Foresight

Infectious Diseases: preparing for the future

OFFICE OF SCIENCE AND INNOVATION

S9: State-of-Science Review – Predictive and real-time epidemiological modelling

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Predictive and real-time epidemiological modelling

1 Introduction

Models are tools that allow us to translate between behaviour at various scales, or extrapolate from the behaviour under one set of conditions to behaviour under another. They allow us to predict the population-level epidemic dynamics from an individual-level knowledge of epidemiological factors, the long-term behaviour from the early invasion dynamics, or the impact of vaccination on the spread of infection. There are no right models, but there are certainly lots of wrong ones. Models come in a variety of forms – from highly complex models that need a range of experts to create and maintain them, to simple 'toy' models that can be easily understood, modified and adapted. Which sort of model is the most appropriate depends on the precision or generality required, the available data and the timeframe in which results are needed. Here, our primary focus is towards detailed predictive models where generality and transparency are frequently sacrificed for greater accuracy. However, only mechanistic models that take into account the known principles of disease transmission will be considered; 'black-box' time-series tools (such as neural-nets) will be ignored, despite their often high degree of accuracy, as it is often difficult, if not impossible, to incorporate novel control measures or behaviours into this model formulation.

Mathematical models of infectious diseases have been in existence for almost 100 years (Hamer 1906). Since that time they have developed from simple caricatures of the infection process to sophisticated tools for understanding and predicting epidemic behaviour. However, it has only been within the last decade that the necessary model complexity and computational power have been available to allow real-time prediction during the course of an epidemic (Ferguson et al*.* 1997, 2001; Keeling et al. 2001; Riley et al. 2003).

Almost all models of infectious diseases are based on a simple set of differential equations:

$$\begin{aligned} \frac{dS}{dt} &= B - \beta SI - dS \\ \frac{dI}{dt} &= \beta SI - gI - dI \end{aligned} \qquad (1)$$

This formulation intuitively translates into the following set of statements:

- All individuals are born (at rate *B*) susceptible to infection, and eventually die (at rate *d*).
- Susceptible individuals (labelled *S*) are infected by infectious individuals (labelled *I*) and then become infectious themselves.
- The risk of infection increases with the proportion of infectious individuals in the population.
- Infectious individuals eventually recover or die (at rate *g*).

These four statements are a general summary of the behaviour of many infectious diseases, from the common cold to HIV, and hence this basic framework of equations has universal applicability; although later models have increased the complexity by incorporating greater individual-level variability in behaviour. The fundamental behaviour of any epidemic process is driven by the non-linear transmission term (βSI) which can lead to a rich variety of dynamical complexity, from constant levels of infection to chaos (Rand and Wilson 1991, Olsen et al*.* 1986). In general, the non-linear transmission rate coupled with the depletion of susceptibles by the epidemic leads to a familiar bell-shaped curve for the number of cases over time (Figure 1). It should be noted that this simple classification of the population, into susceptible, infectious and recovered, ignores all the complexities of pathogen dynamics within the host in favour of a caricature of disease behaviour.

This review is divided into three main sections. The first considers what models can and cannot deliver from an abstract, slightly philosophical, viewpoint. The second reviews the current state-of-the-art models, together with examples of how such models have been utilised in practice. Finally, the last section looks to the future, discusses how predictive models may be improved and utilised over the next 25 years, and how other technological developments may both enhance and benefit from such models.

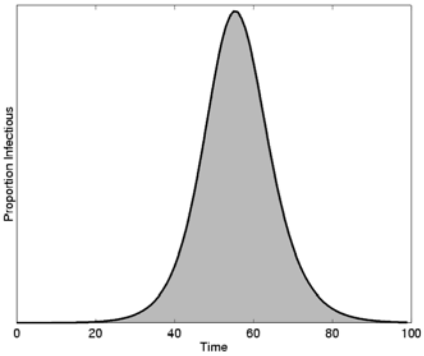

Figure 1: Dynamics of the SIR model (equation 1) showing a rapid epidemic where births and deaths are negligible.

