Non-epistemic factors in epidemiological models. The case of mortality data

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Abstract: The COVID-19 pandemic has made it especially visible that mortality data are a key component of epidemiological models, being a single indicator that provides information about various health aspects, such as disease prevalence and effectiveness of interventions, and thus enabling predictions on many fronts. In this paper we illustrate the interrelation between facts and values in death statistics, by analyzing the rules for death certification issued by the World Health Organization. We show how the notion of the underlying cause of death can change in view of public health goals. This brings us to a general point about how non-epistemic factors, such as values and goals, are reflected in the choice of different measures in epidemiological models. We finally argue that this analysis is not only relevant from a theoretical point of view but also has important practical consequences.

Keywords: cause of death; COVID-19; epidemiological models; non-epistemic factors

1. Introduction

The current pandemic has made it especially visible that mortality data are a key component of epidemiological models, being a single indicator that provides information about various health aspects, such as disease prevalence and effectiveness of interventions, and thus enabling predictions on many fronts. In what follows, we will illustrate the interrelation between facts and values, that is, between epistemic and non-epistemic factors, in determining mortality data and then in realizing epidemiological models. More precisely, in section 2 we will analyze the rules for death

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certification issued by the World Health Organization with a specific focus on COVID-19 and we will show how the notion of the underlying cause of death can change in view of the public health goals of prevention and treatment, that is in view of non-epistemic factors. Then, in section 3, we will explain how mortality data might affect epidemiological models and we will evaluate how the choice of different measures in epidemiological models can also be affected by non-epistemic factors, such as social values and public goals. Finally, in section 4 we will argue that recognizing the presence of both epistemic and non-epistemic factors in epidemiological models does not undermine their objectivity or usefulness, and that our analysis is not only relevant from a theoretical point of view but also has important practical consequences.

2. Facts and values in determining whether COVID-19 is the underlying cause of death

The starting point of our analysis is assessing how a death due to COVID-19 is recorded and certified during the current pandemic. In order to do that, a brief analysis of the rules for the compilation of a death certificate that have been issued by the World Health Organization is necessary. These rules are in fact intended to provide instructions to reliably compile a death certificate, which is the form that contains all the relevant details about the deceased and, in particular, the specification of the so-called underlying cause of death, that is, “(a) the disease or injury that initiated the sequence of morbid events that led directly to death, or (b) the circumstances of the accident or violent act that produced the fatal injury.” This document must be completed by a doctor and a state official within 24 hours of the death, being then available for epidemiological and statistical research.

As we will see in the next section, it is pivotal not only that death certificates are filled in carefully, with the indication of the real cause of death, but also that they are drafted consistently and uniformly across all countries, so that the epidemiological and statistical models developed on their basis can be trustworthy and authentically useful. This becomes particularly relevant

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in the case of a pandemic like that of COVID-19 as the mortality data obtained by looking at death certificates and the epidemiological models built on their basis inform media and institutional communication daily as well as the health policies and measures carried out by different governments.

Apart from small differences from country to country, the current format of a death certificate has been standardized by the WHO, which also establishes the exact codes of all the various diseases, as contained in the International Classification of Diseases, now in its eleventh edition (ICD-11). The WHO’s death certificate has two main parts.

The first and most important part must be filled in with an indication of the exact sequence of diseases or conditions that led to the death, starting with the one that directly caused the death, that is, the so-called precipitating cause, then continuing in the line below with the disease or condition that caused the first one (expressed by the wording ‘due to’), then again in the line below with the disease or condition that caused the second one, and so forth, up to the underlying cause of death. A very simple example could be the following causal sequence: 1) Acute respiratory distress syndrome (precipitating cause), 2) Pneumonia, 3) COVID-19 with positive test (underlying cause of death).

The second part of the death certificate must instead be filled out with the indication of all those conditions that are believed to have increased the risk or the severity of the underlying cause, but that are not part of the causal chain that directly led to death. As an example, if in the first part of the death certificate COVID-19 is indicated as the underlying cause of death, the second part can contain an indication of pre-existing chronic conditions (such as diabetes, coronary artery disease, circulatory diseases or cancers) or conditions that cause a reduction in lung capacity (such as asthma or COPD, that is, chronic obstructive pulmonary disease) capable of aggravating the clinical picture of COVID-19 and thus increasing the risk of death.

