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Modelling of transmission and mitigation

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Overview

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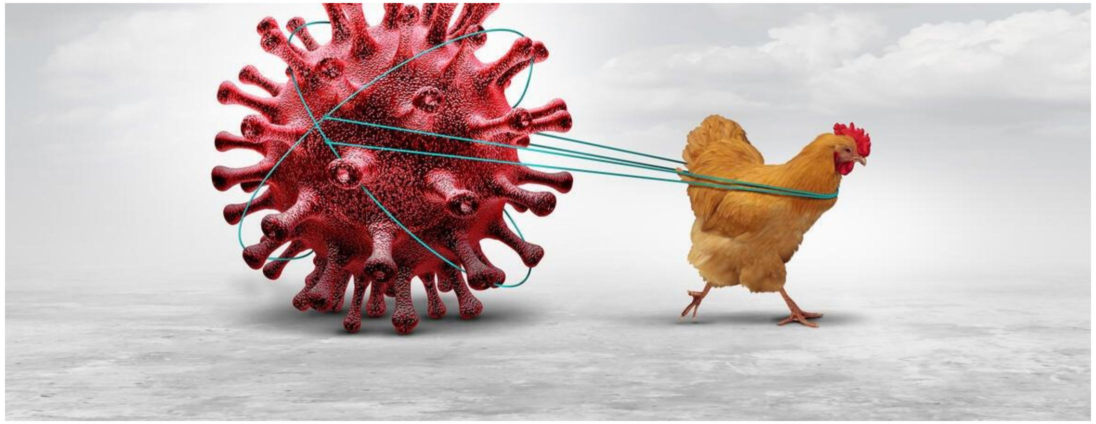
- 2005-8 modelling
- 2009 H1N1
- What's changed since 2008
- Strategic policy goals and drivers
- Data needs
- Decision-making under uncertainty
- Research priorities for modelling