2 What can models deliver?

Despite the advances in modelling that will arise in the coming decades, models will *never* be able to accurately predict if, or when, a particular person, farm or community will become infected. This is for two reasons: (i) the transmission of infection is a stochastic process, such that no two epidemics are identical; (ii) models will always be an approximation, and rare or unforeseen behavioural events can have a significant impact on the disease dynamics (Albert et al*.* 2000; Watts and Strogatz 1998). Consider trying to make an accurate model for a human airborne infection (say influenza). Such a model would need to account for variations in transmission temperature and climate, capture the day-to-day movement and interaction of individuals, and encompass the variability in susceptibility due to genetic factors or past infections. Even if such a model could be built, the chance nature of transmission would still prevent perfect prediction. Therefore, epidemiological modellers are faced with an impossible task; the best they can achieve is to bound the range of plausible epidemic behaviour, predicting which future outcomes are likely and providing confidence intervals for any characteristics of interest.

Despite the inevitable failing of any predictive endeavour, well-parameterised and carefully constructed models can be a powerful public health, veterinary or agricultural tool (Anderson and May 1992; Ferguson et al*.* 2003). Accurate predictive models have four main roles in this area:

2.1 Planning

The prophylactic use of models can produce a range of plausible epidemic scenarios, which will allow decision makers to refine control options and fine-tune the available logistics (Ferguson et al. 2003). The predicted epidemic behaviour from model simulations can be used as the basis for control exercises, assessing how policy makers will respond to a changing epidemic pattern. Such models can also be used to investigate a wide range of control strategies, effectively experimenting *in silico* to assess the advantages and robustness of different measures (Keeling et al. 2003). In this way, it is hoped that models may even allow us to define robust triggers for the implementation of a particular control strategy. For example, in the face of a smallpox or pandemic-influenza epidemic, what are the triggers that necessitate a switch from local control to national vaccination? It is important that models for planning must not only incorporate the stochastic nature of disease transmission, but must also encompass the uncertainties in epidemiological parameters and host behaviour.

2.2 Prediction

During an epidemic, if the epidemiological parameters and host behaviour can be rapidly parameterised, models can be used to predict the size or duration of the epidemic and therefore provide valuable information about the types of logistics and resources that will be necessary in either combating the infection or dealing with the expected number of cases (Ferguson et al. 2001; Keeling et al. 2001). In addition and potentially based on the results from earlier prophylactic simulations, the models can be used to determine which of a range of control policies is optimal. It should be noted that predictions during an epidemic will be continually refined as new data becomes available and as the effects of control measures become apparent. It is therefore clear that the optimal control strategy may also change during the course of an epidemic in response to developing parameters and the changing number and distribution of cases.

2.3 Detection

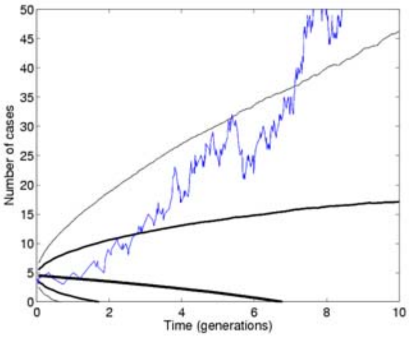

Figure 2: Possible dynamics of a disease at the threshold for invasion (R_0=1). The curves show the 99%, 90% and 50% confidence intervals, while the blue line shows one extreme example.

Models can also be utilised as a powerful statistical tool that can account for the non-linear epidemic dynamics, determining if an observed pattern of reported cases agrees with our beliefs about the epidemic processes and parameters. For widespread, but generally benign, infections (such as meningitis), models can be used to test if the frequency of symptomatic cases is likely to be a chance phenomenon or whether they indicate the start of an epidemic. Similarly, for endemic diseases (or during an epidemic), models can be used to highlight areas in which infection levels are higher than expected or where disease control measures are not operating as effectively as expected. This is illustrated in Figure 2. For these parameters in a deterministic model, the level of infection would remain constant; however, a stochastic variation leads to expanding confidence intervals but a declining mean and eventual disease extinction. The blue line shows one extreme example with these parameters. Differentiating this example, which cannot generate a major epidemic, from one with different parameters that can is a difficult but important problem.

2.4 Understanding

In addition, models can also be used to improve our understanding of the infection processes. Unlike predictive simulations, models used to explore fundamental infection dynamics are often rather simple abstractions, concentrating on the few elements that are under scrutiny (such as spatial structure or temporal variation) while ignoring all other complexities. While such models are of great scientific importance and provide much-needed information on the general behaviour of diseases and the effects of particular heterogeneities, they will not be considered further in this review due to their limited predictive ability.

