15

Pandemic Risk Modelling

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15.1 Introduction

Infectious disease pandemics are among the deadliest events in human history. Events such as the 1918–1919 "Spanish Flu" pandemic and the Black Death have devastated communities, cities and continents, causing sickness and mortality well beyond the burden of disease experienced in normal times.

This chapter will explore the nature of communicable diseases, a brief history of pandemics, and will introduce the mathematical models used to evaluate the risk pandemics pose to human populations. Such modelling is used in a public health context, where modelling past and current events provides insight in how to respond most effectively to a new outbreak. It is also used in the context of risk mutualisation and transfer. As recently as 2013, a survey of 30,000 insurance executives placed global pandemic as the biggest extreme risk facing insurers (Towers Watson 2013). The chapter will introduce the principles used to model these events in the insurance industry and will conclude with a review of the way these models are applied in an unconventional risk transfer context.

Communicable diseases are characterised by pathogens[1] spreading through populations. This is what sets them apart from other diseases and from more geographically localised catastrophic events: where there is contact between

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a pathogenic agent and a susceptible host, it is possible for that disease to spread.

Communicable diseases remain one of the largest causes of death and morbidity globally, accounting for 15.8% of global deaths in 2015 and 19.0% of the global burden of disease in terms of disability-adjusted life years (DALYs)[2] (Figs. 15.1 and 15.2).

While there has been improvement in respect of the mortality and morbidity impact of infectious diseases, both in the long term and since 2000, there remains a substantial proportion of the world's population where the leading cause of death is communicable disease.[3] Communicable diseases ranking in the top 20 causes of death in low-income economies include lower respiratory infectious, diarrhoeal diseases, HIV/AIDS, tuberculosis, malaria and meningitis.[4] Only lower respiratory infectious rank in the top 20 in upper income countries in 2015 (Fig. 15.3).

There are some commonly used terms that are used to describe infectious diseases. These are related to the natural properties of infectious diseases and

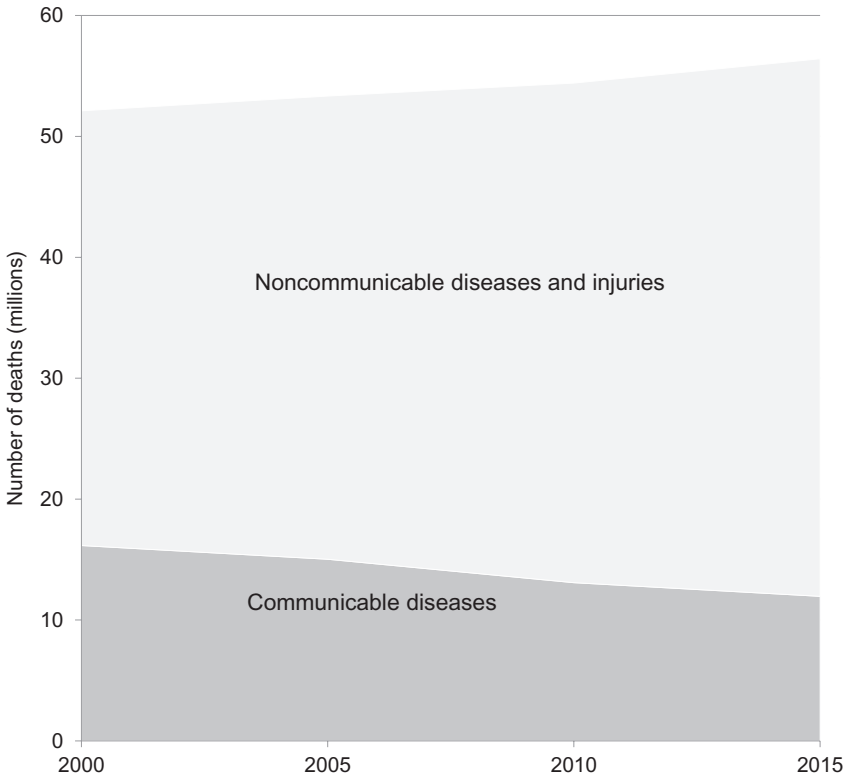

Fig. 15.1 Deaths from communicable diseases and other causes since 2000 (World Health Organization 2016)

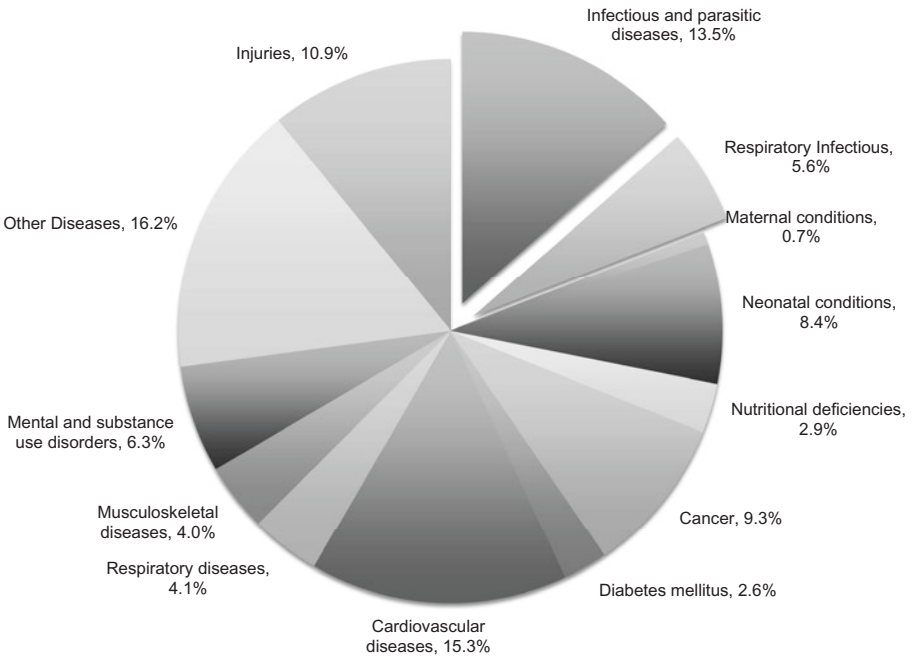

Fig. 15.2 Proportion of global disease burden in respect of DALYs in 2015. Communicable diseases are separated into "infectious and parasitic diseases" and "respiratory infectious" together accounting for 19.1% of DALYs (World Health Organization 2016)

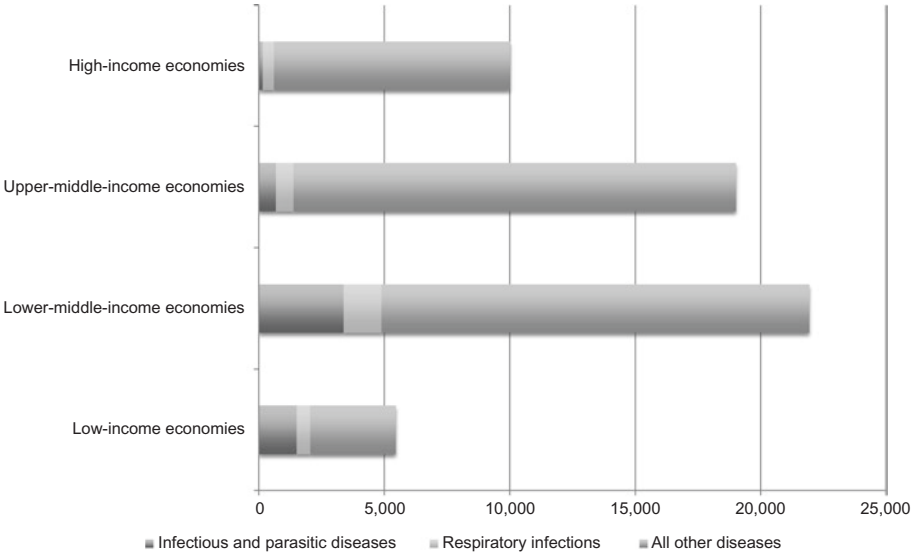

Fig. 15.3 Deaths by cause in 2015 by World Bank classification of economies (World Health Organization 2016)

lend themselves directly towards the mathematical modelling of the impact of an epidemic or pandemic.

