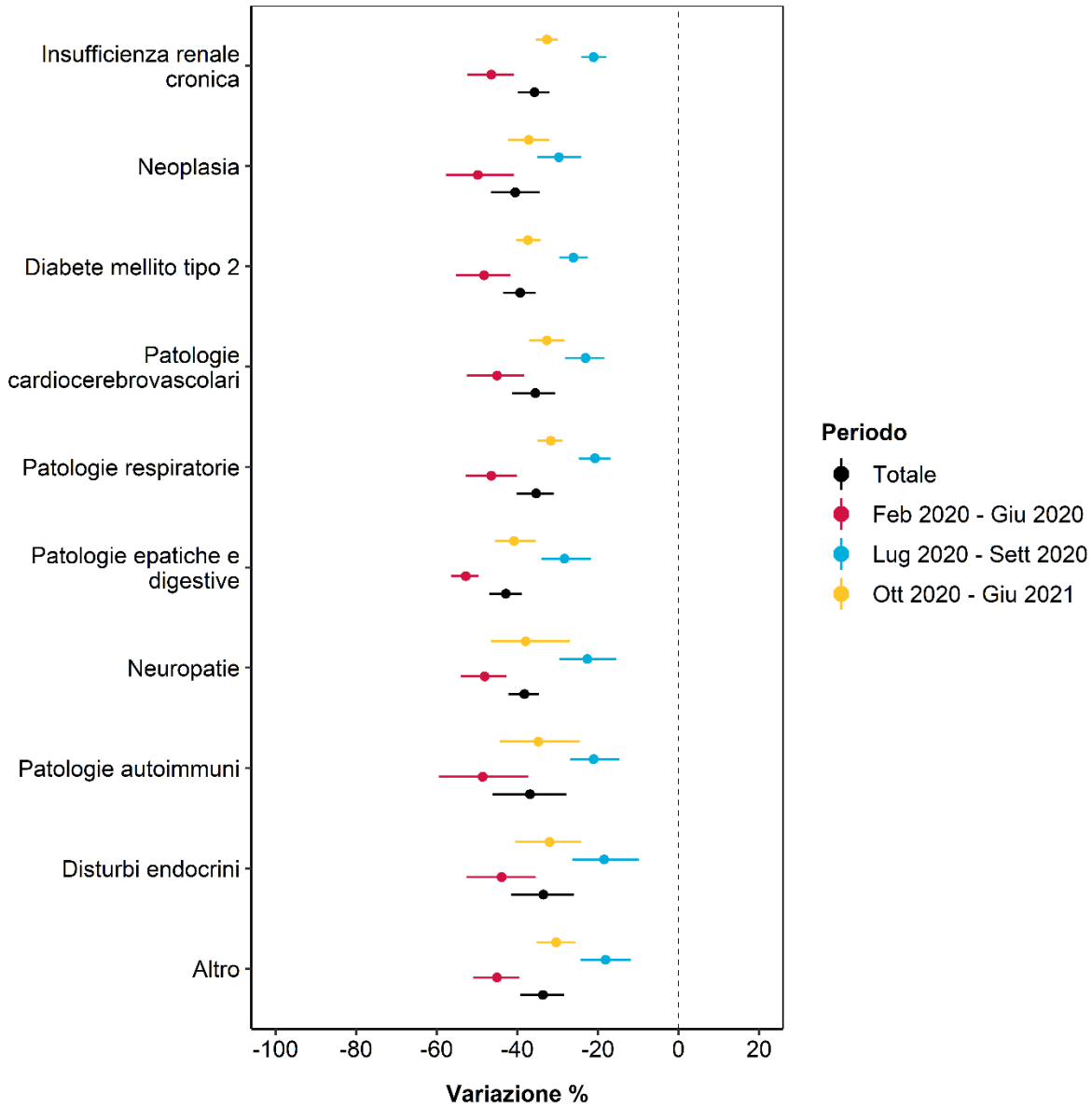


FIGURE 3.13a: Estimated variation of total hospital admissions in patients with chronic condition of Brescia HPA, stratified by comorbidity

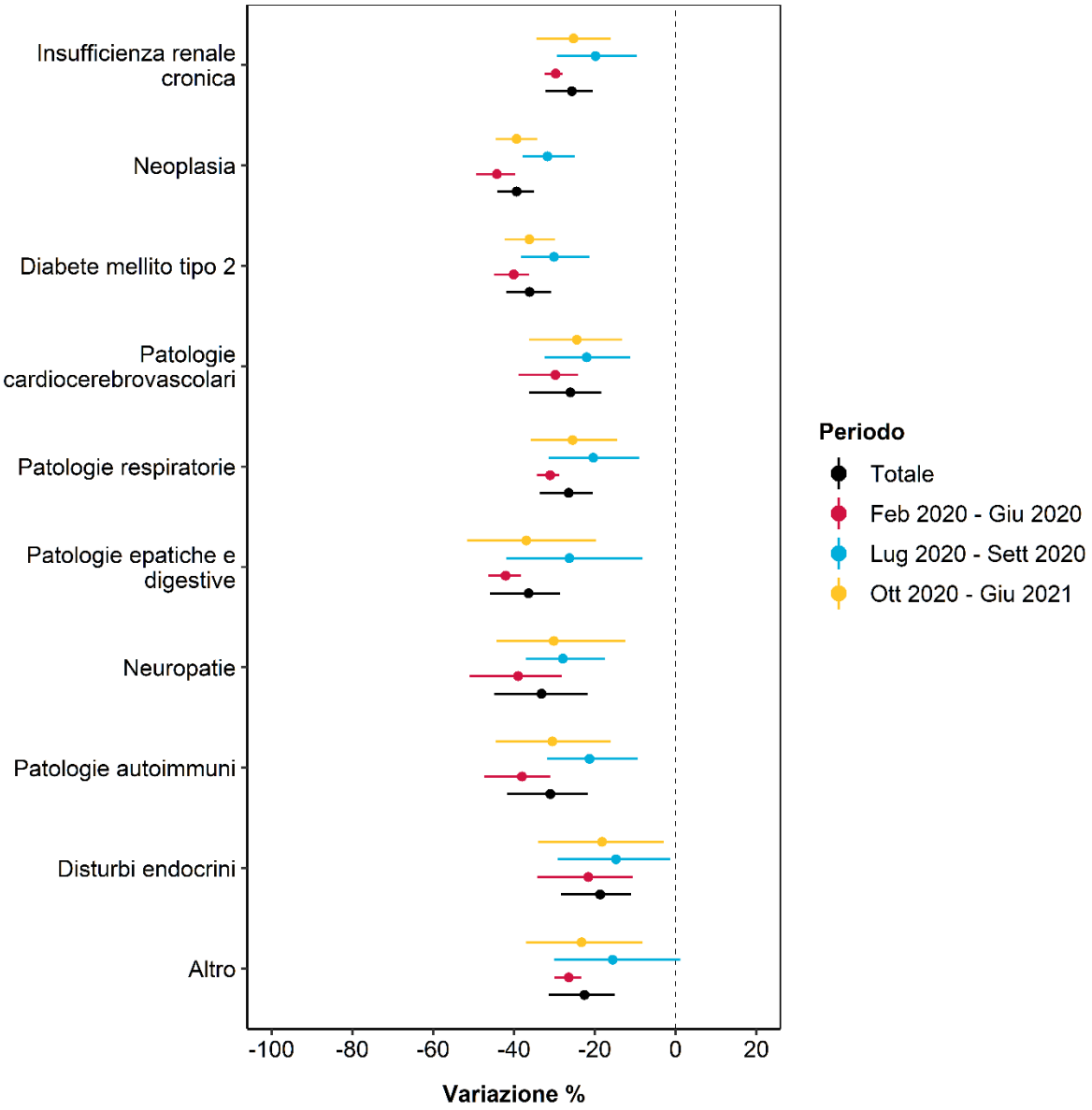


FIGURE 3.13b: Estimated variation of urgent hospital admissions in patients with chronic condition of Brescia HPA, stratified by comorbidity

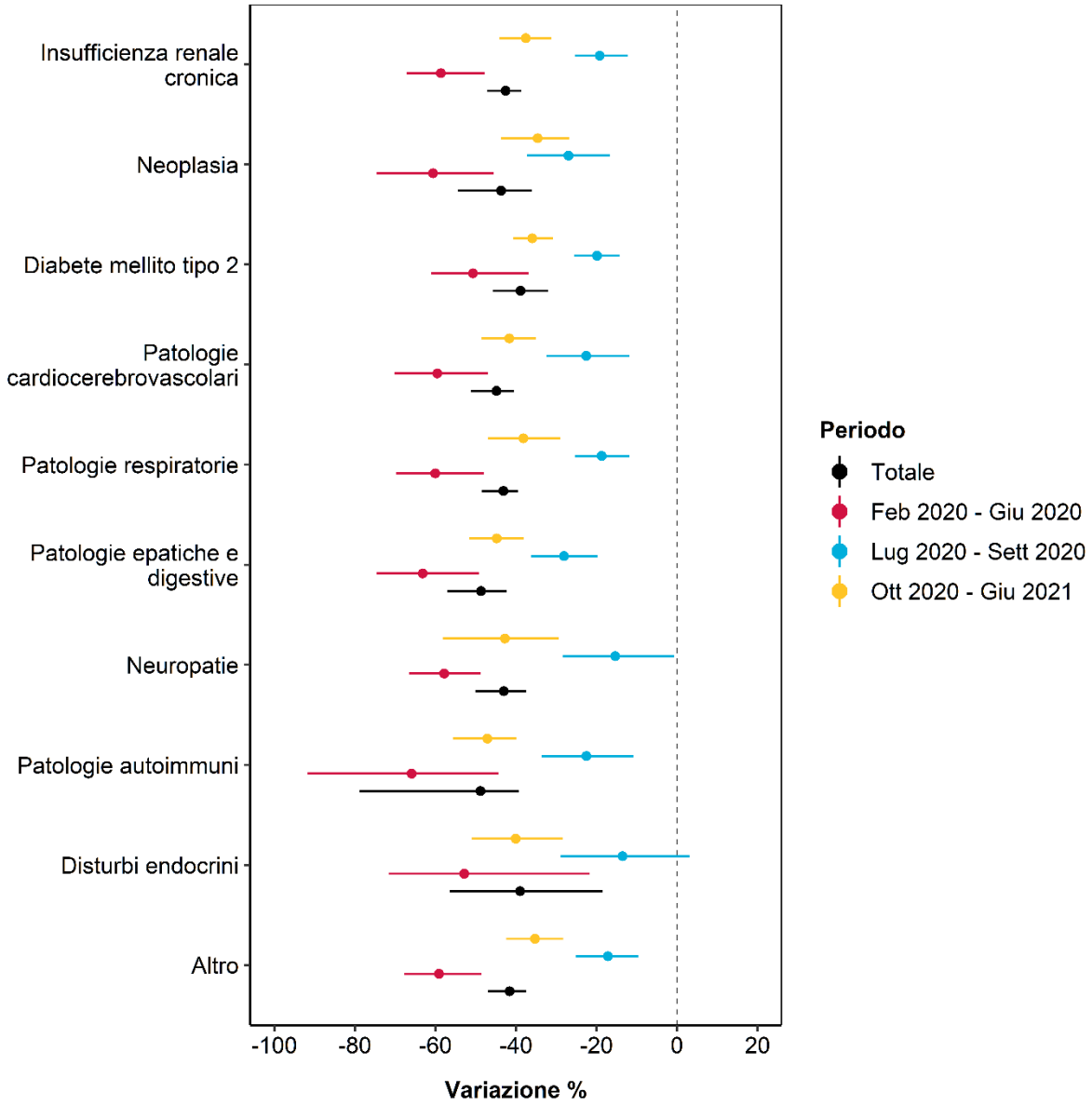


FIGURE 3.13a: Estimated variation of elective hospital admissions in patients with chronic condition of Brescia HPA, stratified by comorbidity

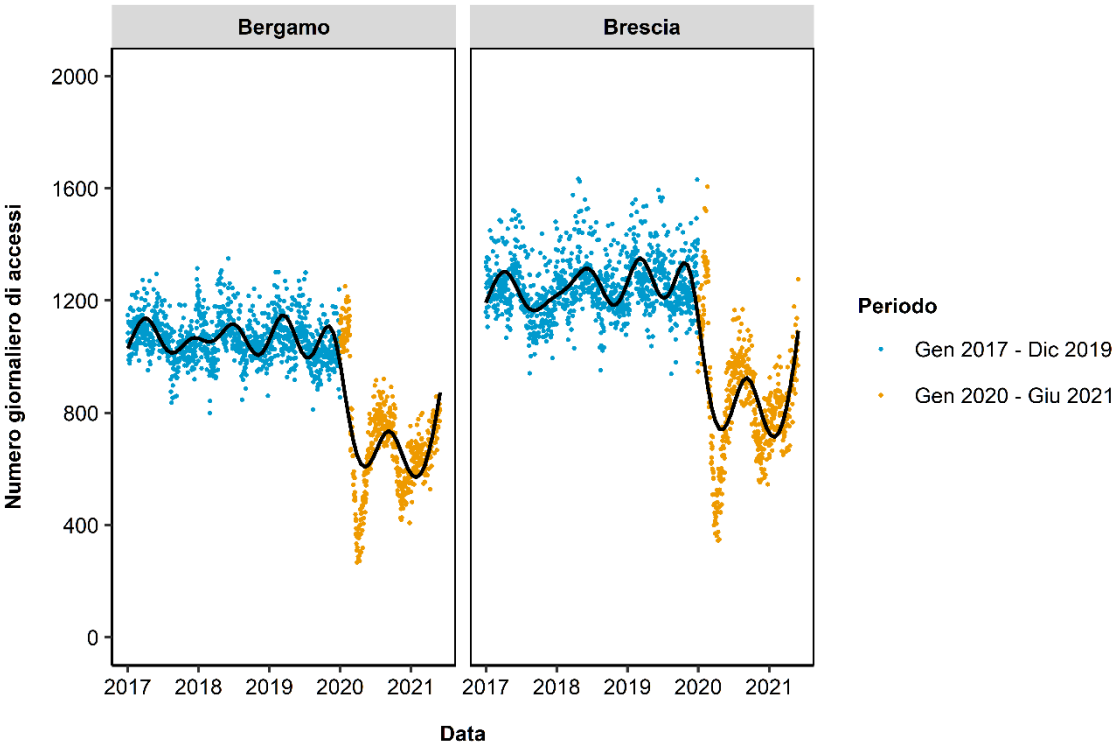


FIGURE 3.14: Time series of the daily number of ED visits in the general population of the two HPAs

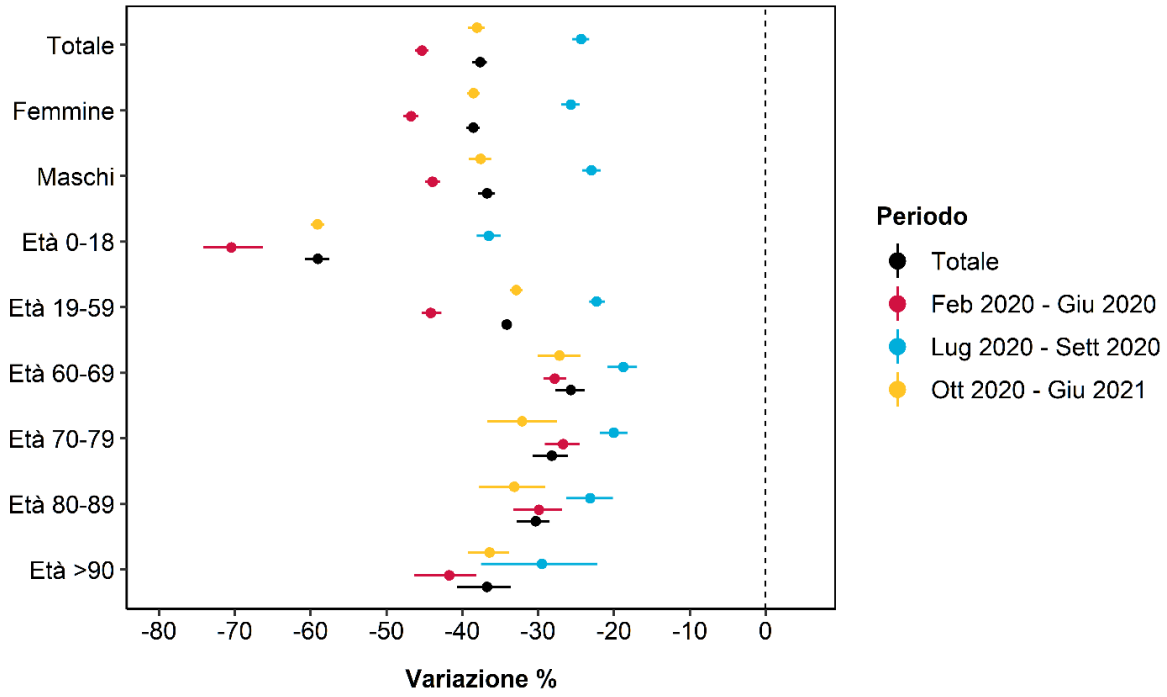


FIGURE 3.15: Estimated variation of ED visits in Bergamo HPA, stratified by sex and age

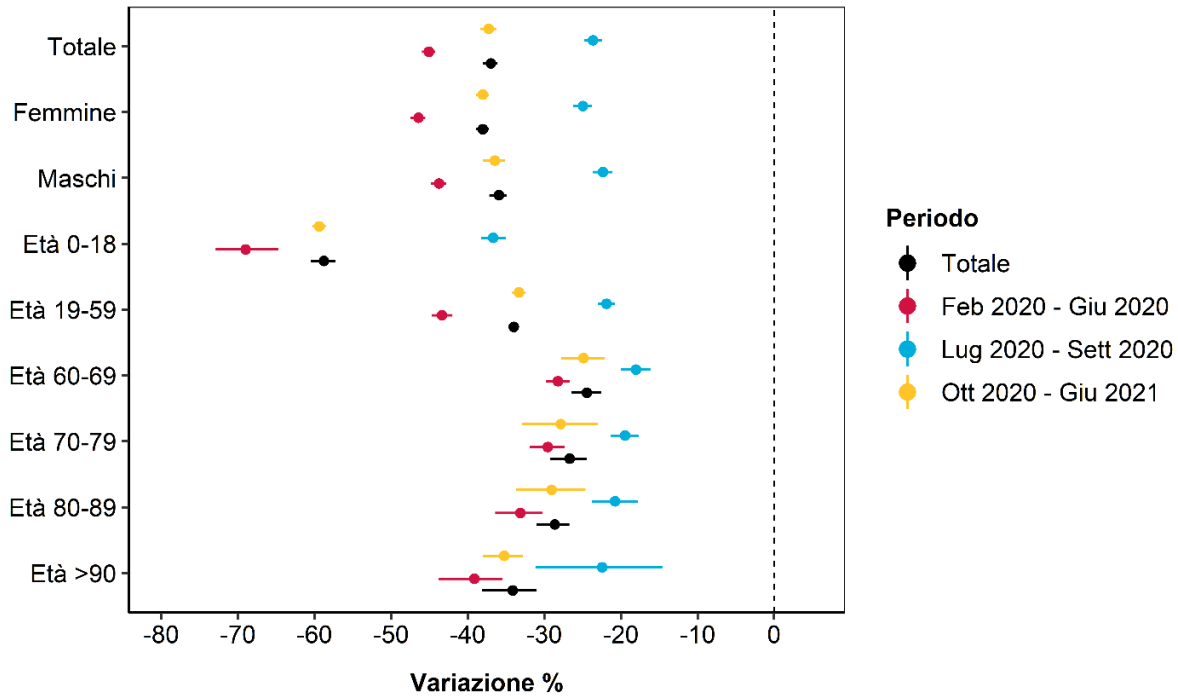


FIGURE 3.16: Estimated variation of ED visits in Brescia HPA, stratified by sex and age

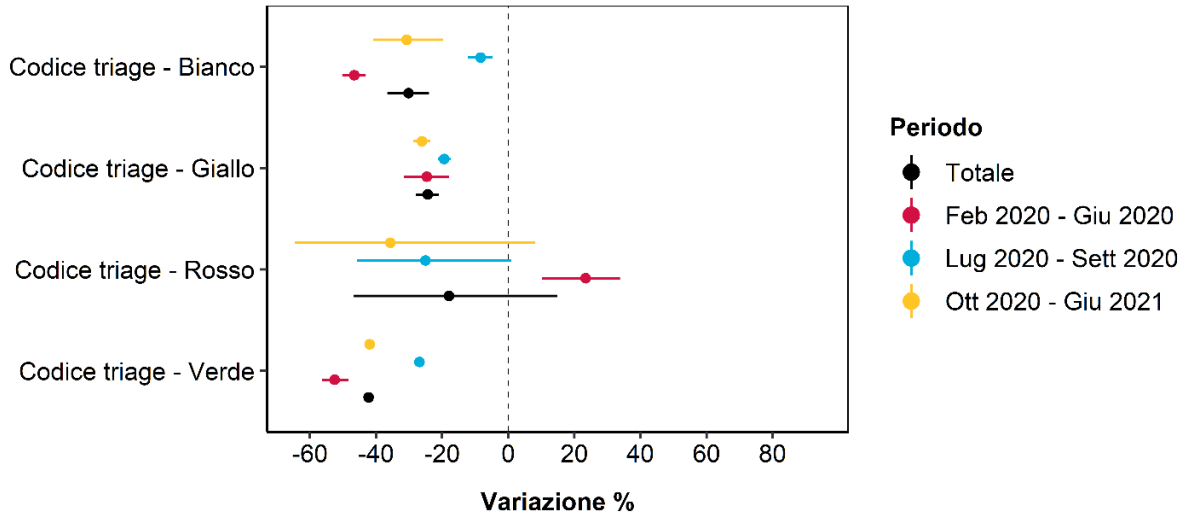


FIGURE 3.17: Estimated variation of ED visits in Bergamo HPA, stratified by triage code

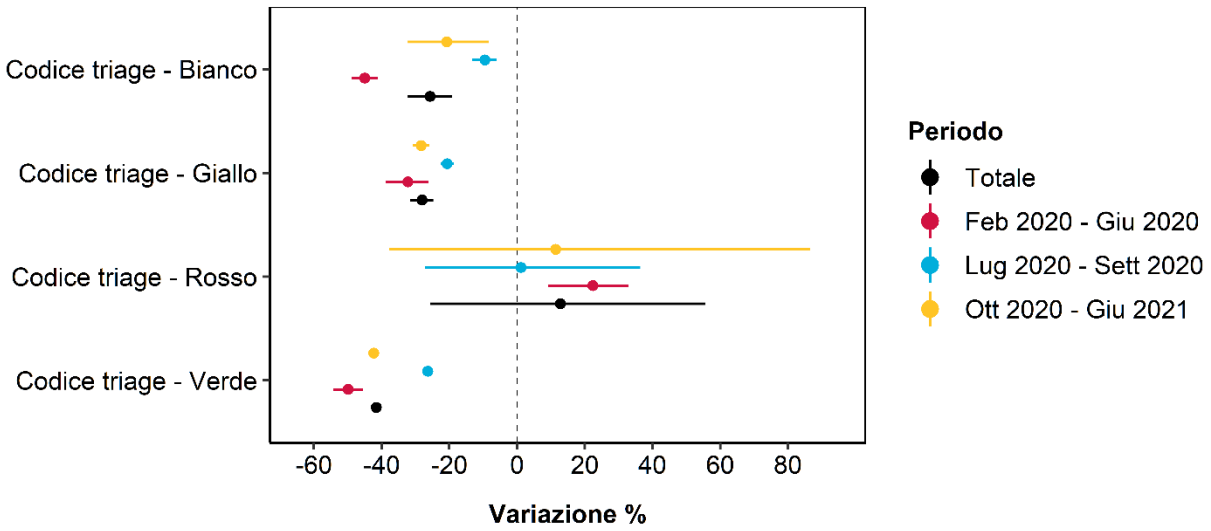


FIGURE 3.18: Estimated variation of ED visits in Brescia HPA, stratified by triage code

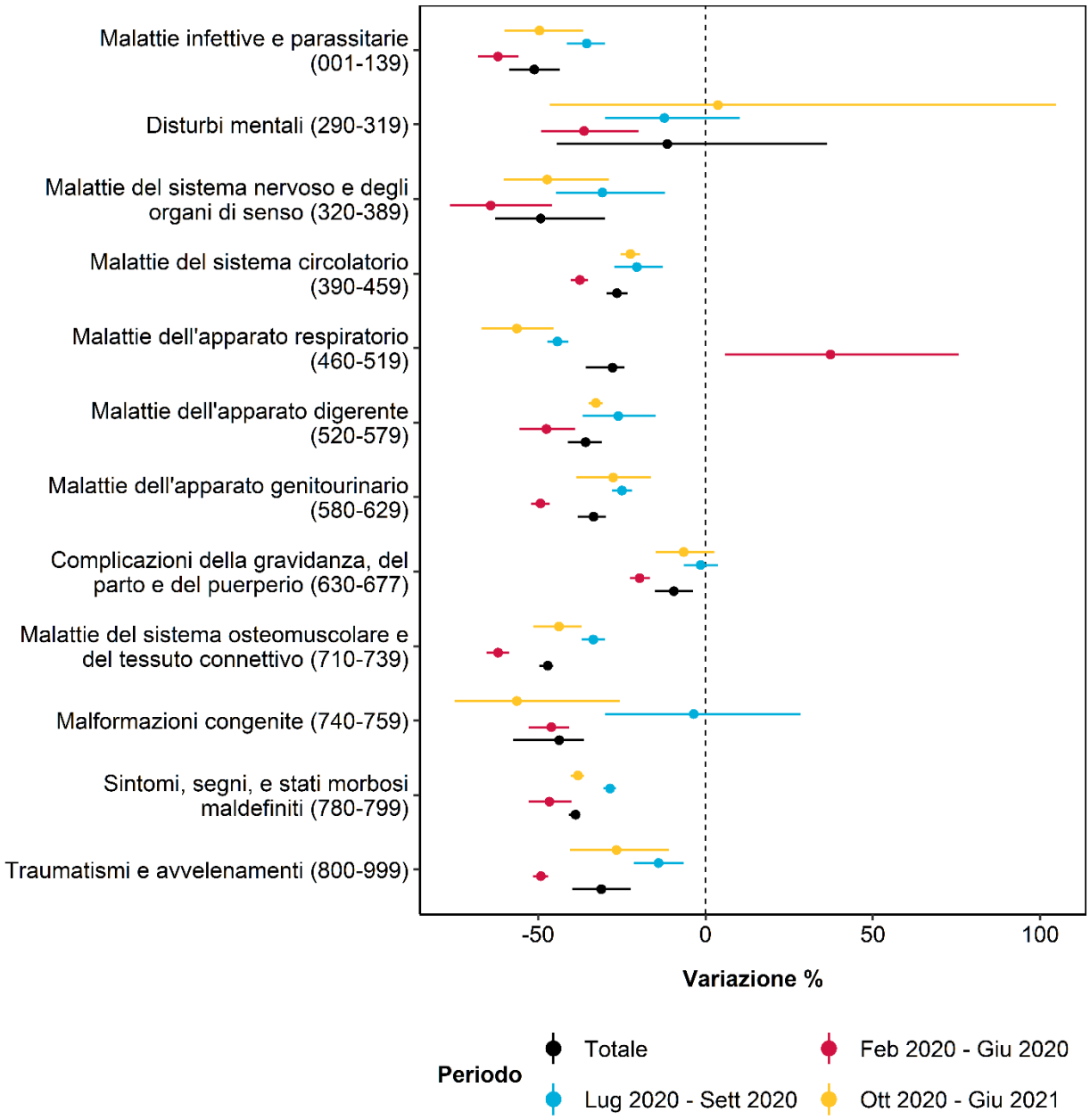


FIGURE 3.19: Estimated variation of ED visits in Bergamo HPA, stratified by main diagnosis (based on ICD-9-CM codes)

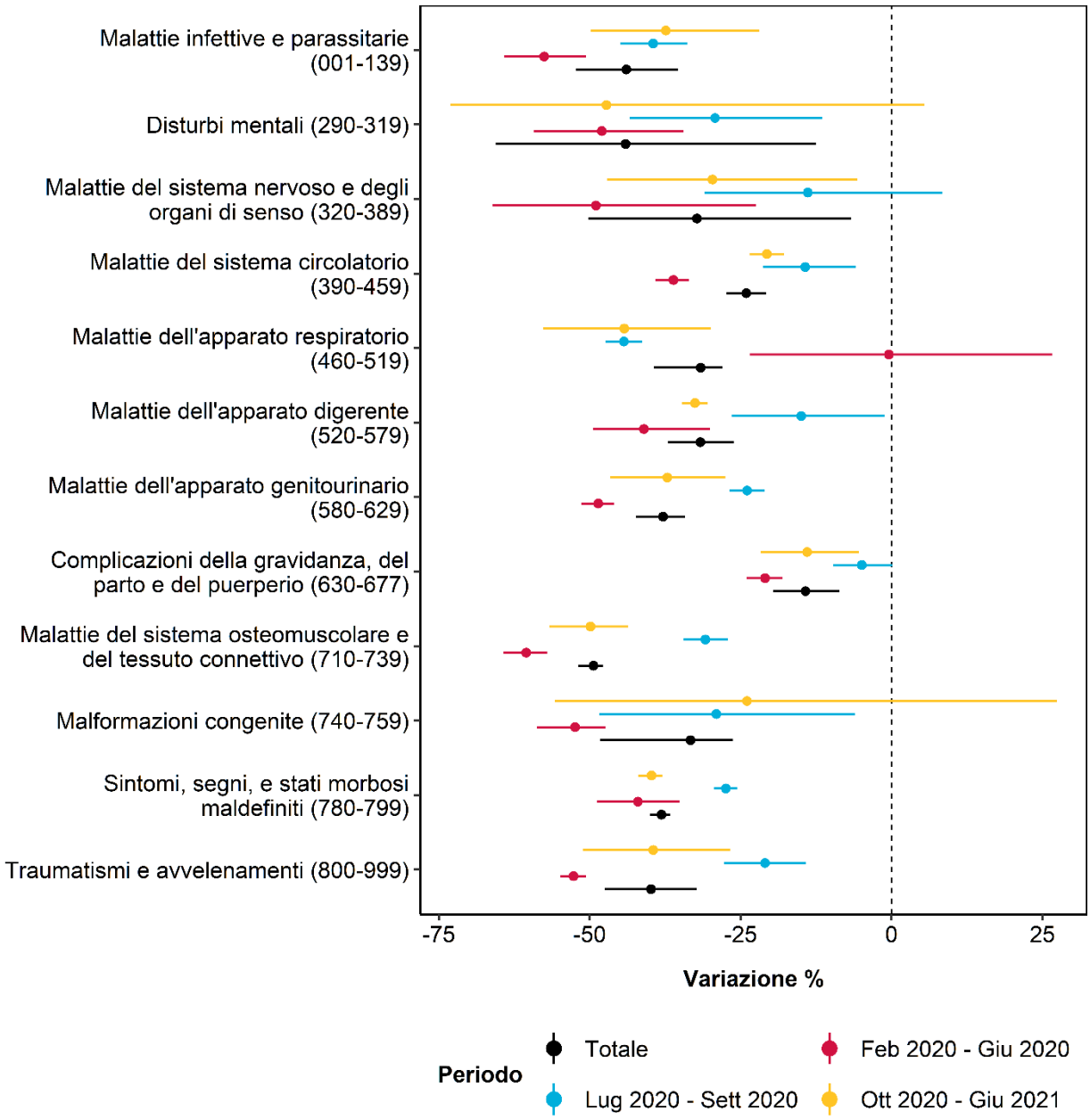


FIGURE 3.20: Estimated variation of ED visits in Brescia HPA, stratified by main diagnosis (based on ICD-9-CM codes)

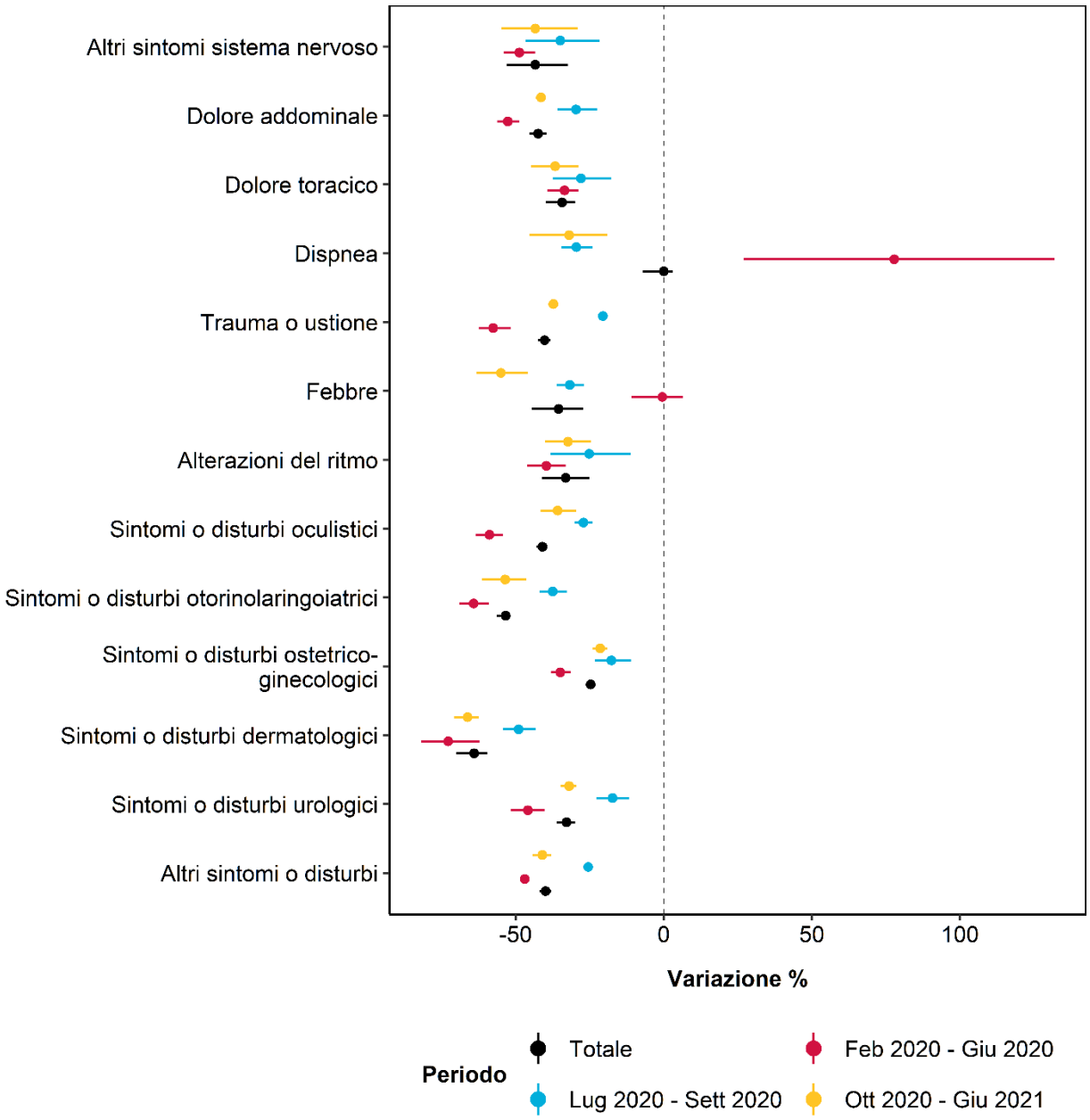


FIGURE 3.21: Estimated variation of ED visits in Bergamo HPA, stratified by presenting complaint

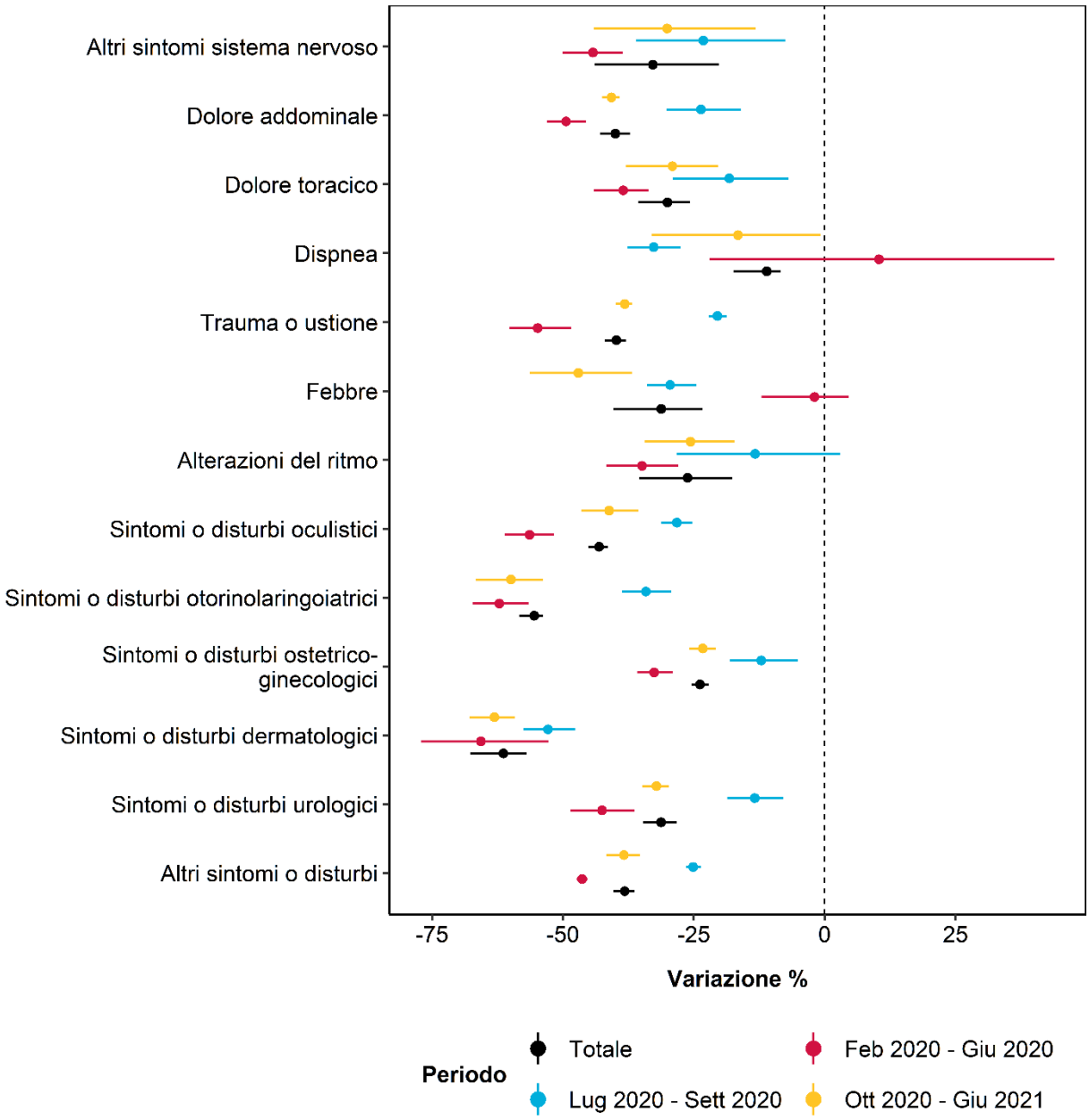


FIGURE 3.22: Estimated variation of ED visits in Brescia HPA, stratified by presenting complaint

