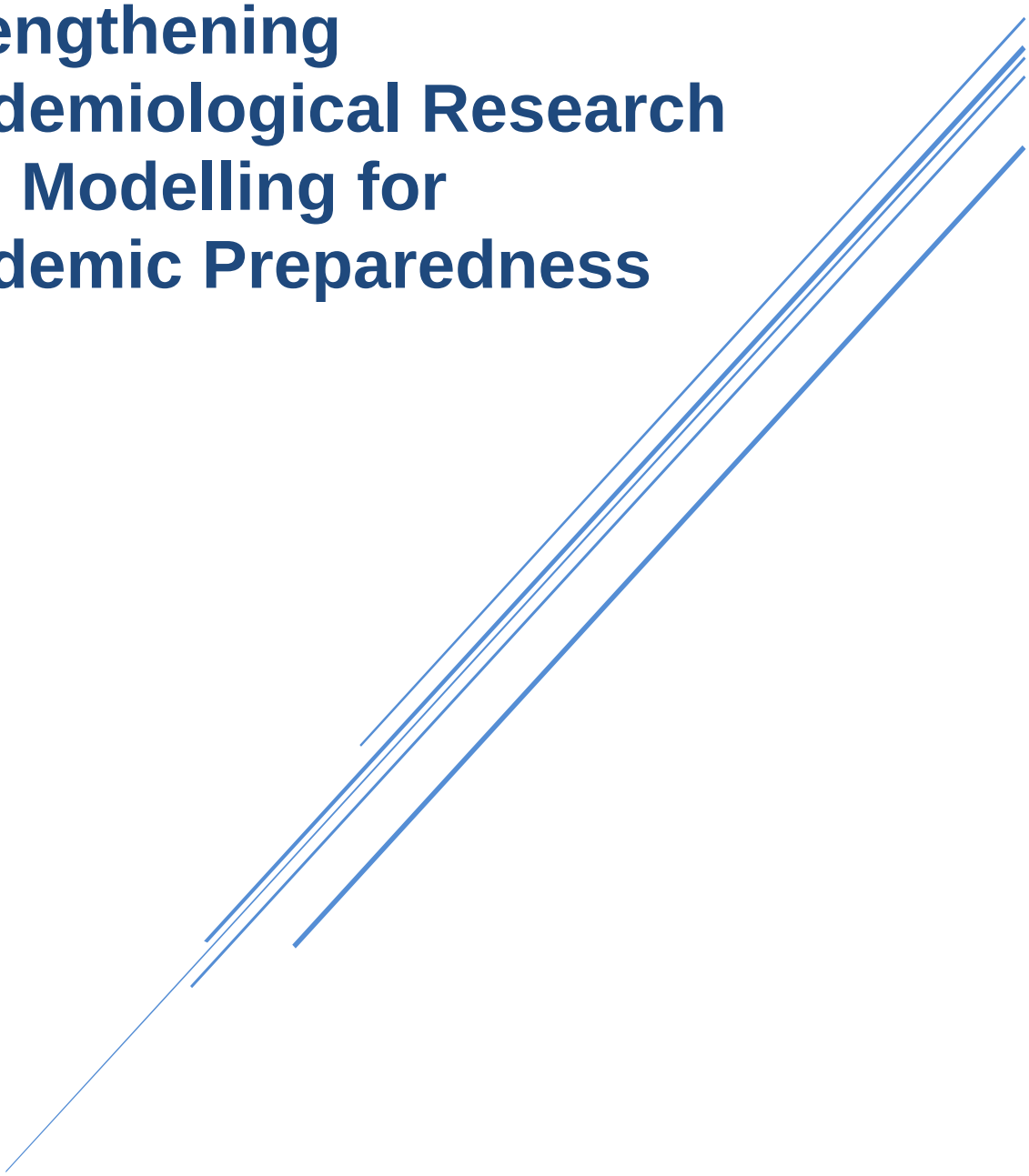
Strengthening Epidemiological Research and Modelling for Epidemic Preparedness



Imperial College London

Acknowledgements

We thank all the participants of the face-to-face workshop, colleagues who contributed case studies, partners around the world who responded to the email survey, and the Wellcome Trust and the UK Foreign, Commonwealth and Development Office (FCDO) (formerly UK Department for International Development) for their input and feedback throughout.

Funding: FCDO-Wellcome Joint Initiative for Research on Epidemic Preparedness and Response

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Summary report

Introduction

Recent outbreaks and epidemics such as the Zika virus epidemic in the Americas, the large West African Ebola epidemic, and ongoing epidemics such as Ebola in the Democratic Republic of the Congo and cholera in Yemen and Bangladesh, reinforce the need for prompt and efficient response at the national level, as well as strengthened mechanisms towards epidemic and pandemic preparedness. As shown in the conceptual representation of the evidence to decision-making pathway on the right, advanced analytics and mathematical models can play a pivotal role in epidemic and pandemic preparedness and decision-making during an outbreak. We use the terms “decision-maker” and “policy-maker” interchangeably and define them as any individual in government or high-level officials in public health agencies typically in charge of or involved in the response.

The types of “modelling” analyses captured and referred to in this report cover a wide range of methods including: i) classical epidemiological studies such as outbreak investigations; ii) statistical models; iii) mechanistic transmission models; and iv) phylogenetic models. A synonym for modelling in this context might be ‘outbreak analytics’.

The Imperial College team was funded by The Wellcome Trust and the UK Foreign, Commonwealth and Development Office (FCDO, formerly Department for International Development) to identify gaps and potential opportunities in the science of using advanced analytics, mathematical models, and epidemiological research during major outbreaks of infectious disease. We conducted a literature review, an online survey and a face-to-face workshop to provide the evidence used in this brief report of our findings and recommendations.

Identified needs

1. Improved coordination between policy-makers, analysts, and epidemiologists

While outbreak analysis and modelling capacity has grown markedly in the last decade, most notably in the USA and UK, much of this growth has been in the academic sector, with many university-based groups having few links to local, national or global public health organisations or policy-makers. Thus, even key organisations such as WHO and US CDC still have limited internal advanced analytical capacity, often relying on a limited number of trusted academic groups to provide support during disease outbreaks.

Our study has therefore identified a need for improved interactions between those collecting data on the ground, country-level decision-makers and those undertaking

advanced analytics and modelling using those data – both by developing local or regional capacity (see below), but also by enhancing engagement between the global modelling community and local policy-makers.

In addition, we have identified a specific need for WHO and its regional offices to be supported to deliver its normative functions in this area: e.g. analysis to inform investments in surveillance and preparedness, undertaking real-time assessment of outbreaks. Furthermore, we have identified that WHO require support to undertake consensus-building across global and regional modelling communities, acting as an interlocutor/interpreter between modellers and national policy-makers, offering informed critiques of newly published model-based analyses which purport to have relevance to an unfolding outbreak.

There was broad consensus among the stakeholders consulted during the workshop that these gaps might most effectively be addressed through the development of expert networks including both academic groups and public health organisations. Investment in this area would:

- Improve coordination between modelling groups and public health policy-makers (nationally and globally) during outbreaks
- Provide opportunities for enhancing research collaborations between public health bodies and academic groups to address outbreak preparedness and response priorities
- Help to develop trust relationships in advance of emergencies, to reduce barriers to data sharing and access, and to develop a community consensus on appropriate and ethical data use.
- Facilitate better understanding of the realities of outbreak response and public health decision-making in modelling groups, and of the role, potential benefits and limitations of modelling within the public health practitioner community, with training materials developed for people operating at different points along the evidence-to-decision-making pathway
- Provide a platform for capacity-building to conduct and understand epidemiological analysis and modelling, notably in LMICs

We did not attempt to define precise templates for such networks in this report, since detailed setting-specific work is required to tailor to local contexts; however, any overarching global network needs to have WHO as a central partner and will need to be flexible in the extent of engagement expected of academic partners. Academic participants will need to support the primary goal of such a network, to enhance epidemic preparedness and response (rather than necessarily to deliver high-impact research publications) – and thus be prepared to commit to the shared, collaborative and public health-focused ethos required to deliver this goal. Funders of academics and academic institutions should be encouraged to value this work appropriately by providing flexibility, recognition, and funding for such applied work.

Suggested activities:

- A fellowship scheme at multiple levels for quantitative scientists (post-doctoral as well as more senior staff) with a requirement for secondment in a public health

agency or government body for an extended period of time to build capacity in translational analytics.

- Coordinated awards with other funding bodies and public health agencies for a modelling network where WHO and its country and regional offices can play a central role in acting as a liaison between modellers and national policy-makers.

- Mechanisms to support coordination and cooperation between different funding bodies during emergencies to enable applied research in the context of epidemics, while delaying funding and deliverables for ongoing research.

2. *Greater analytical capacity, especially in LMICs*

We find compelling evidence in the literature, our email survey and from the workshop that there is a substantial disparity between regions and countries in the technical capacity required to conduct appropriate analysis and modelling during an outbreak. There are excellent case studies of communities of academics and informed public health policy advisors growing substantially in recent years: e.g. in the UK (see Case Study 3), USA [1], Australia, and Hong Kong (see Case Study 4). However, these countries remain the exception, particularly in the extent to which modelling is used to inform policy responses to outbreaks. Most LMICs affected by outbreaks have little or no capability in epidemiological analytics and are therefore nearly entirely reliant on relationships with external partners for the provision of policy-relevant analysis.

In the immediate future, we feel it is not a realistic or appropriate goal to develop advanced outbreak modelling capacity in every LMIC. We conclude a tiered and coordinated approach to capacity-building is required:

- All countries should have baseline capacity to undertake basic epidemiological data collection and analysis, and to be able to effectively consume results from more advanced analysis and modelling (i.e. have an understanding of the potential benefits and limitations of such analyses)
- Regional hubs/centres of excellence (e.g. Africa CDC, SACEMA) should be strengthened to i) build a critical mass of trained analysts and ii) provide more advanced analytical support to countries affected by outbreaks, and to improve regional preparedness (the MAEMOD group at Mahidol University was raised as a successful example).
- International centres of excellence (preferably acting in a coordinated manner via a global network) will continue to provide state-of-the art capabilities in outbreak analytics, surge capacity for major outbreaks, and training materials and software tools for capacity-building at regional and country level

Suggested activities:

- A variety of sustainable and cost-effective mechanisms for delivering such capacity-building should be explored, ranging from fellowships (see point 1), face-to-face short courses, online training materials, exchange programmes, to longer-term support for building local and regional professional communities e.g. similarly to the format of the ICI3D program (www.ici3d.org).

- A reciprocal placement scheme to have country officers from affected countries work in and alongside international centres of excellence during outbreaks, while also deploying epidemiologists and modellers to the field.

- Support for the coordinated development of robust, easy-to-use open source software tools for data capture, cleaning, visualisation and for routine but technically challenging epidemiological analyses that are driven by and adaptable to country needs.

3. *Greater focus on interdisciplinary research priorities in epidemic analysis & modelling*

The literature review identified a substantial body of social science research on recent outbreaks, but this has rarely informed or been linked to epidemiological research or modelling. For outbreaks and emergencies, the deployment of social scientists and anthropologists alongside field epidemiologists and medical personnel is relatively new. However, as such deployments become more frequent, it is likely that behavioural data will be routinely collected resulting in major research challenges for both behavioural research and mathematical modelling to incorporate behavioural change into dynamical models of epidemic progression and the predictive modelling of intervention impact.

In addition, another methodological research gap highlighted in the literature and during the workshop was the lack of integration of health economics into preparedness modelling, even in the context of influenza pandemic planning in high-income countries. Analyses of the costs of epidemics and the investment case for improved surveillance and preparedness in the LMIC context is even more lacking. Such analysis would be particularly valuable to incorporate epidemic preparedness, surveillance and response within the universal health coverage paradigm – thereby allowing investments in that area to be assessed against other services included with a country's health benefits package.

Lack of explicit integration of logistics modelling with epidemic disease models was a further identified gap. For example, estimating where, when, and how many PPEs are needed within the framework of an Ebola model would be particularly relevant and informative for decision-making.

Finally, targeted investment into more basic clinical and non-clinical infectious disease research (such as serological surveys, viral evolution, immunology) is required to better characterise the natural history and epidemiology of known epidemic diseases. The better characterisation of parameters such as the asymptomatic proportion and how infectiousness changes over time during the course of infection is critical for accurate real-time modelling.

Suggested Activities:

- Funding schemes for methodological research focussing on the above-mentioned areas (basic science, logistical, behavioural, economic). This could be in the form of project or fellowship grants, or funding for workshops or "hackathon" type meetings.

4. *Innovative approaches to data collection, data- and benefits-sharing in outbreaks*

More high-quality data, particularly in LMICs, are needed to improve outbreak detection and response. Investments in surveillance and data management systems are more likely to occur if they have a day-to-day benefit for citizen health and in controlling endemic diseases rather than having only an emergency preparedness and response function. Data types and data collection systems with the greatest cost-benefit should be explored.

While open data sharing remains an ideal, epidemiological data collected in an emergency are not research data *per se* and belong to the countries affected. Open sharing of data in outbreaks is often perceived by countries as posing potential risks, and the incentive for openness is further reduced if those collecting the data and the governments of countries affected fail to gain benefits (e.g. from context-specific analyses which address their priorities). There is a need for the development of an innovative data-sharing model specifically for outbreaks and emergencies that ensure that patient confidentiality is respected, credit is given to individuals and agencies who collected the data, and that a clear mechanism is identified by which those sharing data gain benefits (in terms of enhanced situational awareness, policy insights). The context in which the data were collected should also be transparent and those who collected the data should facilitate appropriate interpretation and use of the data by other parties. The recent development of official data sharing policies by WHO specifically addressing health emergencies and routinely collected data, points towards the growing recognition of the importance of sharing data, particularly during emergencies (see Case Study 1). However, data sharing models must still be underpinned by well-developed trust relationships.

Last, the email survey highlighted the improved or increased use of genomic data in outbreaks and emergencies as an important area of growth subject to capacity constraints particularly in LMICs. However, rapidly changing technologies such as portable sequencing methods could make timely collection and analysis of genomic data feasible during outbreaks and facilitate field deployment of such tools.

Suggested activities:

- Recognising that public health data are not research data *per se*, funders should advocate and facilitate data and benefits sharing, working closely with each other, WHO and countries. The discussion around data collection beyond that required for routine care and response should also be highlighted.

5. Sustainable, coordinated, and flexible investment

Recent epidemics (e.g. Ebola, Zika) have seen surges of research funding, including of modelling, but these are rarely sustained and are therefore suboptimal for addressing structural gaps or long-term capacity needs. A focus on preparedness activities with core sustainable funding structures could form the basis of capacity-building for outbreak response. Additionally, because much modelling expertise is provided by the academic sector, the workshop highlighted the need for research grants (both programmatic and project) to explicitly include dedicated resources for applied research and epidemic response.

Addressing the priorities identified above requires sustained (>10 year) funding streams and a coordinated approach by multiple major global funders.

Suggested activities:

- There should be coordination between philanthropic funders, major governmental donors, and WHO in (a) agreeing on a strategy and roadmap to address the gaps detailed above in the development and application of outbreak analytics, and (b) establish a long-term funding and/or training stream to support the activities prioritised by that strategy.

Glossary

CDC	Centers for Disease Control and Prevention
CFR	Case fatality ratio
CoV	Corona virus
CZS	Congenital Zika syndrome
DFID	Department for International Development
ECDC	European Centre for Disease Prevention and Control
FAO	Food and Agriculture Organization of the United Nations
FCDO	Foreign, Commonwealth and Development Office
FETP	Field epidemiology training program
GPEI	Global Polio Eradication Initiative
IGO	Intergovernmental organisation
IHR	International Health Regulations
IPC	Infection prevention control
LMIC	Low- and/or middle-income country
MCM	Medical countermeasures
MERS	Middle East respiratory syndrome
NIPP	National influenza preparedness plan
NPIs	Non-pharmaceutical interventions
OIE	World Organization for Animal Health
pH1N1	Pandemic H1N1 influenza
PHE	Public Health England
PHEIC	Public health emergency of international concern
PPE	Personal protective equipment
R_0	Basic reproduction number
SARS	Severe acute respiratory syndrome
Sitreps	Situational reports
UN	United Nations
WHO	World Health Organization

1: Introduction

Recent emerging events such as the Zika virus epidemic in the Americas, the large West African Ebola epidemic, and ongoing epidemics such as Ebola in the Democratic Republic of the Congo and cholera in Yemen and Bangladesh, reinforce the need for strengthened mechanisms towards epidemic and pandemic preparedness, as well as prompt and efficient response at the national level. Advanced analytics and mathematical models can play a pivotal role in epidemic and pandemic preparedness and decision-making during an outbreak. Well designed and parameterised mathematical models provide situational awareness and allow public health officials to compare a wide range of prevention and control strategies, such as targeted vaccination, and their potential impacts prior to implementation, as well as monitoring effectiveness during implementation. Especially for emerging pathogens, mathematical models can express specific assumptions about the transmission dynamics for a pathogen for which there is no or limited evidence. Thus, models can be used to interpret early data in light of those assumptions and to provide optimised intervention strategies and better support for public health decision-making in the face of uncertainty. Mathematical models informed by these early data can then be used to guide urgent research priorities and to explore the likely impact of interventions.

Mathematical models have contributed to the understanding of the epidemiology of new infectious diseases such as MERS and Zika, as well as those with changing epidemiology such as Ebola and yellow fever. They have been used extensively to estimate the burden of disease e.g. yellow fever [2], influenza [3], and dengue [4], and for risk assessment. Such assessments include quantifying: i) the risk of animal-to-human transmission for zoonoses such as MERS and avian influenza [5,6]; ii) the risk of international spread of yellow fever [7]; and iii) the risk of infection during mass gatherings e.g. the Hajj for MERS and the Rio Olympics in the context of the Zika outbreak [8,9].

Furthermore, advanced analytics and mathematical models can help to improve epidemic preparedness and response by: i) identifying areas at high risk of emerging infectious diseases; ii) quantifying the potential risk of spread should an outbreak occur; iii) defining the potential impact of an outbreak by scenario modelling, especially in high risk groups by means of estimating the number of patients, casualties, and economic impact among other outcomes of interest; iv) assessing the impact of interventions (e.g. changes in the epidemic curve) and other health outcomes; and v) helping to inform the design of new or established surveillance systems.

Countries are increasingly using mathematical modelling to inform public health policy and for strategic decision-making during outbreaks. Pandemic influenza contingency plans in many countries including the UK, USA, and Australia rely heavily on mathematical models and scenario modelling. Insights and outputs from mathematical modelling and epidemiological analysis can add value and evidence to the decision-making pathway. However, the extent to which rigorous data analysis and modelling have been integrated into the decision-making pathway beyond the countries listed above is not clear. Identifying the real and perceived barriers to this, as well as identifying where such outputs can add the most value should be a priority.

This report summarises the work undertaken by Imperial College London funded jointly by the Wellcome Trust and UK Foreign, Commonwealth and Development Office (FCDO, formerly Department for International Development) to:

- Identify pathways, networks, and gaps in the use of epidemiology and mathematical modelling in the evidence-to-decision-making pathway (at both country and global levels) for epidemic preparedness and response.
- Identify gaps and challenges in the use of epidemiology and mathematical modelling, for decision-making for epidemic preparedness with a specific focus on transmission and the use of medical countermeasures.
- Identify ways in which funders could invest in filling identified gaps.

Section 2 describes a scoping literature review undertaken to describe the epidemiological, advanced analytics, and modelling research output available for epidemic response and preparedness. Section 3 describes the types of grey literature available to decision-makers. Section 4 describes the results from the email survey undertaken to solicit expert opinion to identify important research and investment gaps as well as key future developments for decision-making for epidemic preparedness. Section 5 describes the face-to-face workshop consultation of key internal and external stakeholders representing each component of the evidence-to-decision-making pathway at the country-level. Section 6 gives case-studies of the use of modelling for decision-making.

2: Literature Review

Aim and Scope

The purpose of this scoping review was to identify key examples in the published peer-reviewed literature of advanced analytics and modelling for epidemic preparedness and outbreak response to identify: i) examples of how modelling could be used to inform decision-making; ii) the types of epidemiological and modelling studies conducted; iii) and the corresponding data underpinning such analyses.

We chose to review a set of major outbreaks over the last 15 years – that were declared Public Health Emergencies of International Concern (PHEICs) or were close to being named so in our opinion. We chose to focus on these outbreaks as they were most likely to generate policy relevant research and showcase how modelling could be used to inform decision-making. Table 2.1 lists the outbreak, year, and whether a PHEIC was declared. Polio in 2014 was not included in the review as it was an outbreak in the context of eradication and not an emerging infection, and we felt it generated a different set of questions. The review was split into two main categories of epidemic response and epidemic preparedness.

Outbreak Disease	Year	PHEIC declared?
Severe Acute Respiratory Syndrome (SARS)	2002	No
Pandemic H1N1 Influenza (pH1N1)	2009	Yes
Middle East Respiratory Syndrome (MERS)	2012	No
Polio	2014	Yes
Ebola (West Africa)	2014	Yes
Zika	2016	Yes

Table 2.1: Summary of outbreaks and outbreak years for review

Methods

Literature Search

We searched MEDLINE for articles published in English between January 1st 2002 and March 20th 2018 using the search terms:

(Ebola OR zika OR MERS OR (middle east respiratory syndrome) OR (MERS CoV) OR SARS OR (severe acute respiratory syndrome) OR H1N1 OR pH1N1 OR pdm09) AND (outbreak* OR epidemic* OR pandemic*) AND (model* OR epidemiolog*) AND (analy* OR response* OR preparedness OR estimat*) AND ("decision making" OR policy OR "resource allocation" OR mathematica* OR estimat* OR dynamic* OR projection* OR simulat* OR predict* OR forecast* OR projection* OR projected OR counter* OR progression OR modeling OR modelling) NOT (imaging).

The search results were validated against a training set of relevant papers that were informed by expert opinion (Appendix A). “Risk assessment” as a search term was not included. In addition, a supplementary search focusing on the use of analytics and modelling for preparedness was conducted using the following search terms:

(((((pandemic or epidemic) AND (preparedness OR mitigati* OR containment OR containing) AND (modeling OR modelling OR simulation))))).

The title and abstracts of all potentially relevant articles were assessed and included or excluded based on the criteria set out in Appendix B. Our primary diseases of interest were: i) SARS; ii) pandemic 2009 H1N1; iii) MERS; iv) Ebola; v) Zika; as well as vi) preparedness related papers. Each relevant article was also tagged (up to a maximum of three tags) to categorise the type of study. Study categories considered are listed in Table 2. As this was a scoping review and not a systematic review, the exclusion criteria were not explicitly recorded. Instead, the relevant abstracts were categorised by topic (Table 2) and the volume of research pertaining to each research area was quantified.

An additional supplementary search was also conducted for Lassa fever and Nipah using the same search terms and criteria described above.

Category	**Examples**
Forecasting	Incidence, peak timing, magnitude of epidemic.
Key parameters	Estimation of parameters that could inform response. e.g. R_0, serial interval, case fatality ratio.
Scenario modelling	Forward-looking scenario modelling with two or more scenarios, prospective impact of vaccination, trial design.
Impact	Retrospective impact of interventions, vaccination, non-pharmaceutical interventions, cost-effectiveness studies, impact of outbreaks on healthcare systems.
Genomic or Phylogeographic	Studies using genomic data to directly estimate key transmission parameters. Phylogeographic studies.
Preparedness	Modelling to generate results that can be used in preparedness plans.
Burden estimation	Burden of disease, economic burden.
Reviews	Reviews of mathematical models used for epidemic response and preparedness.
Other	Any other relevant paper not captured by the above.

Table 2.2: Summary of tags used to categorise relevant abstracts.

Bibliometric Analysis

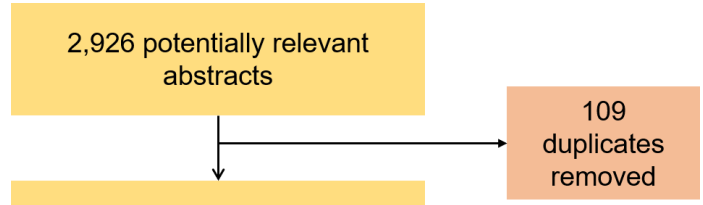
Abstracts were read and then the presence or absence of results for each topic was recorded. This allowed us to assess the general landscape of previous and current research in epidemiology, advanced analytics, and mathematical modelling for outbreak analysis and preparedness. For each topic as described in Table 2, the number of publications over time and citations to this literature was calculated. We also assessed the most productive countries producing research in each topic. We then mapped the co-author country collaboration to assess regions and countries outputting high volumes of modelling research.

For each topic, we extracted the citation metrics for the relevant abstracts. The top 3 cited papers (normalised by the year of publication) were then examined to evaluate the type of analysis conducted (methodological) and the data types informing such analyses.

