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# Best practice assessment of disease modelling for infectious disease outbreaks

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**Review**

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## Abstract

During emerging disease outbreaks, public health, emergency management officials and decision-makers increasingly rely on epidemiological models to forecast outbreak progression and determine the best response to health crisis needs. Outbreak response strategies derived from such modelling may include pharmaceutical distribution, immunisation campaigns, social distancing, prophylactic pharmaceuticals, medical care, bed surge, security and other requirements. Infectious disease modelling estimates are unavoidably subject to multiple interpretations, and full understanding of a model's limitations may be lost when provided from the disease modeller to public health practitioner to government policymaker. We review epidemiological models created for diseases which are of greatest concern for public health protection. Such diseases, whether transmitted from person-to-person (Ebola, influenza, smallpox), via direct exposure (anthrax), or food and waterborne exposure (cholera, typhoid) may cause severe illness and death in a large population. We examine disease-specific models to determine best practices characterising infectious disease outbreaks and facilitating emergency response and implementation of public health policy and disease control measures.

## Introduction

Epidemiological modelling of disease outbreaks has become a crucial tool in public health practice. Information to mitigate impending epidemics is often estimated by post-event modelling from prior outbreaks. Comprehensive predictive models include components representing the 'epidemiologic triad' of disease agent, host and environment [1]. Critical model input information may include the latent, incubation and infectious periods (the 'natural history' of infection), disease surveillance data delineating infection distribution and spread, infection transmission dynamics and medical countermeasures. Population demographics, geographic networks and host movement information are also useful. Other factors not attributable to either disease agent or host within an environment may be appropriate for model inclusion, such as hygiene, cultural/religious practices, climate and reservoirs [2]. We review current epidemiological models for diseases which potentially affect large populations. These include human-to-human disease transmission (Ebola, influenza, smallpox), via aerosol exposure (anthrax), food and waterborne exposure (cholera, typhoid) and co-infections.

## Ebola

The 2014–2016 West African Ebola virus disease (EVD) outbreak had greater geographic spread, duration and magnitude than previous outbreaks [3], which permitted applications from disease modelling for planning purposes [4]. It became evident that absent additional control measures, the outbreak would dramatically increase [5]. As initial African EVD cases emerged, endemic disease 'background noise' (e.g., cholera, Lassa fever, malaria) impeded patient diagnosis, rendering early outbreak identification difficult [6]. Unlike previous outbreaks, the early patient diagnosis was strongly reliant upon patient isolation [7]. Community cultural practices increased disease spread, hindering mitigation measure effectiveness [8]. Information derived from direct medical care best practice [9], helped terminate community transmission. Control measures for EVD eventually included effective measures for contact tracing, case isolation and management, burial guidance, community involvement, enforced sanitary measures [10], establishing field hospitals [11] and laboratories [12], increasing medical supply dissemination [13], enforcement of border controls [14] and international support [5].

Information was required early in the outbreak to determine optimal response. Disease models were designed to predict spatiotemporal spread and magnitude and to estimate best mitigation strategies to end the outbreak. A September 2014 Centers for Disease Control



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and Prevention (CDC) SEIR (susceptible, exposed, infectious, recovered) model predicted the EVD outbreak would cease if 70% of patients received direct medical care [15]. An October 2014 World Health Organization (WHO) model [16] determined that, in the absence of enhanced contact tracing, adequate case isolation, increased clinical management, safe burials and greater community and international engagement, Guinea, Liberia and Sierra Leone would experience thousands more cases and deaths weekly [5].

Ebola outbreak interventions were unequally effective, due to implementation capacity, timing, compliance or extent of completion. Multiple interventions may have unforeseen synergistic effects. Partial implementation of an intervention also may evince different – or no – outbreak amelioration. Non-conventional humanitarian interventions were implemented and included expanded access (compassionate use protocols), novel drugs to treat infected patients (http://www.fda.gov/NewsEvents/PublicHealthFocus/ExpandedAccessCompassionateUse/default.htm) humanitarian military intervention and the use of non-conventional sheltering and food aid resources [17]. Healthcare workers were essential in controlling the EVD epidemic and suffered proportionately (898 cases, 518 deaths) [18–22].

