

Foresight

Infectious Diseases: preparing for the future

OFFICE OF SCIENCE AND INNOVATION

**T8.1: Mathematical modelling
of future infectious diseases risks:
an overview**

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Introduction

This paper provides a brief overview of key outputs and conclusions from a series of quantitative studies of future risks of specified infectious diseases of humans, animals and plants in the UK and sub-Saharan Africa to 2015 and 2030. Foresight commissioned a total of nine individual studies covering the following topics (see links to full reports):

- human **tuberculosis** infection, disease and mortality in sub-Saharan Africa [T8.4]
- population at risk of **malaria** in sub-Saharan Africa [T8.2]
- incidence of paediatric **HIV/AIDS** in sub-Saharan Africa [T8.7]
- risk of **malaria** in the UK [T8.9]
- human **disease vectors** in the UK [T8.5]
- distribution of **cattle trypanosomiasis** in sub-Saharan Africa [T8.8]
- risk of **foot-and-mouth disease** epidemics in UK livestock [T8.6]
- spread of **bluetongue virus** in sheep in Europe [T8.3]
- economic impact of **potato ring rot** in the UK [T8.10].

These studies represent the state of the art in forecasting future risks or burdens of infectious diseases in different settings. Nonetheless, each of the studies is intended to be illustrative rather than definitive. One reason for this is that each study considers only a subset of the many drivers of future disease burden/risk (see *Future Threats*), as is discussed in more detail below. The main drivers considered by this set of studies are:

- **climate change** (malaria in Africa and UK, disease vectors in UK, cattle trypanosomiasis in Africa, bluetongue virus in Europe)
- **demographic change**, e.g. population growth, urbanisation (malaria in Africa, cattle trypanosomiasis in Africa, foot-and-mouth disease in the UK)
- **disease control** and prevention, both technologies and delivery systems (tuberculosis in Africa, paediatric HIV/AIDS in Africa, potato ring rot in the UK).

To varying extents, it is possible to integrate the predicted effects of different drivers but in no case is a fully comprehensive analysis feasible. Even so, the studies are extremely valuable in alerting policy makers to possible future scenarios and helping to identify what kinds of change we should be concerned about.

This paper summarises some of the key findings from the individual studies, identifies some common themes and then discusses the potential contribution of detection, identification and monitoring to mitigating future infectious disease risks in the light of the results from the modelling work.

Key findings

Human tuberculosis in Africa [T8.4]. This study quantifies the relationship between the future burden of tuberculosis (TB) and the efforts to control this disease. The incidence of TB is currently rising and one of the UN Millennium Development Goals is to reverse this trend by 2015. The study concludes that, if this target is to be met in sub-Saharan Africa, current control efforts will need to be significantly stepped up. Case detection rates and percentage successful treatments based on the DOTS programme, already greatly improved in the past 10 years, will need to improve further to achieve this target (Figure 1). Moreover, the DOTS strategy needs to be diversified to include mechanisms for the management of TB linked to HIV, and to support the improvement and reach of health services. The cost of this increased effort is estimated at US\$20 billion over the period 2006 to 2015. The more ambitious target of halving the rate of TB mortality by 2015 (as compared with the 1990 level) does not seem achievable at present; it could be achieved in principle in countries with low HIV rates by even more intensive implementation of DOTS, but not in countries with high HIV rates without some reduction of the incidence of HIV and HIV–TB co-infections (Figure 1). Key drivers of the future burden of TB are thus the successful implementation of more effective HIV/AIDS and TB control programmes.