All analysis was done in the R programming language [10] using the packages *RISmed* [11] and *bibliometrix* [12].

Results

From an initial screen of 2,926 potentially relevant abstracts, 961 abstracts were retained for analysis and were tagged by topic according to the criteria in Table 2.2. Each abstract was also tagged by disease type as listed in Table 2.1. Most of the papers were disease-specific. Pandemic pH1N1 (2009) encompassed the bulk of the search results (574 of 961) followed by Ebola, SARS, Zika, and MERS. Figure 2.1 summarises the search process and breakdown of abstracts by pathogen.



# of disease specific tags	# of abstracts
0	31
1	912
2	17

Pathogen	# of abstracts
SARS	103
pH1N1	574
MERS	41
Ebola	184
Zika	45

Figure 2.1: Abstract screening process and summary of abstracts by i) number of diseases the paper focused on and ii) the pathogen.

The supplementary search on Nipah and Lassa fever (the two remaining high priority pathogens identified by the WHO R&D blueprint) returned only 39 potentially relevant articles of which 14 (6 on Lassa, 8 on Nipah) were retained after title and abstract scanning (not included in figures). Most of these focused on the risk of spill-over infections from animals to humans and ecological niche models [13–16].

As expected, more research on infectious disease epidemiology and modelling came from high-income countries than from LMICs. Figure 2.2 plots the relative percentage of abstracts by author country affiliation for the top 10 productive countries of the 961 abstracts retained for analysis. Hong Kong and China have been captured here likely due to our inclusion of SARS in our focused search. These percentages should be considered relative as authors often have multiple affiliations in more than one country. Looking at the affiliations of authors (Table 2.3), output of modelling research tends to be centred around academic institutions with some collaborations with public health agencies and ministries of health.

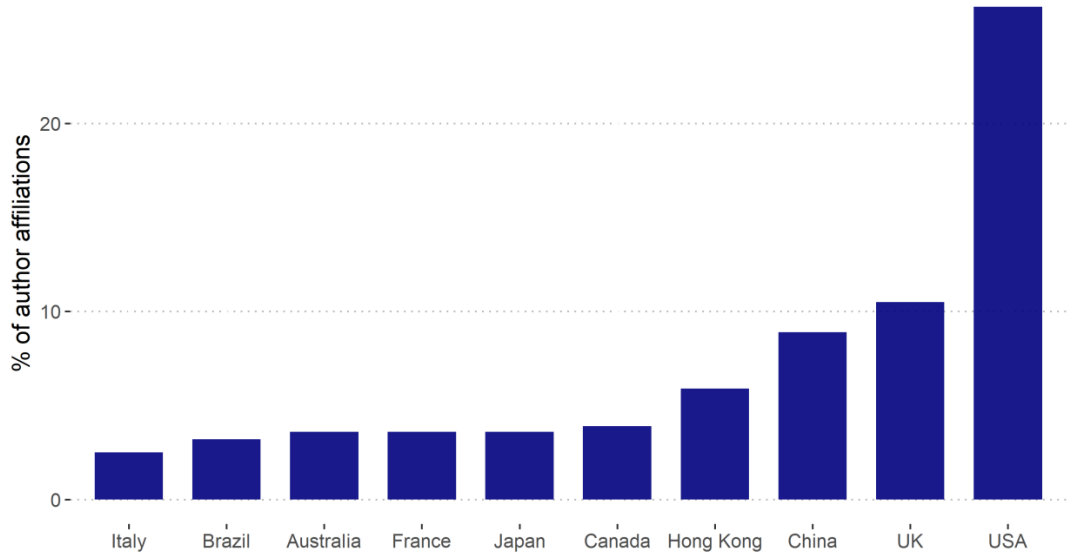


Figure 2.2: Bar plot showing the author country affiliation for the top 10 countries for modelling and epidemiology abstracts focusing on SARS, MERS, pH1N1, Ebola, and Zika.

Literature by research topic and disease

The use of epidemiology and modelling for estimating key parameters such as the basic reproduction number (R_0), case fatality ratio (CFR), and serial interval was the best represented in the peer-reviewed literature with just over 30% of retained abstracts referring to this topic. This was followed by the use of epidemiology and modelling to: i) inform epidemic and pandemic preparedness (16%), ii) quantify the impact of e.g. vaccination and other interventions and cost-effectiveness studies (12%); iii) assess potential scenarios (11%); iv) quantify the burden of disease (9%); and v) forecast the potential course of the epidemic (6%). Of the research topics, the use of genomic data to quantify key parameters and phylogeographic models was least represented at just 3% of all abstracts (Figure 2.3a).

More generally, the volume of epidemiology and modelling in epidemics research has grown substantially since the 2009 H1N1 pandemic, after which there was an increase in research output across all topics (Figure 2.3b). Research in the use of modelling to estimate key outbreak parameters was consistently well represented, as was the use of scenario modelling to assess the potential impact of interventions - although the total volume of research output was much lower.

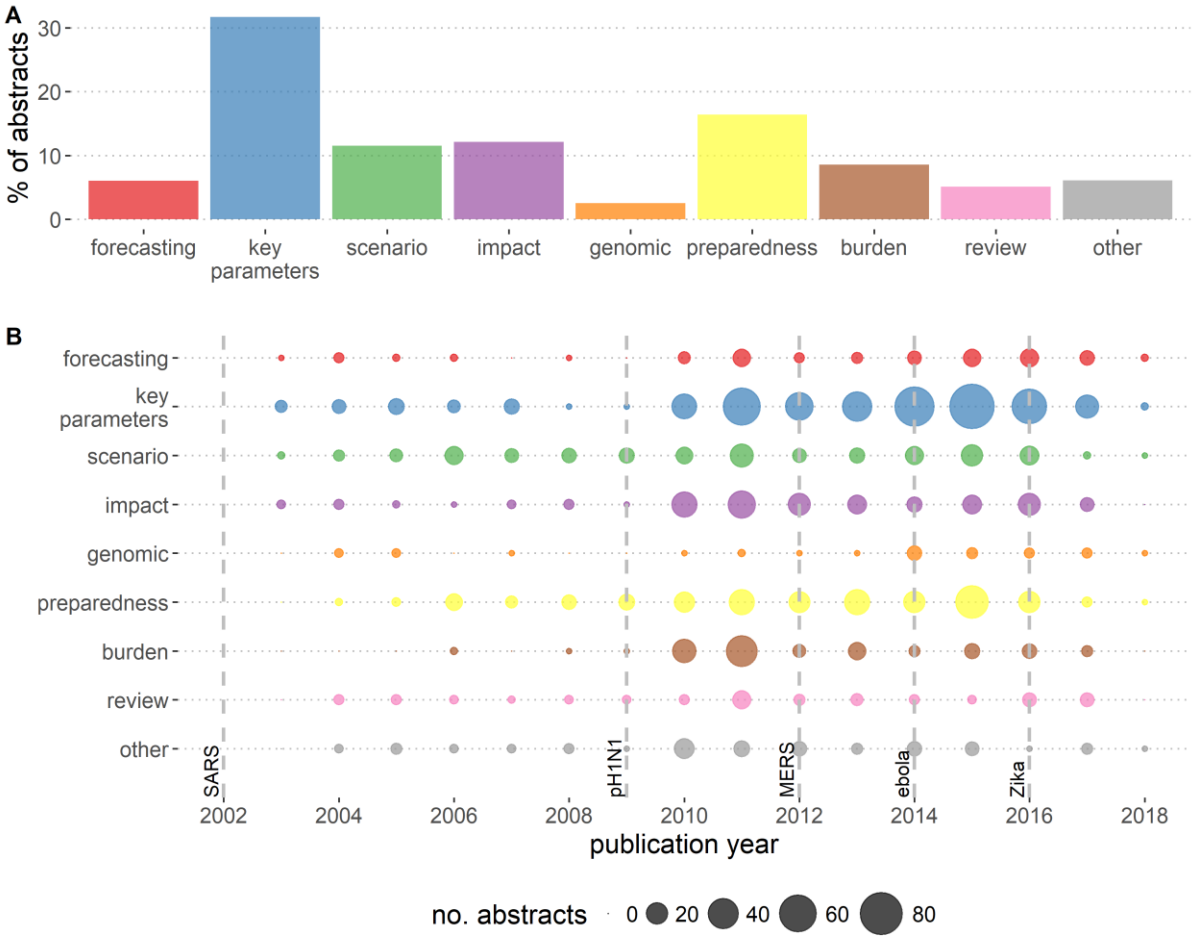


Figure 2.3: Summary of research volume by research topic and year. A) Percentage of total papers by topic. B) The number of topic-specific papers published per year. The vertical dashed lines show the starting year of the outbreaks of interest.

For peer-reviewed literature, there is a substantial time-delay from the actual onset of the outbreak to dissemination of research. This is also shown in Figure 2.4 which summarises the volume of disease-specific literature over time. For each disease, there is little, or no disease-specific research published in the same year of corresponding outbreak onset, with approximately a 1-year delay until the first publications. For example, SARS modelling papers are not captured until 2003 at the earliest. It is notable that over the last 15 years this delay appears to shorten slightly with a substantial number of Ebola modelling papers published in 2014. However, as the figure presents publications by year and not month, there may be some differences depending on the time of year the outbreak started (e.g. outbreaks starting in January allow the most time for publication in the same year).

For H1N1 and Ebola, there was a small volume of modelling and/or epidemiological literature published prior to 2009 and 2014 respectively. We identified only 9 articles specific to Ebola prior to the 2014 West African Ebola epidemic. Three were epidemiological outbreak investigations or estimation of key parameters [17–19], four explored different scenarios and the potential impact of interventions using previous Ebola outbreaks [20–23], one was a phylogeographic study [24], and one was an ecological niche modelling paper [25]. For H1N1, most studies published prior to 2009 were preparedness or scenario modelling papers that used the 1918 H1N1 pandemic as a case study.

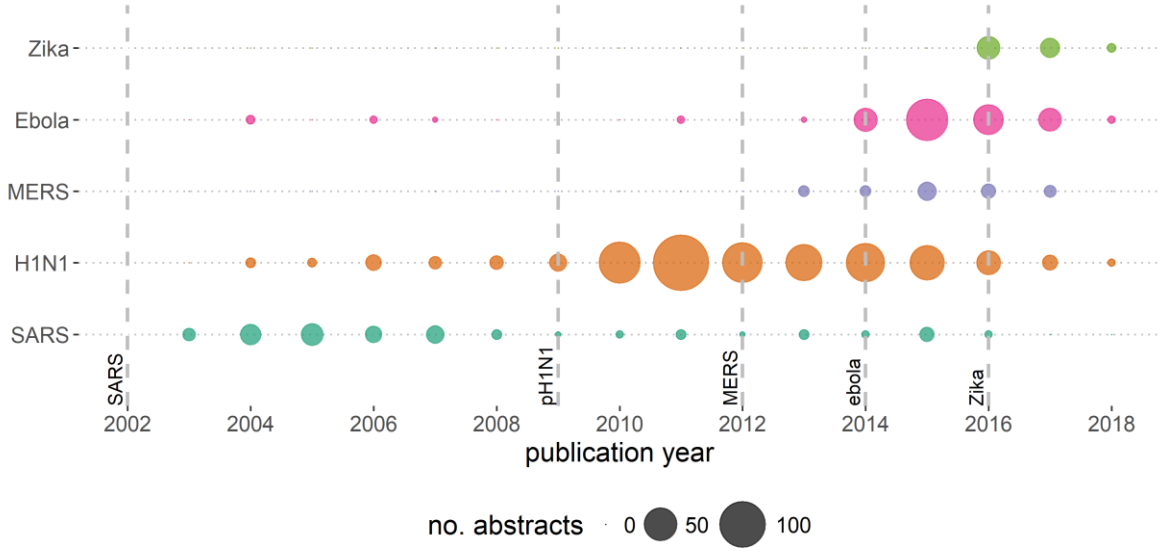


Figure 2.4: Summary of research volume by disease. The vertical dashed lines show the starting year of the outbreaks of interest.

Disease-specific Country Collaborations

Mapping co-author collaborations highlighted again the dominance of European and North American countries, particularly the USA, UK, and France, in advanced analytics and modelling research (Figure 2.5). Hong Kong is shown as the largest node for SARS literature (Figure 2.5a) which reflects both the location of the outbreak and the modelling capacity available. Canada is shown as a smaller node due to the related outbreak in Toronto. For H1N1, the same main countries are represented but with greater international collaborations which reflects the global nature of the pandemic (Figure 2.5b). Japan and Italy are represented in these networks to a smaller extent. This is partly due to several prolific authors having multiple affiliations.

Figure 2.5c shows the country collaborations for MERS where Saudi Arabia and South Korea are visualised as expected, reflecting the geography of affected countries. Interestingly Japan is only connected with South Korea and USA but not Saudi Arabia. This suggests that MERS research in Japan was largely a response to the MERS-CoV outbreak witnessed in neighbouring South Korea. For Ebola (Figure 2.5d), Liberia, Sierra Leone, and Guinea as the 3 affected countries are well connected within the network. Author affiliations from these countries show that both in-country academics and ministry of health were involved with modelling and epidemiological research. However, it is not possible to know from the published literature how it might have informed decision-making during the epidemic. Notably, the Ebola network is the only one in which Switzerland appears, pointing towards the role that the World Health Organization played in coordinating the scientific response to that PHEIC. In comparison to the other 4 diseases, due to its recent emergence, the body of peer-reviewed literature on Zika is still small. Among the countries affected by the Latin American Zika epidemic, Brazil, Colombia, and Mexico were the only countries outputting substantial epidemiological or modelling research (Figure 2.5e).

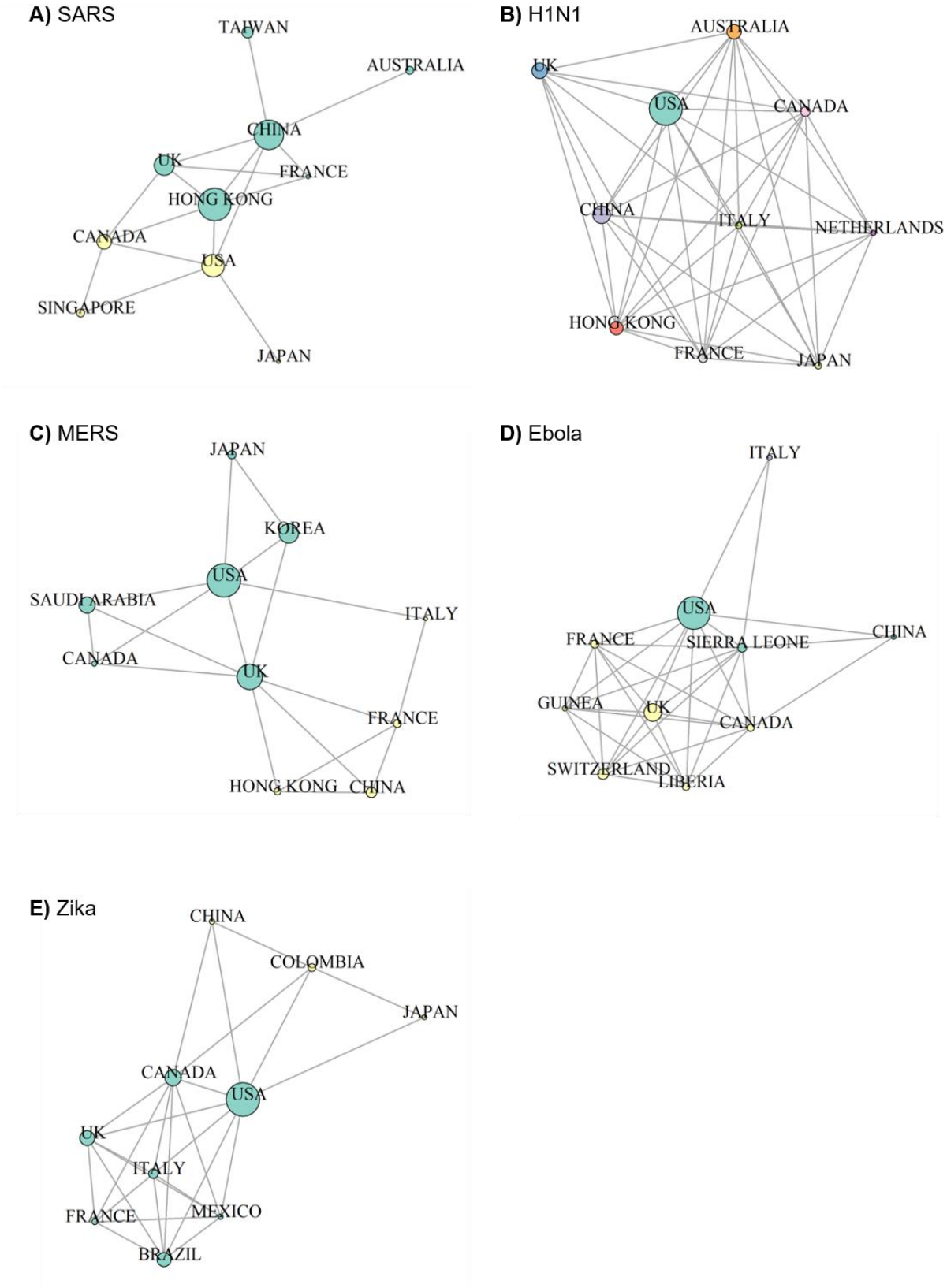


Figure 2.5: Disease-specific country collaborations for the 10 most productive countries. Networks are shown using the Fruchterman layout. A) SARS; B) pandemic H1N1; C) MERS; D) Ebola; and E) Zika. The size of the circles is proportional to the number of articles including authors from that country. Colours of the circles indicate clusters.

Epidemiological, Advanced Analytics, and Modelling Research

For each research topic (Table 2.2) we identified the top cited papers as defined by the MEDLINE database to assess if, or how, these studies (Table 2.3) could help inform decision-making, and the corresponding data required for such analysis. There was some overlap in the top cited papers by research topic as papers often addressed more than one topic e.g. the use of models for scenario planning and preparedness research.

Generally, the papers estimating key outbreak parameters such as R_0, serial interval, or incubation period, relied on the earliest available data from hospital records [26–28]. Such analyses tended to use statistical models such as generalised linear models or logistic models over mechanistic transmission models [26,28,29]. In responding to a known pathogen, assessing whether there have been any changes in R_0 or incubation period will have significant implications for response planning [27]. Particularly for Ebola, early work focused on identifying potential risk factors for a fatal outcome as well as key time periods such as the incubation period - required to assess the length of follow up time of contacts; and intervals between hospital admission and discharge or death – which is indicative of hospital bed demand. The analysis conducted by the WHO Ebola Response Team used patient-level data of all reported cases in the first 9 months of the epidemic shared by the ministries of health of Guinea, Liberia, and Sierra Leone [28]. Smaller studies for Ebola focusing on the clinical outcomes of disease as well as key parameters used hospital records data [30], while other more complex models used a combination of parameter estimates from the literature with detailed demographic data to estimate R_0, generation time, and growth rate [31]. For MERS, as most outbreaks are healthcare-associated outbreaks, detailed clinical data on severity are also taken into consideration which can inform demand for clinical care or highlight differences in clinical outcomes [26,32]. Estimation of reporting rates by comparing the number of reported cases to the expected number of cases can also help to inform surveillance needs and potential future burden on healthcare [32,33].

Forecasts or forward projections of an outbreak can be useful for scaling up (or down) a response, for advocacy purposes, and to anticipate resource requirements. There is a wide range of methods in the literature for forecasting. Projections can be based on estimates of the effective reproduction number R_t, itself generated from the number of new cases over time and the serial interval distribution [28]. Other models use stochastic individual-based models with additional data such as human mobility [34], or make projections using SIR models with key parameter estimates based on previous outbreaks [35]. This type of "forecasting" should be considered as scenario modelling where potential scenarios can be modelled to explore 'worst case' scenarios and potential healthcare demands. While not fit to data and therefore not validated, they can still be informative for decision-making. By simulating the expected number of cases over time, models can make some estimates for vaccine or antiviral stockpile requirements to mitigate further spread.

Scenario planning in turn has significant overlaps with the use of epidemiological analysis and modelling for preparedness. Models are useful to explore the potential effectiveness of intervention strategies and to quantify the associated costs. Preparedness modelling has been most well developed for influenza pandemics and explores the impact of non-pharmaceutical interventions such as school-closures and border restrictions, as well as medical countermeasures (MCMs) including targeted vaccinations and use of antiviral drugs. By exploring 'what-if' scenarios, models can explore which combination of interventions, known as "targeted layered containment", might be most effective [36–38]. These models are often stochastic individual-based models that incorporate travel pattern data but make key assumptions about social contact patterns e.g. assuming double the per-capita contact

rates in schools compared to workplaces. Better quantitative data on context-specific transmission would improve model outputs. Behavioural changes during the course of an influenza epidemic or pandemic are referenced, but not explicitly modelled [36].

Models can also be useful in informing intervention trial design and effectiveness. This type of modelling can also be considered as a type of “scenario modelling”. A prominent use of modelling for trial design during outbreaks was the rVSV-ZEBOV vaccine trial for the West African Ebola epidemic [39]. Such models are fit to incidence data due to their clinical endpoints. Data generated from such trials can then better inform and validate mathematical models that quantify the combined effectiveness of multiple pharmaceutical and non-pharmaceutical interventions [31,39]. This will help to inform priorities for resource allocations, and plan for future response measures.

The use of genomic data for estimating key outbreak parameters or the use of sequence data for phylogeographic studies is underrepresented relative to other areas (Figure 2.3A). For an emerging pathogen, such as Zika, genetic analysis can provide estimated dates of origin or introduction of the pathogen. Such analyses can give insights into how long an epidemic has been ongoing and inform future burden on healthcare systems. This was especially true for Zika where the main burden manifests as microcephaly and congenital Zika syndrome (CZS) in newborns [40]. Sequence data collected during outbreaks can also provide information on the source of the outbreak, reconstruct chains of transmission to identify superspreaders and contacts, and thus key populations for targeted interventions. For zoonotic pathogens such as MERS, coalescent models can be fit to genetic data to quantify rates of mutation and potential adaptations to human-to-human transmission [41]. Due to the resource constraints of sampling and sequencing genetic data, these data are not yet routinely used for real-time outbreak analysis. However, this will become an increasingly important area of research as new and cheaper sequencing technologies become available.

Table 2.3: Summary of top cited papers by research topic

Topic	Title	Author	Year	Journal	Average citation rate* (total times cited)	Ref	Additional tags
Forecasting	Ebola virus disease in West Africa – the first 9 months of the epidemic and forward projections	WHO Ebola Response Team	2014	N Engl J Med	71.6 (358)	[28]	key parameter
	Assessing the international spreading risk associated with the 2014 West African Ebola outbreak	Gomes, MF *et al.*	2015	PLoS Curr	21.3 (85)	[34]	-
	Estimating the future number of cases in the Ebola epidemic – Liberia and Sierra Leone, 2014-2015	Meltzer, MI *et al.*	2014	MMWR Suppl	19.2 (96)	[35]	key parameter, scenario
Key Parameters	Ebola virus disease in West Africa – the first 9 months of the epidemic and forward projections	WHO Ebola Response Team	2014	N Engl J Med	71.6 (358)	[28]	forecasting
	Hospital outbreak of Middle East Respiratory Syndrome coronavirus	Assiri, A. *et al.*	2013	N Engl J Med	36 (216)	[26]	-
	Clinical illness and outcomes in patients with Ebola in Sierra Leone	Schieffelin, JS. *et al.*	2014	N Engl J Med	27.6 (138)	[30]	-
Scenario modelling	Strategies for mitigating an influenza pandemic	Ferguson NM. *et al.*	2006	Nature	39.8 (517)	[36]	preparedness
	Strategies for containing an emerging influenza pandemic in Southeast Asia	Ferguson NM *et al.*	2005	Nature	35.4 (496)	[38]	preparedness
	Superspreading and the effect of individual variation on disease emergence	Lloyd-Smith, JO *et al.*	2005	Nature	27.8 (389)	[42]	review

*Average citation rate = number of times cited / (2018 – publication year).

Table 2.3 continued: Summary of top cited papers by research topic

Topic	Title	Author	Year	Journal	Average citation rate* (total times cited)	Ref	Additional tags
Impact of interventions	Strategies for containing Ebola in West Africa	Pandey, A. *et al.*	2014	Science	14.4 (72)	[43]	forecasting, scenario
	Efficacy and effectiveness of an rVSV-vectored vaccine in preventing Ebola virus disease: final results from the Guinea ring vaccination, open-label, cluster-randomised trials	Henao-Repastro, AM. *et al.*	2016	Lancet	14 (42)	[44]	-
	Spatiotemporal spread of the 2014 outbreak of Ebola virus disease in Liberia and the effectiveness of non-pharmaceutical interventions: a computational modelling analysis	Merler, S. *et al.*	2015	Lancet Inf Dis	13.3 (53)	[31]	key parameters
Genomic	Zika virus in the Americas: Early epidemiological and genetic findings	Faria, NR. *et al.*	2016	Science	66 (198)	[40]	-
	Genetic diversity and evolutionary dynamics of Ebola virus in Sierra Leone	Tong, YG. *et al.*	2015	Nature	13 (52)	[45]	-
	Spread, circulation, and evolution of the Middle East respiratory syndrome coronavirus	Cotten, M. *et al.*	2014	mBio	11 (55)	[41]	-

*Average citation rate = number of times cited / (2018 – publication year).