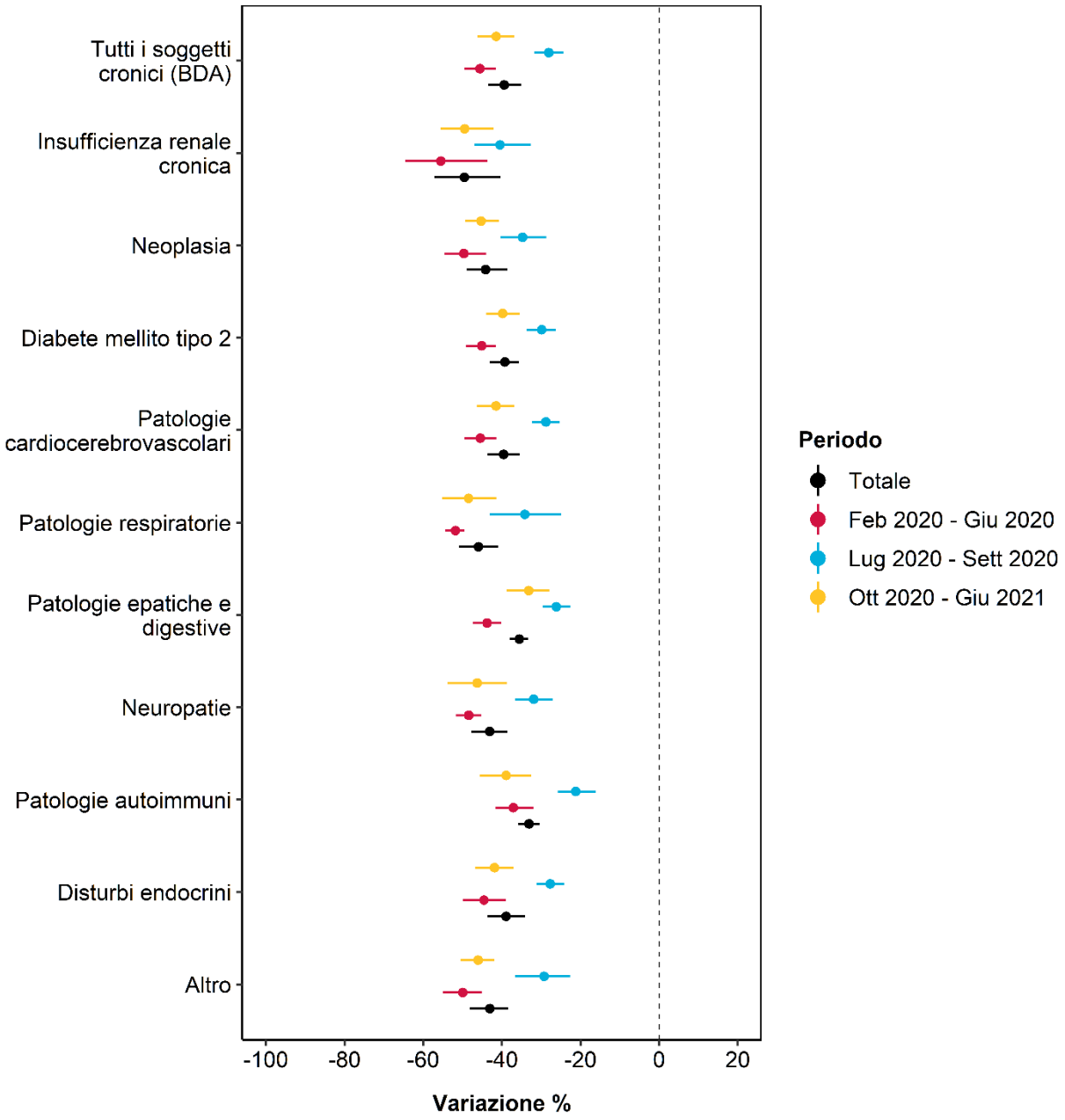


FIGURE 3.23: Estimated variation of ED visits in patients with chronic condition of Bergamo HPA, stratified by comorbidity

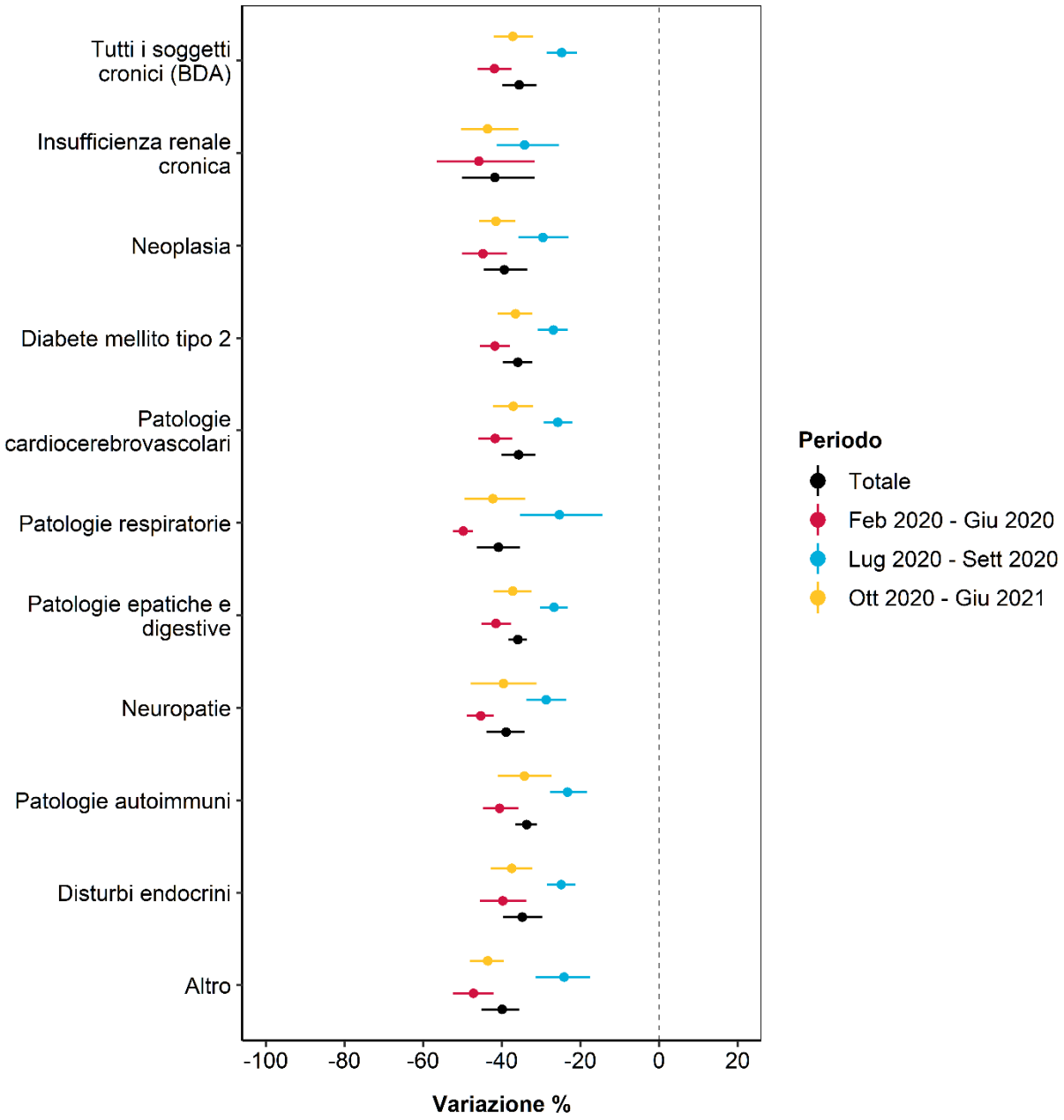


FIGURE 3.21: Estimated variation of ED visits in patients with chronic condition of Brescia HPA, stratified by comorbidity

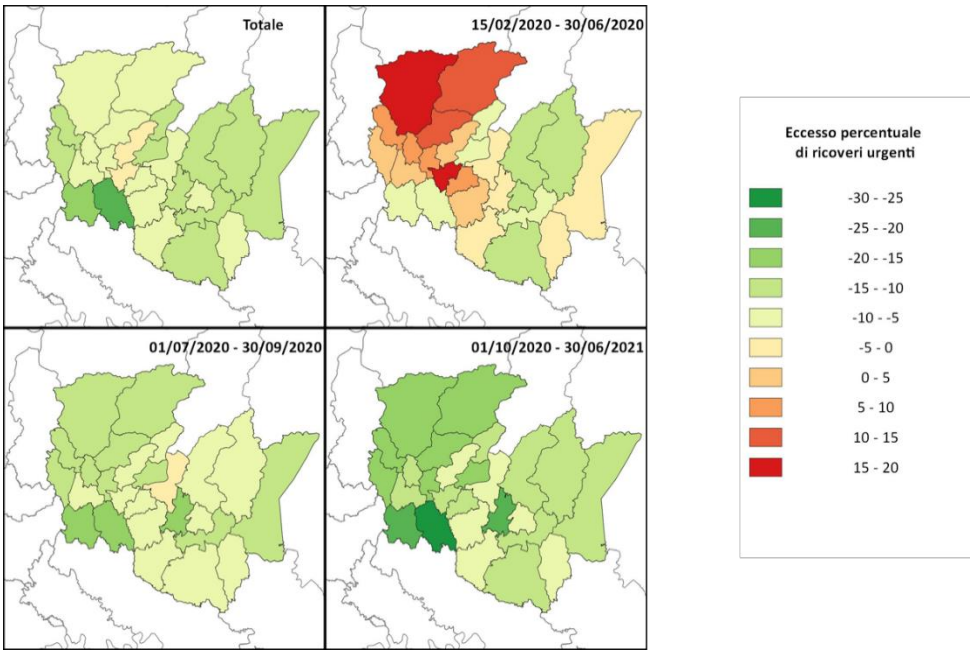


FIGURE 3.25: Geo-spatial distribution of the excess in urgent hospital admissions in HPAs' districts during the first and second waves, and the inter-wave period.

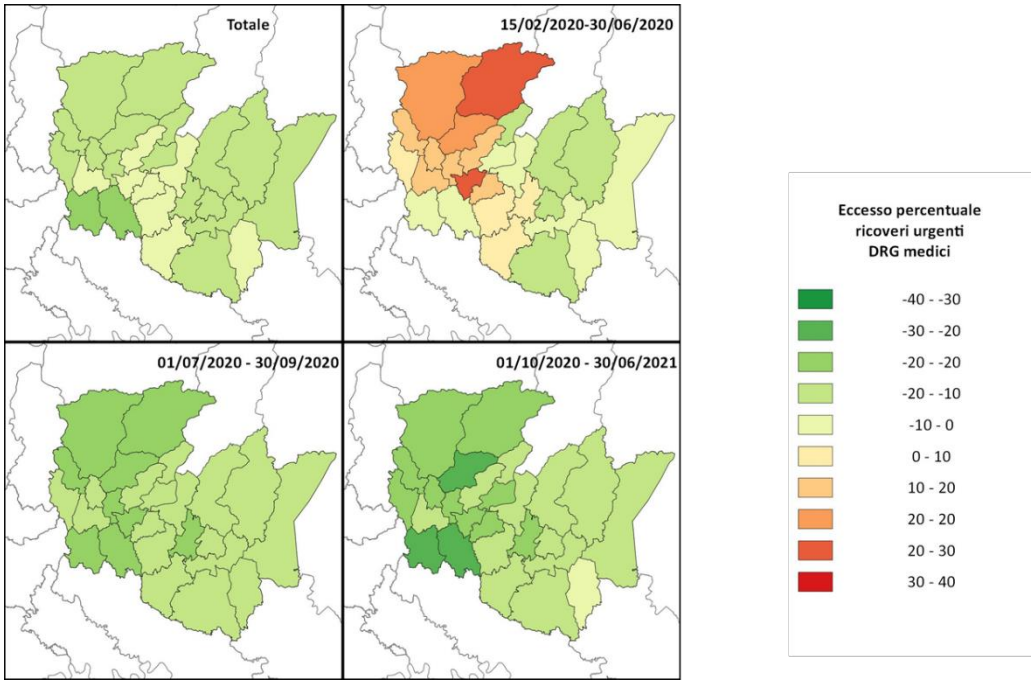


FIGURE 3.26: Geo-spatial distribution of the excess in urgent hospital admissions with medical DRG in HPAs' districts during the first and second waves, and the inter-wave period.

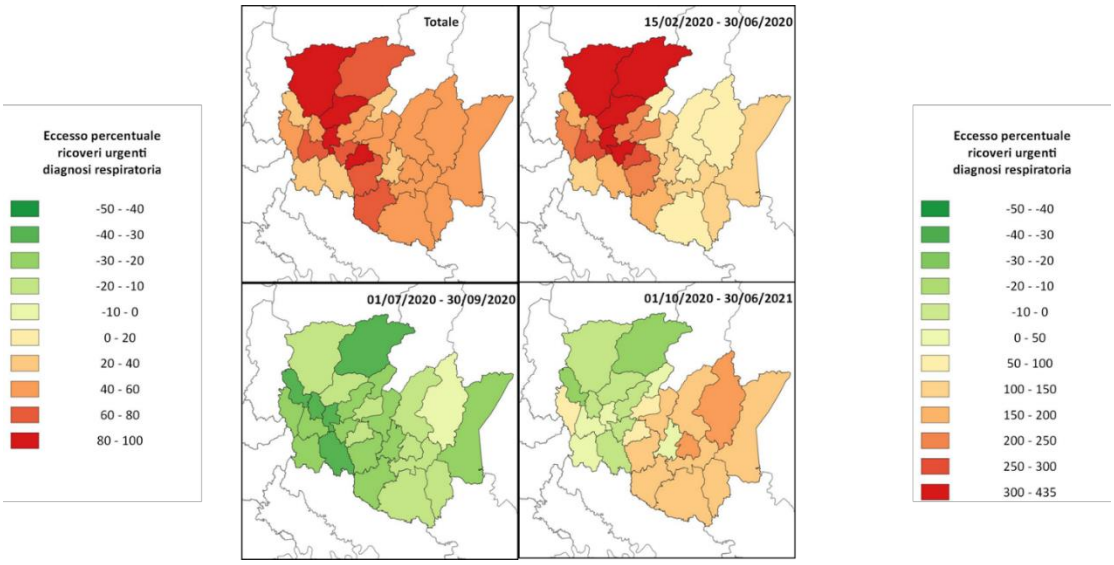


Figure 3.27: Geo-spatial distribution of the excess in urgent hospital admissions for respiratory diagnosis (based on the ICD-9-CM code) in HPAs' districts during the first and second waves, and the inter-wave period. Legend on the left refers to left panels and vice versa.

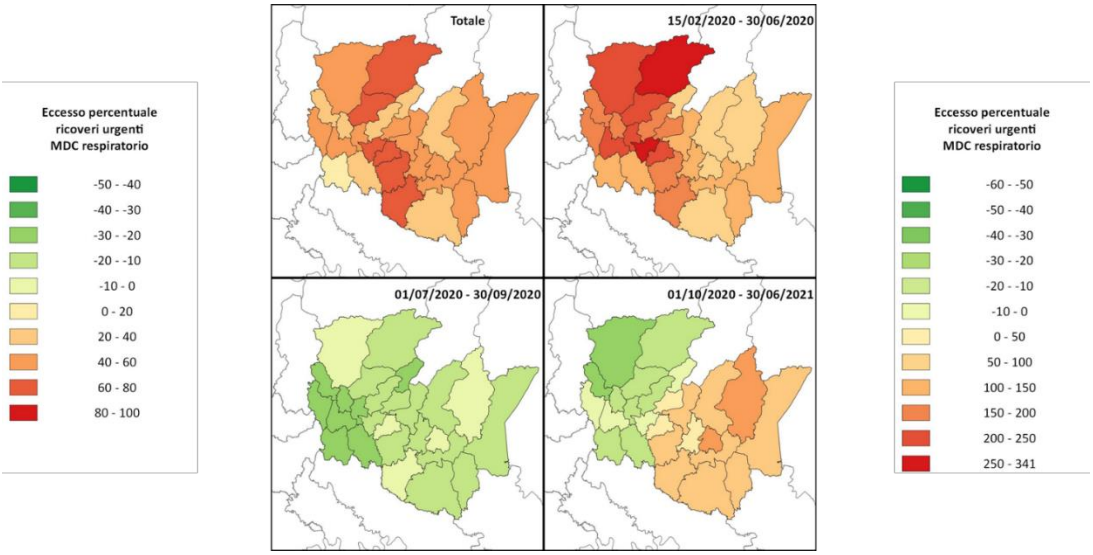


Figure 3.28: Geo-spatial distribution of the excess in urgent hospital admissions with MDC of the respiratory system in HPAs' districts during the first and second waves, and the inter-wave period. Legend on the left refers to left panels and vice versa.

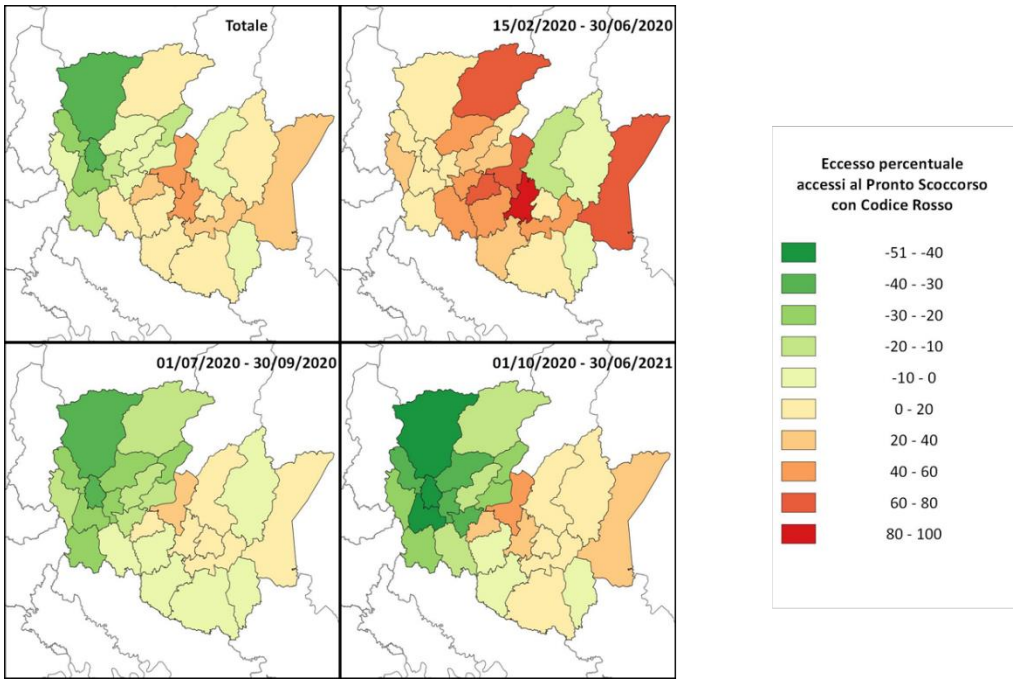


FIGURE 3.29: Geo-spatial distribution of the excess in red-code ED visits in HPAs' districts during the first and second waves, and the inter-wave period.

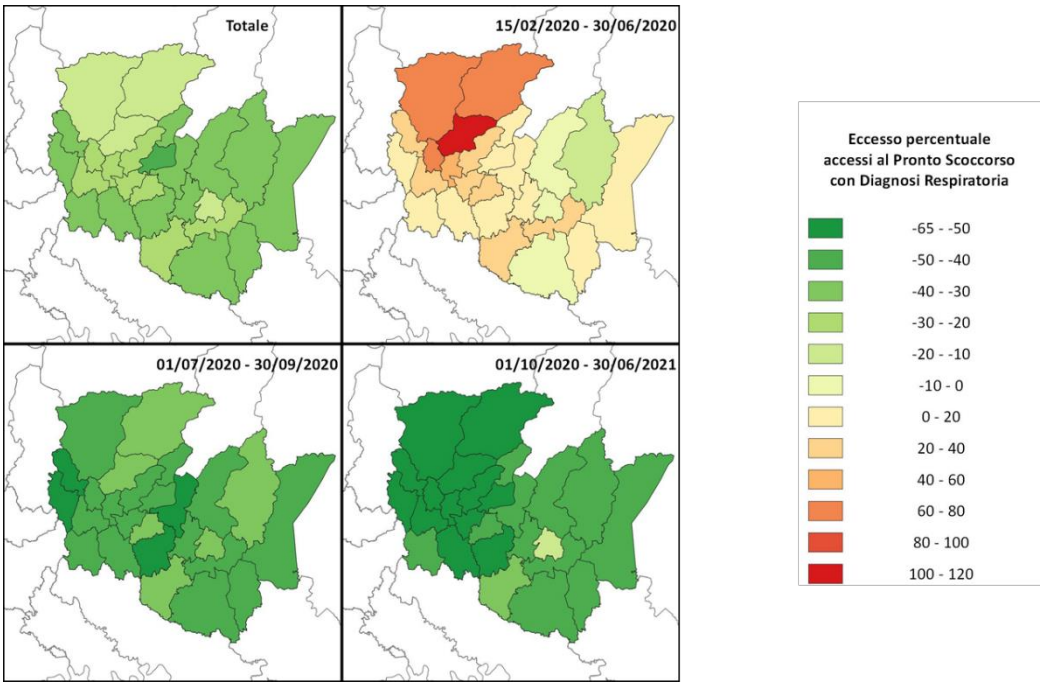


FIGURE 3.30: Geo-spatial distribution of the excess in red-code ED visits with respiratory diagnosis (based on the ICD-9-CM code) in HPAs' districts during the first and second waves, and the inter-wave period.

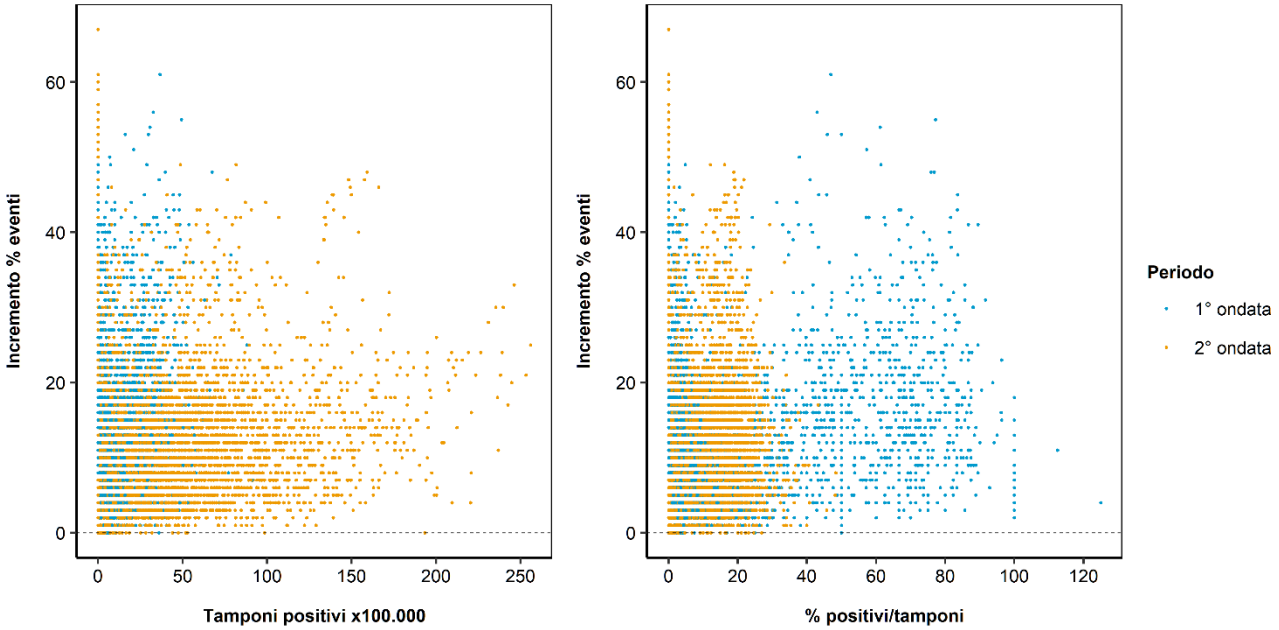


FIGURE 3.31: Scatterplot of the relationship between the daily number of urgent hospital admissions and new positive swabs per 100,000 inhabitants (left panel), or the positive/total swabs ratio (right panel).

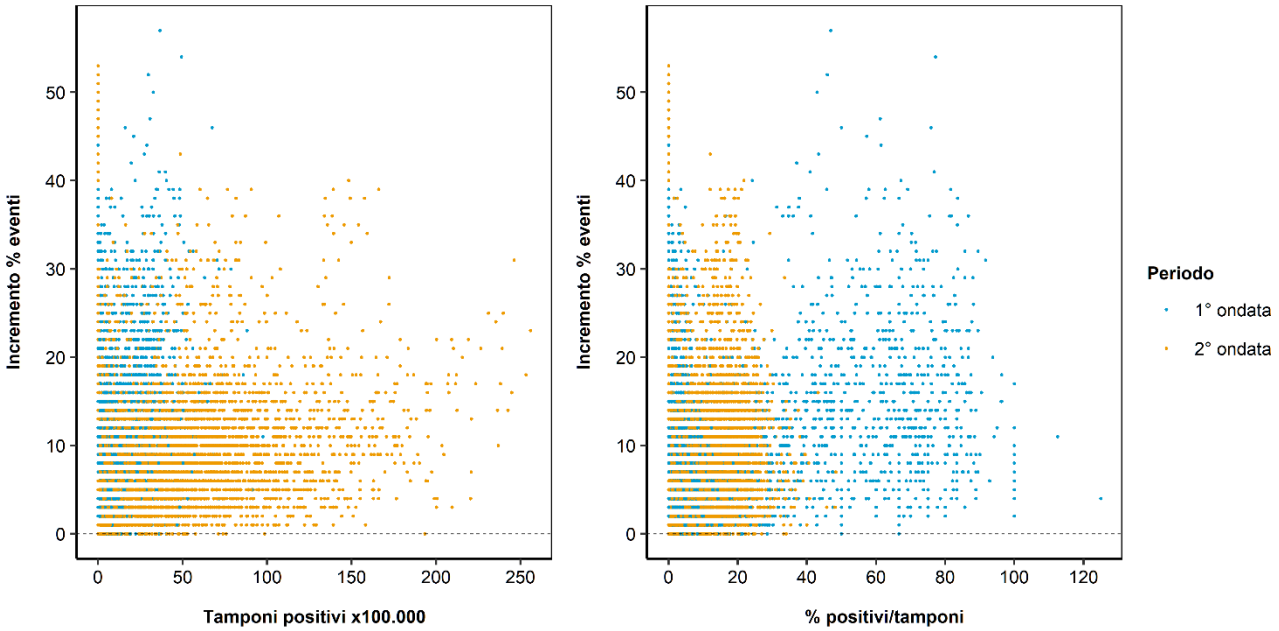


FIGURE 3.32: Scatterplot of the relationship between the daily number of urgent hospital admissions with medical DRG and new positive swabs per 100,000 inhabitants (left panel), or the positive/total swabs ratio (right panel).

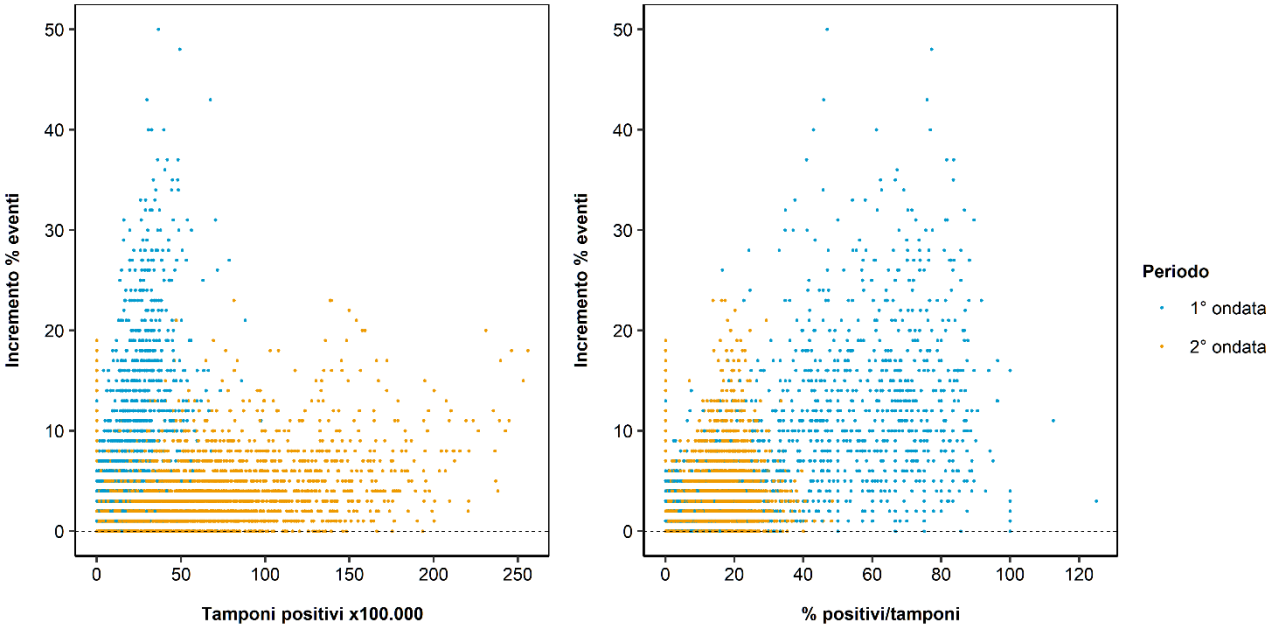


Figure 3.33: Scatterplot of the relationship between the daily number of urgent hospital admissions with respiratory diagnosis and new positive swabs per 100,000 inhabitants (left panel), or the positive/total swabs ratio (right panel).

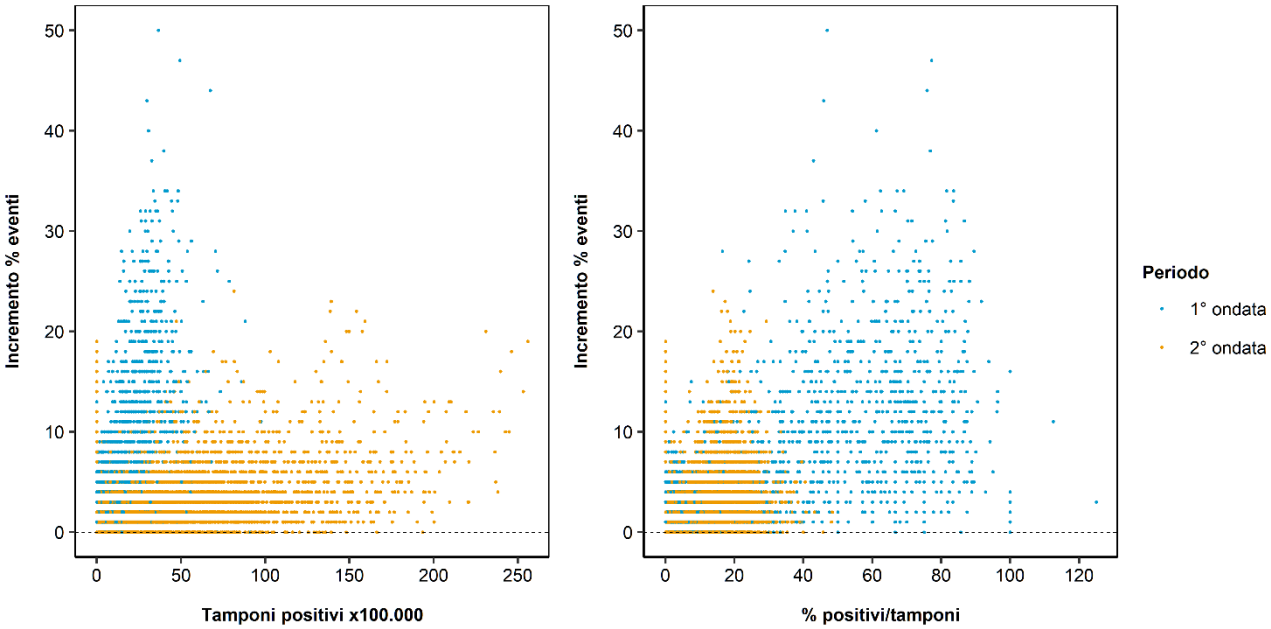


Figure 3.34: Scatterplot of the relationship between the daily number of urgent hospital admissions with respiratory MDC and new positive swabs per 100,000 inhabitants (left panel), or the positive/total swabs ratio (right panel).

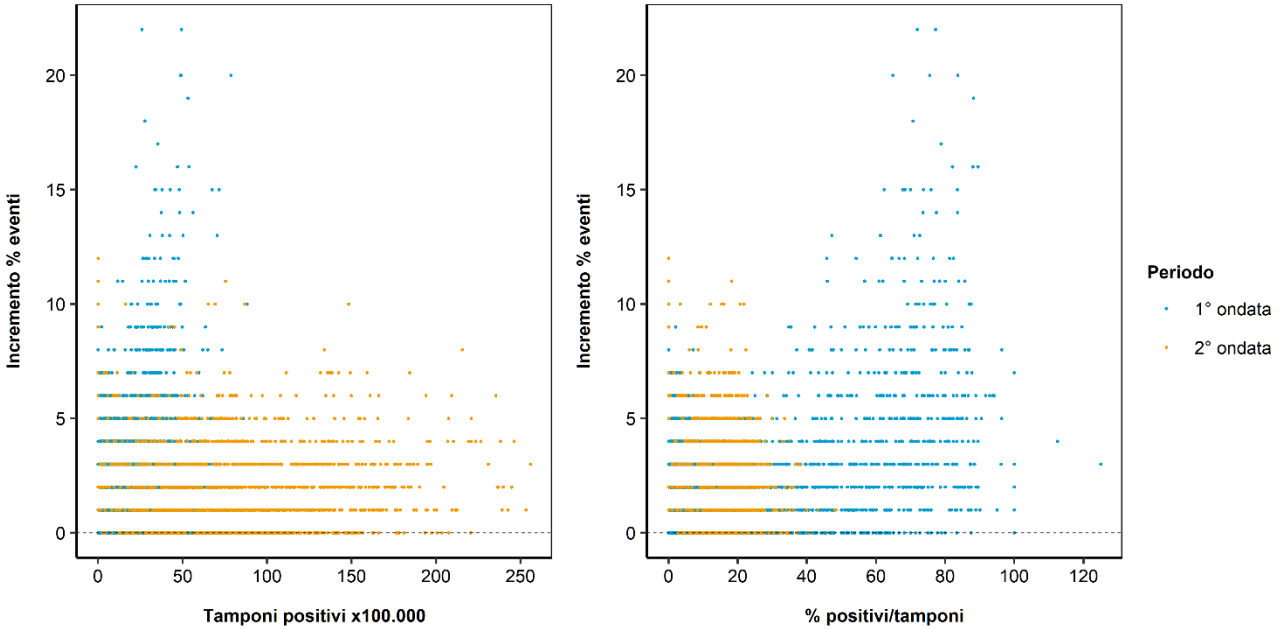


FIGURE 3.35: Scatterplot of the relationship between the daily number of ED visits and new positive swabs per 100,000 inhabitants (left panel), or the positive/total swabs ratio (right panel).

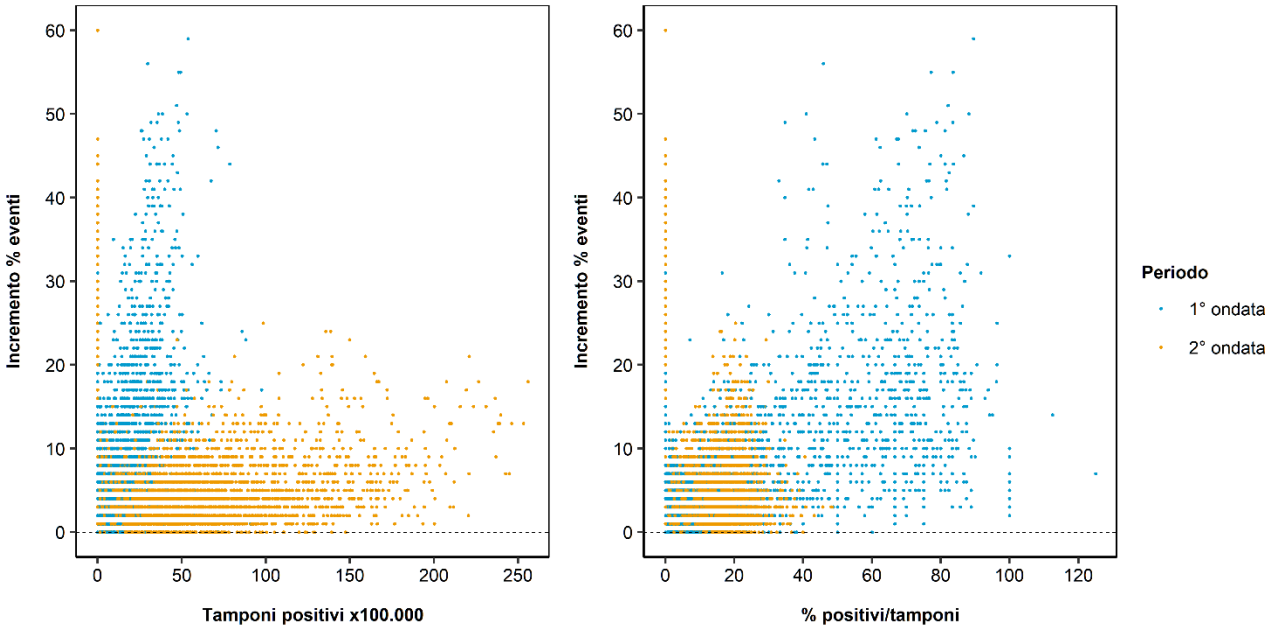


FIGURE 3.36: Scatterplot of the relationship between the daily number of ED visits with respiratory diagnosis and new positive swabs per 100,000 inhabitants (left panel), or the positive/total swabs ratio (right panel).

