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**THE INTERCONNECTED AND CROSS-BORDER NATURE OF RISKS
POSED BY INFECTIOUS DISEASES**

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Abstract

Infectious diseases can constitute public health emergencies of international concern when a pathogen arises, acquires new characteristics, or is deliberately released, leading to the potential for loss of human lives as well as societal disruption. A wide range of risk drivers are now known to lead to and/or exacerbate the emergence and spread of infectious disease, including global trade and travel, the overuse of antibiotics, intensive agriculture, climate change, high population densities, and inadequate infrastructures, such as water treatment facilities. Where multiple risk drivers interact, the potential impact of a disease outbreak is amplified. The varying temporal and geographic frequency with which infectious disease events occur adds yet a further layer of complexity to the issue.

Mitigating the emergence and spread of infectious disease necessitates mapping and prioritising the interdependencies between public health and other sectors. Conversely, during an international public health emergency, significant disruption occurs not only to healthcare systems, but also to a potentially wide range of sectors, including trade, tourism, energy, civil protection, transport, agriculture, and so on. At the same time, dealing with a disease outbreak may require a range of critical sectors for support.

As such, there is a need to move beyond narrow models of risk to better account for the interdependencies between health and other sectors so as to be able to better mitigate and respond to the risks posed by emerging infectious disease. By addressing this topic, this paper will offer a novel and important contribution to discussions about how HFA2 can address complex risk.

1. Introduction

The emergence and spread of infectious diseases is deeply entwined with the circumstances in which human society is organised. This has long been the case; human interactions with animals hosts have led to infectious disease outbreaks dating at least as far back as the Justinian Plague (541-542 AD), while global trade and travel have facilitated disease transmission, whether of the plague in the 14th century, smallpox in the 16th century, SARS or a novel influenza virus in the 21st century (1-3). Indeed, it is often noted that in today's interconnected world a disease can spread nearly anywhere on Earth within 24 hours.

Infectious disease risks are necessarily understood as interconnected and interdependent – but this is not simply because of globalization. A great many factors, some not restricted to the disease control or public health arena, can influence the spread of infectious disease. Assessing disease-related health risks thus necessitates understanding where they might arise and how successful it might be in transmitting. The largest risks tend to occur when novel diseases appear, when familiar diseases appear in novel geographic locations, or when preventative disease control measures break down, whether due to socioeconomic inequalities, lack of resources, accident or conflict.

In this Chapter, the interconnections and interdependencies that create (and are created by) emerging infectious diseases will be introduced, guided by a couple of topical examples. Section 2 will discuss the types of factors that can influence the spread of infectious disease. Section 3 will provide some examples of recent infectious disease incidents that have been created by the interconnectedness of factors introduced in Section 2. Section 4 will discuss some of the integrated risk

modelling approaches that have been developed to attempt to monitor and even predict infectious disease transmission, and Section 5 will summarise this Chapter by reiterating the need for and importance of recognising the interconnected and interdependent nature of infectious disease risks.

2. Infectious disease drivers and interconnected risk

Within the field of health, interconnected risks can be broadly defined as those for which factors traditionally viewed of as "external" to health or disease can nonetheless impact a health risk. Emerging infectious diseases, for example, can easily be viewed of as interconnected because their risk can be driven by a wide range of "externalities". They can be viewed of as interdependent because of their transboundary nature, and because risks from other sectors can interact synergistically or antagonistically. In addition, the emergence of an infectious disease risk can both be amplified by and amplify risks in other areas, from employee absenteeism and workforce shortages to potential social disruption, severe disruptions in energy, healthcare delivery, transportation or other sectors (4, 5).

There are many different ways in which the myriad factors that influence infectious disease could be categorised. For the sake of simplicity, the remainder of this discussion is derived from a study which grouped them according to three broad (and somewhat artificial) categories: globalization and environmental change; social and demographic factors; and health and agriculture (6). It should be noted that although in the following sections each set of factors will be discussed individually, they are themselves often interconnected, adding an additional layer of complexity to the issue. Furthermore, the examples provided below are merely indicative and not exhaustive.

Globalization and environmental change
A wide range of infectious disease drivers can be grouped under this category, including climate change, land-use patterns, global trade and travel, migration, and so on. Climate change involves mean temperature and precipitation increases in many parts of the world, as well as increased likelihood of adverse or even extreme weather events (7-9). Many infectious-diseases are temperature-sensitive, as are the hosts for numerous zoonotic diseases, particularly vector-borne diseases. There is thus a substantial body of research that collectively demonstrates that climate change will likely lead to, at the least, some significant shifts in the geographical ranges within which infectious diseases transmit (10-14).