Ack: UC Riverside

2005-8 modelling

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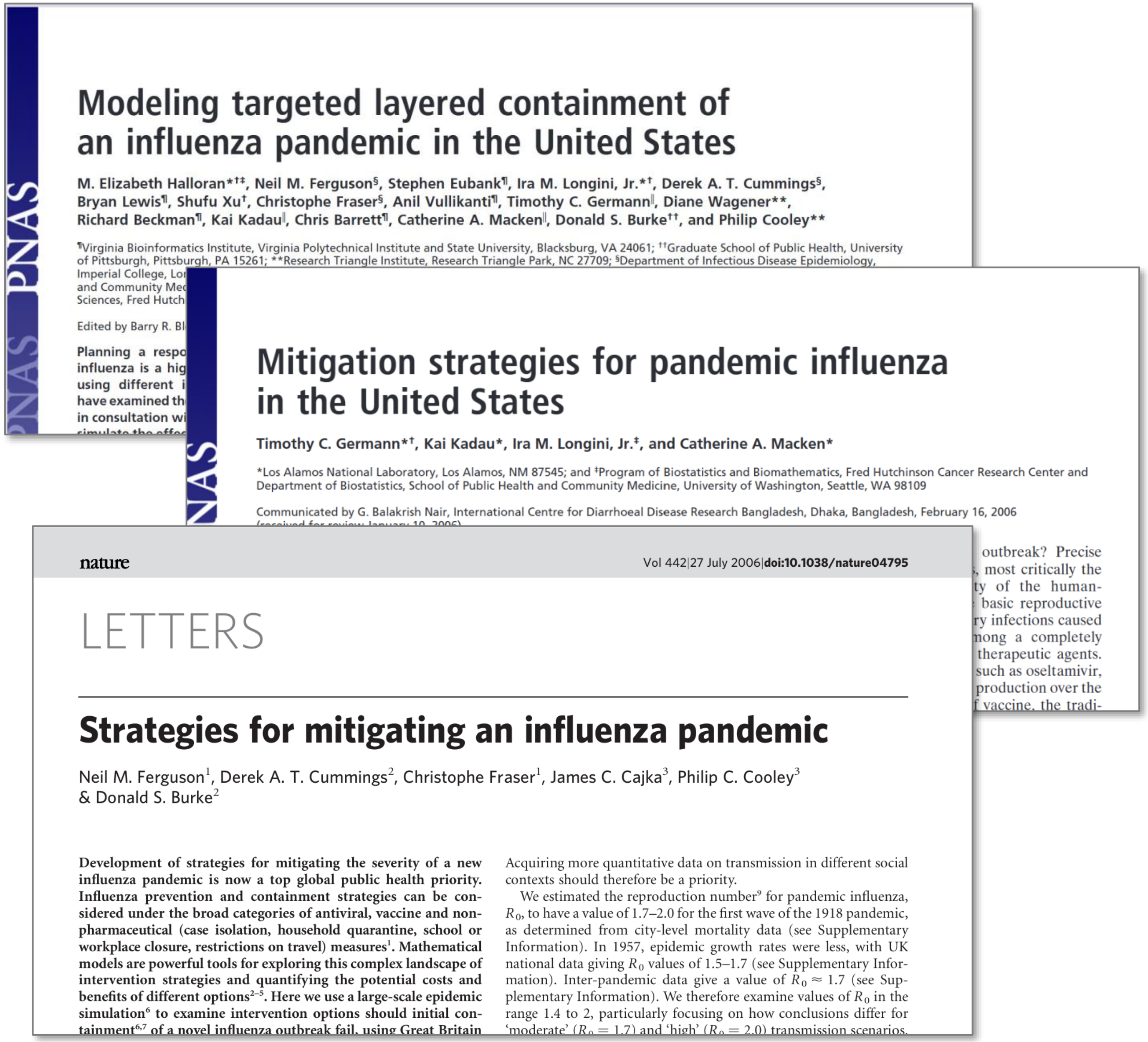
- Examined combinations of NPI, AV and pre-pandemic vaccine use
- PNAS model comparison paper examined incidence-triggered NPI/AV scenarios ranging from “flattening the curve” to suppression
- Ferguson et al. showed 50%+ reductions in health impact possible while still achieving herd immunity



PNAS

Modeling targeted layered containment of an influenza pandemic in the United States

M. Elizabeth Halloran*††, Neil M. Ferguson§, Stephen Eubank¶, Ira M. Longini, Jr.*†, Derek A. T. Cummings§, Bryan Lewis¶, Shufu Xu†, Christophe Fraser§, Anil Vullikanti¶, Timothy C. Germann‖, Diane Wagener**, Richard Beckman¶, Kai Kadau‖, Chris Barrett¶, Catherine A. Macken‖, Donald S. Burke††, and Philip Cooley**

PNAS

Mitigation strategies for pandemic influenza in the United States

Timothy C. Germann*†, Kai Kadau*, Ira M. Longini, Jr.‡, and Catherine A. Macken*

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Communicated by G. Balakrish Nair, International Centre for Diarrhoeal Disease Research Bangladesh, Dhaka, Bangladesh, February 16, 2006

nature Vol 442|27 July 2006|doi:10.1038/nature04795

LETTERS

Strategies for mitigating an influenza pandemic

Neil M. Ferguson[1], Derek A. T. Cummings[2], Christophe Fraser[1], James C. Cajka[3], Philip C. Cooley[3] & Donald S. Burke[2]

Development of strategies for mitigating the severity of a new influenza pandemic is now a top global public health priority. Influenza prevention and containment strategies can be considered under the broad categories of antiviral, vaccine and non-pharmaceutical (case isolation, household quarantine, school or workplace closure, restrictions on travel) measures[1]. Mathematical models are powerful tools for exploring this complex landscape of intervention strategies and quantifying the potential costs and benefits of different options[2–5]. Here we use a large-scale epidemic simulation[6] to examine intervention options should initial con-

Acquiring more quantitative data on transmission in different social contexts should therefore be a priority.