Filling in a death certificate is thus a very complex process, which includes diagnosis, certification and coding. Such a process can give rise to different types of errors, both systematic and accidental. Excluding manual and/or automatic coding errors, both the diagnosis and the identification of the underlying cause of death as well as a description of the exact sequence of diseases or conditions that eventually led to death not only depend on the experience of the physician but can also be influenced by various factors, such as the age and sex of the patient or the context of death.

One of the most relevant issues in compiling a death certificate concerns the uniqueness of the underlying cause of death. On the one hand, the WHO document explicitly states that identifying a single underlying cause of death is fundamental for epidemiological and statistical purposes; on the other hand, it is also recognized that it is increasingly frequent that death occurs in the presence of different diseases or conditions, thus posing a problem of selection. For this reason, the WHO also defines a set of rules to distinguish the underlying cause of death (along with the train of all other diseases or conditions that eventually led to death) from those other diseases or conditions that must simply be considered to have increased the risk or the severity of the underlying cause.

At first glance, it may seem that the underlying cause of death, which triggered the whole sequence of morbid events that led directly to death, must be identified simply looking at the pathogenetic mechanisms that emerged from biomedical research and are certified by scientific consensus, such as the mechanism that describes how the SARS-COV-2 virus binds to human cells and then replicates inside them. Indirect evidence that the WHO adopts a mechanistic view of causality can be represented by the so-called unacceptable or illogical causal sequences, which represent cases of pathogenetic mechanisms that do not exist from a medical point of view and thus cannot be included in a death certificate. For example, infectious diseases – such as COVID-19 – cannot be due to any other condition; so, reporting COPD as the cause of COVID-19 would constitute an illogical causal sequence since COPD cannot cause an infectious disease such as COVID-19.

In the WHO document, however, we also read that “the expression ‘due to’ printed between the lines of the first part of the death certificate apply not only to sequences with a pathological or etiological basis, but also to sequences in which an antecedent condition is held responsible for having prepared the way for the most direct cause.” This means that the choice of a specific causal chain is not wholly based on pure biomedical evidence.

The WHO document also recognizes that it is not easy for a doctor to decide when a certain disease or condition should be listed in the causal sequence that leads directly to death and nor among the diseases or con-

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ditions that simply increase the risk or the severity of the underlying cause. The suggestion – actually rather vague – is to include in the second part of the death certificate all those conditions that are relevant to death but that do not seem to be able to coherently fit into the causal sequence reported in the first part\(^6\). However, it is evident that the selection of the causal sequence that leads directly to death, and in particular of the underlying cause of death, is by no means a simple and linear process.

For example, generally speaking, COVID-19 can be considered the underlying cause of death (and thus included in the first part of a death certificate) when it has triggered all the other diseases or conditions, as recorded by the doctor, which directly culminated in the patient’s death (such as pneumonia or acute respiratory distress syndrome). In this case, potential pre-existing chronic conditions (such as diabetes, coronary artery disease, circulatory diseases, cancers, asthma or COPD) capable of aggravating the clinical picture of COVID-19 and increasing the risk of death must be reported in the second part of the death certificate as they do not coherently fit into the causal sequence that actually led to death and is reported in the first part. On the other hand, COVID-19 can also occur simultaneously with other diseases or conditions that actually lead directly to death. In this case, COVID-19, not being part of the causal sequence that leads directly to death, should not be indicated in the first part of the death certificate, but (possibly) in the second part, among the conditions that increased the risk or severity of the underlying cause. This could be the case of an individual with COVID-19 who has a car accident or a myocardial infarction due to a pre-existing coronary artery disease (which is thus considered the underlying cause of death).

While the two alternatives above are rather clear from a theoretical point of view, they are much less so in practice. Given the sequence of causes listed in the first part of the death certificate, why must COVID-19 – and not, say, pneumonia or acute respiratory distress syndrome – be identified as the underlying cause of death, that is, as the real cause of death? Or, more relevantly, how is it possible to choose the underlying cause of death in the event that there are two or more plausible causal sequences that result in death? To put it differently, how to decide that COVID-19 is the underlying cause of death and coronary artery disease is just an aggravating factor or, vice versa, that coronary artery disease is the underlying cause of death and COVID-19 just an aggravating factor?