Transmissibility is the ease with which the disease spreads from host to host. This can be direct, for example through contact with an infected host or by short-range transmission of the pathogen, or indirect, where there is a vehicle or vector organism that transmits the disease between human hosts.

Pathogenicity is the ability of the pathogen to cause disease within an exposed person.

Virulence is a measure of an infectious disease's severity. Some pathogens cause extreme illness in the host, whereas others may have very little impact in an infected host.

For more information on how these terms relate to, and are borne out of, mathematical models for communicable diseases, see the section "Modelling infectious disease spread".

The two main definitions of communicable diseases in terms of their pattern of occurrence are *endemic* and *epidemic* diseases. An endemic disease is one that has established a stable pattern of transmission. New caseloads may vary from one time period to another and by geographic region, but overall the occurrence is relatively stationary. Epidemic diseases are diseases where the number of cases "spikes", or temporarily exceeds established baseline caseloads. What constitutes an epidemic will depend on the nature and prior history of the pathogenic agent. Features of the exposed population including its size and susceptibility to the pathogen, and the spatio-temporal characteristics of the outbreak are all factors that are used to define whether an epidemic is occurring. Taking Dengue as an example, an epidemic could be characterised by substantial increase in caseloads in an area where Dengue has an established moderate baseline of cases, or if a small number of cases were to emerge in an area that had no prior history of Dengue. Cases of previously unseen pathogenic agents may only need to be small in number in order to be identified as epidemic. An endemic disease may become epidemic if the environment or susceptibility of a population changes.

A *pandemic* is a special case of epidemic, often defined as the situation where a disease reaches epidemic status on multiple continents at the same time or, alternatively, the worldwide spread of an epidemic.

An *emerging infectious disease* is a previously unknown disease. A *re-emerging infectious disease* is a known disease that transitions from a state of being well controlled to achieving sustained (often rapid sustained) transmission in a population.

15.2 History of Pandemics

Given the lack of modern public health practice and the difficulty in communicating long distances, it may seem unlikely that there are much historical data on infectious disease pandemics before the late nineteenth century. However, the scale of pandemics coupled with the fact that they directly impact human populations means we have a relatively long historical record, albeit of unknown completeness (see Table 15.1 for a summary of historical pandemics).

Table 15.1 Pandemics since the middle ages

Years	Reported region	Description	Deaths
1347–1351	Europe	*Bubonic Plague*. The "Black Death" was one of the deadliest pandemics in history. The pathogen responsible for causing the bubonic plague is *Yersinia pestis*, a bacterium that is the disease of rodents and is carried by a vector, the flea *Xenopsylla cheopis* . Through analysis of bones of Black Death victims, comorbidities, particularly malnourishment, but also other health deficits, were significant risk factors in mortality associated with the pandemic (DeWitte 2014).	30–50% of Europe's population
1489	Europe	*Typhus*. Typhus epidemics, caused by the louse-borne bacterium *Rickettsia prowazekii*, typically afflict those living in cramped, unhygienic conditions where the lice thrive. It is for this reason that Typhus has been such a decisive factor in wars over the centuries: in 1489, an army of 25,000 Spanish soldiers were reduced to 8000 by Typhus while besieging the Moors at Granada. The fleeing survivors carried the disease to other parts of Europe, creating the Typhus pandemic of the late fifteenth century and carried on well into the sixteenth century, becoming highly influential in the wars of Western Europe in the 1500s.	Unknown total, but high death counts recorded in military engagements. Case fatality rates often 10–15%.

(*continued*)

Table 15.1 (continued)

Years	Reported region	Description	Deaths
1500s	Europe, Americas	*Smallpox*. Smallpox was the leading cause of death in the sixteenth-century Europe, with a case fatality rate of 30%. When introduced to the Americas, the highly susceptible population with no prior exposure to the disease suffered case fatality rates in the range 80–90%. A highly transmissible epidemic disease, smallpox continued to cause significant mortality well into the twentieth century, until immunisation programmes coordinated by the World Health Organization rendered smallpox extinct in the wild by 1979.	12–25 million deaths in Mexico alone (Acuna-Soto et al. 2002)[a]
1510	Almost all countries of the Old World	*Influenza*. Disease emerged in Asia and spread via trade routes to Europe and Africa. Generally accepted to be the first identified influenza pandemic. Described as a "precipitous illness with coughing and high fever", and a "rheumatic affliction of the head … with constriction of heart and lungs" by medical chroniclers of the day (Morens et al. 2010).	Unknown
1557–1558	Europe	*Influenza*. Chronicled as "quartan agues", "hot agues" and "sweating fevers" in Britain, this likely pandemic came in two waves in 1557 and 1558. Italian writers also refer to epidemics of "catarrhal symptoms" in the years 1557 and 1558 (Creighton 1891).	Reported deaths in Rodwell: 20, 76 and 124 from 1556 to 1558[b]
1580	Asia, Africa, whole of Europe, America	*Influenza*. Believed to have emerged in Asia and to have reached Europe through trade routes via Asia Minor and North Africa. It took six months to spread across the whole of Europe and went on to the Americas (Potter 2001).	8000 in Rome, many in Spanish cities
1635, 1656	Britain, Europe	*Measles*. Elevated infant and child mortality over various periods of approximately five months in England in 1635 and 1656 have been attributed to measles.	Unknown

(*continued*)

Table 15.1 (continued)

Years	Reported region	Description	Deaths
1700s	Americas, Europe, Africa	*Yellow Fever*. Multiple outbreaks of yellow fever afflicted the military campaigns of Europeans in the Americas in the eighteenth century. Epidemics in the USA, Guadeloupe, Cuba, Mexico, Peru, Africa and Spain (Nogueira 2009).	Potential deaths among armed forces of 85,000—more in general population
1729–1730 and 1732–1733	Whole known world	*Influenza*. Emerged in Russia in 1729, before spreading to Europe. Within six months, it had engulfed Europe and continued to transmit to the Americas, Africa and throughout Asia over three years of waves of the disease (Ministry of Health 1920).	High—between 0.5 and 3× normal in London
1761–1762	Americas, Europe	*Influenza*. The 1761–1762 pandemic's origin is suspected to be the Americas, making it the first pandemic likely to have emerged in the New World. This was accompanied by greater study of the clinical manifestations of the disease. It was preceded by a significant equine influenza epidemic, although no causal link has been identified (Taubenberger and Morens 2009).	Substantially milder than 1729–1733, with fewer deaths
1780–1782	China, India, Europe, Americas	*Influenza*. Likely to have originated in China. This outbreak was characterised by extremely high morbidity rates (Hays 1998): 30,000 cases per day were reported in St. Petersburg (Kohn 2007). This pandemic again coincided with outbreaks of equine, as well as canine and feline influenza (Taubenberger and Morens 2009).	Reports of increased death tolls among those with comorbidities[c]
1788–1790	Europe, North America	*Influenza*. Believed to have originated in Russia before being transmitted to Europe and the USA. Significant morbidity rates reported (Kohn 2007).	Low mortality

(*continued*)

Table 15.1 (continued)