Travel restrictions implemented during the outbreak became controversial, with claims that West African travel bans were unsupported by public health science [23] and non-compliant with WHO International Health Regulations (IHR) [24]. Some models indicated travel restrictions were insufficient to prevent the global spread of Ebola, delaying it a few weeks at best [25,26]. One model estimated that, during November 2014, with existing flight restrictions and airport screening guidelines, an average of 2.8 Ebola-infected air travellers per month departed from Guinea, Liberia and Sierra Leone [27]. Later analyses determined that between 4% and 10% of newly-infected Ebola cases migrated to another district within their country, and ⩽23% of this group left their country. Due to underreporting, country differences in cross-border transmission in West Africa was undetermined [28].

## Ebola model findings

Inherent to outbreak model development is that the most accurate model to describe real-world events can be best developed after the outbreak [29–31]. For example, in Sierra Leone, positive associations were found between Ebola transmission and population density, proximity to Ebola treatment centres, cropland coverage and atmospheric temperature. Interventions which interrupted household transmission were discovered to be particularly crucial for EVD transmission cessation [32].

Modelling aided the public health response by analysing potential disease spread and directing interventions. Introduction of burial practices and climatology into agent-based SEIR modelling assisted placement of Ebola treatment centres [33]. Optimal modelling occurred with behavioural factor inclusion [31]. While social and cultural disease determinants were integral to controlling this Ebola outbreak, these factors may not always be considered for outbreak model inclusion but should be where feasible. A CDC SEIR model encouraged increased contact tracing, and improved infection control, reducing new EVD cases [34]. Rapidly reporting newly diagnosed cases and publicising best practices to healthcare providers, health officials and disease modellers enabled contact tracing, calculating transmission dynamics and enhanced disease spread forecasting. Other than known disproportionate healthcare worker disease burden, the level of medical care provided throughout this outbreak cannot be determined to fully support the 2014 CDC model's findings.

When estimating outbreak occurrence in the early stages of disease emergence in a large population, a simpler SEIR model may be best applied [35]. Initial stochastic disease models described transmission dynamics, determined origin and spread, and projected the reproduction number ($R_0$) to inform disease control [5,15]. Early EVD models identified disease dynamics comparable with previous outbreaks [5], and postulated rapid spread due to the populations affected and inadequate control measures. As control measures increased, earlier predictions became irrelevant [36]. Because some models overestimated outbreak growth or underestimated Ebola treatment unit admissions, predicting an earlier peak than had occurred [37], the practicality of disease models was questioned [38]. Later in this outbreak, more detailed mechanistic models included depletion of susceptibles, and specific transmission routes and settings, to help fine-tune public health interventions [39]. These models should be run weekly based on real-time data for best-result forecasting. Travel and border health measures might have prevented EBV spread in West Africa through travel deterrence of symptomatic or exposed individuals and educating travellers about self-protection [40].

## Malaria co-infections: influences on outbreak intervention and an Ebola modelling confounder

In tropical countries, malaria and typhoid are endemic leading public health concerns. False diagnoses due to similar signs and symptoms and false positive test results are major disease management challenges. Modified SEIR models [including carriers (C)] describe co-infection dynamics of malaria and typhoid [41]. A decision tree model analysed a year's preventive malaria treatment costs for patient contacts with EVD in West Africa. Cost per treatment unit admission averted and contact age was calculated. Sensitivity analyses assessed how results varied with malaria parasite prevalence, the daily cost of treatment stay and preventive malaria treatment compliance and effectiveness [42].

## Malaria co-infection model findings

An efficient simultaneous prevention programme will reduce co-infections such that $R_0$ <1, thereby eradicating the disease. Both malaria and typhoid must be simultaneously managed for successful control of co-epidemics [41]. Preventive malaria treatment for contacts of EVD patients was cost-saving. The model indicated that providing preventive malaria treatment to contacts of EVD patients should be considered during EVD outbreaks where high levels of malaria transmission occur, to reduce non-critical healthcare admissions [42].

## Influenza

Influenza is a major public health threat. Beyond seasonal impact, the probability of an influenza pandemic remains among the greatest biological threats to humans. Influenza pandemics could occur by novel virus introduction from reservoir species, coupled with the sustained human-to-human transmission in a susceptible population [43]. During influenza outbreaks, secondary bacterial infections are a leading cause of illness and death [44]. There appears to be lethal synergism between influenza and certain bacteria [45], including *Streptococcus pneumoniae* [46] and Group A *Streptococcus* infection [47].