Land-use patterns, meanwhile, are a crucial driver of infectious disease emergence. It has been estimated that more than 60% of human pathogens are zoonotic (i.e. diseases of animals that can be transmitted to humans) (15). Many human land-use activities, including agriculture, irrigation, hunting, deforestation, and urban expansion, can cause or increase the risk of zoonotic and food- and water-borne diseases (15, 16). For example, one consequence of urban sprawl and deforestation is that wildlife may increasingly need to find

new habitats, sometimes in urban or abandoned environments which can than lead to increased human exposures to infectious pathogens. Meanwhile, the density of human population, also associated with increasing urbanization, has also been shown to be linked to the emergence of many infectious diseases (17).

Intensified global trade and travel, not to mention migration, render political borders irrelevant and create further possibilities for global disease transmission (18-20). There are numerous examples of the arrival, establishment and spread of "exotic" pathogens to new geographic locations, including malaria, dengue, Chikungunya, West Nile, and bluetongue in recent years, aided by shipping or other trade routes (18). This process is facilitated when the environmental conditions in different parts of the world share common characteristics (18). Meanwhile, numerous vaccine-preventable diseases, such as polio, meningitis or measles, can also be introduced or re-introduced to susceptible populations as a consequence of international travel (21).

Social and demographic factors
Social and demographic contexts can significantly influence the transmission of infectious disease, while also creating increased vulnerabilities for some population subgroups. The elderly are at greater risk of many infectious diseases, and the ageing trend in many high income countries could increase the challenges related to nosocomial (hospital-acquired) and nursing-home acquired infections. An additional challenge related to population ageing is that the share of employed workers in a country decreases; the combination of more people to care for and fewer tax-related revenues may challenge publicly financed public health and disease control programmes (6). As migration is a common a strategy to offset population ageing, persons from regions with high endemicity of a given disease may move to ones with lower endemicity, thereby further creating opportunities for disease transmission and challenges for public health.

It is widely established that socially and economically disadvantaged groups suffer disproportionally from disease (22), and this is the same for infectious diseases in Europe (23, 24) and other high and low income settings. Income inequalities are generally widening globally, and this appears to be have been exacerbated in many countries due to the global economic crisis (25). Rising unemployment and the prospect of public health budget cuts can increase the risk of infectious disease transmission (24, 26), with the most prominent example being an outbreak of HIV among people who inject drugs in Greece (see section 3.2) (27, 28). In a similar fashion, it has been speculated that tuberculosis rates could rise in some countries in Central and Eastern Europe (29) .

Social trends and behaviours can also play a significant role in infectious disease transmission. The most notable example would be so-called vaccine hesitancy, the phenomenon through which vaccination coverage rates remain suboptimal due to the varying and complicated reasons that individuals may have for not getting vaccinated (30, 31). In some cases, this might be related to

misconceptions about the safety or efficacy of vaccines (30, 32), whereas in others this may be related to religious or cultural beliefs (33).

Health and agriculture
The delivery of healthcare, the availability of vaccines, antivirals and antibiotics medicines, as well as the avoidance of the over-use of antibiotic consumption, are all important public health factors related to infectious disease control. One critical factor affecting how such services are delivered relates to health system financing. Although the correlation between healthcare system financing and efficacy is not perfect, recent budget cuts to healthcare are of some concern. In part related to the global economic crisis, it has been reported that many high income governments have introduced policies to lower spending through cutting the prices of medical products and, for example, through budget restrictions and wage cuts in hospitals (34). There are many indirect and direct pathways through which budget cuts could affect disease transmission; to provide just one example, it has been estimated that 20-30% of healthcare-associated infections are preventable with intensive hygiene and control programmes [i] – should investments in this area diminish, then healthcare-acquired infections could become an even more problematic issue. There are roughly 4.1 million healthcare-associated infections each year in the EU alone.[ii]

A broader issue related to healthcare provision is population mobility for both healthcare professionals and patients who might increasingly seek work or healthcare in other countries – the provision of cross-border healthcare and the mitigation of cross-border health threats will necessitate collaboration across borders (35, 36) and solutions for the brain-drain of medical personnel from resource-poor countries (37).