Years	Reported region	Description	Deaths
1800s	Europe, Americas, Asia	*Cholera*. Cholera is a bacterial infection caused by strains of *Vibrio cholerae*. It is usually communicated via water or food contaminated with faecal matter containing the bacteria. Five cholera pandemics in India, Russia, the USA and throughout Europe caused mass morbidity and mortality in towns and cities. John Snow's study of the water companies in London gave rise to the theory that cholera was being transmitted via contaminated water. This was one of the first such epidemiological investigations and gave rise to the sanitary reformation that radically reduced mortality in the late nineteenth and twentieth centuries.	50–100 million deaths
1830–1831, 1832–1833	China, Russia, Europe	*Influenza*. Very high morbidity rates and rapid rate of transmission. Lower case fatality rates, rather like 1788 (Patterson 1985).	Thousands of deaths, mainly elderly
1889–1893	Global	*Influenza*. Known as "Russian Flu", this highly transmissible strain had been transmitted to all corners of the globe within four months. Median basic reproductive number (R_0) estimated to be 2.1, similar to that seen in influenza pandemics of the twentieth century. Possibly an H2N2 or H3N8 strain. This was the first pandemic to occur in the modern world, with roads, railways and modern ships connecting populations together (Valleron 2010).	One million. Case fatality rate estimated at 0.1–0.28%
1918–1919	Global	*Influenza*. The most severe known influenza pandemic and one of the most severe health crises in history, the 1918–1919 "Spanish Flu" pandemic spread across the world rapidly, with extremely high morbidity and mortality rates on all continents. H1N1 strain (Taubenberger and Morens 2006).	40–50 million deaths worldwide; case fatality rate >2.5%[d]

(*continued*)

Table 15.1 (continued)

Years	Reported region	Description	Deaths
1957–1958	Global	*Influenza*. "Asian Flu" was a rapidly spreading H2N2 strain. It had high excess mortality rates in school-aged children and young adults (Viboud 2016).	1–1.5 million; case fatality rate 0.13–0.19%
1968	Global	*Influenza*. "Hong Kong Flu" was an H3N2 strain, originating from China. It is likely to have emerged via antigenic shift of the H2N2 1957 virus. Only two weeks passed between the first reported case and 500,000 cases being reported in Hong Kong. The first season had greater mortality in the USA, whereas the second season had greater impact in England (Viboud 2005).	0.75–1 million; case fatality rate <0.1%
1979-	Global	*HIV/AIDS*. Originally identified by previously unseen cases of pneumocystis pneumonia and Kaposi sarcoma in US cities in 1981. HIV is a retrovirus transmitted via certain bodily fluids (blood, semen, breast milk, vaginal fluids). It attacks the immune system of the host, with AIDS rendering the host highly susceptible to death from infection or other complication.	35 million; another 37 million currently living with HIV/AIDS
1977–1978	Global	*Influenza*. 1977 "Russian Flu" was relatively mild in comparison to prior twentieth-century pandemics.	Very low
2009–2010	Global	*Influenza*. 2009 Novel H1N1 "Swine Flu" was a highly transmissible, but ultimately low severity influenza pandemic. It originated via zoonosis in Mexico in April 2009 and continued to transmit throughout summer, autumn and winter of 2009, before gradually declining (Dawood et al. 2012).	284,500, although some estimates are as low as 18,000 or as high as 579,000

[a]Some of these deaths will have been attributable to drought, or more likely the severe drought amplified the mortality effect of the smallpox epidemics in the sixteenth-century Mexico

[b]Rodwell is a parish near Leeds in the North of England

[c]A comorbidity is an existing health problem or disease that occurs at the same time as the primary disease in a patient

[d]Some accounts suppose as many as 100 million deaths were caused by the 1918–1919 pandemic. The case fatality rate was unprecedentedly high, more than ten times what had been seen in previous influenza pandemics

15.2.1 Origins and Properties of Infectious Diseases with Pandemic Potential

Of all known communicable diseases, only some have the transmissibility characteristics to reach pandemic scale. Generally, it is emerging or re-emerging diseases readily transmissible between humans that have the potential to cause pandemics. This is because there is little to no immunity in the world population and because the disease will propagate through the population via usual human-to-human contact, respectively.

Zoonosis is a key biological mechanism by which novel infectious diseases emerge. Taking the 2009 H1N1 pandemic as an example, the origin of this disease was a pig in Mexico. The novel virus emerged via the process of reassortment, where two different strains of influenza, one endemic in North American pigs and the other in Eurasian pigs, infected the same animal. The two viruses exchanged genetic material (RNA) to result in a new virus significantly different from its precursors. This antigenic shift means that the immune systems of humans and swine have never been exposed to this disease before and therefore do not possess the antibodies to halt infection. This coupled with the property that it was relatively readily transmissible resulted in large swaths of the world population being infected (Smith et al. 2009). Table 15.2 displays the zoonotic origins, modes of transmission and further details of a group of diseases with the potential to cause pandemics.

Table 15.2 Transmission modes and zoonotic origins of infectious diseases

Mode of transmission	Disease	Pathogen	Human-to-human	Animal-to-human
Airborne	2009 H1N1 Influenza	Virus	Yes	Pigs*
	2005 H5N1 Influenza	Virus	Very limited	Birds*
	SARS	Virus	Yes	Small mammals*
	MERS-CoV	Virus	Limited	Camels*
	Measles	Virus	Yes	No
	Smallpox	Virus	Yes	No
	Tuberculosis (pulmonary)	Bacteria	Yes	No
	Tuberculosis (bovine)	Bacteria	Yes	Cattle
Blood and serum-borne	Hepatitis B	Virus		
	Hepatitis C	Virus	Yes	No
	Ebola Virus Disease	Virus	Yes	Bats, Primates
	HIV/AIDS	Virus	Yes	No

(*continued*)

Table 15.2 (continued)

Mode of transmission	Disease	Pathogen	Human-to-human	Animal-to-human
Vector-borne	Malaria	Parasite	No	Mosquitoes
	Zika virus	Virus	No	Mosquitoes
	Plague	Bacteria	No	Rat fleas
Water-borne	Cholera	Bacteria	Yes	No

Where the animal is marked with an asterisk (*), this indicates that the disease's zoonotic origin was traced back to the same animal host. Note that where there is no observed recent animal-to-human transmission for some diseases, it remains likely that the disease's earliest origins were via zoonosis. Smallpox's mode of transmission is suspected to be airborne but was not fully confirmed before its extinction in 1979 (Milton 2012)

15.3 Infectious Disease Models

There exist a range of techniques for modelling infectious diseases. The choice of model depends on the type of disease, the use case and the time available. This text sticks to the main use cases of planning responses and interventions against a pandemic and estimating the overall impact of pandemics in a risk management context.

15.3.1 Modelling Infectious Disease Spread

The mathematical models used for pandemics in unconventional risk transfer are based on the mathematical models for communicable diseases. The most commonly used models are called population (compartmental) models. Developments by WH Hamer, Sir Ronald Ross and Kermack and McKendrick between 1910 and 1930 resulted in the core mathematical models that continue to be used to understand and predict the transmission of infectious diseases today (Kermack and McKendrick 1927). These deterministic dynamical models have been extended to stochastic variants for use under certain circumstances, and for modelling diseases with other modes of transmission than those originally studied, as well as for studying endemic and endemo-epidemic diseases. Age structure and spatial structure have been introduced as further features to the dynamical models. More detailed spatial structure between subpopulations, taking account of social groups and travel patterns, captures a subclass of pandemic models with increased spatial heterogeneity. Network models of infectious disease take advantage of modern computing power and increased amounts of readily available social network data to model transmission based on models of individual people's contacts with others in their social groups. Agent-based models go one step further and

explicitly model the interactions of individual hosts, vectors (if applicable) and pathogenic agents, thus removing some of the assumptions underlying the dynamical models and attempting to generate real-world epidemic behaviour directly from the interactions of the agents.[5]

By definition, pandemics occur only if the susceptible population is sufficiently large that sustained transmission can occur over large swaths of the planet. For this to happen, there needs to be low residual immunity in the population: it is emerging or re-emerging pathogens that are likely to give rise to pandemics. Moreover, in an unconventional risk transfer context, the principal use case is to model the risk of emergence of a novel pathogen capable of reaching pandemic scale, and subsequently the size, scale and impact of that pandemic. It is for this reason that industry focuses its attention on population models with spatial heterogeneity: they are able to capture the large-scale behaviour of pandemics relevant to counterparties involved in risk transfer transactions.