\(^6\) Ivi, p. 9.
According to the WHO, the selection of the underlying cause of death must be carried out with a view to preventing premature deaths and thus to hindering the precipitating cause from acting, which are the most effective goals for public health\(^7\). In other words, the choice of the underlying cause of death must be made not only on the basis of biomedical evidence, but also with the primary objectives of prevention and treatment in mind: the underlying cause of death must thus be identified with the disease or condition that can be better manipulated in order to realize the most effective goals for public health\(^8\). As we have already argued\(^9\), the WHO adopts a mechanistic view of causality but with an interventionist criterion to select the real cause of death: among the various plausible causal sequences (that is, the various plausible pathogenetic mechanisms) that led to death, the underlying cause of death must be identified with the disease or conditions that can be acted upon, plausibly at the population level, with prevention and treatment in mind. For example, let us assume that COVID-19 (A) and coronary artery disease (B) both led to death, but preventing A is easier than B, then A must be identified as the underlying cause of death, or if both conditions are equally possible to prevent but blocking A is more effective in avoiding premature deaths, then A must be identified as the underlying cause of death. Non-epistemetic factors thus play a key role in the selection of COVID-19 as the real cause of that.

In the case of COVID-19, moreover, the situation is further complicated by the fact that a death caused by COVID-19 could be correctly recorded on a death certificate even in cases where the infection is only suspected or probable. The WHO in fact defines death caused by COVID-19 in the following way: “A death due to COVID-19 is defined for surveillance purposes as a death resulting from a clinically compatible [symptomatic] disease, in a probable or confirmed case of COVID-19 infection, unless a clearly alternative cause of death exists, which cannot be related to COVID-19 (for example, trauma). There should not be a period of complete recovery from COVID-19 between illness and death. A death due to COVID-19 may not be attributed to another disease (e.g., cancer) and should be considered as such regardless of pre-existing con-
ditions that are suspected to have triggered a severe course of COVID-19. Therefore, COVID-19 can be correctly considered the underlying cause of death even in the case of a mere suspicion, that is in the absence of a swab or serological test or other diagnostic imaging procedure that reliably confirms the infection.

To sum up, the WHO intends to consider COVID-19 as the underlying cause of death in all those cases in which it has actually caused, or is supposed to have caused, or contributed to causing the death of the patient. Such a recommendation may seem rather surprising, but it is in line with other indications in the ICD-11, which explain that the acceptability or otherwise of a causal sequence for the coding of mortality depends not only on biomedical assessments, but also on public health considerations. For this reason, a medically acceptable causal relationship could instead be judged unacceptable in the coding instructions as a later element in the causal chain is deemed more important from a public health perspective. Therefore, in our case, overwhelming public health reasons make it possible to indicate COVID-19 as the underlying cause of death even in the case of a mere unconfirmed suspicion, and thus to identify COVID-19 as the underlying cause of death even in the presence of other and independent causal chains that led to death. Such a rule conforms with the idea that the underlying cause of death must be selected with the primary objectives of prevention and treatment in mind.

3. Facts and values in epidemiological models: choosing between different parameters

As we have seen in the previous section, correctly reporting a COVID-19 infection on a death certificate is essential to understand how many individuals have actually died from COVID-19. Choosing between multiple alternatives and independent causal sequences (or between converging pathogenetic mechanisms) that result in death, however, is not always simple and immediate, and involves not only facts but also values taking into account the objectives of prevention and treatment.

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11 Ibidem.
The philosophical question of what counts as a death due to COVID-19 is philosophically interesting for its own sake, as it involves a reflection on conceptions of causality, and on the problem of the selection among potential concurrent causes. However, it is also and prominently relevant to understand, and ultimately to assess, epidemiological models of the current pandemic.

