

**FORESIGHT ON FUTURE INFECTIOUS DISEASES: DEVELOPING AN INTEGRATIVE RISK
ANALYSIS PROCESS**

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Abstract

This paper derives from the UK Foresight project which reported on the projected risks from infectious diseases of humans, animals and plants over 10- and 25-year time horizons, comparing three geographical regions: the UK, sub-Saharan Africa and China (www.Foresight.gov.uk). This paper reports on the risk analysis of future infectious disease incidence which underpinned this Foresight project and proposes a new decision-making tool to enable better understanding of the socio-economic risk factors of disease to be captured and integrated in the risk analysis process.

Over 300 experts from over 30 countries were consulted using a variety of methods including surveys and specially commissioned expert reviews. Results emphasised the importance of interactions among the drivers, sources and pathways of disease which formed the framework for the risk analysis approach. Using data collected from these expert sources we developed an algorithm-based tool for considering future disease risks and decision-making on the need for and use of detection, identification and monitoring (DIM) technology. The possible application of this decision-making tool is illustrated using exemplars derived from expert case studies. Decision-making in other areas may benefit from a similar modelling approach that allows a complex interdisciplinary risk situation to be broken down into more manageable elements.

Introduction

The UK Foresight Infectious Diseases project on Detection and Identification of Infectious Diseases (DIID) (Foresight, 2006) was conducted by the UK Office of Science and Innovation¹ on behalf of the Chief Scientific Adviser, Professor Sir David King. It aimed “to produce a vision of future systems for the detection, identification and monitoring of infectious diseases, and to assess how they might transform our capabilities in managing the future threat”. The risk analysis element of the project contributed to that aim by developing a basic framework for *Foresight* in the context of infectious diseases that linked scientific and socio-economic aspects promoting or inhibiting disease emergence.

In this paper we will show how we developed this process, leading to a decision-making algorithm, from this empirical work. Detailed empirical results can be found in Tait *et al.* (2006) with highlights available in an article summarising the entire *Foresight* project (King *et al.*, 2006). Using the results from the risk analysis we were able to generate an integrative, interdisciplinary model for a several-step process capturing both natural science and socio-economic risk factors. Designed to complement the work of medical and epidemiological researchers, such a decision-making tool should help policy- and decision-makers understand better the wider picture surrounding an issue of concern – in this case the threat of infectious disease – by assessing scientific data within a broader context.

There is general recognition within the risk literature of the dangers of over-reliance on science and calls for a more holistic and strategic approach to planning for infectious disease outbreaks which integrates natural and social science factors (e.g. Smith, 2006; Casman *et al.*, 2000; Gregory *et al.*, 2006). More widely, others have called for the need

¹ www.dti.gov.uk/science/science-tech-and-dti/index.html

for contextualisation in an attempt to embrace the unpredictable implications of science (Gibbons, 1999). The future of infectious disease outbreaks underscores the simultaneous necessity and impossibility of predicting the unpredictable. Risk analysis is a well-recognised tool for decision-making in the face of uncertainty. It facilitates the communication of risks and their consequences to stakeholders and decision-makers, allowing them to choose appropriate safeguards in a transparent fashion (Giovannini *et al.*, 2004). Not only does risk analysis need to take into account multiple interacting social as well as natural science factors, it must also, if it is to underpin sound risk management, help decision-makers contend continuously with complexity, uncertainty and new and emerging risks, as highlighted here by consideration of future risks of infectious disease. Referring to the inevitability of surprise, the OECD (2001) has noted that risk management strategies need to “better incorporate forward-looking methods, and in particular to evaluate and understand the impact of the driving forces of change.” Contributing to the unpredictability of disease risks is the diversity of factors playing a role and the complexity of their interactions, both of which affect the emergence and spread of diseases, including those already reasonably well understood. For example, Chan *et al.* (1999) promoting an integrated assessment framework for climate change and infectious diseases, noted that climate-influenced changes in the incidence and spread of disease “would be mediated through biologic, ecologic, sociologic and epidemiological processes that interact with each other”, and went on to recognise “the difficulty of including the multitude of always-changing determinants of these diseases.” A report on linkages between globalisation and infectious diseases referred to “the need to pay greater attention to the impacts on the infectious disease burden of policy decisions taken in other sectors e.g. trade and investment, large infrastructure projects (e.g. dam building), migration, agriculture, transportation, communications.” (Saker *et al.*, 2004)

When looking at a future likely to be the result of known and unknown interacting factors and as-yet-unknown emergence of disease, a reasonable goal may well be an effective method to analyse risk qualitatively, rather than an expectation of quantification (Kaferstein *et al.*, 1997). For example, a group of modellers and health policy experts brought together to explore the usefulness of mathematical models in helping with bioterrorism (e.g. smallpox) preparedness and response came to the conclusion that models can be useful, within the context of “reasonable expectations”: noting that, while models will not provide accurate numerical predictions of outcomes, they can provide “a means to systematically compare alternative intervention strategies, determine the most important issues in decision-making, and identify critical gaps in current knowledge” (McKenzie *et al.*, 2004).