Food production systems remain a persistent source for human infectious diseases. Attempts are underway to estimate the global burden of food-borne disease (38), which is likely substantial. Many factors in food production affect human health. A vast range of familiar human pathogens can be acquired through the consumption of animal products and other disease drivers, such as global travel, further provoke this (39). In addition to farmed animals, the hunting and slaughtering of wild animals has led to the emergency of more exotic pathogens: SARS originated in wildlife markets and restaurants in southern China (40) and HIV and Ebola have both been linked to the hunting or slaughtering of primates and other wild animals (15, 41, 42). The density and health of livestock, meanwhile, have been linked to disease in humans (43, 44). Although inconclusive, there is some evidence to suggest that livestock production may lead to increased antibiotic resistance in human pathogens. There are certainly many pathways by which drug resistant pathogens could transmit from livestock to humans, including environmental contamination by excreted veterinary antibiotics (15, 45, 46).

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[i] http://ecdc.europa.eu/en/healthtopics/Healthcare-associated_infections/Pages/index.aspx, accessed January 14, 2014
[ii] http://ecdc.europa.eu/en/healthtopics/Healthcare-associated_infections/Pages/index.aspx, accessed January 14, 2014

3. Examples of interconnections and interdependencies in recent infectious disease events

It is noteworthy that many of the disease drivers discussed above are, from the perspective of other sectors, risks in their own rights. The World Economic Forum's Global Risks Report 2013 identified two infectious disease-specific risks, vulnerability to pandemics and antibiotic resistant bacteria (highlighting the latter) (47). Even more noteworthy, *apropos* the discussion from section 2, many global risks are themselves exacerbating factors for the spread of infectious disease. These include: major systemic financial failure; failure of climate change adaptation; severe income disparity; mismanagement of population ageing; terrorism; land and waterway use mismanagement; mismanaged urbanization; and species overexploitation (47).

It is instructive to provide a few examples of how such risks are interconnected in the context of infectious disease. Literally hundreds of examples from around the world could have been selected. One study identified 335 events leading to an emerging infectious disease between 1940 and 2004, identifying numerous infectious disease "hotspots" across the globe (17). Western Europe is identified as one such hotspot, and as the region within which the authors of this Chapter are most familiar, the examples below will all related to Europe. Nonetheless, while highlighting the interconnections between diverse disease drivers, the global interdependencies inherent to these examples will also be evident. The following examples have been selected to interrogate how different combinations of drivers have affected recent infectious disease risks. In 3.1, the links between environmental factors, climate change, and global trade and travel are discussed. In 3.2, socioeconomic contexts and the impact of the financial crisis are examined for their influence on disease outcomes. 3.3 examines avian influenza in the context of human-animal interfaces and global travel, and 3.4 investigates the impact of terrorism, conflict, and population displacements on infectious disease risk.

3.1 Dengue and Chikungunya in Europe

The sustained transmission of a vector-borne diseases requires the presence of a pathogen, a vector capable of transmitting that pathogen, and a susceptible human population (18). The interconnections between multiple disease drivers and interdependencies created by a globalized world have enabled the global expansion of vector-borne diseases, of which recent examples include the arboviruses dengue (48) and Chikungunya (49, 50).

One critical factor in the expansion of these diseases has been global trade. The mosquito species *Aedes albopictus*, also known as the Asian Tiger mosquito, is a secondary vector of dengue and Chikungunya and is thought to be the most invasive mosquito species of public health importance in the world (51). Over the past few decades it has expanded from its original habitat in Asia to all populated continents in the world (52). It has been documented that this expansion has been enabled by global trade in used tires (51, 53).

In Europe, the climatic conditions have been permissive enough to enable *Ae. albopictus* to gradually expand (often via transportation networks) from its introduction in Italy, where it arrived in 1990 (54). Today, *Ae. albopictus* is established in many regions of the Mediterranean Basin, including in Spain, France, Italy, Croatia, and Greece. In addition, the mosquito has been introduced to regions as far north as Germany, the Czech Republic and Slovakia.[iii] Models based on the known climatic determinants of *Ae. albopictus* suggest that many more areas of Europe could be suitable habitats for the mosquito (55) as well as for Chikungunya transmission, with some regions currently also amenable to dengue transmission (52). Under climate change scenarios, additional areas in central and western Europe, but fewer areas in southern Europe, could be climatically suitable (56, 57).

