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PILLAR 3

STATE OF THE ART

HELICON
Unravelling the long-term and indirect health impact of the COVID-19 crisis in Belgium

Prof Dr Brecht Devleesschauwer (Project Coordinator)

Prof Dr Delphine De Smedt

Prof Dr Sylvie Gadeyne

Prof Dr Niko Speybroeck

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sciensano · Universiteit Gent · VUB Vrije Universiteit Brussel · UCLouvain · KU Leuven · belspo

[Introduction]

The COVID-19 crisis has faced Belgium with unprecedented societal challenges. Although we are gradually gaining control over the virus transmission, large uncertainties exist regarding the multidimensional impact on population health. As depicted in figure 1, the public health burden occurs at different time scales and is borne by different populations. HELICON aims to fulfil three research objectives:

A. Identify sociodemographic (SD) and socio-economic (SE) factors of risk and resilience through the assessment of the social patterning of COVID-19 testing, infection, hospitalizations and mortality (Dimension 1).
B. Describe the medium- and long-term direct health impact of COVID-19 infections with regard to healthcare use after COVID hospitalization (Dimension 1).
C. Assess the indirect health impact of the COVID-19 crisis in terms of non-COVID morbidity and mortality and the health economic impact of delayed health care use (Dimension 2, 3 and 4).

Four guiding principles will be respected: valorisation of administrative health data sources, evaluation of social differentials, evaluation of differentials across the epidemic waves, and knowledge translation and policy transfer.

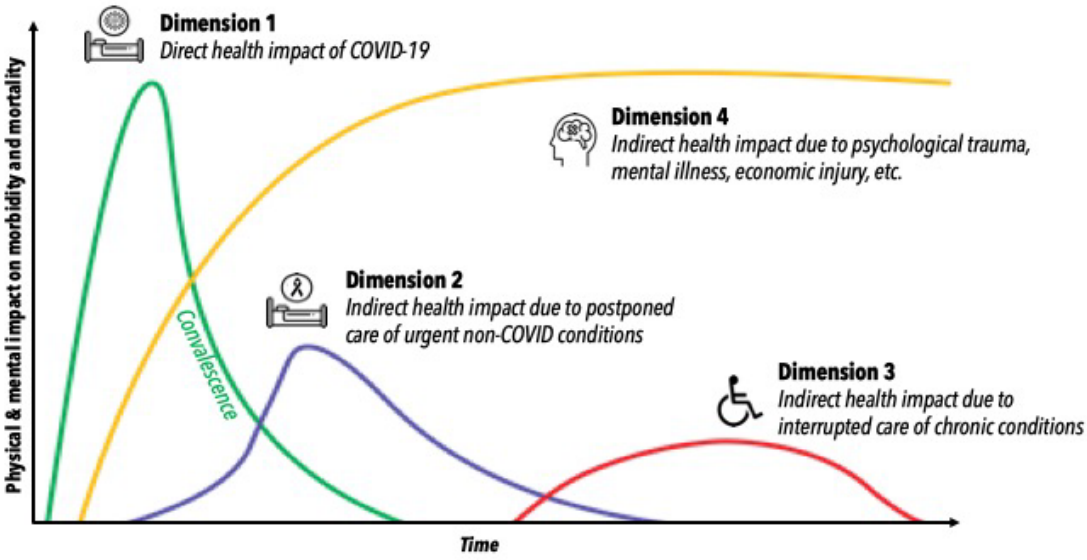

Figure 1 The COVID-19 crisis has a multidimensional impact on population health.

[State of the art]

The pandemic has fuelled research collaborations and scientific productivity resulting in a torrent of COVID-related research. The majority of COVID-19 publications originate from China, the United States and Italy.[1] In the following sections, we synthesize the current literature relevant for the project objectives and methodology. We conclude with a discussion of the policy relevance of the envisaged results.