Matthews and Woolhouse (2005) argue that progress in the rapid detection, identification and assessment of an infectious disease threat requires greater familiarity of public health and animal-health scientists with mathematical modelling, and a greater familiarity of mathematical modellers with the requirements and expertise of public health and veterinary sciences. In the case of newly emerging or changing diseases, for which the dynamics would not be easily predictable, it would be useful to be able to “red flag” those situations most likely to become high-risk. We therefore argue for an additional layer of analysis – beyond mathematical modelling – that augments biological and epidemiological understanding with an appreciation of the social and other drivers likely to come into play. Through such an identification and analysis, decision-makers can gain the capacity to take into account various factors which, while apparently disparate, are necessary to sound consideration of possible futures. Decisions may need to be

taken by a diverse range of actors at varying points in the policy-making process and the effectiveness of the response may hinge on the quality of that decision-making (Smith, 2006).

Understanding the causes of infectious diseases requires an appreciation of macro- and micro-level factors and a multiplicity of analytical approaches (Diez Roux and Aiello, 2005). Non-expert decision-makers need accessible tools to confront this complexity and unpredictability, so that early decisions can be made that are well-grounded and unlikely to miss key factors which might act to accelerate or intensify risk.

Pedersen (1996), for example, encourages “the construction of a new socio-epidemiological model for tracing health determinants, explaining disease resurgence and the emergence of new diseases and epidemics” so as to recognise the full “ensemble” of determinants. A key aim is to improve “understanding of reciprocal relationships between multiple causes and effects, constructing new paradigms and shedding light on the broader social, cultural and political issues influencing the health status and disease experience of large segments of the world population.” The complexity of the challenge is reflected in the array of expertise needed to address it. As noted by senior figures at the US Center for Disease Control, “Gaining a better understanding of zoonotic disease emergence, prevention, and control requires quality basic and applied research, which results from extensive interaction and collaboration among professionals from multiple disciplines” (Marano *et al.*, 2004).

Transboundary and zoonotic diseases that cross species “barriers” epitomise the challenges involved. In the absence of accurate prediction capability, we have developed an approach, based on a simple but multi-faceted model of disease emergence that will allow early and rapid response to future disease risks which combine unpredictability with the potential for enormous social and economic costs.

Thus, a forward-looking analysis of the type we are proposing here can help decision-makers to prioritise at an early stage the level of attention that needs to be paid to new, emerging or expanding/changing risks. Decisions would become more fine-tuned as more data were collected, but a first, broad-brush prioritisation based upon understanding of driving forces of change could accelerate the speed with which potentially high-risk diseases were identified and managed. In coping with risks of the spread of infectious diseases, for example, decision-making might take the form of investment in developing detection, identification and/or monitoring (DIM) technologies tailored to selected disease species or families.

We suggest a simple algorithm, similar to a scenario tree approach (De Vos *et al.*, 2004), as a timely heuristic device for assessing risk using the risk of spread of infectious disease as an illustrative example. Derived from empirical findings of the analysis, the algorithm presented here in a general form could be adapted to suit specific disease contexts. Indeed, this approach could be tailored to algorithms helpful in consideration of other risks shaped by complexity and changes in social as well as technical drivers.

We begin by outlining the key elements of the methodology adopted for the risk analysis component of the *Foresight* project. Next, we describe how we used the empirical data gathered from this expert survey to develop an integrative risk analysis process in order to construct the decision-making algorithm. We then test this algorithm in two ways, first,

using a simplified, hypothetical case and, secondly, using two live situations derived from expert case studies provided by the *Foresight* project. We conclude with a discussion of the likely utility of this approach in the context of other risk studies.