Malaria in sub-Saharan Africa [T8.2]. This study quantifies the impact of climate change and population change on the size of the population at risk of malaria in sub-Saharan Africa. Overall, the population at risk (currently over 600 million) is expected to rise to almost 900 million by 2015 and to 1.1 billion by 2030. This would make another of the Millennium Goals – that the incidence of malaria should start to decline by 2015 – significantly more difficult to achieve. The bulk of the increase in population at risk is due to population growth, although the impact of this is lessened by anticipated increases in urbanisation because urban environments are less conducive to malaria transmission. Even so, population growth emerges as the more important driver: changes in climate account for only one-sixth of the total increase by 2030 and are expected to lead to only relatively small changes in the geographical distribution of malaria by that date (Figure 2). The study points out that other drivers, such as land use and vegetation cover, are also likely to affect future population at risk.

Paediatric HIV/AIDS in sub-Saharan Africa [T8.7]. This study looks at the relationship between the burden of paediatric HIV/AIDS and a range of prevention and control measures for selected countries in sub-Saharan Africa. AIDS accounts for 10% of mortality in children less than five years old worldwide, rising to 80% in some of the worst affected parts of Africa. The UN Millennium Goal of halving childhood mortality by 2015 will not be achieved without tackling this problem. The three main strategies are treatment of infected children, measures to reduce mother-to-child transmission, and reducing levels of maternal infection. The study shows that, in the countries considered, current prevention and control measures will achieve minimal reduction in the number of infected children, but doubling efforts to reduce mother-to-child transmission could have a significant impact, which would be

greatly enhanced by programmes to reduce the prevalence of maternal infections. The key drivers are thus the intensity and effectiveness of the control effort.

Malaria in the UK [T8.9]. This study looks at the relationship between climate change and future risks of malaria outbreaks in the UK. Malaria (specifically vivax malaria, which causes less severe illness than falciparum malaria) used to be endemic in the UK and there are still at least six mosquito species in the country capable of transmitting malaria present. Climate change is expected to increase the likelihood of malaria outbreaks in the UK by increasing both the area and the time during which local transmission is possible (Figure 3), as well as through effects on mosquito habitat (e.g. increased saline wetlands through coastal flooding) and human behaviour (e.g. increased exposure to mosquitoes while outdoors). The study predicts that the risk of malaria outbreaks will increase to 2015 and again to 2030 (Figure 3), although it is not expected that malaria will become endemic in the UK over that period. Outbreaks therefore depend on introductions of malaria from elsewhere. Overall, the risk of future malaria outbreaks are considered to be low [see **T8.5**].

Human disease vectors in the UK [T8.5]. This study looks at the risks of mosquito disease vectors being introduced into the UK and being able to transmit infection, a well-documented example being the occasional cases of airport malaria that occur across Europe, mainly in the summer months. The main routes of disease vector introduction are via airports and seaports; the former are best studied, although seaports may actually present the greater risk for mosquito establishment. In addition to malaria, the mosquito vectors of dengue fever, yellow fever and West Nile virus could all be introduced this way, as well as other disease vectors such as sandflies and ticks. The key drivers considered are the similarity of climate between the UK port and the port of origin and volume of traffic between them. For *Anopheles gambiae* – a mosquito vector of falciparum malaria (which can cause severe illness) – the greatest risk through air travel is considered to be traffic from Lagos or Entebbe to Gatwick or Heathrow during June–September. Climate change is not expected to greatly alter the risk of temporary invasion by mosquito disease vectors by 2015 or 2030, but increased air or sea traffic could. These vectors and the diseases they can carry are not expected to become endemic in the UK over these timescales, but there will be a continued risk of sporadic cases, and an increasing risk of local transmission [see **T8.9**].

Cattle trypanosomiasis in sub-Saharan Africa [T8.8]. This study looks at the relationship between the geographical distribution of the tsetse fly vectors of cattle trypanosomiasis and climate change and human population growth (which drives agricultural activity). Overall, the study suggests that tsetse areas will contract by around 15% by 2030, mostly as a result of population growth. Climate change is expected to result in relatively small changes in the geographical ranges of the most important species of tsetse. However, there are important regional variations. The reduction in tsetse areas will be most dramatic in parts of west Africa, and some reduction is also likely in parts of east and southern Africa. But in Ethiopia and the lowlands of southern Africa,

cattle trypanosomiasis is likely to remain a major constraint on agricultural production. The implication of this study is that, overall, fewer cattle will be at risk of trypanosomiasis in the future than are at present, although the disease will remain a serious problem in some regions without more effective control measures.

