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Modelling pandemics – why so difficult?

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Mathematical models of pandemic trajectories have epistemological challenges and unresolved usefulness.

What repeats itself – for example outbreaks of seasonal flu – can be predicted. Such phenomena can therefore be characterized as *knowns*. What does not repeat itself, and thus cannot be derived from what is known, is an *unknown*. Before the unknown appears, we have no criteria for how it will manifest itself, nor a language to communicate it within. Predicting the unknown is therefore not feasible (1).

The respiratory disease that spread in Wuhan in December 2019 lies within the category of the unknown. But COVID-19 is also a repetition – it is the as yet last in a series of pandemics, and the second viral pandemic since the turn of the millennium. Pandemics can therefore be referred to as *unknown known* phenomena. We do not know when they will appear or in what form, but we know that when they come, they will spread according to established patterns (2). These two aspects can be recognised in emergency plans where the known manifests itself through the principle of infection control and the unknown through the requirement for flexibility in the face of new infectious agents.

Modelling of pandemics

By definition, a pandemic caused by an unknown infectious agent has an undetermined course and outcome. When an outbreak occurs, the health services are nevertheless expected to be able to answer two questions: What will happen, and what should be done? Since the answer to the question of what will happen depends on what is done, it is expedient to have a prediction tool that answers both questions simultaneously.

The most frequently used models for long-term prediction are based on a mechanistic framework that follows the infection from its time of entry into a population of susceptible individuals until it no longer spreads. The population is divided into four groups – susceptible; infected but not ill; ill; and finally immune or dead. Researchers then attempt to estimate the size of each group and for how long individuals remain there before moving to the next group (3). The models are based on adjustable parameters, the most important of which are the reproductive capability of the infectious agent and the time required for transition between the groups. By entering restrictions following from hygiene measures and social distancing, the researchers attempt to arrive at an estimate of how the pandemic will develop and the expected impact of the various measures enacted.

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Mathematical models have a logical structure that lends the predictions a sheen of objectivity and thereby of credibility. However, because models of pandemics are infused with subjectivity, their objectivist appearance can in reality be considered purely ornamental. Their subjectivity is expressed in the choice of parameters, which is based on the principle that simple models are preferable to complex ones (4), in the choice of parameter values, and in the interpretation of results, which is based on reflections and assessments rather than on fixed standards.

Modelling the unknown

Researchers and health authorities attempt to approach the unknown through the use of models that fit the known – i.e. previous epidemics. By adjusting the model's parameter values based on guesswork regarding the effect of the new infectious agent on the human population, a range of outcomes is generated, within which the unknown is expected to become manifest.

This is a highly unreliable approach to capture the contours of the unknown. Even for diseases with similar clinical pictures and infection pathways, the parameter values included in the models may differ considerably. For example, COVID-19 was initially modelled as influenza. However, as COVID-19 gradually became known on its own terms, it also became evident that the diseases differ along key variables. These include the time from infection to onset of illness (2 days for swine flu and 4–12 days for COVID-19), the interval between symptom onset and maximum infectiousness (2 days for swine flu and 0 days for COVID-19), and the basic reproduction rate (1.7 for swine flu and 2.5 for COVID-19) (5). Furthermore, it is highly uncertain whether SARS-CoV-2 leads to protective immunity, as influenza does.

Researchers and health authorities attempt to approach the unknown through the use of models that fit the known – i.e. previous epidemics

Any model that attempts to capture the unknown is expected to fail. The question is not whether the model's predictions will fail or not, but of how *much* they will fail. These considerations also apply to the model that the Norwegian Institute of Public Health uses to study the spread of COVID-19 in Norway. The model, which incorporated infection control measures, reported a one-year scenario plan with 22 000 patients hospitalised and 5 500 patients in intensive care (6). The peak was expected in the middle of the period. A worse scenario was also estimated, but not a milder one. After six months and close to the predicted peak, altogether 10 792 persons had tested positive for COVID-19, 1 250 had been hospitalised and 231 patients had been treated in intensive care units (7). These low figures were also included in the model as a possible outcome, but were not considered realistic by the group of modelling experts.

Wrong, but useful?

Simulation models of pandemics are rarely validated with a view to accuracy (8), and their predictions can therefore hardly be referred to as evidence-based. Despite this, they have had a major influence on the ways in which health authorities of various countries have approached their infection control measures during the COVID-19 pandemic (9).

It can be objected that the degree of consistency between predictions and reality is not the only criterion to be given weight in the appraisal of a pandemic model. Many researchers have, for example, endorsed a view stating that even though the predictions produced by mathematical models are wrong, they may still be useful (3, 10, 11). However, research-based evidence for this assertion is hard to find. It may appear intuitively correct that modelled predictions based on systematised information management work better than predictions that are based on intuition (3). However, justification for this argument is weak. Since intuition is granted argumentative force in the first part of the argument but not in the second, the argumentation is self-referentially inconsistent and thereby methodologically incomplete.

Any model that attempts to capture the unknown is expected to fail

A further reason to be sceptical regarding the assertion that the models are useful is the following: an indefinite number of 'realities' can be derived from one and the same model. Since the models alone cannot determine whether one modelled reality is more correct than another, and since the models predict an as yet unrealised reality, it is impossible to know how close the modelled 'reality' is to the empirically given reality. There is therefore a large risk that the health authorities, who have ordered the modelled predictions, will be governed by a misleading description of reality and thereby promote solutions other than those that the situation demands. If it deviates sufficiently from reality, it can even be argued that this modelled description of reality leads to useless and at worst harmful actions. In this respect, the phrase 'wrong, but useful' appears void of any content.

Why is it so difficult?

Claiming that good models of COVID-19 are difficult to construct because we have little knowledge of the novel virus (11) is too simplistic. The dearth of knowledge is more linked to the effects of the virus on humans and of how humans respond immunologically, psychologically and socioeconomically to the challenges that the virus presents.

Modelling of human predispositions to respond requires an understanding of host-microbe relationships (12). Such insight cannot be obtained by modelling the actors in isolation from the ecological and social systems that have created them. Insight into relational aspects requires an investigation of the pandemic's variable forms of expression as they appear within a dynamic network, as phenomena consisting of a variety of overlapping complex systems where the causal chains within and between the systems are diverse and non-linear.

The more undefined variables that exist for a system, the harder it will be to predict the behaviour of the system. This applies to physical systems such as weather and climate, and even more so for biological and social systems that have a bearing on humans (13). The human being is not only a biological organism that encounters a pandemic infectious agent; it is also a subjective interpreter of the pandemic's effects. Hence, issues such as panic, ignorance and trust come into play. The major challenge associated with modelling outbreaks of pandemics consists in how subjectivity should be accounted for as a model parameter (14).

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