Methodology

In contributing to the *Foresight* project's ability to look to the future of infectious diseases and management of the threats they pose, we developed a basic framework that captures the context of infectious diseases by linking scientific and socio-economic aspects that promote or inhibit disease emergence. This framework was used to structure a questionnaire-based survey of experts in plant, animal and human diseases in Africa and the UK, focusing on future disease risks in 2015 and 2030. The survey was complemented by a series of case studies by expert reviewers, along with responses to a set of open questions based on the risk framework. Finally, the framework was refined to produce an algorithm to aid decision making on the adoption of detection, identification and monitoring (DIM) technology.

Developing the Risk Framework

In order to develop a framework to guide the risk analysis, several workshops were held to explore expert views on future risks, sources, pathways and drivers involved in the future emergence of new infectious diseases or changes in risk patterns of known diseases. Through iterations with scientific experts, a framework for infectious disease processes was developed as the basis for the risk analysis. Figure 1 outlines the basic framework for the risk analysis, involving *drivers* that operate on infectious disease systems, through *sources* of disease emergence and/or through *pathways* of transfer of disease organisms, or both, in order to determine *outcomes* in terms of future diseases and levels of infection. Definitions of these components of the framework, agreed in discussion with project scientists, were:

Disease sources: phenomena or biological events that: give rise to potential new diseases; enable existing diseases to become more harmful; enable existing diseases to infect new hosts; or enable existing diseases to spread to new areas. (Examples of sources might include the emergence of new disease vectors or increased pathogen resistance.)

Pathways: a mechanism or route by which a disease organism can transfer from one host to another, within or between species.

Drivers: social, economic or physical factors that affect disease outcomes by changing the behaviour of disease sources or pathways. Socio-economic drivers arise where human behaviour is directly responsible for creating conditions conducive to disease emergence and/or spread, by bringing together human systems in interaction with one another and/or with the natural world. (The drivers identified were grouped into the following categories: legislation and systems of government; technology and innovation;

conflict and war; economic factors; human activity and social pressures; climate change.)²

Outcomes: plants and animals at the individual, community and ecosystem or farming system level, and humans at individual and societal levels, that are affected by infectious diseases

The subsequent components of the risk analysis were all structured on the basis of this model and descriptions of possible sources, pathways and drivers were derived through iterative discussions with scientific experts and the *Foresight* project's science steering group.

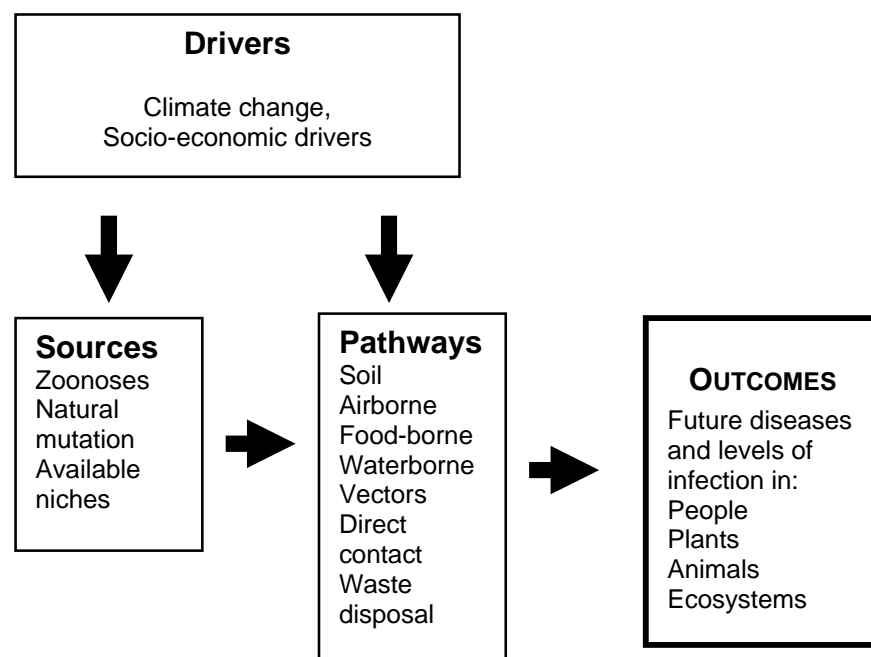


Figure 1. Basic framework for infectious disease risks.

Survey

These lists of possible sources, pathways and drivers were summarised to develop a minimum set of questions which would be suitable for use in a questionnaire-based survey. Six homologous questionnaires were designed, tailored to each of the situations being studied so as to capture developed and developing countries for the three foci of plant, animal and human diseases³.

² A full list of all sources, pathways and drivers identified for this project is given in Tait *et al.* (2006).