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An age- and risk-stratified stochastic SEIR model with Markov Chain Monte Carlo (MCMC) analysis including vaccination data reproduced influenza effects over 14 seasons in the UK. When comparing existing reduction in infections and deaths to no vaccination, vaccination prevented 0.39 infections per vaccine dose and 1.74 deaths per 1000 doses. Targeting 5–16-year-old children increases immunisation effectiveness among influenza transmitters, and increases immunisation efficiency, resulting in overall reduction of 0.70 infections per dose and 1.95 deaths per 1000 doses [48].

Extensive travel restrictions may delay, not prevent, novel influenza virus spread. One review found internal travel and international border restrictions delayed influenza epidemic transmission by 1 week and 2 months, respectively [49]. International travel restrictions delayed the epidemic spread and peak between a few days and 4 months. Travel restrictions can reduce the incidence of new cases by <3%. Travel restriction effectiveness was reduced when implemented >6 weeks after epidemic notification, or with high transmissibility levels. Travel restrictions minimally affect cities with dense populations and travel networks and did not contain influenza within a defined geographical area [49].

As individuals increasingly describe their illness on social media before seeking medical care, Web-based data sources are used for public health surveillance. A 2016 study collected publicly available, de-identified data from the CDC, Google Flu Trends, HealthTweets and Wikipedia for the previous three influenza seasons. Bayesian change point analysis with MCMC detected seasonal changes in each data source. Among Web-based sources, Google had the best sensitivity and PPV (positive predictive value) in detecting a change in influenza-related data. While change points [50] in Google, Twitter and Wikipedia data occasionally aligned well with those captured in CDC influenza-like illness (ILI) data, they did not detect all changes in CDC data [51].

## Influenza model findings

Modelling affirmed that targeting children and older adults are the most efficient vaccine use to reduce overall influenza morbidity and mortality [48]. Travel restrictions have limited specificity for influenza containment during novel virus emergence [49]. While social media data mining demonstrates alignment with CDC ILI data, the CDC data are more comprehensive. Accurate influenza modelling to predict synergistic effects between viral secondary bacterial infections in a susceptible population has yet to be accomplished [52].

## Smallpox

As smallpox was declared eradicated in 1980 [53], smallpox transmission through deliberate virus release should be considered, along with the potential for accidental exposure to unrecognised live virus, as the discovery of unknown viable smallpox virus stored at the US National Institutes of Health (NIH) demonstrated [54]. Contact tracing and case isolation are among initial interventions for a smallpox event. As their effectiveness in a vaccinated population is unknown, evaluation with a multi-type stochastic model (an SIR model with some vaccinated designated fully immune) may assess partially vaccinated populations [55].

The 1967 Abakaliki, Nigeria, smallpox outbreak afforded well-documented data for epidemic modelling. When this outbreak occurred, ~89% of the population was vaccinated. A religious group had refused vaccination, and one smallpox case initiated an outbreak that infected 30 people [56]. An SEIR model variant (susceptible, exposed, with fever, with rash, quarantined or removed) was used to model this outbreak, with Bayesian analysis with MCMC [57]. It suggested the outbreak resulted from population interactions, and that control measures themselves did not end the epidemic. Control measures (case isolation upon detection) introduced during the outbreak reduced the rash period from 16 to 2 days, abating new infections. As with other natural smallpox outbreaks [58], this outbreak ended when susceptible individuals in prolonged and intimate contact with cases became exhausted.

An SEIR-like CDC model estimated smallpox spread following deliberate virus release [59]. Using MCMC, the analysis assumed 100 persons initially infected, each infecting three others. This model estimated combined vaccination and quarantine combined could stop an outbreak with a daily 25% quarantine rate, and sufficient vaccination to reduce smallpox transmission by >33%. Though quarantine itself could halt smallpox transmission, its success requires 50% of symptomatic cases be removed daily. Vaccination alone could reduce population susceptibility, and halt the outbreak within 365 days, after 4200 cases. Historical data provides a median of 2155 smallpox vaccine doses per case will terminate outbreaks.

## Smallpox model findings

Unsurprisingly, modelling demonstrates past vaccination significantly influences outcomes, as does case movement identification. Intervention delays greatly increase total cases. Further recommendations from modelling include assessing delays in case detection and frequency of case contacts among unvaccinated and previously vaccinated populations [54]. Post-release intervention should combine quarantine and vaccination. A ~40 million dose vaccine stockpile should halt a smallpox outbreak in the USA [59].