15.3.2 Compartmental Models

Population (compartmental) models of infectious diseases break down the population into compartments that represent, over time, the populations of various distinct disease states. We have already encountered the term *susceptible*, which is one such compartment that includes anybody who could be infected if they came into contact with an infectious host. *Infective* is another such compartment, which is populated by hosts capable of transmitting the disease to susceptible members of the population. To complete one of the most basic compartmental models of epidemic behaviour, the SIR (susceptible-infective-recovered) model, we introduce a *recovered* compartment, which includes those removed from the susceptible population, as they are now immune to infection. The sum of the three compartments is the total size of the population (Fig. 15.4).

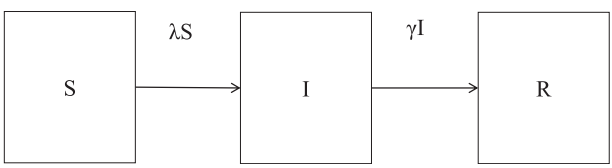

Fig. 15.4 A simple SIR model. Susceptible members of the population are infected at a rate corresponding to the force of infection, λ. Infective people recover at a rate γ corresponding to the rate of recovery

In the SIR model, the force of infection, λ, is modelled as the contact rate (number of contacts one person makes with other people per unit time) multiplied by the fraction of the population that is infective (Fig. 15.4). This captures the logical idea that susceptibles coming into contact with many people are increasingly likely to encounter an infective host as the number of total infectives rises. The rate of recovery, γ, is assumed to be constant in the usual formulation of the SIR model. These epidemiological parameters can be combined to yield a powerful descriptor for the transmissibility of an infectious disease, which combines the population characteristics and behaviour with the communicability of the pathogen. This is the *basic reproduction number*, R_0, which is the expected number of people an infective would infect in an otherwise fully susceptible population. For sustained transmission and an epidemic to occur, R_0 in an SIR model and other similar models must be greater than one. There are various derived terms with their foundations in the basic reproduction number, such as effective R_0 (R' is a measure of reproduction number contingent on the existing immune fraction of the population) and R_t (a measure of reproduction number as an epidemic progresses over time). Table 15.3 provides R_0 values for some key historical pandemics and other epidemic diseases.

The basic SIR model contains a set of assumptions that render it suitable for certain classes of disease model, but deserve closer scrutiny when considering real-world disease outbreaks. One such assumption is that, once exposed, an individual will immediately become infective. Often, there is a latent period where the levels of pathogen are building up in the host and during which the host is not yet infective. This is termed the *exposed* compartment, and its effects are demonstrated in Fig. 15.5. In both the SIR and SEIR deterministic models, for a disease with $R_0 > 1$, the number of infectives (the effective case-

Table 15.3 Basic reproduction numbers of historical influenza pandemics and other epidemic diseases (Taubenberger and Morens 2006; Valleron 2010; Elderd et al. 2006)

Disease	Basic reproduction number (R_0)
Influenza 1889–1893	2.1
Influenza 1918–1919	1.5–2.5
Influenza 1957–1958	1.5–1.7
Influenza 1968	1.5–2.2
Influenza 2009	1.5–2.0
Smallpox	5–7
Measles	12–18
Poliomyelitis	5–7
HIV[a]	1.0–6.5

[a]HIV R_0 estimated using a basic method and based on experience in Uganda from 1996 to 2008

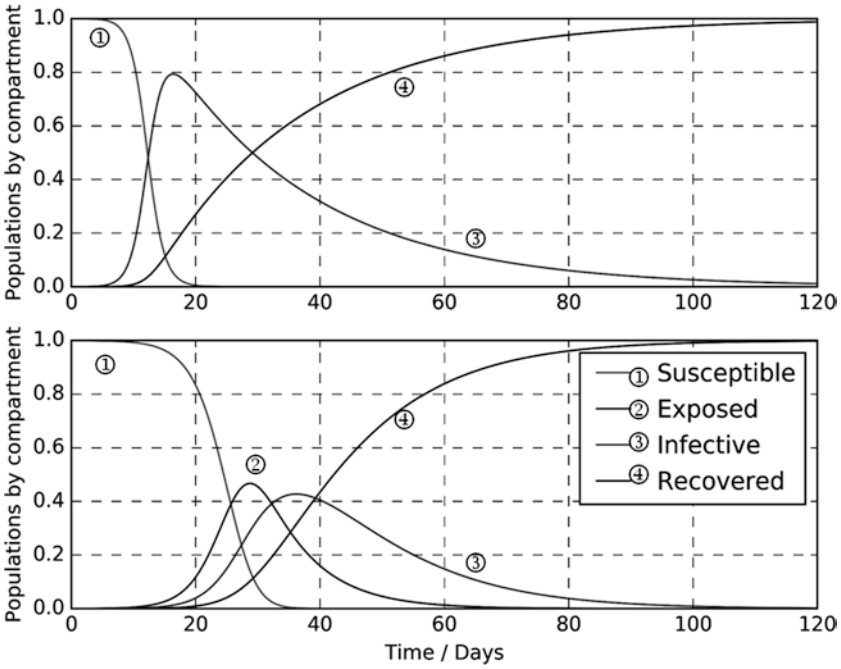

Fig. 15.5 Simple deterministic SIR and SEIR models for smallpox, displaying populations of each compartment relative to the total population. A total of 10^{-4} of the total population is infective at $t = 0$ in an otherwise fully susceptible population. In the SIR model (upper), there is no latent period: susceptibles move directly from susceptible to infective. The SEIR model (lower) incorporates this latent period and yields different dynamics closer to what is seen in smallpox and many other epidemics

load in these models) undergoes exponential growth until it reaches a peak, after which the number of susceptibles available to infect has significantly diminished, resulting in an inflection point where caseloads begin to fall.

Similarly, the formulation of the rate of recovery implicitly assumes that recoveries are exponentially distributed, whereas in reality, other distributions (including those with low variance) of recovery times are typical. Various methods have been proposed and used in tackling this issue, including separating the infective compartment into a sequence of sub-compartments, yielding gamma, normal and delta-distributed recovery times as the number of infective compartments is increased (Wearing et al. 2005).[6]

Another pair of assumptions is that the populations are effectively infinite and the compartments are perfectly mixed. These assumptions may be reasonable approximations to the truth during the peak and late stages of a large epidemic or pandemic. However, consider the case of a novel pathogen. The basic deterministic SEIR model's initial conditions are based on the concept of

a well-mixed proportion of the population starting as infective, whereas in the real-world scenario, there is a single person (index case) that is infective. The subsequent course of the disease will depend on the behaviour of that person and the local characteristics of the population in that area. Thus, while the R_0 may be less than or greater than one when assuming the population is perfectly mixed, whether an epidemic will happen will be uncertain and dependent on a small number of human interactions during these early stages of an outbreak. Introducing demographic stochasticity to the model can improve the realism of this feature (Diekmann and Heesterbeek 2000). Figure 15.6 shows that a disease with a relatively high R_0 of 2.1 may not achieve sustained transmission when starting from a single index case.

