Biostatistics and the COVID-19 Pandemic in Belgium, in 2020 and 2021



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TITRE

La biostatistique et la pandémie de COVID-19 en Belgique, en 2020 et 2021

ABSTRACT

From a statistician's standpoint, the first two years of the COVID-19 epidemic in Belgium are described. First, a narrative of the epidemic evolution is given, with attention for the regional differences within the country. Second, the policy advisory board structure is reviewed. The role of biostatistics is described next, both in terms of scientific research as well as regarding our profession's role in policy making and communication to media and general public. Two sectors are given specific attention: travel and education. Some general conclusions and recommendations are formulated.

Keywords: data sharing, SARS-CoV-2, infection fatality rate, mathematical epidemiology, mathematical modeling, mortality, non-pharmaceutical intervention.

RÉSUMÉ

Les deux premières années de l'épidémie de COVID-19 en Belgique sont décrites du point de vue d'un statisticien. Tout d'abord, un récit de l'évolution de l'épidémie est donné, en tenant compte des différences régionales au sein du pays. Deuxièmement, la structure des conseils consultatifs est examinée. Le rôle de la biostatistique est décrit ensuite, tant en termes de recherche scientifique que du rôle de notre profession dans l'élaboration des politiques et la communication aux médias ainsi qu'au grand public. Deux secteurs font l'objet d'une discussion particulière : les voyages et le tourisme d'une part et l'éducation d'autre part. Quelques conclusions et recommandations générales sont formulées.

Mots-clés : intervention non-pharmaceutique, modélisation mathématique, mortalité, épidémiologie mathématique, partage de données, SARS-CoV-2, taux de létalité de l'infection.

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1. Introduction

To encounter a health crisis of a scale comparable to the SARS-CoV-2 induced COVID-19 pandemic, one has to return to the 1918 H1N1 pandemic – the Spanish flu. For other crises of this magnitude, only world wars and perhaps financial meltdowns come to mind.

The extent of the pandemic is truly global in the sense that not a single country remains unaffected, albeit it to differing degrees.

When the virus spread from Wuhan China, notably in the early months of 2020, countries like Iran, the United States of America, and many European countries were among the earliest ones hit. The first blow on the European continent was dealt to the North of Italy, followed by Spain, France, Belgium, the Netherlands, the United Kingdom, and a range of other countries. Of note is that the more eastern European countries were relatively mildly hit in the early days.

Confronted with a respiratory infection caused by an hitherto novel virus, it is imperative to gauge its epidemiology as soon as possible, and devise a response strategy accordingly. In the early phase, and throughout most of 2020, we could not (yet) count on either of two important lines of defense, i.e., antiviral medication and vaccines. This only left so-called non-pharmaceutical interventions (NPI). Under such circumstances, there are essentially three response strategies.

The first is suppression of the epidemic, which is taken to mean that an extensive set of NPIs is implemented each time there is viral circulation, so as to keep incidence at or near zero. This strategy has been followed, for example, by China (apart from Hubei province in the early phase), Australia, and New Zealand. The advantage is that a society can function relatively normally for larger periods of time, and that measures taken are typically shorter in duration. The disadvantage is that such societies need to be sealed off from others that follow a different strategy. At the other end of the spectrum is so-called herd immunity, where the virus is allowed to circulate in a (nearly) unlimited fashion until the reservoir of susceptibles is so much depleted as to naturally end circulation. Several countries have considered this strategy, such as the United Kingdom, the Netherlands, and Sweden. However, it soon transpired that the hospitalization and mortality rates were such that this strategy is difficult to maintain from an ethical standpoint. In particular, in virtually no society can this strategy be implemented without overwhelming the health care system, thus potentially amplifying the death toll (Hens, Vranckx, and Molenberghs, 2020). The third strategy strikes a middle ground between the other two and is referred to as mitigation: the viral circulation is kept at a level low enough such as to ensure that the health care system is able to cope with the burden of disease induced by the virus.

The strategy of mitigation has been followed by most European countries, especially within the European Union. Given the interconnectedness of the European populations, and the legal framework imposed by the EU, it is very difficult to have radically divergent strategies. However, the time period under investigation here has shown that it is very difficult to regulate the burden of disease; rather, most European countries have had a sequence of waves of varying degrees of severity.