Table 2.3 continued: Summary of top cited papers by research topic

Topic	Title	Author	Year	Journal	Average citation rate* (total times cited)	Ref	Additional tags
Preparedness	Strategies for mitigating an influenza pandemic	Ferguson NM. *et al.*	2006	Nature	39.8 (517)	[36]	Scenario
	Strategies for containing an emerging influenza pandemic in Southeast Asia	Ferguson NM *et al.*	2005	Nature	35.4 (496)	[38]	Scenario
	Containing pandemic influenza at the source	Longini, IM. *et al.*	2005	Science	25.3 (354)	[37]	Scenario
Burden	Estimated global mortality associated with the first 12 months of 2009 pandemic influenza A H1N1 virus circulation: a modelling study	Dawood, FS. *et al.*	2012	Lancet Inf Dis	30.1 (211)	[46]	-
	Global mortality estimates for the 2009 influenza pandemic from the GLaMOR project: a modeling study	Simonsen, L. *et al.*	2013	PLoS Med	12.5 (75)	[3]	-
	Estimating the burden of 2009 influenza A (H1N1) in the United States (April 2009-April 2010)	Shrestha, SS. *et al.*	2011	Clin Infect Dis	12.2 (97)	[47]	-

*Average citation rate = number of times cited / (2018 – publication year).

Discussion

This scoping review of the published literature gives us some information about patterns in the use of advanced analytics and mathematical models that could inform decision-making during outbreaks or emergencies. We have highlighted areas that are scientifically well developed, as well as areas for future progress. Focusing on the PHEICs of the last 15 years demonstrates the increasing importance of epidemiological and mathematical modelling for epidemic analysis (Figure 2.3b). However, epidemiology and modelling capacity is still concentrated in high-income countries, particularly the USA (Figure 2.2).

Reflecting its global nature, the 2009 influenza pandemic generated the largest amount of epidemiological research relative to the other outbreaks of interest, followed by the 2014 West African Ebola epidemic (Figure 2.1). Although the disease-specific country collaboration networks (Figure 2.5) do demonstrate that research has become increasingly internationally collaborative, it is still often the case that the data are provided by LMICs while the analyses are conducted elsewhere.

Looking at the affiliations of authors from Sierra Leone, Liberia, and Guinea visualised in Figure 2.5d (Appendix B), the majority are from the respective ministries of health. This demonstrates that policy-makers are engaged with epidemiological and modelling analysis. However, as several of the major publications from this epidemic do not list author contributions, it is difficult to assess whether any advanced analytics was conducted in-country. During the West African Ebola epidemic, the WHO received patient-level data from the ministries of health, and "…results of these joint analyses… [were] consolidated by the WHO into recommendations to member states for action in the field." [48]. When an outbreak affects more than one country, as was the case for Ebola and pH1N1, the coordinated sharing of data from multiple affected countries can strengthen the analysis by making comparisons between affected regions. This also highlights the important roles that normative agencies such as the WHO have in facilitating data sharing and coordinating analysis efforts.

The delay between the onset of an outbreak and research being made available can hinder the dissemination of important information. Although this has improved since 2002 (Figure 2.4), in the context of emergencies, peer-reviewed literature is most likely not considered in the decision-making process unless policy makers are co-producing the work and aware of the results prior to publication. This publication delay was also demonstrated by Chretien *et al.* who analysed all modelling studies on the 2014 West African Ebola epidemic and quantified the publication lag by analysis type [49]. Efforts have been made to expedite this process, such as the "Zika Open" site created by the WHO Bulletin, where research relating specifically to the Zika outbreak was made publicly available within 24-hours whilst undergoing peer review as per the protocol described by Dye *et al.* [50]. Such "pre-print" mechanisms allow researchers to share vital analyses quickly without being delayed by a long peer-review process.

Methodologically, the use of epidemiology and modelling to estimate key outbreak parameters such as R_0 and the serial interval is well represented in the literature. In contrast, the research output looking at the use of genomic or sequence data in outbreaks or epidemics is smallest (Figure 2.3a). This is likely due to the additional resources required to collect and generate sequence data during outbreak response. However, with new advances in sequencing technologies and field-deployable tools (e.g. MinION) this is an area of increasing importance [51]. Genomic data are often collected during MERS outbreaks and can yield important insights into the transmission chain and origin of infection, both of which are informative in contact tracing and implementing interventions [52].

Behavioural, logistic, or economic modelling studies were not explicitly listed in the inclusion criteria. However, it was clear that although such studies were conducted, very few were integrated into a dynamical model. Although behavioural changes during outbreaks are undoubtedly important in how the epidemic may progress, it is difficult to capture such data quantitatively. Consequently, it is difficult to quantify the impact of interventions targeting behavioural change on the course of an epidemic [53,54]. The South Korean MERS outbreak and 2014 West African Ebola epidemic highlighted the importance of better understanding patient behaviour to optimise control measures [53,55,56]. Incorporating individual behaviour changes into mathematical models has been suggested and demonstrated previously [57]. However, for outbreaks and emergencies, the deployment of social scientists and anthropologists alongside field epidemiologists and medical personnel is relatively new [58]. As this increasingly becomes the norm, it is likely that behavioural data will be more readily incorporated into existing or novel modelling frameworks.

Although the peer-reviewed literature arguably contains the most advanced quantitative analysis of outbreaks, due to the current peer-review process there is inevitably a delay in dissemination of results. However, there is increasingly a push for sharing analyses in emergencies [50,59–61] alongside platforms such as Zika Open, F1000 [62], and bioRxiv [63] that facilitate fast publication of analyses.

As expected, compared to MERS and other PHEICs, the body of epidemiological literature on Nipah and Lassa is very small. Although methods have been developed to better estimate key epidemiological parameters from sparse outbreak data [64], existing surveillance systems are not well calibrated to detect emerging zoonotic events. This points towards a need not only for better baseline surveillance, but also improved integration with animal and veterinary surveillance systems in a one-health approach [65].

Key Findings

- There is a substantial disparity between regions and countries in the technical capacity required to conduct appropriate analysis and modelling during an outbreak. LMICs, although disproportionately affected by epidemics, are often reliant on external partners for epidemiological analysis.
- Although there is a growing body of literature on social science research during recent outbreaks, there are communication, methodological and data gaps which are currently limiting the formal quantitative integration of behavioural science into epidemic disease models.
- There is a lack of integration of health economics and logistics into preparedness and response modelling. Analyses of the cost of epidemics and the investment case for improved surveillance would help inform preparedness measures, while logistics modelling would also help inform response measures.
- Genomic and phylogeographic studies for epidemic modelling are still not common in each of the disease areas highlighted. As genomic data are increasingly collected during outbreaks, this is likely to be a growing area of research.
- Due to the peer-reviewed publication process, there is inevitably a delay between the start of an outbreak and public dissemination of peer-reviewed research. From the peer-reviewed literature it is difficult to know exactly how, or if, academic literature informs decision-making and response measures. In some cases, papers report work that has already been presented to policy-makers; in others, the first time that the work was available to policy-makers was upon academic publication.

- How research is explicitly integrated into decision-making was not clear from the literature search alone.

3: Grey Literature

Aim and Scope

The purpose of the grey literature review was to assess the publicly accessible information and data currently available to decision-makers. A systematic search of grey literature is a complex task due to the lack of standard indexing, lack of controlled vocabulary, and the lack of archiving of such literature. Additionally, given the vast volume of information accessible on the internet it was important to have a pre-defined search strategy to ensure time efficiency.

Therefore, we focussed our search on:

1) Pandemic preparedness plans curated by the WHO.
2) A subset of government and public health agency websites and repositories.
3) Specific publicly available disease alert websites
4) Pre-print servers

We attempted to assess the types of information available to decision-makers for preparedness and whether they referred to epidemiological analysis, advanced analytics, and/or mathematical modelling outputs.

Methods

Pandemic preparedness plans

The pandemic preparedness plans for member states curated by WHO [66,67] were searched and assessed for evidence of epidemiological analysis and modelling. Available documents were searched for all instances of “model*”. If the search returned positive results, the plan was assessed for whether: i) there was any mention of mathematical models; ii) whether models were used for planning purposes e.g. model-based scenario planning; and iii) whether models were used for real-time response. For non-English language preparedness plans, google translate was used to search for “model*” in the relevant language. Due to language constraints, for non-English documents, only whether this search returned positive results was recorded.

Outbreak Situational Reports

The WHO Institutional Repository for Information Sharing (IRIS) [68] was searched for examples of situational reports (sitreps) that are written routinely during outbreaks. Sitreps contain the most up-to-date information about the outbreak, actions taken, and actions planned. Therefore, they should contain information used for decision-making in emergencies. The recent 2017 plague outbreak in Madagascar and the Angolan 2016 Yellow Fever outbreak were taken as case studies. These sitreps were assessed for the type of information routinely reported during outbreak response.

Other sources of publicly available data

The concept of “publicly available outbreak data” is difficult to define precisely. We looked for illustrative examples of easily accessible and publicly available data. These sources were informed by expert opinion. The type of data or evidence reported within these databases was assessed. We limited our search to: ProMed [69], HealthMap [70], and pre-print servers.

For both the sitreps and publicly available data, example data types could include: i) advanced analytical evidence; ii) case counts and simple descriptive analysis such as case

fatality ratios (CFR); iii) epidemic curves; iv) vaccination coverage or other information on relevant interventions; and v) outputs from mathematical modelling.

Results

Pandemic Influenza Preparedness Plans

Of the 194 WHO member states, 93 member states were listed as having national influenza preparedness plans (NIPPs) on publicly available websites. However, 8 had inactive links and we were unable to find preparedness plans via country websites. One member state (Saint Lucia) was listed as not having a publicly available NIPP, when in fact the 2009 plan is available. Therefore, in total, 86 member states have NIPPs available on public websites (Figure 3.1). Of these 86, the majority of plans (61 out of 86) were published in or before 2009, 13 were published or revised between 2010-2013, and 12 were published or revised in or after 2014 (Figure 3.2).

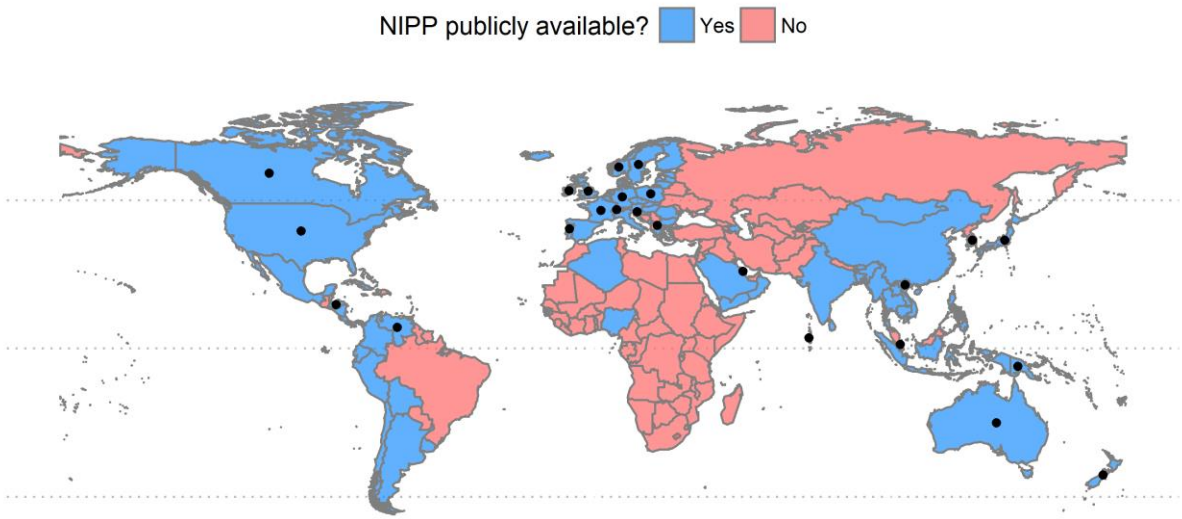


Figure 3.1: Map of WHO member states' national influenza preparedness plan (NIPP) availability. The black points show countries where mathematical models are explicitly mentioned within their NIPPs.

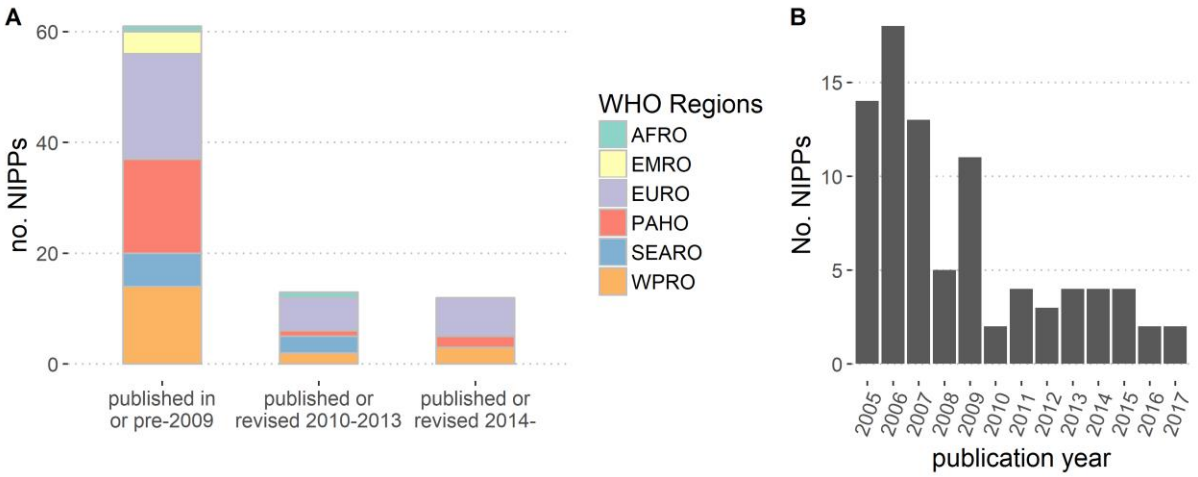


Figure 3.2: Breakdown of publicly available national influenza preparedness plans (NIPPs) by A) WHO region and B) publication year.

There was clearly a deficiency of preparedness plans across the African region, with only two African region member states having publicly available NIPPs (Algeria and Nigeria). Although SEARO, WPRO, and PAHO are relatively well represented, most NIPPs available from these member states were from pre-2009 (Figure 3.2).

24 of 86 NIPPs explicitly mentioned the use of mathematical modelling in their preparedness plans (Appendix C). Of the 24 NIPPs that explicitly mentioned modelling, some referred to previously published modelling work – e.g. the Maldives NIPP states "…estimates based on mathematical modeling suggest that the next influenza pandemic could cause from 2 million to 7.4 million deaths…", but do not make any further reference or use of modelling within their plan. 17 used modelling to set scenarios for preparedness e.g. estimated the potential burden on healthcare or antiviral requirements with a 25% attack rate. Only nine countries explicitly mentioned the use of mathematical modelling for real-time response. Appendix C summarises the information related to mathematical modelling within NIPPs for the 24 countries.

Outbreak Situational Reports

The WHO IRIS system is relatively young within the timeframe of public health events considered by this report. All sitreps typically contained information on: i) the epidemiological situation so far; ii) descriptive statistics such as number of cases and deaths; iii) a map of affected regions; iv) epidemic curve; v) risk assessment; and iv) response measures conducted or planned. There was no information on methodology behind the risk assessment. An overview of the type of information contained in the sitreps is summarised in Figure 3.3.

There were 14 external sitreps available on IRIS for the 2017 plague outbreak in Madagascar. First and last sitreps were available on 4th October 2017 and 4th December 2017 respectively. All 14 sitreps followed a standardised format. Aside from calculation of overall CFR and the epidemic curve, the sitreps did not contain any other estimates of key parameters e.g. the basic reproduction number (R_0), or CFRs by infection type. Despite substantial modelling efforts being undertaken for this outbreak (personal communication, Simon Cauchemez) modelling or modelling outputs were not referred to.

There were 31 sitreps available on IRIS for the 2016 Angolan yellow fever outbreak. The first and last sitreps were available on 5th May 2016 and 28th October 2016 respectively. There was some discrepancy in the formats of the sitreps available, with those released by the incident management team generally containing much more detailed information than sitreps released publicly by WHO. For example, incident management reports contained high-resolution data on the number of confirmed cases by district, the date of onset of the first and last case by district, the target population for vaccination, date of vaccination campaign, and vaccination coverage. Incident management reports also referred to the challenges faced regarding data cleaning and re-analysis due to inconsistent reporting criteria. As the outbreak progressed, the incidence management reports also contained information on the average reporting delays by province and whether there was documented local transmission.

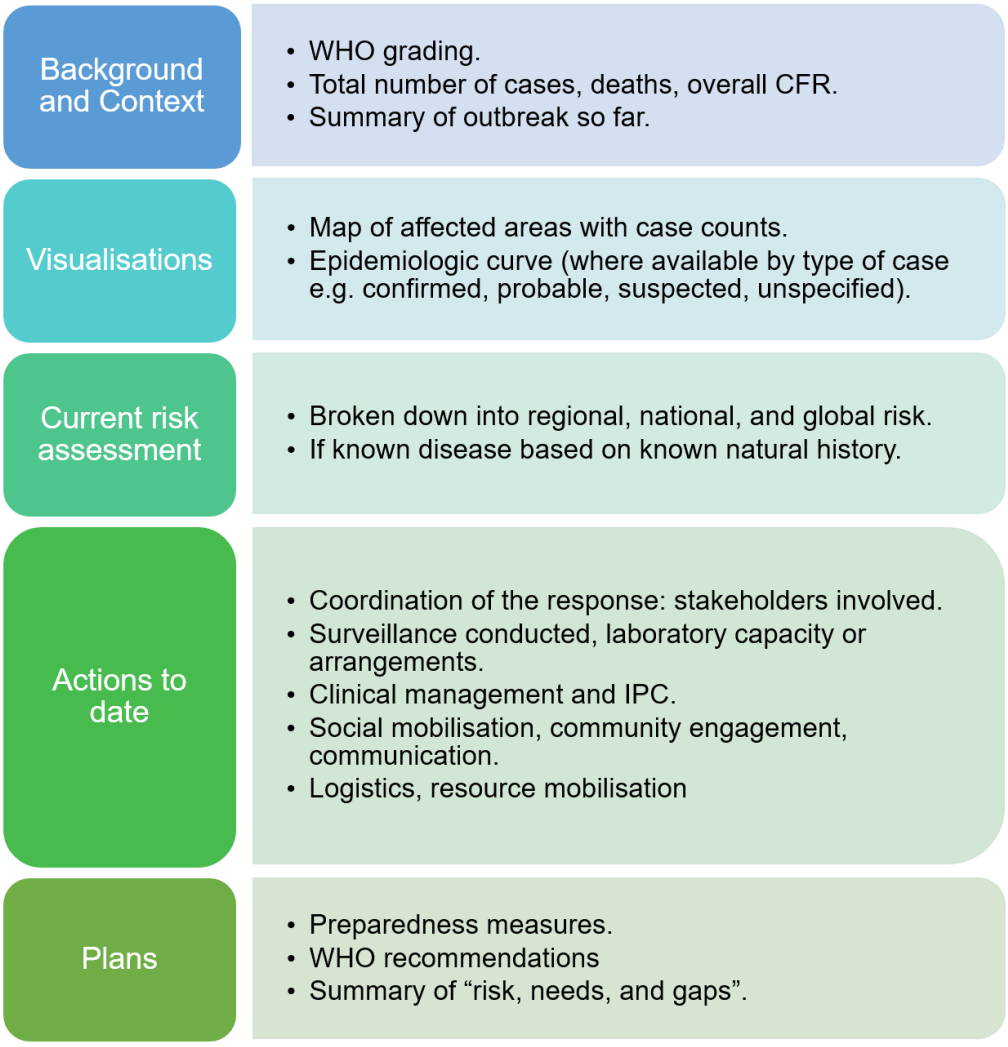


Figure 3.3: Summary of key information typically reported in a situational report (based on the 2016 Angolan yellow fever outbreak and the 2017 Madagascar plague outbreak situation reports).

There was a single reference (out of 31) to the use of modelling for vaccination prioritisation: "…process to identify high risk provinces in need of additional support was started at several levels, including risk prioritization performed by Incident Management System (IMS) team

and [Angolan] Ministry of Health in Luanda in combination with risk modelling performed by WHO…". However, it was not possible to assess what methods were used or how these results were used for decision-making. Again, substantial modelling efforts were being undertaken and communicated but are not evidenced in the situational reports (personal communication Tini Garske). Therefore, it was unclear how insights and results from epidemiological analysis and modelling conducted during outbreaks at the request of agencies such as WHO are used to inform response measures.

Other sources of publicly available data

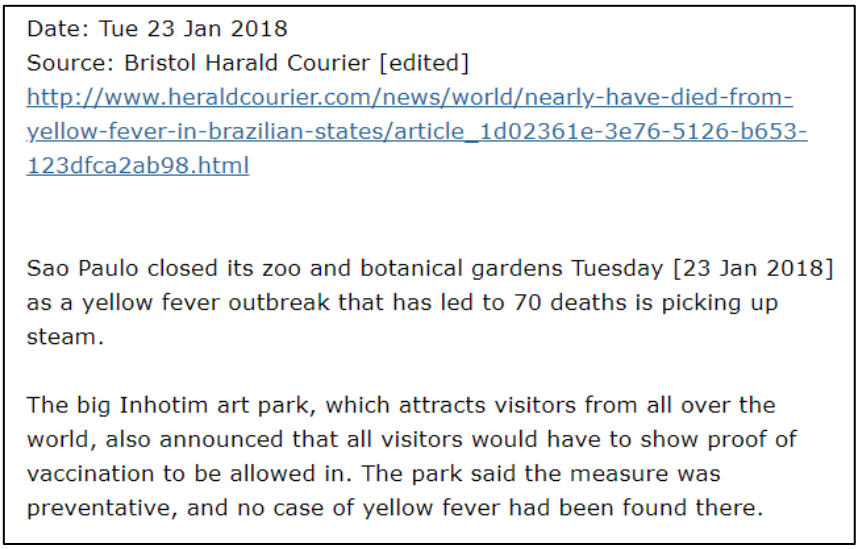
ProMed is an "…internet-based reporting system dedicated to rapid global dissemination of information on outbreaks of infectious diseases … that affect human health.... Electronic communications enable ProMED to provide up-to-date and reliable news about threats to human, animal, and food plant health around the world, seven days a week." [69].

ProMed draws on media reports, official reports, and local observers. The data and information reported are completely open access and are less hindered by political constraints. Therefore, early information disseminated through ProMed is arguably the timeliest. For example, in relation to the West African Ebola epidemic, ProMed were reporting "undiagnosed viral hemorrhagic fever" in Guinea as early as 19th March 2014, with the following notification on 22nd March 2014 confirming Ebola virus as the causative agent. However, the format by which these data are reported makes it difficult to quickly assess whether the outbreak or notification in question may be or become a bigger problem than initially perceived. The standard format of ProMed information is an email notification with a brief update or summary of the current situation, with some simple descriptive analysis (e.g. of CFR), often followed by raw data such as cases and deaths either by region, or time. Figures 3.4 and 3.5 are two examples of recent ProMed updates of yellow fever in the Americas. Figure 3.4 gives a detailed summary of the outbreak thus far, followed by raw data on case counts and deaths by district. In contrast, Figure 3.5 is a notification containing a media report of public park closures due to the outbreak. However, both notifications are in the same email format making it difficult to systematically identify notifications that contain relevant data. Aside from the total number of notifications that might come through for a single pathogen, there is no quantitative way of weighting the importance of certain notifications over others within the current ProMED system. Therefore, it is difficult to know how useful ProMED is for decision-makers.

Some states in the north east and part of the south and south east are not part of the areas currently recommended for vaccination. With the expansion, 77.5 million people in the entire country must be vaccinated. This number corresponds to a current estimate of people not vaccinated in these new areas.