In a deeply interconnected world, there are numerous opportunities for viruses to be introduced into non-endemic regions (20). Each year, millions of people fly between regions of the world endemic to dengue or Chikungunya and European regions that are now home to *Ae. Albopictus*, whose ability to transmit Chikungunya increased after a single genetic mutation in the Chikungunya virus (58). In 2007, a traveller from India, infected with Chikungunya, was bitten by mosquitos in Italy, leading to a local outbreak in which over 200 people were infected (59). Dengue, meanwhile, which is now endemic in many tropical and sub-tropical parts of the world (60), has also been transmitted by *Ae. albopictus* in Europe, as has been documented in France and Croatia (61, 62).

As a result of the continuing expansion of *Ae. albopictus* in Europe, aided by trade and travel networks, climatic conditions, and genetic evolution, two diseases previously "exotic" to Europe now pose a persistent infectious disease risk. This sort of risk is not, of course, restricted to Europe; in late 2013 and early 2014, for example, Chikungunya was introduced and then locally transmitted in a few Caribbean islands, leading to a couple hundred confirmed cases and creating a high risk of further disease spread across the region.[iv]

3.2 Measles among Roma in Bulgaria and HIV among people who inject drugs in Greece

Socioeconomic contexts affect the spread of disease, and particularly among vulnerable populations. When financial circumstances deteriorate, the potential exists that the health burden will continue to be endeared by the most vulnerable members of society. The two examples in this section demonstrate the links between public health provision, income disparities, and infectious disease.

[iii] http://www.ecdc.europa.eu/en/healthtopics/vectors/vector-maps/Pages/VBORNET_maps.aspx, data as of October, 2013. Accessed January 12, 2014.
[iv] http://ecdc.europa.eu/en/press/news/_layouts/forms/News_DispForm.aspx?List=8db7286c-fe2d-476c-9133-18ff4cb1b568&ID=940&RootFolder=/en/press/news, accessed January 12, 2014.

Economic progress of the Roma population in Bulgaria has experienced a number of setbacks, ever since the political and economic transition of the late 80s (63, 64). Discrimination, poor educational attainment, lack of occupational training, poor access to labour markets, and geographic isolation have all contributed to high unemployment rates. The lack of job opportunities discourages further training and education, thereby perpetuating a vicious circle of poor education, poor working opportunities, and worsening living conditions (64). These circumstances, connected to broader cultural, demographic and economic risks, have precipitated one of the worst measles outbreaks in Europe of the past decades. Over 24,000 individuals fell ill and 24 died over a time period of a few months, starting in April 2009 (65). Approximately 90% of the cases were from the Bulgarian Roma community despite the fact that only 4% of the general Bulgarian population are Roma. In this outbreak, the risk for developing severe medical complications such as pneumonia or encephalitis from a measles infection was linked to lower maternal education levels, lower child immunization coverage, and the absence of household incomes (66). Despite that Bulgarian children are eligible for free basic medical services, almost 95% of cases had not received the full course of measles-mumps-rubella (MMR) vaccination.

Although the root causes of measles outbreak are multifactorial, it is noteworthy that Bulgaria had one of the lowest rates of total governmental spending over GDP in 2009 of the European Union (37% vs. 49%, respectively) (67). Declines in public expenditures in Bulgaria over the last two decades have diminished access to health and educational services geared towards highly vulnerable populations. Roma communities remain susceptible to communicable diseases such as the measles outbreak in 2009; outbreaks of hepatitis A, tuberculosis, poliomyelitis have also disproportionally affected the Roma ethnic group (68, 69).

Another highly vulnerable group for infectious diseases in Europe are people who inject drugs (PWID). In the wake of the global economic crisis, many health professionals across Europe anticipated adverse effects in relation to infectious disease incidence and control [66]. An observed rapid increase in reported HIV cases among PWID in both Greece and Romania was thought to be linked to the economic crisis [26]. In Greece, for example, HIV infections among PWID increased 1600% in 2011 [25]. From an epidemiologic standpoint, it is difficult to causally link the economic crisis with an upsurge in HIV in a particular subpopulation. Nonetheless, there are potential causal factors worth noticing. Yearly change in the Greek GDP has been found to be inversely associated with: HIV case reports, homelessness, unemployment among PWID, and HIV prevalence among drug injectors seeking drug in Athens [25]. Meanwhile, causal pathways have been hypothesised to include the following factors: the economic recession increased income disparities, leading to increased homelessness; this contributed to increased injecting network sizes among PWID, which were then exposed to new introductions of HIV from migrant communities, themselves subject to difficult socioeconomic circumstances in their home countries [25]. Transmission risk was intensified by low levels of available injecting equipment and other prevention services

[25]. In this scenario, the economic crisis, which originated in the financial sector, contributed to a large upswing of HIV in a vulnerable population, making conditions among PWID even more tenuous and, simultaneously, leading to fewer resources dedicated to harm prevention.