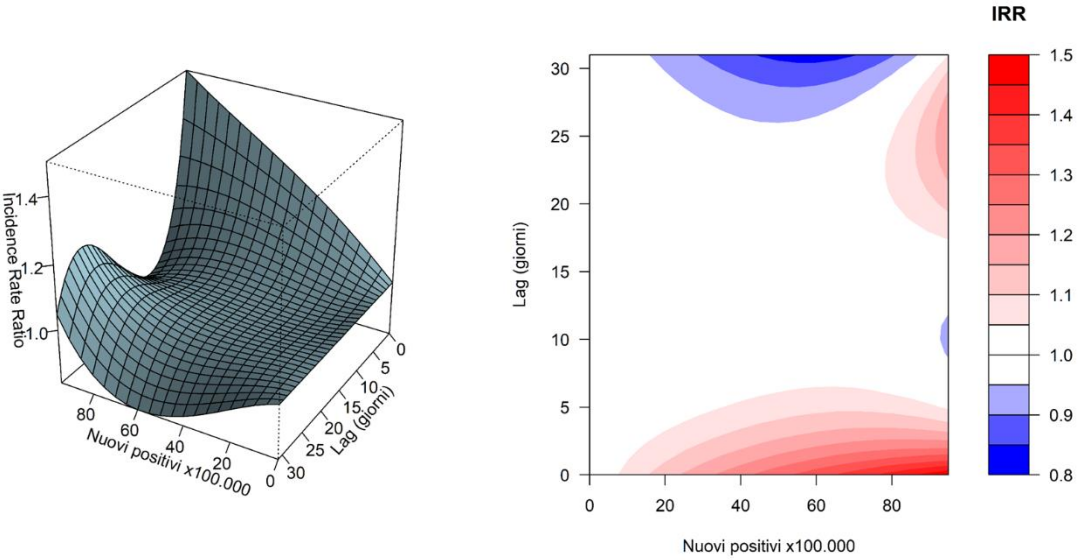


FIGURE 3.37: Tri- and bi-dimensional exposure–lag response surface showing joint effect of lag (days) and new positive swabs per 100,000 inhabitants on predicted incidence rate ratio (IRR) of urgent hospital admission during the first wave

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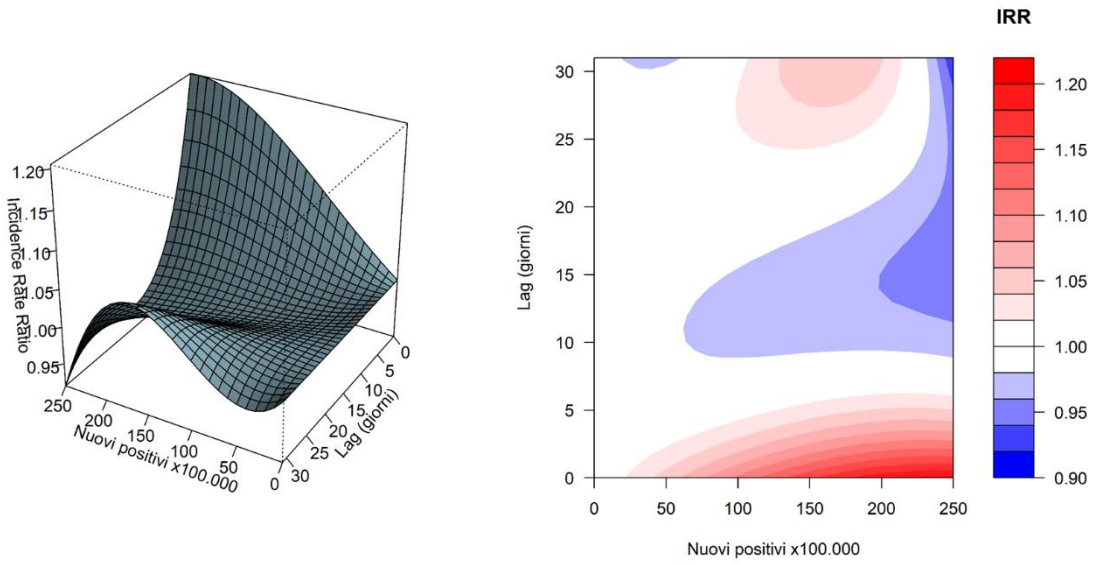


FIGURE 3.38: Tri- and bi-dimensional exposure–lag response surface showing joint effect of lag (days) and new positive swabs per 100,000 inhabitants on predicted incidence rate ratio (IRR) of urgent hospital admission during the second wave

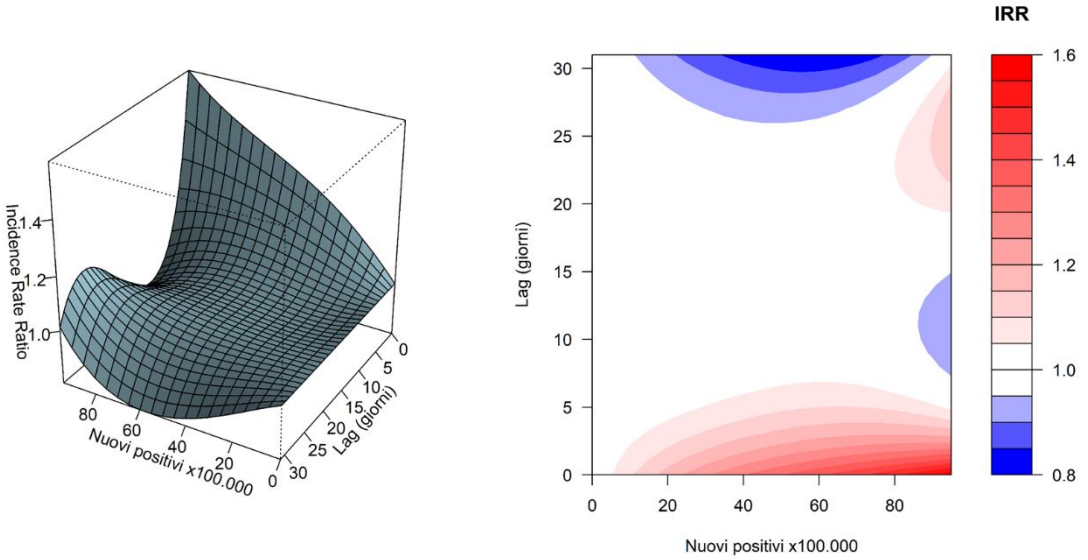


FIGURE 3.39: Tri- and bi-dimensional exposure–lag response surface showing joint effect of lag (days) and new positive swabs per 100,000 inhabitants on predicted incidence rate ratio (IRR) of urgent hospital admission with medical DRG during the first wave

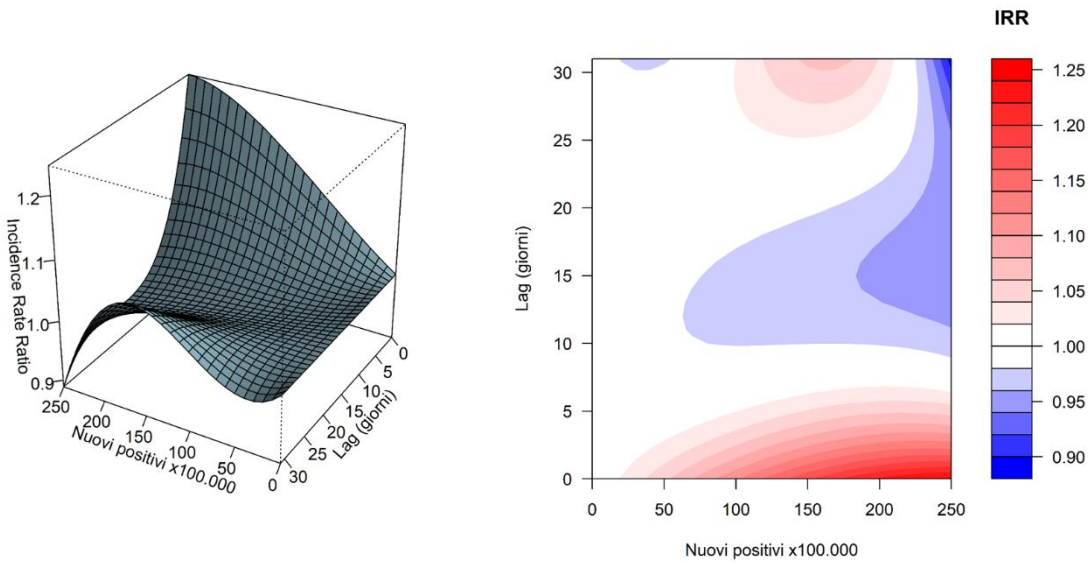


FIGURE 3.40: Tri- and bi-dimensional exposure–lag response surface showing joint effect of lag (days) and new positive swabs per 100,000 inhabitants on predicted incidence rate ratio (IRR) of urgent hospital admission with medical DRG during the second wave

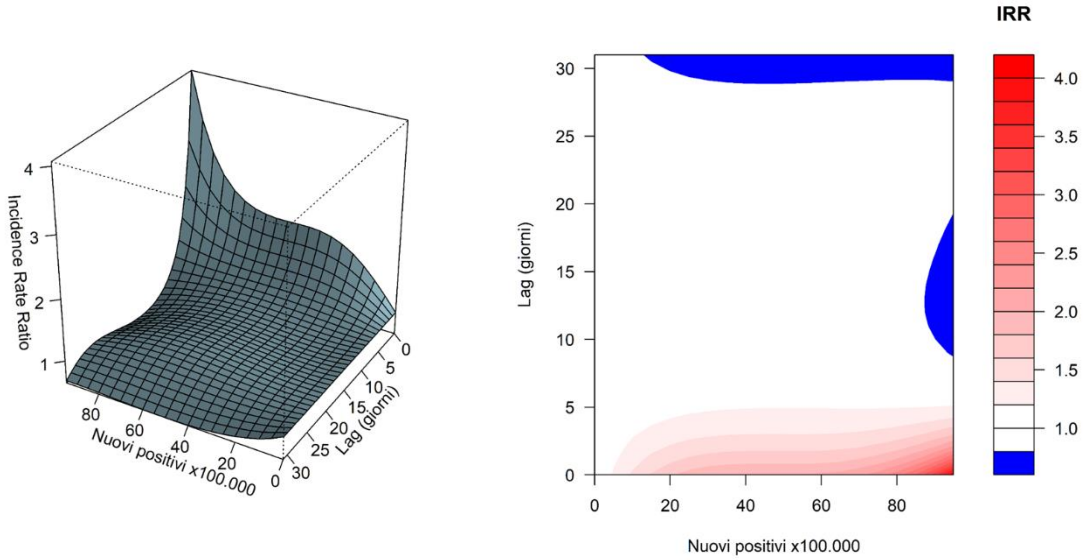


FIGURE 3.41: Tri- and bi-dimensional exposure–lag response surface showing joint effect of lag (days) and new positive swabs per 100,000 inhabitants on predicted incidence rate ratio (IRR) of urgent hospital admission with respiratory diagnosis during the first wave

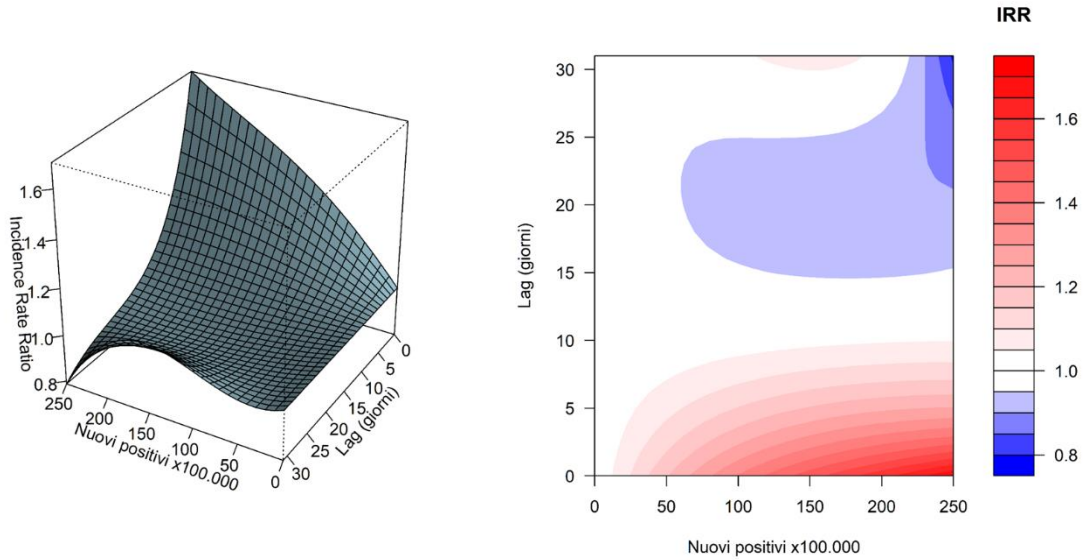


FIGURE 3.42: Tri- and bi-dimensional exposure–lag response surface showing joint effect of lag (days) and new positive swabs per 100,000 inhabitants on predicted incidence rate ratio (IRR) of urgent hospital admission with respiratory diagnosis during the second wave

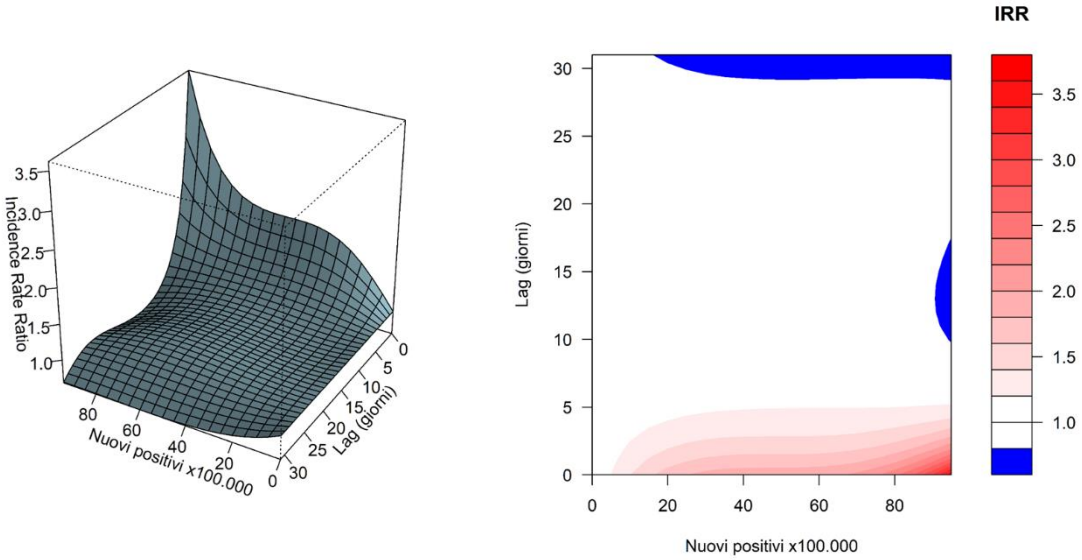


FIGURE 3.43: Tri- and bi-dimensional exposure–lag response surface showing joint effect of lag (days) and new positive swabs per 100,000 inhabitants on predicted incidence rate ratio (IRR) of urgent hospital admission with respiratory system MDC during the first wave

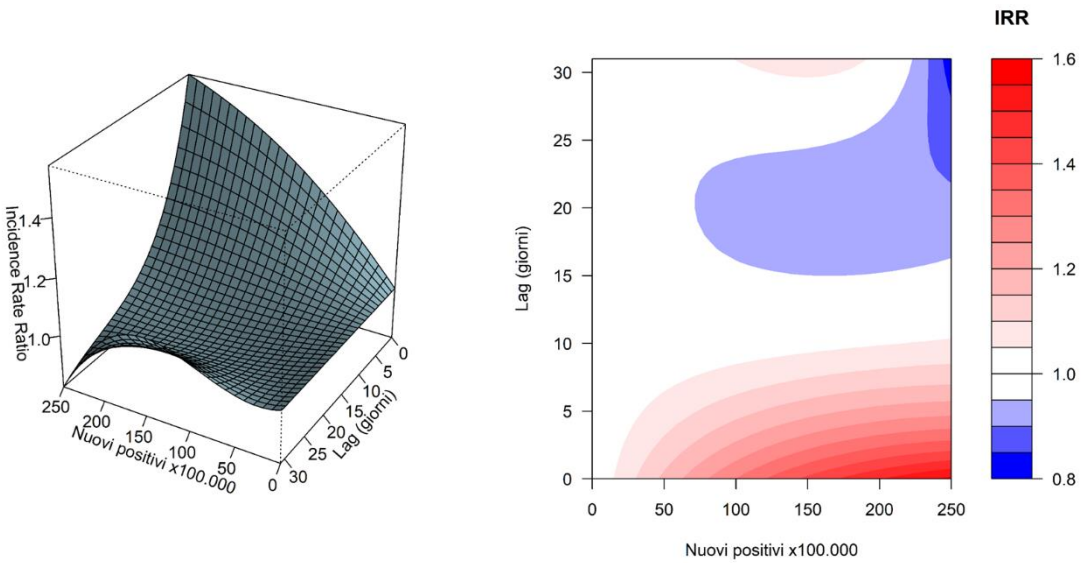


FIGURE 3.44: Tri- and bi-dimensional exposure–lag response surface showing joint effect of lag (days) and new positive swabs per 100,000 inhabitants on predicted incidence rate ratio (IRR) of urgent hospital admission with respiratory system MDC during the second wave

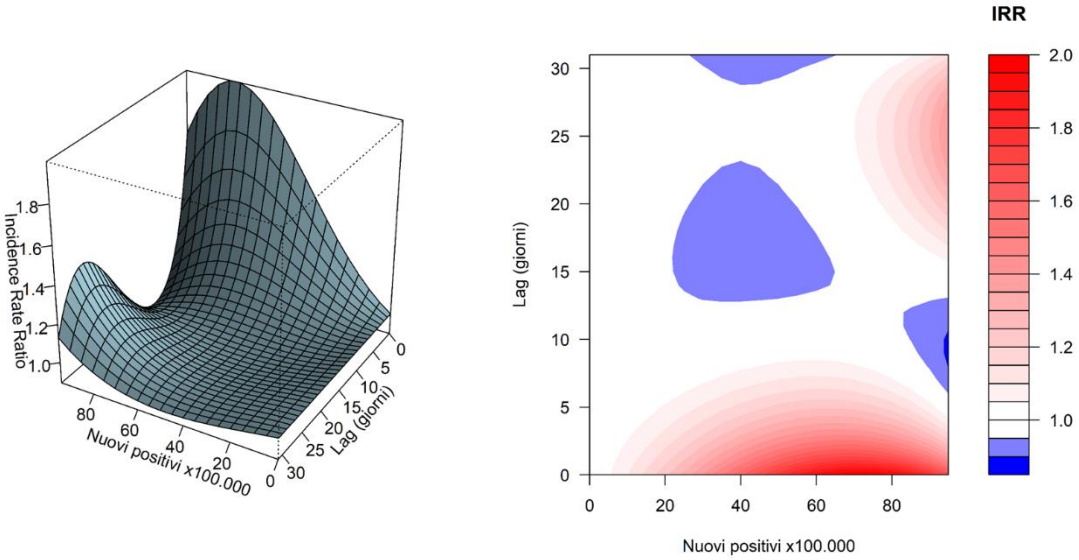


FIGURE 3.45: Tri- and bi-dimensional exposure–lag response surface showing joint effect of lag (days) and new positive swabs per 100,000 inhabitants on predicted incidence rate ratio (IRR) of red-code ED visits during the first wave

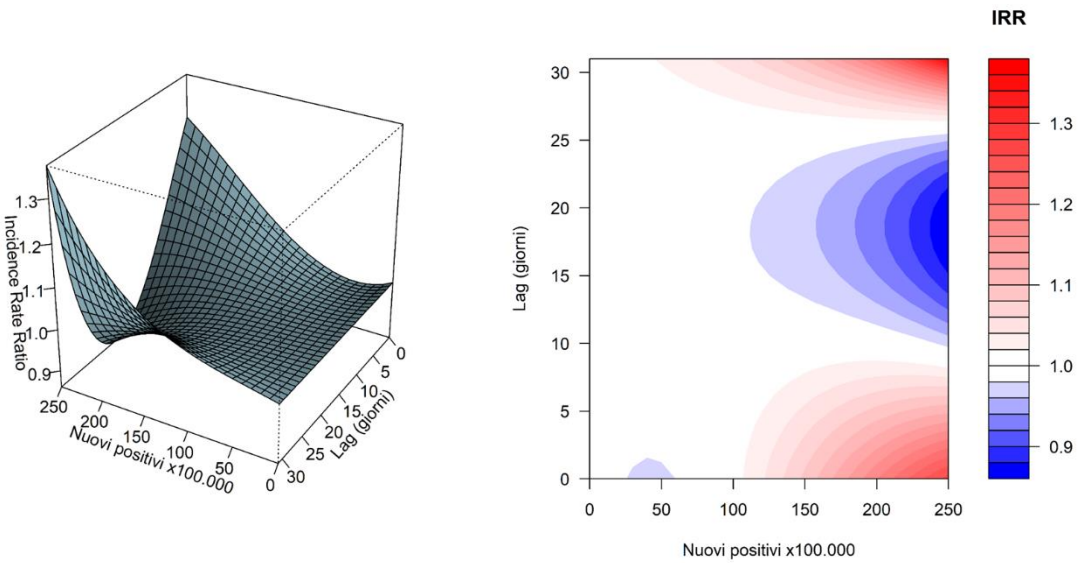


FIGURE 3.46: Tri- and bi-dimensional exposure–lag response surface showing joint effect of lag (days) and new positive swabs per 100,000 inhabitants on predicted incidence rate ratio (IRR) of red-code ED visits during the second wave

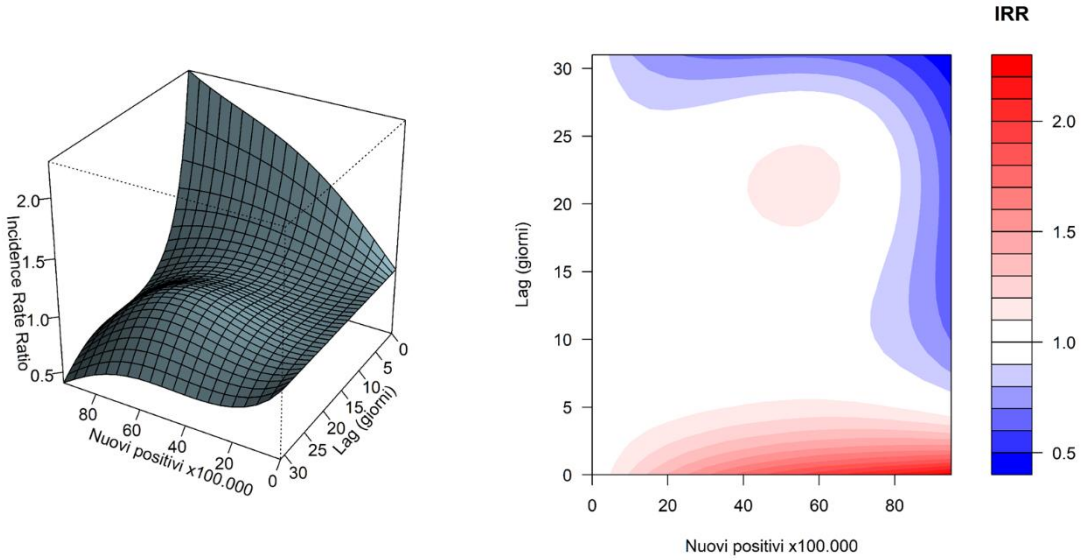


FIGURE 3.47: Tri- and bi-dimensional exposure–lag response surface showing joint effect of lag (days) and new positive swabs per 100,000 inhabitants on predicted incidence rate ratio (IRR) of red-code ED visits with respiratory diagnosis during the first wave

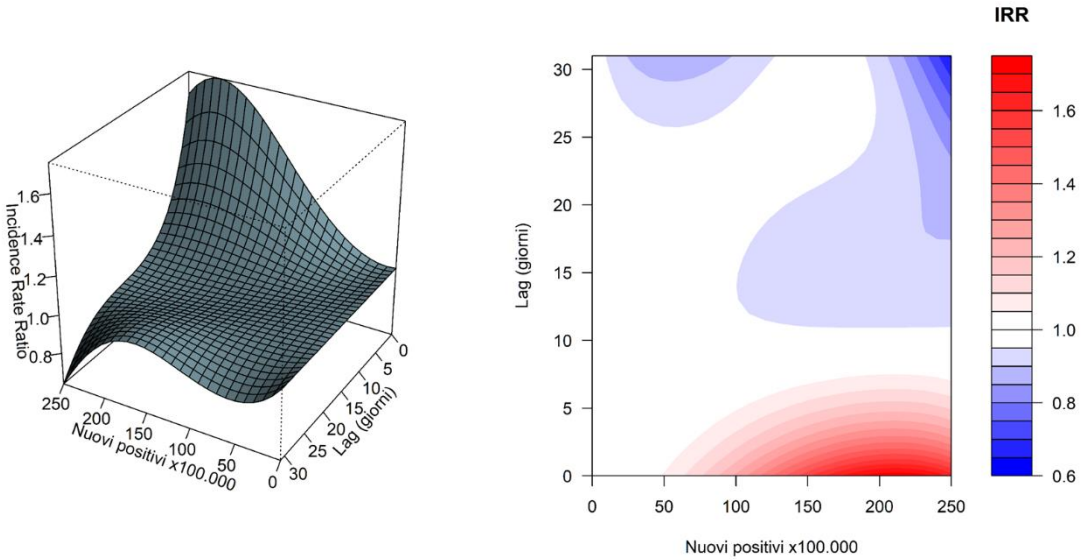


FIGURE 3.48: Tri- and bi-dimensional exposure–lag response surface showing joint effect of lag (days) and new positive swabs per 100,000 inhabitants on predicted incidence rate ratio (IRR) of red-code ED visits with respiratory diagnosis during the second wave

# Chapter 4

# The indirect impact of COVID-19 on hospital outcomes of high-volume, non-deferrable clinical conditions

## *4.1 Introduction*

Chapter 3 describes how the pandemic affected elective and urgent hospitalizations and ED visits in the provinces of Bergamo and Brescia. In summary, hospital and ED admissions generally decreased because of the COVID-19 pandemic and specific age groups and diagnostic categories (e.g., surgical DRGs) were considerably affected (see Chapter 3).

Although providing strong evidence of a change in hospital utilization, the analyses were not designed to investigate whether the pandemic jeopardized effective hospital care pathways. Several COVID-19-related factors might have had a further indirect impact on patient management, particularly for patients with time-dependent conditions. These factors include the overcrowding of hospitals with COVID-19 cases, the shortage of resources and the heavy workload of professionals, the internal reorganization of facilities, the consequences of lockdown measures, and the impact of avoidance for fear of secondary contagion among healthcare consumers (Ferrara et al., 2022*f*; Spadea et al., 2021; Wartelle et al., 2021).

Therefore, the objective of this chapter is to assess whether COVID-19 had an indirect impact on the care pathways for non-deferrable clinical conditions. For this purpose, a longitudinal retrospective study was conducted in the provinces of Bergamo and Brescia to analyse proxies of diagnosis, management, and care outcomes for myocardial infarction (MI), stroke, and trauma—diagnoses chosen for their high volumes (Spadea et al., 2021; James et al., 2020; Roth et al., 2020).

## *4.2 Study population*

A complete overview of the study context and setting is detailed in section 3.2. This analysis focused on all patients admitted to the hospital with a diagnosis of MI, stroke, or trauma within the areas of competence of the Brescia and Bergamo HPAs between January 1, 2019 and May 31, 2021.

*4.3 Data source*

Data were retrieved from the following HADs of the two HPAs: HDR, ED visits, BDA, and COVID-19 integrated surveillance databases.

For a complete overview of the HADs used, please refer to section 3.3.

*4.4 Statistical analysis*

To meet the study objective, data on hospital admission and mortality for MI, stroke, and trauma from January 1, 2019 and May 31, 2021 were selected. Hospitalizations in the month of June 2021 were excluded to account for a sufficiently long follow-up period. For each condition, the health events of interest were traced based on the ICD-9-CM codes recorded in HDRs. These were included in the analysis if they had: (i) a code of initial episode of care for MI (ICD-9-CM diagnosis codes 410.X1) as a main or secondary diagnosis; (ii) a ICD-9-CM code for stroke as a principal diagnosis (codes 430, 431, 433.01, 433.X1, 434.X1, and 436); (iii) a ICD-9-CM code between 800 and 995 for trauma, except for codes 905 to 909 (i.e., late effects of trauma, poisonings, toxic effects, and other external causes). Data from the two HPAs were analysed together due to the small number of some health events.

The case-finding algorithms applied for the case definitions of both MI and stroke showed full validation and had positive predictive values of 94% (95%CI 93% to 95%; Kiyota et al., 2004) and 97% (95%CI 93% to 98%; Roumie et al., 2008), respectively. Cases of a second MI- or stroke-related admission retrieved for a single patient within 28 days of the first event were considered unique events. Trauma was also categorized according to the following causes: work-related accidents, domestic accidents, road trauma, interpersonal violence, self-harm, suicide attempt, and others.

For ED visits, case definitions for the events of interest could not be derived using case-finding validated algorithms. An *ad hoc* analysis of Bergamo and Brescia HPA's HADs showed that ED visits with the same ICD-9-CM code preceded 48.1% and 48.9% of hospitalizations for trauma and stroke, respectively, but only 15.1% of MI hospitalizations, in which presenting complaints could be firstly attributed to other conditions (e.g., angina pectoris, intermediate coronary syndrome, and other cardiac and noncardiac diseases). The analysis of weekly numbers of ED visits were therefore conducted only for trauma- and stroke-related events.

First, the time series of weekly numbers of hospitalizations due to each event and hospitalization rates —defined as the weekly number of hospital admissions over the total person-time at risk (person-weeks)—were computed. 95% CIs were calculated using the Wald test assuming a normal distribution. Trends were further sorted by sex and age group (i.e., < 10, 10–19, 20–29, 30–39, 40–49, 60–59, 60–69, 70–79 and ≥ 80 years). Second, to investigate differences in hospital diagnoses and the management and clinical outcomes of trauma, MI, and stroke, two chronological cohorts were established and epidemiological and clinical data were retrospectively collected from patients with each condition of interest. The cut-off time for the two cohorts was the date of detection of the first confirmed case in Lombardy. Specifically, the first cohort included patients from January 1, 2019 to February 20, 2020 (pre-pandemic cohort) and the second from February 21, 2020 to May 31, 2021 (pandemic cohort). The following outcomes were considered: diagnosis, type of hospital discharge, length of stay, and in-hospital and 28-day mortality. To exclude potentially COVID-19-attributable deaths in patients hospitalized for trauma, MI, and stroke, mortality risk was also stratified according to the presence of a positive SARS-CoV-2 swab test within the previous 21 days. Differences between categorical variables were examined using chi-squared ($\chi 2$) and Fisher exact tests. Continuous variables were evaluated using the Student t test or Wilcoxon rank sum test according to their distributions.

Considering the imbalance between covariates of the two cohorts, propensity score matching (PSM) was performed to reduce or eliminate the effect of confounding factors (Austin, 2011*a*). Each patient was assigned a propensity score that reflected the conditional probability of belonging to either group given confounders predicted using logistic regression. Characteristics were sex, age, presence of chronic or long-term conditions (e.g., autoimmune disease, cancer, chronic respiratory disease, CKD, CVD, gastrointestinal disease, HIV or AIDS, neuropathy, organ transplant, thyroid disorders, and type 1 or 2 diabetes mellitus [T1DM] or T2DM)), the month of hospital admission and, for trauma patients, type and cause of trauma. According to optimal PSM match ratio and calliper widths for the estimation of differences in means and proportions in observational studies, we matched respondents in a 1:1 ratio using the nearest neighbouring method and fixing an absolute standardized difference of covariates less than 0.1 as a cut-off for optimal matching (Rassen et al., 2021; Austin, 2011*a*).

Differences between categorical variables in the matched cohorts were examined using the Neyman–Pearson test and continuous variables were evaluated using the Student t test or Wilcoxon rank sum test according to the distribution. A

28-day survival probability was determined using Kaplan–Meier curves and the mean survival time, which was estimated as the area under the survival curve in the interval 0 to $t_{max}$, was compared using the Klein and Moeschberger test (Klein and Moeschberger, 2003).

All *p*-values ≤ .05 were assumed to be statistically significant.

## *4.5 Results*

Results are presented separately for each of the health events included.

### *4.5.1. Trauma*

The 2019–2021 total and sex-standardized time series of weekly hospitalizations for trauma are plotted in Figure 4.1. During the first wave and up to the first week of May 2020 (i.e., when the first lockdown was eased), the number of trauma admissions was halved from 350 to 175 per week (Figure 4.1, panel A). The following trends reflect the SARS-CoV-2 incidence curve and peaks (October–December 2020) and the extent of lockdown measures. Time-varying weekly hospitalizations for trauma were similar across the sexes (Figure 4.1, panels B–C) and age groups except for the older groups, in whom substantial reductions were observed over the entire pandemic period (Figure 4.2, panels A–I). Figures 4.3 and 4.4 report the time series by age and sex. The sex- and age-adjusted hospitalization rate for 2019 was approximately 140 admissions per 1,000,000 person-weeks. The rate dropped to 40 and 100 admissions per 1,000,000 person-weeks in March–May 2020 and during the second national lockdown, respectively, and subsequently returned to higher volumes toward the end of the observation period (Figure 4.5). Trends in weekly ED visits mirrored those of hospitalizations, with major reductions observed between March and May 2020 (Figure 4.6).

Comparisons between cohorts of patients hospitalized for trauma showed that the pre-lockdown cohort was younger (18,178 vs. 16,005 patients), included a high proportion of males, and had different distributions of chronic conditions, trauma type, and discharge modality (Table 4.1). The 28-day mortality rate was higher in the pandemic cohort (3.5% vs. 2.9%, *p*-value < .01), though it equalled that of the pre-pandemic period (~2.9% in both cohorts) when patients who had confirmed SARS-CoV-2 infection within the prior 21 days were excluded.

No differences in hospital outcomes were observed when cohorts' characteristics were matched in PSM (Table 4.1), except for 28-day mortality when

patients with positive SARS-CoV-2 swab within the prior 21 days were included in the analysis (p-value .02; Figure 4.7).

### *4.5.2 Acute myocardial infarction*

The weekly number of hospitalizations for MI ranged between 40 and 90 in 2019 and between 20 and 60 during the first pandemic wave in Italy. Levels following the first wave remained lower than those of the pre-pandemic period. No difference was observed across the sexes (Figure 4.8).

When stratifying by sex and age, a trend of a constant small number of weekly hospitalizations was observed in women aged 70 years and under and men aged 60 years and under. The patterns in older age groups were similar to those observed in the general population (Figures 4.9–4.11).

The sex- and the age-adjusted weekly hospitalization rate dropped during the first wave to 14 hospitalizations per 1,000,000 person-weeks (Figure 4.12).

Overall, 4,069 and 3,969 patients were hospitalized for incident MI during the pre-lockdown period and the following months, respectively (Table 4.2). The first cohort was older (median age 72 vs. 70 years, *p*-value < .0001) and had different comorbid conditions. A longer length of stay (7 vs. 6 days, *p*-value .0004), lower 28-day mortality (9.6% vs. 11.0%, *p*-value .04) and lower in-hospital mortality (6.6 % vs 7.9%, *p*-value .03) were observed in the pre-lockdown cohort compared with those observed in the following months. However, differences became statistically non-significant after excluding patients who tested positive to SARS-CoV-2 infection in the previous 21 days.

The 1:1 matching resulted in 2,487 hospitalized MIs in each cohort (Table 4.2). Standardized group differences across covariates were less than 0.1, representing negligible differences except for the proportion of patients referred to other health facilities, a shorter length of stay (7 vs. 6 days, *p*-value < .05) and the greater mortality rate (10.8% vs 8.4%, *p*-value .002) in the COVID-19 period (Table 4.2; Figure 4.13). When deaths in patients with prior SARS-CoV-2 infection (positive swab in the previous 21 days) were excluded, mortality from MI was similar in the two cohorts (9.0% vs 8.3%, *p*-value .40). Similarly, the 28-day mortality differed only when patients with prior infection were included in the analysis (*p*-value .003; Figure 4.13, panels A and B). The discharge probability during the 28-day follow-up was statistically higher in the pre-lockdown cohort (p-value .004; Figure 4.13, panel C).

### *4.5.3 Stroke*

The weekly number of hospitalizations for stroke decreased over the entire pandemic period compared with that in 2019 (Figure 4.14). Analyses stratified by age and sex indicated an overall persistent trend in all ages, with a marked reduction in women 80 years and older (Figures 4.15–4.17).

Figure 18 shows the age- and sex-standardized weekly hospitalization rate. A slight decrease was observed during the first lockdown period when the rate reached three admissions per 1,000,000 person-weeks. The overall trend was consistent over the entire period.

Weekly stroke-attributable ED visits decreased during the first months of the pandemic and stably increasing in the months that followed, but still under the pre-pandemic level. From March to May 2020, the lowest weekly number was 10 ED visits, compared with a median of 33 ED visits in the pre-pandemic period (Figure 4.19).

The total number of patients hospitalized for incident stroke was 2,168, with 1,154 patients in the pre-lockdown period and 1,014 patients in the pandemic period (Table 4.3). Those admitted during the first period were older (median age 78 vs. 77 years, *p*-value .04) and had a higher prevalence of previous neuropathies (8.9% vs. 6.2%, *p*-value .02) recorded in the BDA.