My personal role can be described as follows. From a scientific perspective, I have been involved in research, among others, on COVID-19 mortality (Molenberghs *et al.*, 2022), education (Bekkering *et al.*, 2020), the role of higher education (Natalia *et al.*, 2022), spatial aspects of the pandemic (Neyens *et al.*, 2020; Vranckx *et al.*, 2021), COVID-19 in the labor force sectors (Verbeeck *et al.*, 2021), and vaccine willingness (Delporte *et al.*, 2021). I was a member of CELEVAL and, at the time of writing, of both RAG and GEMS. Apart from frequent interaction with policy makers, I have taken up a role in communicating with both written and spoken mainstream media.

In Section 2, we will briefly describe the course of the epidemic in Belgium, and place it in a European perspective, with particular attention for the neighboring countries (France, the Netherlands, Germany, Luxembourg, but also the United Kingdom, given its proximity). Some attention is devoted to the typical regional differences within Belgium. The advisory board structure is reviewed in Sec-

tion 3. Section 4 focuses on the role played by biostatisticians from a research perspective. Their role in policy making, communication, and public debate is discussed in Section 5. Scientific government advisors often also provide advice to specific sectors. In Section 6, two examples are given. In Section 6.1, we address the specific challenge posed by transborder travel, as well as intra-European and international travel. One of the sectors of great importance is education, both compulsory and higher education. In Section 6.2 we turn to this sector and briefly discuss what measures were taken to essentially keep compulsory education open during the school year 2020–2021.

2. The Epidemic in Belgium, in 2020 and 2021

2.1. The Epidemic's Evolution

The first wave hit Belgium relatively soon after the virus arrived in Europe, facilitated by, among others, travel related to winter holidays and carnival festivities. The Belgian regions most severely hit were, broadly, situated in an east-west band in the middle of the country. The first confirmed corona death was registered on March 10, 2020. There was a rapid rise in cases, even though in the early days it was difficult to quantify because of very limited testing capacity. Hospitalization, ICU beds taken, and mortality were more reliable indicators. The ICU peak was reached on April 8, 2020, with 1286 beds taken, implying that normal capacity had to be scaled up and non-COVID care postponed.

Relatively stringent measures, of a lockdown type, were in place during this period, although less so than in, for example, Italy, Spain, or France. Because measures taken can take a variety of forms, the so-called *stringency index* was developed, for the purpose of the current pandemic, by the University of Oxford based Blavatnik School of Government (Hale *et al.*, 2020). Stringency is 0 when there are no measures taken, with 100 being the highest value. Table 1 shows the stringency indices for Belgium and selected countries, on the first day of April 2020, July 2020, and February 2021, respectively.

Country	01/04/2020	01/07/2020	01/02/2021
Belgium	81.5	50.0	63.0
France	88.0	51.9	63.9
Italy	91.7	58.3	78.7
Spain	85.2	41.2	71.3

Table 1: Stringency indices for Belgium, France, Italy, and Spain, on the first day of April 2020, July2020, and February 2021.

It is clear that, apart from early summer 2020, Belgium had the mildest stringency among the four countries listed, whereas Italy maintained the most stringent measures throughout.

The epidemic situation improved in late April and May, and sectors started to gradually reopen. Like in many European countries, measures were drastically relaxed by the start of summer 2020, and international travel, in particular for tourist purposes, resumed. The number of cases in Belgium started to rise again from mid-July 2020 onwards, this time predominantly in the north of the country (Province of Antwerp) and Brussels. Of note is that particularly densely populated inner city areas were affected. The stringency of the NPIs was increased again in late July 2020, a curfew in the city of Antwerp. Because of these, and arguably supported by the seasonal effect, the rapid rise in the Province of Antwerp was countered. By the end of August 2020, roughly 400 cases per day were confirmed – as opposed to roughly 100 by the beginning of Summer.



Figure 1: Increment function of the confirmed cases in Belgium, over the period September 1, 2020 – March 25, 2022. The increment is defined as the percentage change of the 7-day incidence at a given date relative to the immediately preceding period of seven days. Data source: Sciensano daily epidemiological bulletin (https://covid-19.sciensano.be/fr/covid-19-situation-epidemiologique).