## Anthrax

The spores of *Bacillus anthracis*, the causative organism of anthrax disease, can be used as a weapon through aerosol dissemination. Such an aerosol release is often modelled using the Hazard Prediction and Assessment Capability (HPAC) or similar programme [60]. An MCMC algorithm to simulate anthrax release demonstrated that early targeted prophylactic treatment minimised overall mortality, based on estimates from the initial five cases [61]. A CDC model combines inhalational anthrax caseload, effects of variable post-exposure prophylaxis (PEP), and healthcare facility surge capacity to project hospitalisations and casualties. This model confirmed the value of PEP initiation, predicting that deaths peak 5 days post-exposure, hospital treatment volume will peak 15 days post-exposure and recovery peaks 23 days post-exposure [62].

## Anthrax model findings

Modelling illustrated the possibility of early estimates derived from initial anthrax cases to characterise location and geographic spread of an outbreak [60]. Delays in detection and response to a large-scale anthrax aerosol release in a large city nullify a mass prophylaxis campaign to prevent a surge in hospitalisations [63]. The CDC model's publicly-available software (Anthrax Assist) enables health officials to examine predictive scale and consequences of alternative responses to an anthrax event, and

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uses disease surveillance data, allowing available data input. It demonstrates realistic benefits of public health countermeasures and inherent value of PEP [61].

## Cholera

Cholera, a bacterial disease caused by *Vibrio cholerae*, causes severe diarrhoea and subsequent dehydration. It is preventable with clean drinking water access and vaccination. Interventions and treatments include water sanitation, antibiotics, oral rehydration therapy and supportive care. Cholera is endemic in some countries and imported in others. In October 2010, imported cholera caused the first modern outbreak in Haiti. Cholera outbreaks have recently occurred in Afghanistan, Bangladesh, Dominican Republic, Democratic Republic of Congo, Iraq, Kenya, Malawi, Mozambique, Nigeria, Somalia, South Sudan, Tanzania, Yemen and Zimbabwe [64–66].

A cholera SEIR model can include data for potential interventions, population demographics, surveillance data, timescale evaluations [67], and *Vibrio* characteristics, including dose and viability [68]. Cholera modelling parameters may differentiate seasonal endemic cholera outbreaks from epidemics exacerbated by natural or man-made disasters. An outbreak model for a non-endemic region's population could include minimal population immunity, a high attack rate, similar attack rates among age groups and high symptomatic groups. Some models approximate drinking water bacterial concentration [69]. A comprehensive extended compartmental model for Haitian cholera transmission specified rapid human-to-human transmission and slower human-to-environment and environment-to-human transmission [68] while incorporating cholera incidence and remote sensing data. Notably, the environmental compartment source of *V. cholerae* exposure was modelled separately, and incorporated environmental considerations of bacterial pathogenesis. Unsurprisingly, this model indicated that cholera outbreaks will likely continue. The uncertainties inherent in cholera modelling are such that errors in a single parameter can eliminate model predictive value [66].

Limited vaccine models were used to assess strategies for cholera outbreak control in Haiti [70]. Targeting 1 000 000 doses of vaccine (enough for two doses for 5% of the population) could reduce total cases by 11%. Vaccine available for 30% of the population, coupled with hygienic improvements, could reduce cases by 55% [66]. A static cholera model was used to estimate the potential number of cholera cases averted through improvements in water, sanitation and hygiene (WASH), oral cholera vaccine (OCV), or both. Cholera incidence over 20 years was estimated using Malawian data [71]. Over the next two decades, scalable WASH interventions could avert 57 949–78 567 cholera cases, OCV could avert 38 569–77 636 cases and combined WASH and OCV interventions could avert 71 586–88 974 cases [72].

Recently, immunisation against cholera has improved. While studies have evaluated two-dose regimens (i.e., Dukoral and Shanchol) for cholera vaccination [73], a single-dose [74] licensed cholera vaccine (Vaxchora) [75] now exists [76,77]. A consideration for Vaxchora, which warrants model forecasts, may be its prohibitive cost [78] for resource-poor nations, compared with two-dose vaccines [72]. Further, studies estimating cholera vaccination cost-effectiveness may neglect disease transmission predictions [79,80]. During large, prolonged outbreaks, transmission dynamics among most susceptible populations are crucial for modelling and enable a better estimate of interventions, including vaccination [81].

## Cholera model findings

Modelling cholera transmission provides cost–benefit evaluation for potential interventions [82,83]. Cholera models should include contaminated water ingestion. Modelling cholera infections is difficult due to relationships between human hosts and environmental components, requiring a combined human–environment epidemiological model [84]. In a country with an increased susceptible population, the presence of *V. cholerae* in the environment, and absence of drinking water, sanitation and infrastructure improvement, cholera will likely continue. Vaccine distribution in high-risk areas is maximally efficient. Multiple modelling efforts have predicted that increased hygienic improvements, coupled with a limited vaccination campaign, may have synergistic cholera reduction effect. Sensitivity analyses of cholera models may help refine model prediction.