The median length of stay was 9 days regardless of the study period (*p*-value .87). The 28-day mortality rate was higher in the lockdown cohort (31.7% vs 27.0%, *p*-value .01) but decreased to 29.0% when patients with prior SARS-CoV-2 infection (positive swab in the previous 21 days) were omitted from the analysis (*p*-value .27). During the COVID-19 pandemic, patients had a higher probability of being referred to other health facilities rather than being sent home.

After PSM, 572 hospitalized patients for each group entered the final analysis and the two cohorts were balanced according to covariates, with a standardized mean difference of less than 0.10 (Table 4.3). The risk of death appeared to be higher in the "lockdown" cohort, but the difference did not reach statistical significance when patients with prior SARS-CoV-2 infection were excluded. No differences in the 28-day risk of death and the probability of discharge were observed across cohorts (Table 4.3; Figure 4.20).

### *4.6 Concluding remarks*

This chapter provides interesting insight into the indirect impact of COVID-19 on hospital care for high-volume, non-deferrable conditions such as trauma, MI, and stroke.

A large number of COVID-19 cases in northern Italy overwhelmed hospitals and created the need for rapid adaptation to address the substantial flow of patients and control viral transmission (Ferrara et al., 2022*f*; Ferrara and Albano, 2020; Spadea et al., 2021; Voza et al., 2021). Adaptations included hospital bed cuts in several specialty departments (Ministry of Health, 2022).

Hospital admissions for trauma, MI, and stroke declined during the lockdown periods, especially from March to May 2020. In particular, trauma such as work- and road trauma halved during the lockdown, presumably because of the considerable reduction in outdoor activities, the cessation of non-essential work activities, and lengthy quarantine (Benazzo et al., 2020). Similarly, admissions for MI and stroke—two life-threatening conditions—suffered considerable reductions, with only scant differences in proxies of hospital outcomes (length of stay, discharge modality and probability, and mortality risk) except for a higher death rate in patients with recent SARS-CoV-2 infection.

The results of this study are roughly comparable to findings on the effect of the pandemic and national lockdown on the non-deferrable clinical conditions of interest reported in various contexts. Measures taken during COVID-19 resulted in a predictable decrease in the total number of patients with trauma (Benazzo et al., 2020; Fahy et al., 2020; van Aert et al., 2021).

Evidence highlighted slight decreases in the number of stroke cases during COVID-19, but the quality of care remained largely unchanged (Brunssen et al., 2022; Rydell et al. 2022). This is particularly relevant given the evolving epidemiology of stroke and the importance of timely and high-quality care. Notably, although a reduction in the total incidence is observed, there is an increase in the rate of stroke at a young age and an increase in the global prevalence of people living with stroke-attributable disability, which underlines the improvement of acute phase therapies (GBD 2019 Dementia Collaborators, 2021).

An analysis conducted in the Emilia-Romagna Region in Central Italy similarly described a decrease in MI hospitalizations during the first wave of the COVID-19 pandemic but did not indicate changes in the management and outcomes of hospitalized MI patients except for those with SARS-CoV-2 infection. However, a concomitant increase in out-of-hospital cardiac mortality was observed (Campo et al., 2021; Sanmarchi et al., 2022).

While appreciating the present findings, the analysis is nonetheless limited to patients who received a hospital diagnosis for any of the investigated health events that were traceable in HADs. Thus, the analysis cannot be completely free of ascertainment bias given that data did not include members of the target population

who did not have access to the hospital or ED during the COVID-19 pandemic, particularly during the first wave. Notably, previous analyses conducted in the same Lombard provinces during the first wave indicated an overall increased mortality risk among males and the elderly, highlighting that cumulative deaths were highest in the 70–79-year age group while COVID-19 attributable death was highest in individuals aged 80 years and higher (Conti et al., 2020*a*; VICES-SMIRE Study Group, 2022). As suggested by Conti et al., discrepancies might be due to a more clear-cut direct and indirect impact of COVID-19 in individuals 60 years and older in whom underlying functional status is a more important predictor of mortality because of acute life-threatening conditions (Conti et al., 2020*a*).

In summary, the empirical characterization of changes in healthcare pathways is important in guiding the post-pandemic management of resources (EOHSP, 2021). The relative stability of non-deferrable—and likely life-threatening—conditions indicate that the indirect impact of COVID-19 might not have been considerable in the provinces of Bergamo and Brescia. Future research should focus on monitoring hospital care and outcomes of patients with these conditions during further course of the COVID-19 pandemic.

### *4.7 Tables and Figures*

### *4.7.1 Tables*

TABLE 4.1: Hospitalized trauma patients before and after propensity score matching

| | *Before matching* | | | *After matching* | | |
|---|---|---|---|---|---|---|
| | **COVID-19 cohort** | **Pre-COVID cohort** | ***p-value*** | **Pre-COVID cohort** | **COVID-19 cohort** | ***p-value*** |
| N | 16005 | 18178 | | 9318 | 9318 | |
| Sex, n (%) | | | *0.0013* | | | |
| Female | 8037 (50.22) | 8811 (48.47) | | 4667 (50.09) | 4667 (50.09) | |
| Male | 7968 (49.78) | 9367 (51.53 | | 4651 (49.91) | 4651 (49.91) | |
| Age (in years) | | | *0.0065* | | | |
| Mean ± SD | 59.2 ± 25.2 | 58.2 ± 25.7 | | 56.81 ± 26.08 | 56.79 ± 26.05 | |
| Median (IQR) | 63 (43-80) | 63 (40-80) | | 60 (37-80) | 60 (38-80) | |
| Age classes, n (%) | | | *< 0.0001* | | | |
| <10 | 657 (4.10) | 677 (3.72) | | | | |
| 10-19 | 1076 (6.72) | 1407 (7.74) | | | | |
| 20-29 | 952 (5.95) | 1311 (7.21) | | | | |
| 30-39 | 899 (5.62) | 1115 (6.13) | | | | |
| 40-49 | 1375 (8.59) | 1678 (9.23) | | | | |
| 50-59 | 2239 (13.99) | 2234 (12.29) | | | | |
| 60-69 | 2047 (12.79) | 2115 (11.63) | | | | |
| 70-79 | 2419 (15.11) | 2753 (15.14) | | | | |
| 80+ | 4341 (27.12) | 4888 (26.89) | | | | |
| Comorbidities, n (%) | | | | | | |
| Organ transplant | 5 (0.03) | 4 (0.02) | *0.3207* | 0 (0) | 0 (0) | |
| Chronic kidney disease | 374 (2.34) | 450 (2.48) | *0.0421* | 79 (0.85) | 79 (0.85) | |
| HIV/AIDS | 53 (0.33) | 47 (0.26) | *< 0.0001* | 0 (0) | 0 (0) | |
| Cancer | 1800 (11.25) | 1715 (9.43) | *0.0062* | 683 (7.33) | 683 (7.33) | |
| Cardiovascular disease | 6440 (40.24) | 6431 (35.38) | *0.3799* | 3343 (35.88) | 3343 (35.88) | |
| Chronic respiratory disease | 805 (5.03) | 889 (4.89) | *0.8753* | 225 (2.41) | 225 (2.41) | |
| Gastrointestinal disease | 512 (3.2) | 505 (2.78) | *0.2145* | 82 (0.88) | 82 (0.88) | |
| Neuropathy | 698 (4.36) | 935 (5.14) | *0.5999* | 247 (2.65) | 247 (2.65) | |
| Autoimmune disorder | 425 (2.66) | 415 (2.28) | *0.0897* | 67 (0.72) | 67 (0.72) | |
| Thyroid disorder | 2569 (16.05) | 2415 (13.29) | *0.2864* | 1067 (11.45) | 1067 (11.45) | |

| | *Before matching* | | | *After matching* | | |
|---|---|---|---|---|---|---|
| | **COVID-19 cohort** | **Pre-COVID cohort** | ***p-value*** | **Pre-COVID cohort** | **COVID-19 cohort** | ***p-value*** |
| Type 1 diabetes mellitus | 19 (0.12) | 28 (0.15) | *0.3588* | 0 (0) | 0 (0) | |
| Type 2 diabetes mellitus | 1603 (10.02) | 1662 (9.14) | *0.1670* | 595 (6.39) | 595 (6.39) | |
| Others | 185 (1.16) | 244 (1.34) | *0.8515* | 16 (0.17) | 16 (0.17) | |
| Trauma cause, n (%) | | | | | | |
| Work | 737 (4.6) | 779 (4.29) | *0.1523* | 414 (4.44) | 414 (4.44) | |
| Home | 4778 (29.85) | 5267 (28.97) | *0.0752* | 2741 (29.42) | 2741 (29.42) | |
| Traffic | 1323 (8.27) | 1678 (9.23) | *0.0017* | 759 (8.15) | 759 (8.15) | |
| Interpersonal violence | 108 (0.67) | 178 (0.98) | *0.0020* | 38 (0.41) | 38 (0.41) | |
| Self-harm with or without intent to kill oneself | 99 (0.62) | 137 (0.75) | *0.1323* | 22 (0.24) | 22 (0.24) | |
| Others | 7437 (46.47) | 8281 (45.56) | *0.0915* | 4532 (48.64) | 4532 (48.64) | |
| Unknown | 1523 (9.52) | 1858 (10.22) | *0.0293* | 812 (8.71) | 812 (8.71) | |
| ICD-9-CM diagnoses (and code) | | | | | | |
| Fracture (800-829) | 11424 (71.38) | 12646 (69.57) | *0.0003* | 7617 (81.75) | 7617 (81.75) | |
| Dislocation (830-839) | 274 (1.71) | 356 (1.96) | *0.0909* | 98 (1.05) | 98 (1.05) | |
| Sprains and strains of joints and adjacent muscles (840-848) | 968 (6.05) | 1223 (6.73) | *0.0104* | 577 (6.19) | 577 (6.19) | |
| Intracranial injury, excluding those with skull fracture (850-854) | 776 (4.85) | 890 (4.9) | *0.8386* | 244 (2.62) | 244 (2.62) | |
| Internal injury of chest, abdomen, and pelvis (860-869) | 365 (2.28) | 384 (2.11) | *0.2895* | 114 (1.22) | 114 (1.22) | |
| Open wound (870-897) | 776 (4.85) | 757 (4.16) | *0.0023* | 374 (4.01) | 374 (4.01) | |
| Injury to blood vessel (900-904) | 57 (0.36) | 60 (0.33) | *0.6805* | 4 (0.04) | 4 (0.04) | |
| Superficial injuries (910-919) | 51 (0.32) | 54 (0.3) | *0.7189* | 4 (0.04) | 4 (0.04) | |
| Contusion with intact skin surface (920-924) | 271 (1.69) | 467 (2.57) | *< 0.0001* | 66 (0.71) | 66 (0.71) | |
| Crushing injury (925-929 | 59 (0.37) | 59 (0.32) | *0.4882* | 13 (0.14) | 13 (0.14) | |
| Effects of foreign body entering through orifice (930-939) | 121 (0.76) | 124 (0.68) | *0.4192* | 33 (0.35) | 33 (0.35) | |
| Burns (940-949) | 95 (0.59) | 126 (0.69) | *0.2517* | 23 (0.25) | 23 (0.25) | |
| Injury to nerves and spinal cord (950-957) | 77 (0.48) | 82 (0.45) | *0.6841* | 10 (0.11) | 10 (0.11) | |

| | *Before matching* | | | *After matching* | | |
|---|---|---|---|---|---|---|
| | **COVID-19 cohort** | **Pre-COVID cohort** | ***p-value*** | **Pre-COVID cohort** | **COVID-19 cohort** | ***p-value*** |
| Certain traumatic complications and unspecified injuries 958-959 | 95 (0.59) | 131 (0.72) | *0.1480* | 15 (0.16) | 15 (0.16) | |
| Poisoning by drugs, medicinal and biological substances (960-979) | 194 (1.21) | 281 (1.55) | *0.0085* | 38 (0.41) | 38 (0.41) | |
| Toxic effects of substances chiefly nonmedicinal as to source (980-989) | 40 (0.25) | 61 (0.34) | *0.1454* | 4 (0.04) | 4 (0.04) | |
| Other and unspecified effects of external causes (990-995) | 362 (2.26) | 477 (2.62) | *0.0308* | 84 (0.9) | 84 (0.9) | |
| Discharge type | | | | | | |
| Home | 12078 (75.46) | 14048 (77.28) | *<0.0001* | 7113 (76.34) | 7196 (77.23) | *0.0818* |
| Against medical advice | 91 (0.57) | 119 (0.65) | *0.3096* | 42 (0.45) | 46 (0.49) | *0.7493* |
| Other hospital | 360 (2.25) | 381 (2.1) | *0.3313* | 156 (1.67) | 140 (1.5) | *0.3666* |
| Other unit (same hospital) | 801 (5) | 972 (5.35) | *0.1543* | 482 (5.17) | 541 (5.81) | *0.0527* |
| Home with medical support | 9 (0.06) | 6 (0.03) | *0.3063* | 156 (1.67) | 140 (1.5) | *0.3666* |
| Home with nursing support | 86 (0.54) | 68 (0.37) | *0.0245* | 5 (0.05) | 2 (0.02) | *0.4531* |
| Residential or nursing facility | 1922 (12.01) | 1967 (10.82) | *0.0006* | 42 (0.45) | 31 (0.33) | *0.2416* |
| Long-term facility | 359 (2.24) | 316 (1.74) | *0.0008* | 1148 (12.32) | 1075 (11.54) | *0.0764* |
| Death | 299 (1.87) | 301 (1.66) | *0.1358* | 195 (2.09) | 176 (1.89) | *0.3268* |
| Length-of-stay (in days) | | | *0.2168* | | | *0.9824* |
| Mean ± SD | 6.7 ± 7.8 | 6.9 ± 8.7 | | 6.23 ± 6.83 | 6.30 ± 7.21 | |
| Median (IQR) | 4 (2-9) | 4 (2-9) | | 4 (2-8) | 4 (2-8) | |
| Mortality, n (%) | | | | | | |
| In-hospital | 299 (1.87) | 301 (1.66) | *0.1358* | 135 (1.45) | 111 (1.19) | *0.1157* |
| *Without prior SARS-CoV-2 infection** | *255 (1.59)* | *299 (1.64)* | *0.7062* | 110 (1.18) | 111 (1.19) | *1.0000* |
| Within 28 days from discharge | 552 (3.45) | 522 (2.87) | *0.0023* | 254 (2.73) | 209 (2.24) | *0.0197* |
| *Without prior SARS-CoV-2 infection** | *462 (2.89)* | *514 (2.83)* | *0.7438* | 202 (2.17) | 207 (2.22) | *0.8265* |
| After 28 days from discharge | 253 (1.58) | 221 (1.22) | *0.0040* | 119 (1.29) | 98 (1.05) | *0.1412* |
| *Without prior SARS-CoV-2 infection** | *207 (1.29)* | *215 (1.18)* | *0.3555* | 92 (0.99) | 96 (1.03) | *0.8170* |

* Positive SARS-CoV-2 swab test within the previous 21 days

Abbreviations: COVID-19, coronavirus disease 2019; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; HIV, Human Immunodeficiency Virus; AIDS, Acquired Immuno-deficiency Syndrome; ICD-9-CM, International Classification of Diseases, 9th Revision, Clinical Modification; SD, standard deviation; IQR, interquartile range

TABLE 4.2: Hospitalized MI patients before and after propensity score matching

| | *Before matching* | | | *After matching* | | |
|---|---|---|---|---|---|---|
| | **COVID-19 cohort** | **Pre-COVID cohort** | ***p-value*** | **Pre-COVID cohort** | **COVID-19 cohort** | ***p-value*** |
| N | 3969 | 4069 | | 2487 | 2487 | |
| Sex, n (%) | | | *0.0734* | | | |
| Female | 1236 (31.14) | 1343 (33.01) | | 736 (29.59) | 736 (29.59) | |
| Male | 2733 (68.86) | 1226 (66.99) | | 1751 (70.41) | 1751 (70.41) | |
| Age (in years) | | | *<.0001* | | | |
| Mean ± SD | 69.8 ± 13.1 | 71.2 ± 13.3 | | 70.10 ± 12.88 | 70.24 ± 12.95 | |
| Median (IQR) | 70 (60-80) | 72 (61-82) | | 71 (60-80) | 71 (60-81) | |
| Age classes, n (%) | | | *0.0008* | | | |
| <10 | 1 (0.03) | 1 (0.02) | | | | |
| 10-19 | 1 (0.03) | 1 (0.02) | | | | |
| 20-29 | 22 (0.55) | 21 (0.52) | | | | |
| 30-39 | 250 (6.30) | 212 (5.21) | | | | |
| 40-49 | 675 (17.01) | 643 (15.80) | | | | |
| 50-59 | 946 (23.83) | 929 (22.83) | | | | |
| 60-69 | 996 (25.09) | 960 (23.59) | | | | |
| 70-79 | 1078 (27.16) | 1301 (31.97) | | | | |
| 80+ | | | | | | |
| Comorbidities, n (%) | | | | | | |
| Organ transplant | 2 (0.05) | 0 (0) | *0.2438* | 0 (0.00) | 0 (0.00) | |
| Chronic kidney disease | 193 (4.86) | 260 (6.39) | *0.0030* | 67 (2.69) | 67 (2.69) | |
| HIV/AIDS | 26 (0.66) | 31 (0.76) | *0.5684* | 3 (0.12) | 3 (0.12) | |
| Cancer | 506 (12.75) | 569 (13.98) | *0.1039* | 232 (9.33) | 232 (9.33) | |
| Cardiovascular disease | 2324 (58.55) | 2557 (62.84) | *<.0001* | 1479 (59.47) | 1479 (59.47) | |
| Chronic respiratory disease | 222 (5.59) | 273 (6.71) | *0.0375* | 77 (3.1) | 77 (3.1) | |
| Gastrointestinal disease | 147 (3.7) | 145 (3.56) | *0.7370* | 28 (1.13) | 28 (1.13) | |
| Neuropathy | 112 (2.82) | 128 (3.15) | *0.3937* | 24 (0.97) | 24 (0.97) | |
| Autoimmune disorder | 98 (2.47) | 117 (2.88) | *0.2590* | 14 (0.56) | 14 (0.56) | |
| Thyroid disorder | 1013 (25.52) | 1140 (28.02) | *0.0116* | 611 (24.57) | 611 (24.57) | |
| Type 1 diabetes mellitus | 39 (0.98) | 32 (0.79) | *0.3473* | 4 (0.16) | 4 (0.16) | |
| Type 2 diabetes mellitus | 11 (0.28) | 4 (0.1) | *0.0632* | 1 (0.04) | 1 (0.04) | |

| | *Before matching* | | | *After matching* | | |
|---|---|---|---|---|---|---|
| | **COVID-19 cohort** | **Pre-COVID cohort** | ***p-value*** | **Pre-COVID cohort** | **COVID-19 cohort** | ***p-value*** |
| Others | 819 (20.63) | 963 (23.67) | *0.0011* | 444 (17.85) | 444 (17.85) | |
| Discharge type | | | | | | |
| Home | 2742 (69.09) | 2763 (67.9) | *0.2542* | 1743 (70.08) | 1726 (69.4) | *0.6076* |
| Against medical advice | 23 (0.58) | 14 (0.34) | *0.1190* | 15 (0.6) | 11 (0.44) | *0.5413* |
| Other hospital | 240 (6.05) | 308 (7.57) | *0.0068* | 139 (5.59) | 193 (7.76) | *0.0022* |
| Other unit (same hospital) | 81 (2.04) | 123 (3.02) | *0.0051* | 49 (1.97) | 59 (2.37) | *0.3634* |
| Home with medical support | 1 (0.03) | 0 (0) | *0.4938* | 0 (0.00) | 0 (0.00) | - |
| Home with nursing support | 6 (0.15) | 8 (0.2) | *0.6252* | 3 (0.12) | 5 (0.2) | *0.7266* |
| Residential or nursing facility | 515 (12.98) | 553 (13.59) | *0.4167* | 308 (12.38) | 338 (13.59) | *0.2212* |
| Long-term facility | 47 (1.18) | 30 (0.74) | *0.0397* | 35 (1.41) | 11 (0.44) | *0.0005* |
| Death | 314 (7.91) | 270 (6.64) | *0.0276* | 195 (7.84) | 144 (5.79) | *0.0032* |
| Length-of-stay (in days) | | | *0.0004* | | | *0.0489* |
| Mean ± SD | 8.7 ± 7.9 | 9.0 ± 7.7 | | 8.59 ± 8.05 | 8.84 ± 7.91 | |
| Median (IQR) | 6 (5-10) | 7 (5-10) | | 6 (5-10) | 7 (5-10) | |
| Mortality, n (%) | | | | | | |
| In-hospital | 436 (10.99) | 389 (9.56) | *0.0352* | 269 (10.82) | 208 (8.36) | *0.0019* |
| *Without prior SARS-CoV-2 infection** | *354 (8.92)* | *386 (9.49)* | *0.3792* | 223 (8.97) | 206 (8.28) | *0.3945* |
| Within 28 days from discharge | 314 (7.91) | 270 (6.64) | *0.0276* | 195 (7.84) | 144 (5.79) | *0.0032* |
| *Without prior SARS-CoV-2 infection** | *256 (6.45)* | *267 (6.56)* | *0.8390* | 163 (6.55) | 142 (5.71) | *0.2209* |
| After 28 days from discharge | 122 (3.07) | 119 (2.92) | *0.6948* | 74 (2.98) | 64 (2.57) | *0.4228* |
| *Without prior SARS-CoV-2 infection** | *98 (2.47)* | *119 (2.92)* | *0.2078* | 60 (2.41) | 64 (2.57) | *0.7789* |

* Positive SARS-CoV-2 swab test within the previous 21 days

Abbreviations: MI, acute myocardial infarction; COVID-19, coronavirus disease 2019; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; HIV, Human Immunodeficiency Virus; AIDS, Acquired Immuno-deficiency Syndrome; SD, standard deviation; IQR, interquartile range

TABLE 4.3: Hospitalized stroke patients before and after propensity score matching

| | *Before matching* | | | *After matching* | | |
|---|---|---|---|---|---|---|
| | **COVID-19 cohort** | **Pre-COVID cohort** | ***p-value*** | **Pre-COVID cohort** | **COVID-19 cohort** | ***p-value*** |
| N | 1014 | 1154 | | 572 | 572 | |
| Sex, n (%) | | | *0.5075* | | | |
| Female | 532 (52.47) | 589 (51.04) | | 294 (51.4) | 294 (51.4) | |
| Male | 482 (47.53) | 565 (48.96) | | 278 (48.6) | 278 (48.6) | |
| Age (in years) | | | *0.0348* | | | |
| Mean ± SD | 73.0 ± 15.2 | 73.9 ± 16.1 | | 72.99 ± 15.15 | 73.65 ± 15.10 | |
| Median (IQR) | 77 (63-84) | 78 (66-85) | | 77 (63-84) | 78 (65-85) | |
| Age classes, n (%) | | | *0.3978* | | | |
| <10 | 4 (0.39) | 5 (0.43) | | | | |
| 10-19 | 2 (0.20) | 3 (0.26) | | | | |
| 20-29 | 7 (0.69) | 12 (1.04) | | | | |
| 30-39 | 18 (1.78) | 16 (1.39) | | | | |
| 40-49 | 45 (4.44) | 66 (5.72) | | | | |
| 50-59 | 118 (11.64) | 114 (9.88) | | | | |
| 60-69 | 133 (13.12) | 133 (11.53) | | | | |
| 70-79 | 264 (26.04) | 279 (24.18) | | | | |
| 80+ | 423 (41.72) | 526 (45.58) | | | | |
| Comorbidities, n (%) | | | | | | |
| Organ transplant | 2 (0.2) | 2 (0.17) | *1.0000* | 0 (0.00) | 0 (0.00) | |
| Chronic kidney disease | 44 (4.34) | 47 (4.07) | *0.7575* | 5 (0.87) | 5 (0.87) | |
| HIV/AIDS | 4 (0.39) | 5 (0.43) | *1.0000* | 0 (0.00) | 0 (0.00) | |
| Cancer | 147 (14.5) | 187 (16.2) | *0.2718* | 48 (8.39) | 48 (8.39) | |
| Cardiovascular disease | 578 (57) | 689 (59.71) | *0.2025* | 320 (55.94) | 320 (55.94) | |
| Chronic respiratory disease | 47 (4.64) | 62 (5.37) | *0.4330* | 7 (1.22) | 7 (1.22) | |
| Gastrointestinal disease | 35 (3.45) | 33 (2.86) | *0.4300* | 5 (0.87) | 5 (0.87) | |
| Neuropathy | 63 (6.21) | 103 (8.93) | *0.0178* | 19 (3.32) | 19 (3.32) | |
| Autoimmune disorder | 26 (2.56) | 22 (1.91) | *0.2991* | 0 (0.00) | 0 (0.00) | |
| Thyroid disorder | 219 (21.6) | 263 (22.79) | *0.5052* | 95 (16.61) | 95 (16.61) | |
| Type 1 diabetes mellitus | 11 (1.08) | 9 (0.78) | *0.4587* | 0 (0.00) | 0 (0.00) | |
| Type 2 diabetes mellitus | 1 (0.1) | 2 (0.17) | *1.0000* | 0 (0.00) | 0 (0.00) | |

| | *Before matching* | | | *After matching* | | |
|---|---|---|---|---|---|---|
| | **COVID-19 cohort** | **Pre-COVID cohort** | ***p-value*** | **Pre-COVID cohort** | **COVID-19 cohort** | ***p-value*** |
| Others | 138 (13.61) | 178 (15.42) | *0.2321* | 48 (8.39) | 48 (8.39) | |
| Discharge type | | | | | | |
| Home | 348 (34.32) | 449 (38.91) | *0.0270* | 204 (35.66) | 219 (38.29) | *0.3750* |
| Against medical advice | 5 (0.49) | 1 (0.09) | *0.1043* | 3 (0.52) | 0 (0.00) | *1.0000* |
| Other hospital | 84 (8.28) | 91 (7.89) | *0.7340* | 45 (7.87) | 55 (9.62) | *0.3481* |
| Other unit (same hospital) | 90 (8.88) | 75 (6.5) | *0.0373* | 47 (8.22) | 33 (5.77) | *0.1302* |
| Home with medical support | 0 (0) | 1 (0.09) | *1.0000* | 0 (0.00) | 0 (0.00) | - |
| Home with nursing support | 8 (0.79) | 9 (0.78) | *0.9810* | 3 (0.52) | 2 (0.35) | *1.0000* |
| Residential or nursing facility | 196 (19.33) | 248 (21.49) | *0.2135* | 111 (19.41) | 120 (20.98) | *0.5544* |
| Long-term facility | 41 (4.04) | 36 (3.12) | *0.2462* | 22 (3.85) | 11 (1.92) | *0.0522* |
| Death | 242 (23.87) | 244 (21.14) | *0.1294* | 137 (23.95) | 132 (23.08) | *0.7651* |
| Length-of-stay (in days) | | | *0.8669* | | | *0.5328* |
| Mean ± SD | 13.2 ± 14.0 | 12.6 ± 12.7 | | 12.25 ± 11.38 | 12.25 ± 11.38 | |
| Median (IQR) | 9 (5-17) | 9 (5-15) | | 9 (5-15) | 9 (5-15) | |
| Mortality, n (%) | | | | | | |
| In-hospital | 322 (31.76) | 311 (26.95) | *0.0141* | 194 (33.92) | 164 (28.67) | *0.0431* |
| *Without prior SARS-CoV-2 infection** | *294 (28.99)* | *310 (26.86)* | *0.2695* | 170 (29.72) | 163 (28.50) | *0.6782* |
| Within 28 days from discharge | 242 (23.87) | 244 (21.14) | *0.1294* | 137 (23.95) | 132 (23.08) | *0.7651* |
| *Without prior SARS-CoV-2 infection** | *224 (22.09)* | *244 (21.14)* | *0.5929* | 122 (21.33) | 132 (23.08) | *0.5001* |
| After 28 days from discharge | 80 (7.89) | 67 (5.81) | *0.0542* | 57 (9.97) | 32 (5.59) | *0.0088* |
| *Without prior SARS-CoV-2 infection** | *70 (6.90)* | *66 (5.72)* | *0.2566* | 48 (8.39) | 31 (5.42) | *0.0675* |

* Positive SARS-CoV-2 swab test within the previous 21 days

Abbreviations: COVID-19, coronavirus disease 2019; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; HIV, Human Immunodeficiency Virus; AIDS, Acquired Immuno-deficiency Syndrome; SD, standard deviation; IQR, interquartile range

### *4.7.2 Figures*

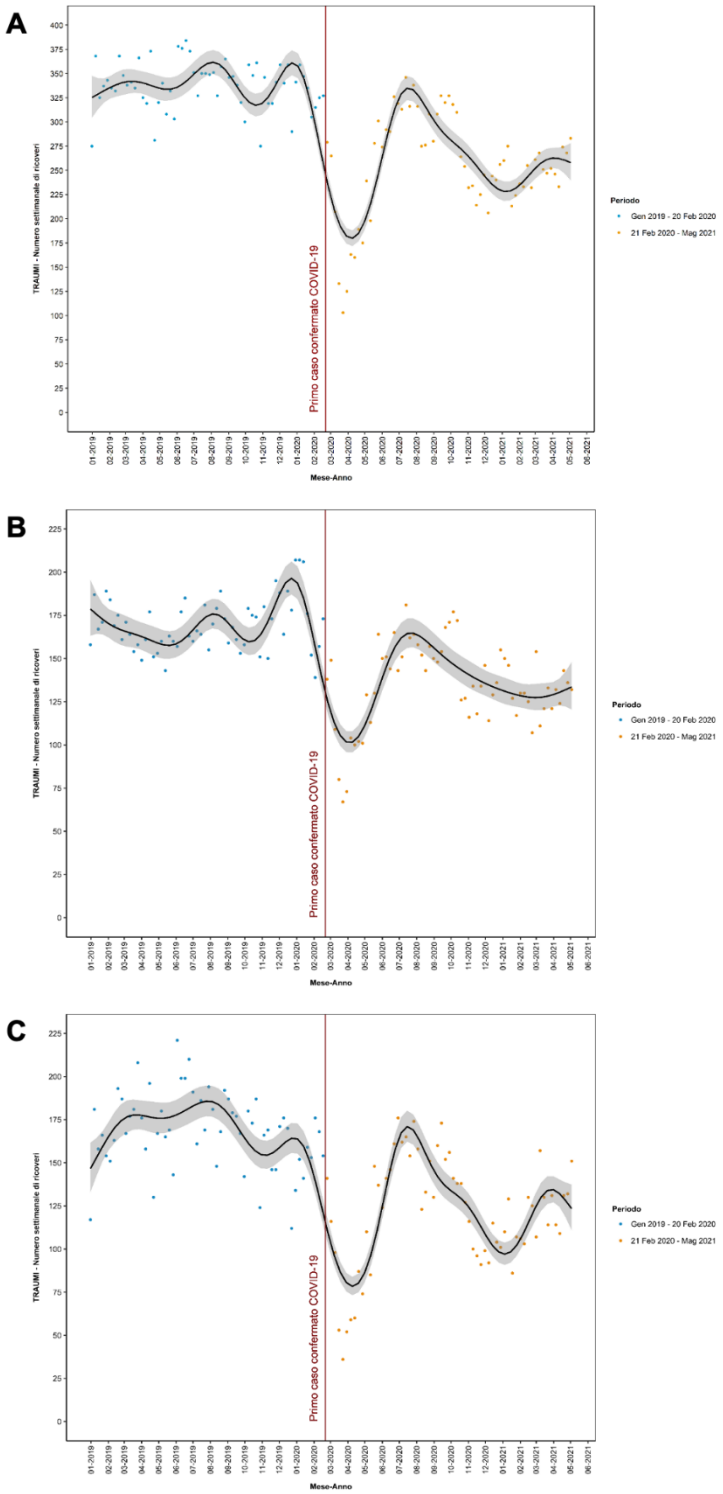


FIGURE 4.1. Time series of weekly number of trauma hospitalizations. Panel A, general population; Panel B, female; Panel C, male

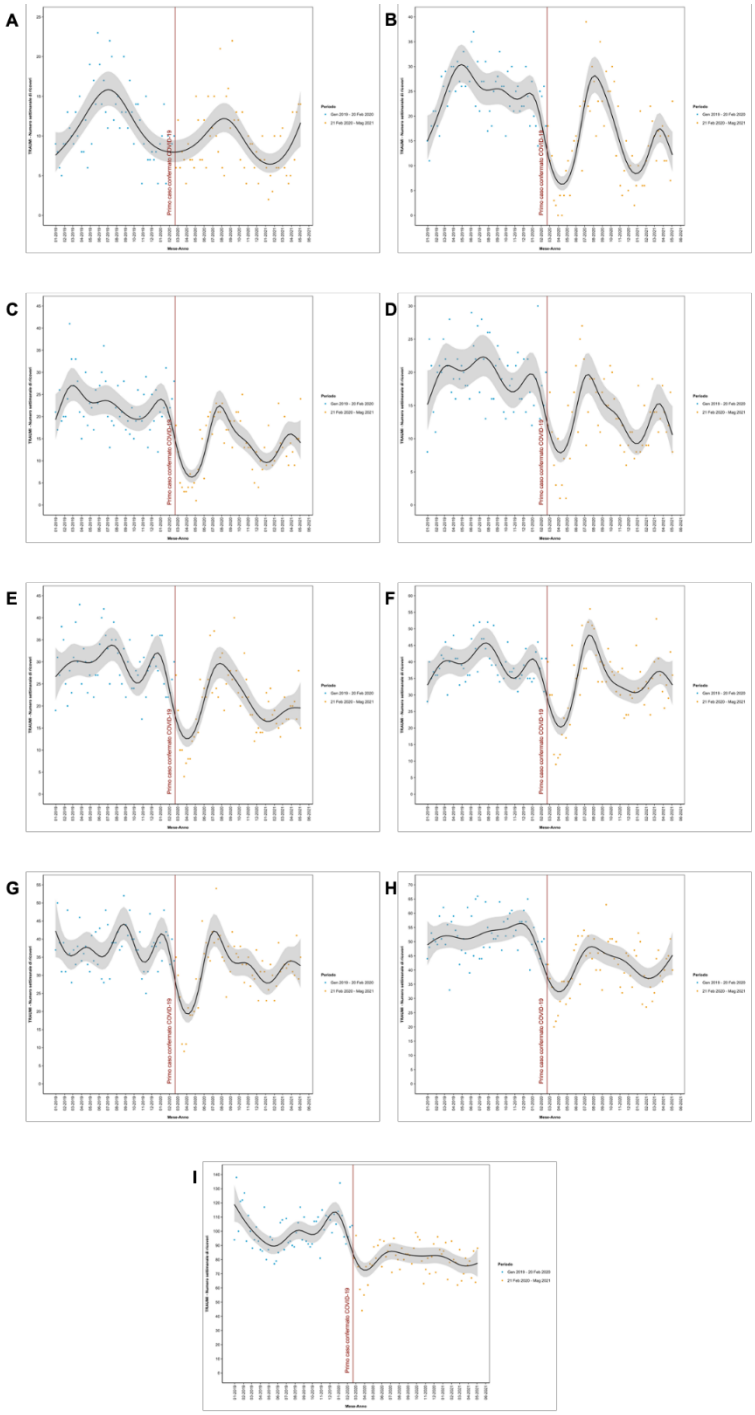


FIGURE 4.2. Time series of weekly numbers of trauma hospitalization, stratified by age classes (2019-2021). Panel A, 0-9 years; Panel B, 10-19 years; Panel C, 20-29 years; Panel D, 30-39 years; Panel E, 40-49 years; Panel F, 50-59 years; Panel G, 60-69 years; Panel H, 70-79 years; Panel I, 80+ years

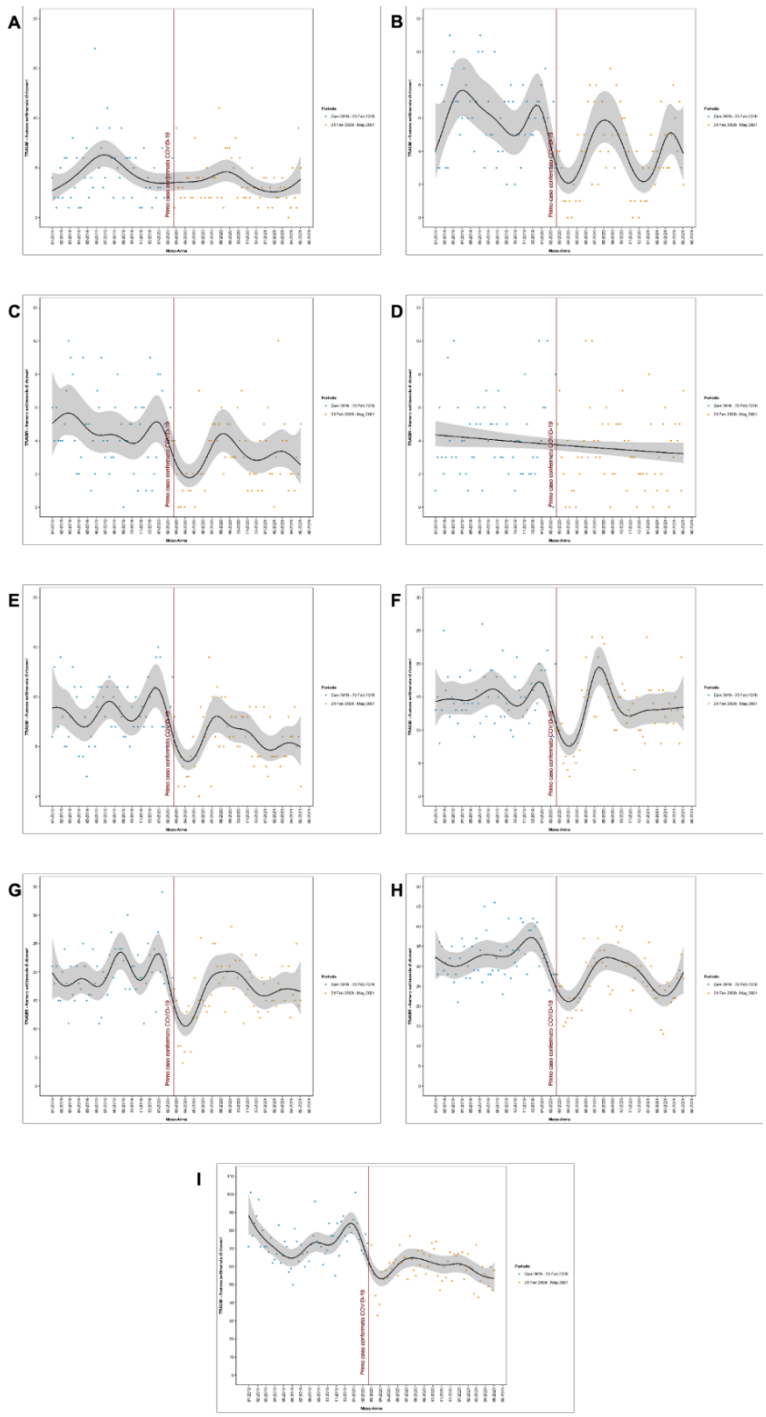


FIGURE 4.3. Time series of weekly numbers of trauma hospitalization in female population, stratified by age classes (2019-2021). Panel A, 0-9 years; Panel B, 10-19 years; Panel C, 20-29 years; Panel D, 30-39 years; Panel E, 40-49 years; Panel F, 50-59 years; Panel G, 60-69 years; Panel H, 70-79 years; Panel I, 80+ years