Distribution of reported yellow fever cases from 1 Jul 2017 to 20 Mar 2018
Federal units / Reported / Discarded / Under investigation / Confirmed / Deaths
Acre (AC) / 1 / 1 / - / - / -
Alagoas (AL) / 8 / 2 / 6 / - / -
Amapái (AP) / 4 / 2 / 2 / - / -
Amazonas (AM) / 7 / 4 / 3 / - / -
Parã (PA) / 32 / 23 / 9 / - / -
Rondãnia (RO) / 9 / 8 / 1 / - / -
Roraima (RR) / 2 / 2 / - / - / -
Tocantins (TO) / 16 / 14 / 2 / - / -
Bahia (BA) / 44 / 27 /17 / - / -
Ceara (CE) / 2 / 1 / 1 / - / -
Maranhão (MA) / 5 / 3 / 2 / - / -

Figure 3.4: Example of a ProMed notification published 25 March 2018, for a yellow fever outbreak in Brazil containing a situational report and raw data by district (archive number: 20180325.5708856 [71]. [Image has been cropped – full email not shown.]



Date: Tue 23 Jan 2018
Source: Bristol Harald Courier [edited]
http://www.heraldcourier.com/news/world/nearly-have-died-from-yellow-fever-in-brazilian-states/article_1d02361e-3e76-5126-b653-123dfca2ab98.html

Sao Paulo closed its zoo and botanical gardens Tuesday [23 Jan 2018] as a yellow fever outbreak that has led to 70 deaths is picking up steam.

The big Inhotim art park, which attracts visitors from all over the world, also announced that all visitors would have to show proof of vaccination to be allowed in. The park said the measure was preventative, and no case of yellow fever had been found there.

Figure 3.5: Example of a ProMed notification published 24 January 2018 for the same yellow fever outbreak as Fig. 3.5 containing media reports of public park closures due to the outbreak (archive number 20180124.5582416, [72]). [Image has been cropped – full email not shown.]

HealthMap is a publicly available website that aggregates freely available information from i) ProMED Mail; ii) the WHO; iii) GeoSentinel, a clinician-based sentinel surveillance system on travellers; iv) OIE the World Organization for Animal Health; v) FAO the Food and Agriculture Organization; vi) Eurosurveillance – a peer-reviewed journal published by ECDC; vii) Google News; viii) Moreover – a commercial news feed aggregation service; ix) the Wildlife Data Integration Network; x) Baidu News; and xi) SOSO Info. Data are aggregated through an automated process and visualised by geo-location. As it visualises multiple data sources, it provides a graphic overview of disease alerts globally (Figure 3.6). However, similarly to ProMED it is difficult to assess whether a specific news alert may be more cause for concern than another.

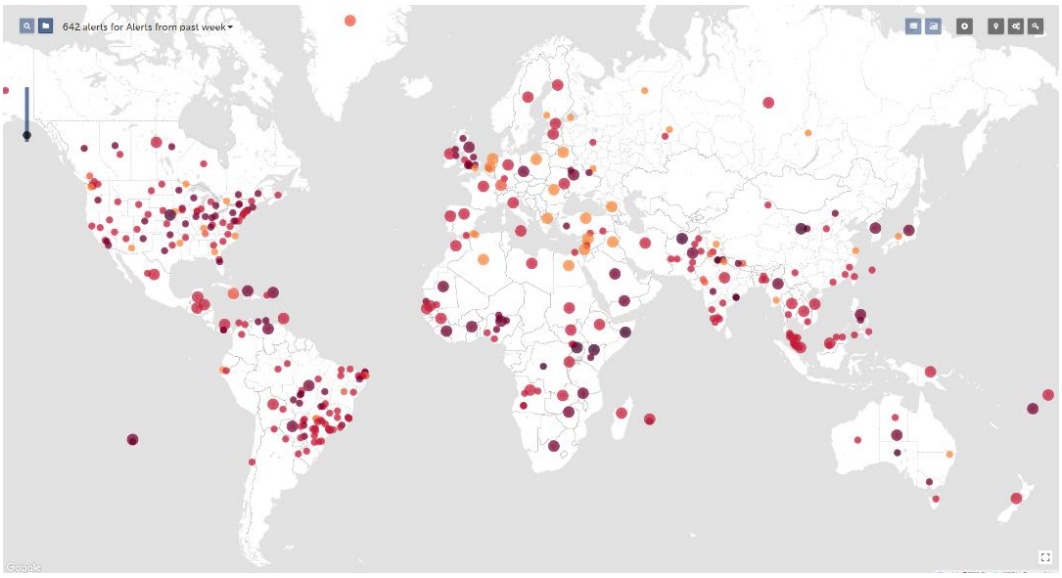


Figure 3.6: HealthMap.org landing page that visualises all disease alerts in the past week. Clip taken on 02/05/2016 from www.healthmap.org.

Pre-print servers such as arXiv [73], bioRxiv [63], and F1000 Research [62] are platforms where non-peer reviewed research is hosted. They are often used to disseminate new research quickly before submission for peer-review. The use of pre-print servers is very common in other areas of science and has been common for a long time. For example, arXiv was started in 1991 and passed 1 million articles in 2014. bioRxiv was established in 2013 and is being increasingly used for biomedical sciences: it has received substantial recent investment from the Chan-Zuckerburg Foundation. Major outbreaks have also prompted new platforms for sharing research such as PLoS Currents Influenza in response to the 2009 pandemic. It initially acted as both a journal and a pre-print server, but its main objective was the latter. The dual action was stopped during 2010 and in May 2013 the scope was expanded beyond influenza to all infectious disease outbreaks and became the online journal “PLoS Currents Outbreaks” [74]. However, in August 2018, it was announced that PLoS Currents Outbreaks would be discontinued due to the increased use of pre-print servers during outbreaks. The pre-print server system of publishing research was prominent during the Latin American Zika outbreak, when the Bulletin of the World Health Organization created the “Zika Open” site where research relating specifically to the Zika outbreak was made publicly available within 24-hours whilst undergoing peer review as per the protocol described in Dye *et al.* [50]. This enabled researchers to share vital data and analyses quickly without being hampered by a long peer-review process. There had already been discussion with first responders and public health agencies for a push towards open data sharing prior to publication of any paper related to outbreak analysis in response to the 2014 West African Ebola epidemic [59,75]. However, the Zika Open platform was arguably the first time this had been implemented by a normative agency. Despite this, there were still more papers made available on traditional pre-print servers during this time. 91 papers on Zika were published on bioRxiv between January 1st 2015 and 30th November 2016 when WHO announced the end of the Zika epidemic compared to only 34 in the WHO Bulletin for the same time period. A recent study however, showed that only a minority of Ebola and Zika papers were made available on pre-print servers [76]. Authors performing real-time analysis should be encouraged to use pre-print servers, and barriers to doing so should be investigated further.

Key Findings

- There is a deficiency of preparedness plans across LMICs, particularly across the African continent.
- Even amongst countries with an up-to-date National Influenza Preparedness Plan (NIPP), very few explicitly use modelling for preparedness, and fewer still for real-time response. The extent to which modelling is used reflects the local epidemiological and modelling capacity.
- Preparedness decisions are still made based on the local capacity to respond, the surveillance systems already available, and the regional networks that can be used. This was especially the case for LMICs.
- The situational reports arguably contain information that policy-makers routinely consider for decision-making. However, the sitreps do not contain results from the modelling analysis undertaken during the two outbreaks taken as case studies (yellow fever in Angola and plague in Madagascar). Therefore, it is possible that results of advanced analytics and modelling are considered at a different level of the response such as resource allocation rather than the day-to-day response.
- The publicly available grey literature such as ProMed and HealthMap are not readily accessible for decision-making due to their notification format.
- It is unclear to what extent, and how consistently research posted on pre-print servers such as bioRxiv directly inform outbreak response. However, during the most recent Ebola outbreak in the Democratic Republic of the Congo, the communications team at WHO and other senior officials pro-actively prepared responses to potential questions from the media in relation to research published on different platforms.
- Authors performing real-time analysis should be encouraged to use pre-print servers, and barriers to doing so should be investigated further.

4: Expert Opinion Email Survey

Objectives

Decision-making and evidence needs during outbreaks and emergencies are likely to be highly country- and context-specific. Identifying the reasons behind these differences (among LMICs, between LMICs and high-income countries) as well as the commonalities will be useful in focusing investment. An email survey was conducted to solicit expert opinion from a wide range of stakeholders, including field epidemiologists, researchers, and decision-makers, to ensure the entire evidence-to-decision-making pathway was represented. Many of these stakeholders had direct high-level experience of the specific outbreaks we considered in the literature review.

The objectives of this survey were to identify pathways, networks, and gaps in the use of epidemiology and mathematical modelling in the evidence-to-decision-making pathway for epidemic preparedness and response.

Methods

The survey focused on 5 key areas of activity:

i) modelling and analysis to inform risk assessment, preparedness, and investment decisions;
ii) modelling and analysis to inform real-time response;
iii) data availability, data needs, and data synthesis;
iv) coordination and networks; and
v) capacity-building.

Each section was designed to assess whether there were funders actively funding work in each area, for example funding for capacity-building in modelling and epidemiological analysis. We then asked respondents to rank how important they thought each sub-topic was for effective outbreak preparedness and/or response, rank and comment on how each topic could be improved and highlight gaps and suggest examples of successes and failures. See Appendix E for the full questionnaire.

Sample Construction and Methodology

The initial sample (66 individuals) was constructed based on the complete workshop invitation list, which was agreed during discussion with Wellcome and FCDO. Invitees were selected to be representative of current roles and geography and to have experience of key recent outbreaks. Focal points for specific funding agencies and other relevant respondents were then identified from existing contacts and networks within Imperial, Wellcome, and FCDO (10 individuals). “Snowball sampling” was used to ensure disease-area and geographic representation by asking respondents to nominate others whose opinion should be sought.

The survey was conducted using Survey Monkey (www.surveymonkey.com). Individuals were contacted via email with a web link to the survey. All responses were collected using Survey Monkey and results were analysed in the statistical software SAS. All responses except respondent institution were anonymised provided there was more than 3 responses from the same institution.

In the summary presented here, we have combined the responses “Agree strongly” and “Somewhat agree” to be “Yes”, and all other responses (including no response in partially completed surveys) to be “Not yes”. For example, in response to the question, “Do you think the use of modelling and analysis for risk assessment is important?”, responses were categorised as “Yes” or “Not yes”, the latter including “Somewhat” and “Not sure/NA”.

Results

The following results are based on the 61 responses submitted by 25th June 2018.

Survey Respondents

A total of 61 individuals completed the survey. Of these, the majority were from academic or research institutions (n=30), followed by public health agencies (n=11), funders (n=9), government (n=6), and other (n=5). Those who were categorized as “other” all had recent experience either in government or public health agencies. 74% of respondents (45 of 61) stated that they were responsible for, or undertook, epidemiological analysis and/or modelling research as part of their role. Of the respondents who filled out the “Background Information” questions, 18 respondents were individuals who did not attend the “Consultation on Epidemic Modelling” workshop held 10-11 May 2018 in London, UK.

Institutional Definitions of “Public Health Emergency”

According to the 2005 IHR definition, a public health emergency of international concern (PHEIC) is defined as “an extraordinary event which is determined, as provided in these Regulations: (i) to constitute a public health risk to other States through the international spread of disease and (ii) to potentially require a coordinated international response” [77].

Only 14 respondents said that their institution had an explicit definition of a “public health emergency”. Of these, only the World Health Organization had a well-defined description – “…an occurrence or imminent threat of an illness or health condition, caused by bio terrorism, epidemic or pandemic disease, or (a) novel and highly fatal infectious agent or biological toxin, that poses a substantial risk of a significant number of human facilities or incidents or permanent or long-term disability (WHO/DCD, 2001).” Most of the remaining positive respondents quoted the IHR regulations, or that their institutions aligned their definitions with those of the WHO or the United Nations (UN). One Ministry of Health defined a “public health emergency” as an “outbreak of diseases more than expected leading to public panic and disturbances”.

It is clear that not many institutions have a pre-defined definition of a public health emergency, and that the WHO as a normative agency and the only UN agency able to declare a PHEIC acts as the baseline for many other countries or institutions.

Funding activity

Based on 18 respondents who stated that their institution currently or have previously provided funding for epidemiological analysis or modelling work all survey topics had some form of active or past funding. Modelling and analysis to inform risk assessment, preparedness, or investment decisions had the most positive responses (14 of 18), followed by modelling and analysis to i) inform real-time response, ii) to refine data collection, surveillance, or improve data sharing, and iii) capacity-building (all 9 of 18). Funding for modelling networks had the fewest positive responses (8 of 18).

Topic specific results

Modelling and analysis to inform risk assessment, preparedness, investment decisions, and real-time response

There was a clear discrepancy between how important individuals thought the use of modelling and epidemiological analysis was for most topics compared with how well developed they thought each area was, and even more so for whether epidemiological and modelling outputs were routinely used for decision-making (Figure 4.1).

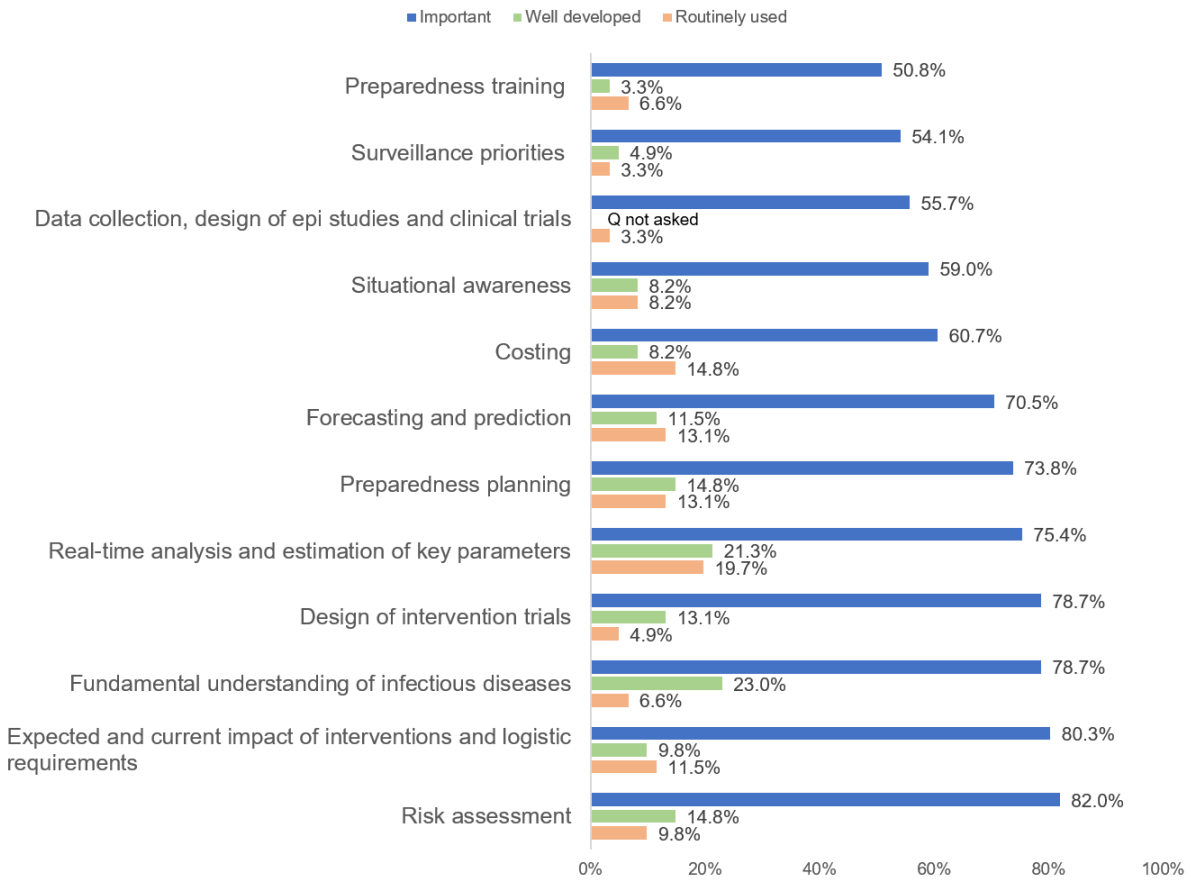


Figure 4.1: Percentage of survey respondents (N=61) that thought modelling and epidemiological analysis was important (blue), well developed (green), and routinely used (orange) for each topic.

Of the topic areas, the use of epidemiological analysis and modelling for real-time analysis of outbreaks and estimation of key parameters scored relatively well across the three questions. In contrast, despite the “use of epidemiological analysis and modelling for risk assessment (e.g. risk of spread or risk of new outbreaks)” scoring highest for importance, only 14.8% and 9.8% of respondents thought this topic area was well developed and routinely used respectively. Although modelling for decision-making was not perceived as routinely used for any topic, among the topics considered, real-time analysis and estimation of key parameters and costing scored highest (19.7% and 14.8% respectively). However, the use of epidemiology and modelling for costing was thought to be poorly developed (8.2%) respectively. For preparedness planning, it was highlighted that epidemiology and an

understanding of the natural history of the pathogen would help to better target appropriate investment for preparedness e.g. new containment units and border screening.

Data availability, data needs, and data synthesis

Of the topics within data availability, needs, and synthesis the areas that respondents thought was most important were, in descending order: i) data sharing during emergencies and outbreaks; ii) data sharing after emergencies and outbreaks; iii) the use of genomic data for epidemic preparedness and response; and iv) the use of big data for epidemic preparedness and response (Figure 4.2). However, respondents thought these areas were not well developed, nor routinely used (0% – 7.5%). There was shared opinion that the use of genomic data or epidemic preparedness and response could be an important area for growth and a "powerful tool". Although sequence data have been used extensively in other areas such for the Global Polio Eradication Initiative (GPEI), it has not yet been "integrated in decisions" for other outbreaks. Concerns were also raised as "…capacity is limited…for these analyses and many policy makers do not have these kinds of analyses on their 'radar' as possible tools". Others raised the rapidly changing technologies such as portable sequencing methods (e.g. MinION) that could make collection and analysis of such data timelier in outbreaks and facilitate field deployment of such tools. The useful sources of 'big data' for epidemic response such as mobile phone and healthcare utilisation data were highlighted as difficult to access. In contrast social media data or internet search query data may be easier to access but may not yield useful information. The use of diagnostics in the generation of reliable data was also raised. In many LMICs the lack of access to diagnostic tests prohibits the timely detection of new outbreaks outside of emergency NGO responses.

Although there was consensus that data sharing during and after emergencies was important (Figure 4.2), respondents highlighted the need to be sensitive regarding data ownership and confidentiality. The different levels of data sharing that needed to be improved was also raised – "…the biggest issue is data sharing at field level…. between agencies, between case management, and lab…between everyone and the [emergency operation center] EOC". An incentive structure for countries to openly share their data was also suggested "…for example by receiving additional funding and international assistance". Generally, respondents thought that data should be shared openly, however there were some concerns about data being misinterpreted and "…shared publicly without context and so cause undue panic in the broader population".

Coordination and Networks

Networks were thought to be important for facilitating early interactions between modellers and policy makers. The lack of formal networks to access epidemiological and modelling expertise for outbreaks was flagged as a potential gap and area for future development by several respondents. Previous successful examples given were the WHO Informal Network for Mathematical Modelling for Pandemic Influenza H1N1 2009, RAPIDD and MIDAS in the USA, and SPI-M in the UK. However, beyond these networks based in the USA and Europe, respondents highlighted the lack of such networks or indeed comparable modelling capacity in LMICs. "…There has been very little emphasis in [capacity] building….in Latin America, Africa, or Asia…where arguably the biggest problems lie". Some respondents also thought networks could facilitate better dialogue between academic groups and policy makers, leading to better informed decision-making. The potential importance of networks between

emergencies was also highlighted to “test out models, to build on experience and to ensure capacity when needed”.

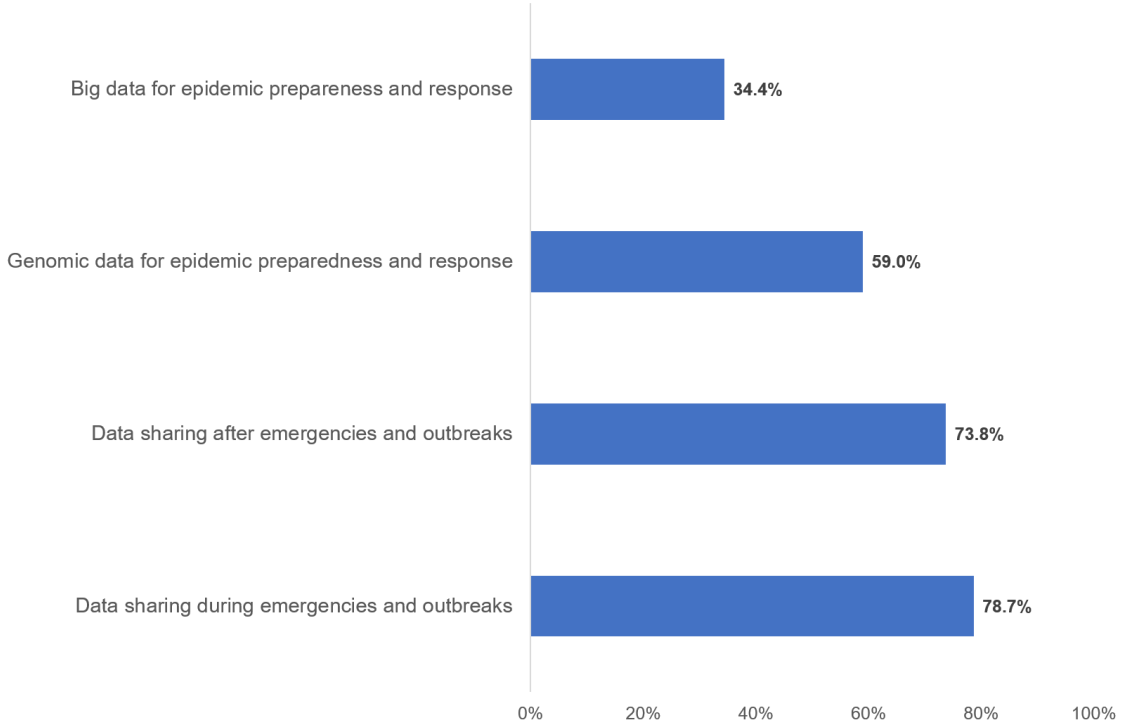


Figure 4.2: Percentage of survey respondents (N=61) that thought each of the topic areas within data needs, synthesis, and sharing was important.

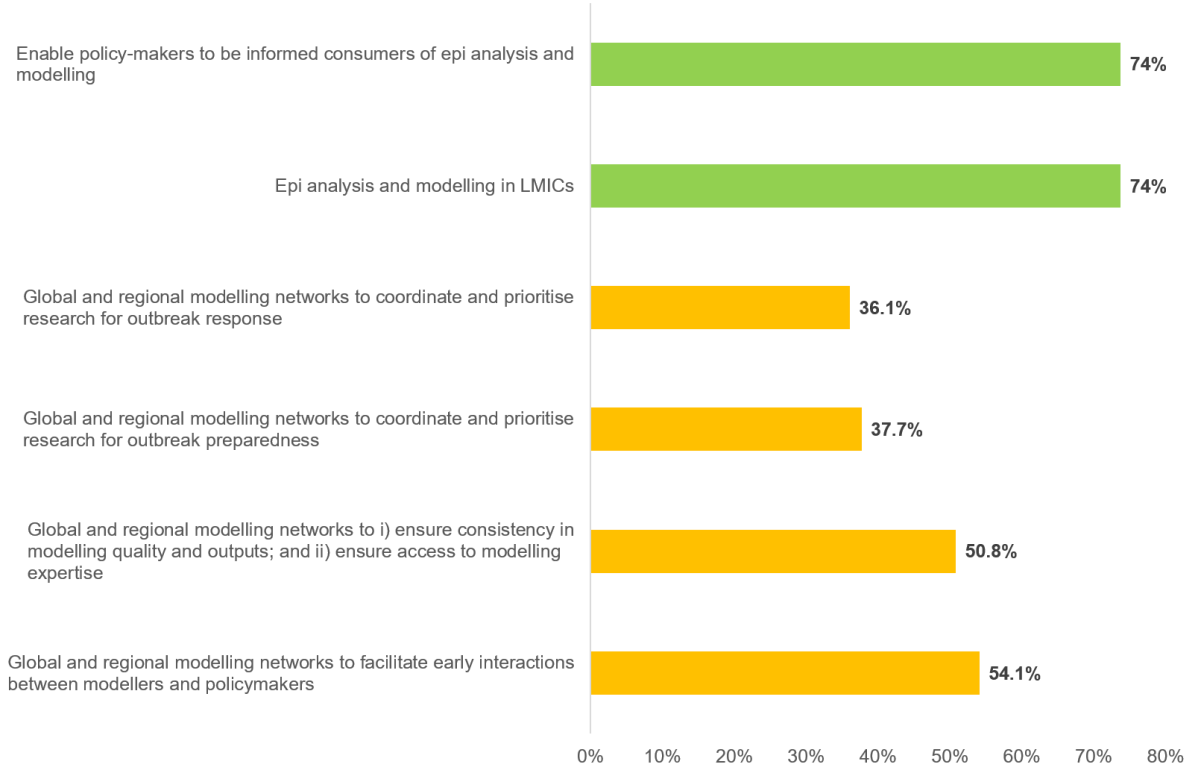


Figure 4.3: Percentage of survey respondents (N=61) that thought each of the topic areas was important. Green and orange bars indicate questions/answers related to capacity-building and networks, respectively.