## Typhoid

Multi-year epidemics of *Salmonella enterica* serovar Typhi have recently been reported from eastern and southern African nations, and a large outbreak occurred in Malawi in 2014 [85]. This increase in typhoid cases may be linked to the emergence of the H58 haplotype, which often exhibits multiple drug resistance (MDR). An SIR model fitted to culture-confirmed *Salmonella typhi* infections at a Malawian hospital showed an increase in typhoid transmissibility due to the emergence of drug resistance associated with the H58 haplotype may help to explain the typhoid outbreaks [86]. The model included compartments for carriers and environmental reservoir, to account for regional transmission dynamics.

## Typhoid model findings

Modelling supported the hypothesis that Malawian outbreaks were caused by the emergence of multiple drug resistance and recent African introduction of the H58 haplotype [85], rather than urbanisation [87], overcrowding [88] or changing immunological susceptibility [89].

## Discussion

Current disease models optimally build upon previous work, allowing a greater understanding and inclusion of significant factors affecting disease transmission. Existing efforts differ for each disease. Bernoulli's model of smallpox transmission was published in 1766 [90], while comprehensive cholera outbreak models are recent developments [91]. Initial models constructed during the EVD outbreak included values derived from earlier outbreaks [15]. Co-infection models build upon knowledge from separate modelling for each disease [41].

During the evolving EVD epidemic, it was difficult for modellers to rapidly determine effective outbreak cessation measures. While epidemiologic models have demonstrated utility in post-intervention evaluation [92], the inability to control the EVD epidemic brought an immediacy for disease modelling to provide solutions. Partially because of the extended nature of the outbreak, and subsequent direct discovery of sustainable successful interventions, modelling could provide vetting of proposed interventions prior to implementation. Timely modelling informed specific EVD outbreak intervention through confirming effective intervention with increased patient management capacity,

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**Table 1.** Contemporary outbreak modelling characteristics

| Disease modelled | Disease transmission | Data sources used for model | Benefit of modelling | Lessons learned | Optimisation goals for future models |
|---|---|---|---|---|---|
| Ebola | • Person-to-person | • Real-time during outbreak (March 2014–March 2016)<br>• Retrospective | A persistent outbreak allowed for model fine-tuning in real time | • Early models created with incomplete assumptions.<br>• Model incorporation of social and cultural disease determinants informed outbreak response | Incorporate known disease and healthcare data into a comprehensive predictive model |
| Malaria co-Infections (EVD confounder) | • Vector-borne<br>• Person-to-person | Data obtained during West Africa Ebola outbreak (2014–2016) | Modelling demonstrates treatment of co-infection permits improved EVD response | Co-infections may be reduced by efforts guided by targeted predictive modelling | Apply probable co-infection modelling for other outbreaks |
| Influenza | • Person-to-person | • Annual influenza outbreak.<br>• Pandemic years (1918, 2009) | Continuous monitoring of influenza transmission allows for real-time modelling | Influenza models useful for pandemic predictions | Incorporate influenza and bacterial co-infections into model |
| Smallpox | • Aerosol<br>• Person-to-person<br>• Laboratory accident[a] | • Historical data<br>• 1967 Nigeria outbreak | Disease eradication ensures modelling will remain top priority for outbreak control | Vaccination and quarantine limits, and synergistic effects estimates derived by modelling | Model disease agent release scenarios with infected individuals at multiple locations |
| Anthrax | • Aerosol<br>• Ingestion<br>• Direct contact through handling infected animals, meat | • 1979 Sverdlovsk data, primary source for extrapolated exposure[b] | Mass exposure prophylaxis plans have been developed from modelling | Information obtained from initial anthrax cases can be used in modelling to help shape response | Refine models to optimally respond to natural outbreaks |
| Cholera | • Environment-to-person<br>• Person-to-person | Outbreaks modelled from Haitian and Malawian data | Cholera modelling can be used to provide cost–benefit of large outbreak interventions | Modelling innovative approaches such as one-dose of a less costly two-dose vaccine can provide effective guidance | Cholera remains a global scourge of low resource nations. Sensitivity analysis should be used to modify model prediction |
| Typhoid | • Person-to-person<br>• Food and water transmission | 2014 Malawian outbreak data | Modelling helped demonstrate effects of MDR and genomic changes in Malawian typhoid | Inclusion of typhoid carriers and environmental reservoir refined the model | Continuing model refinement to model additional geographic typhoid locales |