3 State-of-the-art models

It is clear, from what has already been said, that no model is perfect, and no model can accurately predict the detailed outcome of an infection process. However, there are two key points that define a good model. Firstly, a model should be suited to its purpose, having an appropriate balance of accuracy, transparency and flexibility. A model built for accurate prediction should provide a comprehensive picture of the full dynamics, and should include all the relevant features of the disease and host, although determining which factors are relevant and which may be safely ignored is a complex and skilled process. Secondly, the model should be parameterisable from available data. Thus, while a predictive model requires the inclusion of many features, it is important that they can all be parameterised from available data. Hence, in many situations it may be impossible to produce a good predictive model simply due to the lack of sufficiently detailed data. Therefore, it is clear that what constitutes a good model is context-dependent.

All epidemiological models of infectious diseases are based on the approximation for the transmission of infection between infectious and susceptible individuals that is given in equation 1. More complex, state-of-the-art models include additional structure that hopefully lends greater accuracy to the predictions. Here, we categorise this additional structure before considering how state-of-the-art models have been utilised during three recent epidemic threats. The additional modelling elements that can be found in many predictive models can be subdivided into stochasticity, heterogeneity, greater individual-level accuracy and spatial structure. While not all state-of-the-art models contain all of these additional elements, the inclusion of these features often separates conceptual from predictive models.

3.1 Stochasticity

Stochasticity is a ubiquitous element of disease dynamics. It refers to the fact that all events (such as infection or recovery) are chance processes, although their underlying average rate is predictable by deterministic equations. Stochastic models in general deal with integer numbers of individuals (and integer changes to the number of individuals). Such an approach is therefore especially important during the early and late phases of an epidemic when the number of infectious cases is low (Keeling 1997; Renshaw 1991). All state-of-the-art models should incorporate this chance element into the disease dynamics, which is essential if questions of disease persistence, epidemic duration or disease eradication are to be addressed. It is important to realise that the results of stochastic models may be highly variable, and thus multiple simulations will be needed to provide bounds and confidence intervals on any predictions (see Figure 2). In this manner, most stochastic simulations can be viewed as a means of generating large amounts of detailed surrogate data which require a battery of statistical tools to extract the underlying patterns.

3.2 Heterogeneity

Heterogeneity describes the variability in the basic epidemiological parameters between individuals. The simplest disease models assume that all individuals are identical. However, models have illustrated the importance of variability for both the initial growth of an epidemic (Ferguson et al. 2001; Keeling et al. 2001; Riley et al. 2003 (and for the prevalence of infection (Hethcote and Yorke 1984), therefore state-of-the-art models should include this factor. A wide variety of heterogeneities can be included, usually by partitioning the population into groups with similar characteristics. Age-structure, and the preferential mixing between individuals of a similar age, is seen as a vital component of childhood infections (Anderson and May 1992; Bolker 1993; Schenzle 1984) and may be crucial for diseases such as smallpox or pandemic influenza, where older generations may have partial immunity. Age-structured models may also be important when disease severity is a function of age (Anderson and May 1983; Medley et al. 2001).

Figure 3 shows predicted cases of rubella in woman of child-bearing age as both the level of vaccination and the reproductive ratio (R_0) vary. From this figure, it is clear that if rubella is highly transmissible (R_0 is large), intermediate levels of vaccination may lead to more potential cases in pregnant women and therefore increase the adverse effects of this infection.

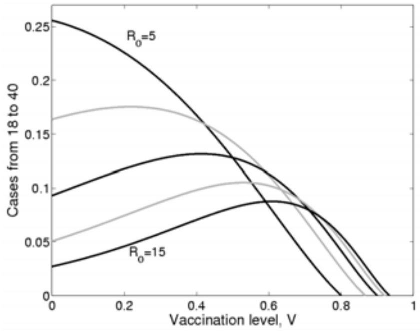

Figure 3: Level of rubella infection in women of child-bearing age as the basic reproductive ratio of the disease (R_0) and the proportion of individuals vaccinated at birth varies.

Heterogeneous risk-structured models are therefore constructed to account for differences in susceptibility to and transmission of infection. There are many instances where the increased risk of a proportion of the population needs to be accounted for: intravenous drug users for a variety of pathogens, sex-workers for sexually transmitted infections (Hethcote and Yorke 1984*;* Rothenberg 2003), doctors and nurses for the spread of MRSA in hospitals (Cooper et al. 2004), and large mixed-species farms for foot-and-mouth disease (FMD) (Ferguson et al. 2001; Keeling et al*.* 2001). The number and type of heterogeneities included in any modelling project are limited only by our understanding of relevant risk factors and the availability of suitable data. Such heterogeneous models allow us to consider targeting control towards particular sections of the community. In general, it is found that targeting high-risk individuals is a very efficient and effective control strategy.