We estimated the reproduction number[9] for pandemic influenza, R_0, to have a value of 1.7–2.0 for the first wave of the 1918 pandemic, as determined from city-level mortality data (see Supplementary Information). In 1957, epidemic growth rates were less, with UK national data giving R_0 values of 1.5–1.7 (see Supplementary Information). Inter-pandemic data give a value of $R_0 \approx 1.7$ (see Supplementary Information). We therefore examine values of R_0 in the range 1.4 to 2, particularly focusing on how conclusions differ for

2005-8 modelling: limitations

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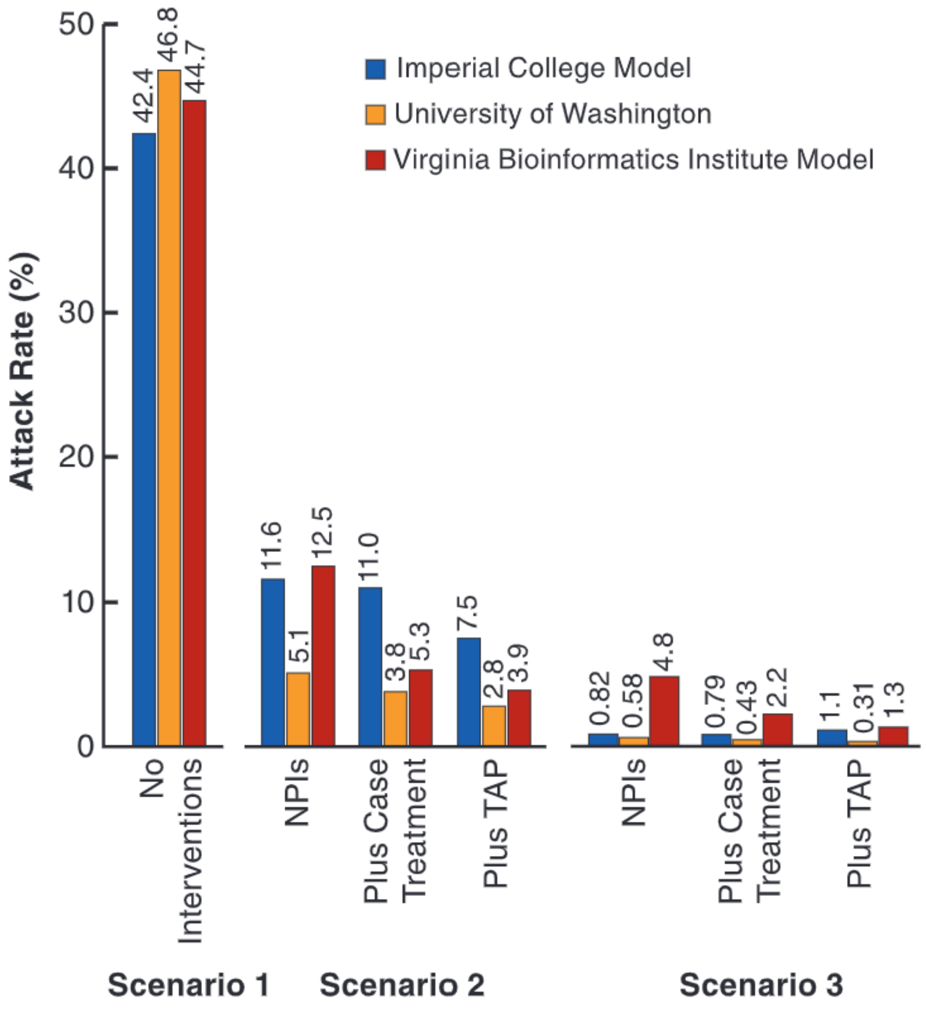
- Optimistic assumptions about symptomatic case ascertainment (60%+)
- AV and vaccine scenarios assumed stockpiles to be substantial fraction of population size
- Human influenza-like epidemiological parameters assumed (R_0, T_g)
- Not modelled:
    - Viral evolution
    - Adaptive policies (other than incidence triggers)
    - Border restrictions (some work done separately)
    - Contact tracing (only household/school/workplace)
    - Healthcare demand/mortality
    - Economic impacts (separate analyses)