Generally speaking, epidemiological models are mathematical tools built to explain complex medical phenomena, such as the COVID-19 pandemic. Most of them have the structure of so-called SEIR models, that is, they represent individuals in a population as moving through four states – Susceptible to the disease, Exposed, Infected, and Removed (deceased or recovered) – as affected by various factors. They can have the goal of predicting infection rates or death rates for a time and population, and/or to test the effect of mitigation strategies or other policies enforced by governments, as well as the effect of other factors such as schools reopening or seasonal change in infections and deaths. They are currently what national and local institutions mostly base their strategies on. Prominent models from the beginning of the pandemic were the Imperial College Model, the Institute for Health Metrics and Evaluation (IHME) Model, the London School of Hygiene & Tropical Medicine (LSHTM), and the Youyang Gu (YYG) model.

As the number of Infected is always unknown (as not everyone is tested), most of these models ‘fit’ confirmed deaths and calculate back how many infections would have been likely to produce such a result. As we illustrated in the previous section, confirmed deaths due to COVID-19 are formally registered by national health authorities in a standardized way, so they make for ‘good’ data in this context. Models of the pandemic also build on data about the virus (the notorious R, the basic reproductive number, that is the average number of cases generated by a single infected individual), and about the population, such as age, mobility, health status, and family structure.

Data of all these sorts can come in either good or bad quality, and they can be scarce or sufficient, they can be either freshly collected, or rather retrieved from registries and repositories filled out in the past, with no control by the re-

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searchers now working on the model. Whatever the merits of these criticisms, the general point they presuppose is that for their epistemic credentials – in order to qualify as providing explanations and predictions of the phenomenon – models depend on the quality of data they are fed with. This is a point we will not pursue further, as it has been widely discussed in the recent literature\(^\text{15}\).

In the first part of this paper, we discussed a definition, that of death due to COVID-19, and showed that in itself it is value-laden. This means that epidemiological models that use data about the number of deaths due to COVID-19 are assuming data that are not ‘pure’ but constitutively dependent on non-epistemic values, such as the importance of prevention and treatment. However, models also depend crucially on parameters and definitions of parameters. These are not data, but conceptual tools that epidemiologists pick and choose – albeit with a limited degree of freedom – in order to manage data, with a view to the explanation and prediction of a phenomenon. Let us now broaden the view, and consider different parameters related to death, from which epidemiologists can, and do, pick and choose in model-building.

The first is infection fatality ratio (IFR), which estimates this proportion of deaths among all infected individuals. The second death-related parameter is case fatality ratio (CFR), which estimates this proportion of deaths among identified confirmed cases. They are both measures of the severity of the disease. Moreover, both IFR and CFR have the definition of death due to COVID-19 as an ingredient, and thus inherit, so to say, the value component we highlighted in the previous section. However, they are also significantly different.

IFR is the most speculative parameter, so to say, as it heavily depends both on testing, and on prior biological knowledge of the mechanisms of virus transmission. CFR is less speculative, but it is nevertheless exposed to specific biases (systematic errors). On a WHO fact sheet published in August 2020, we read that if deaths are more likely to be reported than recoveries, CFR will be overestimated, and the reverse leads to underestimation\(^\text{16}\). Biases apart, it is known that risk of death from COVID-19 is unevenly distributed among groups stratified by age, socio-economic status and ethnicity\(^\text{17}\). Choosing an undifferentiated CFR parameter is likely...
to mask such differences in the predictions of a model, whereas choosing stratified CFR measures is likely to make them apparent. Such a choice involves social and ethical considerations, as models are intended to guide institutional interventions.

Another death-related parameter is the number of overall excessive deaths in a population – for example, the number of overall excessive deaths in Lombardy, Northern Italy, in March 2020, compared to the same region in November 2020 or March 2019. The choice of a measure of overall excessive deaths, versus deaths due to COVID-19 only, can show how the virus impacts on the overall health of the population, for example by limiting the quality and access of treatments for other pathologies, such as cancers, cardiovascular diseases, and so on. Therefore, the choice of this measure also implicitly assumes that actions aimed at preventing such an impact are worth taking.

Finally, using death parameters implies focusing on the goal of preserving life in general, and treating all deaths equally. Preserving life in general and treating all deaths equally is obviously good from an ethical point of view, but it can be qualified further when it comes to choosing the goals of healthcare strategies. A possible alternative to death parameters is counting Potential Years of Life Lost (PYLL). PYLL is a measure of the time a person would have lived had he or she not died prematurely. Choosing PYLL as a parameter means that not all deaths are treated equally, as greater weight is given to deaths at a younger age and a lower weight to deaths at an older age.