The evolution of the epidemic in Belgium is represented by the increment function over the period September 1, 2020 – February 28, 2022. The increment is defined as the percentage increase or decrease of confirmed cases, accumulated over a seven-day time period, as opposed to the immediately preceding seven days. Precisely, let W_1 be the total number of confirmed cases over a given 7-day period and W_0 the total number of the immediately preceding week, then the increment function for the last day of W_1 is defined as $(W_1 - W_0)/W_0$. Working with 7-day periods mitigates dayof-the-week effects. The function supplements the information in the curve representing the cases itself, like a derivative function does; of course, the latter is very variable because of daily fluctuations. During the first half of September 2020, there was a rapid rise in cases, to a large extent provoked by seeding via returning travelers, as is corroborated by both phylogenetic (Hodcroft et al., 2020) as well as epidemiological (Natalia et al., 2022) evidence. During the second half of September 2020, the increase in cases slowed but did not revert to a decrease, only to pick up again in October 2020, this time catalyzed by, among others, higher education. A typical Belgian phenomenon is that students sojourn near the educational institution during weekdays, to then return to their home town over the weekend. Such "conveyer belts" of contacts led to a quick spread across the country, but this time with focus on Wallonia. The second wave that ensued reached its peak early November 2020, with maximal ICU occupancy of 1474 on November 9, 2020. Around the peak, roughly 20,000 cases per day were confirmed. The 14-day incidence per 100,000 inhabitants in Belgium peaked near 1800, whereas the incidence for the three regions at peak was about 1000 for Flanders, 2000 for Brussels, and 3000 for Wallonia.

Early December 2020, the number of confirmed cases per day had fallen to roughly 2000 per day. NPIs were made less stringent, and a relatively long "plateau phase" began. A resurgence around Christmas and New Year was avoided as no relaxations were implemented for this period, in part also with the emergence of the alpha variant in mind, and supported by mathematical modeling, which showed that relaxing measures before Christmas 2020 could have led to a considerable peak. Of note, such peaks appeared in Ireland and Portugal at that time. The gradual increase of the alpha variant necessitated frequent revision of measures over the winter and early Spring 2021 period, but eventually a new wave ensued, on top of the plateau phase. On April 13, 2021, the number of beds occupied in ICU equaled 947. The alpha variant provoked a higher burden of disease, even against the background of a well progressing vaccination campaign.

Over the months of May and June 2021, the numbers declined rapidly, and early July 2021, the number of confirmed cases per day was around 300–400, with about 20 hospital admissions per day, ICU occupancy below 100, and about 5 deaths per day.

From July 2021 onwards, the epidemic curves started rising again (as is also clear from Figure 1), a process that continued at a relatively gentle pace, until a fourth (delta) wave occurred in October-November 2021. At the end of 2021, the delta wave gave way to its omicron successor.

2.2. Some Key Regional Differences in Belgium

Belgium's three regions have considerable differences. The Northern Flanders is Dutch speaking, the Walloon south is French speaking, with the Brussels Capital Region bilingual, though with a vast majority of French speakers. Brussels being a city region with both a national and an international mission, it differs in various aspects from the other two regions. For example, Brussels welcomes more foreign travelers per capita than the other two regions, as is clear from Figure 2. It is also a very diverse region, with varying access to official government communication and mainstream media.



Figure 2: Travel rates (number of incoming travelers per 100 inhabitants) for each of the three Belgian Regions: Brussels. Flanders. Wallonia, starting and January 2021. Based on the Sciensano weekly bulletins from 1 epidemiological (https://covid-19.sciensano.be/fr/covid-19-situation-epidemiologique).

For various reasons, therefore, it is not surprising that the 14-day incidence curves for the three regions are not always synchronized, as is clear from Figure 3. During the Fall wave of 2020, the incidence in Wallonia rose to about 3000, whereas it topped off at about 2000 and 1000 for Brussels and Flanders, respectively. However, in the Fall wave of 2021, it was Flanders who reached the highest incidence, during the delta wave.

The latter fact is a bit surprising at first sight, given the high vaccination rate in Flanders. Indeed, on 31 December 2021, 60% of the entire Brussels population was fully vaccinated, whereas the number for Flanders is 81% and 72% for Wallonia. However, as vaccines provide good but not perfect protection, the high incidence in Flanders should be seen against the background of more extensive (high risk) contact behavior in the region in the Fall of 2021, as compared to the other two.