2009 H1N1 pandemic

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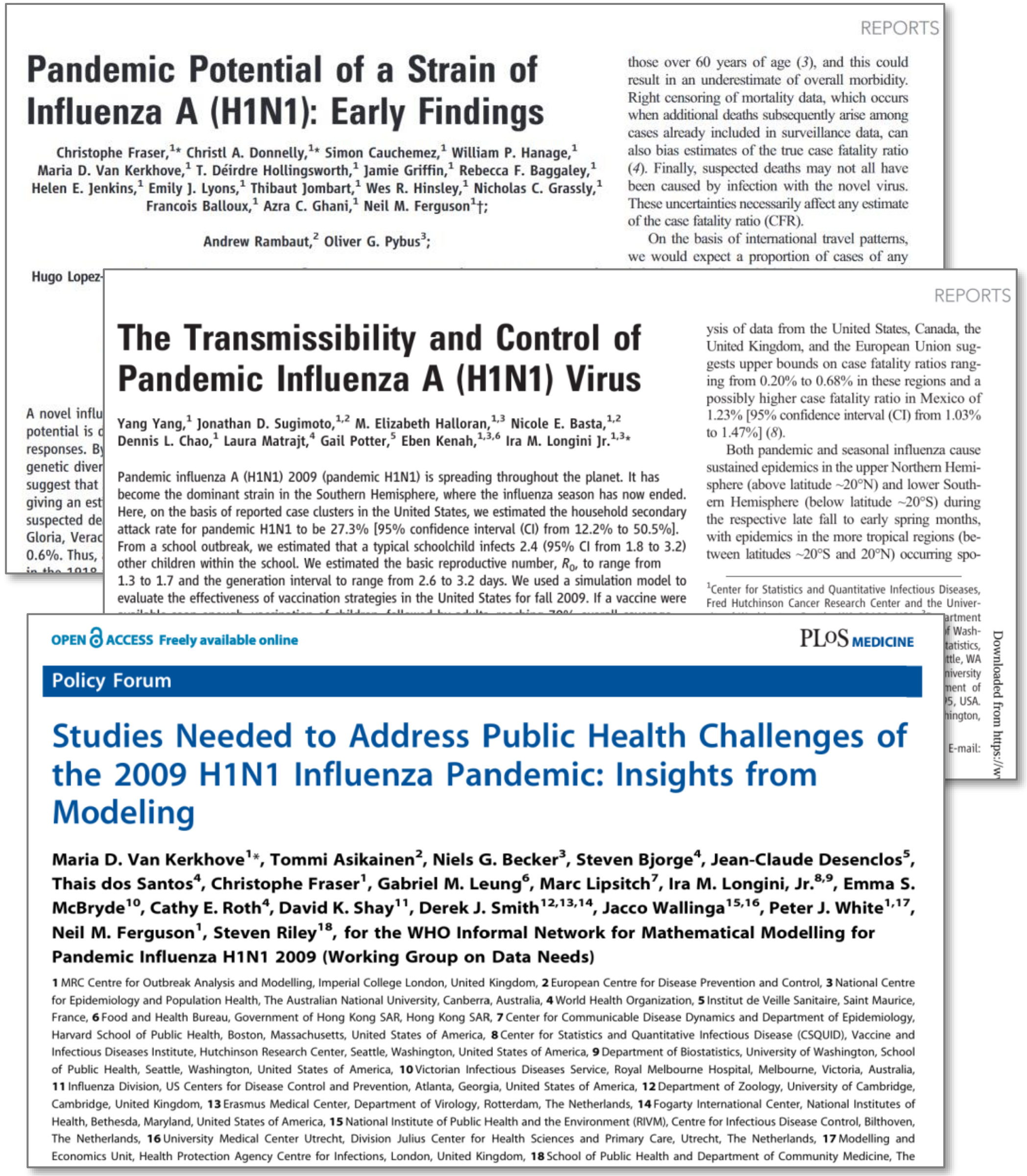
- Rapid early quantitative epidemiological characterisation of virus
- Real-time modelling influenced policy in several countries
- Real-time forecasting of incidence trends started to be a priority
- BUT:
  - Early estimates of CFR/IFR insufficiently precise for policymakers
  - Some policymakers struggled with changing epidemiological estimates (esp upper bound of IFR)
  - Data gaps – serology, case ascertainment/testing, …
  - Some drew the wrong lessons about the future chances of a severe pandemic and ongoing risk from H5N1



