Mathematical models, Pandemic Complexity and the Over-Estimation of Lives Saved by Covid-19 Vaccinations

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Author contributions

Conceptualisation: HW; formal analysis; HW, RJK; writing - original draft: HW, RJK

Conflicts of Interest

The authors declare that they have no conflicts of interest related to this publication.

Funding: No funding was received for writing this commentary.

Abstract

In a recent modeling study Watson et al. (Lancet Infect Dis 2022;3099:1–10) claim that Covid-19 vaccinations have helped to prevent roughly 14-20 million deaths in 2021. This conclusion is based on an epidemiological susceptible-exposed-infectious-recovered-susceptible (SEIRS) model trained on partially simulated data and extrapolated to a hypothetical scenario in which no vaccinations would have occurred. We point out several caveats of this model and caution against believing in its implications. In particular, the model was calibrated on uncertain data, leading to a potentially false posterior parameter distribution for the reproduction number which was also used in the hypothetical scenario without vaccinations. However, we take an argument from critical realism that absences have causal powers too, so that the absence of vaccinations would yield differ reproduction numbers than its presence. We use this example to point out some general problems of SEIRS models of which many have vastly over-predicted Covid-19 deaths in the past, because they oversimplify the complex interplay between biomedical, social and cultural dimensions of health. In reality, too many mechanisms which are the subject of different scientific disciplines are at play than could be modelled, so that pandemic forecasting should not be used to guide public health policy.

Key words

Covid-19 deaths; Epidemiology; SARS-Cov-2; SEIRS epidemic model; SIR (Susceptible Infected Recovered) model

Introduction

In a modeling study recently published in *The Lancet Infectious Diseases,* Watson et al. (2022a) claim that Covid-19 vaccinations have prevented roughly between 14 and 20 million deaths worldwide during the first year of the vaccination campaign (i.e. until December 2021). This claim is derived from an extended Bayesian SIR-model (susceptible-infected-recovered) they have published previously (Hogan et al., 2021; Walker et al., 2020). This model was calibrated on another model-derived dataset of world-wide excess death counts (the 'Economist model', see appendix of (Watson et al., 2022a)) up until 7th December 2021. Alternatively, officially reported Covid-19 deaths were used for model calibration. After model fitting, the protective effect of the vaccines was removed from the model, while the biweekly varying reproduction numbers were kept, simulating a counterfactual scenario in which no vaccinations would have been applied. The number of deaths prevented by vaccination was then estimated by subtracting the number of deaths of the originally fitted model from the estimated deaths of the counterfactual model without vaccinations, resulting in posterior estimates of 19.8 and 14.4 million averted deaths when using the excess mortality or Covid-19 death data, respectively. Thus, the authors conclude that "more lives could have been saved if vaccines had been distributed more rapidly to many parts of the world and if vaccine uptake could have been strengthened worldwide" and that "[v]accine distribution and delivery infrastructure also needs to be scaled up worldwide and misinformation combatted to improve vaccine demand" (Watson et al., 2022a). Here, we will argue that the model by Watson et al. has failed to incorporate the multiple mechanisms at play during the Covid-19 crisis, leading to blown-up estimates of vaccine efficacy that are reminiscent of the lockdown efficacy overestimations in previous modeling studies by the same group (Ferguson et al., 2020; Flaxman et al., 2020).

Details of the Watson et al. model

First of all, early on in the pandemic critical voices were raised that the success of SIR models is highly dependent on the parameters chosen (Daunizeau, Moran, Mattout, & Friston, 2020). Yet, Watson and colleagues did calibrate their model on partially simulated data coming from another – the

Economist – model whose accuracy is far from clear (David Adam, 2022), thus forecasting the expected deaths without vaccination from uncertain model data. It is important to notice that the Economist model data do not refer to actual Covid-19 deaths, but reflect excess mortality which is assumed to be a better proxy for Covid-19 mortality than the official numbers (David Adam, 2022). However, this claim is problematic because excess deaths may have been due to multiple reasons not directly related to Covid-19 as a disease, including the economic consequences of non-pharmaceutical interventions (NPIs) and vaccination side effects which appear to be non-negligible (Fraiman et al., 2022; Mörl, Günther, & Rockenfeller, 2022; Walach, Klement, & Aukema, 2022). Although Watson et al. performed a second analysis calibrating their model with officially reported Covid-19 death numbers, the latter are also highly uncertain and in some cases over- instead of under-reported (Ioannidis, 2021). In our opinion, the large uncertainties in the data the model was calibrated with could easily lead to wrong distributions for the many model parameters that were fine-tuned to fit the calibration data.