Foot-and-mouth disease in the UK [T8.6]. This study looks at future risks of foot-and-mouth disease (FMD) outbreaks as a function of projected changes in UK livestock populations to 2015. The 2001 UK FMD epidemic cost the national economy an estimated £6 billion and highlighted the need to identify factors affecting the likelihood of FMD 'taking off' should the disease be re-introduced. Demographic projections suggest that little change is anticipated in total livestock numbers but that cattle and pigs (though not sheep) are expected to be found in a smaller number of larger farms. Overall, there is a very slight decrease in risk and there are some small shifts in which areas are most likely to experience major epidemics, although the regions most at risk remain southern Scotland/northern England, mid-Wales and south-west England. However, changes in livestock demography could be much greater than indicated by the projections used in this study. For example, reform of the Common Agricultural Policy would significantly alter the economics of livestock production in the UK and so lead to major changes in livestock numbers and distributions. Other drivers could also be important, such as an improved capability to detect FMD (see below).

Bluetongue virus in Europe [T8.3]. This study looks at the impact of climate change on the geographical distribution of bluetongue virus. Bluetongue is an important disease of ruminants which has spread 800km northwards of its previous geographical limits since 1998. The virus is transmitted by *Culicoides* midges, different species of which occur in all parts of Europe. The study illustrates that, although the effects of climate change on vector distributions may be quite minor, the effects on disease distributions may be much greater if climate change allows new species of vector to become involved in transmission. This seems to have occurred with bluetongue, either because the virus has come into contact with new potential vectors and/or because of changes in vector abundance or activity. The study predicts that further northward spread of bluetongue is likely by 2030, possibly reaching northern France and south-eastern UK. However, this spread could become much more dramatic if other *Culicoides* species abundant in northern Europe were to become involved in transmission.

Potato ring rot in the UK [T8.10]. This study looks at the economic benefits of keeping the UK free of potato ring rot. Although the UK is currently considered to be at very low risk of potato ring rot, the study suggests that its impact, if it were to be introduced, would be very substantial, so the economic benefit of exclusion over the next 30 years is estimated to be on average £2.6 million per year. This is a stochastic model, designed to expose the uncertainty around predicting the impact of possible future events, in order to better inform policy making. The model is then used to predict the impact of changing future conditions. If trade liberalisation, for instance, were to increase the risk of disease introduction from very low to moderate, the

average benefit of disease exclusion could increase four-fold, even allowing for expected reduction in the area under cultivation due to cheaper imports (Figure 4). New and more cost-effective disease control technology will reduce the average benefit of exclusion, and this reduction can be used to estimate the value of investing in new control methods. The key drivers in this study are economics (costs of disease and costs of control), trade, and prevention and control technologies.

Themes

Drivers – climate change. Several of these studies explore the relationship between climate change and future distributions of infectious diseases. Although there is considerable interest in both the short- and long-term consequences of climate change [T7.1], it is not in itself regarded as one of the main drivers of changing infectious disease risks to 2015 and 2030 [T2]. The modelling studies largely confirm this impression, but they also illustrate some of the complexities around the issue.

For human and animal diseases the impact of climate change has been most carefully considered in connection with vector-borne diseases (e.g. malaria [T8.2, T8.9], trypanosomiasis [T8.8], bluetongue [T8.3]). Here, climate change acts mainly by shifting the geographical areas where the climate is suitable for the vector. Although climate change may affect some other kinds of pathogen, e.g. cholera, it is unlikely to have major direct effects on diseases such as TB, AIDS or FMD (the situation may be different for plants where not only vector-borne pathogens but also a variety of infections, especially fungal infections, transmitted by other routes are likely to be influenced by climate change [T7.3]). But even for many vector-borne diseases, only relatively minor shifts in vector distributions are expected in the next 25 years due to climate change. Therefore, other factors that affect vector distributions, such as land use and vegetation cover, may turn out to be much more important.