3.3 Avian influenza

Specific subtypes of influenza A viruses that circulate in birds can infect humans. Influenza infections of avian origin occur through both direct and indirect exposure to infected animals, whether alive or dead. One important unique feature of influenza viruses is their ability to cause both annual epidemics (seasonal influenza) and, from time to time, more serious pandemics (70). Each emerging strain has the potential to become seasonal.

Birds are a natural reservoir for influenza viruses, and A virus subtypes H5, H7 and H9 have all led to outbreaks in human populations (71). In recent years, the most significant outbreaks have been related to H5N1 and H7N9. Although a limited number of human cases infected with influenza A(H5N1) has been reported, the high case fatality and its potential ability to adapt to human hosts have raised concern at the global level (72). More recently, in the spring of 2013, 145 people in China were infected by the avian influenza strain A(H7N9), leading to 45 deaths (73). The virus was detected in poultry but also in the environment. The closure of live poultry markets in April 2013 did lead to a dramatic drop in the number of cases (74) although sporadic cases have been reported through the end of 2013.[v]

A broad combination of factors can trigger and sometimes amplify avian influenza outbreaks (75, 76). Ecological and environmental factors play a key role. Population density of both human and animals – as well as the proximity between them – are known risk factors for avian influenza infections in humans. Live bird markets and human consumption patterns of poultry and other avian species are also known to contribute to the risk of both influenza emergence as well as infection (77). Seasonality is another influencing factor, although different hypotheses exist as to why winter seasons are traditionally driving influenza transmission (78). Bird migratory patterns, particularly where migratory birds might interact with livestock poultry, create potential pathways for introductions of the virus into new regions. Air travel can quickly lead to the rapid global spread of influenza (2). Meanwhile, level of available public health measures, from molecular surveillance to rapid vaccine production, are important determinants of the impact that any given influenza outbreak might have (79). Significantly, different avian influenza have different characteristics, further challenging the public health response. For example, influenza A(H5N1)

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http://ecdc.europa.eu/en/press/news/_layouts/forms/News_DispForm.aspx?List=8db7286c%2
Dfe2d%2D476c%2D9133%2D18ff4cb1b568&ID=930&RootFolder=%2Fen%2Fpress%2Fnews
%2FLists%2FNews&Source=http%3A%2F%2Fecdc%2Eeuropa%2Eeu%2Fen%2Fhealthtopics
%2Favian%5Finfluenza%2FPages%2Findex%2Easpx&Web=86661a14%2Dfb61%2D43e0%2D
9663%2D0d514841605d, accessed January 10, 2014.

is highly pathogenic in birds, leading to natural sentinel surveillance sytems, while influenza A(H7N) may circulate among healthy birds, thereby remaining undetected (80).

The global and sectoral interdependencies related to influenza have been well documented. A widespread pandemic could quickly disrupt activities in many sectors, including trade (including potential trade bans) (81), transportation, healthcare delivery, critical infrastructure, and so on. School closures and workplace absenteeism are oft-cited control measures that might also have substantial impact on society. Numerous economic estimates indicate that the direct costs (use of healthcare services) and indirect costs (productivity losses) related to seasonal influenza can amount to billions of dollars globally (82). An economic scenario analysis of pandemic influenza in the UK indicated potential costs of 0.5%-1% of GDP in low fatality scenario and 3.3%-4.3% in a high fatality scenario (83).

3.4 Regional conflicts and the eradication of polio

Political unrest, armed conflict and related population displacements are well known to be severe barriers to the provision of public health programmes (including immunization programmes). Needless to say, conflicts also lead to significant vulnerabilities among populations, whilst population movements create further opportunities for disease spread.