A disease transmitted by a living organism from one animal to another is known as vector-borne. Examples include malaria and Dengue, both of which are transmitted by mosquitos. Vector-borne diseases can be modelled using compartmental models.

To relax another of the assumptions of these models and to improve realism, spatial effects can be incorporated. Knowledge of long-range interactions

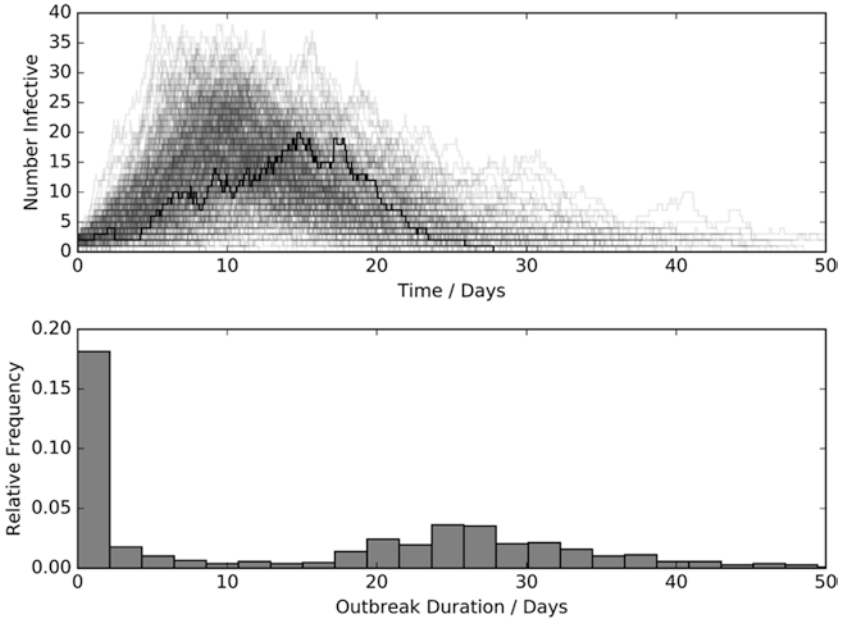

Fig. 15.6 Results of the SIR model incorporating demographic stochasticity for a single infective introduced to a community of 100 people. The R_0 of this disease is 2.1, and the model was run for 500 simulations. The black line represents an example simulated scenario. The histogram shows that even outbreaks with R_0 much larger than unity can peter out if a critical mass of infectives is not reached

(e.g. between cities or countries) and short-range interactions (e.g. between households) can be incorporated into the deterministic and stochastic formulations of the compartmental models via metapopulation modelling, where the population is modelled as consisting of a set of well-mixed homogeneous patches which are coupled together. Such models can range from the relatively simple where the coupling is homogeneous and requires only minor extensions to the compartmental models described above, to the complex. Heterogeneous coupling and network models of detailed population dynamics such as commuting and travel patterns can be taken into account in such models. Such additional complexity is accompanied by a need to infer additional parameters, which can be done to varying degrees of success depending on the complexity of the model and the availability of data globally (Ball et al. 1997; Colizza and Vespignani 2008). The contact features of metapopulation and network models are described schematically in Fig. 15.7.

15.3.3 Agent-Based Models

The inclusion of networks of subpopulation connectedness into pandemic models can be taken to a more granular level by turning to agent-based models (ABMs). ABMs are simulation models that attempt to capture the real-world

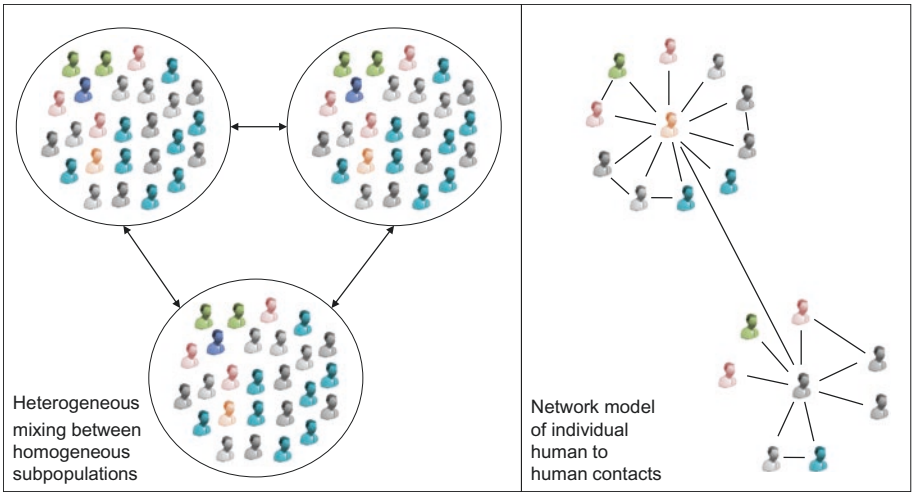

Fig. 15.7 A schematic of a metapopulation model and a network model of infectious disease spread. The metapopulation model has the assumption of homogeneous mixing within each subpopulation alongside heterogeneous connectivity and interactions between subpopulations. A network model captures the contacts between individuals directly based on knowledge or assumptions of their contact network

interactions between a set of autonomous agents. Similar to network models, rather than the dynamics being specified from the top down as in compartmental models, the dynamics emerge from the bottom-up descriptions of the agents' behaviours and their interactions. ABMs go beyond contact network models to incorporate local knowledge of demographic data, household data, healthcare system and infrastructure, details of the epidemiologic and evolutionary characteristics of the pathogen, host–host and host–pathogen interactions, and other real-world features (Sietttos and Russo 2013). Such models have been used in epidemic intervention planning, for example in the suggestion to stockpile antiviral drugs in order to halt progress of the 2005 H5N1 outbreak in South East Asia (Ferguson et al. 2005).

15.4 Inferring Key Epidemiological Model Parameters During a Pandemic

Having selected the appropriate model structure to capture the dynamics of disease spread, the next stage is to infer the model's parameters. There are many techniques used to do this, so here we will just consider a selection and will focus on the transmissibility and the virulence.

One simple method to estimate the basic reproduction number in the early stages of an epidemic is to estimate it directly from contact tracing. The approach is simple: the epidemiologist will trace all the people the primary case has made contact with and count which of those became secondary cases. Repeating this and averaging over a sufficient number of primary cases yields an estimate of the R_0 and the uncertainty around it.

Another approach is to find features in population-level data that permit direct estimation of the epidemiological model's parameters. For example, by recasting the exponential growth phase (early stages) of the outbreak into a linear problem, it is possible to estimate the R_0 simply by linear regression. An advantage of this approach is its simplicity, but a drawback is that it does not make much use of the caseload data available. A more sophisticated approach is to use a Bayesian approach to estimate the (posterior) parameters given the model structure and the data. The key advantages of this approach are that prior knowledge of the distributions of the transmission parameters can be incorporated, and that estimates of the uncertainty of the parameters are obtained directly from the model. It also makes full use of the observational data (Elderd et al. 2006). Disadvantages include computational complexity, choice of appropriate priors for each parameter and the more perplexing issue

that varying the model structure and rerunning the process may yield equally compelling explanations of the data and equally uncertain parameter estimates (Babtie et al. 2014).

It should be noted that estimates of R_0 may be very different for the contact tracing approach when compared to the population-based approaches, even when ensuring contact assumptions are the same at individual and population levels. Therefore, great care must be taken when making modelled projections about future caseloads using R_0 inferred from contact tracing (Keeling and Grenfell 2000; Breban et al. 2007).