³ Africa-Animals, Africa-Humans, Africa-Plants, UK-Animals, UK-Humans, UK-Plants.

The survey generated qualitative risk estimates that allowed us to compare the importance of a range of sources, pathways and drivers in contributing to future disease outcomes for animals, plants and humans in 2015 and 2030, in Africa and the UK. We then developed road maps to disease outcomes using a strategic planning tool, Decision Explorer, widely used in research on strategic planning to provide visual descriptions summarising and comparing the outcomes of discussions or analyses. In this case, the maps – termed “Influence Maps” (see e.g. Casman *et al.* 2000) – showed, among other things, the much denser array of sources, pathways and drivers expected to be leading to high levels of risk in 2030 in Africa compared to the UK. Visualising the findings in this way facilitated the identification of patterns, outliers and linkages, thus contributing to the bigger picture of the analysis while still retaining individual points⁴.

Expert Reviews

Questionnaire-based surveys inevitably constrain the views of experts within a predetermined framework. In this project, the linear framework developed in Figure 1 enabled us to simplify the survey results to make their implications easier to understand. Yet in reality for any evolving or emerging new disease, the impact on human, animal or plant populations will probably only be significant and sustained if several drivers interact with each other and with a source and/or pathway, creating feedback that, in turn, leads to build-up of populations of disease organisms to dangerous levels.

To investigate these more subtle interactions we invited eleven selected experts to write case studies, explaining and predicting the course and impacts of various key diseases, along with the risk parameters and interactions that influence these dynamics. Important in themselves, these studies provided background information for the development of our understanding of future risks in various disease categories⁵. Responses amplified the understanding generated by the survey and shed light on linkages across plant, animal and human diseases. These experts also considered early warnings of risk and pointed to potential critical inflection points where interactions among drivers may trigger unexpectedly rapid emergence of new diseases, or changes in prevalence or range of existing diseases. In addition, they highlighted important areas of uncertainty and challenge in detection and identification.

Developing an Integrative Risk Analysis Process

A key message from the expert reviews was that dynamic interactions among drivers, sources and pathways can greatly amplify, or indeed diminish, the hazards generated by any one factor in isolation.

Reviewers also emphasised the stochasticity of evolutionary processes in disease *sources*, leading to the unpredictability of new diseases. Zoonoses are of very real concern; these are human diseases emerging from other species' reservoirs, usually from association with livestock, animal-based food products, exotic game animals as in

⁴ Detailed survey results and analysis including Influence Maps are provided in Lyall *et al.* (2006), Tait *et al.* (2006), and Suk *et al.* (Innogen WP54).

⁵ These studies are published as Disease Case Studies T5.1 to T5.12 at www.foresight.gov.uk/Previous_Projects/Detection_and_Identification_of_Infectious_Diseases/Reports_and_Publications/Final_Reports/Index.html

the bushmeat trade, or pets. Again, such interactions are shaped by changing social and behavioural trends.

The future development of an infectious disease may well be influenced by multiple, interacting factors, with combinations of pathways and drivers often playing an important role, as hypothesised for the emergence in humans of HIV and hepatitis B from chimpanzees, involving animals killed as a food source being cross-contaminated with hepatitis B and HIV-bearing blood, facilitation of disease spread by sexual intercourse, poor hygiene and/or tattooing, and extension internationally by global air travel and sexual tourism. Social drivers as well as biological parameters were clearly seen as necessary to inform effective modelling for complex situations, with one African respondent noting, for example, the need to incorporate changes in drivers such as access to/coverage of interventions, settlement patterns, land use and population growth, as well as influences such as HIV, poverty and nutritional status.

A recurring message was that detection and identification technologies will inevitably be deployed in situations shaped by changes in disease sources, pathways and multiple drivers, and by the interactions among these factors. Future disease management will require appreciation of all these factors and of their interactions, particularly in the face of newly emerging diseases.

When asked to identify ways of using early warnings of likely high risk, and to consider critical inflection points at which investment in detection and identification technologies could make a significant difference, experts frequently referred to the challenges of detecting and identifying novel disease agents, with a need for “vigilance” in rapidly diagnosing emergent diseases and identifying key indicators of the likelihood of spread, along with monitoring and control. In other words, some risk management will need to be prioritised and implemented before all the data regarding possible risks are available.