Capacity-building in epidemiological analysis and modelling

As expected, the majority (74%) of respondents thought capacity-building was important both in LMICs for epidemiological analysis and modelling, but also to enable policy makers to be informed consumers of such outputs (Figure 4.3). That this figure of 74% is not higher reflects that while none of the respondents scored capacity-building as “not important”, some respondents skipped this question entirely and so were coded “not yes”. Different areas for capacity-building were raised including: i) regional field epidemiology training programmes (FETPs) as good mechanisms for building and retaining local capacity; ii) senior policy makers to better understand how epidemiological outputs and modelling could be useful; and iii) advanced analytical training.

Key Findings

- Although most respondents generally thought that each of the topic areas highlighted in the email survey was important, there was a clear discrepancy between importance and whether this was well developed or routinely used.
- Some key gaps highlighted were the use of epidemiological analysis and modelling for risk assessment. This was the area that was thought to be most important. Although methods exist for risk assessment, <15% of respondents considered these methods to be “well developed”, and the lack of data early in an outbreak will be a limiting factor in the context of outbreak response.

- The use of genomic data for preparedness and response was also thought to be an increasingly important area for development. However, there was some scepticism regarding the resources required for sequencing particularly in LMICs. Hence, this may be an area for development for outbreak response where external organisations may be involved but less feasible for smaller outbreaks where fewer resources are mobilised.
- The use of modelling for (i) costing response or preparedness requirements and (ii) estimating the expected and current impact of interventions and logistic requirements was thought to be relatively routinely used. However, this has not been explicitly integrated into dynamic disease modelling (Figure 4.3). This integration is an area that requires more methodological research.
- Capacity-building for both policy makers and local analysts was clearly identified as an important area. The gap between the existing analytical capacity and interactions between modelling groups and policy makers in Australia, UK, and USA compared to LMICs was highlighted by respondents.
- Although FETPs were raised as a good example of building local or regional capacity, the survey did not ask the question of “how” best to build capacity in such areas. Some free text suggestions included secondments of individuals from academic institutions to Ministries of Health or other decision-making agencies.
- Respondents also noted that although there is currently no formal framework for an epidemic modelling network, such regional or global networks would help to facilitate essential interactions across sectors and disciplines.
- The term "modelling", which is used as shorthand, including in this report, was viewed by some as vague and potentially confusing: there are different types of modelling and different types of modeller, with different skill sets. This can lead to the wrong type of “modellers” being asked to answer a particular question. For example, most health economic “modellers” have expertise in non-infectious diseases, but limited experience of modelling transmission dynamics of infectious diseases, which can lead to flawed analyses being produced. Infectious and non-infectious diseases are fundamentally different in their epidemiology and require fundamentally different models, developed by people with relevant expertise.

5: Workshop Summary

Background

A focused consultation workshop was held at Wellcome Trust, London, UK 10-11th May 2018 to solicit expert opinion and feedback on the key findings, gaps and future developments in epidemiology and modelling for epidemic preparedness and response. A total of 53 participants attended the workshop representing academic institutions, public health agencies, ministry of health or other policy makers, social scientists, health economists, and funding agencies. The complete list of participants and the meeting agenda is given in Appendix F. The relevant results of the literature review and the email survey were presented to the workshop participants at the start of each session.

Objectives

1. Identify **pathways, networks, and gaps** in the use of **epidemiology and mathematical modelling in the evidence-to-decision-making pathway** for epidemic preparedness and response, including transmission and the use of medical and non-pharmaceutical countermeasures.
2. Share **lessons learned** from past experiences of the use of epidemiology and mathematical modelling in infectious disease outbreaks and emergencies, including novel pathogens.
3. Identify **priorities** for future research, coordination, and investment.

Key findings from the workshop

Networks and Capacity-Building

There was strong consensus on the need for a network or 'professional body' to better facilitate the use of quantitative evidence for decision-making during outbreaks. A multi-disciplinary "network-of-networks" approach was suggested that would allow interactions within and between different parties e.g. a network of modellers to establish standard operating procedures and best practices for coding and analysis, as well as a network of modellers and decision-makers to facilitate early and useful interactions between the two parties during an outbreak. This would also ensure that epidemiologists and modellers would be embedded in the 'lessons learnt' exercises that could inform preparedness and data collection for future outbreaks and to better understand other factors that must be considered for a policy decision to be made, whether that be political, personal, or logistical. A systematic review of 'lessons learnt' exercises was suggested to analyse how models have been used during outbreaks. Since dissemination via peer-reviewed literature is so important – and can be highly influential on mainstream media reporting during outbreaks – the proposed professional body would have an important role in promoting rigorous standards of reviewing, e.g. in developing a set of standards that journal editors would be encouraged to adopt. Published standards would promote openness and facilitate interactions with and input from other relevant disciplines such as physics, engineering, and computer science.

There was also consensus that such networks should have different geographical tiers – national, regional, and global, with an explicit capacity-building element to ensure that in-country epidemiologists can gain new skills and experiences. This will also help to retain

local capacity and embed modelling expertise within the existing country infrastructure. In the long-term this will also bring analysis closer to decision-making. Networks or similar frameworks to address the barrier of entry of individuals from LMICs to modelling was suggested. Networks will need to have a clear structure, operational framework, and focal points to ensure rapid response to calls for technical assistance. Having a clear operational framework would also accelerate data sharing during emergencies, by having a clear data sharing agreement or 'clear rules of engagement' in place with countries who wish to engage with such networks.

Long-term sustainable funding for such networks not just during outbreaks but also during "peace time" would help to build closer collaborations, institutional relationships, and trust. During such times, there could be a focus on 'endemic' diseases, to build local capacity by enabling modellers to develop their skills, developing robust data pipelines, and enable decision-makers to become acquainted with modelling, as well as providing useful information to inform public-health decision-making but without the high-stakes associated with epidemics. The Wellcome Trust funded institutions such as KEMRI and OUCRU were raised as examples of good models for capacity-building. However, any such networks or modelling work must be driven by country needs, and the function and sustainability of regional networks will need to be considered carefully. In relation to frameworks to find and retain analytical capacity in-country, the need for innovative approaches to identify other areas of existing quantitative expertise (such as mathematics, engineering, or physics) that could be drawn into public health was raised. More local but also broader disciplinary engagement (i.e. with local capacity in other quantitative disciplines) may address some of these issues.

Funding of networks would also facilitate continuous engagement between modellers and policy-makers to build and sustain institutional memory. The need for coordinated funding was also raised to ensure that efforts were not duplicated. It was also clear there was a need for grants in the area of infectious disease analysis to be more flexible. Researchers are often funded to deliver a specific project and work on outbreaks can detract from and be detrimental to both the original project and potential career paths. Extra funding for research is often made available in response to major outbreak or epidemics. However, such calls should include funds not just for an immediate response, but also ensure sufficient funds to make sure any response actions during an outbreak or capacity-building are consolidated.

Improving modelling for decision-making

There was a clear call for better communication between analytical groups, decision-makers, and those on the ground collecting the data. From experience, it was raised that often the context in which the data were collected was lost as the data were reported upstream. Important qualitative information such as the social and cultural context of where the data originated, who collected the data, and the intent behind why the data were collected was not conveyed to those doing the analysis. There was consensus that data on behavioural changes and drivers during outbreaks needed to be better considered, by improving communication between modellers and anthropologists. There is also a need to measure 'baseline' data to determine the nature and magnitude of any change in behaviour. However, there were differing opinions on whether behavioural changes during outbreaks should be explicitly included within a disease modelling framework. Incorporation of behavioural parameters in dynamical models was raised as a potential methodological research gap.

There is clearly a need for a "common language" and to "bridge the disconnect" between all parties, from different sectors and disciplines, involved in an outbreak response. Networks

as described above were raised as a way to embed social scientists within the evidence-to-decision-making pathway and improve communication. Funding a network of institutions with a mandate to work with countries on diseases of local priority with surge capacity to respond to outbreak disease was suggested along with funds for research positions where individuals are embedded part time in government of policy-orientated institutions and part time in an established research institute. This co-location of both parties would also help facilitate trust and incorporate 'on the job' training. However, this will require capacity-building for all parties and at different levels. Drawing from the UK experience, if such capacity-building is not feasible on a large scale, then it is important to train individuals to be the focal point or interface between policy makers and analysts.

Additionally, the term "modelling", which is used as shorthand, including in this report, was thought to be potentially confusing. For example, "modelling" can encompass a wide range of models (as described in the literature review), and decision-makers need to have a clear understanding of what types of model are required to address their particular policy questions using the data available. Infectious diseases are fundamentally different in their epidemiology from non-infectious diseases and require fundamentally different models.

There is a need to improve understanding among policy-makers of the limitations of modelling, the context in which modelling outputs should be considered, and the uncertainty often surrounding results. In turn, epidemiologists and modellers need to better understand the policy environment and decision-makers' requirements: decision-makers typically need much less precision than modellers try to achieve. The key question is often: "under what range of circumstances is a particular intervention option appropriate or not?". Speed of analysis is critical in emergency situations, and many modellers are not comfortable with this. For modelling and analysis outputs to be actionable, they need to be timely, pragmatic, and targeted. Modelling should also be better integrated into outbreak response to inform the response needs, as well as informing longer term prevention efforts.

In discussions, the point was made that for decision-makers, having multiple views is important but there is a key challenge in determining the quality of modelling work. There is a critical need in an emergency situation to appraise third-party modelling work because there are often contradictory claims made by different groups. Maintaining public confidence is an important component of effective emergency response and whilst public debate in the context of genuine scientific uncertainty is desirable there have also been examples of less robust modelling results being reported. Typically, these groups have used only published data (or no data) and therefore data-sharing agreements requiring responsible behaviour would not solve the problem.

The UK has formal structures for appraising scientific evidence to inform policy-making (e.g. SPI-M) through which third-party (or non-governmental – often academic) modelling work would be evaluated, and this is part of the solution that other countries could adopt. However, it would be preferable for seriously flawed analyses not to be published in the first place, particularly due to the potential to harm public confidence and effect on behaviour.

Data cleaning and quality control

An essential activity that is typically given too little attention is the need for quality control of data and the need for considerable resources to be required for checking data and correcting errors. Typically, modellers have to spend as much time undertaking data

cleaning as doing data analysis. It is also common for data to be changed retrospectively, potentially causing confusion. There should be a proper 'audit' process logging the recording of data, changes to data made in the field, and imputations made by modellers in the cleaning process. Improving these processes should be a priority during "peace-time".

Data collection, access, and sharing

In relation to improving outbreak response, generally, there is a need for more and better-quality baseline surveillance data. There is a need for capacity-building along the entire evidence-to-decision-making pathway to better understand the benefits of collecting higher quality, or additional, data to those routinely collected. Investments in such capacity are more likely to occur if they have a day-to-day benefit in controlling endemic diseases rather than having only an emergency preparedness and response function; however, the latter function must be acknowledged in the intent of the funding, as structures and processes built for the purpose of dealing with routine problems are unlikely to meet the needs of an emergency response.

Recognising that consistently open data sharing is difficult to achieve, the need for an alternative strategy was raised. Suggestions included: i) giving local value, i.e. external groups are not allowed to analyse the data unless the direct benefit to the local communities are made clear; ii) a systematic set of rules and policies for data storage and sharing; iii) making clear the considerations of ethical remits and imperatives (including patient confidentiality and data ownership); and iv) making feedback of data analysis results back to local communities compulsory.

However, questions were raised over *how* best to institutionalise best practices for data analysis and data sharing. There are legal barriers to be overcome, e.g. in the 2009-10 influenza pandemic the then-Health Protection Agency (now PHE) shared anonymised individual-level data in real-time across Europe, facilitated by harmonised data protection regulations across and within the European Union (EU). However international common data protection laws did not extend beyond the EU and data sharing was not permitted outside of Europe. However, barriers are not only legal: no other European country followed the UK's lead in sharing data in the influenza pandemic.

Summary

- Decision-making pathways are country- and context-specific. Decision-making will depend on multiple issues such as resources available and political will.
- There is no systematic approach to decision-making for outbreaks and/or emergencies even within the same organisation.
- A multidisciplinary and geographically representative "network-of-networks" would facilitate better interactions between policy-makers and modellers, as well as other parties involved in outbreak response.
- Such networks should also provide capacity-building for all parties involved as well as ensuring a clear framework for "rules of engagement" between the different groups.
- There is a need for long-term sustainable funding to build collaborations and capacity during "peace-time" but also to provide surge capacity during emergencies.
- There is a clear need for improved communication and development of a "common language" between modellers and decision-makers. A need to train individuals to sit on the interface of policy and analytics was highlighted. This is especially important when multiple modelling groups are involved, and a consensus view is required.

- The explicit integration of social science or behavioural data into dynamic modelling was raised as a key methodological research gap.
- Improvements in data collection methods and an auditing process would be beneficial to ensure the context in which the data were collected is retained.
- Improvements in surveillance systems and data collection are more likely to occur if investment leads to a day-to-day benefit in addition to benefits in emergencies. Data sharing remains a complex and sensitive issue that requires careful consideration of patient confidentiality, ethics, and code of conduct or rules of engagement.

6: Case Studies

Motivation

Recognising that evidence-informed decision-making is often highly context-specific, throughout the consultation process (email survey and workshop) we identified several case studies to illustrate key points and experiences relevant to specific points along the evidence-to-decision-making pathway:

1) *Sharing data*:
    - WHO data sharing principles for all data and during emergencies.
2) *Improving and sustaining interactions between policy-makers and analysts*:
    - Setting up meaningful, long-term partnerships between government institutions in LMICs and epidemiology research groups.
3) *Epidemiology, advanced analytics, and modelling for real-time decision-making*:
    - Providing real-time epidemiological, advanced analytics, and modelling analysis during PHEICs.
4) *Capacity-building*:
    - Building local capacity after an emergency for the development of advanced analytics.

Individuals were contacted in person or via email and asked to provide their insights and experiences of specific topics listed above.

Case Study 1 – Sharing Data

WHO Data Sharing Principles - Chris Dye

The World Health Organization has had no general policy on the sharing and use of data that are provided to WHO by member states, which are then shared by the Organization with third parties. Between December 2016 and August 2017, a wide consultation was carried out within and outside WHO to develop and finalize a *Policy on Use and Sharing of Data Collected in Member States by WHO Outside the Context of Public Health Emergencies.* Based on this consultation involving over 150 individuals and organisations, WHO have now developed two policies for data sharing:

i) For during emergencies under the International Health Regulations (IHR);
ii) For all data.

Data sharing in health emergencies covers data (but not biological samples) on: i) surveillance, epidemiology and emergency response, including health facilities; ii) genetic sequences; and iii) observational studies and clinical trials. The data sharing policy outside of emergencies addresses: i) essential elements of data collection, use and sharing; ii) the benefits of data sharing and measures to mitigate potential risks; iii) measures to ensure ethical and secure use of data; and iv) additional safeguards.

WHO consider data sharing to be part of a broader debate on open access to information (i.e. words as well as numbers), and WHO have also launched a fully open access publishing policy. Data sharing and data protection are inherently linked and must be

considered and discussed jointly. However, in order to adequately protect patient identity and adhere to ethical data sharing, it is clear that trade-offs are required as a general rule.

Although these are now official policies that WHO staff must adhere to (Appendix G), it remains to be seen how these policies will change action in member states and other organisations. The policies support health information sharing as a public good and brings WHO in line with other governmental and intergovernmental organisations, research, and funding agencies globally. However, it is important to acknowledge that the WHO, as an intergovernmental organisation with 194 member states or "clients", is fundamentally different from other organisations such as funding bodies or NGOs.

Key Points

The development of official data sharing policies by WHO specifically addressing health emergencies and routinely collected data points towards the growing recognition of the importance of sharing data, particularly during emergencies. There is now "…consensus that data should be shared by default, but with an opt-out policy, to ensure that the knowledge generated becomes a global public good." It will be important to ensure confidentiality, and that countries share the benefits arising from sharing their data with WHO and third parties. Analyses of country data should be driven by country needs.

Case Study 2 – Improving and sustaining interactions between policy-makers and analysts

Meaningful partnerships within LMICs and co-production of evidence - Emily Gurley

Collaboration between government and academic collaborators on outbreak response: Nipah virus in Bangladesh as a case study

During January 2004, outbreaks of fatal encephalitis in Rajbari and Faridpur Districts were identified and suspected to be caused by Nipah virus. Due to the international concerns about Nipah virus, the Government of Bangladesh requested assistance from the World Health Organization, and local partner icddr,b (International Centre for Diarrheal Disease Research, Bangladesh), an international public health research institute located in Dhaka. The lead for the response from icddr,b was a secondee from the US Centers for Disease Control and Prevention, and the US government supported the collaborative investigation with staff and resources. These initial collaborative efforts were driven by acute needs for resources and expertise. However, this was the beginning of a long-term collaboration on Nipah virus between the Institute for Epidemiology, Disease Control and Research (IEDCR) at the Ministry of Health and Family Welfare, the icddr,b, and US CDC.

When another suspect Nipah virus outbreak was reported in 2005, IEDCR, icddr,b and US CDC collaborated again to detect cases and investigate risk factors for illness. In particular, the icddr,b team included social scientists, who helped to identify how humans may have been infected by bats. This was the first outbreak where drinking date palm sap was identified as a route of transmission. All collaborators worked together to analyze and disseminate the results, through local publications and international, peer-reviewed journals.

During 2006 -2008, leadership at collaborating institutes sought to build on past successes and formalize the partnership on Nipah virus and improve the systematic identification of Nipah virus through surveillance activities and outbreak investigation. There were a number

of components of this collaboration that made it successful. First, a formal memorandum of understanding was signed between the institutes, setting out their intentions to collaborate on surveillance and outbreak activities. A formal organizational agreement made the collaboration sustainable as it was not reliant on specific persons. Second, funds were raised to support the collaboration. The US CDC provided funding to begin hospital-based surveillance for Nipah virus cases and for a full-time outbreak investigation team that could investigate Nipah virus outbreaks, as well as any other outbreaks of interest for the collaboration. IEDCR also committed funding for these outbreak efforts, including provision of transportation and staff time. An important feature of this outbreak team was that one physician-epidemiologist was seconded from icddr,b to IEDCR specifically for the purpose of outbreak investigation. The staff member was paid by icddr,b with US CDC funds, but reported to the Director of IEDCR on a daily basis, and supported government investigations and activities. Third, the team developed protocols that would be used for surveillance and outbreak investigation activities and trained the teams on procedures before any outbreak occurred. This sets expectations for data collection and quality and ensured that scientific goals were advanced during each outbreak opportunity. Fourth, a central theme of the collaboration was capacity building and the laboratory infrastructure at the IEDCR labs was strengthened, including training at the US CDC for laboratory staff, so that the routine Nipah surveillance testing could be conducted at IEDCR. Finally, one of the most important components was the clarification of the rules of engagement and responsibilities of each collaborator. IEDCR had the mandate for surveillance and outbreak investigation and response and was responsible for reporting cases to WHO and making them public; icddr,b and the US CDC were responsible for bringing technical support and resources to the effort. The databases were shared, and scientific manuscripts included co-authors from each institute.

The collaboration continues in 2018. A highlight of the collaboration was when the Government of Bangladesh used the epidemiologic data from outbreaks to inform policy; they declared that date palm sap should not be consumed raw, due to the risk that Nipah virus posed.

Case Study 3 – Epidemiology, advanced analytics, and modelling for real-time decision-making

Providing real-time analysis during the 2014 West African Ebola Epidemic – Christl Donnelly

In August 2014, the World Health Organization (WHO) contacted Neil Ferguson, the Director of the WHO Collaborating Centre for Infectious Disease Modelling seeking assistance in the analysis and modelling of data from the West African Ebola epidemic.

WHO Collaborating Centre for Infectious Disease Modelling: MRC Centre for Outbreak Analysis and Modelling, Imperial College London [1]

Designated in 2010, the terms of reference are:

1. Provide rapid analysis of urgent infectious disease problems, notably outbreaks and events of international concern.
2. Provide technical research capability in specific disease areas
3. Provide training/capacity building in modelling

4. Coordination of expertise in infectious disease modelling
5. Contribute to WHO information products as indicated and related activities in the workplan, subject to WHO approval

A formal data sharing agreement between WHO and Imperial College was drafted in August 2014 and contained terms including:

i. to use the data "for the exclusive purpose of epidemiological analysis, including mathematical modelling and risk assessment, as well as response and impact evaluation";
ii. to treat the data as "strictly confidential and proprietary. They will not be used for any purpose other than the [aforesaid] Purpose";
iii. to "on at least a weekly basis, share all major analyses conducted and/or ongoing on the Ebola data, describing all major insights and/or findings arising from these analyses";
iv. not to "present any findings and/or analyses arising from the Ebola data in any public forum…. without the written consent of the Member State" that has provided these data.

On this basis, case-based line-list data on Ebola virus disease (EVD) cases were shared by WHO. Collaborating Centre (CC) staff were quickly mobilised to analyse the data. Initial goals [see appendix] were mutually agreed and aimed to improve situational awareness, including investigating whether the epidemiology suggested that the Ebola virus in West Africa was substantially different from the viruses which caused earlier Ebola outbreaks.

What followed were ongoing collaborative discussions and a series of over 37 reports and supplementary analyses written by CC staff sent only to WHO initially (who distributed the reports to key individuals in affected countries), but later – with WHO permission – distributed to key partners involved in the operational response (e.g., US CDC and a number of UK Government departments).

Epidemiological topics of the reports included:

i. case fatality ratio (CFR)
ii. delay distributions (such as onset-to-hospitalisation, hospitalisation-to-recovery, etc)
iii. estimation of key epidemiological parameters (including the basic reproduction number)
iv. analysis of incidence time series data, overall and by district
v. projection of future incidence
vi. exposures and risk factors associated with the spread

Amongst these topics, analysis of the case fatality ratio and projections of future incidence were particularly informative for decision-making. Estimates of CFR [2,3] were used to assess whether the Ebola virus was more virulent compared to past epidemics, and how the risk of dying varied with age, sex, and geographical location. The formal analysis was the basis of better understanding the risk of death by programme managers, donors, politicians, and others. Second, the projection of future incidence [2] came at a critical time when case numbers were still growing at a close to exponential rate. The numbers of cases forecast to the beginning of November 2014 added urgency to the response and informed WHO's strategic planning and budgeting. These forecasts carried credibility in being perceived as technically sound and objective in stating the threat.

The initial peer-reviewed publication of this collaborative work was published in September 2014 [2]. Prof Christl Donnelly (Imperial College London) and Dr Chris Dye (Director of Strategy, WHO) held a joint press conference in Geneva at the time of publication. Subsequent papers were published, providing updates on the overall situation [3,4], while others were focused on EVD in children [5], on EVD and gender [6], and a detailed analyses of contact data [7].

References

1. http://apps.who.int/whocc/Detail.aspx?cc_ref=UNK-226&cc_subject=influenza&
2. WHO Ebola Response Team. Ebola Virus Disease in West Africa — The First 9 Months of the Epidemic and Forward Projections. *New England Journal of Medicine* 371, 1481-95, 2014. Published online 23 September 2014. doi: 10.1056/NEJMoa1411100
3. WHO Ebola Response Team. West African Ebola epidemic after one year--slowing but not yet under control. *New England Journal of Medicine* 372, 584-7, 2015. Published online 24 December 2014. doi: 10.1056/NEJMc1414992
4. WHO Ebola Response Team. After Ebola in West Africa: infections are unpredictable but epidemics are preventable. *New England Journal of Medicine* 375: 587-596, 2016. doi: 10.1056/NEJMsr1513109
5. WHO Ebola Response Team. Ebola virus disease among children in West Africa. *New England Journal of Medicine* 372, 1274-7, 2015. doi: 10.1056/NEJMc1415318.
6. WHO Ebola Response Team. Ebola virus disease among male and female persons in West Africa. *New England Journal of Medicine* 374, 96-8, 2016. doi: 10.1056/NEJMc1510305
7. International Ebola Response Team. Exposure patterns driving Ebola transmission in West Africa: A retrospective observational study. *PLoS Medicine* 13(11): e1002170, 2016. doi: 10.1371/journal.pmed.1002170

Appendix Case Study 3: Workplan for Ebola analysis and modelling

Collaboration between the World Health Organization, Imperial College London and University of Oxford

The following workplan was developed in discussions with the World Health Organization (WHO) to support WHO and its member states responding to the current Ebola outbreak via provision of epidemiological and geospatial analysis and modelling. It describes priorities for analyses that the MRC Centre for Outbreak Analysis and Modelling at Imperial College London (WHO Collaborating Centre for Infectious Disease Modelling, Director Prof. Neil Ferguson) and Oxford University (WHO Collaborating Centre for Geospatial Modelling, Prof. Simon Hay) will conduct for WHO. The timelines provided below are estimated and will depend on the quality and completeness of the data available.