However, while climate change may have relatively minor direct effects, it does have the potential to influence many of these other drivers, not only land use and vegetation cover but also such factors as agricultural practices, population density and human behaviour, all of which may in turn affect infectious disease risks. Moreover, climate change may act synergistically with other drivers. For example, the northward spread of bluetongue in Europe may be due partly to climate change and partly to a switch to a new vector species facilitated by climate change [T8.3]. Finally, we are concerned here with relatively short time periods – up to 25 years. The impact of climate change may be far greater (though also far more uncertain) in the longer term.

Drivers – demography. A major driver of future infectious disease burdens is the demography of the population at risk, as several of the modelling studies illustrate. Population growth in regions of sub-Saharan Africa suitable for malaria emerges as a key driver of future risk [T8.2], although this effect is lessened by increased urbanisation. The burden of AIDS in children is inevitably linked to birth rates in countries with high prevalences of HIV infection [T8.7]. Human population growth is likely to mean smaller areas at risk of cattle

trypanosomiasis through loss of habitat suitable for the vector [T8.8]. The risk of major FMD outbreaks in the UK is linked to the density of livestock [T8.6]. Other demographic factors, such as changes in age structure, may also be important for many diseases. The examples provided here illustrate a more general observation that, in order to estimate future infectious disease risks, we need to consider the future demography of the population at risk.

Drivers – disease control and disease control technologies. For many infectious diseases, potentially effective control measures are available, and a major driver of future disease burdens is how well or how badly these are implemented. The future of disease control is itself difficult to predict with any confidence [D3.1;D3.2;D3.3], not least because it is closely linked with economics and governance, but some of the modelling studies are able to explore the expected impact of changing control efforts in the future. The studies of TB [T8.4] and paediatric HIV/AIDS [T8.7] illustrate this in the context of achieving the UN Millennium Goals of reducing the incidence of major infectious diseases and halving childhood mortality by 2015. Both studies predict a wide range of possible future outcomes but suggest that: (i) the Millennium Goals are unlikely to be met in sub-Saharan Africa given current control efforts; (ii) the Millennium Goals could, in principle, be met using existing technologies given a quantifiable increase in the control effort, although improved technologies could make the task a great deal easier.

Uncertainty. This set of modelling studies covers only a few of the drivers that will affect future infectious disease risks [see T2]. An important issue is predicting changes in the driver. Sophisticated, quantitative projections are readily available for climate change and population growth and can be incorporated into epidemiological models. Equally important is quantifying the relationship between the driver and the disease. The relationship between levels of disease and control measures is relatively easily expressed and has been the subject of epidemiological modelling for over a century [S9]. Other drivers are much more difficult to consider, either because projections are unavailable and/or because the relationship between the driver and the disease is hard to quantify. Drivers such as improved international co-operation, increased numbers of refugees, health services, illegal imports, reform of the Common Agricultural Policy and many others fall into this category. Alternative approaches are required to examine their likely impact [T2].

The reports of the modelling studies consistently stress that, even for the most readily quantifiable and best understood drivers, there is considerable uncertainty associated with model projections. Various techniques are used to capture this uncertainty in the models. This underlines the importance of reporting not just average values of projections but also some measure of the likely range. Modelling frameworks can be helpful for exploring uncertainties, – for example, making disease projections based on different climate change scenarios. Uncertainty may itself be a subject of analysis; for example, there may be considerably more doubt about future malaria risks around the margins of its range [T8.2], making such areas appropriate targets for surveillance efforts.