The Influence Maps, derived from experts’ responses to surveys, assisted us in tackling the question of future risks of emergence of infectious diseases, but only in a general context. If related to specific disease contexts, however, these diagrams could contribute to early warnings of high risk situations, and to related decisions on management such as investment in detection, identification and prioritisation of monitoring in order to constrain the spread of disease. The use of such tools needs to be grounded in research and in expert understanding. The Influence Maps thus have the potential to be translated into the sort of forward-looking method desired by many, in that they provide a clear framework of high, moderate and low drivers of change that influence the incidence and spread of disease. We suggest that survey data on expected sources, pathways and drivers of future disease risk can be combined with information from the more discursive expert reviews to feed into an integrative risk decision-making tool (Figure 2).

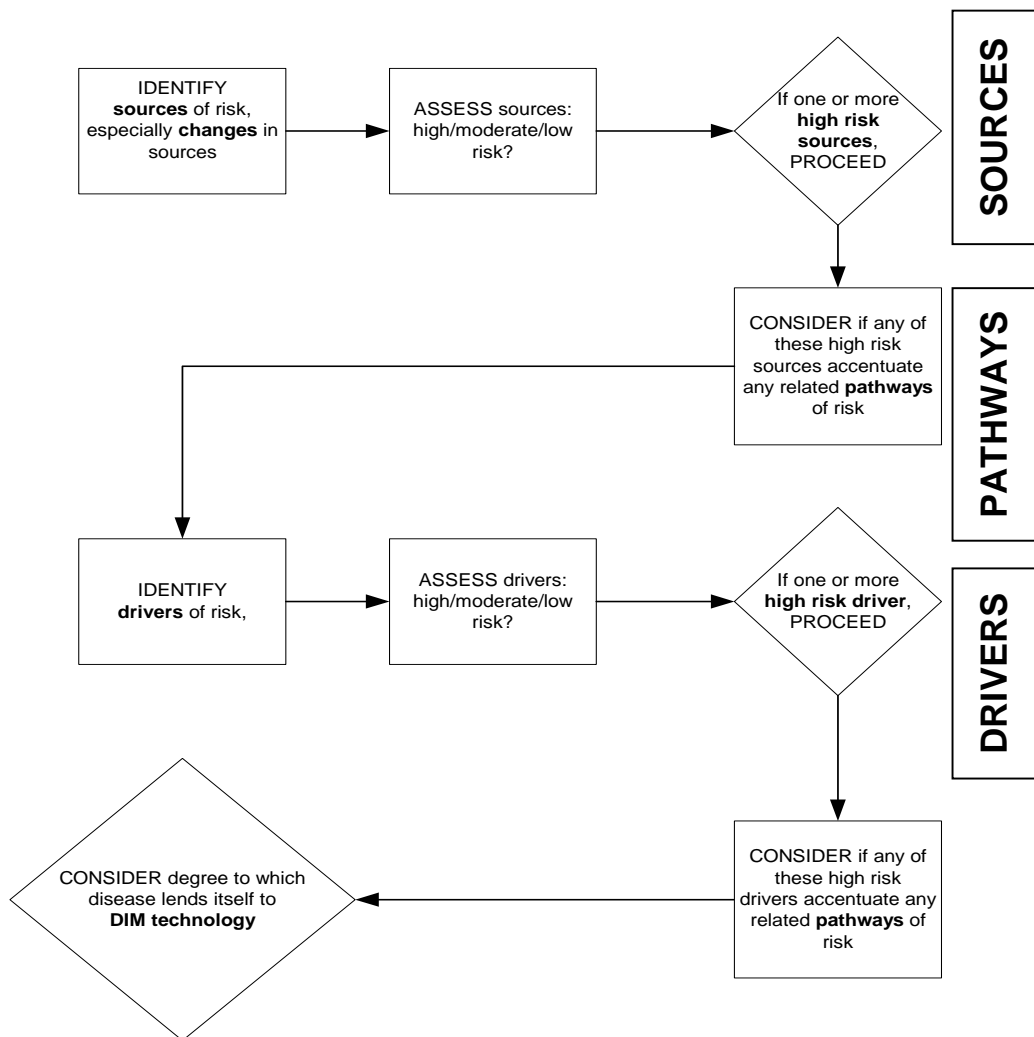


Figure 2. Integrative risk decision-making tool

By incorporating social with other factors, this layer of analysis can complement real-time data on incidences of disease and other epidemiological considerations, for which a flow chart or algorithm is a familiar concept. The user can apply the algorithm or framework suggested here as a series of checklists when considering the likely risk of disease.