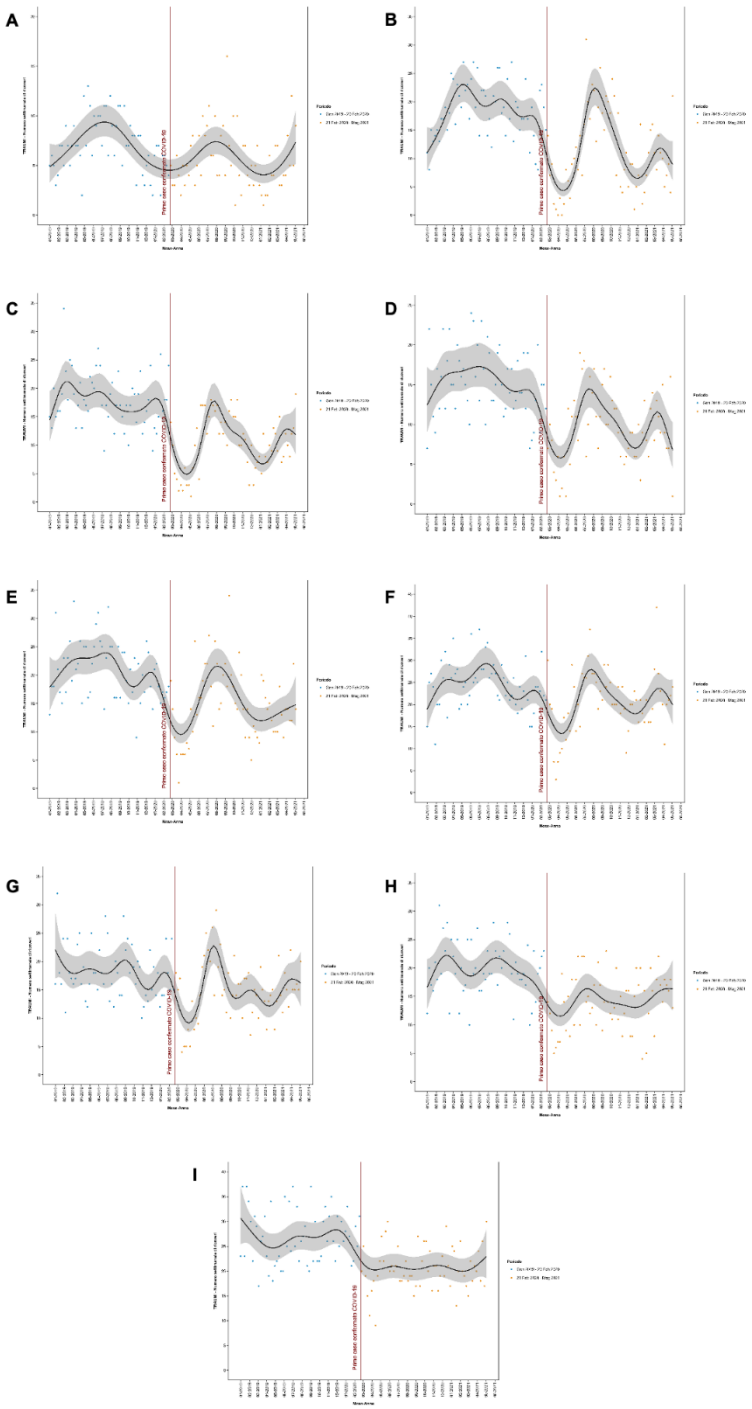


FIGURE 4.4. Time series of weekly numbers of trauma hospitalization in male population, stratified by age classes (2019-2021). Panel A, 0-9 years; Panel B, 10-19 years; Panel C, 20-29 years; Panel D, 30-39 years; Panel E,

40-49 years; Panel F, 50-59 years; Panel G, 60-69 years; Panel H, 70-79 years; Panel I, 80+ years

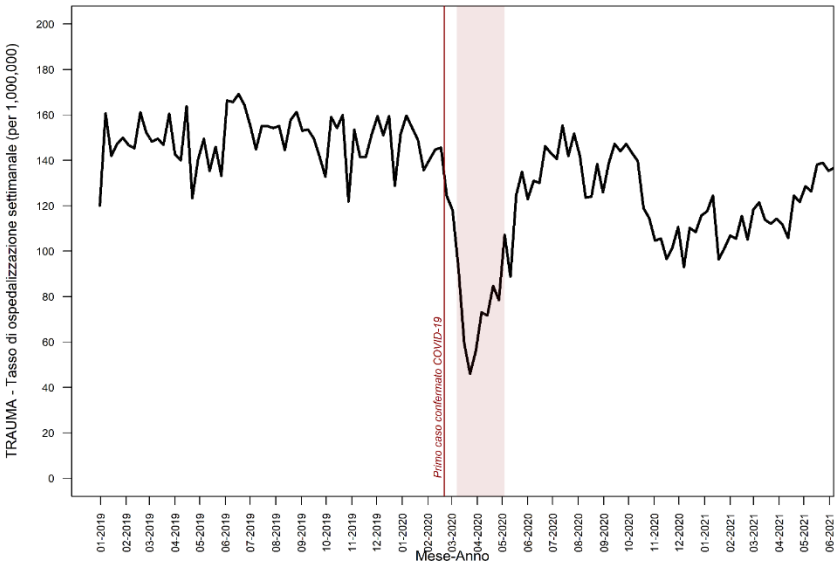


FIGURE 4.5. Weekly rate of trauma hospital admissions (trend 2019-2021)

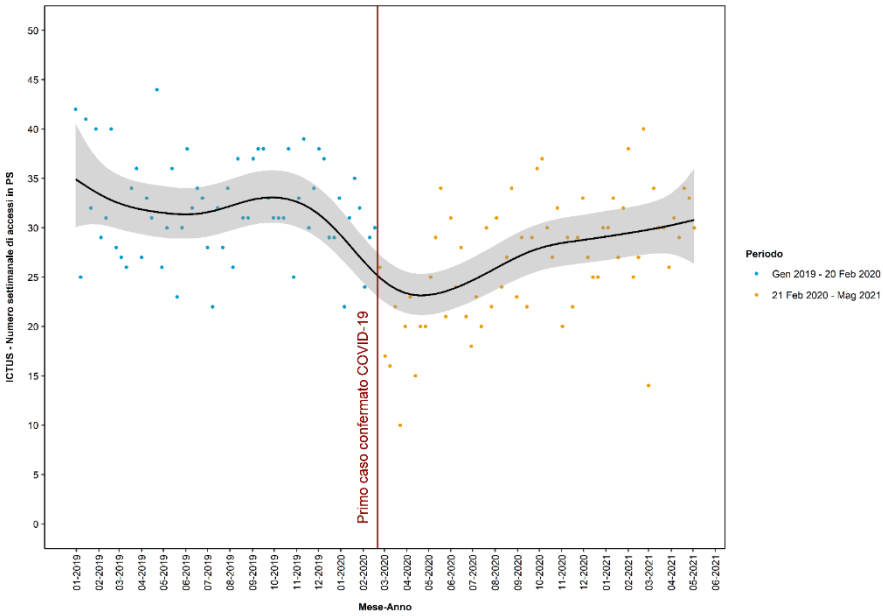


FIGURE 4.6. Weekly numbers of trauma ED visits (trend 2019-2021)

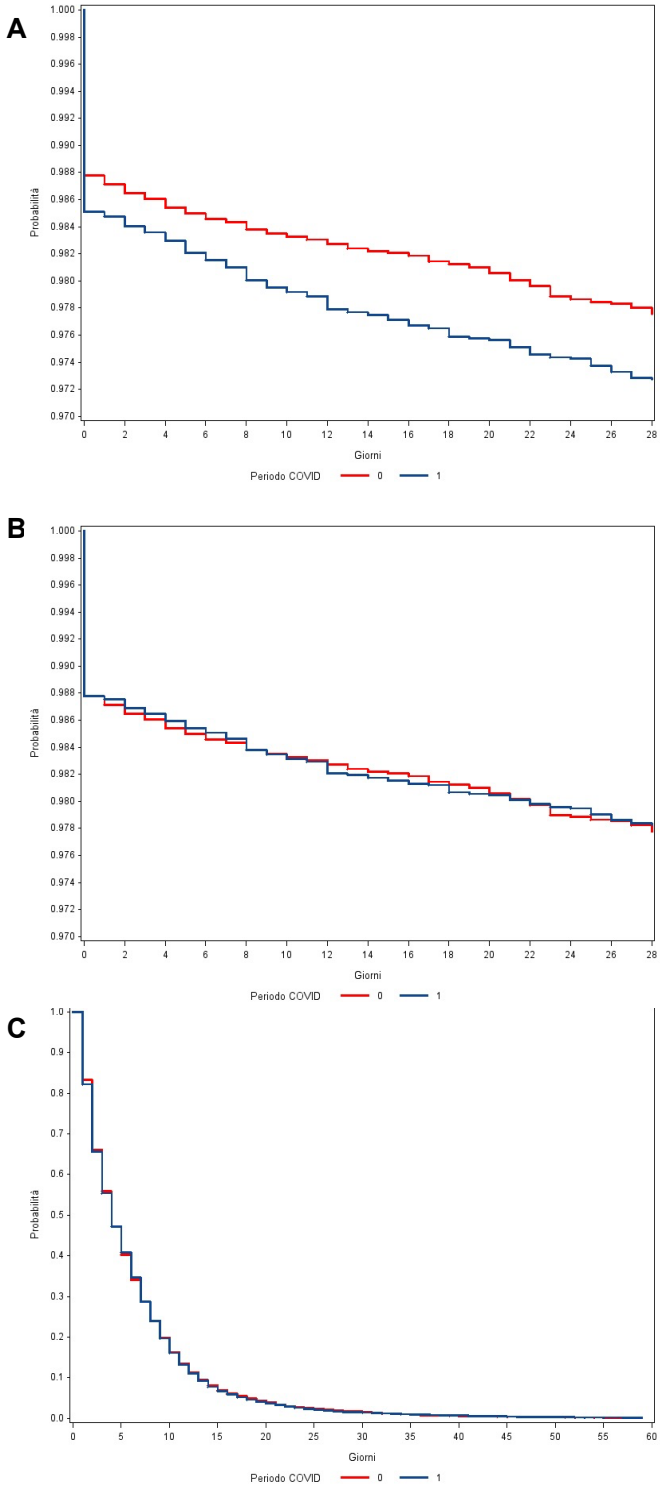


FIGURE 4.7. Kaplan-Meier curves in matched cohorts of hospitalized trauma patients. Panel A, time-to-death (*p*-value = 0.0033); Panel B, time-to-death in patients without previous SARS-CoV-2 infection (*p*-value = 0.9144); Panel C, time-to-discharge (*p*-value = 0.2653)

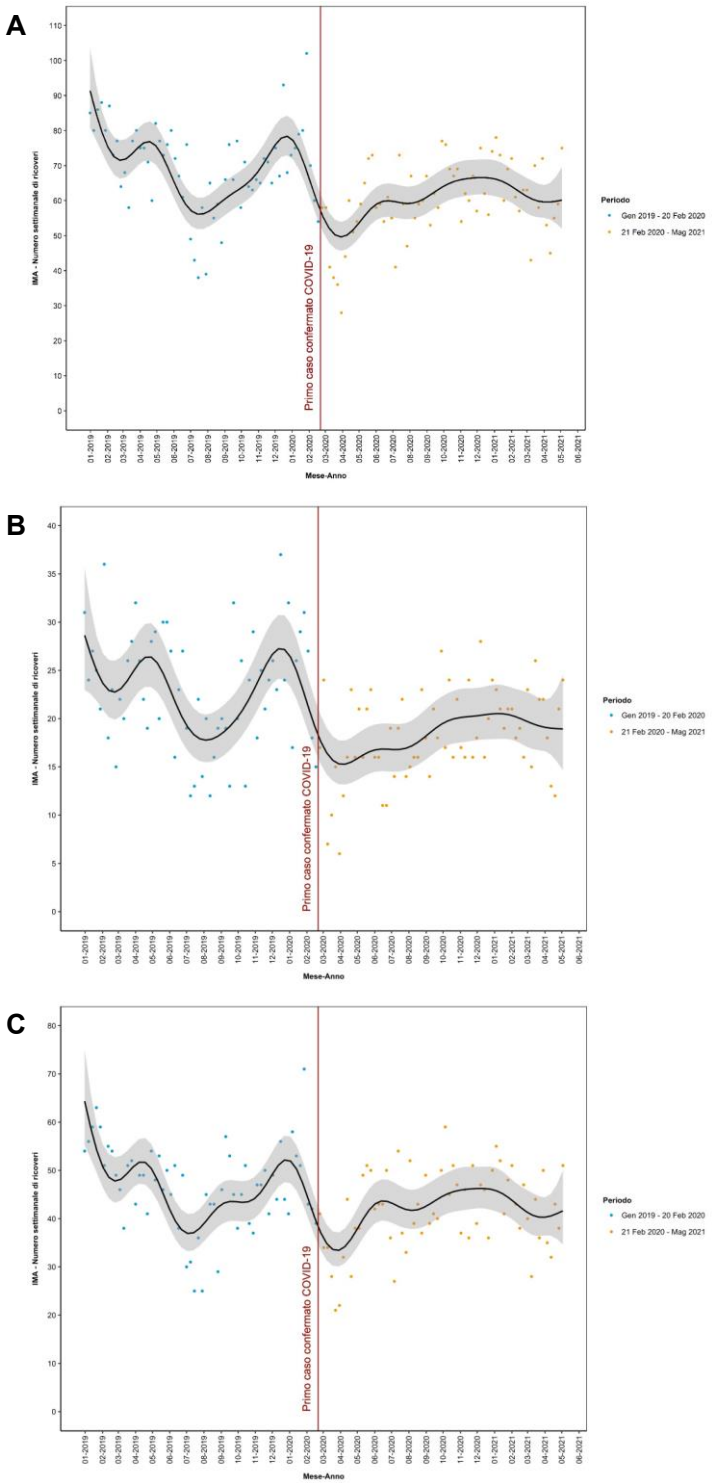


FIGURE 4.8. Time series of weekly number of hospitalizations for acute myocardial infarction (MI). Panel A, general population; Panel B, female; Panel C, male

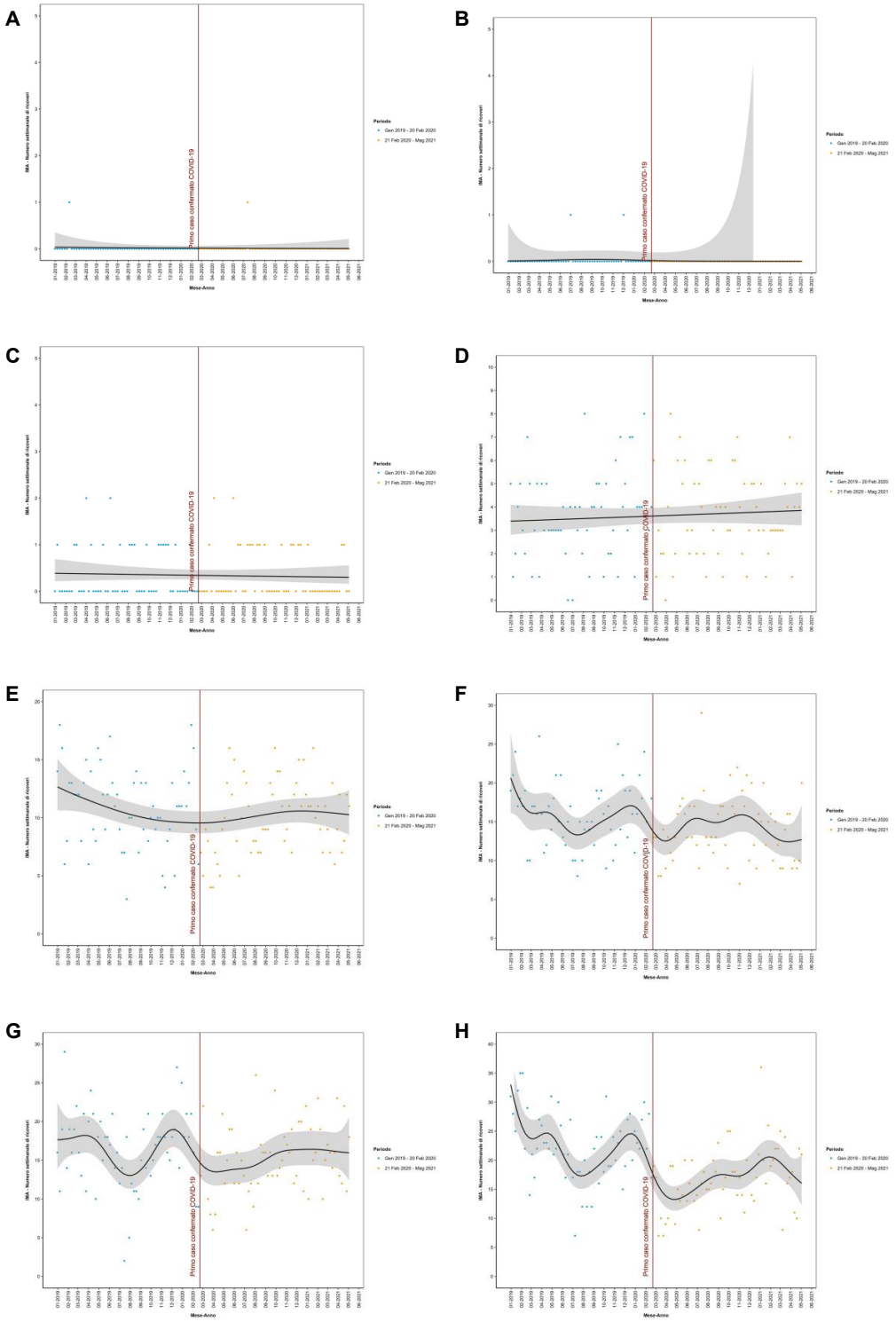


FIGURE 4.9. Time series of weekly numbers of MI hospitalization, stratified by age classes (2019-2021). Panel A, 10-19 years; Panel B, 20-29 years; Panel C, 30-39 years; Panel D, 40-49 years; Panel E, 50-59 years; Panel F, 60-69 years; Panel G, 70-79 years; Panel H, 80+ years

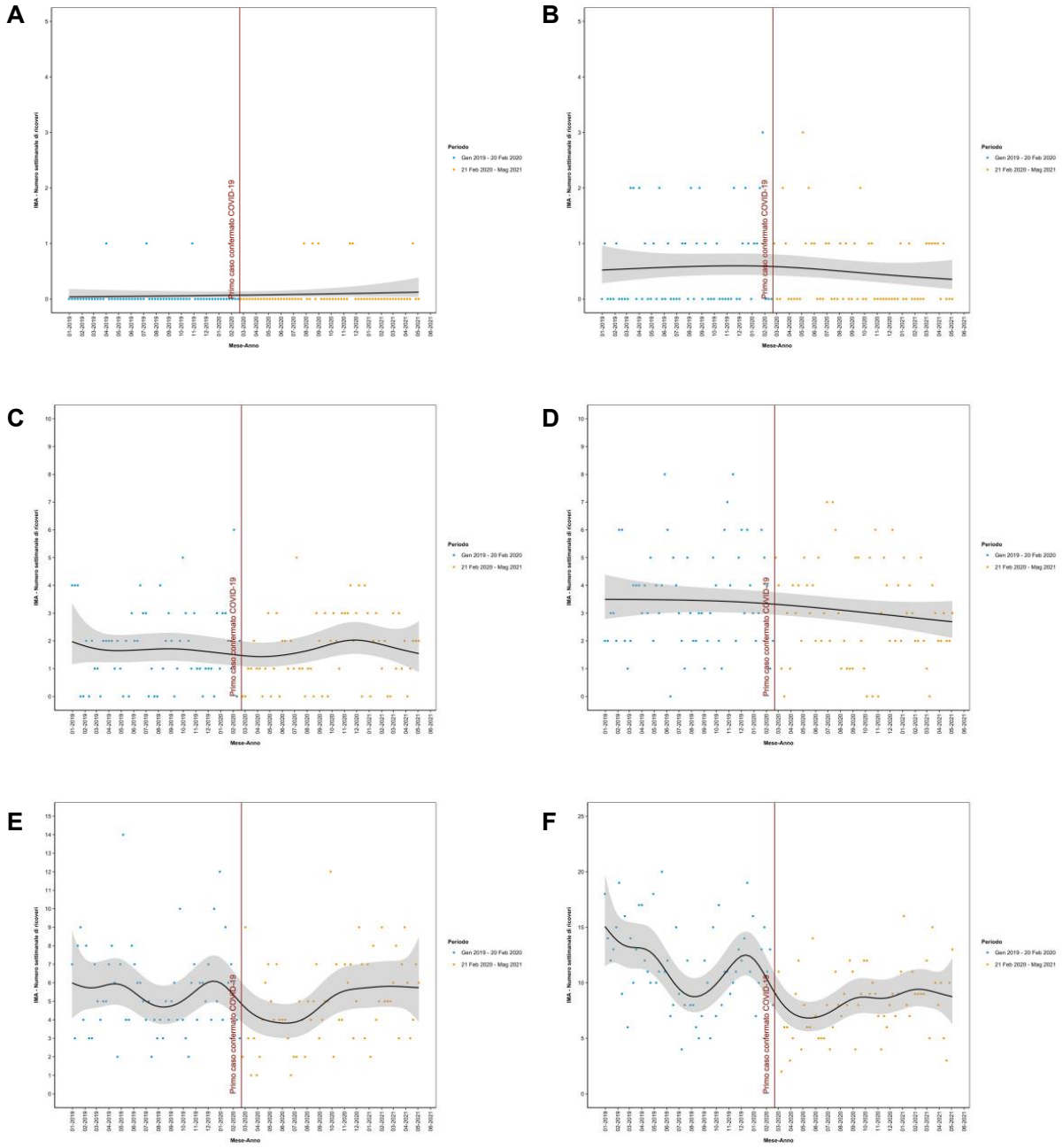


FIGURE 4.10. Time series of weekly numbers of MI hospitalization in female population, stratified by age classes (2019-2021). Panel A, 10-19 years; Panel B, 20-29 years; Panel C, 30-39 years; Panel D, 40-49 years; Panel E, 50-59 years; Panel F, 60-69 years; Panel G, 70-79 years; Panel H, 80+ years

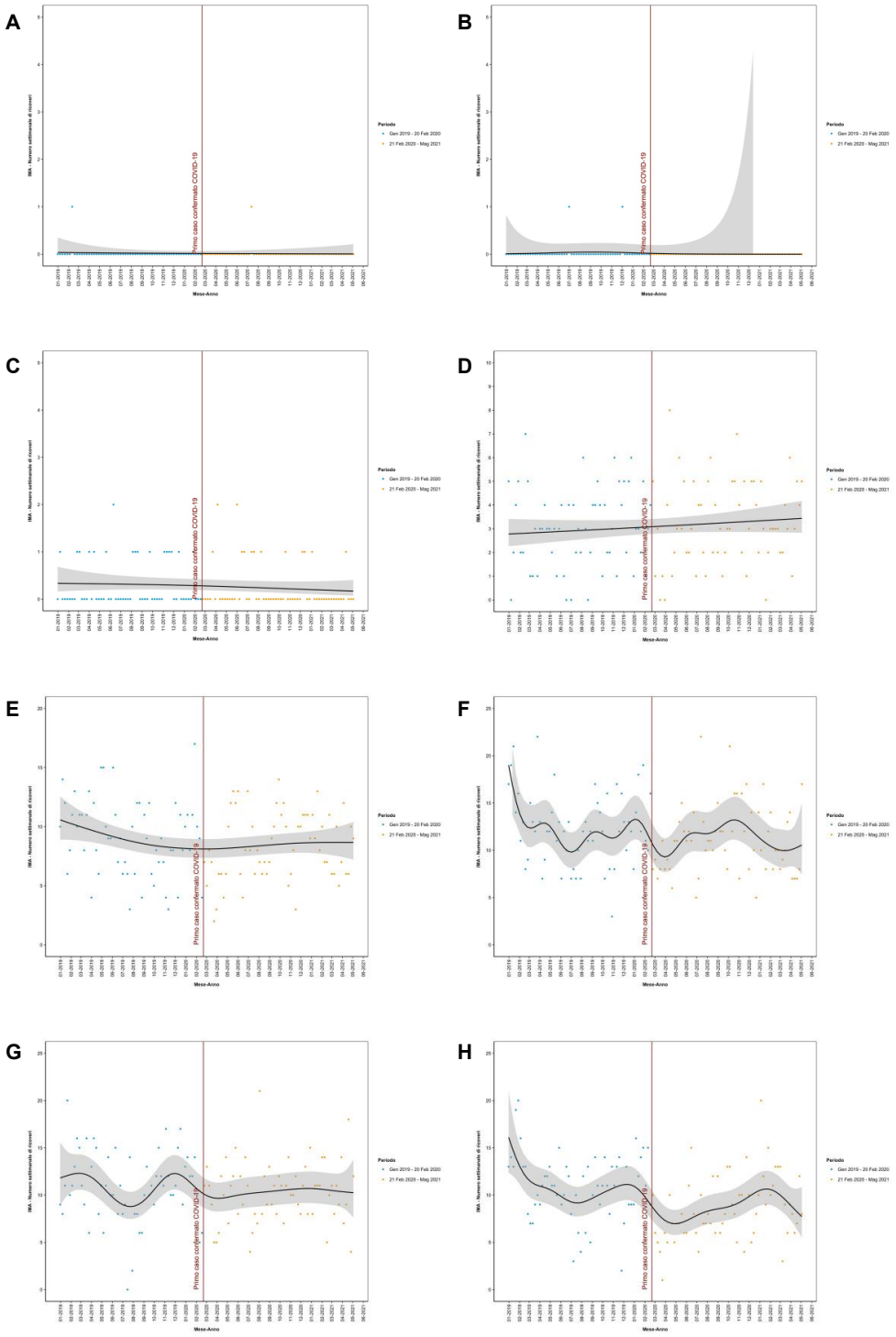


FIGURE 4.11. Time series of weekly numbers of MI hospitalization in male population, stratified by age classes (2019-2021). Panel A, 10-19 years; Panel B, 20-29 years; Panel C, 30-39 years; Panel D, 40-49 years; Panel E, 50-59 years; Panel F, 60-69 years; Panel G, 70-79 years; Panel H, 80+ years

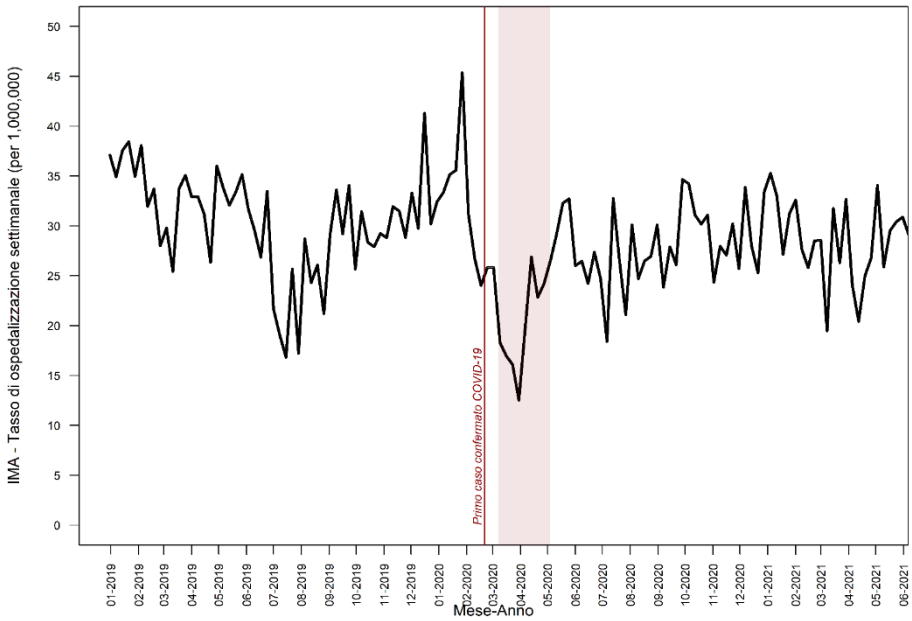


FIGURE 4.12. Weekly rate of MI hospital admissions (trend 2019-2021)

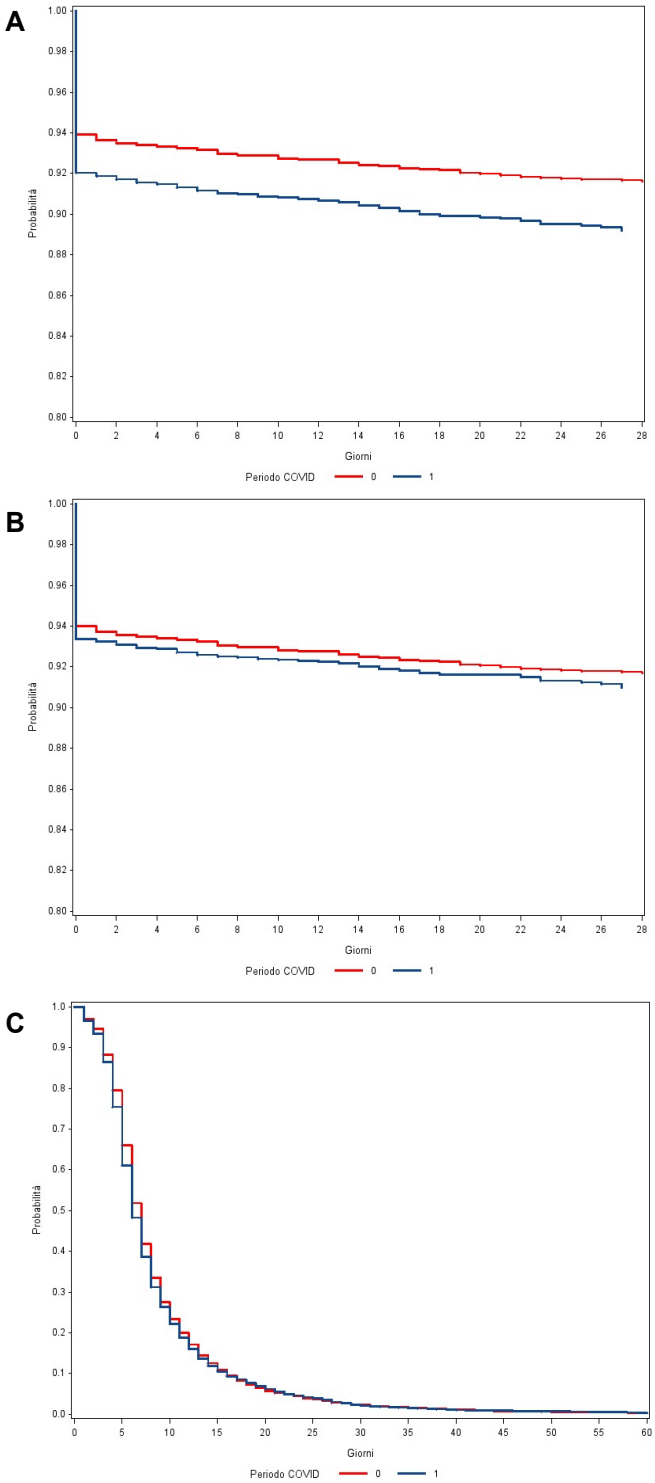


FIGURE 4.13. Kaplan-Meier curves in matched cohorts of hospitalized MI patients. Panel A, time-to-death (*p*-value = 0.0036); Panel B, time-to-death in patients without previous SARS-CoV-2 infection (*p*-value = 0.1882); Panel C, time-to-discharge (*p*-value = 0.0036)

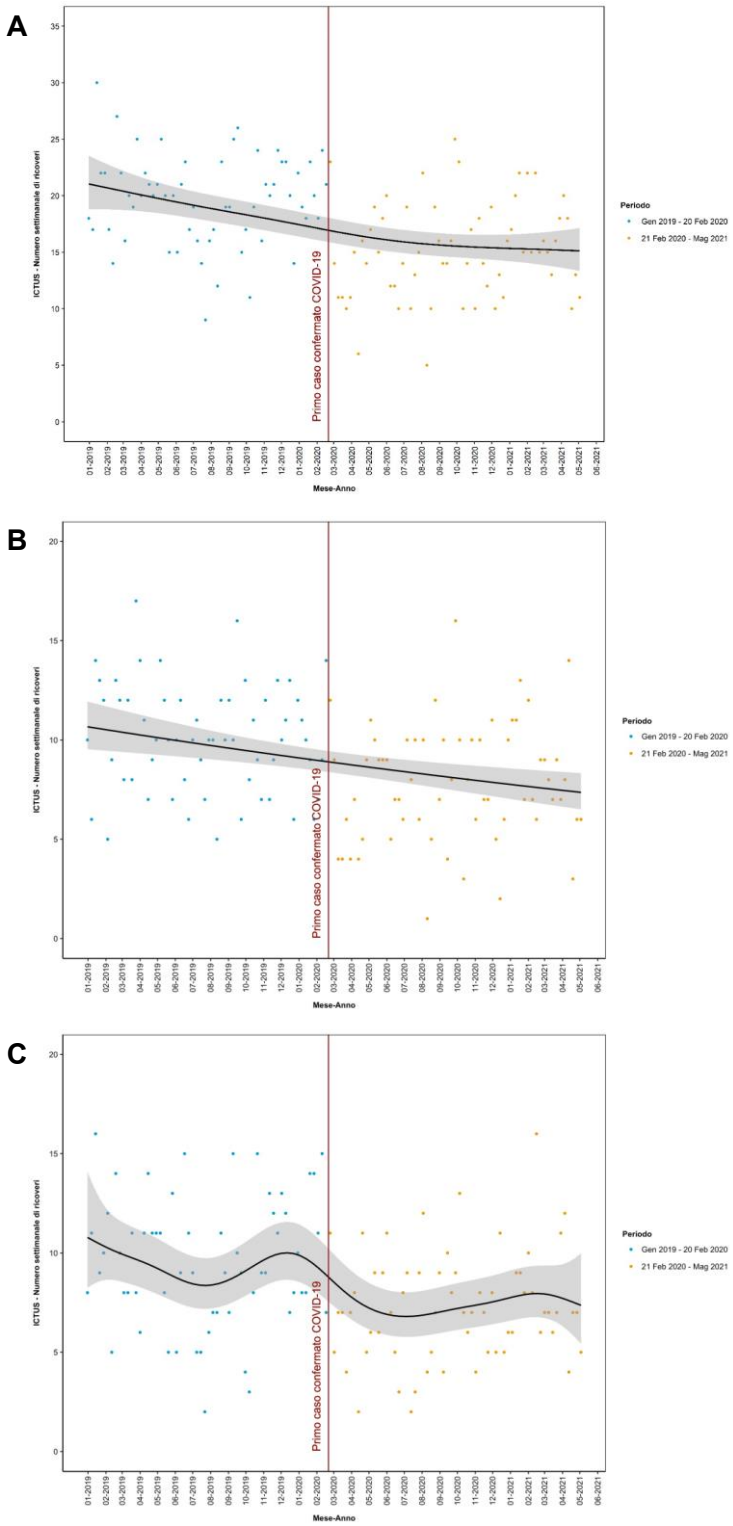


FIGURE 4.14. Time series of weekly number of stroke hospital admissions. Panel A, general population; Panel B, female; Panel C, male

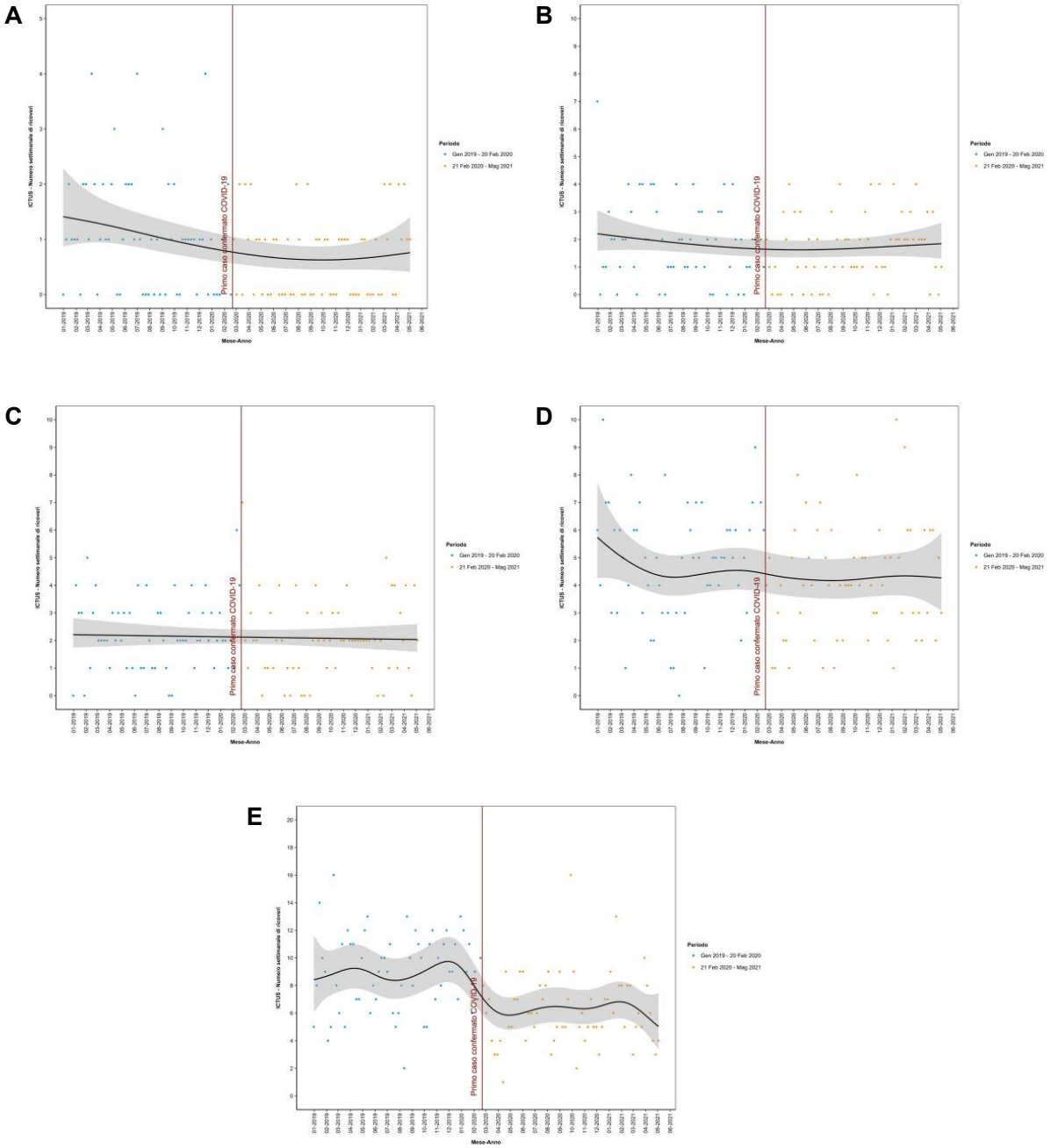


FIGURE 4.15. Time series of weekly numbers of stroke hospital admissions, stratified by age classes (2019-2021). Panel A, 40-49 years; Panel B, 50-59 years; Panel C, 60-69 years; Panel D, 70-79 years; Panel E, 80+ years