Belgium swiftly installed active surveillance systems at the beginning of the crisis to monitor the number of COVID-19 cases, hospitalizations and deaths in real-time. These data provide valuable insights in the direct health impact of COVID-19 in Belgium – with current estimates reaching over 25,000 deaths, over 78,000 hospitalized patients, and almost 1.2 million confirmed cases.[2] Early research efforts suggest a heavy direct impact of COVID-19 on population health in Belgium. A European comparison of excess mortality – a well-established proxy for the total COVID-19 associated mortality- shows Belgium experienced substantial excess mortality during the first and second wave of the epidemic in 2020.[3,4] Despite the wealth of information that is being gathered on the current, immediate impact of COVID-19, **three important knowledge gaps** remain – i.e., (1) the social patterning of COVID-19; (2) the long-term direct health impacts of COVID-19 infections; and (3) the indirect health impacts of the COVID-19 crisis. Although Belgium has a number of rich data collections to address these issues, these databases provide fragmentary perspectives on the clinical health situation, the SD/SE context or the health care expenditures. The interoperability and reuse of these different clinical and administrative data sources pose a number of technical, administrative and data security

challenges. While these data linkage opportunities remain under-exploited in Belgium, data linkage systems have proven to be a powerful tool in combatting the epidemic and managing the aftermath in several other nations (e.g., England, Wales, Scotland, Denmark, Taiwan).[5–9]

⇨ HELICON will set up a number of individual-level data linkages between Sciensano, Statistics Belgium, the Intermutualistic Agency, the Belgian Cancer Registry, and the FPS Health, Food Chain Safety and Environment. The expected result is a population-based data structure covering in- and post-pandemic health information, as well as SD/SE characteristics, health care use and related costs.

Social health inequalities

The COVID-19 crisis has been described as a syndemic pandemic, meaning that it interacts with and is exacerbated by social, economic and health inequalities.[10] Risk factors and comorbidities (e.g., obesity) are expected to be intertwined, interactive and cumulative. COVID-19 severity has been clearly associated with two SD indicators: advanced age and male sex.[11,12] There is a growing body of literature recognising the social patterned distribution of COVID-19-related health outcomes, with indications of higher risks for exposure, infection, symptom severity, hospitalization and death among disadvantaged groups (e.g., low-income groups, people with a migrant background) and certain occupations (e.g., health care workers).[10,13–15] The scarce Belgian research on SD and SE differences in COVID-19 health largely supports these international findings. Only one study investigated COVID-19 incidence at the municipal level. The working paper suggests significant relations with area characteristics such as the income level per capita, the share of elderly, the share of care home residents and the share of migrant groups during the first wave.[16] Studies comparing the number of deaths from all causes during the first wave of the COVID-19 crisis with the pre-pandemic mortality patterns show that the heaviest burden of excess mortality is born by the **elderly population**. Although negative social gradients are found for educational attainment and personal income in the population aged 64 and younger, these differences lie within the bounds of expected social health inequalities for Belgium.[17,18] Interestingly, Gadeyne and colleagues report significantly higher excess deaths among low-educated women, high-income men and individuals living in collective households for this middle-aged group.[17] For the population aged 65 and older, results also show clear significant negative gradients for **education and income**, but only for individuals who did not live in a nursing home. [17,18] Decoster, Minten en Spinnewijn report for the group of elderly non-residents that more than twice as many excess deaths occurred in the bottom income decile compared to the top income decile. Because of the large income mortality differences in pre-pandemic times, the COVID-19 crisis seems to have caused only a relatively modest increase in the income mortality gradient during the first wave.[18] **Nursing home residents** have been identified as an extremely vulnerable group with increased risk of COVID-19 hospitalization and mortality, most likely due to the accumulation of risk factors related to old age, comorbidities and increased exposure risks in collective living arrangements.[11,19,20] Although no clear social health gradients were found for excess mortality in this group,[17,18] some specific subgroups may be even more vulnerable. For example, Willaert examined excess mortality among members of the socialist health insurance fund during the first wave and found significantly higher mortality risks among nursing home residents entitled to supplemented refunds.[21]

In addition, specific **migrant communities** seem to be bear increased COVID-19-related health risks. Vanthomme and colleagues investigated excess mortality in the Belgian population by migrant origin group during the first wave.[22] Significant excess mortality was reported for men and women of sub-Saharan African origin, as well as for Turkish elderly men after accounting for other SD and SE indicators. A non-representative survey of migrants and refugees in Brussels indicates that this population group experienced difficulties in accessing health care during the first wave of the epidemic, especially when having a precarious legal status.[23]