Application of the algorithm is most likely to be useful for early warnings in the case of new, emerging, changing or expanding diseases. If the use of this algorithm flags up a synergistic combination of sources, pathways and drivers that has the potential to generate a serious disease threat, then this should signal a range of precautionary responses. In the context of a specific disease setting, such a combination of alerts or “Red Flags” generated through the algorithm could lead to an expectation that the outcome is likely to be significant spread of the disease. For example, an emerging, potentially serious disease which lacks a relevant pathway and involves no high-risk drivers may be unlikely to spread beyond a limited area. At the other end of the spectrum, if an emerging disease involves a high-risk source which could readily take advantage of one or more transmission pathways, and also involves two or three high risk drivers, at least one of which accentuates the ability of a pathway to transmit the

disease, a series of precautionary measures should be considered, depending on the nature of the disease.

Between the two ends of the spectrum lies the province of judgement. However, if consideration of relevant drivers indicates potentially synergistic interactions and the source is itself high-risk, then it would be prudent to pay serious attention.

If the cumulative level of risk is indeed high, such that the cost/benefit ratio is likely to be positive for early investment in technologies, the next step is to consider the degree to which the disease lends itself to effective detection, identification or monitoring by technologies (such as those identified by other authors in the suite of "Infectious Futures" publications) and also whether there are treatments available.

Thus, a decision-maker working through this algorithm would be able to consider in a logical manner those diseases which would merit investment in dedicated detection, identification or monitoring technology. Accelerated development of such technology, targeted to high risk situations, may well be worth the investment, as illustrated in the following hypothetical case study.

Hypothetical case study: Human Diseases

A new human Disease A has emerged from an animal reservoir, transmitted via meat preparation and consumption (Red Flag for Source of Other Species). It has arisen first in a poverty-stricken area torn by war (Red Flag for Drivers 'Conflict' and 'Economic Factors') and characterised by movements of populations with their livestock (Red Flag for Driver 'Movement').

Conditions of poor hygiene prevail (Red Flag for Driver 'Reduced Quality of Sanitation' and 'Foodborne' pathway), and capacity for controlling disease is compromised (Red Flag for Driver 'Lack of Adequate Systems for Disease Control'). The area also receives international aid workers (Red Flag for Driver 'Increased Travel'). The local drivers accentuate the effectiveness of the pathway of faecal contamination (Red Flag for Pathway).

This disease should merit rapid and intense response, with heavy investment in the development and implementation of detection and identification technology, even if identifying the right target molecules requires significant work.

On the other hand, if a new human Disease B emerges from a source that may be potentially high-risk but is characterised by none of the high or even moderate risk Drivers above, it is less likely to warrant a full scale initiative for developing new detection and identification technologies.

Two Case Studies of Possible Adoption

While this may seem rather obvious in a simplified, hypothetical example, it would not be so clear-cut in a real case, particularly in the early stages of an emerging infectious disease where there are likely to be gaps in information making it difficult to judge the relative importance of specific risk factors. Having demonstrated how the algorithm might work in a hypothetical case, we therefore sought to test it with actual disease

occurrence examples drawn from the *Foresight* project⁶. The following are summaries of our detailed interrogation of two of these case studies using the algorithm to assess whether, in each case, there was a synergistic combination of sources, pathways and drivers with the potential to generate a serious disease threat.

Case Study 1 - MRSA Infection

Identify and assess changes in sources of risk: Methicillin-resistant *Staphylococcus aureus* (MRSA/Methicilin) is an example of increased pathogen resistance to antibiotics, expected to continue to evolve in new forms. While seen now as an example of a hospital-acquired infection, it is likely to spread into the wider community, with new strains possibly highly transmittable. At the same time, the number of vulnerable people with compromised immune systems continues to grow in society. Thus the upcoming disease threat will be “community-acquired infections”.

Do these changes in sources accentuate pathways of risk?: Humans can carry and spread the pathogen without themselves manifesting the illness or being diagnosed as carriers. Spread outward into the community is likely via host-to-host infection, through people and association with livestock, pets and wild birds.

Identify and assess drivers of risk: Use of antibiotics has given rise to rapidly evolving antibiotic-resistant organisms such as *Staphylococcus aureus* that is resistant to methicillin (MRSA). Particularly as the pathogen spreads out into the wider community, beyond hospitals (which themselves may be challenged by restrictions in budgets or facilities), there is currently a lack of adequate systems for detection and identification, surveillance and control, along with a lack of sufficiently effective drugs for control of “community-acquired MRSA”. Yet, the number of “easy targets” out in the community is rising rapidly, due to, for example, medical capacity to prolong lives of immunocompromised individuals, growing incidence of HIV infection globally, and an increased number of people in non-hospital settings that concentrate vulnerable populations (such as long-term care homes).