Techniques for estimating the virulence of a disease are based on statistical approaches for parameter estimation. The virulence is the severity of the disease in an infected host. It is a means of quantifying the pathogenicity in the host. In a mortality context, the case fatality rate is the most common measure of virulence: this is the probability that a particular host dies after being infected by the disease. Other quantities, such as expected time until death from infection and lethal dose, are measures of virulence that focus on the mortality impact of the disease (Day 2002). DALYs and disease state-specific morbidity rates are used in the context of infectious disease morbidity.

Estimating a crude case fatality rate can be done as simply as dividing the total number of deaths in the population by the number of cases. However, this approach can be confounded by the fact that most epidemics will have a significant proportion of cases where the outcome is unknown at the point in time of estimation, particularly during the early stages of an emerging infectious disease. Methods have been developed to counteract this issue that make use of data on survival times for diagnosed patients (Ghani et al. 2005). Furthermore, for many diseases, there is incomplete caseload data because of unreported or asymptomatic cases. Other methods for reducing biases in case fatality rate estimation have been developed and can be employed in risk modelling (Lipsitch et al. 2015).

The same pathogen may have different virulence in different hosts. Sometimes, this difference is marked. For example, seasonal flu tends to be more virulent in young children and the elderly, whereas the 1918–1919 pandemic flu had noticeably higher mortality in the young adult population (Taubenberger and Morens 2006). The reason for this elevated mortality has been investigated in animal models in the lab. The conclusion of this study was that individuals who had been exposed to influenza once prior to 1918 were rendered vulnerable to experiencing a pathological immune response when infected with the 1918 H1N1 strain. The 2009 H1N1 pan-

demic had a different age mortality distribution again, with age-specific case fatality rates in teenagers and young adults significantly higher than in seasonal flu, whereas they were much lower in over 65s (Fig. 15.8). One possible explanation for this is that of residual immunity: those over-65s had some degree of immunity conferred from exposure to an H1N1 virus during childhood (Lemaitre and Carrat 2010). From these examples, it is clear that not just the age of the host is relevant: prior experience of previous strains will impact the virulence of future strains within the cohorts exposed to them. Sometimes these effects may reduce virulence, whereas in others, they may increase it.

It is also important to note that the prior health status of the individual plays an important role in the severity of a case. By studying bone fragments of victims of the Black Death, it has been shown that a disproportionate number of victims were malnourished or already suffering from prior health deficits (DeWitte 2014). More recent evidence from the 1918 and 2009 pandemics indicates that wealth and health, in particular the presence of comorbidities, is highly influential in determining the outcome of pandemic influenza cases. The case fatality rate in the lowest socioeconomic segment in the USA in 1918 was three times that of the highest (Sydenstricker 1931). In the 2009

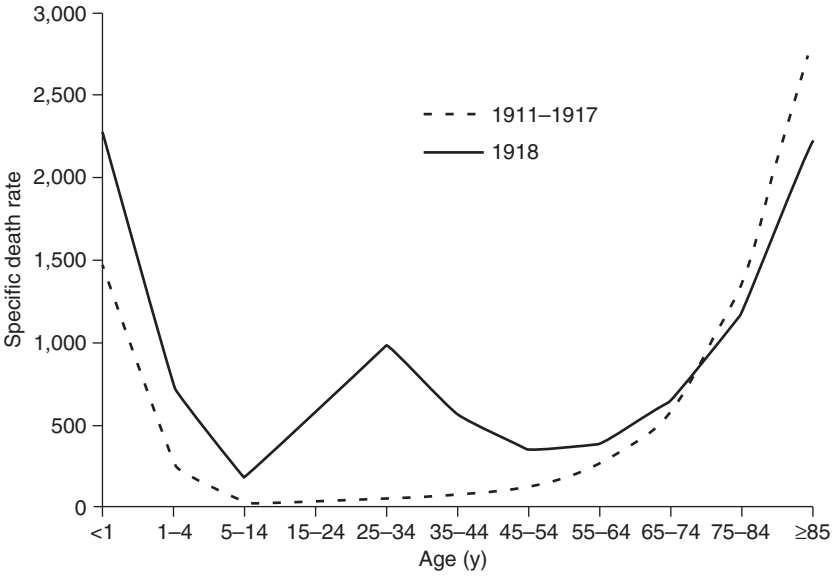

Fig. 15.8 Annualised age-specific mortality rates for deaths attributed to influenza or pneumonia per 100,000 cases in the USA for 1911–1917 and 1918. Notice the peak in mortality rates among young adults. Source: CDC (Taubenberger and Morens 2006)

pandemic, over 70% of deaths had an underlying risk factor for severe influenza (Peabody et al. 2010).

15.5 Medical Interventions and Public Health Countermeasures

As knowledge and understanding of epidemic transmission and virulence have increased, methods have been devised to combat them. Prior to the modern epidemiological theory, major progress had already been made. The canonical example is Edward Jenner's development of the smallpox vaccine, so-named because it was derived from the related disease, cowpox ("vacca" is the Latin for cow). This development and subsequent developments of other vaccines using the same fundamental immunological principles has perhaps saved (or extended) more lives than any other single medical innovation in history. Vaccines remain the most powerful tool used by public health practitioners to protect populations against transmission of epidemic diseases.

One caveat of the use of vaccination is that, by definition, a vaccine will not be available for an emerging infectious disease. Some prior biological material from the pathogen or a close relative (e.g. deactivated virus particles) is required to develop a vaccine, and these either will not exist or will not be known at the early stages of an outbreak. Recent experience from the 2009 H1N1 pandemic indicates that a time period of 5–6 months is required from first isolation of the novel virus to availability of the first batches of influenza vaccine (World Health Organization 2009). During this interval, depending on the transmissibility, a large fraction of the world population may have already been infected. For other emerging infectious diseases, this interval may be much longer. There remains no vaccine for HIV even 18 years after the first vaccine trials began (Koff 2014).

Using the simple SEIR formulation, modelling the impact of vaccinations can simply be done by including a rate at which people transition from susceptible to a fifth compartment, "vaccinated". This can be done in conjunction with all the other features that can be introduced to compartmental models, including age, demographic and spatial effects. Using ABMs, it is possible to go a step further and include more detail about the strategy for vaccination and the likely uptake in different individuals. One current application of such modelling is a Dengue vaccine that has recently been licenced for use in six countries. The clinical trials of the vaccine demonstrated its ability to success-

fully confer immunity to those who had already been infected by Dengue; however, for people with no prior exposure to Dengue the vaccine increases risk of a more severe Dengue infection in future. Advanced modelling of the age groups vaccinated and the local transmission intensity suggests that vaccination of selected subgroups according to age and level of local transmission can have significantly superior outcomes versus traditional vaccination approaches (Ferguson et al. 2016).

Pharmaceutical countermeasures beyond vaccines fall into categories used to combat the infection, thus reducing the effective case fatality rate in treated patients. Antibiotics are an example of such an approach, where a patient suffering a bacterial infection may be treated with a high degree of efficacy (depending on the specific pathogen). Antibiotics can also be valuable in reducing mortality in pandemics where the pathogen is a virus. While the antibiotic does not directly have any impact on viral load, in historical pandemics such as 1918, very large numbers of deaths have been attributed to secondary bacterial infections, such as bacterial pneumonia (Morens et al. 2008). Modelling the effect of antibiotics over the course of such a pandemic can be done as follows: (i) assess antibiotic efficacy against secondary bacterial infections in the infected individual, yielding proportion of mortality reduced per secondary infection; (ii) multiply this by the proportion of secondary infections that occur; (iii) compare against the baseline of the primary infection case fatality rate. Reconstructions of the 1918 pandemic scenario assuming the ability to treat secondary bacterial infections have shown that use of antibiotics may have been able to reduce mortality by 60% (RMS 2012).