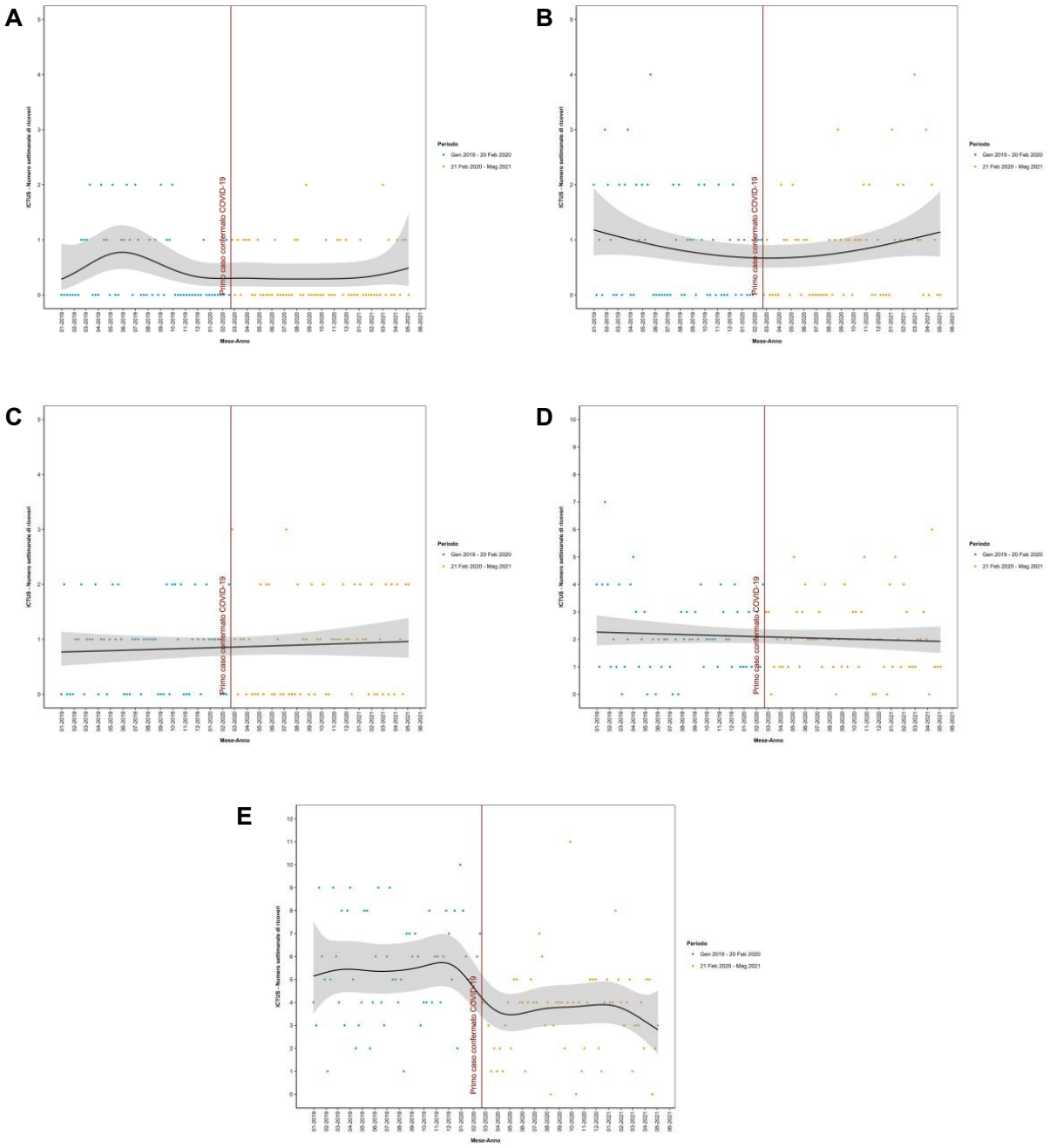


FIGURE 4.16. Time series of weekly numbers of stroke hospital admissions in female population, stratified by age classes (2019-2021). Panel A, 40-49 years; Panel B, 50-59 years; Panel C, 60-69 years; Panel D, 70-79 years; Panel E, 80+ years

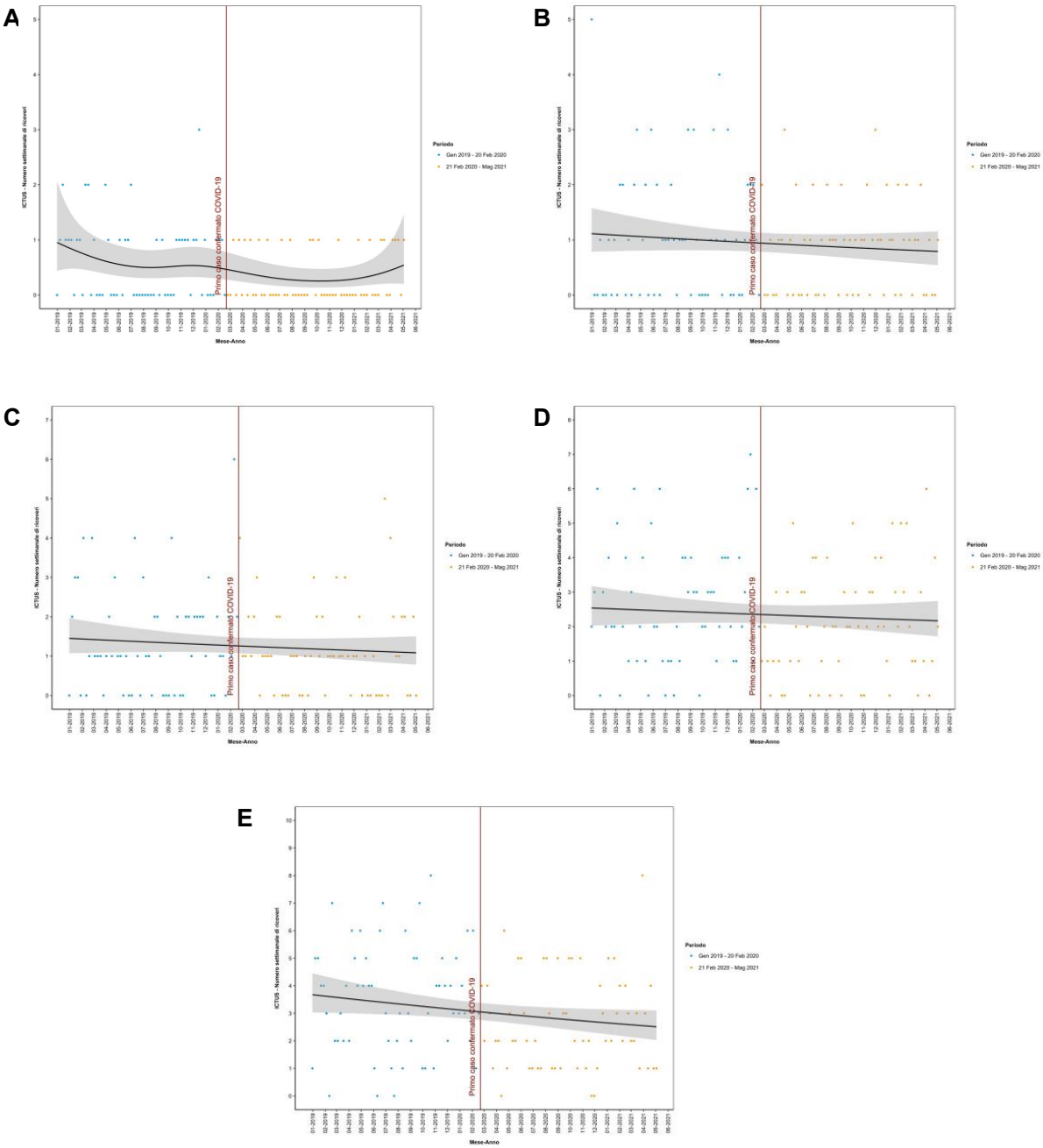


FIGURE 4.17. Time series of weekly numbers of stroke hospital admissions in male population, stratified by age classes (2019-2021). Panel A, 40-49 years; Panel B, 50-59 years; Panel C, 60-69 years; Panel D, 70-79 years; Panel E, 80+ years

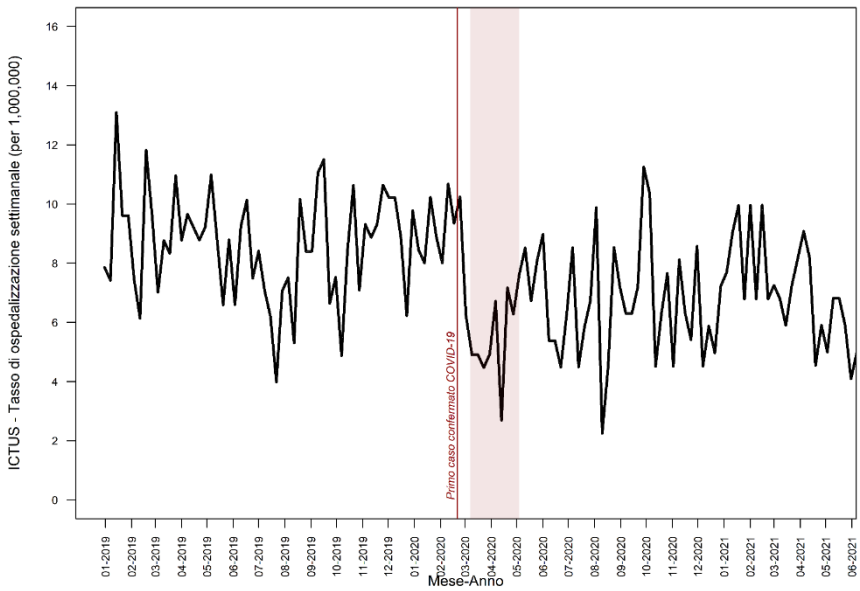


FIGURE 4.18. Weekly rate of stroke hospital admissions (trend 2019-2021)

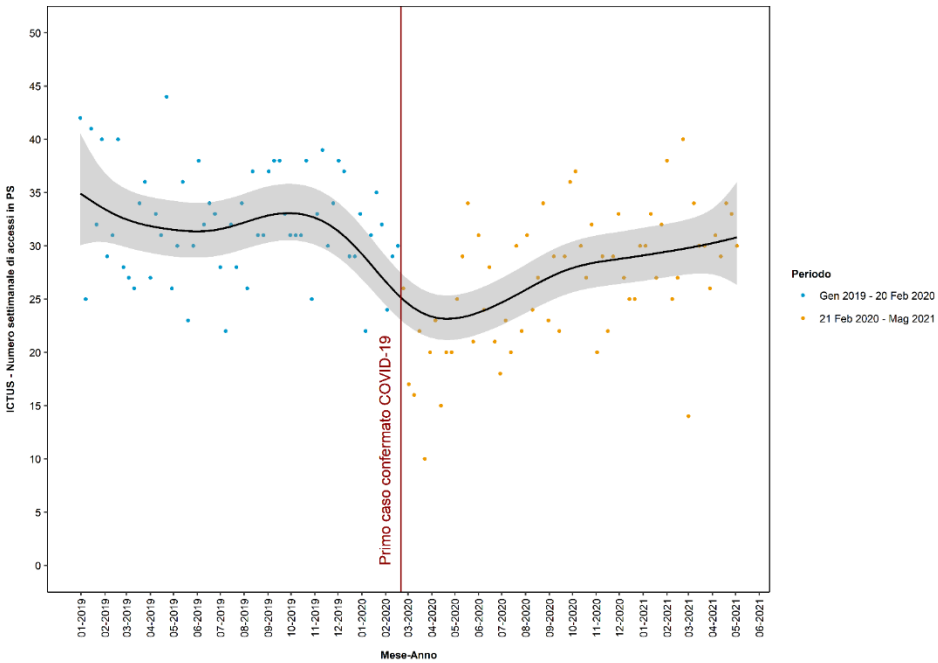


FIGURE 4.19. Weekly numbers of stroke ED visits (trend 2019-2021)

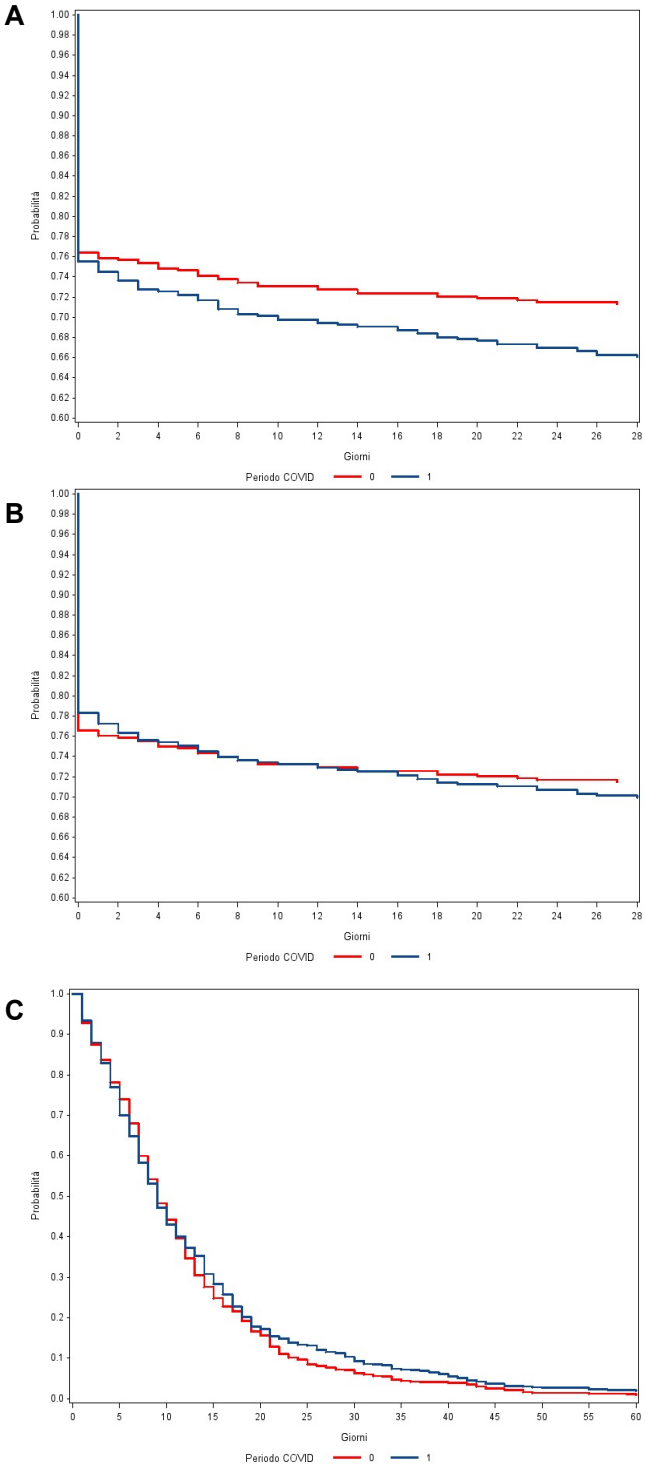


FIGURE 4.20. Kaplan-Meier curves in matched cohorts of hospitalized stroke patients. Panel A, time-to-death (*p*-value = 0.0892); Panel B, time-to-death in patients without previous SARS-CoV-2 infection (*p*-value = 0.3819); Panel C, time-to-discharge (*p*-value = 0.4689)

# Chapter 5

# The use of syndromic surveillance systems for the detection of early anomalous COVID-19 clusters in healthcare administrative databases

## *5.1 Introduction*

The rapid spread of COVID-19 raised questions about the potential presence of COVID-19 cases and hotspots (i.e., areas with a high level of transmission) before late February 2020 that may have remained undetected because of the virus's incubation, the absence of specific clues to diagnosis, and the delay in organizing community mitigation strategies (Güemes et al., 2021; Jombart et al., 2021; Roberts et al., 2021).

Several attempts have been made to retrospectively describe and date the earliest circulation of SARS-CoV-2 in the epicentre of the Italian outbreak using measures currently used to describe the burden of COVID-19, such as counts of confirmed infections, population serosurveys, patients' hospitalizations, admissions into intensive care units, and deaths (Conti et al., 2020*a*; Della Valle et al., 2021; Tomaselli et al., 2022). An epidemiological analysis of officially recorded cases in Lombardy estimated over 520 symptomatic cases in the weeks before the first patient diagnosed with COVID-19 infection and suggested that SARS-CoV-2 was circulating in approximately 15% of regional municipalities based on its transmission dynamics (Cereda et al., 2021).

To rapidly detect possible epidemic-prone clusters, potential COVID-19 outbreaks—and other infectious diseases' dynamics—must be monitored by specific periodic surveillance (Jombart et al., 2021). To this end, combining traditional public health methods with the syndromic surveillance of time series of cases and the ongoing incidence is crucial. Syndromic surveillance is defined by the Centers for Disease Control as an investigational approach that allows the monitoring of disease indicators in real or near-real time and aims to detect disease outbreaks earlier than would otherwise be possible with traditional epidemiological monitoring systems (Buehler et al., 2004; Noufaily et al., 2019). Syndromic surveillance relies on patient-level information sourced from existing HADs and

uses clinical outcomes prompted by the early onset of symptoms as an alert of changes in disease activity (Hope et al., 2006; Noufaily et al., 2019).

Considering the above, data from healthcare information systems in the provinces of Bergamo and Brescia, which registered the first SARS-CoV-2 infections in Italy, represent an important opportunity to verify whether establishing a surveillance pipeline for the identification of abnormal activity in hospital admissions and ED visits is effective in detecting potential early anomalous COVID-19 clusters.

### *5.2 Study population*

A complete overview of the study context is detailed in section 3.2.

### *5.3 Data source*

Data were retrieved from the following HADs of the two HPAs: HDRs, ED visits, BDA, and COVID-19 integrated surveillance databases (see section 3.3).

### *5.4 Statistical analysis*

The health events considered are those that showed significant excess on the basis of the analyses conducted in Chapter 3. The analysis was conducted at the territorial level charted as HPA districts (see Figure 3.1). To account for weekly fluctuations of counts, the time series for each outcome of interest included the cumulative events in the 7 days before any index date. These time series were then examined to detect possible breakpoints or aberrations (e.g., days in which the event counts abnormally increased) and possible structural changes (e.g., changes in the temporal trend or average counts). Breakpoints were identified using the following algorithms:

- Farrington flexible, which takes range values of the surveillance time series and uses a quasi-Poisson regression model for each time point, with seasonality and linear trends of events' distribution as explanatory variables: in this algorithm, alarms are flagged for surveillance days where the 'exceedance score' is greater than 1, i.e, when model residuals exceed a threshold based on expected counts (Farrington et al., 1996; Noufaily et al., 2019);

- Early Aberration Reporting System (EARS), version EARS-NB, which implements Shewhart regression Poisson or negative binomial charts based on the generalized likelihood ratio statistic: here, an alarm is produced when multiplicative shift in mean occurs (Hutwagner et al., 2003; Höhle and Paul, 2008; Noufaily et al., 2019).

Changes in the trends and means of events were analysed applying segmented regression models to events' time series, in particular: (i) segmented linear regression, (ii) segmented linear regression with first-order autoregressive component, and (iii) segmented linear regression with second-order autoregressive component.

*5.5 Results*

Based on surveillance data, the time series of overall urgent hospital admissions detected the first fluctuations after February 21, 2020, except for the analysis based on the Farrington flexible algorithm, which identified 7-day persistent aberrations in three HPA areas in Brescia—namely BS12, Valle Sabbia; BS01, Brescia; and BS02, Brescia Ovest—starting from January 1, February 4, and February 18, respectively (Table 5.1; Figures 5.1–5.5). Restricting the analysis to urgent hospital admissions with medical DRGs, a similar pattern was seen (Table 5.2; Figures 5.6–5.10).

No excesses in urgent hospital admissions with diagnosis of the respiratory system were observed before February 21 in all areas. These events started in late February in BG08, Val Seriana (between February 23 and 28); BS08, Bassa Bresciana Occidentale (between February 25 and 29); and BG03, Seriate (between February 29 and March 3) (Table 5.3; Figures 5.11–5.15).

The only early aberration in urgent hospital admissions with MDC of the respiratory system (MDC 04) using the Farrington flexible algorithm was registered in BS02, Brescia Ovest on 2 January (Table 5.4; Figures 5.16–5.20).

According to various surveillance approaches, abnormal counts in code-red and respiratory ED visits (Tables 5.5 and 5.6; Figures 5.22–5.25 and 5.27–5.30) started in March, although the Farrington algorithm tracked a few signals for ED visits during the previous months (Tables 5.5 and 5.6; Figures 5.21 and 5.26).

*5.6 Concluding remarks*

Here, validated tools for largescale syndromic surveillance widely used by public health institutes were applied to identify early abnormally high counts of hospital admissions and ED visits (which showed significant excesses owing to COVID-19) in defined geographical HPA districts within Bergamo and Brescia. Reports of excesses in these events coincided with the identification of the first official COVID-19 cases in February 2020, except for scattered noise detected through the Farrington flexible algorithm in urgent hospital admissions and ED visits. Of note, no excesses were observed in the number of urgent admissions with diagnosis of the respiratory system before February 21, 2020 across all explored areas.

Whether the signals detected using Farrington flexible algorithm were sufficiently reliable for first identifying a COVID-19 outbreak remains unclear, especially considering the absence of confirmation with complementary surveillance approaches. Although this algorithm has been considered a suitable benchmark for measuring COVID-19-related aberrations, it is worth noting that, however, the use of all surveillance approaches depends on the situation and the algorithms' detection accuracy, such as their sensitivity and specificity in detecting outbreaks (Jombart et al., 2021; Noufaily et al., 2019; Yoneoka et al., 2021).

Farrington flexible tends to have a low power of detection (i.e., the probability of an alarm at least once during a spiked outbreak or the probability of detecting the outbreak) while it has the highest sensitivity (i.e., the proportion of alarms among spike outbreak days) and specificity (i.e., the proportion of no alarms among non-outbreak days). It can trace the emergence of very rare fluctuations that do not always constitute outbreaks, particularly when these fluctuations are censused on a defined local level. Therefore, Farrington flexible may be preferred if the priority is for periodic alarms that are as accurate as possible. Conversely, when the detection of an outbreak is the aim, other complementary algorithms that are more precise (i.e., have a higher positive predictive value) should be used (Farrington et al., 1996; Hulth et al., 2010; Jombart et al., 2021; Noufaily et al., 2019; Yoneoka et al., 2021).

In this regard, it should also be considered that signals detected using Farrington flexible can likely be attributable to other outbreak-prone infections, such as influenza, or to the meningococcal disease outbreak that occurred in the provinces of Bergamo and Brescia since late December 2019 (ISS, 2020*c*).

Beyond the epidemiological importance of describing the abnormally high activity of health events, public health interest focuses primarily on the timeliness and sensitivity of a detection system—one with no or a short delay between

infection and reporting. The unpredictable dynamics that characterized the earliest weeks of the COVID-19 outbreak have challenged the capabilities of specific syndromic surveillance systems. Moreover, several hypotheses have been proposed for what could have been the most suitable approaches for detecting disease indicators as early as possible in the course of the COVID-19 outbreak (Buehler et al., 2004; Güemes et al., 2021; Ibrahim, 2020; Pekar et al., 2021).

More generally, the considerable pressure on Lombardy's healthcare system in the very first weeks of the pandemic was very likely rooted in the high but silent transmissibility of SARS-CoV-2 during mid-February 2020 (Balasco et al., 2021; Cereda et al., 2021). However, early anomalous COVID-19 clusters are hardly detectable through existing HADs. Although the possibility of filtering noise and detecting aberrations in healthcare information data flows are capabilities of common syndromic surveillance systems and tools (Buehler et al., 2004), informing the outbreak of infectious diseases and the related healthcare impact using HADs is challenging for local health authorities in Lombardy and more broadly in Italy. Although data are uniformly available to HPAs from all areas covered, their use is hampered by variable organizational factors that mediate the transmission of health data over a unique data environment. These factors include the complexity of administrative procedures, differences in data collection systems, and lead time in data transmission systems at health facilities. This lead time in particular jeopardizes the capacity to monitor the occurrence of outbreaks using early indicators of possible outbreak-related healthcare impacts and results indicate that epidemic risks—such as the transmission of SARS-CoV-2—cannot be traced using such systems in real time or near-real time (Güemes et al., 2021).

Nevertheless, prompt recognition of potential epidemic outbreaks allows the implementation of epidemiologic investigations and public health community mitigation measures (Ferrara et al., 2022*a*; Ferrara et al., 2022*g*; Menni et al., 2020). Therefore, using surveillance systems—the application of which depends on the choice of prespecified parameters and the performance scores of algorithms—to detect and filter any aberrations in the previous trend as early as possible is of utmost importance (Noufaily et al., 2019; Yoneoka et al., 2021).

The efficiency of an acute health event warning thus relies on approaches to pre-emptive data collection at the source. In this context, our research confirms that HADs are unable to assist in the early identification of infectious outbreaks. A rapid approach to the detection of potential temporal clusters is instead required and must include prompt reports from healthcare workers—namely general practitioners, clinicians, and laboratory personnel—who are in direct contact with the patient and

are specifically trained using structured educational interventions to respond to possible future epidemics (Nayahangan et al., 2021). One Health approaches also foster the crucial role of communities in participatory surveillance systems to ensure timely disease outbreak detection surveillance (Crawley et al., 2021; Smolinski et al., 2017). In addition, measures for expanding epidemic intelligence and improving health safety support the adoption of digital health interventions, which provide valuable opportunities for strengthening epidemic preparedness and the health response (EOHSP, 2021; Güemes et al., 2021; Mahmood et al., 2020).

## 5.7 Tables and Figures

### 5.7.1 Tables

TABLE 5.1: Date of first signal detection in urgent hospital admissions

| HPA district | Outbreak start date | | | | |
|---|---|---|---|---|---|
| | **Farrington Flexible algorithm** | **Early Aberration Reporting System algorithm** | **Segmented linear regression** | **Segmented linear regression with first-order autoregressive component** | **Segmented linear regression with second-order autoregressive component** |
| **Bergamo** | | | | | |
| 01 - Bergamo | 11/03/2020 | 11/03/2020 | 03/03/2020 | 02/03/2020 | 01/03/2020 |
| 02 - Dalmine | 12/03/2020 | 12/03/2020 | 03/03/2020 | 02/03/2020 | 01/03/2020 |
| 03 - Seriate | 10/03/2020 | 16/03/2020 | 03/03/2020 | 02/03/2020 | 01/03/2020 |
| 04 - Grumello | 12/03/2020 | 14/03/2020 | 05/03/2020 | 04/03/2020 | 03/03/2020 |
| 05 - Val Cavallina | 17/03/2020 | 18/03/2020 | 10/03/2020 | 09/03/2020 | 08/03/2020 |
| 06 - Bronzone/Basso Sebino | 11/03/2020 | 12/03/2020 | 02/03/2020 | 28/03/2020 | |
| 07 - Alto Sebino | 25/03/2020 | | | | |
| 08 - Val Seriana | 04/03/2020 | 05/03/2020 | 25/02/2020 | 24/02/2020 | 23/02/2020 |
| 09 - Val Seriana Sup/Val di Scalve | 16/03/2020 | 16/03/2020 | 08/03/2020 | 07/03/2020 | 06/03/2020 |
| 10 - Val Brembana | 07/03/2020 | 09/03/2020 | 28/02/2020 | 27/02/2020 | 26/02/2020 |
| 11 - Val Imagna/Villa d'Almè | 14/03/2020 | 18/03/2020 | 03/03/2020 | 02/03/2020 | 01/03/2020 |
| 12 - Isola Bergamasca | 13/03/2020 | 14/03/2020 | 05/03/2020 | 08/03/2020 | 03/03/2020 |
| 13 - Treviglio | 16/03/2020 | 18/03/2020 | 04/03/2020 | 10/03/2020 | 09/03/2020 |
| 14 - Romano di Lombardia | 14/03/2020 | 17/03/2020 | 06/03/2020 | 06/03/2020 | 03/04/2020 |
| **Brescia** | | | | | |
| 01- Brescia | **04/02/2020** | | 04/03/2020 | 30/03/2020 | 29/03/2020 |
| 02 - Brescia Ovest | **18/02/2020** | 15/03/2020 | 02/03/2020 | 09/03/2020 | 08/03/2020 |
| 03 - Brescia Est | 17/03/2020 | 22/03/2020 | 06/03/2020 | 05/03/2020 | |
| 04 - Valle Trompia | 21/03/2020 | | 11/04/2020 | 10/04/2020 | 09/04/2020 |
| 05 - Sebino | 19/03/2020 | | 11/03/2020 | | |
| 06 - Monte Orfano | 20/03/2020 | 21/03/2020 | 11/03/2020 | 10/03/2020 | 09/03/2020 |
| 07 - Oglio Ovest | 19/03/2020 | 20/03/2020 | 12/03/2020 | 12/03/2020 | 11/03/2020 |
| 08 - Bassa Bresciana Occidentale | 05/03/2020 | 07/03/2020 | 27/02/2020 | 26/02/2020 | 25/02/2020 |
| 09 - Bassa Bresciana Centrale | 10/03/2020 | 13/03/2020 | 02/03/2020 | 01/03/2020 | 29/02/2020 |
| 10 - Bassa Bresciana Orientale | 17/03/2020 | 19/03/2020 | 29/03/2020 | | |
| 11 - Garda | | | 26/03/2020 | | |
| 12 - Valle Sabbia | **02/01/2020** | | 28/03/2020 | 27/03/2020 | 26/03/2020 |

TABLE 5.2: Date of first signal detection in urgent hospital admissions with medical Diagnosis Related Group

| HPA district | Outbreak start date | | | | |
|---|---|---|---|---|---|
| | **Farrington Flexible algorithm** | **Early Aberration Reporting System algorithm** | **Segmented linear regression** | **Segmented linear regression with first-order autoregressive component** | **Segmented linear regression with second-order autoregressive component** |
| **Bergamo** | | | | | |
| 01 - Bergamo | 09/03/2020 | 10/03/2020 | 03/03/2020 | 02/03/2020 | 01/03/2020 |
| 02 - Dalmine | 11/03/2020 | 12/03/2020 | 03/03/2020 | 02/03/2020 | 01/03/2020 |
| 03 - Seriate | 10/03/2020 | 12/03/2020 | 03/03/2020 | 02/03/2020 | 01/03/2020 |
| 04 - Grumello | 11/03/2020 | 13/03/2020 | 05/03/2020 | 04/03/2020 | 03/03/2020 |
| 05 - Val Cavallina | 17/03/2020 | 18/03/2020 | 10/03/2020 | 09/03/2020 | 08/03/2020 |
| 06 - Bronzone/Basso Sebino | 11/03/2020 | 12/03/2020 | 02/03/2020 | 28/03/2020 | |
| 07 - Alto Sebino | 23/03/2020 | | | | |
| 08 - Val Seriana | 02/03/2020 | 04/03/2020 | 25/02/2020 | 24/02/2020 | 23/02/2020 |
| 09 - Val Seriana Sup/Val di Scalve | 15/03/2020 | 16/03/2020 | 08/03/2020 | 07/03/2020 | 06/03/2020 |
| 10 - Val Brembana | 07/03/2020 | 08/03/2020 | 28/02/2020 | 27/02/2020 | 26/02/2020 |
| 11 - Val Imagna/Villa d'Almè | 13/03/2020 | 16/03/2020 | 03/03/2020 | 02/03/2020 | 01/03/2020 |
| 12 - Isola Bergamasca | 11/03/2020 | 12/03/2020 | 05/03/2020 | 08/03/2020 | 03/03/2020 |
| 13 - Treviglio | 14/03/2020 | 13/03/2020 | 04/03/2020 | 10/03/2020 | 09/03/2020 |
| 14 - Romano di Lombardia | 14/03/2020 | 14/03/2020 | 06/03/2020 | 06/03/2020 | 03/04/2020 |
| **Brescia** | | | | | |
| 01- Brescia | **04/02/2020** | 21/03/2020 | 04/03/2020 | 30/03/2020 | 29/03/2020 |
| 02 - Brescia Ovest | **19/02/2020** | 16/03/2020 | 02/03/2020 | 09/03/2020 | 08/03/2020 |
| 03 - Brescia Est | 18/03/2020 | 21/03/2020 | 06/03/2020 | 05/03/2020 | |
| 04 - Valle Trompia | 20/03/2020 | | 11/04/2020 | 10/04/2020 | 09/04/2020 |
| 05 - Sebino | 19/03/2020 | 22/03/2020 | 11/03/2020 | | |
| 06 - Monte Orfano | 19/03/2020 | 20/03/2020 | 11/03/2020 | 10/03/2020 | 09/03/2020 |
| 07 - Oglio Ovest | 11/03/2020 | 19/03/2020 | 12/03/2020 | 12/03/2020 | 11/03/2020 |
| 08 - Bassa Bresciana Occidentale | 04/03/2020 | 08/03/2020 | 27/02/2020 | 26/02/2020 | 25/02/2020 |
| 09 - Bassa Bresciana Centrale | 10/03/2020 | 12/03/2020 | 02/03/2020 | 01/03/2020 | 29/02/2020 |
| 10 - Bassa Bresciana Orientale | **22/01/2020** | 19/03/2020 | 29/03/2020 | | |
| 11 - Garda | 25/03/2020 | | 26/03/2020 | | |
| 12 - Valle Sabbia | 22/03/2020 | 23/03/2020 | 28/03/2020 | 27/03/2020 | 26/03/2020 |

TABLE 5.3: Date of first signal detection in urgent hospital admissions with diagnosis of the respiratory system

| HPA district | Outbreak start date | | | | |
|---|---|---|---|---|---|
| | Farrington Flexible algorithm | Early Aberration Reporting System algorithm | Segmented linear regression | Segmented linear regression with first-order autoregressive component | Segmented linear regression with second-order autoregressive component |
| **Bergamo** | | | | | |
| 01 - Bergamo | 06/03/2020 | 06/03/2020 | 03/03/2020 | 02/03/2020 | 01/03/2020 |
| 02 - Dalmine | 06/03/2020 | 10/03/2020 | 03/03/2020 | 02/03/2020 | 01/03/2020 |
| 03 - Seriate | 29/02/2020 | 29/02/2020 | 03/03/2020 | 02/03/2020 | 01/03/2020 |
| 04 - Grumello | 10/03/2020 | 09/03/2020 | 05/03/2020 | 04/03/2020 | 03/03/2020 |
| 05 - Val Cavallina | 06/03/2020 | 07/03/2020 | 10/03/2020 | 09/03/2020 | 08/03/2020 |
| 06 - Bronzone/Basso Sebino | 08/03/2020 | 08/03/2020 | 02/03/2020 | 28/03/2020 | |
| 07 - Alto Sebino | 17/03/2020 | 19/03/2020 | | | |
| 08 - Val Seriana | 28/02/2020 | 29/02/2020 | 25/02/2020 | 24/02/2020 | 23/02/2020 |
| 09 - Val Seriana Sup/Val di Scalve | 05/03/2020 | 12/03/2020 | 08/03/2020 | 07/03/2020 | 06/03/2020 |
| 10 - Val Brembana | 05/03/2020 | 05/03/2020 | 28/02/2020 | 27/02/2020 | 26/02/2020 |
| 11 - Val Imagna/Villa d'Almè | 10/03/2020 | 11/03/2020 | 03/03/2020 | 02/03/2020 | 01/03/2020 |
| 12 - Isola Bergamasca | 09/03/2020 | 10/03/2020 | 05/03/2020 | 08/03/2020 | 03/03/2020 |
| 13 - Treviglio | 09/03/2020 | 09/03/2020 | 04/03/2020 | 10/03/2020 | 09/03/2020 |
| 14 - Romano di Lombardia | 05/03/2020 | 11/03/2020 | 06/03/2020 | 06/03/2020 | 03/04/2020 |
| **Brescia** | | | | | |
| 01- Brescia | 09/03/2020 | 10/03/2020 | 04/03/2020 | 30/03/2020 | 29/03/2020 |
| 02 - Brescia Ovest | 08/03/2020 | 10/03/2020 | 02/03/2020 | 09/03/2020 | 08/03/2020 |
| 03 - Brescia Est | 08/03/2020 | 10/03/2020 | 06/03/2020 | 05/03/2020 | |
| 04 - Valle Trompia | 10/03/2020 | 16/03/2020 | 11/04/2020 | 10/04/2020 | 09/04/2020 |
| 05 - Sebino | 15/03/2020 | 15/03/2020 | 11/03/2020 | | |
| 06 - Monte Orfano | 04/03/2020 | 11/03/2020 | 11/03/2020 | 10/03/2020 | 09/03/2020 |
| 07 - Oglio Ovest | 06/03/2020 | 09/03/2020 | 12/03/2020 | 12/03/2020 | 11/03/2020 |
| 08 - Bassa Bresciana Occidentale | 29/02/2020 | 03/03/2020 | 27/02/2020 | 26/02/2020 | 25/02/2020 |
| 09 - Bassa Bresciana Centrale | 05/03/2020 | 07/03/2020 | 02/03/2020 | 01/03/2020 | 29/02/2020 |
| 10 - Bassa Bresciana Orientale | 09/03/2020 | 12/03/2020 | 29/03/2020 | | |
| 11 - Garda | 11/03/2020 | 12/03/2020 | 26/03/2020 | | |
| 12 - Valle Sabbia | 12/03/2020 | 13/03/2020 | 28/03/2020 | 27/03/2020 | 26/03/2020 |