Detection, identification and monitoring

The modelling studies illustrate possible benefits of improved detection, identification and monitoring in several different contexts. TB control in sub-Saharan Africa is a good example [T8.4]. Better TB control depends to a significant extent on better case detection. Case detection has improved (to around 50% now from around 25% ten years ago), but needs to improve still further (to at least 70% and perhaps as high as 90%) if TB burdens are to be reduced in line with the Millennium Goal targets. Improved case detection is likely to require point-of-care diagnostics which are cheap, simple and quick, but to achieve very high levels of case detection would require active screening of 'at risk' populations. More investment now in finding and treating patients means that there will be fewer patients later (through reduced transmission) and may even result in a net economic gain.

Appropriate technologies already exist (e.g. see www.finddiagnostics.org) but technological improvements are still urgently needed (e.g. the smear test is now 100 years old) and we also need better packaging and delivery systems [T8.4]. Further progress could be achieved by rapid diagnosis of TB–HIV co-infections, if this could be coupled with HIV treatment.

A reduction in the burden of paediatric HIV/AIDS also requires improved diagnostics. Modelling [T8.7] suggests that the future burden could be reduced by over 30% by 2030 by preventing mother-to-child transmission, which in turn requires identification of HIV-infected mothers in order to implement preventive measures. The barriers to doing this are not purely technological but also include social, economic and governance issues [T8.7].

During epidemics, rapid detection of the presence of infection in the population and rapid identification of newly infected individuals are both vital for successful control. This is well illustrated by FMD in livestock [T8.6], which remains a significant threat to the UK. If early detection is accompanied by early and effective intervention (e.g. movement restrictions, quarantine, treatment or vaccination), the size of an epidemic can be greatly reduced (Figure 5). Again, this is most likely to be achieved by use of point-of-care/pen-side diagnostics.

The economic benefits of detection are illustrated by the case study of potato ring rot in the UK [T8.10]. This study illustrates that there may be a net economic gain from strengthening procedures to exclude pathogens from the UK, although the study also reveals an economic trade-off between prevention and control: more cost-effective control reduces the economic return on disease exclusion. But if the costs of disease control remain high, investment in high-throughput screening or other technologies that could contribute to pathogen exclusion would make good economic sense.

Concluding remarks

Predicting future infectious disease risks is a formidable scientific challenge. This reflects the complexity of the problem. Disease risks, burdens and

impacts are influenced by a huge number of different drivers. To predict changes in disease risk we need to have an underlying expectation of changes in these drivers (which is often a formidable challenge in its own right). Putting the two together requires an appropriate mathematical or statistical framework (itself a rapidly developing subject; see **S7**) which reflects a detailed biological understanding of the relationships between drivers and disease (some of which may be well understood, others much less so).

Despite these difficulties, in some circumstances mathematical modelling is a valuable tool offering a way of exploring the future that can provide valuable insights and add to the evidence base available to policy makers, as the studies discussed here illustrate. Even so, there will be many other circumstances where formal, quantitative analyses are not (yet) practicable and qualitative approaches are more appropriate (see **T2**). Perhaps the most useful insights from quantitative studies come not from predicting absolute changes in disease risk or burden but from comparing different scenarios, both to suggest a range of possible outcomes and to identify scenarios most likely to be associated with favourable or adverse outcomes. At the same time, models may be valuable for quantifying uncertainty in outcomes and identifying the most important sources of that uncertainty.

One of the key messages from this set of modelling studies is that the future infectious disease situation is likely to be different from today's. This may reflect demographic change, increased (or decreased) efforts at control and prevention, climate change or change in any of a large number of other drivers, including improved technologies for combating infectious diseases and systems for delivering those technologies where they are needed. However, the scale and, in some cases, even the direction of change remain very uncertain. In certain scenarios, some disease problems in some places may get worse, in others they may get better. We have to anticipate that, in the next 25 years, the disease risks and burdens faced by the UK, sub-Saharan Africa and elsewhere in the world will be different than they are now.