To treat non-bacterial primary infections, drugs such as antivirals, antifungals and antiparasitics may be used. Antivirals work by directly attacking viruses. Examples of antivirals used against influenza include oseltamivir and zanamivir, both of which inhibit reproduction of the virus in the host cell. These drugs and others have been stockpiled in response to emerging influenza pandemics because research at the time indicated they would help to reduce transmission and case fatality rates associated with the pandemic (Ferguson 2005). While the strategies remain reasonable in theory, the efficacy of these drugs in reducing influenza transmission and virulence has been called into question after more extensive study of their effectiveness (Jefferson et al. 2014).

The final intervention at our disposal is supportive care. This involves the stabilisation of the patient, treatment of dehydration via provision of fluids, monitoring and maintaining oxygen levels and blood pressure and treating secondary infections as they occur. Cholera is an example of a disease where,

when used appropriately, supportive care should reduce the case fatality rate to below 1% (Wong 2015). When supportive care is inadequately administered, case fatality rates are much higher, for example up to 12% in a community in Kenya in a recent epidemic (Loharikar et al. 2013). Modelling the impact of supportive care involves assessing the joint distribution of efficacy of supportive care against each pandemic pathogen with the availability of and access to supportive care in the region in question.

Non-pharmaceutical countermeasures, such as isolation, quarantine, curfews and school closures can be useful tools to combat the spread of infectious diseases. Isolation is at its most useful when a disease becomes communicable after the onset of symptoms. One example of such a disease is Ebola virus, where effective isolation of suspected and known cases has been shown to reduce transmissibility significantly and can be incorporated into epidemic models (Shan et al. 2015). In examples such as influenza, however, such strategies do not work because onset of symptoms is some time after the infective period has begun. Non-pharmaceutical countermeasures used to reduce influenza spread are therefore focused on reducing contact rates and improving public practices around personal hygiene in the context of the pandemic. Evidence from some epidemiological and a number of modelling studies suggests that school closures may be an effective tool in reducing the peak load on hospitals and health infrastructure during a flu pandemic and may buy time to roll out the vaccine (Earn et al. 2012; Jackson et al. 2014).

15.6 Probabilistic Models

This section provides a review of how the epidemiological models described under "Modelling infectious disease spread" have been adapted to the use case of modelling the probability distribution of cases, morbidity and deaths over a future short- to medium-term time horizon. Borrowing from catastrophe modelling, this problem is broken down into two components:

- Frequency—how many pandemics will occur in the time period; and
- Severity—how many cases and deaths and how much morbidity these pandemics may cause.

First, we consider the earlier pandemic risk models used in the life insurance industry. The first pandemic risk models used in a risk transfer context did not include treatment of the way infectious diseases transmit through the population. The first such model involved in an excess mortality transaction

was a statistical model designed to capture the mortality risk associated with influenza. This was an actuarial model that drew from analysis of the relatively small number of influenza pandemics for which we have mortality data.[7] In the years 1918–1919, 1957–1958 and 1968, the three historical pandemics were included in the model. An additional scenario was incorporated, which was a version of the 1918–1919 pandemic with an adjustment based on assumptions about the change in the world population and health environment between 1918 and the vintage of the model. From these four data points, a heavy-tailed probability distribution was fit to form the severity distribution. Some further epidemiological information on seasonality was included to complete the severity component. The frequency distribution was based on the assumption that future flu pandemic prevalence would be similar to the past and draws from the literature of known and suspected flu pandemics through the ages (Bagus 2008).

This type of modelling falls short when trying to capture the range of plausible future outcomes once a pandemic has already begun, for example in the 2009 H1N1 pandemic. In order to tackle this specific issue, modellers made use of epidemiological models of infectious disease. Consistent with this, the majority of pandemic models used now in the insurance industry are adapted from compartmental models and aim to quantify the distribution of morbidity and mortality rates future pandemics may wreak on a population (Fig. 15.9).

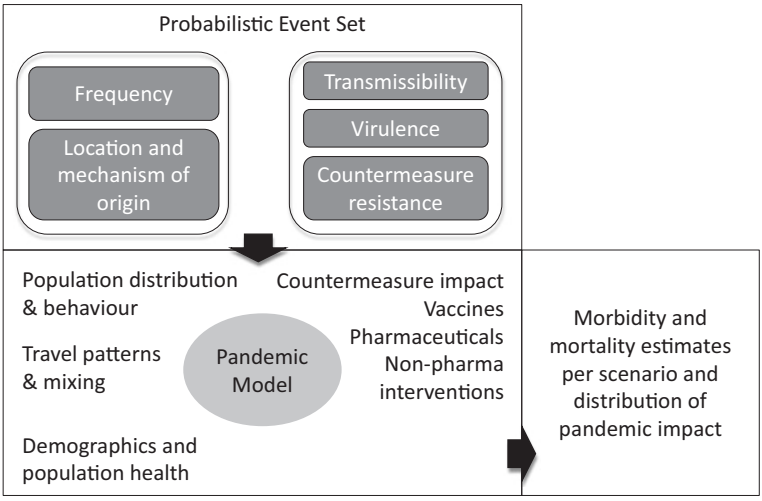

Fig. 15.9 Example of a structure of a probabilistic pandemic model

15.6.1 Frequency and Origin

As evident from Table 15.1, true pandemics are relatively rare events, even in the context of catastrophes. For this reason, there is no single generally accepted approach to model frequency of novel pandemic emergence. Models may draw on a combination of the historical record, the behaviour of hosts, the interactions between hosts, pathogens, vectors, and the environment, and the fundamental evolutionary processes that give rise to novel pathogens. Most models start with the historical record.

Owing to the relatively large number of influenza pandemics in the historical record, pandemic models are typically broken down into two or more submodels—one for influenza, and the other model(s) capturing other emerging or re-emerging infectious diseases. It can be seen that between 3 and 4 influenza pandemics occurred per century within the timeframe of the historical record. This provides a top-down view of the frequency of the outcome of myriad random processes. A frequency model based on the assumption that flu pandemics are independent events with a rate of between 3 and 4 per century has been used as a starting point for modelling (Bagus 2008; RMS 2012; AIR 2015). Beyond independence, this includes the tacit assumption that the behaviour of the world's population has not changed significantly over time and that the probabilities associated with the underlying processes leading up to a novel influenza strain. Moreover, while the historical record goes back centuries, the rare nature of pandemic disease means there are not many events from which to infer a frequency distribution.

Further sources of information can be used to establish a frequency distribution for pandemic influenza, and the same principles can be extended to other pandemic-capable diseases too. This begins with understanding the evolutionary processes behind zoonosis. The process of genetic reassortment underpinning pandemic flu zoonosis may occur only when a single animal is infected with two strains of influenza. Therefore, data on the zoonotic reservoir of the disease can be useful in estimating future pandemic frequency. Influenza viruses circulate among animal, notably avian and swine populations. Where swine or poultry is kept in closely confined conditions and where viral strains that may be common in animal populations in other regions are introduced to a new region, the chance of reassortment is increased. Close human contact with animals, for example, sleeping in close proximity or frequent manual handling can increase the chance of a novel pathogen being transmitted to humans. We can, therefore, use proxies derived from these principles to gain insight on the probability of reassortment occurring and

its transmission to humans. Extensive mapping projects are conducted by the Food and Agriculture Organization of the United Nations and are used in modelling frequency and location of origin of novel animal pathogens and zoonoses (Robinson et al. 2014).