TABLE 5.4: Date of first signal detection in urgent hospital admissions with Major Diagnostic Category of respiratory system (MDC 04)

| HPA district | Outbreak start date | | | | |
|---|---|---|---|---|---|
| | **Farrington Flexible algorithm** | **Early Aberration Reporting System algorithm** | **Segmented linear regression** | **Segmented linear regression with first-order autoregressive component** | **Segmented linear regression with second-order autoregressive component** |
| **Bergamo** | | | | | |
| 01 - Bergamo | 06/03/2020 | 06/03/2020 | 03/03/2020 | 02/03/2020 | 01/03/2020 |
| 02 - Dalmine | 05/03/2020 | 10/03/2020 | 03/03/2020 | 02/03/2020 | 01/03/2020 |
| 03 - Seriate | 01/03/2020 | 02/03/2020 | 03/03/2020 | 02/03/2020 | 01/03/2020 |
| 04 - Grumello | 08/03/2020 | 10/03/2020 | 05/03/2020 | 04/03/2020 | 03/03/2020 |
| 05 - Val Cavallina | 06/03/2020 | 07/03/2020 | 10/03/2020 | 09/03/2020 | 08/03/2020 |
| 06 - Bronzone/Basso Sebino | 07/03/2020 | 09/03/2020 | 02/03/2020 | 28/03/2020 | |
| 07 - Alto Sebino | 17/03/2020 | 19/03/2020 | | | |
| 08 - Val Seriana | 28/02/2020 | 02/03/2020 | 25/02/2020 | 24/02/2020 | 23/02/2020 |
| 09 - Val Seriana Sup/Val di Scalve | 05/03/2020 | 12/03/2020 | 08/03/2020 | 07/03/2020 | 06/03/2020 |
| 10 - Val Brembana | 05/03/2020 | 05/03/2020 | 28/02/2020 | 27/02/2020 | 26/02/2020 |
| 11 - Val Imagna/Villa d'Almè | 09/03/2020 | 11/03/2020 | 03/03/2020 | 02/03/2020 | 01/03/2020 |
| 12 - Isola Bergamasca | 09/03/2020 | 10/03/2020 | 05/03/2020 | 08/03/2020 | 03/03/2020 |
| 13 - Treviglio | 09/03/2020 | 09/03/2020 | 04/03/2020 | 10/03/2020 | 09/03/2020 |
| 14 - Romano di Lombardia | 04/03/2020 | 10/03/2020 | 06/03/2020 | 06/03/2020 | 03/04/2020 |
| **Brescia** | | | | | |
| 01- Brescia | 09/03/2020 | 10/03/2020 | 04/03/2020 | 30/03/2020 | 29/03/2020 |
| 02 - Brescia Ovest | **02/01/2020** | 10/03/2020 | 02/03/2020 | 09/03/2020 | 08/03/2020 |
| 03 - Brescia Est | 10/03/2020 | 11/03/2020 | 06/03/2020 | 05/03/2020 | |
| 04 - Valle Trompia | 10/03/2020 | 16/03/2020 | 11/04/2020 | 10/04/2020 | 09/04/2020 |
| 05 - Sebino | 15/03/2020 | 14/03/2020 | 11/03/2020 | | |
| 06 - Monte Orfano | 04/03/2020 | 11/03/2020 | 11/03/2020 | 10/03/2020 | 09/03/2020 |
| 07 - Oglio Ovest | 05/03/2020 | 10/03/2020 | 12/03/2020 | 12/03/2020 | 11/03/2020 |
| 08 - Bassa Bresciana Occidentale | 02/03/2020 | 03/03/2020 | 27/02/2020 | 26/02/2020 | 25/02/2020 |
| 09 - Bassa Bresciana Centrale | 05/03/2020 | 08/03/2020 | 02/03/2020 | 01/03/2020 | 29/02/2020 |
| 10 - Bassa Bresciana Orientale | 09/03/2020 | 11/03/2020 | 29/03/2020 | | |
| 11 - Garda | 11/03/2020 | 12/03/2020 | 26/03/2020 | | |
| 12 - Valle Sabbia | 13/03/2020 | 13/03/2020 | 28/03/2020 | 27/03/2020 | 26/03/2020 |

TABLE 5.5: Date of first signal detection in red-code emergency department visits

| HPA district | Outbreak start date | | | | |
|---|---|---|---|---|---|
| | **Farrington Flexible algorithm** | **Early Aberration Reporting System algorithm** | **Segmented linear regression** | **Segmented linear regression with first-order autoregressive component** | **Segmented linear regression with second-order autoregressive component** |
| **Bergamo** | | | | | |
| 01 - Bergamo | **02/02/2020** | 14/03/2020 | 03/03/2020 | 02/03/2020 | 01/03/2020 |
| 02 - Dalmine | **31/01/2020** | 17/03/2020 | 03/03/2020 | 02/03/2020 | 01/03/2020 |
| 03 - Seriate | 12/03/2020 | 15/03/2020 | 03/03/2020 | 02/03/2020 | 01/03/2020 |
| 04 - Grumello | 08/03/2020 | 14/03/2020 | 05/03/2020 | 04/03/2020 | 03/03/2020 |
| 05 - Val Cavallina | 10/03/2020 | 15/03/2020 | 10/03/2020 | 09/03/2020 | 08/03/2020 |
| 06 - Bronzone/Basso Sebino | **03/02/2020** | 18/03/2020 | 02/03/2020 | 28/03/2020 | |
| 07 - Alto Sebino | 12/03/2020 | | | | |
| 08 - Val Seriana | **10/02/2020** | 03/03/2020 | 25/02/2020 | 24/02/2020 | 23/02/2020 |
| 09 - Val Seriana Sup/Val di Scalve | 05/03/2020 | 11/03/2020 | 08/03/2020 | 07/03/2020 | 06/03/2020 |
| 10 - Val Brembana | 08/03/2020 | 08/03/2020 | 28/02/2020 | 27/02/2020 | 26/02/2020 |
| 11 - Val Imagna/Villa d'Almè | 21/03/2020 | 20/03/2020 | 03/03/2020 | 02/03/2020 | 01/03/2020 |
| 12 - Isola Bergamasca | 14/03/2020 | 15/03/2020 | 05/03/2020 | 08/03/2020 | 03/03/2020 |
| 13 - Treviglio | 22/03/2020 | 22/03/2020 | 04/03/2020 | 10/03/2020 | 09/03/2020 |
| 14 - Romano di Lombardia | 15/03/2020 | 16/03/2020 | 06/03/2020 | 06/03/2020 | 03/04/2020 |
| **Brescia** | | | | | |
| 01- Brescia | 21/03/2020 | | 04/03/2020 | 30/03/2020 | 29/03/2020 |
| 02 - Brescia Ovest | **25/01/2020** | 20/03/2020 | 02/03/2020 | 09/03/2020 | 08/03/2020 |
| 03 - Brescia Est | 24/03/2020 | 24/03/2020 | 06/03/2020 | 05/03/2020 | |
| 04 - Valle Trompia | 24/03/2020 | 28/03/2020 | 11/04/2020 | 10/04/2020 | 09/04/2020 |
| 05 - Sebino | 17/03/2020 | 17/03/2020 | 11/03/2020 | | |
| 06 - Monte Orfano | 15/03/2020 | 17/03/2020 | 11/03/2020 | 10/03/2020 | 09/03/2020 |
| 07 - Oglio Ovest | **20/01/2020** | 16/03/2020 | 12/03/2020 | 12/03/2020 | 11/03/2020 |
| 08 - Bassa Bresciana Occidentale | **26/01/2020** | 16/03/2020 | 27/02/2020 | 26/02/2020 | 25/02/2020 |
| 09 - Bassa Bresciana Centrale | 14/03/2020 | 15/03/2020 | 02/03/2020 | 01/03/2020 | 29/02/2020 |
| 10 - Bassa Bresciana Orientale | 16/03/2020 | 18/03/2020 | 29/03/2020 | | |
| 11 - Garda | 25/03/2020 | | 26/03/2020 | | |
| 12 - Valle Sabbia | | | 28/03/2020 | 27/03/2020 | 26/03/2020 |

TABLE 5.6: Date of first signal detection in emergency department visits with respiratory diagnosis

| HPA district | Outbreak start date | | | | |
|---|---|---|---|---|---|
| | **Farrington Flexible algorithm** | **Early Aberration Reporting System algorithm** | **Segmented linear regression** | **Segmented linear regression with first-order autoregressive component** | **Segmented linear regression with second-order autoregressive component** |
| **Bergamo** | | | | | |
| 01 - Bergamo | **18/02/2020** | 09/03/2020 | 03/03/2020 | 02/03/2020 | 01/03/2020 |
| 02 - Dalmine | 07/03/2020 | 12/03/2020 | 03/03/2020 | 02/03/2020 | 01/03/2020 |
| 03 - Seriate | 07/03/2020 | 14/03/2020 | 03/03/2020 | 02/03/2020 | 01/03/2020 |
| 04 - Grumello | 11/03/2020 | 18/03/2020 | 05/03/2020 | 04/03/2020 | 03/03/2020 |
| 05 - Val Cavallina | 10/03/2020 | 19/03/2020 | 10/03/2020 | 09/03/2020 | 08/03/2020 |
| 06 - Bronzone/Basso Sebino | 14/03/2020 | 22/03/2020 | 02/03/2020 | 28/03/2020 | |
| 07 - Alto Sebino | 17/03/2020 | 21/03/2020 | | | |
| 08 - Val Seriana | 25/02/2020 | 03/03/2020 | 25/02/2020 | 24/02/2020 | 23/02/2020 |
| 09 - Val Seriana Sup/Val di Scalve | 09/03/2020 | 12/03/2020 | 08/03/2020 | 07/03/2020 | 06/03/2020 |
| 10 - Val Brembana | 04/03/2020 | 07/03/2020 | 28/02/2020 | 27/02/2020 | 26/02/2020 |
| 11 - Val Imagna/Villa d'Almè | **01/02/2020** | 16/03/2020 | 03/03/2020 | 02/03/2020 | 01/03/2020 |
| 12 - Isola Bergamasca | **05/02/2020** | 15/03/2020 | 05/03/2020 | 08/03/2020 | 03/03/2020 |
| 13 - Treviglio | 13/03/2020 | 19/03/2020 | 04/03/2020 | 10/03/2020 | 09/03/2020 |
| 14 - Romano di Lombardia | 04/03/2020 | 21/03/2020 | 06/03/2020 | 06/03/2020 | 03/04/2020 |
| **Brescia** | | | | | |
| 01- Brescia | 14/03/2020 | **01/01/2020** | 04/03/2020 | 30/03/2020 | 29/03/2020 |
| 02 - Brescia Ovest | **02/01/2020** | 16/03/2020 | 02/03/2020 | 09/03/2020 | 08/03/2020 |
| 03 - Brescia Est | 13/03/2020 | 21/03/2020 | 06/03/2020 | 05/03/2020 | |
| 04 - Valle Trompia | 12/03/2020 | 20/03/2020 | 11/04/2020 | 10/04/2020 | 09/04/2020 |
| 05 - Sebino | **23/02/2020** | 18/03/2020 | 11/03/2020 | | |
| 06 - Monte Orfano | 16/03/2020 | 22/03/2020 | 11/03/2020 | 10/03/2020 | 09/03/2020 |
| 07 - Oglio Ovest | 12/03/2020 | 23/03/2020 | 12/03/2020 | 12/03/2020 | 11/03/2020 |
| 08 - Bassa Bresciana Occidentale | 04/03/2020 | 09/03/2020 | 27/02/2020 | 26/02/2020 | 25/02/2020 |
| 09 - Bassa Bresciana Centrale | 12/03/2020 | 15/03/2020 | 02/03/2020 | 01/03/2020 | 29/02/2020 |
| 10 - Bassa Bresciana Orientale | 10/03/2020 | 22/03/2020 | 29/03/2020 | | |
| 11 - Garda | 13/03/2020 | | 26/03/2020 | | |
| 12 - Valle Sabbia | 14/03/2020 | 25/03/2020 | 28/03/2020 | 27/03/2020 | 26/03/2020 |

### 5.7.2 Figures

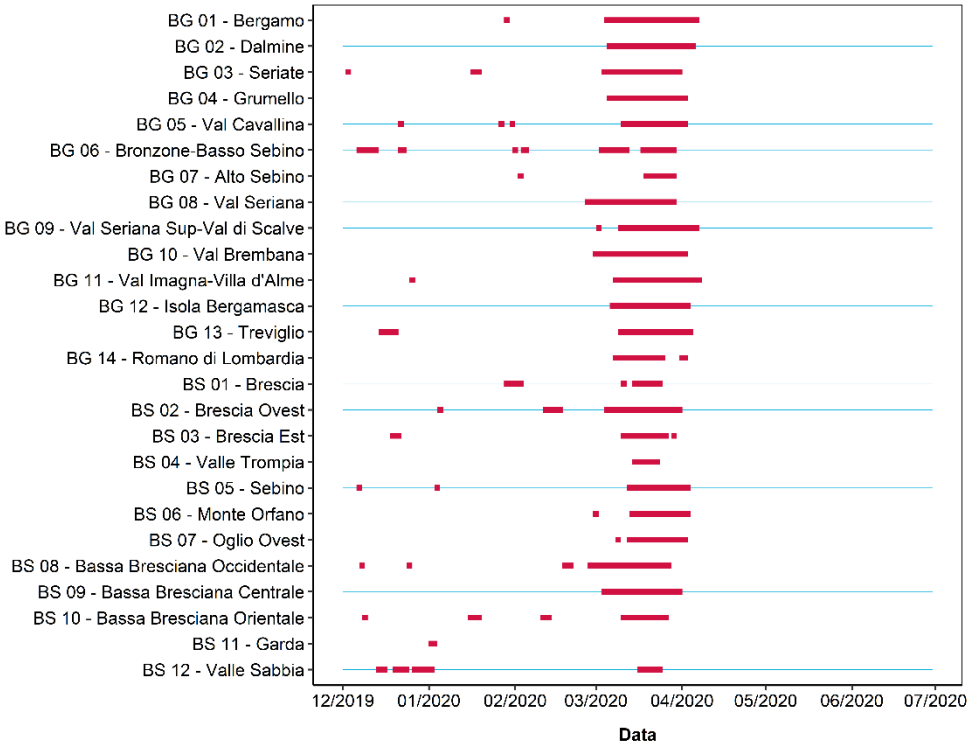


FIGURE 5.1: Outbreak detection in urgent hospital admission using Farrington Flexible algorithm


FIGURE 5.2: Outbreak detection in urgent hospital admission using Early Aberration Reporting System algorithm

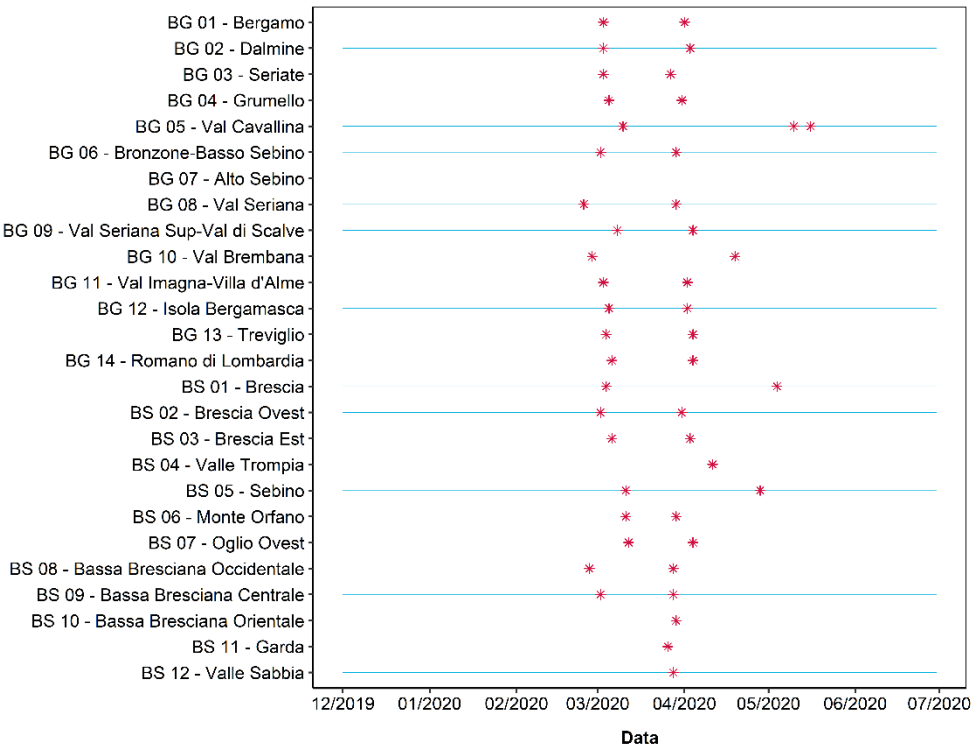


FIGURE 5.3: Outbreak detection in urgent hospital admission using segmented linear regression

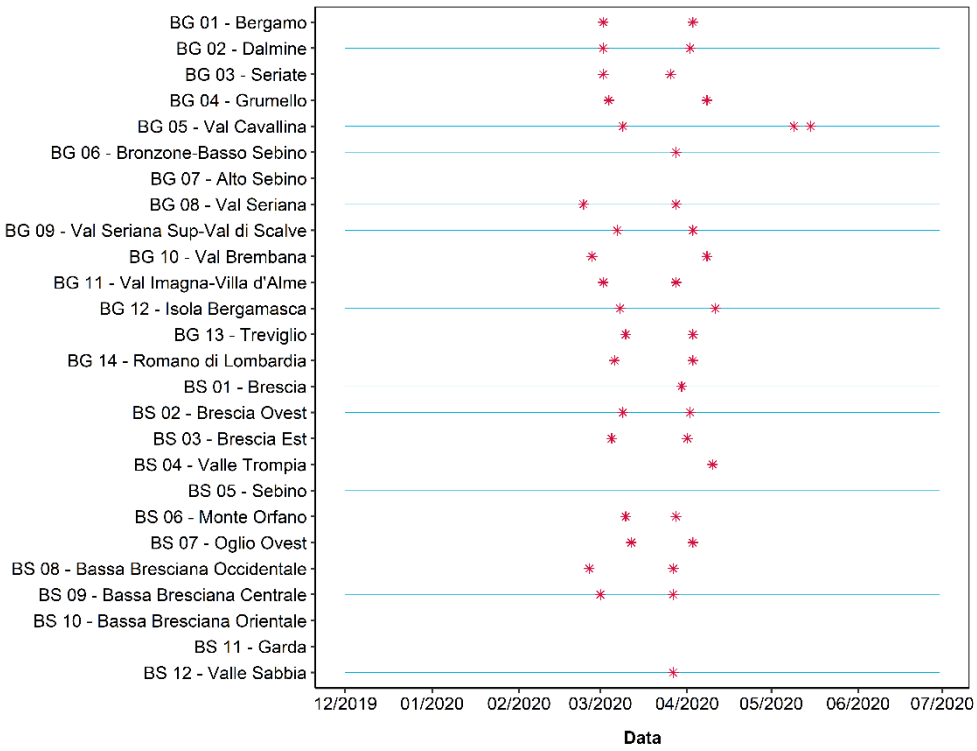


FIGURE 5.4: Outbreak detection in urgent hospital admission using segmented linear regression with first-order autoregressive component

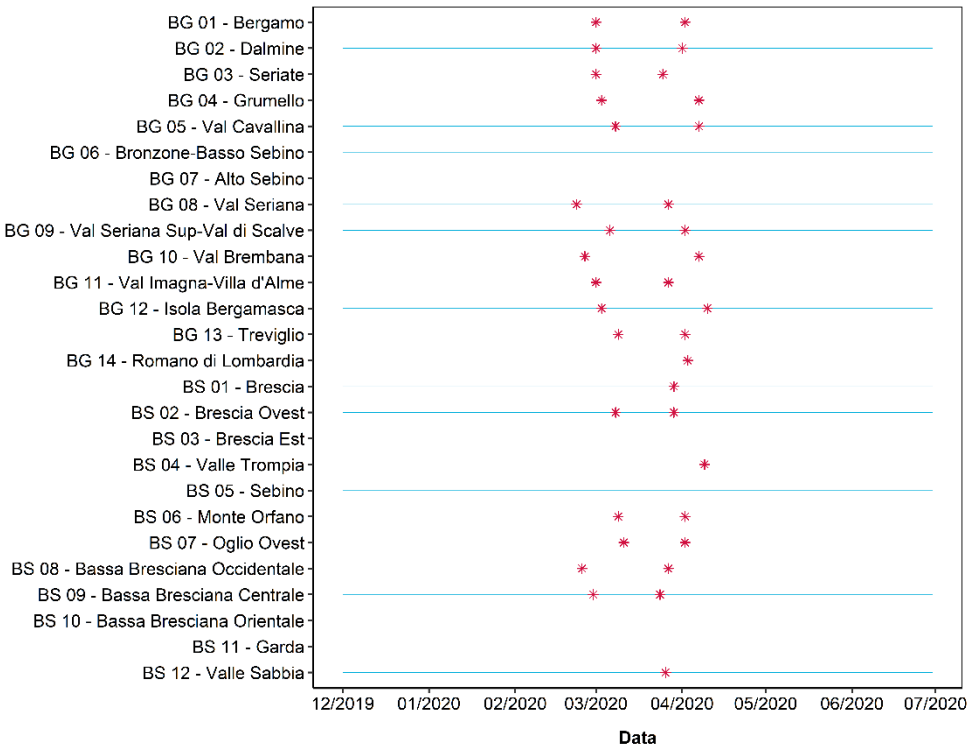


FIGURE 5.5: Outbreak detection in urgent hospital admission using segmented linear regression with second-order autoregressive component


FIGURE 5.6: Outbreak detection in urgent hospital admission medical DRG using Farrington Flexible algorithm

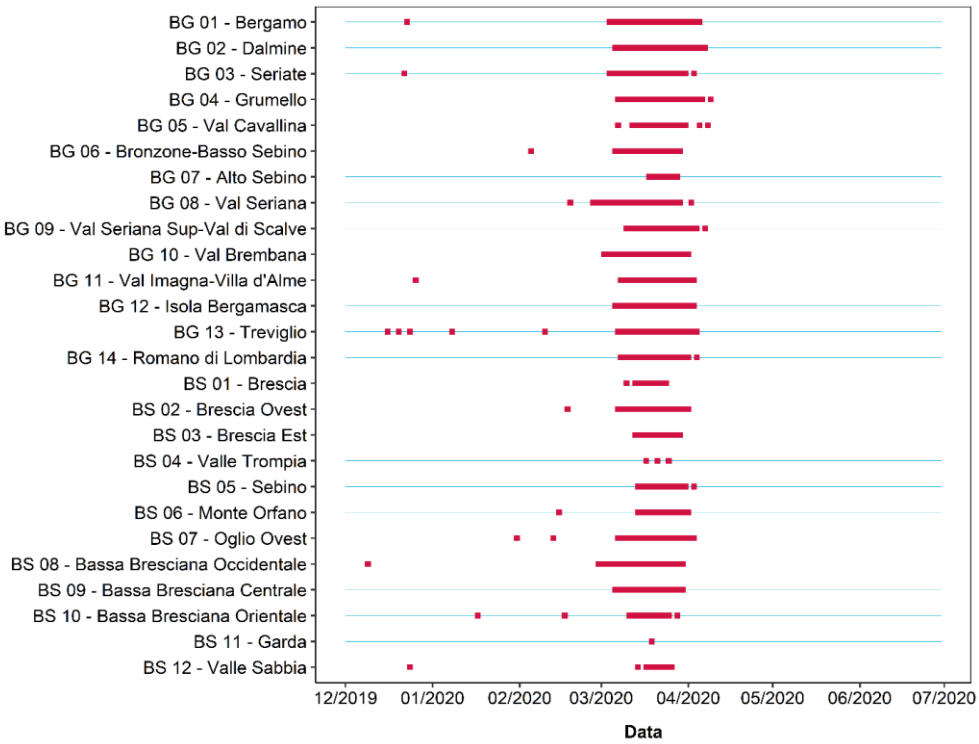


FIGURE 5.7: Outbreak detection in urgent hospital admission with medical DRG using Early Aberration Reporting System algorithm

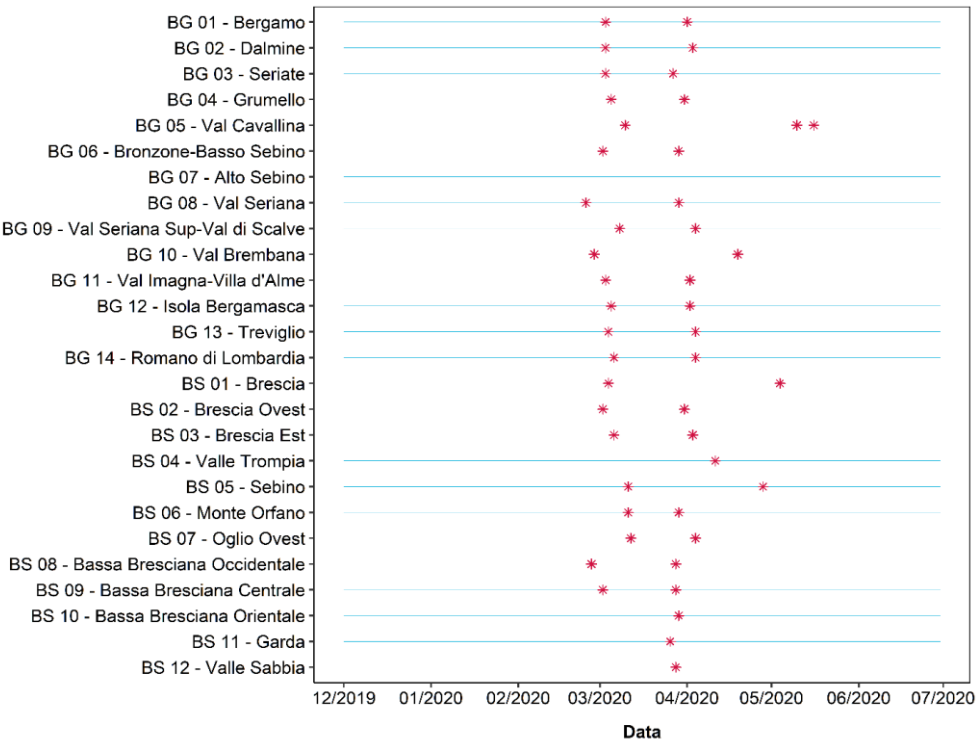


FIGURE 5.8: Outbreak detection in urgent hospital admission with medical DRG using segmented linear regression

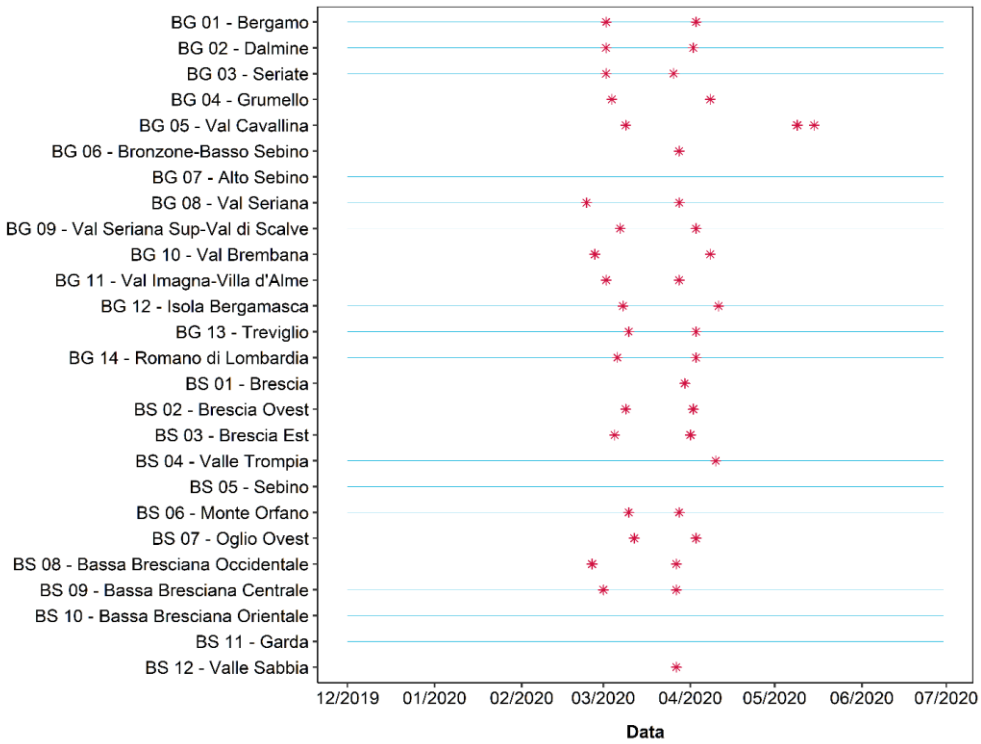


FIGURE 5.9: Outbreak detection in urgent hospital admission with medical DRG using segmented linear regression with first-order autoregressive component

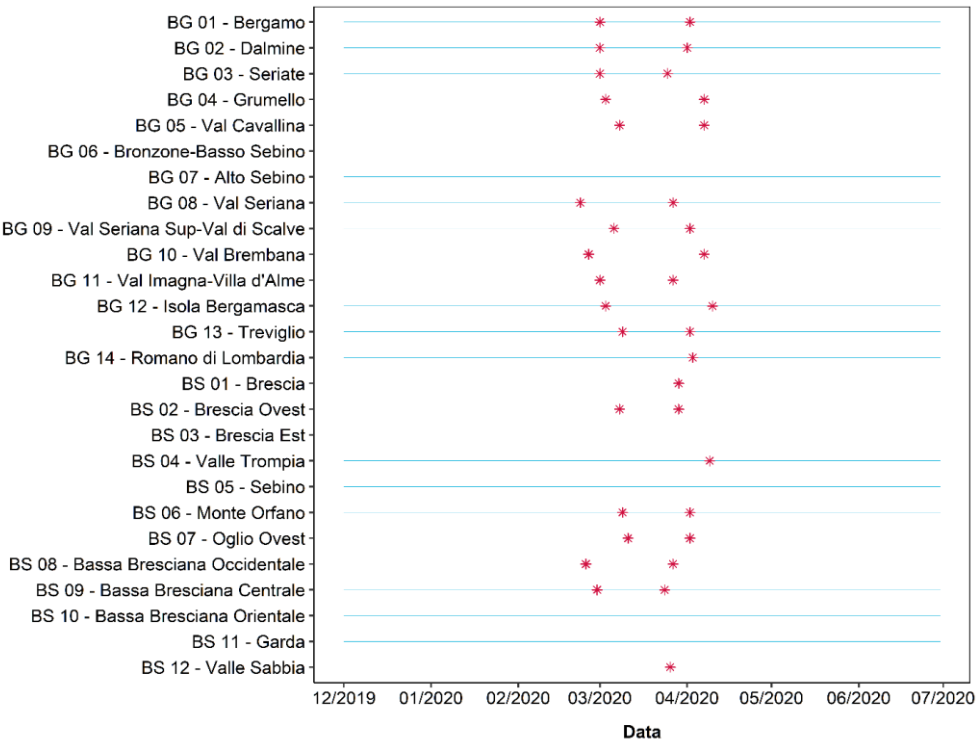


FIGURE 5.10: Outbreak detection in urgent hospital admission with medical DRG using segmented linear regression with second-order autoregressive component


FIGURE 5.11: Outbreak detection in urgent hospital admission with respiratory diagnosis using Farrington Flexible algorithm

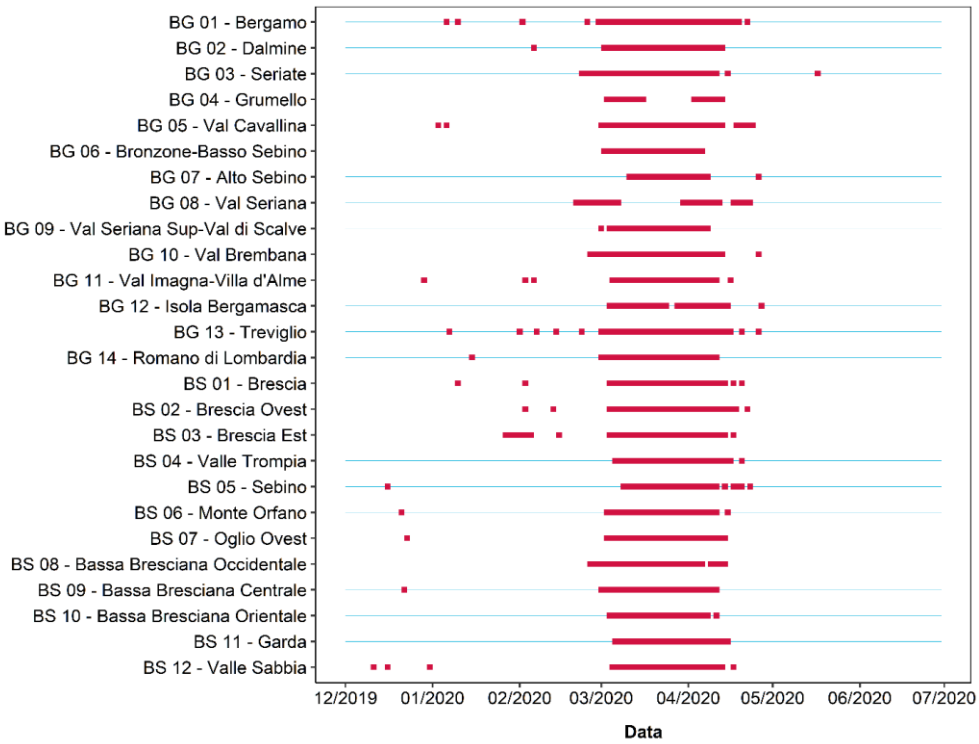


FIGURE 5.12: Outbreak detection in urgent hospital admission with respiratory diagnosis using Early Aberration Reporting System algorithm

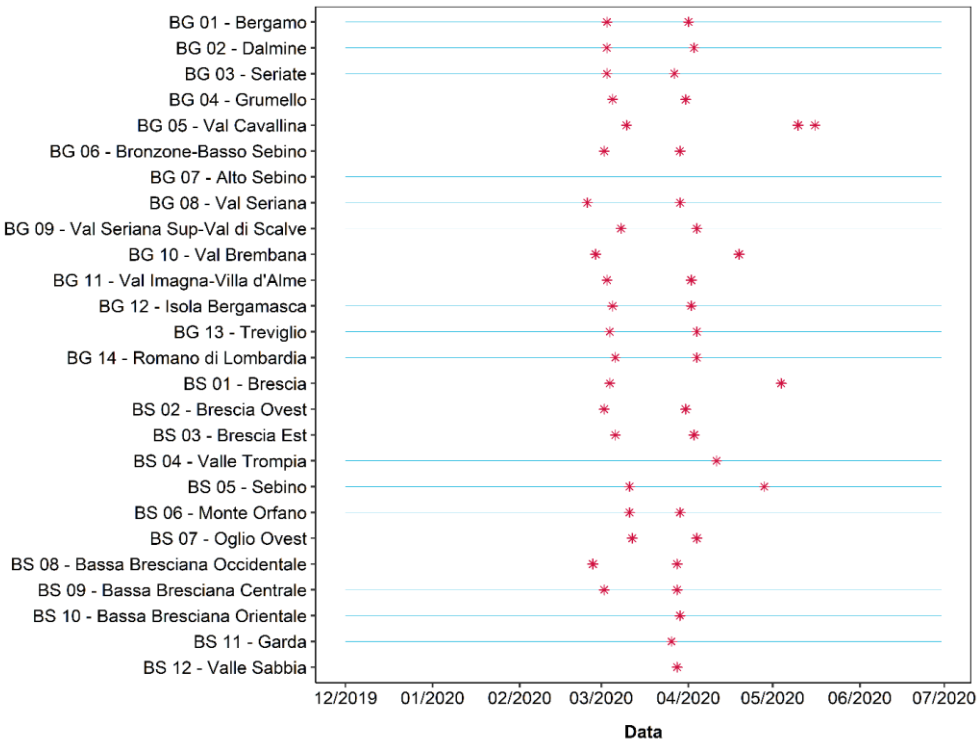


FIGURE 5.13: Outbreak detection in urgent hospital admission with respiratory diagnosis using segmented linear regression

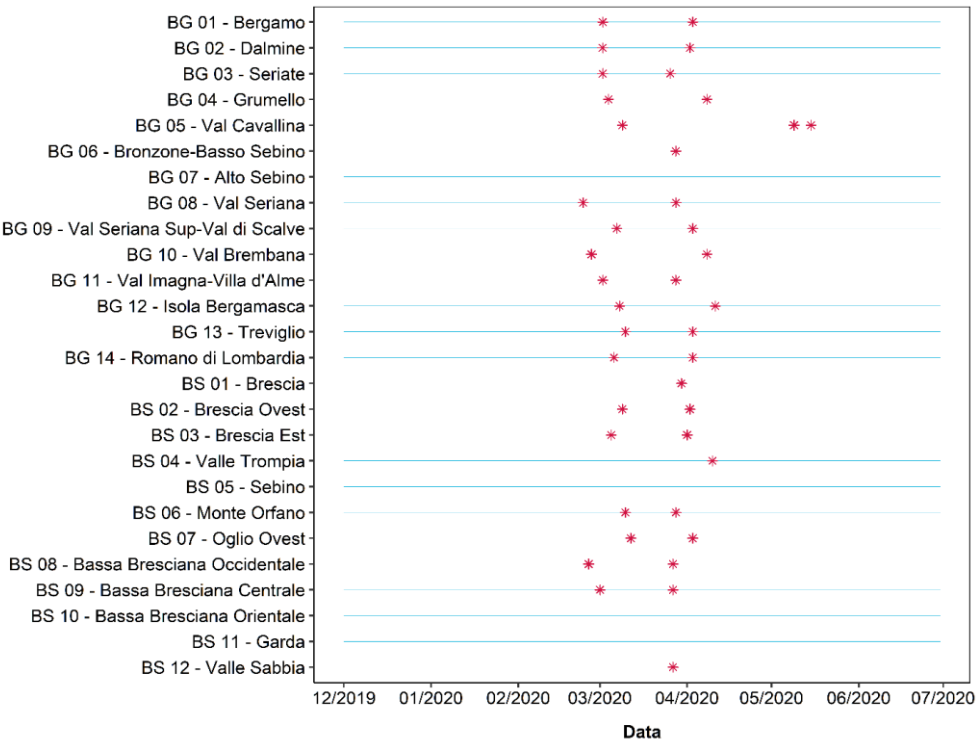


FIGURE 5.14: Outbreak detection in urgent hospital admission with respiratory diagnosis using segmented linear regression with first-order autoregressive component