Acknowledgement

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Figure 1: Control of human TB in sub-Saharan Africa. Projected mortality rate to 2015 in countries with high HIV prevalence and given different intervention strategies: no DOTS (red line); DOTS improving to 2005 (blue line); continued improvement in DOTS to 2015 (green line); and intensive implementation of DOTS with active screening (purple line). Horizontal broken line represents the Millennium Goal target. For full details see T8.4.

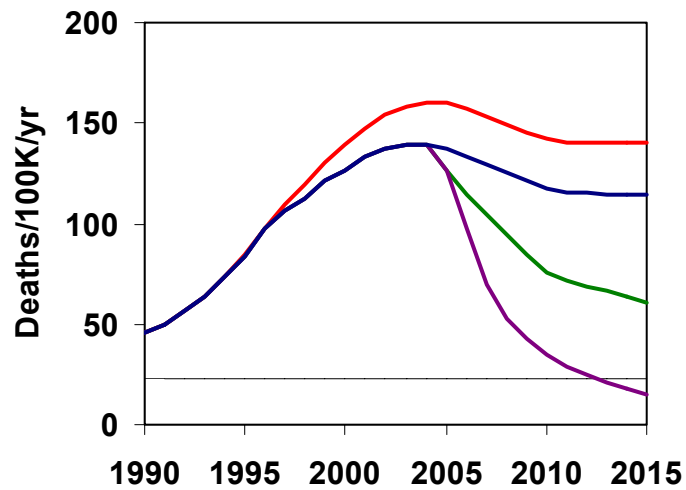
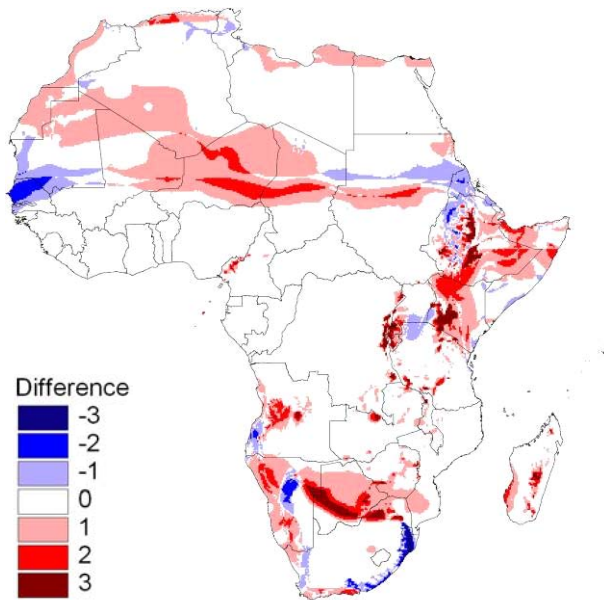


Figure 2: Maps showing the change in fuzzy climate suitability class (red = more suitable; blue = less suitable) across Africa between 2005 and 2030: (a) as a result of climate change; (b) projected population growth over the same period. The combination of maps allows the visualisation of the population at risk of malaria and how it may change in the next 25 years. For full details see T8.2.

a)



b)