3.3. Greater individual-level accuracy

Greater individual-level accuracy comes from a detailed understanding of the epidemiology of infection. Most simple models assume a constant transmission rate from all infectious individuals, and a constant (stochastic) rate of recovery leading to exponentially distributed infection times (Anderson and May 1992). In practice, neither of these assumptions are generally true, and both can have a dramatic impact on the disease dynamics and the types of control measures that are needed (Fraser et al. 2004). Parameterising the individual-level behaviour with the results from detailed observations of patients can have fundamental effects on the model behaviour (Ferguson et al. 1997, 2001; Fraser et al*.* 2004; Riley et al. 2003). Generally, this parameterisation leads to a distribution of infectious periods with less variation and infectivity that varies throughout the infectious period.

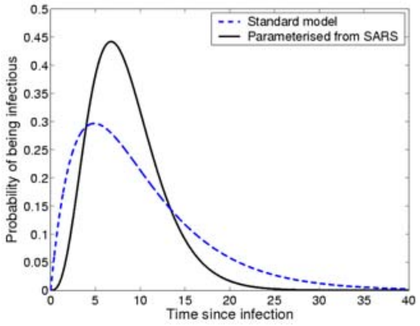

Figure 4: Comparison of individual-level infection profile from an SEIR model (with an exposed but none infectious class, E) to a more realistic model profile fitted to data from SARS patients. Parameters are from Riley et al (2003).

3.4 Spatial structure

Spatial structure must be included if models are to capture the intuitive observation that transmission of disease is fundamentally a local process. Two particular scales of spatial structure can be included within models, and both may be important in determining the epidemic behaviour. Large-scale spatial structure captures the separation of a national population into discrete local communities (Grenfell and Harwood 1997; Keeling et al. 2004), with strong random mixing within each community and weaker mixing between communities representing the frequency of the associated transmission events. As such, this form of spatial structure informs about the effects of long-range movement and regional control measures. On a more local scale, a contact network defines the potential transmission links between individuals and is a necessary tool if we are to interpolate from individual-level behaviour to a population-level prediction (Halloran et al. 2002*;* Keeling et al*.* 2001) or if we wish to understand local control measures such as contact tracing (Eames and Keeling 2003). Generally, spatial models display a much slower epidemic increase compared to traditional (random-mixing) models due to the rapid depletion of susceptible individuals in the local environment. This is clearly a factor that must be included in predictive models if the transmission of infection is based on proximity.

4 Disease case-studies

To observe how such additional modelling elements feature in and affect state-of-the-art models, we focus on three recent outbreaks or epidemiological scares. It is said that 'Necessity is the mother of invention,' and for predictive models this saying also holds true as the threat of an epidemic tends to lead to substantial advances in techniques and expertise. It is hoped that by comparing and contrasting the models used for FMD, smallpox and severe acute respiratory syndrome (SARS), we can develop a general understanding of current modelling ability.

4.1 Smallpox

Although smallpox was effectively eradicated worldwide in 1979, it still poses a potential threat as a bioterrorist weapon due to the high mortality associated with this infection. From 2001 to 2003, a variety of modelling papers were produced in an attempt to quantify the risk and determine the optimal control measures – generally concentrating on the trade-off between contact tracing and mass vaccination. While all these models had similar goals and attempted to model similar epidemics, they differed widely in their methodology, parameterisation and predictions. Meltzer et al*.* (2001) produced by far the simplest model, in which the number of infectious cases increased exponentially before vaccination and decreased slowly but exponentially after vaccination. By contrast, Halloran et al*.* (2002) formulated an individual-based model in which contacts within a population of 2,000 individuals were created to mimic known patterns of social structure – hence this model is stochastic, spatial (in terms of social space) and socially heterogeneous.