[a]Although all of the diseases listed may be contracted in a laboratory accident, the 2014 discovery of viable smallpox stored unrecorded for over 60 years in an unauthorised repository laboratory demonstrates this possibility.
[b]Meselson et al.[115]

surveillance and contact tracing [93]. During this epidemic, behavioural patterns in affected areas were difficult to assess. One solution was the inclusion of stochastic agent-based modelling, incorporating behavioural, demographic and movement interactions in a synthetic population with notional households, distributed according to census data. This was used by US government modellers to provide assessments to policy makers and others [33]. Once initiated and sustained, behavioural change significantly impacted disease spread [94].

In future large-scale epidemics, public health authorities may not have the liberty of extensive time from outbreak initiation and spread to implement model-based interventions. Predictive models are reliable as the parameters used for their construction, and essential information may be lacking early in an outbreak. Model development for subsequent intervention proposals during a novel rapidly occurring future pandemic [95] is especially challenging, in the absence of historic outbreak data. Further, decision makers may value uncomplicated models which can be more readily modified upon request and easier to understand. This is particularly relevant as the primary purpose of disease modelling has been to inform the decision-making process.

The contemporary outbreak models are assessed in Table 1 regarding disease transmission, data sources used for the model, and benefit and lessons learned from modelling, with future model optimisation goals described. Further suggested model improvements based upon this review include:

- In a post-EVD outbreak and influenza pandemic world, models should include potential local, regional and global health resource infrastructure effects [96,97].

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- Include social, geographic, behavioural and cultural disease determinants as appropriate.
- Evaluate the effect of co-infections on endemic diseases when modelling a susceptible population. Widespread co-infections potentially impact interventions in resource-poor nations [98–100].
- Re-examine existing disease models when new therapies and interventions have been developed.
- Consider model design for scenarios other than anticipated and previously modelled. One example is to model natural anthrax transmission in an endemic area [101], as most anthrax models consider deliberate epidemics [63,102].
- As available and practicable, include relevant disease agent genomic input, which may inform models with more precise pathogenicity estimation [103,104].
- Modelling should allow for scenarios where at least initial interventions become partially or wholly ineffective, i.e. 'good', 'bad, and 'ugly' estimates. Potential causes may include decreased global antibiotic effectiveness [105], diminished public health [106] or financial resources [107] and others.

As demonstrated during the EBV epidemic, it is exceedingly difficult for modelling to rapidly determine effective outbreak cessation measures. There are multiple inherent inaccuracies in data assessments used in disease modelling. Particularly in the early stages of an epidemic, imperfect knowledge as to which parameters are most useful for inclusion may facilitate imperfect model results [108]. In this regard, optimal disease models are best constructed upon conclusion of an epidemic. Useful prerequisites for modelling accuracy include:

- Access to best available disease surveillance data, necessarily dependent upon sensitivity and specificity of the diagnostic test used, data collection methods, and assessment of underreporting [2].
- Interactions between risk factors (synergy) may increase disease probability and should be incorporated into a model when known. Conversely, interventions may also have synergistic effects.
- Climate and temperature effect vector transmission [109].
- Appreciate that certain behaviours are powerful risk factors for disease transmission [110].
- Knowledge of intrinsic characteristics, including herd susceptibility and population immunity.
- Knowledge that model assumption of early exponential growth can overestimate epidemic size when early disease transmission is slowed [111].
- Knowledge that highly detailed data input required for a complex model may not necessarily generate more accurate predictive results than a simplified model [112].
- A simplified model is not simplistic; this design may be used to model more inclusive and comprehensive concepts [113].
- Understand that frequent model validation is required [114].

## Conclusion

Predictive disease models constructed for past and ongoing epidemics have demonstrated value formulating the public health response. Disease models permit effects estimation for various transmission modalities, interactions between populations, and mitigating applications of antimicrobials, vaccines and other public health measures. Public health intervention planning models for some diseases should be regularly examined in consideration of currently available pharmaceutical and non-pharmaceutical interventions. Diseases considered for modelling as deliberate releases should be more extensively modelled as natural outbreaks. Increasing demands will likely be made that future modelling for emerging diseases provide more rapid results and greater utility to achieve a successful outbreak response.

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