Do these changes in drivers accentuate pathways of risk?: Concentration of vulnerable individuals, in hospitals and in various settings out in the wider community, facilitates the spread of the pathogen.

Consider degree to which disease lends itself to DIM technology: Technological advances have already been made in detection and, potentially, control within the hospital setting. Speeding up rapid microbiological detection methods will be key to early accurate diagnosis, effective treatment or indeed steps addressing dispersal out in the community. This might take place, for instance, through molecular probes for genetic markers that differentiate the “superbugs”, combined with a cost-effective automated detection system. Although it would not necessarily be cost-effective (or indeed feasible),

⁶ Eleven expert reviews were commissioned for the project. These two sample cases – MRSA infection and Potato late blight – were selected as representative of the breadth of topics covered in these reviews and in order to illustrate a human and a plant disease. The original case studies can be found in Foresight reports T5.1 and T5.7 at www.foresight.gov.uk/Previous_Projects/Detection_and_Identification_of_Infectious_Diseases/Reports_and_Publications/Final_Reports/Index.html

development of a simple, sensitive screening technology would help MRSA to be detected within the larger numbers of a wider population; however, a significant challenge to surveillance would need to be overcome: that individuals may carry different MRSA strains (which rapidly evolve) and sampling will be difficult as MRSA is not evenly distributed even within one individual.

Decision: Even as steps are being taken to decrease endemic MRSA levels in hospitals, “community-acquired MRSA” is likely to increase, in part via concentrations of vulnerable individuals outside of hospitals, posing challenges not only to health care but also to technological development. Investment in technologies for rapid, early diagnosis would facilitate early treatment, in hospitals and beyond, and could inform steps to limit spread. A more detailed cost/benefit analysis, combining scientific, technological and financial/policy considerations, would be needed to determine whether or not large-scale screening or surveillance technology would be a viable goal.

Case Study 2 – Potato late blight (*Phytophthora infestans*)

Identify and assess changes in sources of risk: *Phytophthora infestans* was originally introduced to Europe from overseas. New genotypes and, importantly, a new mating type have recently been introduced from Mexico. The sexual reproduction made possible by the second mating type could facilitate emergence of new strains of the pathogen.

Do these changes in sources accentuate pathways of risk: Spores can disperse via air; infection can spread via infected tubers over-wintering in soil in fields or disposal piles. Subclinically infected seed potatoes or ware tubers can spread infection, as when they are imported.

Identify and assess drivers of risk: Pathogen spread is usually caused by importation of subclinically diseased tubers, so trade is a key driver. Poorer countries are more susceptible, being less able financially to tackle the disease. Breeding for resistance is difficult. A conservative industry’s requirements for familiar cultivars can lead to highly susceptible cultivars suffering yield loss and spreading infection to other crops. Trends in demands from consumers and environmentalists exert pressure on farmers to use less fungicide and/or justify use in some detail, although fungicides are the primary control method. A rise in temperature, with a predicted increase in relative humidity, could act as a climate change driver increasing risk.

Do these changes in drivers accentuate pathways of risk?: Various pathways can spread the disease; the introduction via trade of aggressive new genotypes and a new mating type greatly accentuate risk in Europe.

Consider degree to which disease lends itself to DIM technology: New molecular methods have the potential to increase sensitivity and speed of detection, potentially effective even in bulk samples. Some detection methods may be developed for field use, but some detection may take place too late to bring the disease under control. If molecular markers could be developed for resistance to the pathogen, breeding host plants for resistance would benefit. Improved blight forecasting models could help farmers ensure that they are not applying more fungicide than necessary (and justify their decisions to others), if they become able to combine complexity with practicality.

Decision: Potato late blight is an aggressive disease attacking a major crop globally; it can cause total crop destruction and consequent human/social costs, as seen most dramatically in the Irish potato famine. Between depressed yield and cost of (usually fungicide) control, its negative impact worldwide has been estimated at \$5 billion, annually. Wherever potatoes are grown the blight is found so, as a threat it is omnipresent. New techniques for detection could be useful: 1) in assessing imports, especially as seed potatoes and ware tubers can be infected at subclinical levels; 2) in finding infection *early* in the field, for a particular farm. Development of molecular markers for (complex) resistance to the pathogen could be very helpful in tackling the challenge of breeding resistant cultivars.