4.2 FMD

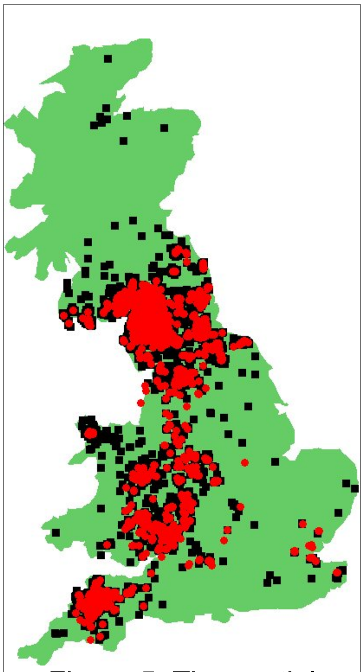
Figure 5: The spatial location of culled farms (black) and farms reporting infection with FMD (red) from the 2001 epidemic.

When FMD was identified in the UK in February of 2001, several teams of modellers were asked to provide input. Within a few months, three detailed models were being simultaneously used to predict the epidemic dynamics and assess control measures. Interspread (Morris et al. 2001) used by DEFRA is a spatial, stochastic and heterogeneous model. It is the most complex of the three models and can incorporate a wide number of different factors leading to a large number of parameters. The model by Ferguson et al. (2001), by contrast, is deterministic and approximates spatial clustering, but includes both farm-level heterogeneity and variability, and could be readily parameterised from the 2001 data. Finally, the model by Keeling et al. (2001) falls between the other two – it is spatial and stochastic but, due to its lack of parameters, it can be parameterised from the epidemic data, although this is a time-consuming process. Despite the differences in the model formulation, all three models provided similar advice, showing that the level of control in the first few months of the epidemic was insufficient and that a more intensive culling programme would actually reduce the loss of livestock.

4.3 SARS

During the widespread SARS epidemic of 2003, there was only one major model developed by the scientific community (Riley et al. 2003). This model for SARS in Hong Kong is stochastic, spatially structured into 18 districts, and accounts for both risk-structured heterogeneity and individual-level variability – as such, it includes all four modelling elements listed above.

These three example situations raise a number of issues that can be explained by the role that models were expected to play.

Firstly, the models for FMD provided similar recommendations and yet the models for smallpox were widely conflicting. For FMD, models were used predictively – based on very detailed epidemiological data all the models could be parameterised to match the observed behaviour of the disease. In contrast, for smallpox, the models were used for planning – data on significant smallpox outbreaks in the developed world is generally over 50 years old and it is difficult to translate this epidemic behaviour to a contemporary scenario. Therefore, while for FMD, all three models were required to fit to the observed epidemic, the models for smallpox were not so constrained and a variety of assumptions could be utilised. This highlights the need for reliable data and a thorough investigation of plausible parameter space in any predictive modelling exercise.

The second question that arises is why many smallpox models were produced, while there were only three FMD models and just one SARS model. While some of this discrepancy may be due to obtaining access to the necessary data, again the use of model results clearly plays a role. For SARS, there were very few questions for models to address. Isolation and quarantine were the only available control measures and the uncertain nature of human movement patterns makes precise prediction very difficult. For FMD, there was the clear question of whether additional control measures would save more farms than it would cull. Finally, for smallpox, there was the highly publicised question of whether mass vaccination or localised control would be most effective .

Finally, although many of these models would be considered state of the art, they do not all include the four modelling elements listed above. Which elements are included in a model, and which are ignored, is largely based on the judgement of the modeller who must consider which effects are likely to be important, and which effects can be parameterised from available data. It is interesting to note that for the two human diseases (smallpox and SARS), only the model by Halloran et al. (2002) includes local social structure. This is not due to modellers viewing this effect as unimportant but due to the difficulty of robustly parameterising models of social interaction.

5 The future

If we look back 25 years, to the early 1980s, Anderson and May had just published *Population Biology of Infectious-Diseases. 1* (1979), which lays much of the original foundation for robust modelling of infectious diseases. Since those early days, models have increased in both complexity and accuracy – it is likely that the next 25 years will witness just as great a development in modelling techniques and applications. In addition, following Moore's Law (Moore 1965), the available computational power is also likely to increase substantially in the next 25 years, making the simulation of structured individual-based models with multiple heterogeneities a relatively quick process. The diseases that pose a challenge to public health today are unlikely to be substantially reduced (or eliminated) within the next 25 years, and will continue to pose a burden. In addition, other pathogens may emerge (as HIV, Ebola and SARS have arisen in the past 20–30 years), increasing the number of diseases that must be considered. It is therefore important that control methods for tackling these infections are targeted as efficiently as possible, delivering the maximum impact for the minimum effort. Predictive models can play a vital role in achieving this goal.