Furthermore, the burden per **economic group** seems to depend heavily on the timing and the prioritization of the protective policy measures, the testing strategy and the vaccination strategy. During the autumn of the second wave, the sectors most at risk for a COVID-19 infection were human health activities (e.g., working in a nursing home) and sport activities (e.g., working at a fitness club).[24] By the spring of 2021, Molenberghs and colleagues found a clear protective effect of the vaccination strategy among health care workers in their occupational comparison of COVID-19 incidence rates. With strict sector protocols and shutdowns for many recreational activities, no elevated incidence risks were found for sport activities. Instead, occupational risks groups during the spring of the second wave include workers in waste management and cleaning; private security; manufacturing industries; public transportation; call centres; and packaging services.[25] Further Belgian research is needed understand the SD/SE distributional patterns in COVID-related health outcomes and how these develop during the different waves of the pandemic and afterwards. An ecological study from the USA shows that the relationship between SE indicators and COVID-19 incidence and mortality can change

drastically over time.[26] More detailed information may provide new insights with regard to SD/SE differences in increased vulnerability (e.g., pre-existing comorbidities); increased susceptibility (e.g., smoking); increased exposure (e.g., no possibility to telework); and increased transmission (e.g., high-density housing).[10]

⇨ HELICON will investigate SD (e.g., sex, age, migration background, household status) and SE (e.g., educational attainment, employment status, income level) differences in COVID-19 testing, hospitalization and death at population level for Belgium. The analyses will account for intersectionality and the dynamic nature of the epidemic.

Long-term health and social impact

It is becoming increasingly clear that COVID-19 has the potential of causing long-lasting health effects.[27,28] Some people report health impairments after being first infected with the virus, even after mild or asymptomatic infections. A range of neurologic, cardiovascular, respiratory, gastro-intestinal and dermatological symptoms have been reported in the aftermath, of which the most prevalent are fatigue and shortness of breath.[29,30] These various symptoms can last weeks or months after the infection, or can even occur weeks after recovering from COVID-19. Despite considerable research efforts, difficulties remain in defining, characterizing, explaining and treating the diverse mid- and long-term health conditions related to a COVID-19 infection.[31] There is a rapidly growing body of literature addressing **Post-COVID Syndrome (PCS)**. Much of the current research is oriented towards recognizing specific symptom clusters; identifying existing syndromes (e.g., Post-Intensive Care Syndrome [32] and Post-Viral Fatigue Syndrome [33]); shedding light on the underlying mechanisms (e.g. multi-organ damage and inflammatory response mechanisms [34]) and describing new COVID-specific syndromes. These fine-grained analyses are essential in understanding the natural history of this disease and developing effective treatments. At the same time, a more comprehensive overview of the long-term consequences of COVID-19 is needed from a public health perspective. The aftershock of COVID-19 may further increase the human burden, intensify public health demands and exacerbate social health inequalities for an indefinite period. Considerable differences have already been reported for **hospitalized from non-hospitalized** patients in terms of the type, severity and frequency of PCS symptoms. A meta-analysis of 33 international studies indicates that 79% of hospitalized patients showed one or more PCS symptoms up to 60 days after hospital admission compared to 56% of non-hospitalized patients up to 60 days after symptom onset.[29] A comparison with a matched control group from the English general population shows that COVID-19 hospitalized patients experience increased rates of multiorgan disfunction, hospital readmission and mortality.[35] In addition, there are indications of important demographic and clinical differences between hospitalized and non-hospitalized patients. The COVID-19 hospitalized population includes more elderly, men and ethnically diverse people compared to the COVID-19 non-hospitalized population. Pre-existing comorbidities seem to be more prevalent in hospitalized patients than in non-hospitalized patients, potentially obscuring a causal association when comorbidities and PCS share common risk factors.[29] So far, Belgian evidence on the subject remains scarce and lacks the scope to provide insights into the long-term health consequences on population level.[11,36,37] Further research is urgently needed to identify vulnerable populations groups and estimate the public health costs related to the aftermath of COVID-19.

⇨ HELICON will provide a comprehensive assessment of health complications and pre-mature mortality during and after a COVID-19 positive test or hospitalization, as well as assess evolutions in health care expenditure. In addition, the project includes data validation tasks to further open up research opportunities for post-COVID patients.