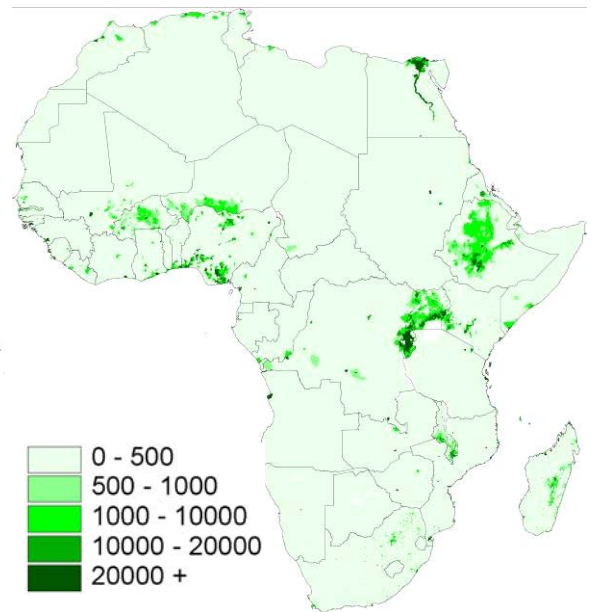


Figure 3: Predictions of changing malaria risk in the UK as a result of climate change. Number of months in which climate could support vivax malaria if introduced: (a) Present day; (b) 2030. For full details see T8.9.

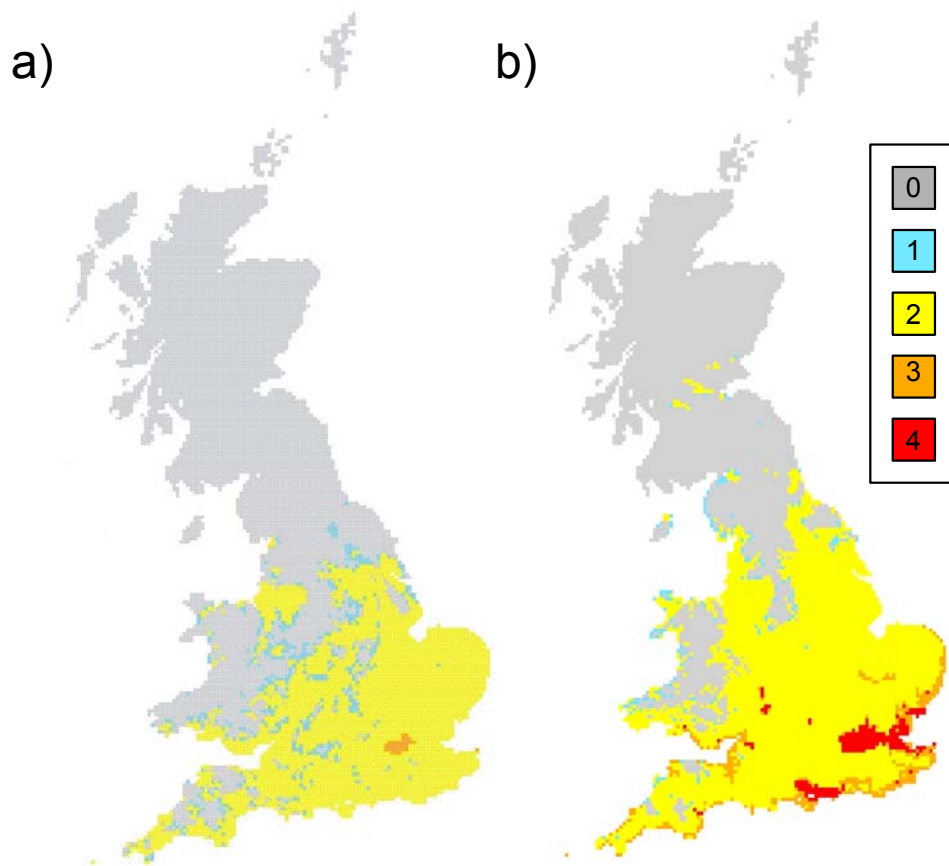


Figure 4: Projected economic benefits from successfully excluding potato ring rot from the UK for three different future scenarios: current conditions (control case); increased risk of introduction as a result of trade liberalisation; and reduced costs of disease due to improvement in control technologies. For full details see T8.10.