Also the booster campaign is evolving at a different in the three regions, with on 25 February 2022,

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booster vaccination rates among the 18+ population of 46% in Brussels, 83% in Flanders, and 65% in Wallonia.

Because of the multilingual structure of Belgium, the regions consume different media, and have their own public opinion foci. This implies that the balance between the sanitary, economic, and well-being aspects may not always be drawn in the same way. For example, when NPIs were reinstated in Summer 2020, this was perceived in the South as primarily for the purpose of counteracting the reemergence of the virus in the North (in particular in the Antwerp area). This might explain why there was a stronger reaction against the continuing measures from Southern actors in September-October 2020. In the Fall of 2021, in Flanders the impression existed that the epidemic was under control because of the high vaccination rate, whereas a more cautious attitude was adopted in Brussels and Wallonia. Thus, while at macro level all regions have been moving through the same set of waves, the relative ordering of the regions changed over time.



Region-specific 14-day incidence curves

Figure 3: 14-day incidence curves from March 2020 until week 2022/10, for each of the three Belgian Regions: Brussels, Flanders, and Wallonia. Data source: ECDC (https://www.ecdc.europa.eu/en/publications-data/weekly-subnational-14-day-notification -rate-covid-19)

3. A Complex Advisory and Policy Making Structure

Belgium has a complex federal system. For example, the health care and public health competencies are split over the federal, regional (Flemish, Brussels, and Walloon Regions), and community levels (Flemish, Wallo-Brux, and German Communities). For simplicity, we will simply refer to the federal and regional levels. For example, hospitals are largely but not entirely federal matter, whereas nursing homes, playing such a key role in the pandemic, are a regional competency.

Thus, data that need to be consolidated, originate from various levels within the Belgian federal system. Hospital mortality is collected by the federal authorities, whereas nursing home mortality is collected by the three Regions. Data-related issues may arise for nursing home residents that are transferred to hospital and then die. It is crucial of course that every death is counted, and counted

only once. The national public health institute Sciensano had to set up data sharing protocols with both Regions and the federal authorities for this matter. In addition, this has to be done in real time, whereas in non-pandemic times, cause of mortality data become available with a couple of years of delay.

Likewise, the political, scientific, and administrative advisory structure has been complex. A number of factors are worth attention.

First, the onset of the crisis was set against the background of an acting rather than fully empowered federal government.

Second, because there is no natural hierarchy among the country's governments, dedicated coordination structures had to be invoked or put in place. Until October 2020, the principal ministers of the various governments met the National Security Country; thereafter, when the government-Wilmès was succeeded by the government-De Croo, this role was assumed by the so-called Coordination Committee.

Third, a large number of structures and boards, scientific and other, have been active in the management of the crisis. We discuss these in turn.

- **Sciensano.** The national public health institute, responsible, among others, for surveillance, data collection, and reporting on the pandemic.
- **National Crisis Center.** This permanent structure is responsible for both crisis communication as well as regular examination as to whether the country is prepared to face the challenges imposed by the pandemic (e.g., readiness of the health care system).
- **Risk Assessment Group (RAG).** Sciensano hosts the RAG, consisting of scientific members of the administration, supplemented with scientists located in universities and other research institutes. The RAG's task is to carefully describe the state of the epidemic and its evolution, and to offer scientific advice to the authorities. The RAG is a permanent structure that can be invoked to handle various public health crises, not only the current pandemic.
- **Risk Management Group (RMG).** The RAG's input is received by the RMG, at which level the scientific advice is used to generate policy advice. The RMG consists of members of the administration and governmental cabinets.
- **Group of Experts on the Exit Strategy (GEES).** In the Spring and early Summer of 2020, the *ad hoc* GEES was charged with offering policy advice on successive relaxations of measures, directly to the Prime Minister and the key ministers involved. The board consisted of the disciplines: biostatistics, epidemiology, virology, infectiology, economy, social inequality, and European affairs.
- **Evaluation Cell (CELEVAL).** This is a permanent but usually dormant cell, at the level of the Ministry of Public Health, but with representatives from various other ministries (such as Interior Affairs, Foreign Affairs, etc.). It was conceived at the time of the Tjernobyl nuclear crisis, and invoked again during the Summer of 2020. Like the RAG, it is populated according to the crisis at hand. Whereas RAG evaluates the epidemiological situation, CELEVAL formulated policy advice, e.g., proposed the establishment or lifting of NPIs.