The academic parties will additionally provide support (in the form of staff or program code) to WHO in developing code for data visualisation and analysis for use in daily/weekly situation reports.

Task	Data Needs	Analysis Plan*	Timeline*
1. Epidemiological assessment			
A. Estimating key epidemiological parameters (incubation period, generation time, distribution of times from onset to death, etc)	Line list with data at the individual case level; contact tracing data	Maximum likelihood fitting of distributional models, correcting for censoring	~1 week
B. Estimating transmission intensity (R) and its spatiotemporal variation	Line list with data at the individual case level; population data for affected region	Renewal equation models, branching process models &/or infection tree analysis undertaken at regional, country and provincial/district level	1-2 weeks
C. Assessing relative contribution of	Line list with data at the individual case level including information on clinical outcomes; contact tracing data	Results of 1A, 1B, survival analysis	1-2 weeks

different stages of infection (early symptomatic, late symptomatic, dead) and modes of contact (household prior to death, healthcare contacts, funeral contacts) to transmission	with details of contact types; data from historical outbreaks		
D. Geospatial analysis of spatial spread of infection and risk of infection being imported to unaffected areas	Line list with data at the individual case level; population data for affected region; genetic sequencing data; human movement data	Branching process models &/or infection tree analysis of the entire outbreak, weighting probability of long-range movement of infection using data on human mobility. Sequence data also able to be used (e.g. via Outbreaker software)	2-6 weeks
2. Disease burden assessment			
A. Estimating the case fatality ratio and how it varies by age, sex and other covariates	Line list with data at the individual case level including information on clinical outcomes	Results of 1A, survival analysis	~1 week
B. 'Now-casting' - estimating the numbers	Line list with data at the individual case level	Results of 1A, 1B, 2A, simple renewal equation models.	1-2 weeks

currently infected (*not* correcting for overall under ascertainment), correcting for incubation period, reporting delays			
C. Estimate the true scale of the epidemic by estimating the degree of case under-ascertainment	Line list with data at the individual case level; population data for affected region; genetic sequencing data; human movement data	Analysis will draw on 1A-C. Two approaches: (a) genetic analysis – using viral diversification rate to estimate numbers infected; (b) fitting model of the rate of spatial spread to estimate likely scale of outbreak at different time points	2-6 weeks
3. Evaluation of interventions			
A. Assessment of required follow up period for contacts of cases	Line list with data at the individual case level; contact tracing data	(a) Using results of from 1A, assess follow-up period required to detect 80%, 90%, 95%, 99% of infections in contacts. (b) Using results from 1B, assess proportion of cases in contacts needing to be detected in order to achieve control of transmission (R<1)	~1 week for (a), 1-2 weeks for (b)
B. Prioritisation of types of contacts to follow up	Line list with data at the individual case level including information on clinical outcomes; contact tracing data with details of contact types; data from historical outbreaks	Using results of 1A-C, assess minimum subset of contact types required to achieve control of transmission (R<1)	~2 weeks

C. Assessment of impact of current interventions **C-1 Evaluate potential impact of various control modalities (from strategies such as "containment" to operational factors e.g., PPE, treatment, social mobilization, contact tracing, etc) to prioritize resource allocation**	Line list with data at the individual case level; contact tracing data; details of interventions used for particular cases, areas	Analysis of correlations between local transmission intensity (or individual case reproduction number) and intervention-related covariates	2-6 weeks
D. Assessment of likely impact of novel interventions	Line list with data at the individual case level; contact tracing data; preliminary efficacy data (or proxies thereof)	Using results of 1A-D & 2A, simulate impact using branching process or transmission models	3-6+ weeks
E. Predicting capacity/logistical needs for current and future interventions	Estimates of case numbers, resource requirements per case (& or head of population), healthcare centre or region	Simple logistical/supply-chain/health economic models, coupled to epidemiological models developed above	2+ weeks

*Will depend on the quality and completeness of the data available.

Case Study 4 – Capacity-Building

Building local capacity after an emergency for the development of advanced analytics – Steven Riley and Ben Cowling

During the 2003 SARS outbreak Hong Kong had very little modelling or advanced analytical capacity (in infectious diseases). Therefore, the local academic teams in receipt of the data from the Hong Kong government reached out and formed collaborative links with UK and US groups, resulting in real-time epidemiological and modelling analyses, followed by a number of key scientific publications.

Immediately following the outbreak, the government of Hong Kong established the Research Fund for the Control of Infectious Diseases (RFCID) with the explicit goal of building local capacity in all aspects of the science of infectious disease control. As well as small project grants, the RFCID also made large awards that could fund junior faculty appointments on soft money, resulting in the recruitment of analytical and modelling staff from the UK and US.

These resources were used largely to conduct follow-up research on the SARS outbreak and then to develop the science of pandemic influenza preparedness, leading to more general epidemiological research on influenza. Therefore, during the 2009 influenza pandemic, there was strong local capacity for the analysis of early data in real time and there were ongoing epidemiological studies of influenza that could be re-tasked to the pandemic. In addition, a key member of one research group (Gabriel Leung, HKU) was appointed in summer 2008 as Under Secretary for Health in government. This resulted in a highly efficient channel for collaboration between academic groups and a government in a health emergency such as the 2009 pandemic.

The net result of post-SARS capacity-building for advanced analytics and modelling of infectious disease in Hong Kong can be seen in the collaboration bubble charts in Figure 2.5 (Chapter 2) where Hong Kong, with a population of ~7 million, features for SARS, H1N1 and MERS. Hong Kong's successful capacity development illustrates how the establishment of a small core group of individuals with the right network can lead to a healthy community in a relatively short period of time.

Appendix A: Training set of peer reviewed papers

The following peer-reviewed papers were used as a training set for the literature review (Section 2) to ensure that our search terms captured key papers in each topic. The papers below were chosen based on expert opinion.

Ebola

1. Strategies for containing **Ebola** in West Africa. (Pandey A, Atkins KE, Medlock J, Wenzel N, Townsend JP, Childs JE, Nyenswah TG, Ndeffo-Mbah ML, Galvani AP.)

2. **Ebola** virus **disease** in West Africa--the first 9 months of the **epidemic** and forward **projections**. WHO **Ebola Response** Team

3. **Dynamics** and control of **Ebola** virus transmission in Montserrado, Liberia: a **mathematical modelling analysis**. (Lewnard JA, Ndeffo Mbah ML, Alfaro-Murillo JA, Altice FL, Bawo L, Nyenswah TG, Galvani AP.)

4. West African **Ebola epidemic** after one year--slowing but not yet under control. WHO Ebola Response Team

5. Other WHO Ebola Response Team / International Ebola Response Team papers:
    - Heterogeneities in the case fatality ratio…
    - Exposure patterns driving Ebola transmission in West Africa…
    - Ebola virus disease among children in West Africa

6. Measuring the impact of **Ebola** control measures in Sierra Leone. Kucharski AJ, Camacho A, Flasche S, Glover RE, Edmunds WJ, Funk S.

7. Temporal Changes in **Ebola** Transmission in Sierra Leone and Implications for Control Requirements: a Real-time **Modelling** Study. Camacho A, Kucharski A, Aki-Sawyerr Y, White MA, Flasche S, Baguelin M, Pollington T, Carney JR, Glover R, Smout E, Tiffany A, Edmunds WJ, Funk S.

H1N1 influenza

1. **Pandemic** potential of a strain of **influenza** A (H1N1): early findings. Fraser C, Donnelly CA, Cauchemez S, Hanage WP, Van Kerkhove MD, Hollingsworth TD, Griffin J, Baggaley RF, Jenkins HE, Lyons EJ, Jombart T, Hinsley WR, Grassly NC, Balloux F, Ghani AC, Ferguson NM, Rambaut A, Pybus OG, Lopez-Gatell H, Alpuche-Aranda CM, Chapela IB, Zavala EP, Guevara DM, Checchi F, Garcia E, Hugonnet S, Roth C; WHO Rapid Pandemic Assessment Collaboration

2. Closure of schools during an **influenza pandemic**. Cauchemez S, Ferguson NM, Wachtel C, Tegnell A, Saour G, Duncan B, Nicoll A. *pure epi – maybe include?

3. Improving **pandemic influenza** risk assessment. Russell CA, Kasson PM, Donis RO, Riley S, Dunbar J, Rambaut A, Asher J, Burke S, Davis CT, Garten RJ, Gnanakaran S, Hay SI, Herfst S, Lewis NS, Lloyd-Smith JO, Macken CA, Maurer-Stroh S,

Neuhaus E, Parrish CR, Pepin KM, Shepard SS, Smith DL, Suarez DL, Trock SC, Widdowson MA, George DB, Lipsitch M, Bloom JD. Elife.

4. Studies needed to address public health challenges of the 2009 H1N1 **influenza pandemic**: insights from **modeling**. Van Kerkhove MD, Asikainen T, Becker NG, Bjorge S, Desenclos JC, dos Santos T, Fraser C, Leung GM, Lipsitch M, Longini IM Jr, McBryde ES, Roth CE, Shay DK, Smith DJ, Wallinga J, White PJ, Ferguson NM, Riley S; WHO Informal Network for Mathematical **Modelling** for **Pandemic Influenza**H1N1 2009 (Working Group on Data Needs).

Zika

1. Comparative **Analysis** of Dengue and **Zika** Outbreaks Reveals Differences by Setting and **Virus**. Funk S, Kucharski AJ, Camacho A, Eggo RM, Yakob L, Murray LM, Edmunds WJ.

1. Countering the **Zika** epidemic in Latin America. Ferguson NM, Cucunubá ZM, Dorigatti I, Nedjati-Gilani GL, Donnelly CA, Basáñez MG, Nouvellet P, Lessler J.

2. After the epidemic: **Zika virus projections** for Latin America and the Caribbean. Colón-González FJ, Peres CA, Steiner São Bernardo C, Hunter PR, Lake IR.

3. Potential for **Zika virus** introduction and transmission in resource-limited countries in Africa and the Asia-Pacific region: a **modelling** study. Bogoch II, Brady OJ, Kraemer MUG, German M, Creatore MI, Brent S, Watts AG, Hay SI, Kulkarni MA, Brownstein JS, Khan K.

2. Transmission Dynamics of **Zika Virus** in Island Populations: A **Modelling Analysis** of the 2013-14 French Polynesia Outbreak. Kucharski AJ, Funk S, Eggo RM, Mallet HP, Edmunds WJ, Nilles EJ.

4. Transmission Dynamics of **Zika Virus** in Island Populations: A **Modelling Analysis** of the 2013-14 French Polynesia Outbreak. Kucharski AJ, Funk S, Eggo RM, Mallet HP, Edmunds WJ, Nilles EJ.

5. A Cost-Effectiveness Tool for Informing Policies on **Zika Virus** Control. Alfaro-Murillo JA, Parpia AS, Fitzpatrick MC, Tamagnan JA, Medlock J, Ndeffo-Mbah ML, Fish D, Ávila-Agüero ML, Marín R, Ko AI, Galvani AP.

6. Spread of **Zika virus** in the Americas. Zhang Q, Sun K, Chinazzi M, Pastore Y Piontti A, Dean NE, Rojas DP, Merler S, Mistry D, Poletti P, Rossi L, Bray M, Halloran ME, Longini IM Jr, Vespignani A. *although I think we've discussed previously this one has some serious flaws.

3. Quantifying **Zika**: Advancing the Epidemiology of **Zika** With Quantitative Models. Keegan LT, Lessler J, Johansson MA.

MERS

1. Estimation of MERS-Coronavirus Reproductive Number and Case Fatality Rate for the Spring 2014 Saudi Arabia **Outbreak**: Insights from Publicly Available Data. Majumder MS, Rivers C, Lofgren E, Fisman D.

1. Middle East respiratory syndrome **coronavirus**: quantification of the extent of the epidemic, surveillance biases, and transmissibility. Cauchemez S, Fraser C, Van Kerkhove MD, Donnelly CA, Riley S, Rambaut A, Enouf V, van der Werf S, Ferguson NM.

2. Estimating Potential Incidence of **MERS**-CoV Associated with Hajj Pilgrims to Saudi Arabia, 2014. Lessler J, Rodriguez-Barraquer I, Cummings DA, Garske T, Van Kerkhove M, Mills H, Truelove S, Hakeem R, Albarrak A, Ferguson NM; MERS-CoV Scenario Modeling Working Group; MERS-CoV Scenario Modeling Working Group

3. Preliminary epidemiological assessment of **MERS**-CoV outbreak in South Korea, May to June 2015.Cowling BJ, Park M, Fang VJ, Wu P, Leung GM, Wu JT.

4. Synthesizing data and models for the spread of **MERS**-CoV, 2013: key role of index cases and hospital transmission. Chowell G, Blumberg S, Simonsen L, Miller MA, Viboud C.

5. Unraveling the drivers of **MERS**-CoV transmission. Cauchemez S, Nouvellet P, Cori A, Jombart T, Garske T, Clapham H, Moore S, Mills HL, Salje H, Collins C, Rodriquez-Barraquer I, Riley S, Truelove S, Algarni H, Alhakeem R, AlHarbi K, Turkistani A, Aguas RJ, Cummings DA, Van Kerkhove MD, Donnelly CA, Lessler J, Fraser C, Al-Barrak A, Ferguson NM.

SARS

1. **Modeling** and public health emergency responses: lessons from **SARS**. Glasser JW, Hupert N, McCauley MM, Hatchett R.

2. **Dynamically modeling SARS** and other newly emerging respiratory illnesses: past, present, and future. Bauch CT, Lloyd-Smith JO, Coffee MP, Galvani AP. *review not primary research paper.

3. The epidemiology of **severe acute respiratory syndrome** in the 2003 Hong Kong **epidemic**: an **analysis** of all 1755 patients. Leung GM, Hedley AJ, Ho LM, Chau P, Wong IO, Thach TQ, Ghani AC, Donnelly CA, Fraser C, Riley S, Ferguson NM, Anderson RM, Tsang T, Leung PY, Wong V, Chan JC, Tsui E, Lo SV, Lam TH.

4. Transmission **dynamics** of the etiological agent of **SARS** in Hong Kong: impact of public health interventions. Riley S, Fraser C, Donnelly CA, Ghani AC, Abu-Raddad LJ, Hedley AJ, Leung GM, Ho LM, Lam TH, Thach TQ, Chau P, Chan KP, Lo SV, Leung PY, Tsang T, Ho W, Lee KH, Lau EM, Ferguson NM, Anderson RM.

5. Epidemiological determinants of spread of causal agent of severe acute respiratory syndrome in Hong Kong. Donnelly CA, Ghani AC, Leung GM, Hedley AJ, Fraser

C, Riley S, Abu-Raddad LJ, Ho LM, Thach TQ, Chau P, Chan KP, Lam TH, Tse LY, Tsang T, Liu SH, Kong JH, Lau EM, Ferguson NM, Anderson RM.

See excel spreadsheet attachments for full set of abstracts.

Appendix B: Peer-reviewed literature inclusion criteria and author list

Inclusion Criteria

Inclusion*(Primary Diseases of Interest: SARS, MERS, pH1N1 2009, Ebola, Zika, Preparedness)	**Examples of papers excluded**
Forecasting • e.g. incidence, peak timing, magnitude	• Clinical outcome prediction models. • Clinical risk factors for disease outcome analysis. • Vaccine uptake hesitancy models. • Change in vaccine uptake post-H1N1. • Genetic studies looking at evolution of pathogen that do not include estimation of disease dynamic parameters. • Theoretical models of infectious disease transmission alone. E.g. not used for preparedness or analysis. • KAP studies (not mechanistic model). • Basic science, protein/immunological modelling studies. • Clinical case studies. • Transfusion risk studies and models. • Animal studies.
Estimation of key parameters that could inform response • e.g. R_0, serial interval, CFR, other measures of severity etc.	
Forward looking scenario modelling • Abstract states clearly two or more alternate future scenarios. • Prospective impact of vaccination or other interventions.	
Retrospective impact of interventions and impact of the epidemic on healthcare* • Include both statistical and mechanistic analysis. • Modelling studies looking at the impact of outbreaks on healthcare systems or healthcare provision of other diseases. • Cost-effectiveness studies e.g. pandemic flu vaccination.	
Genomic or Phylogeographic studies • Studies using genomic data that directly estimate key transmission parameters. • Phylogeographic studies looking at source-sink/seeding or spatial patterns of spread.	
Preparedness • Stating that a model has been used to generate a result that can be used in planning for an outbreak or pandemic	
Burden estimation • Including pandemic influenza 2009 but not seasonal influenza. • Economic impact of epidemics.	
Reviews • Papers focusing on mathematical models and epidemiological analysis of epidemics or preparedness strategies.	
Other • Any other potentially relevant papers	

*Excluding impact of seasonal influenza vaccination studies.

Authors listed in Figure 2.5 of the author country collaboration network plots

SARS Authors

PMID	Author	Country*
26336062	Chowell, G., Abdirizak, F., Lee, S., Lee, J., Jung, E., Nishiura, H., Viboud, C	USA;USA;USA;USA;JAPAN;JAPAN;JAPAN;KOREA;KOREA;KOREA;USA;USA;USA;USA
26133021	Virlogeux, V., Fang, VJ., Wu, JT., Ho, LM., Peiris, JS., Leung, GM., Cowling, BJ	CHINA;FRANCE;HONG KONG;HONG KONG
17555781	Liang, W., McLaws, ML., Liu, M., Mi, J., Chan, DK	CHINA;AUSTRALIA;CHINA;AUSTRALIA;CHINA
17493952	Pitzer, VE., Leung, GM., Lipsitch, M	USA;HONG KONG;USA
17254984	Kwok, KO., Leung, GM., Lam, WY., Riley, S	CHINA;HONG KONG;HONG KONG;UK
17235210	Cowling, BJ., Muller, MP., Wong, IO., Ho, LM., Louie, M., McGeer, A., Leung, GM	HONG KONG;HONG KONG;CANADA
16494726	Cauchemez, S., Boelle, PY., Donnelly, CA., Ferguson, NM., Thomas, G., Leung, GM., Hedley, AJ., Anderson, RM., Valleron, AJ	FRANCE;FRANCE;UK;UK;HONG KONG;HONG KONG;UK
16237660	Farewell, VT., Herzberg, AM., James, KW., Ho, LM., Leung, GM	UK;CANADA;HONG KONG
16076827	Ghani, AC., Donnelly, CA., Cox, DR., Griffin, JT., Fraser, C., Lam, TH., Ho, LM., Chan, WS., Anderson, RM., Hedley, AJ., Leung, GM	UK;UK;UK;UK;UK;HONG KONG;HONG KONG;UK;HONG KONG
15909256	Leung, GM., Ho, LM., Chan, SK., Ho, SY., Bacon-Shone, J., Choy, RY., Hedley, AJ., Lam, TH., Fielding, R	CHINA;HONG KONG;HONG KONG
15825024	Yu, IT., Wong, TW., Chiu, YL., Lee, N., Li, Y	CHINA;HONG KONG;HONG KONG
15809907	Lan, YC., Liu, TT., Yang, JY., Lee, CM., Chen, YJ., Chan, YJ., Lu, JJ., Liu, HF., Hsiung, CA., Ho, MS., Hsiao, KJ., Chen, HY., Chen, YM	CHINA;TAIWAN
15781959	Yip, PS., Lau, EH., Lam, KF., Huggins, RM	CHINA;HONG KONG;HONG KONG
15539054	Tang, CS., Wong, CY	CHINA;HONG KONG;HONG KONG
15520422	Leung, GM., Hedley, AJ., Ho, LM., Chau, P., Wong, IO., Thach, TQ., Ghani, AC., Donnelly, CA., Fraser, C., Riley, S., Ferguson, NM., Anderson, RM., Tsang, T., Leung, PY., Wong, V., Chan, JC., Tsui, E., Lo, SV., Lam, TH	CHINA;HONG KONG;HONG KONG;HONG KONG;HONG KONG;UK;UK;UK;UK;UK;UK
15466494	Li, Y., Yu, IT., Xu, P., Lee, JH., Wong, TW., Ooi, PL., Sleigh, AC	CHINA;HONG KONG;HONG KONG
15306395	Anderson, RM., Fraser, C., Ghani, AC., Donnelly, CA., Riley, S., Ferguson, NM., Leung, GM., Lam, TH., Hedley, AJ	UK;UK;UK;UK;UK;UK;HONG KONG;HONG KONG

12766207	Lipsitch, M., Cohen, T., Cooper, B., Robins, JM., Ma, S., James, L., Gopalakrishna, G., Chew, SK., Tan, CC., Samore, MH., Fisman, D., Murray, M	USA;USA;USA;USA;SINGAPORE;SINGAPORE;SINGAPORE;SINGAPORE;SINGAPORE;USA;CANADA;USA
12766206	Riley, S., Fraser, C., Donnelly, CA., Ghani, AC., Abu-Raddad, LJ., Hedley, AJ., Leung, GM., Ho, LM., Lam, TH., Thach, TQ., Chau, P., Chan, KP., Lo, SV., Leung, PY., Tsang, T., Ho, W., Lee, KH., Lau, EM., Ferguson, NM., Anderson, RM	UK;HONG KONG;HONG KONG;UK;HONG KONG;UK;UK;UK
12781533	Donnelly, CA., Ghani, AC., Leung, GM., Hedley, AJ., Fraser, C., Riley, S., Abu-Raddad, LJ., Ho, LM., Thach, TQ., Chau, P., Chan, KP., Lam, TH., Tse, LY., Tsang, T., Liu, SH., Kong, JH., Lau, EM., Ferguson, NM., Anderson, RM	UK;UK;HONG KONG;HONG KONG;UK;UK;UK;HONG KONG;HONG KONG;HONG KONG;HONG KONG;HONG KONG;HONG KONG;HONG KONG;HONG KONG;HONG KONG
21489421	Liu, X., Kakade, M., Fuller, CJ., Fan, B., Fang, Y., Kong, J., Guan, Z., Wu, P	USA;USA;USA;CHINA;CHINA;CHINA;USA

**as authors can have multiple affiliations, the countries are not necessarily in the order of the author names.*

H1N1 Authors

PMID	Author	Country*
29510904	Ejima, K., Nishiura, H	USA;JAPAN;JAPAN;JAPAN
29335536	Wang, L., Wu, JT	CHINA;CHINA;HONG KONG;HONG KONG;HONG KONG;HONG KONG
28369163	Arinaminpathy, N., Kim, IK., Gargiullo, P., Haber, M., Foppa, IM., Gambhir, M., Bresee, J	UK;USA;AUSTRALIA
27914853	Leung, K., Lipsitch, M., Yuen, KY., Wu, JT	CHINA;CHINA;CHINA;HONG KONG;HONG KONG;HONG KONG;HONG KONG;HONG KONG;HONG KONG;USA
28222682	Chong, KC., Zee, BC., Wang, MH	CHINA;CHINA;CHINA;CHINA;CHINA;CHINA;HAITI;HAITI;HONG KONG;HONG KONG;HONG KONG;HONG KONG;HONG KONG;HONG KONG;HONG KONG;HONG KONG;HONG KONG;HONG KONG;HONG KONG
27707909	Chowell, G., Viboud, C., Simonsen, L., Moghadas, SM	CANADA;DENMARK;USA;USA;USA;USA;USA
27449665	Jamotte, A., Chong, CF., Manton, A., Macabeo, B., Toumi, M	AUSTRALIA;FRANCE;FRANCE;FRANCE;FRANCE;SINGAPORE;SINGAPORE;SINGAPORE;SINGAPORE
27125572	Wong, JY., Wu, P., Lau, EH., Tsang, TK., Fang, VJ., Ho, LM., Cowling, BJ	CHINA;CHINA;CHINA;CHINA;CHINA;CHINA;CHINA;HONG KONG;HONG KONG;HONG KONG;HONG KONG;HONG KONG;HONG KONG;HONG KONG;HONG KONG;HONG