Indirect health impact

In order to prevent the healthcare system from being submerged by an unmanageable number of COVID-19 patients, regular health care in Belgium was suspended from 14 March 2020 until 4 May 2020.[38] All non-urgent and selective primary and hospital care were postponed to reserve maximum capacity for triage and hospitalization of COVID patients. This postponement is likely to have unintended but significant consequences on access to care, diagnosis and treatment. Even after the restart of the regular health care, the delays in diagnosis and treatment may produce knock-on effects which could overwhelm health services in the coming years. There are also indications that patients were less prone to seek professional help for their health problems during the COVID-19 crisis.[39] International research shows reductions in health care for acute, chronic and mental health disorders.[40,41] However, it remains unclear in what way these reflects changes in missed care opportunities or in disease frequencies (e.g., due to beneficial effects of increased exercise during the lockdown). We will investigate three priority disease groups: acute life-threatening cardiovascular diseases,

cancers, and mental disorders, respectively.
For **acute cardiovascular diseases**, Belgian research for the first wave shows hospital admissions for ST elevation myocardial infarction dropped by 26% compared to the pre-pandemic levels.[42] The study further reveals that the time between admission and treatment was higher during the lockdown. Delayed diagnosis and delayed treatment can result in worse prognosis and increased mortality.[43]
Cancer diagnoses in Belgium were heavily impacted during the first wave, with 44% less diagnoses of invasive tumours compared to the pre-pandemic situation. The rate of diagnosis returned to the baseline levels by June 2020 and remained relatively stable until the second wave. The impact of the second wave seems limited with only 2% less cancer diagnosis in the Autumn of 2020.[44] Preliminary evidence for the first wave shows a 33% increase in mortality among the cohort of Belgian cancer patients diagnosed in 2013-2018.[45] This result is similar to the mortality increase in the general population, suggesting a limited impact of delayed treatment for this cohort during the first wave. However, much remains uncertain regarding the further evolution throughout the epidemic, the loss on healthy life years and potential increases in resource use related costs.
Mental health has deteriorated significantly in Belgium since the start of the COVID-19 crisis with more than half of the Belgian population experiencing mild to extreme anxiety or depression during the first and second wave.[46] This may be caused by the traumatic experience of the crisis itself and related mental health risk factors such as financial insecurity, the lack of social support and disruptions of the daily routine.[47] We need more detailed information, especially on the persons may require increased mental health care in the future. One of most vulnerable groups is persons who already suffered with severe mental health issues prior to the outbreak. Severe mental disorders such as bipolar disorder, schizophrenia, and major depressive disorders can be considered as chronic conditions that require continuous surveillance and maintenance treatment to avoid relapse and rehospitalization.[48] To our knowledge, no Belgian studies have been published on severe mental health related the COVID-19 crisis. Italian evidence shows that the number of psychiatric admissions decreased during the lockdown, but that these admissions were more often long-stay admissions.[49] Admissions normalised again in the post-lockdown period but significantly more patients reported suicidal ideation. Furthermore, there are indications that this group also has increased COVID-19 health risks. According to a large Swedish population-based study, COVID-19 mortality risks are three times higher for persons diagnosed with severe mental health problems compared to persons without such a diagnosis, even after adjusting for comorbidities (e.g. diabetes).[50] It is crucial to gain more insights into how mental health patients are impacted by the COVID-19 crisis in terms of disease severity, as well as to understand potential changes in mental and non-mental health care needs.

⇨ HELICON will investigate the indirect impact of the COVID-19 crisis on morbidity and mortality related to acute, chronic and mental health disorders. We consider changes in health care use and associated expenses, as well as losses in the quality and quantity of life lived.

Policy implications

The immediate impact of HELICON will lie in the generation of new scientific knowledge on the long-term and indirect impact of the corona crisis, and the social inequalities therein. This new knowledge will not only be highly relevant for better understanding the Belgian context, it will also have international significance – e.g., new evidence on long-term complications of COVID-19.
HELICON will assess the validity of routine administrative data sources for research on novel health threats such as COVID-19. These findings will have implications for the valorisation and management of administrative health data collections – indeed, a better understanding of the validity of such data sources will allow better interpretation and use of these data, and may identify opportunities for improving the quality of these data sources. These activities will also provide a strong precedent for new collaborations between data producers and researchers to take on future federal societal challenges.
In the medium and long term, HELICON aims to have a significant impact on policy and public services, with expected gains in terms of health and economic development. As one of the key guiding principles, HELICON will have an explicit focus on knowledge translation and policy transfer, translating the research findings into actionable policy messages. Insights in social inequalities in health will be able to support social policy and resilience measures, insights in the long-term complications of COVID-19 will support clinical practice, and insights in the indirect consequences of the corona crisis will put evidence in the scale to define balanced mitigation measures. While we acknowledge (and hope) that at the end of the project, the corona crisis will be behind us, these findings can of course serve a broader purpose and can be used to help prepare for the next pandemic.

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