Discussion and Conclusion

The challenges of forward-looking risk analysis and management generally can be highlighted by consideration of future risks of infectious disease. The future will be a dynamic, ever-changing world in which new diseases arise, the range of some existing diseases expands and the toll taken by certain diseases appears to increase as the diseases change or find new targets. On the other hand, some currently important diseases will diminish in their impact, and some potential new or expanding diseases will fail to find conditions that allow them to reach epidemic status, for example where the necessary combination of drivers and pathways does not materialise. False alarms can have huge economic costs and can seriously undermine public confidence, making it just as important to avoid causing unnecessary alarm as it is to predict accurately serious new, emerging and changing disease outbreaks. Epidemiology, population dynamics, clinical surveillance, and new methods of detection and identification will all contribute to our ability to recognise new and emerging disease phenomena and to predict their future status.

Decision-makers may also find it useful to draw upon additional understanding when forced to make early decisions as to the likely importance of particular disease phenomena. This risk analysis has drawn together several lines of evidence, based on surveys, and augmented by case studies, expert views and workshops. These have contributed to the development of a Risk Framework and Influence Maps that enabled this analysis to meet its objective of informing the 'Infectious Futures' Project on factors relevant to future infectious disease outcomes for humans, animals and plants in Africa and the UK. The request to carry out this risk analysis represented a considerable challenge as we were not able to identify any precedents on which we could build. Thus, the process we developed to conduct the analysis may prove to be a useful basis for future studies of disease risks, or perhaps indeed other sorts of risks.

In the past, there has been concern that, if epidemiology moves beyond the scope of the natural sciences, then it will lose credibility in the scientific community (Vandenbroucke, 1994 cited in Wilby, 2005) but others have argued that a more holistic, multidisciplinary systems approach to the study and control of emerging infectious diseases could improve the process of public health policy-making and that these approaches cannot always be based in the languages and models of mathematics or natural science (Wilby, 2005). We concur with Wilby in concluding that it is only prudent to expand the range of disciplines used in the investigation of emerging infectious diseases to identify proactively emergent properties and that the human, social and political interests represented through qualitative data gathering and the technical and practical interests

represented through quantitative data gathering be incorporated into the same databases.

Although a body of published literature does exist in the area of interconnection, and there have been calls to consider a more integrated, holistic approach to risk by developing conceptual models for understanding infectious disease, and the implications of such a model for public policy (Koren and Crawford-Brown, 2004), few have included economic, political or social science factors in these models, despite the fact that these are clearly critical factors in any public policy.

Those making decisions on the management of infectious diseases will already be knowledgeable about, and comfortable with, conventional biological parameters and indicators of disease dynamics. However, the integrative risk analysis algorithm outlined here can help to enrich decision-making by bringing together information about sources, pathways, drivers and their interactions and by indicating how or why they might combine to generate important new risks. The algorithm is thus a form of predictive model to estimate the severity of effect and combines an analysis framework approach with a conceptual model. The former shows the steps in analysis or decisions that must be performed to get from problem formulation to risk assessment. The latter approach shows the entities and/or activities that play a causal role in producing that risk (Koren and Crawford-Brown, 2004). By helping decision-makers deal with the complexity of interacting contextual factors, this algorithm could thus contribute to delivering better decisions as to investments on, or use of, detection, identification and monitoring technology for a particular emerging disease.

In general, government policy is not good at tackling multi-factorial problems in an integrated manner (Lyll and Tait, 2005). The *Foresight* project highlighted the importance of fostering interdisciplinary approaches to infectious diseases in order to bring to bear a better understanding of the socio-economic factors that influence disease spread. Determining the relations between these factors and understanding the dynamic relationships between sources, pathways and drivers of disease remains a challenge. The framework, methods and algorithm developed here are offered as a set of tools which could be adapted to suit specific circumstances as new infectious diseases emerge or existing diseases expand in range or increase in virulence.

The process by which this set of tools was developed could also be adapted to generate tools useful for decision-makers dealing with risks other than diseases. As appreciation grows for the roles that socio-economic drivers play in the nature, degree and dynamics of future risks in a variety of areas, decision-makers may want to incorporate such drivers into their considerations of risk and prioritisation of risk management action steps. Development of a multi-faceted, accessible, easily utilised algorithm from expert input could make the unmanageable a bit more manageable and help prioritise response, particularly at the early stages of emerging, complex risk situations.

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