In the Fall of 2020, GEES and CELEVAL have been discontinued and succeeded by new structures.

Corona Commissariat. A government Corona Commissioner has been appointed in the Fall of 2020, to coordinate all activities of all advisory boards.

- Group on the Exit Management Strategy (GEMS). The GEMS can be seen as the successor of both GEES and CELEVAL; it reports to the Corona Commissariat. In spite of its name, GEMS has had to propose both increases as well as decreases in NPI stringency.
- **Task Forces.** Finally, there are several Task Forces, charged with advice regarding specific aspects of pandemic response, such as on Testing and Tracing, on Ventilation, and on Vaccination. They advice on the policy related to their charge, and work with federal and regional authorities towards smooth implementation of decisions taken (e.g., the testing centers, the vaccination campaign).

Like the GEES, the other advisory boards have always been populated in a multi-disciplinary fashion, with members having a biomedical, exact sciences, or humanities background. These include virologists, infectiologists, vaccinologists, economists, health economists, labor force specialists, psychologists, sociologists, and pediatricians. Psychologists and sociologists have been instrumental in surveying the public regarding such key topics as mental wellbeing, motivation to follow the NPIs, vaccination willingness, etc. People working with disfavored groups have provided valuable advice to increase vaccination rates in target groups. Not surprisingly, the remit of the pediatricians is children's wellbeing, and providing advice around measures in schools and for extra-curricular activities. Because of the GEMS' larger size, it was easier to have a wider scientific representation than with, for example, GEES.

In spite of this relatively multi-disciplinary approach, there has been criticism, throughout the pandemic, that there was a certain dominance of biomedical and exact sciences on the board. This might have been provoked, at least in part, by certain constraints that applied. For example, for the GEES, the government had chosen for a board of not too large a size, 10 members to be precise. Given this small size, it was as multi-disciplinary as possible. Indeed, apart from the disciplines: biostatistics, epidemiology, virology, infectiology, there were members representing economy (Pierre Wunsch, Johnny Thys, and Mathias Dewatripont), social inequality (Céline Nieuwenhuys), and European affairs (Inge Bernaerts). It is fair to say that the balance could have been struck a bit differently, and that perhaps a slightly larger board would have been better. This is why GEMS has been composed of 25 rather than 10 people.

For the purpose of this article, it is important to mention that at several levels, statisticians and epidemiologists have been active; for example, in the capacity of members of GEES, CELEVAL, RAG, and GEMS.

4. Biostatistics Research

Biostatisticians have played various roles throughout the crisis. Biostatistics refers to the use of statistical and mathematical methods in the broad sense, including medicine, public health, biology, agriculture, and forestry. Evidently, in the current pandemic, the focus is on human health on the one hand, and the societal implications of the measures taken on the other.

In this section, we will focus on scientific research. A detailed description of the various research endeavors can be found in Molenberghs *et al.* (2020). A large fraction of the research efforts take place in a multi-disciplinary environment, encompassing one or more of the disciplines already mentioned.

A considerable part of the research efforts are geared towards modeling and monitoring the epidemic. For example, mathematical models are progressively tailored to the ever expanding and oftentimes changing epidemiological knowledge about the virus and the disease that it causes. The teams at Hasselt and Antwerp universities have over two decades of experience in mathematical modeling of infectious diseases, and could hence take part in rapid response from a biostatistical perspective.

Such elements include the existence of a pre-symptomatic period as well as fully asymptomatic infec-

tions, the length of the incubation period, the onset of infectiousness, the length of the serial interval, the phenomenon and extent of superspreading, the emergence of variants with quite different characteristics, and progressing vaccine uptake. This knowledge is, in turn, relevant towards optimally informing mathematical models (e.g., Abrams *et al.*, 2020).