We can easily see how death-related values and life-years lost values come apart when, as in the case of COVID-19, mortality is unevenly distributed on ages, and disproportionally affects the elderly. Differently, the Spanish flu killed people with average age of 28 and its burden in terms of number of life-years lost has been calculated as about 1,000-times higher than COVID-19 as of June 2020.

Governments’ mitigation strategies and interventions can be affected by the choice of death-related or years-lost related parameters in a predictive model. It is plausible that, in some contexts, closing schools may

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have an immediate decreasing effect on death-related values, but also an increasing effect on life-years lost in the long term, as life expectancy is known to decrease with school-years lost\textsuperscript{19}. A model with only one of the two parameters would have the effect of orienting political decisions in favor or against school closing, while a model incorporating both could give a wider picture. Admittedly, effects of interventions on PYYL are more difficult to quantify and predict, as they locate in the distant future. However, not to consider such parameters at all in modeling a phenomenon is in itself a choice, and one that cannot be made on purely factual grounds\textsuperscript{20}.

4. Conclusions

To sum up, the aim of this paper was to unpack the various roles that non-epistemic factors might have in the making of epidemiological models of COVID-19, first by a zoom-in on the definition of death due to COVID-19 (section 2), then with a bird’s-eye view on different parameters that can be incorporated into predictive epidemiological models (section 3). Specifically, the definition of a death due to COVID-19 rests on a choice, the choice of positively evaluating the goal of fostering public health through disease prevention and treatment, over the goal of preserving the epistemic and biomedical soundness of a causal inference about the underlying cause of death. In its turn, this definition figures as a component of death-related parameters, such as IFR and CFR. Death-related parameters, however, collectively represent only one option, as other measures may optionally be considered when modeling, such as life-years lost. Choosing between different parameters in epidemiological modeling does not depend on facts only, but also on goals and value assumptions, that is on non-epistemic factors.

Arguing that non-epistemic factors play a key role not only in determining what counts as a death due to COVID-19 but also in realizing the epidemiological models of the current pandemic, we do not mean to claim that such mortality data and epidemiological models are flawed, un-


reliable, useless or non-purely scientific. That non-epistemic factors play an important and unavoidable role in the scientific enterprise – not only in medicine but also in the so-called 'hard' sciences – is a widely recognized and well-documented issue, defended on historical, sociological, and philosophical grounds\textsuperscript{21}. More importantly, it has convincingly been argued that the presence of non-epistemic factors within the various sciences does not undermine their epistemic reliability and objectivity but can possibly strengthen it\textsuperscript{22}. For instance, Helen Longino\textsuperscript{23} argues that scientific objectivity lies in the fact that scientific statements and models can be inter-subjectively tested and criticized, thus being a social product. Alternatively, Sandra Harding\textsuperscript{24} claims that certain standpoints – those of marginalized and underprivileged social groups – are epistemically privileged or advantaged and thus the presence of their associated values in the scientific enterprise can be beneficial.

The fact that the mortality data of COVID-19 and the epidemiological models attempting to describe the current pandemic depend on both epistemic and non-epistemic factors is not only relevant from a theoretical point of view but also has many important practical consequences. Specifically, it makes it clear that such data and models should be explained and discussed publicly. On the one hand, the interplay of facts and values must be made explicit to the general public and the two components must be carefully separated and evaluated independently. On the other hand, and more importantly, it must be clarified that whereas facts can only be acknowledged, values and goal-related choices may and should be rationally discussed on practical and ethical grounds (this is why knowing where they are located, in the complex machinery of models, can be extremely useful). For example, are prevention and treatment good things to be pursued? Should all deaths be considered equally? What conflicting values are possibly at stake? Such a discussion must be open and public,


\textsuperscript{24} S. Harding, \textit{Whose science?}, cit.
and not concealed in some secret cabinet, as the consequences of a choice of alternative values and goals will have a great impact on everybody’s lives. In this paper we do not aim at assessing potential different choices along with their consequences, but simply at suggesting the importance of making these choices explicit in order to improve the collective understanding of the current pandemic and to clarify the rationale of specific health policies and measures, as well as political decisions.