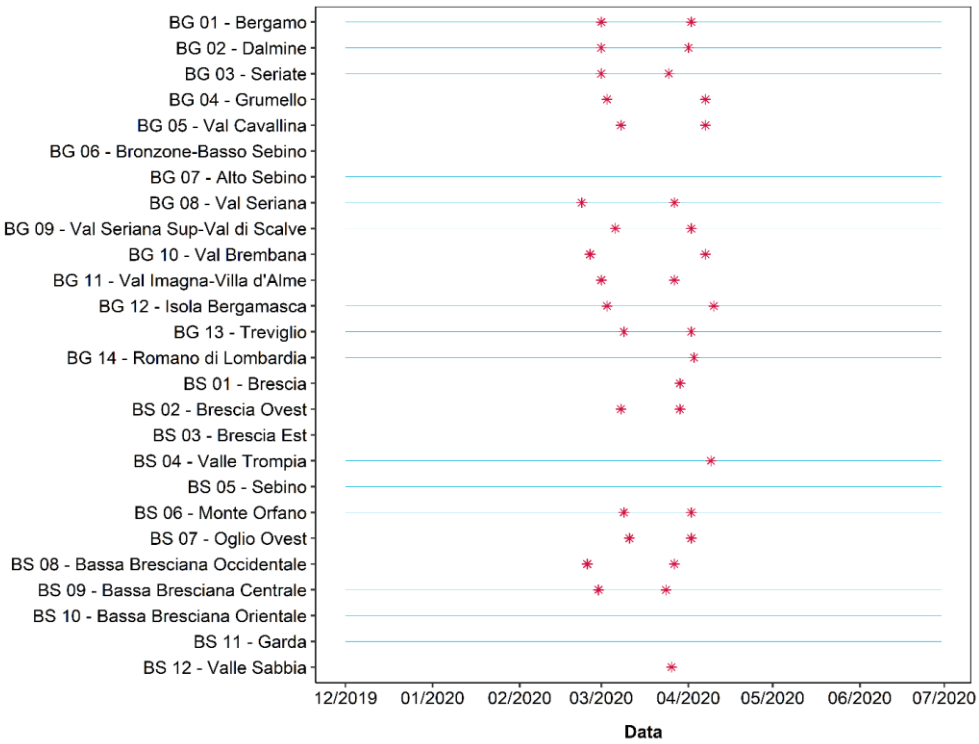


FIGURE 5.15: Outbreak detection in urgent hospital admission with respiratory diagnosis using segmented linear regression with second-order autoregressive component


FIGURE 5.16: Outbreak detection in urgent hospital admission with MDC of the respiratory system using Farrington Flexible algorithm

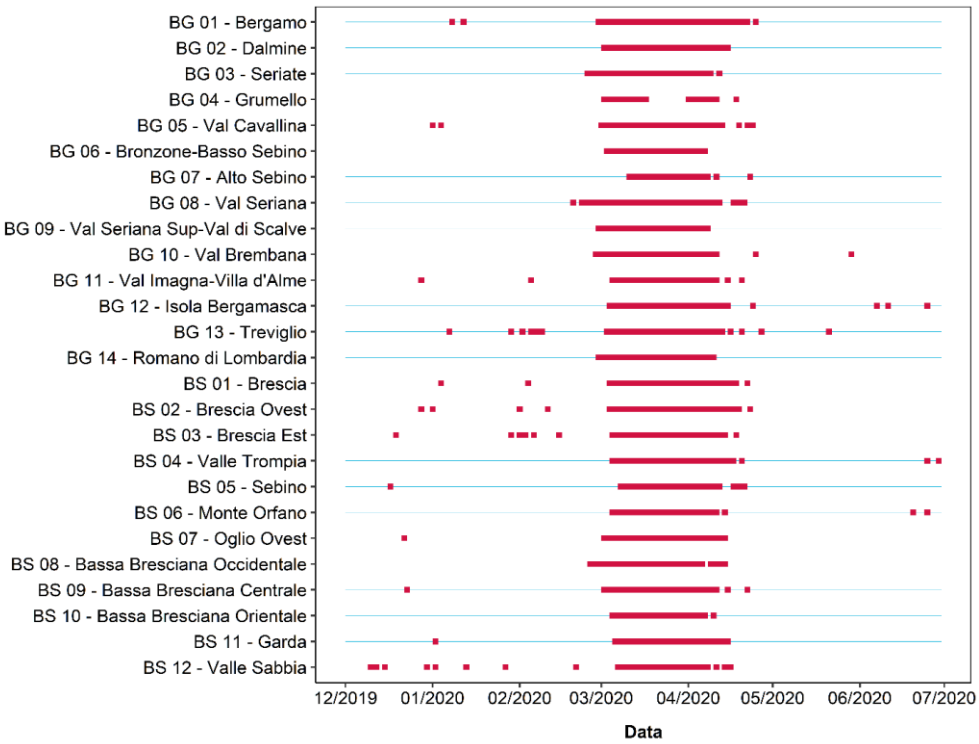


FIGURE 5.17: Outbreak detection in urgent hospital admission with MDC of the respiratory system MDC using Early Aberration Reporting System algorithm

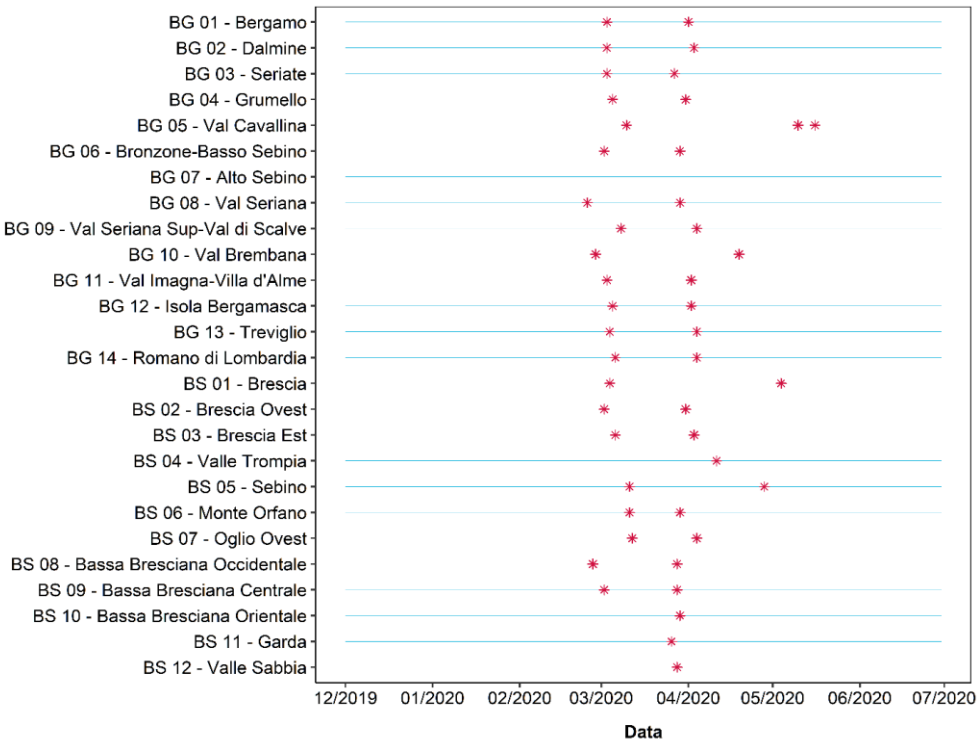


FIGURE 5.18: Outbreak detection in urgent hospital admission with MDC of the respiratory system using segmented linear regression

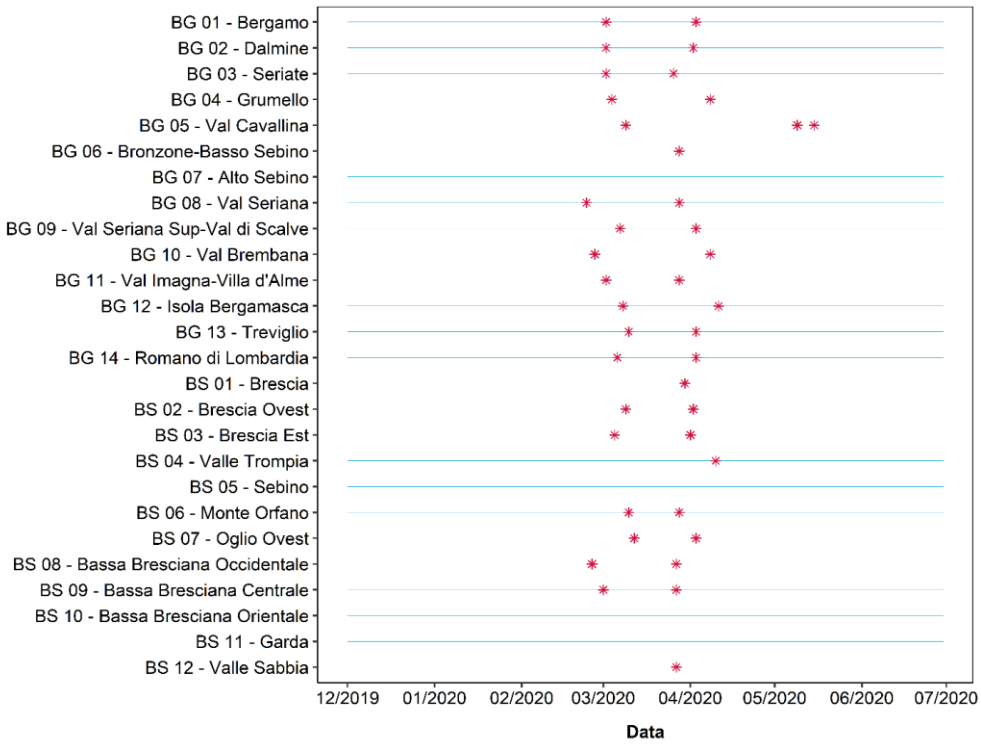


FIGURE 5.19: Outbreak detection in urgent hospital admission with MDC of the respiratory system using segmented linear regression with first-order autoregressive component

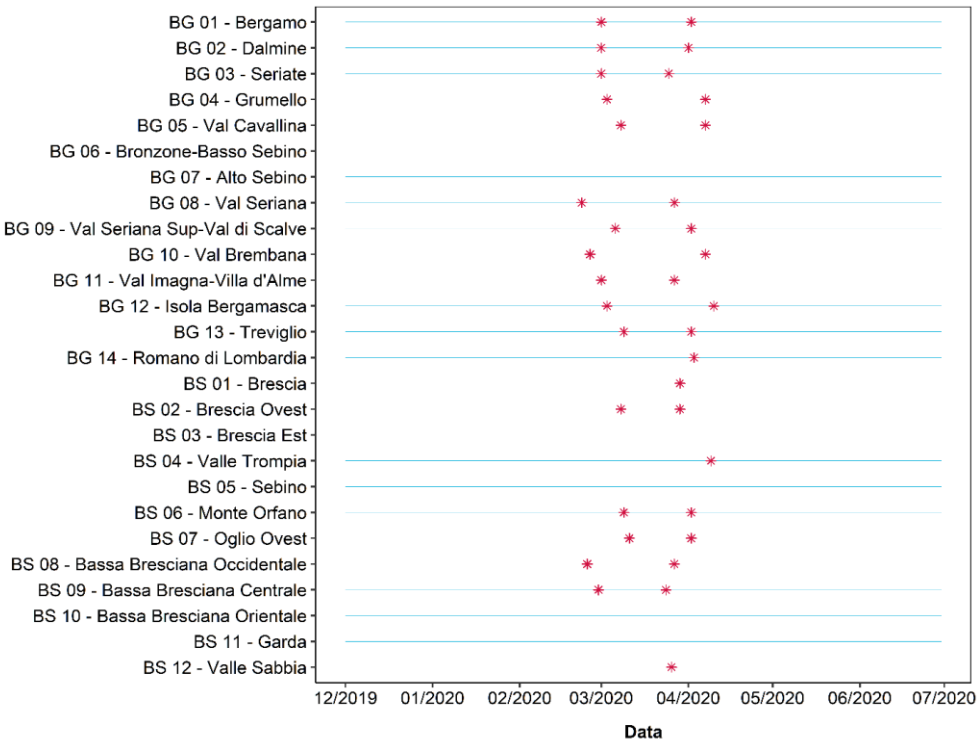


FIGURE 5.20: Outbreak detection in urgent hospital admission with MDC of the respiratory system using segmented linear regression with second-order autoregressive component

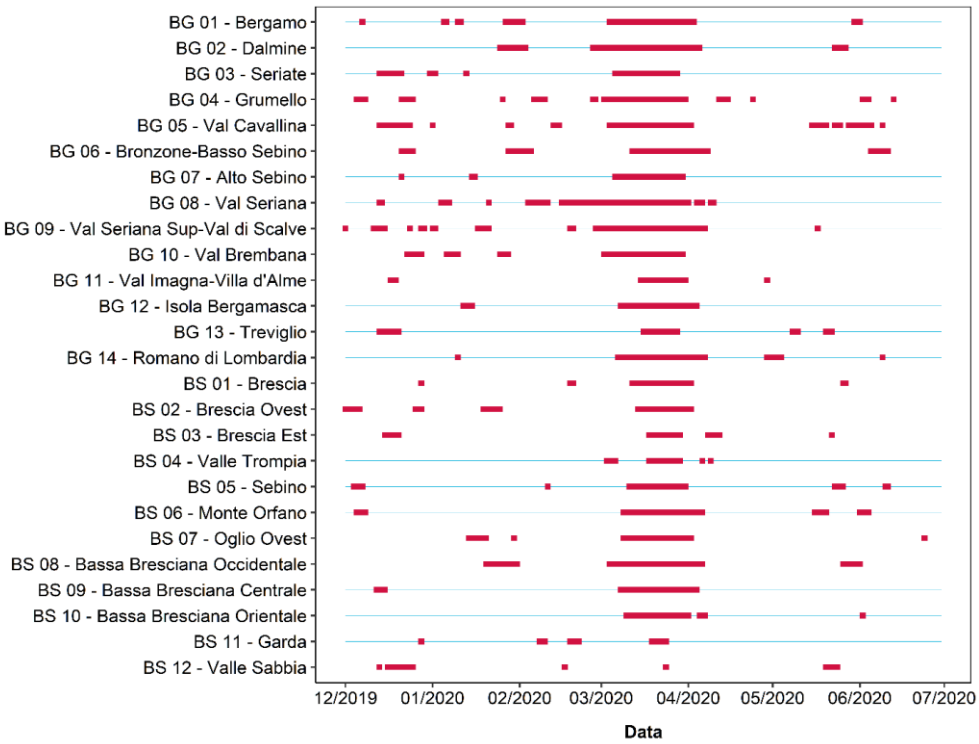


FIGURE 5.21: Outbreak detection in total red-code ED visits using Farrington Flexible algorithm

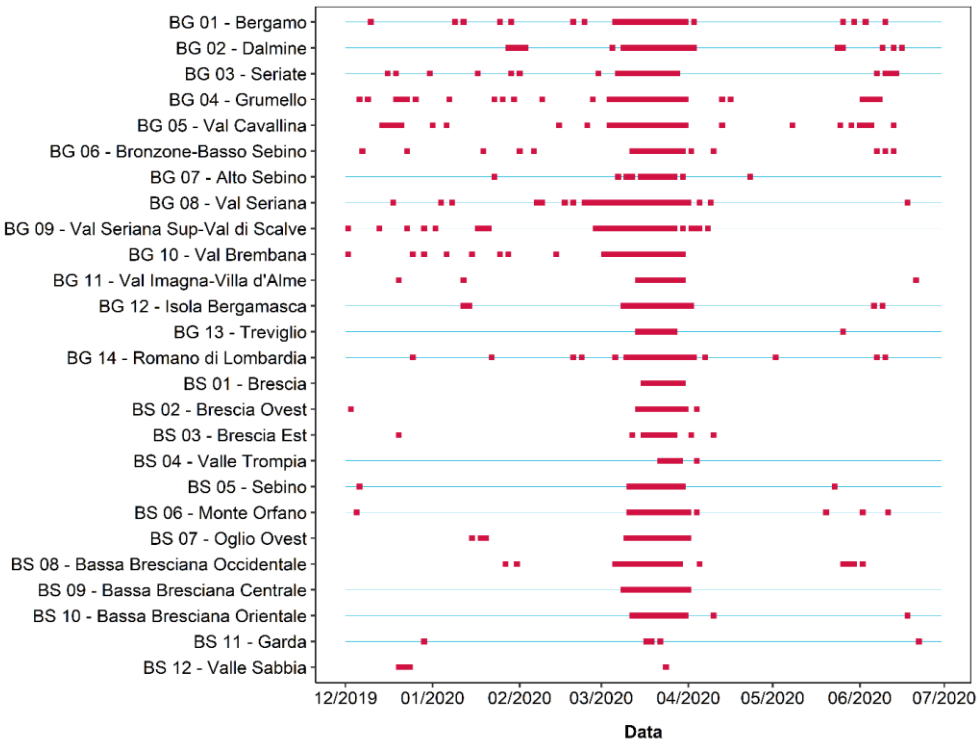


FIGURE 5.22: Outbreak detection in total red-code ED visits using Early Aberration Reporting System algorithm

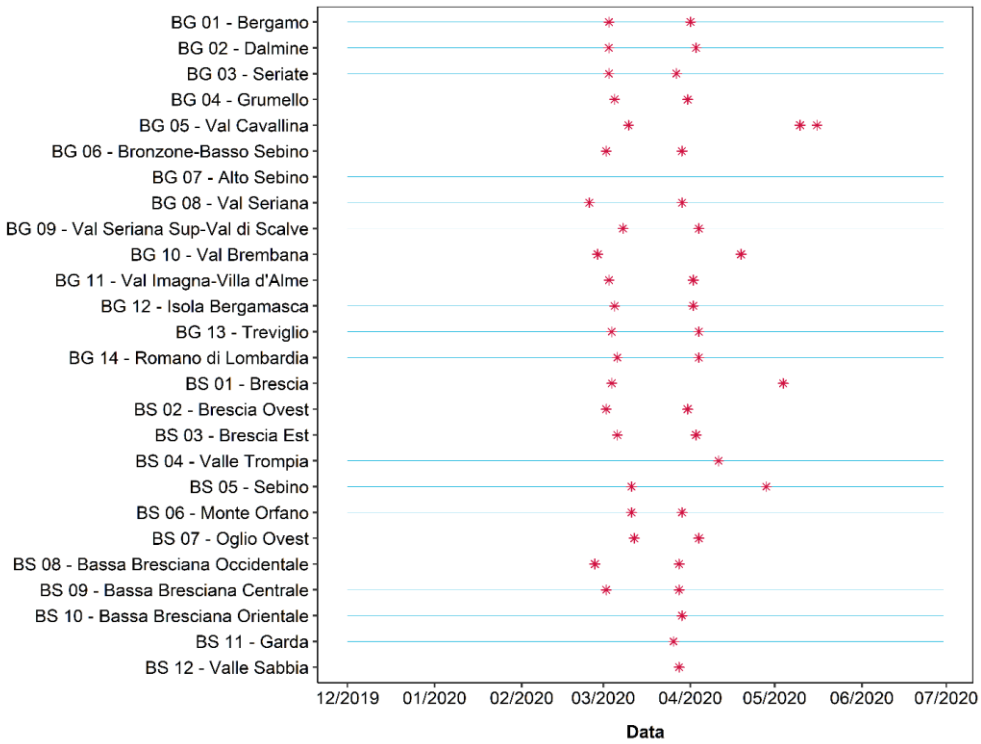


FIGURE 5.23: Outbreak detection in total red-code ED visits using segmented linear regression

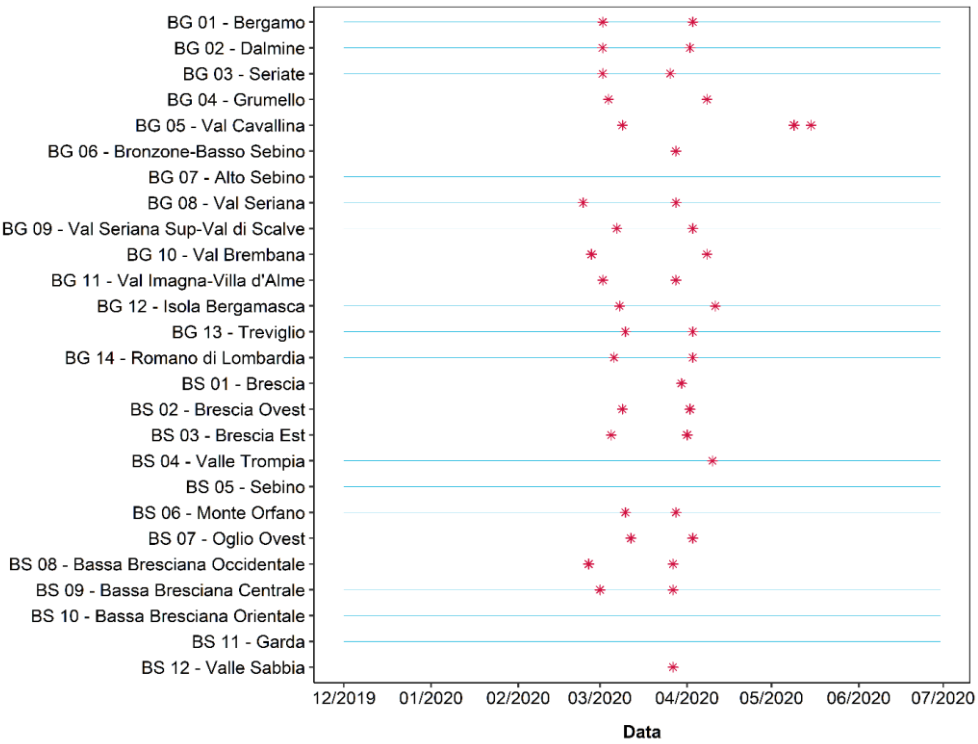


FIGURE 5.24: Outbreak detection in total red-code ED visits using segmented linear regression with first-order autoregressive component

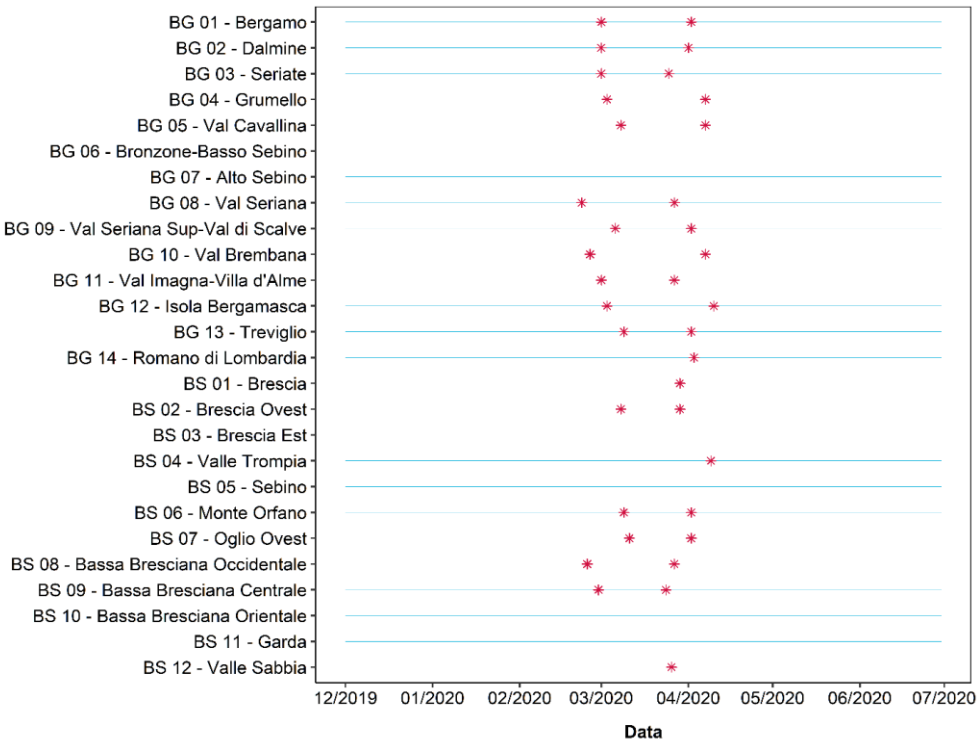


FIGURE 5.25: Outbreak detection in total red-code ED visits using segmented linear regression with second-order autoregressive component

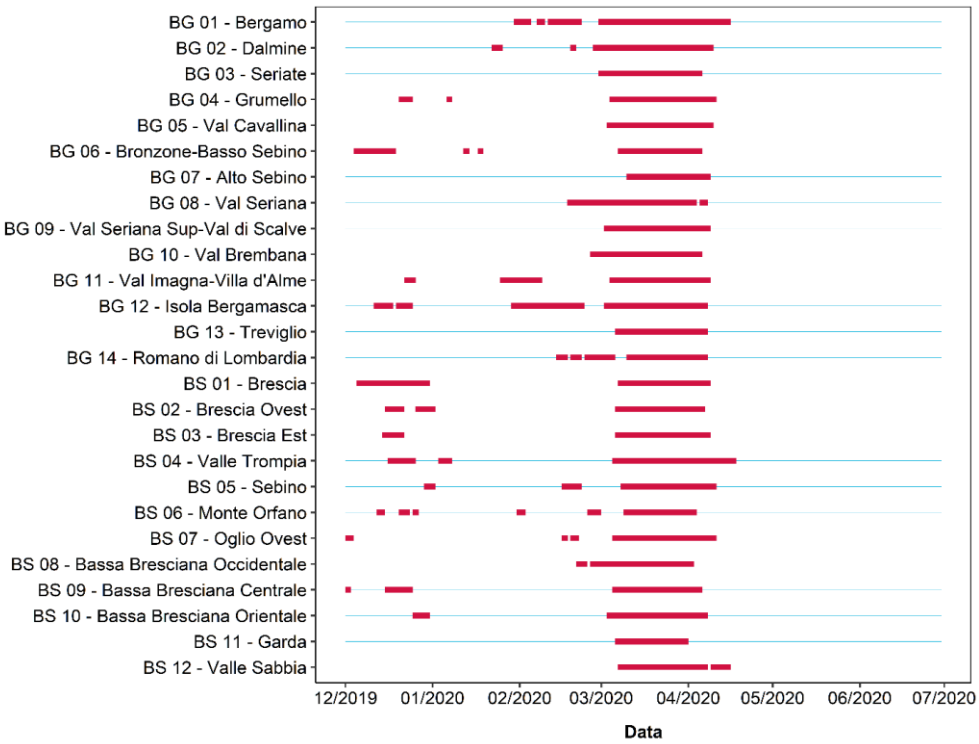


FIGURE 5.26: Outbreak detection in ED visits with respiratory diagnosis using Farrington Flexible algorithm


FIGURE 5.27: Outbreak detection in ED visits with respiratory diagnosis using Early Aberration Reporting System algorithm

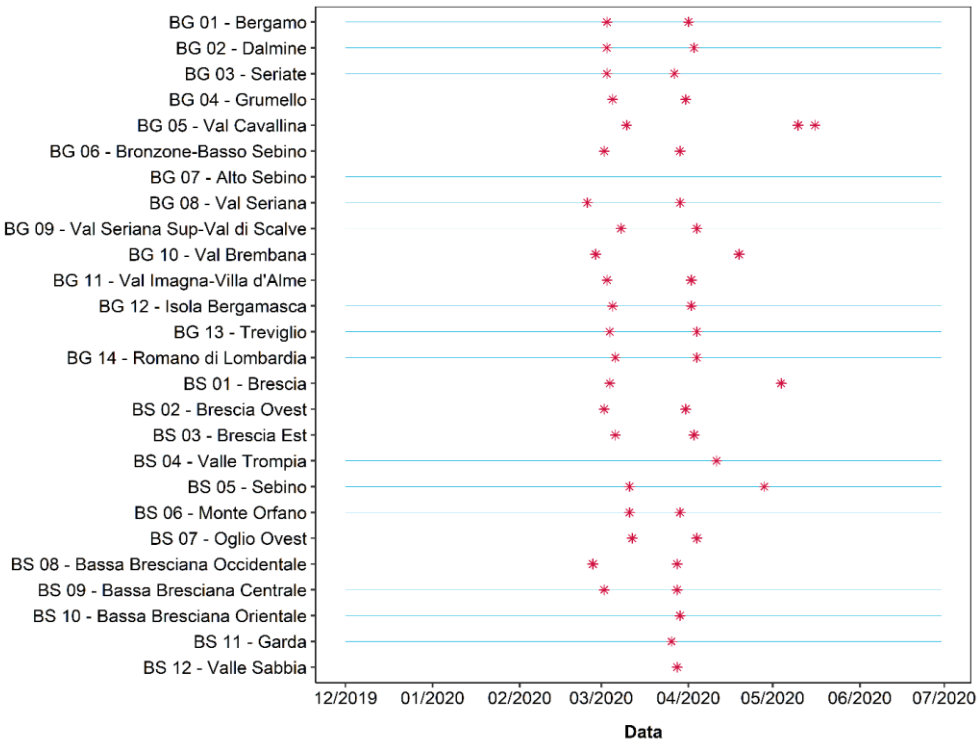


FIGURE 5.28: Outbreak detection in ED visits with respiratory diagnosis using segmented linear regression

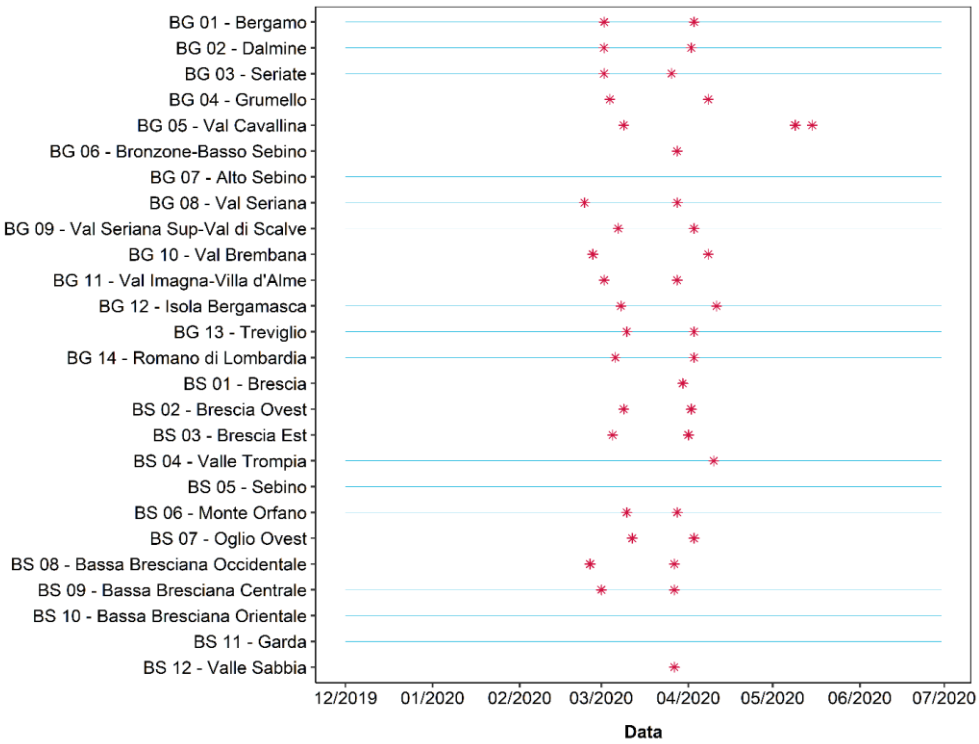


FIGURE 5.29: Outbreak detection in ED visits with respiratory diagnosis using segmented linear regression with first-order autoregressive component

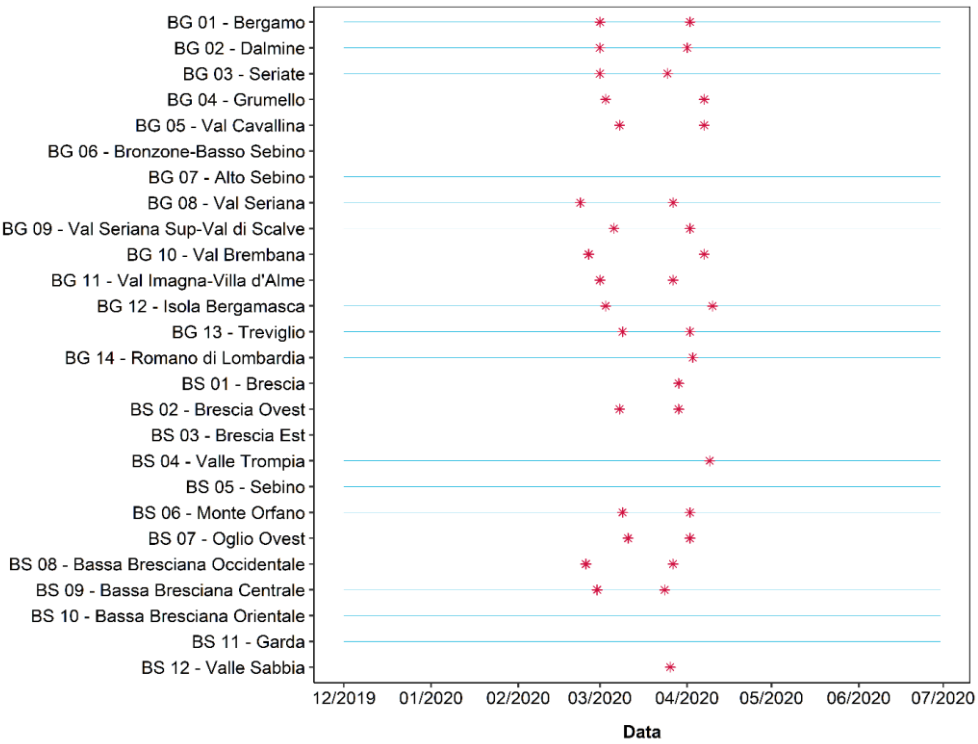


FIGURE 5.30: Outbreak detection in ED visits with respiratory diagnosis using segmented linear regression with second-order autoregressive component

# Conclusions

This research described how the COVID-19 outbreak changed hospital utilization and activity during the pandemic period in Bergamo and Brescia, which include densely populated areas of the Lombardy region and represented a critical epidemic burden. Results provide context to strengthen the response of health services to meet patients' needs and promote options to address possible backlogs, including a prompt adaptation of services and the reorganization of elective hospital and community care.

Given that no major health area has been exempt from the adverse impact of COVID-19, commissioners and providers are called upon to adjust and implement multiple strategies to address the tension that has arisen in healthcare management under pandemic conditions to ensure healthcare service quality and the sustainability of health systems.

In Italy as in other contexts, the current "hospital-centric" architecture of healthcare has caused the crowding of hospital units and EDs and has pressured hospitals to deliver an inefficient and unsafe level of care. Over the past two years, the SARS-CoV-2 pandemic has exacerbated health systems' pre-existing issues related to the provision of both acute and elective care for conditions other than COVID-19, although the management and outcomes of patients hospitalized for non-deferrable conditions appear to have remained unchanged, except for those with SARS-CoV-2 infection.

Evidence related to the COVID-19 outbreak has been generated with astounding speed. Therefore, the present approaches provide actionable metrics that could be useful to tie specific actions to observed results and may help reveal insightful analogies and differences between periods and contexts in the development of the pandemic and data reporting. Indeed, focusing on a robust methodology to learn how existing health service capacity should be (re)distributed is important for leading and governing the COVID-19 response, reducing barriers to healthcare, and meeting universal health coverage objectives. Adjusting facilities and referral processes in the care delivery system toward value-based models—in which the management of care and services is reallocated in the most appropriate setting according to the degree of complexity—is critical.

Adopting a more integrated, patient-centred care model means considering the rising demand for care services from dynamic populations and ensuring that patients—especially chronic patients—always receive the most appropriate assessment, treatment, and care.

This is particularly important in Italy, where the NHS has to operate in a complex and evolving environment and the ISS estimates that one individual out of five lives with a noncommunicable disease. Recently, the government steered the National Recovery and Resilience Plan (PNRR), which focuses on strategies to better serve high-need patients in a more robust and sustainable NHS using funds from the European Union's NextGenerationEU plan, a temporary recovery instrument to help repair the economic and social disruptions brought about by the COVID-19 pandemic in Europe. In doing so, the Ministry of Health is leading the transformation of community-based care services through specific guidelines, released in the first semester of 2022, for preparing and adopting a range of interventions designed to provide the right care in the right place from the right person at right time.

Therefore, the PNRR offers an irreplaceable opportunity to redesign the Network of Care in Italy envisaged by the Ministerial Decree 70 of 2015 by using the efficiency of current hospital structures, and creating and strengthening advanced territorial organizational models outlined in the Ministerial Decree 77 of 2022 that is projected to deliver care outside the hospital setting.

In brief, the PNRR provides the impetus for building longer-term NHS resilience and preparedness, including community health development and community engagement, surge procurement, and financial planning. These interventions are specifically intended to redesign and strengthen primary care models and facilities on a national level, with a focus on proximity networks, facilities, and telemedicine for territorial healthcare assistance. The ultimate goal is to align services to the needs of patients.

Although more research is required to learn the real extent of COVID-19 on care services and population health, identifying the top-priority needs for maintaining essential health coverage is an open-ended question. The PNRR's push to strengthen continuity of care is necessary but likely insufficient without an effective longer-term response. The main issues in this response should include recruiting health workers according to identified staffing requirements and identifying program-specific tracer care areas, with a particular focus on care for older people, cancer care, and reproductive, maternal, and child health.

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