Another crucial model parameter is the time-dependent reproduction number R(t). The reproduction number R(t) was updated every two weeks so that R(t)/R(t-1) followed a F distribution with degrees-of-freedom parameters 40 and 40, which according to Watson et al. 'maintains near symmetry in increases/decreases [of R(t)]' (see their Supplementary Table 1). This distribution has a mean of 1.05 and mode at 0.90, but appears unsuited to model the behavior of R(t), because in reality, for a finite population, R(t) must necessarily be a monotonically decreasing function since the number of infections would otherwise diverge (Kuhbandner & Homburg, 2020). In another previous modelling study from the same group that aimed to estimate the impact of NPIs on Covid-19 deaths, similarly unrealistic assumptions about R(t) had been used, because R(t) was only allowed to decrease by the implementation of NPIs or else would remain constant (Flaxman et al., 2020).[1] The Flaxman et al. study led BCC News to announce on June 8th 2020 that "Lockdowns in Europe saved millions of lives" (Gallagher, 2020), a doubtful statement given that the efficacy of NPIs was subsequently shown to be

[1] Further flaws of the Flaxman et al. (2020) study have been pointed out by Klement (2020a)

small or even negligible in many analyses of real-world data (Annaka, 2021; De Larochelambert, Marc, Antero, Le Bourg, & Toussaint, 2020; Herby, Jonung, & Hanke, 2022; Klement & Walach, 2022). Finally, Watson et al. derived the posterior distribution of R(t) by fitting the model to the actual situation in which large parts of the population had been vaccinated and then retained that distribution while removing the protective effects of vaccinations to model the counterfactual scenario. However, it is highly questionable whether the reproduction number distribution without vaccinations (the counterfactual scenario) would really have been the same as the one obtained by fitting the model to data that – even if partially simulated themselves – implicitly include the fact that vaccinations have been rolled out globally. The reason is that absences (all that is not present) have causal powers on their own, an insight that is particularly emphasized by critical realism (Alderson, 2021; Mingers, 2014). Clearly, the mechanisms leading to a decline of R(t) triggered by the absence of vaccinations, such as the achievement of natural herd immunity, have not been taken into account.

Previous failures of Covid-19 forecasting models

In general, models such as the one by Watson et al. appear empirically inadequate (Ioannidis, Cripps, & Tanner, 2022). For instance, the basic model (Walker et al., 2020) predicted that in high income countries with a good health system and rapid installation of non-pharmaceutical interventions (NPIs) like Germany approximately 5,000 deaths per million would be seen until approximately April 2021 (Figure 4E in Ref. (Walker et al., 2020)). This translates to roughly 419,000 deaths due to Covid-19 in Germany (using the population size of 83,783,945 from (Walker et al., 2020)). The actual number of Covid-19-related deaths at the end of April 2021, however, was 82,850 according to Our World in Data (OWID; https://ourworldindata.org/covid-vaccinations; accessed August 5th); the discrepancy cannot be explained by vaccinations since at this time only 7.8% of Germans were fully vaccinated. For a low-income country like Uganda, where the population has limited access to a poor healthcare system, the model predicted that nearly 100% of the population would get infected (Fig. 1E in (Walker et al., 2020)) and that approximately 7,000 deaths per million would have occurred

(Fig. 4E in (Walker et al., 2020)), totaling 320,000 deaths due to Covid-19 (assuming a population size of 45,741,000). However, OWID reports 342 Covid-19-related deaths at the 30th April and a negligible proportion of vaccinated people. Even allowing for a lack of thorough reporting in Africa it is difficult to square the empirical data with the model predictions and attribute the difference to the vaccination campaign.

Another influential model predicting a high effectiveness of NPIs was published by Dehning et al. (2020) in the prestigious journal *Science*, but later also found to be grounded on a shaky database and plainly wrong (Kuhbandner, Homburg, Walach, & Hockertz, 2022). There are many more examples for the failure of epidemic or pandemic forecasting models some of which have been reviewed by Ioannidis and colleagues who stated:

> *Failure in epidemic forecasting is an old problem. In fact, it is surprising that epidemic forecasting has retained much credibility among decision-makers, given its dubious track record* (Ioannidis et al., 2022).

Reasons for forecasting failures

Empirical inadequacy of models such as the one used by Watson et al. (2022a) stems from the tremendous complexity of the Covid-19 situation which includes multiple feedback loops on the political, societal, individual and environmental level (Klement, 2020b). The difficulty with forecasting is grounded in a level of reality which the philosopher Roy Bhaskar has termed the domain of the 'Real' and in which multiple discipline-spanning mechanisms interact:

> *… outside a few experimentally (and even fewer naturally occurring) closed contexts a multiplicity of causes, mechanisms and potentially theories is always involved in the explanation of any event or concrete phenomenon* (Bhaskar & Hartwig, 2016).