Complex security situations have played a role in slowing down global efforts at polio eradication. In Pakistan, two workers associated with the World Health Organization (WHO) and its polio vaccination campaign were shot dead in July, 2012 (84), and it has since been reported that 31 people associated with polio campaigns were killed in the country between July 2012 and December 2013; reputedly, polio workers have been targeted for killing with terrorist intentions.[vi] Vaccination campaigns in Pakistan have been further hindered by public mistrust (84), a situation that likely further deteriorated after it was revealed that one doctor had run a fake vaccination campaign as part of a collaboration with the US Central Intelligence Agency efforts to find Osama bin Laden (85, 86). Pakistan had a reported 85 polio cases in 2013, up from 55 in 2012.[vii] Assuming that roughly 95% of polio infections are asymptomatic and another 4.5% have mild or non-paralytic symptoms, this means that at least a few thousand additional people could be currently carrying and transmitting the virus in the country. Meanwhile, polio eradication programmes have pushed back their target completion dates, and it is has been reported that 350,000

[vi] http://www.aljazeera.com/indepth/features/2013/12/pakistan-polio-workers-targeted-killing-20131211836485137.html, accessed January 14, 2014.
[vii] http://www.polioeradication.org/Dataandmonitoring/Poliothisweek.aspx, accessed January 14, 2014.

children in Pakistan's Federally Administered Tribal Areas have not received polio vaccinations since mid-2012.[viii]

Spill-over into neighbouring countries is one consequence of halted polio eradication. Although analyses are underway, it appears that an introduction of polio from Pakistan into the broader region led to viral circulation in Israel, Egypt and, potentially, Syria (87). In Israel, circulation of polio virus occurred despite an estimated vaccination coverage of greater than 95% of the general population (87, 88). In Syria, meanwhile 17 laboratory-confirmed cases were identified in 2013, implying widespread circulation of poliovirus (88). The combination of conflict and circulating poliovirus is potentially highly problematic, as there are currently more than two million Syrian refugees globally, with an increase of 700,000 since July 2013(88). This vast number, with high numbers children, many of whom may be unvaccinated, creates the potential for further regional spread of poliovirus. In a globalised world, this risk is not localised; in the EU, for example, ten per cent of new asylum applications in between January 1 and August 31, 2013, were from Syria, while the number of undocumented migrants from Syria has also increased (88). Such circumstances increase the risk of poliovirus reintroduction and transmission in Europe.

There are many tragic dimensions to a humanitarian crisis such as the one in Syria, and dealing with the health aspects of such crises is both challenging and fraught with danger. This example demonstrates that inadequate global coordination of the health response (89), in combination with the interconnection of key risks such as low vaccination coverage, conflict and terrorism, population displacement, have the potential to amplify an already serious risk to global health.

4. Analysing interconnected and interdependent infectious disease risks

There is a growing awareness within the health sector that the wide range of factors – many of them risks generated from other sectors – that can combine to affect the transmission of infectious disease need to be better and more holistically monitored, assessed, and acted upon. This is reflected by calls to approach the topic from a broader systems perspectives (6, 15, 90-93), which tend to emphasise the need for integrating insights from multiple sectors and disciplines. Similarly, the One Health approach, which recognises the intimate relationship between environmental conditions, animal health, and human health, has been promoted at the global level[ix]; ways of operationalizing One Health concepts have also gained traction (94). Growing attention to the social

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[viii] http://www.cdc.gov/media/releases/2013/p1121-polio-progress.html, accessed January 14, 2014.

[ix] http://www.oie.int/en/for-the-media/editorials/detail/article/one-world-one-health/, accessed January 14, 2014.

determinants of health, meanwhile, is another crucial development for assessing and monitoring infectious disease related risks.

In concert with the growing awareness of the need to broadly assess the interconnected nature of infectious disease risk, there have been growing calls to develop tools and methodologies for predictive modelling of infectious disease outbreaks that assess, to some degree, the amplifying role that non-health factors play in propagating disease risk (13, 95, 96). Lagging behind have been analyses of vulnerabilities as well as strong evidence bases on the status and efficacy of public health preparedness (97)– two critical determinants of the magnitude of impact that any disease outbreaks might have.

There are a wide range of approaches to predictive infectious disease modelling approaches (96). One of the more promising developments has been research into the links between environmental variables and infectious disease spread. As discussed in section 2, many environmental drivers can be considered as epidemic precursors of disease, and thus monitoring changes in environmental conditions can help anticipate or even forecast an upsurge of disease (98). In recent years, work in this area has been greatly enabled by rapid developments in Geographic Information Systems (GIS), which have facilitated the management and use of spatial data for analytic epidemiology. Climatic, weather and environmental data can now be linked and integrated with data on health, disease vectors, and so on, to provide support tools for decision makers (98).