		KONG;HONG KONG;HONG KONG;HONG KONG;HONG KONG;HONG KONG
26727660	Poon, LL., Song, T., Rosenfeld, R., Lin, X., Rogers, MB., Zhou, B., Sebra, R., Halpin, RA., Guan, Y., Twaddle, A., DePasse, JV., Stockwell, TB., Wentworth, DE., Holmes, EC., Greenbaum, B., Peiris, JS., Cowling, BJ., Ghedin, E	AUSTRALIA;AUSTRALIA;CHINA;CHINA;CHINA;CHINA;HONG KONG;HONG KONG;HONG KONG;HONG KONG;HONG KONG;HONG KONG;HONG KONG;USA;USA;USA;USA;USA;USA;USA;USA;USA;USA;USA;USA;USA;UK;UK
26820982	Wong, ZS., Goldsman, D., Tsui, KL	AUSTRALIA;CHINA;USA;USA;HONG KONG;HONG KONG;UK;UK;USA
26427725	Tsang, TK., Fang, VJ., Perera, RA., Ip, DK., Leung, GM., Peiris, JS., Cauchemez, S., Cowling, BJ	CHINA;CHINA;FRANCE;HONG KONG;HONG KONG;HONG KONG;HONG KONG
26715075	Ip, DK., Lau, EH., Tam, YH., So, HC., Cowling, BJ., Kwok, HK	CHINA;CHINA;CHINA;CHINA;CHINA;CHINA;HONG KONG
26097505	Worby, CJ., Chaves, SS., Wallinga, J., Lipsitch, M., Finelli, L., Goldstein, E	NETHERLANDS;USA;USA;USA;USA;USA;USA
26372219	Kwok, KO., Davoudi, B., Riley, S., Pourbohloul, B	CANADA;CANADA;CANADA;CHINA;CHINA;HONG KONG;HONG KONG;HONG KONG;HONG KONG;HONG KONG;HONG KONG;HONG KONG;UK
26188191	Wong, JY., Kelly, H., Cheung, CM., Shiu, EY., Wu, P., Ni, MY., Ip, DK., Cowling, BJ	HONG KONG;CHINA;AUSTRALIA;UK
26161740	Liu, R., Leung, RK., Chen, T., Zhang, X., Chen, F., Chen, S., Zhao, J	CHINA;CHINA;CHINA;CHINA;CHINA;CHINA;CHINA;CHINA;HONG KONG;HONG KONG
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25255809	Pelat, C., Ferguson, NM., White, PJ., Reed, C., Finelli, L., Cauchemez, S., Fraser, C	FRANCE;UK;UK;UK;UK;UK;USA;USA
25004134	Lynfield, R., Davey, R., Dwyer, DE., Losso, MH., Wentworth, D., Cozzi-Lepri, A., Herman-Lamin, K., Cholewinska, G., David, D., Kuetter, S., Ternesgen, Z., Uyeki, TM., Lane, HC., Lundgren, J., Neaton, JD.	USA;USA;AUSTRALIA;ARGENTINA;USA;UK;POLAND;ARGENTINA;UK;USA;USA;DENMARK
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24107289	Chong, KC., Fong, HF., Zee, CY	CHINA;CHINA;HONG KONG;HONG KONG;HONG KONG;HONG KONG;USA
24815805	Muthuri, SG., Venkatesan, S., Myles, PR., Leonardi-Bee, J., Al Khuwaitir, TS., Al Mamun, A., Anovadiya, AP., Azziz-Baumgartner, E., Báez, C., Bassetti, M., Beovic, B., Bertisch, B., Bonmarin, I., Booy, R., Borja-Aburto, VH., Burgmann, H., Cao, B., Carratala, J., Denholm, JT., Dominguez, SR., Duarte, PA., Dubnov-Raz, G., Echavarria, M., Fanella, S., Gao, Z., Gérardin, P., Giannella, M., Gubbels, S., Herberg, J., Iglesias, AL., Hoger, PH., Hu, X., Islam, QT., Jiménez, MF., Kandeel, A., Keijzers, G., Khalili, H., Knight, M., Kudo, K., Kusznierz, G., Kuzman, I., Kwan, AM., Amine, IL., Langenegger, E., Lankarani, KB., Leo, YS., Linko, R., Liu, P., Madanat, F., Mayo-Montero, E., McGeer, A., Memish, Z., Metan, G., Mickiene, A., Mikic, D., Mohn, KG., Moradi, A., Nymadawa, P., Oliva, ME., Ozkan, M., Parekh, D., Paul, M., Polack, FP., Rath, BA., Rodríguez, AH., Sarrouf, EB., Seale, AC., Sertogullarindan, B., Siqueira, MM., Skret-Magierlo, J., Stephan, F., Talarek, E., Tang, JW., To, KK., Torres, A., Törün, SH., Tran, D., Uyeki, TM., Van Zwol, A., Vaudry, W., Vidmar, T., Yokota, RT., Zarogoulidis, P., Nguyen-Van-Tam, JS., Aguiar-Oliveira, Mde L., Al Masri, M., Amin, R., Araújo, WN., Ballester-Orcal, E., Bantar, C., Bao, J., Barhoush, MM., Basher, A., Bautista, E., Bettinger, J., Bingisser, R., Bouza, E., Bozkurt, I., Chan, KK., Chen, Y., Chinbayar, T., Cilloniz, C., Cox, RJ., Cuezzo, MR., Cui, W., Dashti-Khavidaki, S., Du, B., El Rhaffouli, H., Escobar, H., Florek-Michalska, A., Fraser, J., Gerrard, J., Gormley, S., Götberg, S., Hoffmann, M., Honarvar, B., Hu, J., Kemen, C., Khandaker, G.,	ARGENTINA;ARGENTINA;ARGENTINA;ARGENTINA;ARGENTINA;ARGENTINA;AUSTRALIA;AUSTRALIA;AUSTRALIA;AUSTRIA;BANGLADESH;BANGLADESH;BANGLADESH;BRAZIL;BRAZIL;BRAZIL;BRAZIL;CANADA;CANADA;CANADA;CANADA;CANADA;CANADA;CHINA;CHINA;CHINA;CHINA;CHINA;CROATIA;DENMARK;EGYPT;EGYPT;FINLAND;FRANCE;FRANCE;FRANCE;FRANCE;GERMANY;GERMANY;GREECE;HONG KONG;HONG KONG;HONG KONG;HONG KONG;INDIA;INDIA;IRAN;IRAN;IRAN;ISRAEL;ISRAEL;ITALY;JAPAN;JORDAN;LITHUANIA;LITHUANIA;MEXICO;MEXICO;MEXICO;MEXICO;MONGOLIA;MOROCCO;NETHERLANDS;NORWAY;NORWAY;POLAND;POLAND;SAUDI ARABIA;SAUDI ARABIA;SAUDI ARABIA;SERBIA;SINGAPORE;SINGAPORE;SINGAPORE;SINGAPORE;SLOVENIA;SLOVENIA;SOUTH AFRICA;SPAIN;SPAIN;SPAIN;SPAIN;SPAIN;SWITZERLAND;SWITZERLAND;TURKEY;TURKEY;TURKEY;TURKEY;USA;USA;USA;USA;USA

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24699693	Wu, JT., Leung, K., Perera, RA., Chu, DK., Lee, CK., Hung, IF., Lin, CK., Lo, SV., Lau, YL., Leung, GM., Cowling, BJ., Peiris, JS	CHINA;CHINA;CHINA;CHINA;CHINA;CHINA;CHINA;CHINA;CHINA;CHINA;CHINA;CHINA;CHINA;CHINA;HONG KONG
24674239	Liao, Q., Cowling, BJ., Lam, WW., Ng, DM., Fielding, R	CHINA;HONG KONG;HONG KONG
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24641156	Gunaratnam, PJ., Tobin, S., Seale, H., Marich, A., McAnulty, J	AUSTRALIA;AUSTRALIA;AUSTRALIA;AUSTRALIA;AUSTRALIA;UK

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24373289	Wu, P., Goldstein, E., Ho, LM., Wu, JT., Tsang, T., Leung, GM., Cowling, BJ	CHINA;HONG KONG;HONG KONG
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22074735	Yang, L., Chan, KP., Cowling, BJ., Chiu, SS., Chan, KH., Peiris, JS., Wong, CM	CHINA;HONG KONG;HONG KONG
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22325010	Dorigatti, I., Cauchemez, S., Pugliese, A., Ferguson, NM	UK;UK;ITALY;UK
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21878814	Klick, B., Nishiura, H., Ng, S., Fang, VJ., Leung, GM., Peiris, JS., Cowling, BJ	CHINA;HONG KONG;HONG KONG
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21990967	Wu, JT., Ho, A., Ma, ES., Lee, CK., Chu, DK., Ho, PL., Hung, IF., Ho, LM., Lin, CK., Tsang, T., Lo, SV., Lau, YL., Leung, GM., Cowling, BJ., Peiris, JS	CHINA;HONG KONG;HONG KONG

21387184	Ohkusa, Y., Sugawara, T., Taniguchi, K., Okabe, N	JAPAN;USA
21624784	Flasche, S., Hens, N., Boëlle, PY., Mossong, J., van Ballegooijen, WM., Nunes, B., Rizzo, C., Popovici, F., Santa-Olalla, P., Hrubá, F., Parmakova, K., Baguelin, M., van Hoek, AJ., Desenclos, JC., Bernillon, P., Cámara, AL., Wallinga, J., Asikainen, T., White, PJ., Edmunds, WJ	UK;UK;UK;LUXEMBOURG;SWEDEN;FRANCE;SLOVAKIA;NETHERLANDS;BELGIUM;BELGIUM;ITALY;BULGARIA;UK;ROMANIA;NETHERLANDS;PORTUGAL;SPAIN;SPAIN;FRANCE
20949342	Liao, Q., Cowling, BJ., Lam, WW., Fielding, R	CHINA;HONG KONG;HONG KONG
21477133	Khandaker, G., Dierig, A., Rashid, H., King, C., Heron, L., Booy, R	AUSTRALIA;UK
20561390	Leung, YH., Li, MP., Chuang, SK	CHINA;HONG KONG
20964521	Wu, JT., Ma, ES., Lee, CK., Chu, DK., Ho, PL., Shen, AL., Ho, A., Hung, IF., Riley, S., Ho, LM., Lin, CK., Tsang, T., Lo, SV., Lau, YL., Leung, GM., Cowling, BJ., Malik Peiris, JS	CHINA;HONG KONG
20805752	Cowling, BJ., Lau, MS., Ho, LM., Chuang, SK., Tsang, T., Liu, SH., Leung, PY., Lo, SV., Lau, EH	CHINA;HONG KONG;HONG KONG
20967280	Liao, Q., Cowling, B., Lam, WT., Ng, MW., Fielding, R	CHINA;HONG KONG;HONG KONG
20830210	Gilbert, GL., Cretikos, MA., Hueston, L., Doukas, G., O'Toole, B., Dwyer, DE	AUSTRALIA;UK
20735923	Muscatello, DJ., Cretikos, MA., Macintyre, CR	AUSTRALIA;UK;UK
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16881729	Wu, JT., Riley, S., Fraser, C., Leung, GM	CHINA;HONG KONG;HONG KONG
27526868	Huang, C., Liu, X., Sun, S., Li, SC., Deng, M., He, G., Zhang, H., Wang, C., Zhou, Y., Zhao, Y., Bu, D	CHINA;CHINA;CHINA;CHINA;CHINA;CHINA;CHINA;CHINA;CHINA;CHINA;CHINA;CHINA;CHINA;HONG KONG
25878298	Biggerstaff, M., Reed, C., Swerdlow, DL., Gambhir, M., Graitcer, S., Finelli, L., Borse, RH., Rasmussen, SA., Meltzer, MI., Bridges, CB	AUSTRALIA;USA;USA
16642006	Ferguson, NM., Cummings, DA., Fraser, C., Cajka, JC., Cooley, PC., Burke, DS	UK;UK;USA;USA;USA;USA
16079797	Ferguson, NM., Cummings, DA., Cauchemez, S., Fraser, C., Riley, S.,	UK;USA;USA;HONG KONG;THAILAND

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26796333	Fumanelli, L., Ajelli, M., Merler, S., Ferguson, NM., Cauchemez, S	FRANCE;ITALY;ITALY;ITALY;UK
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26420593	Mizumoto, K., Endo, A., Chowell, G., Miyamatsu, Y., Saitoh, M., Nishiura, H	USA;USA;JAPAN;JAPAN;JAPAN;JAPAN;JAPAN;JAPAN;JAPAN;JAPAN;JAPAN;JAPAN;JAPAN;JAPAN;USA;USA
26336062	Chowell, G., Abdirizak, F., Lee, S., Lee, J., Jung, E., Nishiura, H., Viboud, C	USA;USA;USA;USA;JAPAN;JAPAN;JAPAN;KOREA;KOREA;KOREA;USA;USA;USA;USA
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26132767	Cowling, BJ., Park, M., Fang, VJ., Wu, P., Leung, GM., Wu, JT	CHINA;HONG KONG;HONG KONG
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25685624	Lessler, J., Rodriguez-Barraquer, I., Cummings, DA., Garske, T., Van Kerkhove, M., Mills, H., Truelove, S., Hakeem, R., Albarrak, A., Ferguson, NM., Aguas, R., Algarni, H., AlHarbi, K.,	SAUDI ARABIA;SAUDI ARABIA;SAUDI ARABIA;USA;USA;USA;USA;UK;UK;UK;UK;UK

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25356657	Blumberg, S., Funk, S., Pulliam, JR	UK;USA;USA;USA;USA;USA;USA
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24549846	Cotten, M., Watson, SJ., Zumla, AI., Makhdoom, HQ., Palser, AL., Ong, SH., Al Rabeeah, AA., Alhakeem, RF., Assiri, A., Al-Tawfiq, JA., Albarrak, A., Barry, M., Shibl, A., Alrabiah, FA., Hajjar, S., Balkhy, HH., Flemban, H., Rambaut, A., Kellam, P., Memish, ZA	UK;SAUDI ARABIA;UK;UK;SAUDI ARABIA;SAUDI ARABIA;SAUDI ARABIA;SAUDI ARABIA;SAUDI ARABIA;SAUDI ARABIA;UK;USA;SAUDI ARABIA;
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28207062	Kirsch, TD., Moseson, H., Massaquoi, M., Nyenswah, TG., Goodermote, R., Rodriguez-Barraquer, I., Lessler, J., Cumings, DA., Peters, DH	LIBERIA;LIBERIA;LIBERIA;LIBERIA;USA;USA;USA;USA;USA;USA;USA;USA
28193880	Lau, MS., Dalziel, BD., Funk, S., McClelland, A., Tiffany, A., Riley, S., Metcalf, CJ., Grenfell, BT	SWITZERLAND;SWITZERLAND;UK;UK;USA;USA
28351674	Nouvellet, P., Cori, A., Garske, T., Blake, IM., Dorigatti, I., Hinsley, W., Jombart, T., Mills, HL., Nedjati-Gilani,	UK;UK;UK;UK;UK;UK;UK;UK;FRANCE

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28024952	Camacho, A., Eggo, RM., Goeyvaerts, N., Vandebosch, A., Mogg, R., Funk, S., Kucharski, AJ., Watson, CH., Vangeneugden, T., Edmunds, WJ	BELGIUM;BELGIUM;BELGIUM;USA;USA;UK;UK;UK
27524644	Taylor, BP., Dushoff, J., Weitz, JS	CANADA;USA;USA;USA;USA;USA;USA
27806049	Merler, S., Ajelli, M., Fumanelli, L., Parlamento, S., Pastore Y Piontti, A., Dean, NE., Putoto, G., Carraro, D., Longini, IM., Halloran, ME., Vespignani, A	ITALY;ITALY;ITALY;ITALY;ITALY;ITALY;ITALY;USA;USA;USA;USA;USA;USA;USA
27721505	Burghardt, K., Verzijl, C., Huang, J., Ingram, M., Song, B., Hasne, MP	CHINA;CHINA;NETHERLANDS;SINGAPORE;SINGAPORE;SINGAPORE;USA;USA;USA;USA
27707909	Chowell, G., Viboud, C., Simonsen, L., Moghadas, SM	CANADA;DENMARK;USA;USA;USA;USA;USA
27600737	Ajelli, M., Merler, S., Fumanelli, L., Pastore Y Piontti, A., Dean, NE., Longini, IM., Halloran, ME., Vespignani, A	ITALY;ITALY;ITALY;ITALY;USA;USA;USA;USA;USA;USA;USA
27434164	Krauer, F., Gsteiger, S., Low, N., Hansen, CH., Althaus, CL	SWITZERLAND;SWITZERLAND;SWITZERLAND;SWITZERLAND;TANZANIA;UK
27188404	Bower, H., Smout, E., Bangura, MS., Kamara, O., Turay, C., Johnson, S., Oza, S., Checchi, F., Glynn, JR	SIERRA LEONE;SIERRA LEONE;SIERRA LEONE;SIERRA LEONE;UK;UK;UK;UK
27135922	Abbate, JL., Murall, CL., Richner, H., Althaus, CL	FRANCE;FRANCE;GERMANY;SWITZERLAND;SWITZERLAND;SWITZERLAND
27029911	Wong, JY., Zhang, W., Kargbo, D., Haque, U., Hu, W., Wu, P., Kamara, A., Chen, Y., Kargbo, B., Glass, GE., Yang, R., Cowling, BJ., Liu, C	AUSTRALIA;CHINA;CHINA;CHINA;CHINA;CHINA;CHINA;CHINA;HONG KONG;HONG KONG;HONG KONG;HONG KONG;HONG KONG;HONG KONG;SIERRA LEONE;SIERRA LEONE;SIERRA LEONE;SIERRA LEONE;SIERRA LEONE;USA;USA
27035948	Fang, LQ., Yang, Y., Jiang, JF., Yao, HW., Kargbo, D., Li, XL., Jiang, BG., Kargbo, B., Tong, YG., Wang, YW., Liu, K., Kamara, A., Dafae, F., Kanu, A., Jiang, RR., Sun, Y., Sun, RX., Chen, WJ., Ma, MJ., Dean, NE., Thomas, H., Longini, IM., Halloran, ME., Cao, WC	CHINA;CHINA;CHINA;CHINA;CHINA;CHINA;CHINA;CHINA;CHINA;CHINA;CHINA;CHINA;CHINA;CHINA;CHINA;CHINA;SIERRA LEONE;SIERRA LEONE;SIERRA LEONE;SIERRA LEONE;SIERRA LEONE;SIERRA LEONE;SIERRA LEONE;SIERRA LEONE;SIERRA

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26928839	Atkins, KE., Pandey, A., Wenzel, NS., Skrip, L., Yamin, D., Nyenswah, TG., Fallah, M., Bawo, L., Medlock, J., Altice, FL., Townsend, J., Ndeffo-Mbah, ML., Galvani, AP	UK;USA;LIBERIA;UK;USA;LIBERIA;UK;USA;LIBERIA
26959413	Lokuge, K., Caleo, G., Greig, J., Duncombe, J., McWilliam, N., Squire, J., Lamin, M., Veltus, E., Wolz, A., Kobinger, G., de la Vega, MA., Gbabai, O., Nabieu, S., Lamin, M., Kremer, R., Danis, K., Banks, E., Glass, K	AUSTRALIA;AUSTRALIA;AUSTRALIA;AUSTRALIA;AUSTRALIA;CANADA;CANADA;CANADA;CANADA;FRANCE;NETHERLANDS;SIERRA LEONE;SIERRA LEONE;SIERRA LEONE;SIERRA LEONE;SIERRA LEONE;SIERRA LEONE;SIERRA LEONE;SIERRA LEONE;SIERRA LEONE;SWEDEN;SWITZERLAND;UK;UK;UK
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26607790	Ajelli, M., Parlamento, S., Bome, D., Kebbi, A., Atzori, A., Frasson, C., Putoto, G., Carraro, D., Merler, S	ITALY;ITALY;ITALY;ITALY;ITALY;ITALY;ITALY;SIERRA LEONE;SIERRA LEONE

26559683	Yang, W., Zhang, W., Kargbo, D., Yang, R., Chen, Y., Chen, Z., Kamara, A., Kargbo, B., Kandula, S., Karspeck, A., Liu, C., Shaman, J	CHINA;CHINA;CHINA;CHINA;CHINA;SIERRA LEONE;SIERRA LEONE;SIERRA LEONE;SIERRA LEONE;SIERRA LEONE;SIERRA LEONE;SIERRA LEONE;SIERRA LEONE;SIERRA LEONE;SIERRA LEONE;SIERRA LEONE;SIERRA LEONE;SIERRA LEONE;USA;USA;USA;USA
26544705	Loubet, P., Mabileau, G., Baysah, M., Nuta, C., Taylor, M., Jusu, H., Weeks, H., Ingels, A., Perennec-Olivier, M., Chapplain, JM., Cartier, N., Mendiharat, P., Raguin, G., Tattevin, P., Yazdanpanah, Y	FRANCE;FRANCE;LIBERIA
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26116183	Plucinski, MM., Guilavogui, T., Sidikiba, S., Diakité, N., Diakité, S., Dioubaté, M., Bah, I., Hennessee, I., Butts, JK., Halsey, ES., McElroy, PD., Kachur, SP., Aboulhab, J., James, R., Keita, M	GUINEA;GUINEA;GUINEA;GUINEA;GUINEA;GUINEA;GUINEA;GUINEA;USA;USA;USA;USA;USA;USA;USA;USA;USA;USA;USA;USA
25970247	Tong, YG., Shi, WF., Liu, D., Qian, J., Liang, L., Bo, XC., Liu, J., Ren, HG., Fan, H., Ni, M., Sun, Y., Jin, Y., Teng, Y., Li, Z., Kargbo, D., Dafae, F., Kanu, A., Chen, CC., Lan, ZH., Jiang, H., Luo, Y., Lu, HJ., Zhang, XG., Yang, F., Hu, Y., Cao, YX., Deng, YQ., Su, HX., Sun, Y., Liu, WS., Wang, Z., Wang, CY., Bu, ZY., Guo, ZD., Zhang, LB., Nie, WM., Bai, CQ., Sun, CH., An, XP., Xu, PS., Zhang, XL., Huang, Y., Mi, ZQ., Yu, D., Yao, HW., Feng, Y., Xia, ZP., Zheng, XX., Yang, ST., Lu, B., Jiang, JF., Kargbo, B., He, FC., Gao, GF., Cao, WC., Tong, YG., Qian, J., Sun, Y., Lu, HJ., Zhang, XG.,	CHINA;SIERRA LEONE;SIERRA LEONE;SIERRA LEONE;SIERRA LEONE;SIERRA LEONE;SIERRA LEONE;SIERRA LEONE;SIERRA LEONE

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26064785	Siettos, C., Anastassopoulou, C., Russo, L., Grigoras, C., Mylonakis, E	GREECE;GREECE;ITALY;USA;USA
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25575618	Merler, S., Ajelli, M., Fumanelli, L., Gomes, MF., Piontti, AP., Rossi, L., Chao, DL., Longini, IM., Halloran, ME., Vespignani, A	ITALY;ITALY;ITALY;ITALY;USA;USA;USA;USA;USA;USA;USA;USA
25347321	Yamin, D., Gertler, S., Ndeffo-Mbah, ML., Skrip, LA., Fallah, M., Nyenswah, TG., Altice, FL., Galvani, AP	USA;USA;USA;LIBERIA
25372658	Bah, EI., Lamah, MC., Fletcher, T., Jacob, ST., Brett-Major, DM., Sall, AA., Shindo, N., Fischer, WA., Lamontagne, F., Saliou, SM., Bausch, DG., Moumié, B., Jagatic, T., Sprecher, A., Lawler, JV., Mayet, T., Jacquerioz, FA., Méndez Baggi, MF., Vallenas, C., Clement, C., Mardel, S., Faye, O., Faye, O., Soropogui, B., Magassouba, N., Koivogui, L., Pinto, R., Fowler, RA	GUINEA;UK;UGANDA;USA;SWITZERLAND;SENEGAL;USA;CANADA;FRANCE
25503921	Kilmarx, PH., Clarke, KR., Dietz, PM., Hamel, MJ., Husain, F., McFadden, JD., Park, BJ., Sugerman, DE., Bresee, JS., Mermin, J., McAuley, J., Jambai, A	SIERRA LEONE;USA;ZIMBABWE;USA;USA;USA;USA;USA;USA;ZAMBIA;SIERRA LEONE
25480136	Camacho, A., Kucharski, AJ., Funk, S., Breman, J., Piot, P., Edmunds, WJ	UK;UK;UK;UK;UK;USA
25455986	Lewnard, JA., Ndeffo Mbah, ML., Alfaro-Murillo, JA., Altice, FL., Bawo, L., Nyenswah, TG., Galvani, AP	LIBERIA;LIBERIA;USA;USA;USA;USA;USA;USA;USA;USA;USA;USA
25353969	Schieffelin, JS., Shaffer, JG., Goba, A., Gbakie, M., Gire, SK., Colubri, A., Sealfon, RS., Kanneh, L., Moigboi, A., Momoh, M., Fullah, M., Moses, LM., Brown, BL., Andersen, KG., Winnicki, S., Schaffner, SF., Park, DJ., Yozwiak, NL., Jiang, PP., Kargbo, D., Jalloh, S., Fonnie, M., Sinnah, V., French, I., Kovoma, A., Kamara, FK., Tucker, V., Konuwa, E., Sellu, J., Mustapha, I., Foday, M., Yillah, M., Kanneh, F., Saffa, S., Massally, JL., Boisen, ML., Branco, LM., Vandi, MA., Grant, DS., Happi, C., Gevao, SM., Fletcher, TE., Fowler, RA., Bausch, DG., Sabeti, PC., Khan, SH., Garry, RF.	USA;USA;SIERRA LEONE;USA;NIGERIA;UK;CANADA;PERU