Because only some of the actual events produced by the interaction of the multiple mechanisms which constitute the Real are subject to experience within any given discipline, an interdisciplinary approach is necessary in order to gain knowledge about this domain. This is especially the case for science dealing with public health and well-being were biological, social and cultural dimensions interact (Correia & Willis, 2022; Price, 2021). The necessity of interdisciplinarity in epidemic modeling has also been emphasized by Ioannidis et al. (Ioannidis et al., 2022) who proposed to "ensure that the modelers' teams are diversified and solidly grounded in terms of subject matter experience" (Ioannidis et al., 2022). Examples for the complexity behind Covid-19 hospitalizations and deaths are the interplay between SARS-CoV-2 infections and smoking (Kashyap et al., 2020), obesity (Kwok et al., 2020), non-communicable diseases (Ahmad Malik et al., 2022), environmental factors (Shakil, Munim, Tasnia, & Sarowar, 2020) and vitamin D status (Klement & Walach, 2022), to name just a few. Other often overseen or consciously ignored factors at play consider political, economic and cultural influences (Alderson, 2021). These factors are usually not incorporated into epidemic forecasting models and where not taken into account by Watson et al. (2022b) either. Table 1 lists further recommendations made by Ioannidis et al. (Ioannidis et al., 2022) to improve epidemic forecasting which were not incorporated into the Watson et al. model. Finally, we point out that Watson et al. did not examine adverse effects resulting from the socio-economic consequences of NPIs (Brenner & Bhugra, 2020; Kundu et al., 2022) and vaccine toxicity (Kostoff et al., 2021; Seneff & Nigh, 2021; Walach, Klement, & Aukema, 2021; Yamamoto, 2022); these effects may induce secondary deaths that should be co-estimated together with the putatively prevented Covid-19 deaths by NPIs or vaccination campaigns predicted by epidemic forecasting models in order to obtain the "big picture, covering multiple dimensions" (Ioannidis et al., 2022).

Implications

It is understandable that in a desperate situation scientists want to produce early results. But it is inappropriate and irresponsible to use simulated data to train a model and make counterfactual predictions, or to incorporate unrealistic assumptions about the reproduction number R(t) and other crucial parameters. In the best case, the Watson et al. model is considered a starting point for integration of empirical aspects of disease transmission, age-dependent susceptibility to hospitalization and death and the impact of vaccination campaigns, with the potential for further incorporation of multiple mechanisms. Given the authors' conclusions cited in the Introduction, however, we fear that this model can be potentially harmful, if used to inform policies as has been done with previous models of this group such as the famous report 9 (Ferguson et al., 2020) whose exaggerated death predictions justified the implementation of strict lockdowns in many countries. The clear alignment between the call for a rapid roll-out of Covid-19 vaccinations supported by this model and the interests of the funders of the Watson et al. study such as Gavi, the Vaccine Alliance or the Bill & Melinda Gates Foundation should be one more reason to be extremely careful in believing the claim that Covid-19 vaccinations have saved 18 million lives; this is besides the fact that this claim is based on a shaky database and unsupported by factual evidence as we have shown in this article. After all, conflicts of interest and entanglements between scientists and the pharmaceutical industry belong to this level of reality that we referred to above as the domain of the Real. It includes unseen causal mechanisms including those considered as 'political' which are usually excluded from mathematical models. However, as real mechanisms they have an impact in the World which should be considered when interpreting the predictions of models based on empirical data – else, the forecasts of these models can quickly become misleading.

Conclusions

The Watson et al. study provides another case supporting the conclusion that extreme care must be taken when interpreting the predictions of SIR-type models applied to the Covid-19 crisis, because they do not (and cannot) adequately account for the complexity of the biological, social and cultural dimensions of health (Correia & Willis, 2022).

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Table 1: Recommended necessary amendments for improving epidemic model predictions

Recommendation	**Comment regarding the non-incorporation in the Watson et al. model**
Invest more on collecting, cleaning, and curating real, unbiased data, and not just theoretical speculations	Violated, because the world-wide excess death counts used to calibrate the model were itself based on a model (the 'Economist model')
Continuously monitor the performance of any model against real data and either re-adjust or discard models based on accruing evidence	Possible in a future model update
Incorporate the best epidemiological estimates on age structure and comorbidities in the modeling	Age-specific infection fatality rates taken into account, but not country-specific information about comorbidities
Focus on quality-adjusted life-years rather than deaths	Not done, model only considers deaths
Avoid unrealistic assumptions about the benefits of interventions; do not hide model failure behind implausible intervention effects	No cost-to-benefit ratio of Covid-19 vaccines due to their side effects was incorporated into the model. Vaccine efficiency prior distributions derived from the manufacturer's clinical trials which mimic closed systems, while human societies are open systems with multiple upstream and downstream interacting mechanisms, questioning the external validity of these parameters distributions.
Promote interdisciplinarity and ensure that the modelers' teams are diversified and solidly grounded in terms of subject matter expertise	Failure to promote interdisciplinarity by neglecting toxicology (vaccine side effects), psychoneuroimmunology (impact of comorbidities, vitamin D, stress from NPIs), environmental medicine (air pollution, temperature, humidity), sociology (secondary socio-economic deaths)
Maintain an open-minded approach and acknowledge that most forecasting is exploratory, subjective, and non-pre-registered research	Authors' interpretation reported in their abstract sounds very certain that "COVID-19 vaccination has substantially altered the course of the pandemic, saving tens of millions of lives globally."

The recommendations are taken from Ioannidis et al. (2022). NPIs: Non-pharmaceutical interventions.