Another strand of research is geared towards so-called nowcasting and early warning. To this effect, knowledge about the delay between symptom onset and hospitalization, hospital length of stay, etc. are needed, so that short-term predictions can be made. Important predictors for hospitalizations include, evidently, confirmed cases, the positivity rate, the workload of the first line of health care (general practitioners), etc. Many of these indicators come with their own issues. For example, the numbers of confirmed cases are influenced by the testing policy. In the first half of 2020, about 62,000 cases were confirmed; the number for the second half of 2020 is about 590,000, and for the first half of 2021 it is about 470,000. However, model-based estimates of the total number of cases are approximately 1 million, 1.5 million, and again 1 million, respectively. Without such an adjustment, the numbers of COVID-19 deaths would be implausible. They are, again roughly, 10,000; 10,000; and 5,000 for each of the three periods, respectively. In the Fall of 2020, the infection fatality rate (fraction of deaths among those infected, whether confirmed or not) had dropped somewhat (10,000 deaths, but among 50% more cases), due to somewhat better protection of the vulnerable population, and modest advance in antiviral treatment.

A perpetual strand of research for biostatisticians is towards the design and analysis of studies geared towards antiviral medication and vaccine development. Of course, the circumstances, including timelines, were very different. Apart from COVID-19 related trials, biostatisticians have to be concerned with the pandemic's effect on ongoing trials in other therapeutic areas.

We also mention the estimation of important epidemiological indicators, such as seroprevalence, contribution towards testing and contact tracing efforts, and design an analysis of public opinion surveys. Such surveys are undertaken, for example, to gauge the state of the population's wellbeing in the face of a relatively long pandemic and the restrictions that come with it.

5. Biostatisticians in the Public Spotlight

Unlike in non-pandemic times, biostatisticians' role in research and policy making was often the subject of political and public debate. Moreover, they have frequently been called upon to explain various quantitative aspects of the Belgian epidemic and the pandemic at large.

While over the first months of the pandemic there was a general public consensus that appropriate measures (NPIs) were needed, and that they had been successful in flattening the curve, against the background of very severe conditions in Wuhan, China, in Bergamo, Italy, as well as in several other places, including in the south of the Belgian Limburg Province, there was a clear shift in the public opinion over the summer of 2020, in Belgium as well in a range of other countries. Arguably, this was due to the very unwelcome flare up that happened in Belgium and elsewhere in Europe, necessitating reinforced measures. Scientists, politicians, and the public realized that the pandemic would not be over with a single wave.

In Belgium, the fact that a large second wave could be avoided invoked the prevention paradox – because the intervention taken avoids an undesirable situation, it appears that this intervention was unnecessary.

5.1. Criticisms of Biostatisticians

Biostatisticians and epidemiologists and their expertise started to be called into question much more than before. Let us briefly consider three examples.

First, the death toll has been the subject of ongoing debate (Molenberghs et al., 2021). For example, on July 31, 2020, Belgium had the highest number of deaths per million (849 DPM) on the planet, except for some ministates. Skeptics argued that the high death toll underscored the inefectiveness of the NPIs. However, also here, counterfactual reasoning is important: What would the death toll have been, had no NPIs been implemented, or had less stringent measures been taken. A second point of criticism was towards Belgium's reporting of COVID-19 mortality. Indeed, both test confirmed as well as clinically confirmed cases were reported, whether they occurred in a hospital or nursing home setting. Given the very restrictive testing policy during the early weeks of the pandemic, not counting clinically confirmed cases would have drastically altered the apparent death toll - given the discrepancy between the 62,000 confirmed cases versus the estimated one million of total cases over the first half of 2020. Likewise, the death toll would have been drastically lower if only hospital mortality were reported. As Aron et al. (2020) showed, the reported Belgian COVID-19 mortality was close to reality, unlike in some countries such as the Netherlands and Spain, where only around 50-60% of COVID-19 deaths were reported. Upon completion of 2020, it turned out that Belgium's excess mortality and reported COVID-19 mortality were in agreement, in the sense that excess mortality, defined as the difference between the 2020 mortality and the average over the preceding five years, was about 85% of COVID-19 mortality.

Second, a debate, also well-known in other countries, that emerges when the number of confirmed cases increases is whether this is a genuine increase or rather a consequence of an expanding testing policy. To exacerbate the problem, initially increasing case numbers sometimes happen against the background of non-increasing or even decreasing hospitalization rates. Of course, this is a classical epidemiological issue. Commonly, the people being tested do not form a random sample from the population. Rather, the reason for being tested is related to the test outcome itself, such as a high risk contact or the emergence of symptoms. Nevertheless, when policies remain constant, the *evolution* of confirmed cases may be an important though impure indicator. This is why it is often considered jointly with other indicators, such as the positivity rate, or it is stratified over age and/or testing reason categories. Of course, ideally regular repeated samples should be taken according to proper survey design, such as in a sentinel network. This is one of the many important lessons that should be drawn from the pandemic, i.e., the need for properly designed, efficient surveillance networks.