To illustrate how this has can be done, the European Centre for Disease Prevention and Control developed the European Environment and Epidemiology (E3) Network to help monitor environmental conditions related to infectious disease threats (98). The initial building-block of the E3 Network is data from the Emerging Diseases in a Changing European Environment project (EDEN), a research initiative funding by the Directorate-General for Research and Innovation of the European Commission.[x] The aggregation of these data sets, and those continuously acquired from other sources, with regular outputs from advanced scientific analysis, serve as a starting point for analysis of disease risk and vulnerable regions.

This approach has been used to predict the environmental suitability of malaria transmission in Greece (99). Malaria was eradicated from Greece in 1974, but in 2009 (and subsequent years), locally acquired cases were identified. Remotely sensed data were used to describe the environmental and climatic conditions where future transmission could happen in Greece. Sea-level altitude and the mean and annual variation of land-surface temperature, both for daytime and night-time, were predictors in this model. Defining the areas of high risk helped guide the public health responses and to integrate preparedness and response activities, including targeted epidemiological and entomological surveillance, vector control activities, and awareness rising among the general population and health workers, in the areas environmentally suitable for transmission.

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[x] http://www.eden-fp6project.net/, accessed January 14, 2014.

In another example, the E3 Network hosts a real-time model for the environmental suitability of *Vibrio* spp. in marine waters worldwide, taking into account temperature and salinity (100).   It uses daily-updated remotely sensed data to assess environmental suitability conditions for *Vibrio spp.* infections according to a model developed by Baker-Austin et al (101). Infections caused by Vibrio species (other than *V. cholerae*) can cause serious problems for immunocompromised persons, although the overall occurrence is generally low. Nonetheless, early information about the environmental suitability of *Vibrio spp.* infections will be of public health interest, and also demonstrates a proof-of-concept for predictive disease modelling more generally.

5 Conclusion

As has been stressed in this Chapter, infectious diseases are very often the product of a wide range of intermingling and interconnected factors, and disease outbreaks create many cross-sectoral interdependencies. There is an emerging body of research on deploying holistic analyses of the many factors affecting infectious disease risks, and there are now even early-stage predictive modelling frameworks that show promise. Information from these analyses can be used to set public health priorities and to inform civil society about potential consequences that factors external to health, such as global change, have on infectious disease control.

Moving forward, more research into the efficacy and status of public health preparedness and further work on the cross-sectoral dependencies created by disease outbreaks will be important areas for development.   Meanwhile, methodological development of approaches for analysing priorities for public health preparedness activities and tools for facilitating cross-sectoral collaboration were recently highlighted by participants representing more than 30 countries at a Joint ECDC-WHO Consultation on Pandemic and All-Hazard Preparedness, held in November, 2013.[xi] These will be developed by ECDC in the coming years.

At the European policy level, the multifactorial, interconnected and interdependent nature of infectious disease risks has been recognised. On 6 November 2013, a new EU Decision on serious cross border threats to health entered into force.[xii] Two of the main features of this legal instrument are its "all-hazard" approach and its emphasis on inter-sectoral collaboration. Both aspects are of strong relevance for an integrated approach towards interconnected risks.

[xi]
http://ecdc.europa.eu/en/press/events/_layouts/forms/Event_DispForm.aspx?List=a8926334-8425-4aae-be6a-70f89f9d563c&ID=242&ContentTypeId=0x010082EE625D0C434588A3E95C31FC12D7A701070052267A797710AF45AB21E1D53B49B228, accessed January 14, 2014.
[xii] http://ec.europa.eu/health/preparedness_response/policy/decision/index_en.htm, accessed January 14, 2014.

The all-hazard component implies a shift from a cause-driven to an impact-driven assessment and management of health threats. In this sense, the Decision builds on the EU's extensive experience in the field of communicable diseases and expands it to other types of threats from biological, chemical or environmental origin, ensuring a consistent European response across countries and across types of public health emergencies. The inter-sectoral component aims at enhancing the joint preparedness and response planning among European countries, resulting in comprehensive assessments of emergency situations and a formulation of responses addressing the whole range of their potential impacts. This Decision thus draws attention to the need for integrated approaches towards the identification, assessment and management of inter-connected risks.

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