Combining the four forms of structure detailed above (stochasticity, heterogeneity, greater individual-level accuracy and spatial structure) and building ever-more complex and involved models is largely a matter of computing power, the researcher’s patience and dedication, and the availability of data to parameterise the various aspects of the model. There will always be a place for such comprehensive models, as they often offer the most accurate methods of prediction. For complex models to be of practical use, however, requires a robust understanding of how each complexity influences the dynamics and how the complexities interact. In particular, we need to know which details of epidemiology and host behaviour are vital for the accurate prediction of the dynamics and determination of the optimal control policies, and which are largely superfluous. Therefore research also needs to be focused on more fundamental science, determining when complexity and additional details are required and when simpler approximations can be used.

With increasing model complexity comes an increasing number of parameters that must be determined from limited data (Ferguson et al. 2003). Considerable future research will inevitably focus on novel methods to extract the maximum information from the available data and the development of new techniques for acquiring large amounts of data on the general population. Rapid parameterisation in the face of an epidemic is a must if models are to aid decision making in the early stages of the epidemic when controls are most effective. Markov Chain Monte Carlo (MCMC) techniques offer a promising means of parameterisation for the future, as they are able to deal with very high-dimensional parameter spaces and hence large amounts of missing data. At each step, MCMC requires the calculation of the likelihood of obtaining the observed epidemic from the model parameters and assumed values of the missing data. As many millions of steps may be required, MCMC can be prohibitively slow and while this may be overcome by the advances in computation speed, other parameterisation tools and improvement in statistical techniques will still be required.

We now focus briefly on how some of the disciplines featured in this review will impact on disease modelling, and how models may influence the deployment and implementation of these new technologies.

- Detailed predictive models that are parameterised with known human (or animal) movement patterns, or known dispersal patterns of pathogens, can be used to direct the surveillance for sources of infection. Such predictive models will be able to identify *hotspots*, where infection is likely to be found during the early stages of an epidemic, or *critical locations* where the presence of infection is often a trigger for a large-scale epidemic. Such hotspots or critical locations for human diseases are likely to be areas where people congregate, such as shopping malls, underground stations or hospitals; for animal diseases, markets, distribution centres or particular farms may be the focus; whereas, for plant diseases, attention may be directed towards nurseries. In addition, for human, animal and plant infections, entry points into a disease-free country or region, such as ports, airports and boarder crossings are always likely to be critical locations as these act as bottlenecks in the transmission route. Once identified, these hotspots or critical locations are the ideal sites in which automated sensors, rapid non-invasive scanners or sentinel organisms should be placed.

- Models can additionally be used to provide a guide to the dynamic targeting of testing or detection. It is plausible, that once an invading pathogen is identified, the number and position of critical locations may change, so it is important that detection technology can be routinely moved to regions where perceived risk is greatest. Consider the 2001 UK FMD epidemic – models were able to predict that risk of infection was greatest for large farms close to an infectious source. This lead to the localised (contiguous premise) culling of many animals, of which a significant proportion were not infected. A rapid and reliable test for FMD, which could detect early infection, targeted towards local large farms may have allowed a much more discriminating response and leading to the same control of infection and less loss of livestock. Additionally, although state-of-the-art models will predict a range of possible epidemic scenarios, targeted detection may be able to quickly eliminate many of these possibilities. Finally, accurate forecasting may allow control measures to be rapidly and efficiently targeted, resulting, for example, in the swift vaccination of those people most at risk.
- Models should also be used to analyse the results from detection and identification sensor or devices. While the detection of a single infected individual is a worthwhile goal in its own right, it is only when such data are collated and analysed that a comprehensive picture of infection risk emerges. At the moment, the Health Protection Agency in the UK and the Centers for Disease Control in the USA currently collect information from a variety of national sources in an effort to detect changes in disease profiles. However, this data represents only a very small sample of the true epidemiological status of the nation. A more complete sampling system, linked to predictive models, would be able to ascertain epidemic patterns far sooner. It is clearly possible with current technology to collect and collate information from GP surgeries, although this would place an extra burden on already overworked GPs. However, the ability to gather a large quantity of remotely sensed information, in people's homes, at hotspots or at critical locations, would generate a qualitative shift in the type of analysis and prediction that could be performed.
- In the future, it is plausible that large-scale models could be developed that include the tracking and personal history of every individual. Advances in mobile-phone technology and geographical positioning systems (GPS) mean that it is now relatively easy to track an individual to a high degree of accuracy. This, in principle, means that close contacts that would allow the transmission of infection could be monitored in real-time, providing a huge jump in the potential accuracy of simulations. Of course, such privileged information may be highly sensitive and questions of anonymity and personal privacy would need to be considered. Using such information it may be possible, once an infectious case is identified, to perform detailed contact tracing automatically. This has the advantage over current contact tracing, which is relatively slow, labour-intensive and relies on the infectious individual remembering every encounter or knowing everyone they meet. Individuals traced automatically could be contacted for more detailed screening for infection and then possible treatment. This type of real-time information may be vital if we are to predict the spread of a major