Third, in Belgium as much as elsewhere, there have been continual debates over the sense and nonsense of NPIs, such as social distancing, face mask mandates, and curfews. Many opponents of NPIs argue that there is no randomized evidence for or against such measures and that there is no control group. This debate is similar to that in other areas of epidemiology, such as around the relationship between smoking and lung cancer. The problem is that gathering evidence about the impact of NPIs prior to their implementation and in roughly the same circumstances as present themselves in the field is virtually impossible. For example, there is evidence about the use of face masks from various angles: based on historic data in earlier pandemics, from routine use in clinical and industrial contexts, from dedicated laboratory experiments. But the evaluation of an NPI's impact arguably is possible only *after* implementing it. Even then, it is imperative to carefully correct for confounding factors. In addition, most NPIs are not taken in isolation, but rather in varying combinations (Liu *et al.*, 2021; Bo *et al.*, 2021).

5.2. Policy Advice and Communication

At first sight, policy advice towards government and administration on the one hand and general public communication on the other appear to be very different tasks. While they are, there is at the same time a strong connection.

A common factor is that, from a scientific and epidemiological standpoint, a pandemic like the current one is complex and multi-faceted. Many aspects are counterintuitive. We already referred to the difficulties with counterfactual thinking ("What if no NPIs had been implemented?") and the near impossibility to conduct controlled experiments, let alone in a timely fashion. In addition, statisticians will realize that outside their field and that of the exact sciences, exponential growth is poorly understood.

This implies that there is a constant need to warn against the risk of resurgence when NPIs are relaxed up to too low a stringency level. At a political level, it is important to have eye for public health, well-being, and the economy. While these are often seen as opposing forces, in fact a prudent management of the pandemic is the best way to ensure that simultaneously well-being and economy are optimally protected. Careful and frequent public opinion surveys are imperative in this regard (Neyens *et al.*, 2020; De Coninck *et al.*, 2021). Many countries have experienced the risks associated with relaxing NPIs too much or too quickly. Statisticians are well-positioned to gauge the impact of changing measures on human contact behavior and hence the spread of the virus, based on detailed data collection and analysis (Coletti *et al.*, 2020) as well as on insight in the general principles.

All of this implies that at the same time there is a great need for frequent communication on the one hand, while the political and societal context can be challenging, even tense at times. In Belgium, a relatively large number of scientists have taken the stage in conventional and social media to inform the public opinion. This includes scientists who also serve on advisory boards. This aspect alone requires a constant reflection on the equilibrium between academic freedom and loyalty as an advisor in a formal role. This is especially true when the public role provokes a strong response from certain factions within society, sometimes even taking the form of death threats. While it is not unnatural that a crisis of this magnitude and length leads to the search for scapegoats, it is a fate for the researcher uncommon in non-pandemic times.

6. Advice to Specific Sectors

Scientific government advisors, including statisticians, are often called upon to provide *ex officio* advice to certain sectors, such as the labor force, the cultural sector, travel, education, and higher education. We briefly expand on a few of these.

6.1. Travel

In the early phases of the epidemic, national borders quickly closed and (air) travel was reduced but did not stop. For example, Belgians undertook over 22 million trips in 2019, which reduced to 11 million in 2020. Brussels National Airport saw its volume of passengers reduce to roughly 25% over normal figures, over the pandemic months (excluding January and February 2020). For details, see https://www.brusselsairport.be/fr/notre-aeroport/faits-chiffres/de-trafic-mensuels.