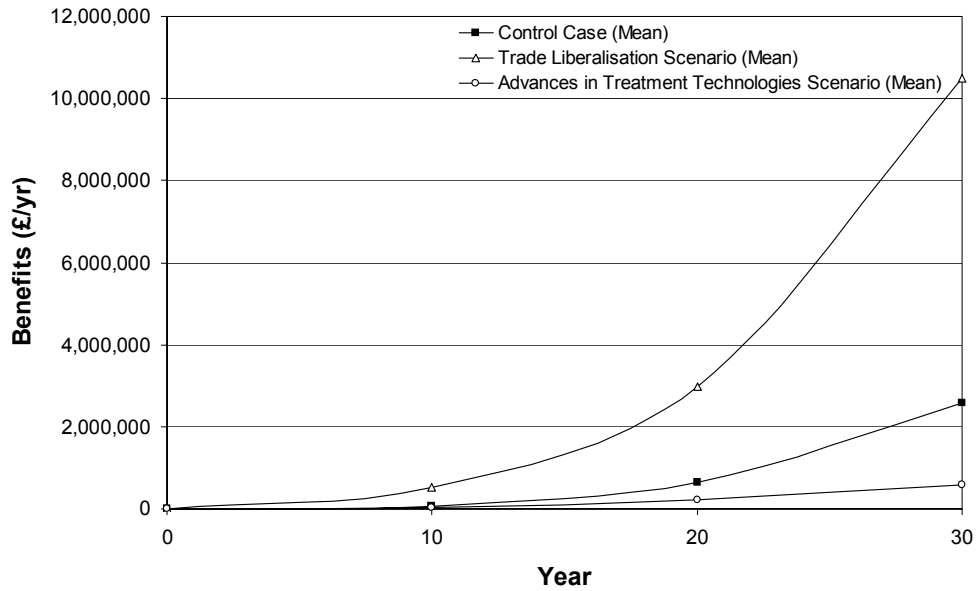
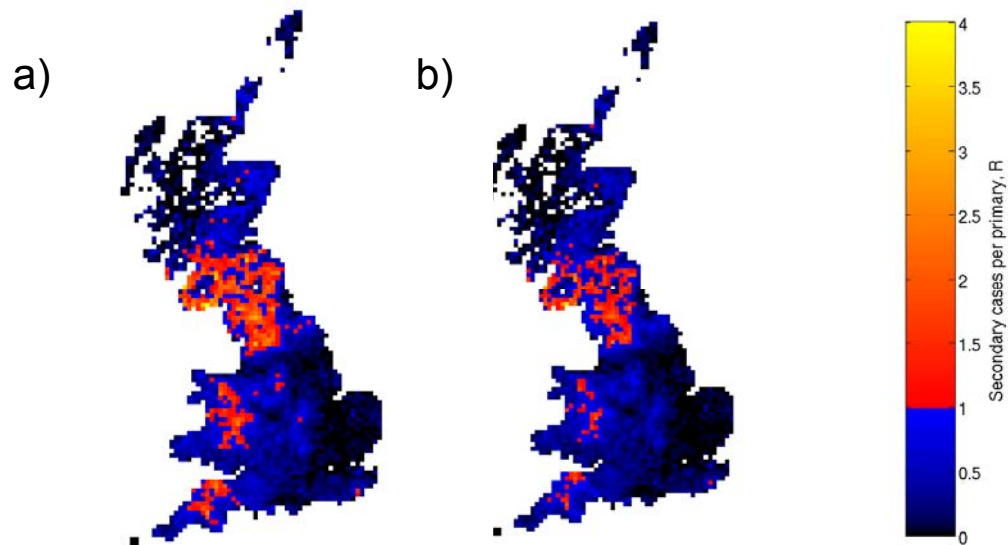


Figure 5: Predicted impact of more rapid diagnosis on risk of FMD in the UK in 2015. Risk is expressed as reproduction ratio (R) through local spread, assuming: (a) 7 days to detection of disease on farm; (b) 5 days to detection. The proportion of 10km x 10km squares where the average R is >1 is 15% and 9% respectively, illustrating the benefit of early detection and control at the farm level for reducing the likelihood of a major epidemic. For further details see T8.6.



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