human epidemic, when panic may lead individuals to behave unpredictably. In the UK, the cattle tracing system (CTS) and the animal movement licences scheme (AMLS) provide this kind of information for the livestock industry, allowing us to monitor the movement of animals between farms and markets. This means that the transmission routes of future outbreaks of livestock infections may be traced, which can be especially important for detecting the long-range movement of infection into naive areas.

- Epidemiological models are based on quantifying the infectious status of individuals, which is in direct contrast to medical considerations that focus on the diseased status of individuals. This difference in emphasis means that individual-level parameters for infection dynamics are difficult to obtain directly. However, new molecular and immunological techniques (such as those detailed within this review) are providing ever-more detailed information on the within-host dynamics of infection, which can be used to determine the individual-level behaviour. Hopefully, such information will not only provide a detailed temporal picture of infection levels and transmission potential, but will also allow modellers to characterise the variability between individuals.
- Finally, molecular and immunological techniques could be used to determine the population-level susceptibility (or resistance) to the pathogen of interest. In many modelling scenarios, such as pandemic influenza or smallpox, the level of susceptibility is largely a matter of informed guesswork. However, this parameter can be vitally important for predicting disease dynamics and the types of controls that are required. In addition, individual-level susceptibility data may highlight regions or social groups that are particularly at risk from infection, and therefore should be either the main target of controls or closely monitored for signs of disease.

If future models are to be of practical use to policy makers, they must be driven by the need to answer particular policy decisions (such as whether it is 'optimal' to mass vaccinate against an epidemic). In addition, such models must also consider the logistics and economics of control measures. This dimension has generally been largely ignored by the majority of the modelling community, but is necessary if models are to consider trade-offs between various options. Therefore, the future of modelling relies on closer integration with policy makers and public health practitioners so that control constraints carefully match what is achievable in practice.

The vast majority of modern state-of-the-art models are for directly transmitted infectious diseases. However, vector-borne pathogens (such as malaria) are responsible for millions of deaths worldwide and may invade new areas under the effects of climate change. Bluetongue, a disease of sheep and goats, was once originally confined to the tropics and subtropics, but in recent years outbreaks have occurred in Spain, Italy Greece, Corsica, Bulgaria, Croatia, Macedonia, Kosova and Yugoslavia. It is clear that this disease is moving north driven by the expansion of the vector species. Vector-borne diseases have both advantages and disadvantages when it comes to control. One advantage is that control can be targeted at different elements, either limiting the transmission from infected hosts, limiting the transmission from infected vectors or simply reducing the number of vectors. The disadvantages are the inability to easily detect infection in vectors and the inability to control the movement of vectors. It is important that the scientific community addresses this modelling deficiency, creating detailed well-parameterised models that can account for the ecology and natural history of the insect vector, as well as the associated transmission dynamics.

At the moment, modellers (and experimentalists) tend to study either human, animal or plant pathogens, with little or no transfer of skills between these areas. There is, however, a great deal that such modellers could learn from each other. Human diseases tend to be the most studied, with the greatest understanding of the infection dynamics and the longest recorded patterns of incidence. However, understanding and predicting the movement and interaction of humans is extremely complex. In contrast, while animal diseases are less well studied and reported, their movement patterns are far better described. While plants differ from animals due to their lack of a full immune system, plants are far more amenable to experiments allowing researchers to compare models and experiments in tightly controlled situations. Bringing together the expertise from these three fields is clearly an important goal in the near future.

Finally, as exemplified by the SARS epidemic, due to the increase in international travel, it may no longer be appropriate to model diseases at a national scale. Instead, we must see the UK as one element in a much larger patchwork, with infections being imported from a variety of sources. Concerns over emergent pathogens from Asia demands a global perspective, with prompt detection and action when and where infections first arise often being the best way of limiting cases within the UK

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