25414312	Pandey, A., Atkins, KE., Medlock, J., Wenzel, N., Townsend, JP., Childs, JE., Nyenswah, TG., Ndeffo-Mbah, ML., Galvani, AP	LIBERIA;USA;USA;USA;USA;USA;USA;USA;USA;USA
25914858	Volz, E., Pond, S	UK;USA
25244186	Aylward, B., Barboza, P., Bawo, L., Bertherat, E., Bilivogui, P., Blake, I., Brennan, R., Briand, S., Chakauya, JM., Chitala, K., Conteh, RM., Cori, A., Croisier, A., Dangou, JM., Diallo, B., Donnelly, CA., Dye, C., Eckmanns, T., Ferguson, NM., Formenty, P., Fuhrer, C., Fukuda, K., Garske, T., Gasasira, A., Gbanyan, S., Graaff, P., Heleze, E., Jambai, A., Jombart, T., Kasolo, F., Kadiobo, AM., Keita, S., Kertesz, D., Koné, M., Lane, C., Markoff, J., Massaquoi, M., Mills, H., Mulba, JM., Musa, E., Myhre, J., Nasidi, A., Nilles, E., Nouvellet, P., Nshimirimana, D., Nuttall, I., Nyenswah, T., Olu, O., Pendergast, S., Perea, W., Polonsky, J., Riley, S., Ronveaux, O., Sakoba, K., Santhana Gopala Krishnan, R., Senga, M., Shuaib, F., Van Kerkhove, MD., Vaz, R., Wijekoon Kannangarage, N., Yoti, Z	Group authorship consisting of authors from: SWITZERLAND;LIBERIA;GUINEA;NIGERIA;SIERRA LEONE;UK
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28195145	Rulli, MC., Santini, M., Hayman, DT., D'Odorico, P	ITALY;ITALY;NEW ZEALAND;USA;USA;USA

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28538727	Faria, NR., Quick, J., Claro, IM., Thézé, J., de Jesus, JG., Giovanetti, M., Kraemer, MUG., Hill, SC., Black, A., da Costa, AC., Franco, LC., Silva, SP., Wu, CH., Raghwani, J., Cauchemez, S., du Plessis, L., Verotti, MP., de Oliveira, WK., Carmo, EH., Coelho, GE., Santelli, ACFS., Vinhal, LC., Henriques, CM., Simpson, JT., Loose, M., Andersen, KG., Grubaugh, ND., Somasekar, S., Chiu, CY., Muñoz-Medina, JE., Gonzalez-Bonilla, CR., Arias, CF., Lewis-Ximenez, LL., Baylis, SA., Chieppe, AO., Aguiar, SF., Fernandes, CA., Lemos, PS., Nascimento, BLS., Monteiro, HAO., Siqueira, IC., de Queiroz, MG., de Souza, TR., Bezerra, JF., Lemos, MR., Pereira, GF., Loudal, D., Moura, LC., Dhalia, R., França, RF., Magalhães, T., Marques, ET., Jaenisch, T., Wallau, GL., de Lima, MC., Nascimento, V., de Cerqueira, EM., de Lima, MM., Mascarenhas, DL., Neto, JPM., Levin, AS., Tozetto-Mendoza, TR., Fonseca, SN., Mendes-Correa, MC., Milagres, FP., Segurado, A., Holmes, EC., Rambaut, A., Bedford, T., Nunes, MRT., Sabino, EC., Alcantara, LCJ., Loman, NJ., Pybus, OG	ARGENTINA;AUSTRALIA;BRAZIL;CANADA;FRANCE;FRANCE;GERMANY;GERMANY;ITALY;MEXICO;MEXICO;MEXICO;USA;USA;USA;USA;USA;USA;USA;USA;USA;USA;USA;USA;USA;UK;UK;UK;UK;UK;UK;UK
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	EL., Kelly, Y., Castro, C., Carrasquilla, G., Halloran, ME., Longini, IM	
27312324	Gao, D., Lou, Y., He, D., Porco, TC., Kuang, Y., Chowell, G., Ruan, S	CHINA;CHINA;CHINA;USA;HONG KONG;HONG KONG;HONG KONG;HONG KONG;USA;USA;USA;USA
27366586	Chowell, G., Hincapie-Palacio, D., Ospina, J., Pell, B., Tariq, A., Dahal, S., Moghadas, S., Smirnova, A., Simonsen, L., Viboud, C	CANADA;COLOMBIA;DENMARK;USA;USA;USA;USA;USA;USA;USA;USA;USA;USA;USA;USA
27205899	Alfaro-Murillo, JA., Parpia, AS., Fitzpatrick, MC., Tamagnan, JA., Medlock, J., Ndeffo-Mbah, ML., Fish, D., Marín, R., Ko, AI., Galvani, AP	USA;USA;USA;COSTA RICA;COSTA RICA;BRAZIL
27060613	Nishiura, H., Mizumoto, K., Villamil-Gómez, WE., Rodríguez-Morales, AJ	COLOMBIA;COLOMBIA;COLOMBIA;COLOMBIA;COLOMBIA;COLOMBIA;COLOMBIA;COLOMBIA;CUBA;ECUADOR;ECUADOR;JAPAN;JAPAN;JAPAN;JAPAN;JAPAN;JAPAN
27013429	Faria, NR., Azevedo, RDSDS., Kraemer, MUG., Souza, R., Cunha, MS., Hill, SC., Thézé, J., Bonsall, MB., Bowden, TA., Rissanen, I., Rocco, IM., Nogueira, JS., Maeda, AY., Vasami, FGDS., Macedo, FLL., Suzuki, A., Rodrigues, SG., Cruz, ACR., Nunes, BT., Medeiros, DBA., Rodrigues, DSG., Queiroz, ALN., da Silva, EVP., Henriques, DF., da Rosa, EST., de Oliveira, CS., Martins, LC., Vasconcelos, HB., Casseb, LMN., Simith, DB., Messina, JP., Abade, L., Lourenço, J., Alcantara, LCJ., de Lima, MM., Giovanetti, M., Hay, SI., de Oliveira, RS., Lemos, PDS., de Oliveira, LF., de Lima, CPS., da Silva, SP., de Vasconcelos, JM., Franco, L., Cardoso, JF., Vianez-Júnior, JLDSG., Mir, D., Bello, G., Delatorre, E., Khan, K., Creatore, M., Coelho, GE., de Oliveira, WK., Tesh, R., Pybus, OG., Nunes, MRT., Vasconcelos, PFC	BRAZIL;CANADA;CANADA;CANADA;USA;USA;USA;USA;USA;UK;UK;UK;UK;UK;UK
27134732	Rodriguez-Morales, AJ., Galindo-Marquez, ML., García-Loaiza, CJ., Sabogal-Roman, JA., Marin-Loaiza, S., Ayala, AF., Lozada-Riascos, CO., Sarmiento-Ospina, A., Vásquez-Serna, H., Jimenez-Canizales, CE., Escalera-Antezana, JP	CHINA;COLOMBIA
27111294	Lednicky, J., Beau De Rochars, VM., El Badry, M., Loeb, J., Telisma, T., Chavannes, S., Anilis, G., Cella, E., Ciccozzi, M., Rashid, M., Okech, B., Salemi, M., Morris, JG	HAITI;HAITI;HAITI;ITALY;ITALY;USA;USA;USA;USA;USA;USA;USA;USA;USA;USA;USA;USA;USA;USA;USA;USA;USA;USA;USA;USA;USA

28542540	Watts, AG., Miniota, J., Joseph, HA., Brady, OJ., Kraemer, MUG., Grills, AW., Morrison, S., Esposito, DH., Nicolucci, A., German, M., Creatore, MI., Nelson, B., Johansson, MA., Brunette, G., Hay, SI., Khan, K., Cetron, M	CANADA;CANADA;CANADA;CANADA;CANADA;CANADA;CANADA;CANADA;USA;USA;USA;USA;USA;USA;USA;USA;UK;UK;UK;UK;USA;USA;USA;USA;USA;USA;USA;USA;USA
27066299	Monaghan, AJ., Morin, CW., Steinhoff, DF., Wilhelmi, O., Hayden, M., Quattrochi, DA., Reiskind, M., Lloyd, AL., Smith, K., Schmidt, CA., Scalf, PE., Ernst, K	USA;USA;USA;USA;USA;USA;USA;UK

Appendix C: Summary of WHO Member states that mention mathematical models in their National Influenza Preparedness Plans (NIPPs)

Country (Language)	Modelling-based scenario planning	Modelling for real-time response	Examples of scenarios modelled or parameters estimated using models	Comments or Example data types explicitly linked to modelling within NIPP
Australia (English)	Yes	Yes	i) PPE; ii) border controls or travel bans; iii) voluntary isolation; iv) exit screening; v) social distancing; vi) school-closures (pro-active and reactive); vii) workplace closures; viii) cancellation of mass gatherings; ix) antiviral use (response, pre- and post-exposure prophylactic use)	i) "*Contact tracing* to obtain surveillance data to support modelling of pandemic impact levels." ii) "Early molecular and syndromic diagnosis to obtain surveillance data to support modelling of impact of antiviral use."
Bahrain (English)	Yes	Yes	i) Modelling of peak absenteeism; ii) social distancing measures; iii) general feasibility of control measures.	"Government will need regular timely information on the extent and impact of the pandemic across the whole country; the mathematical modelers will need timely, early data in order to refine their estimates of the impact"
Canada (English)	Yes	Yes	i) Vaccination prioritization; ii) estimating transmissibility; iii) impact of public health measures (NPIs e.g. school-closures, self-isolation etc.).	NA
France (English)	NA	Yes	i) "evaluation of the situation and anticipation"; ii) "modelling of the evolution of the pandemic" to develop anticipation capacities.	NA
Germany* (German)	NA	NA	NA	Describes the importance of clarifying limitations and potential usefulness of models for scenario analysis.

Appendix C continued: Summary of WHO Member states that mention mathematical models in their National Influenza Preparedness Plans (NIPPs).

Country (Language)	**Modelling-based scenario planning**	**Modelling for real-time response**	**Examples of scenarios modelled or parameters estimated using models**	**Comments or Example data types explicitly linked to modelling within NIPP**
Honduras (English)	Yes. Refer to CDC planning model by Meltzer *et al*.	No	i) Refer to modelling outputs looking at potential interventions.	NA
Ireland (English)	Yes. Use of UK model to structure scenarios for planning.	Yes	i) Attack rate; ii) CFR; iii) hospitalisation rate; iv) ICU requirements; v) R0 estimation; vi) vaccination prioritisation; vii) containment strategies; viii) antiviral use; ix) severity; x) duration of pandemic.	NA
Japan (English)	Yes. CDC Estimation Model (FluAid2.0 Meltzer et al.)	No	i) Scale of epidemic; ii) GP consultations; iii) mortality estimation; iv) requirements for antiviral drugs.	NA
South Korea (English)	Yes. FluAid2.0 + 10 national experts + Delphi.	No	i) Attack rate; ii) duration of pandemic; iii) prioritisation of high risk groups; iv) mortality; v) hospitalisations; vi) outpatient visits.	NA
Maldives* (English)	No	No	-	"Conservative estimates based on mathematical modeling suggest that the next influenza pandemic could cause from 2 million to 7.4 million deaths although an upper limit of 150 million has also been quoted."

*countries where NIPP refers to modelling but plan does not use modelling for planning or real-time response.

Appendix C continued: Summary of WHO Member states that mention mathematical models in their National Influenza Preparedness Plans (NIPPs).

Country (Language)	**Modelling-based scenario planning**	**Modelling for real-time response**	**Examples of scenarios modelled or parameters estimated using models**	**Comments or Example data types explicitly linked to modelling within NIPP**
New Zealand (English)	Yes	Yes	i) containment modelling; ii) quarantine modelling; iii) post-exposure prophylaxis; iv) targeted layered containment	i) ILI; ii) EpiSurv; iii) sentinel surveillance; iv) virological; v) travel; vi) impact on health services; vii) antiviral use; vii) ICU usage; viii) absenteeism.
Norway (Norwegian)	Yes	No.	i) R0; ii) attack rates; iii) duration; iv) peak; v) peak timing.	Emphasized importance of quickly collecting data to adjust attack and mortality rates.
Papua New Guinea* (English)	No	No	-	"…modelling studies that show that adherence to quarantine can be below 100% and still be effective"
Poland (English)	Yes – but specific parameters not listed.	NA	"…consider introducing population-wide measures to reduce the number of cases and death. Decisions can be guided by mathematical and economy modeling. If modeling indicates a reduction in the absolute numbers of cases and deaths, decision to introduce measures involving multiple government sectors will then need to balance the protection of priority functions against the risk of social and economic disruption."	"- facilitate and support central databases (e.g., Flunet and the LANL sequence database) for recording epidemiological, virological and genetic information, and for modeling purposes"

*countries where NIPP refers to modelling but plan does not use modelling for planning or real-time response.

Appendix C continued: Summary of WHO Member states that mention mathematical models in their National Influenza Preparedness Plans (NIPPs).

Country (Language)	**Modelling-based scenario planning**	**Modelling for real-time response**	**Examples of scenarios modelled or parameters estimated using models**	**Comments or Example data types explicitly linked to modelling within NIPP**
Portugal (Portuguese)	Yes. FluAid2.0	No	i) Scenario planning using different attack rates; ii) R0	-
Singapore* (English)	No	No	"Modeling studies notwithstanding, predictions of how particular disease strains will evolve remain highly speculative. Continued surveillance and monitoring of the global developments in the evolution of acute respiratory infections as well as pandemic preparedness and planning will serve to prepare us against the emergence of the next pandemic."	Mention of modelling, but no further details.
Slovenia (Slovenian)	Yes. UK model used for scenario planning	No	-	-
Sweden* (Swedish)	No. Post-pandemic analysis and future preparedness.	No	"… register studies, analysis with modeling, … It is crucial that the needs are specified in advance, so that data needed for the post-analysis is already collected during the outbreak"	-

*countries where NIPP refers to modelling but plan does not use modelling for planning or real-time response.

Appendix C continued: Summary of WHO Member states that mention mathematical models in their National Influenza Preparedness Plans (NIPPs).

Country (Language)	**Modelling-based scenario planning**	**Modelling for real-time response**	**Examples of scenarios modelled or parameters estimated using models**	**Comments or Example data types explicitly linked to modelling within NIPP**
Switzerland (French, German, Italian)	Yes	Yes	i) modelling excess mortality (as part of routine influenza surveillance); ii) school closures; iii) banning of mass gatherings; iv) allocation/distribution of medical interventions.	i) Contact managements; ii) identification of at risk groups; iii) contact tracing. Use of "consensus models"
Republic of Macedonia (English)	Yes. Use of previous model outputs for scenario planning.	No	i) school closures; ii) travel restrictions; iii) household prophylaxis.	-
UK	Yes	Yes	i) early estimates of severity and impact of pandemic; ii) forecasting likely course of the pandemic; iii) assess requirements for public health interventions e.g. school closures; iv) outbreak analytics – CFR, at risk groups, clusters, and "other aspects… associated with the new virus to inform real-time modelling.	i) Early stages, first-few hundred (FF100) data and ad hoc outbreak studies for initial assessment of key parameters; ii) aggregate data from multiple sources in age and regionally structured SEIR model within Bayesian evidence synthesis framework; iii) current estimates and uncertainties; iv) household secondary attack rates; v) serial interval; vi) symptomatic proportion of cases; vii) antibody dynamics; viii) R0; ix) incubation period; x) case severity ratio; xi) effectiveness of clinical countermeasures.

Appendix C continued: Summary of WHO Member states that mention mathematical models in their National Influenza Preparedness Plans (NIPPs).

Country (Language)	**Modelling-based scenario planning**	**Modelling for real-time response**	**Examples of scenarios modelled or parameters estimated using models**	**Comments or Example data types explicitly linked to modelling within NIPP**
USA (English)	Yes	Yes	i) Forecasting spread; ii) burden; iii) impact of pandemic; iv) clinical guidance; v) response strategies involving use of medical countermeasures (MCMs); vi) product needs and gaps for stockpiling purposes.	"Developing and applying epidemiological modeling tools…to inform policy, clinical guidance, and response strategies involving the use of MCMs." Leverage "big data" for modelling.
Venezuela (Spanish)	Yes. FluAid2.0	No	NA	
Vietnam* (English)	No	No	Strategic plan to: … "review international studies on models and scenarios to improve pandemic planning".	"Improved modelling of selected diseases based on better quality field data".

*countries where NIPP refers to modelling but plan does not use modelling for planning or real-time response.

Appendix D: Sources of grey literature

Pandemic Preparedness Plans

- http://www.who.int/influenza/preparedness/plans/en/
- https://extranet.who.int/sph/influenza-plan

WHO Institutional Repository for Information Sharing (iris)

- http://apps.who.int/iris/

ProMED

- https://www.promedmail.org/

HealthMap

- http://www.healthmap.org

Pre-print Servers

- arXiv - https://arxiv.org/
- BioRxiv - https://www.biorxiv.org/
- F1000Research - https://f1000research.com/

Appendix E: Email survey questionnaire and additional information

Email survey questionnaire

See attachment.

Additional information on organisations highlighted in survey responses

- SPI-M is an advisory group of the UK Department of Health, with members from Public Health England and academic institutions including LSHTM, Imperial, and Warwick that provide modelling capacity and technical expertise to the UK government primarily for influenza. It is part of the UK's pandemic influenza preparedness and response structure, which has been in place for more than a decade. (https://www.gov.uk/government/groups/scientific-pandemic-influenza-subgroup-on-modelling)
  - Successful as it draws on existing in-country expertise and its members are highly-experienced in doing modelling work to inform policy. The long establishment of the group means that members have a good understanding of their roles and of the policy-making process.
  - Peter Grove was also critical in its success as a "bridge/translator" between the modelling groups and government policy makers.

- MIDAS is a US based network of modelling groups (https://www.midas.pitt.edu/index.php?option=com_content&view=article&id=89&Itemid=131)
  - Originally set up in response to 9/11 and smallpox risks, to focus on analysis of infectious disease threats.
  - Organised by NIGMS (part of NIH).
  - Principal initial goals were to build modelling capacity in the US.
  - Close links with Federal government policy-makers in its first 10 years, but these links have since weakened.
  - Scope has recently changed and MIDAS in its original form (i.e. with MIDAS-specific calls for proposals) will end next year.

- RAPIDD was another US-based group of modelling networks:
  - funded by DHS (Homeland security).
  - focused more on fundamental research than applied policy-relevant activity.
  - remit included animal diseases.
  - largely run by two individuals – Bryan Grenfell and Ellis McKenzie.
  - main modus operandi was the running of large numbers of specialist technical workshops in key research priority areas.
  - also provided seed funding for research in these areas to early-career researchers.
  - Now ended.

Appendix F: Consultation on Epidemiology and Modelling for Epidemic Preparedness and Response, 10-11th May 2018

List of Participants

Name		Institution
Emmanuel	Agogo	Nigerian Center for Disease Control
Robert	Agyarko	African Risk Capacity
Virgina	Asin-Oostburg	CARPHA
Kevin	Bardosh	University of Florida
Caroline	Buckee	University of Harvard
Lenio	Capsaskis	Wellcome Trust
Kalipso	Chalkidou	Imperial College London
Hannah	Clapham	Wellcome Oxford University Clinical Research Unit, Vietnam
Kori	Cook	Wellcome Trust
Ben	Cooper	Wellcome Trust Mahidol Oxford Research Unit
Ben	Cowling	Hong Kong University
Inger	Damon	US Centers for Disease Control and Prevention
Basu	Dev Pandey	Nepal Ministry of Health
Christl	Donnelly	Imperial College London
Bianca	D'Souza	LSHTM
Chris	Dye	University of Oxford
John	Edmunds	London School of Hygiene and Tropical Medicine
Lukas	Engelmann	University of Edinburgh
Neil	Ferguson	Imperial College London
Josie	Golding	Wellcome Trust
Peter	Grove	UK Department of Health
Emily	Gurley	Johns Hopkins Bloomberg School of Public Health
Peter	Hart	Wellcome Trust
Richard	Hatchett	Coalition for Epidemic Preparedness Innovations (CEPI)
Daniel	Hogan	GAVI
Peter	Horby	University of Oxford
Natsuko	Imai	Imperial College London
Michael	Johansson	US CDC
Gerald	Keusch	Boston University
Anna	Kinsey	The Medical Research Council, UK

Name	Institution

Justin	Lessler	Johns Hopkins Bloomberg School of Public Health
Marc	Lipsitch	University of Harvard
Nicole	Lurie	Independent Consultant
Sophie	Mathewson	GAVI/Wellcome
Keith	McAdam	LSHTM
Jodie	McVernon	University of Melbourne
Hinta	Meijerink	Coalition for Epidemic Preparedness Innovations (CEPI)
Marcela	Mercado	National Institute of Health Colombia
Oliver	Morgan	Health Emergency Information and Risk Assessment (HIM), WHO
James	Nokes	KEMRI-Wellcome
Mead	Over	Centre for Global Development
Erica	Pufall	Wellcome Trust
Juliet	Pulliam	SACEMA
Joao	Rangel de Almeida	Wellcome Trust
Steven	Riley	Imperial College London
Cathy	Roth	UK Department for International Development (DFID)
Anna	Ruddock	Wellcome Trust
Henrik	Salje	Institut Pasteur
Jennifer	Stuart	UK Department of Health
Bob	Taylor	Wellcome Trust Mahidol Oxford Research Unit
Maria	Van Kerkhove	Infectious Hazard Management (IHM) Department, WHO
Charlotte	Watts	UK Department for International Development (DFID)
Peter	White	Imperial College London

Workshop Agenda

Consultation on epidemiology and modelling for epidemic preparedness and response, 10-11 May 2018

215 Euston Road, London, NW1 2BE, UK

Day 1		
09:30-10:00	*Coffee*	
10:00-10:20	Goals of the meeting	Wellcome/Imperial
10:20-11:05	Introductions	45 mins
Session 1: Evidence-to-decision-making in an ideal world		
11:05-11:35	Framing the discussion	Neil Ferguson
11:35-12:30	Group discussion: What would the ideal look like? • Please see group allocation list	55 mins (breakout)
12:30-13:30	*Lunch*	60 mins
Session 2: Identifying and prioritising key gaps		
13:30-13:55	Feedback from breakout sessions	25 mins
13:55-14:55	Group discussion: identification of key gaps	60 mins
14:55-15:20	Feedback from breakout sessions	25 mins
15:20-15:50	*Coffee*	30 mins
Session 3: Breakout session – risk assessment, response, preparedness		
15:50-16:50	Topic specific discussion: risk assessment, real-time response, and preparedness	60 mins
16:50-17:30	Feedback from breakout sessions and aims for day 2	40 mins
17:30-	*Drinks and dinner hosted by Wellcome Trust*	

Day 2 Session 4: Data		
08:30-09:00	*Coffee*	
09:00-10:00	Topic specific discussion: Data needs, data sharing, and data synthesis.	60 mins
10:00-10:40	Feedback	40 mins
10:40-11:00	*Coffee*	20 mins
Session 5: Networks and Capacity		
11:00-12:00	Topic specific discussion: Networks and capacity-building	60 mins
12:00-12:40	Feedback	40 mins
12:40-14:00	*Lunch*	80 mins
Session 6: Plenary discussion, next steps, and recommendations		
14:00-15:30	Plenary discussion – summary of conclusions, key priorities, the role of funder networks.	90 mins
15:30-16:00	Next steps, and thanks	30 mins
16:00	*Close*	

Appendix G: Supporting documents from Case Studies

Sharing Data (Chris Dye)

Policy Statement on Data Sharing by the World Health Organization in the Context of Public Health Emergencies: http://www.who.int/ihr/procedures/SPG_data_sharing.pdf

WHO policy on the use and sharing of data collected by WHO in Member States outside the context of public health emergencies:

1) http://www.who.int/publishing/datapolicy/en/
2) http://www.who.int/publishing/datapolicy/Policy_data_sharing_non_emergency_final.pdf
3) http://www.who.int/publishing/datapolicy/FAQs_datasharing_website_final.pdf

Improving and sustaining interactions between policy-makers and analysts (Emily Gurley)

1) Cluster of Nipah Virus Infection, Kushtia District, Bangladesh, 2007
    a. http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0013570

2) Nipah Virus Infection Outbreak with Nosocomial and Corpse-to-Human Transmission, Bangladesh
    a. https://wwwnc.cdc.gov/eid/article/19/2/12-0971_article

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