Over certain time periods, there were travel bans even within a country, or other limitations of movement, such as a perimeter. A controversial situation arose when also intra-EU borders ended up being closed. When travel resumed in June 2020, Belgium assumed an exceptional position by retaining a ban on travel to red zones, against the background of an ever changing color coded map. This exception was lifted in the Fall of 2020, only to be replaced by a full travel ban on non-essential travel in the early days of January 2021, and until the middle of April 2021. This implied, for example, that only about 20,000 travelers entered Belgium in, say, a week in February 2021, whereas this number approached 400,000 in the last week of July 2021. As stated before, seeding by incoming travelers has played an important role throughout, but especially during the high tourist season. The role of travel restrictions has always been controversial, but as more and more data accumulated, from a phylogenetic as well as epidemiological nature, it became clear that travel bans and/or strict hygienic measures on travelers (testing, tracing, quarantine, isolation) play an important role in controlling the local epidemic. Such measures are particularly relevant when variants of concern emerge that are not yet present in the country. This situation arose in December 2020 and the following months, with the advent of the alpha variant, a little later with the beta and gamma variants, and then in May–July 2021 with the coming of the delta variant.

From an epidemiological standpoint, it is important to minimize as much as possible introduction from incoming travelers. From a statistical point of view, it is crucial to have good data on border crossing, including background data, such as available in the Passenger Locator Form, as well as test result data, vaccination status data, and contact tracing follow up data.

6.2. Education and Higher Education

As soon as the pandemic struck Belgium, schools and higher education institutions reverted to distance learning. Policy advice, based on modeling, kept schools almost fully closed throughout the remainder of the school year 2019–2020, with the exception of a very limited number of face-to-face teaching days in primary and secondary schools. In the higher education system, there were on-site exams in Flanders, but not in the French speaking universities.

The school and academic years 2020–2021 opened against the background of an expanding epidemic. Color codes were developed for all educational systems. The compulsory education system opened at full capacity, but with a face mask mandate in secondary schools. When the epidemic worsened, it was decided to supplement the regular one-week Autumn break with an additional holiday week, after which time the second and third grades of secondary schools reverted to hybrid education (essentially 50% on-site and 50% online). In February 2021, when the delta variant started spreading, extra-scholarly activities were limited, a situation that continued until Easter 2021. Once again, the Easter holiday was extended by an extra week. The face mask mandate was extended to the fifth and sixth year of primary school. Schools returned to full-time on-site presence in June 2021 only. While the school year 2020–2021 was unusual, there no longer were extended and extensive closures, unlike in the preceding school year. See also Bekkering *et al.* (2020).

Also higher education started the academic year in so-called code yellow, meaning that lecture halls and classrooms could receive 50% of the students, effectively implementing a hybrid system. As stated earlier, one of the driving forces of the Fall 2020 wave were student activities, and after only a few weeks, universities reverted to code orange, further reducing on-campus teaching to 20%. After the Autumn break, this became code red, where in-person teaching was no longer allowed. Essential practical sessions that could not be organized online were still allowed. Apart from exam sessions, this situation continued almost throughout the entire academic year, apart from some slight relaxations for on-campus presence and exam sessions.

Statistical and epidemiological advice and modeling has played a role in policy advice to the education sectors throughout the epidemic.

7. Concluding Remarks

Biostatistics, epidemiological, and mathematical modeling research during a global pandemic serves the role, apart from furthering scientific knowledge, of offering advice to the national, regional, and local governments, to specific sectors. Furthermore, it is used as a solid basis for communication to science-oriented as well as general and even popular media, and hence to the general public.

Especially when there are neither vaccines nor anti-viral medicinal products, society has to revert to NPIs, of which the main effect is to keep the epidemic curves under control. The side effects are undesirable but unavoidable impact on well-being and economy.

As a comprehensive understanding of the global pandemic and national epidemics is complicated, especially from a mathematical and statistical point-of-view, quantitative scientists are continually challenged regarding the proportionality or even mere necessity of NPIs. This is especially true at times when numbers are low and/or decreasing, and even when they are mildly increasing. The characteristics of SARS-CoV-2, especially the long incubation period and serial interval, the time lapse between infection and hospitalization, combined with a high basic reproduction number, often make it difficult for scientists, politicians, and society, including key players from affected sectors, to properly assess the timing and stringency of measures to be taken. While models and the associated scenario analysis can help in communicating the potential risks for the immediate, medium, and longer term perspective, they themselves are surrounded with uncertainty. While naturally understood by statisticians, the communication of uncertainty takes specific skill.

Arguably, for these reasons combined, biostatisticians and scientists in related fields need to combine scientific with didactic skills.

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