15.6.2 Transmissibility and Virulence

The transmissibility and virulence parameters in an emerging pandemic can be estimated using the methods described in the section "Inferring key epidemiological model parameters during a pandemic". In the case of a probabilistic model, realistic distributions of transmissibility and virulence need to be parameterised for each disease class covered by the model. These distributions can then be sampled to generate the events of the probabilistic event set.

To parameterise the event set's transmissibility distribution, it is typical to fit a long-tailed parametric distribution to the historical R_0 estimates from prior epidemics and pandemics. Expert epidemiological judgement is required to ensure that the tail of this distribution is reasonable (Sullivan 2010). Unabated case fatality and morbidity rates would also be derived by inferring the appropriate distribution from prior data on infectious disease virulence.

Some probabilistic pandemic models incorporate a degree of negative correlation between transmissibility and virulence on the grounds that highly virulent diseases are more debilitating and therefore readily self-limit (Woo 2015). The argument is that this self-limiting behaviour means such diseases would be under negative selective pressure and are therefore less common. While this argument has been criticised for assuming group selection,[8] further evolutionary arguments and simulations suggest that an intermediate level of virulence is preferred (Lenski and May 1994). This is captured in the models by sampling from a joint distribution of transmissibility and virulence.

Estimates of the other factors influencing the post-intervention transmissibility and virulence of the disease are based on assessment of experience in prior pandemics, published countermeasure efficacy where available, and stated best (and actual) practices of government agencies and NGOs in countering infectious disease. These are likely to be simple distributions and are open to be adjusted and stress-tested by the end user in some probabilistic pandemic modelling software packages (RMS 2014).

15.6.2.1 Infectious Disease Modelling in Comparison to Catastrophe Modelling

Scenario-based and probabilistic models for pandemics are similar in structure to natural catastrophe models for geophysical hazards. Table 15.4 shows a comparison of the main elements of these models used in the insurance industry. A key difference between most natural catastrophe events and pandemics is the timeframe over which they develop. Many natural catastrophes, in terms of physical hazard, are over within hours, days or weeks of the first damage. However, even pandemics with a short caseload doubling time can go on for many months, even years.[9] This results in a further type of scenario modelling for pandemics—emerging event modelling.

Table 15.4 Comparison of the functional components of pandemic models versus natural catastrophe models

	Natural hazard model	Pandemic model
Historical reconstructions	Estimate the impact of an event with hazard equivalent to estimated hazard in the historical event on today's built environment	Estimate the impact of a novel pathogen emerging with transmissibility and virulence characteristics similar to the historical event, but applied to today's population and under modern world travel, medical and non-medical countermeasure assumptions
Stochastic scenarios	Generate an event with plausible physical characteristics and estimate impact on built environment	A novel emerging or re-emerging pathogen with plausible biological characteristics. Estimate its impact on population
Emerging event modelling	–	A real-world emerging pathogen with uncertain characteristics and upon which epidemiological study is being carried out. Model its progress and estimate the impact on the population
Probabilistic model	Generate a suite of events—a stochastic event set—composed of a large set of stochastic scenarios, with statistical properties based on the modelled frequency and physical properties of those events	A set of stochastic scenarios based on the modelled frequency distribution and distributions of biological and medical characteristics associated with the type of pathogen

An actual versus expected assessment of RMS's model for the novel H1N1 influenza pandemic provides anecdotal evidence that good performance can be achieved when applying probabilistic pandemic risk models to real-world emerging events (RMS 2010).

15.7 Applications

Epidemic and pandemic spread models have been used in a public health context for many years, both to explain the patterns seen in previous events and to make projections for events that are emerging. When a new pathogen exhibiting sustained transmission has been identified, models can be used to estimate the range or distribution of potential outcomes. This is relevant to public health practitioners or task forces focussed on reducing the scale and impact of the outbreak, as well as to governments and organisations exposed to the impacts of the outbreak. For example, the range of possible control effects of using various countermeasures can be assessed by modelling their impact on the simulated pandemic, yielding a distribution of the net impact of the intervention. Ring vaccination—vaccination of traceable direct and indirect contacts of infected persons—for Ebola virus was trialled during the latter stages of the 2014–2015 epidemic in Guinea. Results of the field trial indicated that a ring vaccination strategy using the candidate vaccine could be highly effective at reducing transmission of the disease (Henao-Restrepo et al. 2015). This theory was tested further via computer simulation of ring vaccination strategies, which supported this finding in the latter stages of an epidemic, but with the caveat that the same strategy could be substantially less effective during the early stages of an outbreak (Kucharski et al. 2016).

In an insurance risk transfer context, there are three main types of transaction that pandemic risk models support. The first is the excess mortality bond. The first such bond, Vita Capital Ltd was issued by Swiss Re in 2003; it and some other insurers and reinsurers have actively participated in the issuance of excess mortality bonds since that time. These instruments provide the sponsor a financial hedge against short-term (one- or two-year long) increases in mortality rates relative to the baseline mortality experienced in recent, normal times. Their purpose is to make a payout to life insurers and reinsurers in the event a qualifying excess mortality rate is achieved. The one to two calendar-year timeframe is particularly relevant for influenza pandemics, which are typically around that duration. These are parametric bonds, insofar as their payout structure is not based on an

indemnity loss to the sponsor. Instead, it is based on national statistics agency-provided mortality data for the population of the covered countries. Since 2003, excess mortality bonds with a cumulative face value of $3.4 billion have been issued.

Beyond mortality, a transaction has been devised to provide coverage against extreme increases in cost of healthcare for a health insurer. A large surge in demand and used of health services and pharmaceuticals could drive a major loss to a health insurer, so pandemic risk modelling contributed to quantifying and transferring that risk to the capital markets.

Further applications to risk transfer include the World Bank's proposed Pandemic Emergency Facility, which provides early stage surge funding to finance the response against a novel infectious disease outbreak. This facility was proposed following the 2014–2015 Ebola virus disease epidemic. The principle is that a well-funded rapid response will halt some outbreaks much earlier than would otherwise be possible, thus saving orders of magnitude of lives and reducing the cost of the ultimate response.

15.8 Conclusion

This chapter has explored the nature of pandemic diseases, their history and the mathematical models that can be used to estimate their probability of emergence and future progress. Modelling of infectious diseases remains an active area of scientific research and plays an important role in maintaining public health and resilience to catastrophic mortality events. It also underpins appropriate management of excess mortality risk by life insurers and reinsurers, including providing the means to quantify such risks for the purpose of risk transfer.

Beyond the pure mortality impact, the emergence of a highly transmissible infectious disease could have a major impact on the global economy by way of less willingness to travel, reduced economic participation and confidence.

Notes

1. A virus, bacterium or parasite that can cause disease.
2. DALYs: Disability-adjusted life years are measured as number of years of life lost caused by disability, ill-health or premature death.
3. Mortality in this context is number of deaths per unit population by cause of death. Morbidity is the rate of disease in a population.

4. The World Bank classifies economies on the basis of income, using the following four categories: low, lower-middle, upper-middle and high income.
5. A vector is any agent that carries and transmits a pathogen from one living organism to another.
6. The gamma distribution is commonly used to model non-negative random variables. The Dirac delta distribution is a distribution with zero variance.
7. Actuarial models are extrapolations of past data used for forecasting future outcomes.
8. Group selection assumes natural selection will happen at the level of a group of organisms rather than at the level of an individual or gene. The units of selection remain an active area of research among evolutionary biologists.
9. Doubling time is the time period required for the number of cases to double during the exponential growth phase of an epidemic.

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