REPORTS

Pandemic Potential of a Strain of Influenza A (H1N1): Early Findings

Christophe Fraser,[1*] Christl A. Donnelly,[1*] Simon Cauchemez,[1] William P. Hanage,[1] Maria D. Van Kerkhove,[1] T. Déirdre Hollingsworth,[1] Jamie Griffin,[1] Rebecca F. Baggaley,[1] Helen E. Jenkins,[1] Emily J. Lyons,[1] Thibaut Jombart,[1] Wes R. Hinsley,[1] Nicholas C. Grassly,[1] Francois Balloux,[1] Azra C. Ghani,[1] Neil M. Ferguson[1]†; Andrew Rambaut,[2] Oliver G. Pybus[3]; Hugo Lopez-

those over 60 years of age (3), and this could result in an underestimate of overall morbidity. Right censoring of mortality data, which occurs when additional deaths subsequently arise among cases already included in surveillance data, can also bias estimates of the true case fatality ratio (4). Finally, suspected deaths may not all have been caused by infection with the novel virus. These uncertainties necessarily affect any estimate of the case fatality ratio (CFR).

On the basis of international travel patterns, we would expect a proportion of cases of any

A novel influ… potential is c… responses. By… genetic diver… suggest that… giving an est… suspected de… Gloria, Verac… 0.6%. Thus, …

REPORTS

The Transmissibility and Control of Pandemic Influenza A (H1N1) Virus

Yang Yang,[1] Jonathan D. Sugimoto,[1,2] M. Elizabeth Halloran,[1,3] Nicole E. Basta,[1,2] Dennis L. Chao,[1] Laura Matrajt,[4] Gail Potter,[5] Eben Kenah,[1,3,6] Ira M. Longini Jr.[1,3*]

Pandemic influenza A (H1N1) 2009 (pandemic H1N1) is spreading throughout the planet. It has become the dominant strain in the Southern Hemisphere, where the influenza season has now ended. Here, on the basis of reported case clusters in the United States, we estimated the household secondary attack rate for pandemic H1N1 to be 27.3% [95% confidence interval (CI) from 12.2% to 50.5%]. From a school outbreak, we estimated that a typical schoolchild infects 2.4 (95% CI from 1.8 to 3.2) other children within the school. We estimated the basic reproductive number, R_0, to range from 1.3 to 1.7 and the generation interval to range from 2.6 to 3.2 days. We used a simulation model to evaluate the effectiveness of vaccination strategies in the United States for fall 2009. If a vaccine were

ysis of data from the United States, Canada, the United Kingdom, and the European Union suggests upper bounds on case fatality ratios ranging from 0.20% to 0.68% in these regions and a possibly higher case fatality ratio in Mexico of 1.23% [95% confidence interval (CI) from 1.03% to 1.47%] (8).

Both pandemic and seasonal influenza cause sustained epidemics in the upper Northern Hemisphere (above latitude ~20°N) and lower Southern Hemisphere (below latitude ~20°S) during the respective late fall to early spring months, with epidemics in the more tropical regions (between latitudes ~20°S and 20°N) occurring spo-

[1]Center for Statistics and Quantitative Infectious Diseases, Fred Hutchinson Cancer Research Center and the Univer-

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Policy Forum

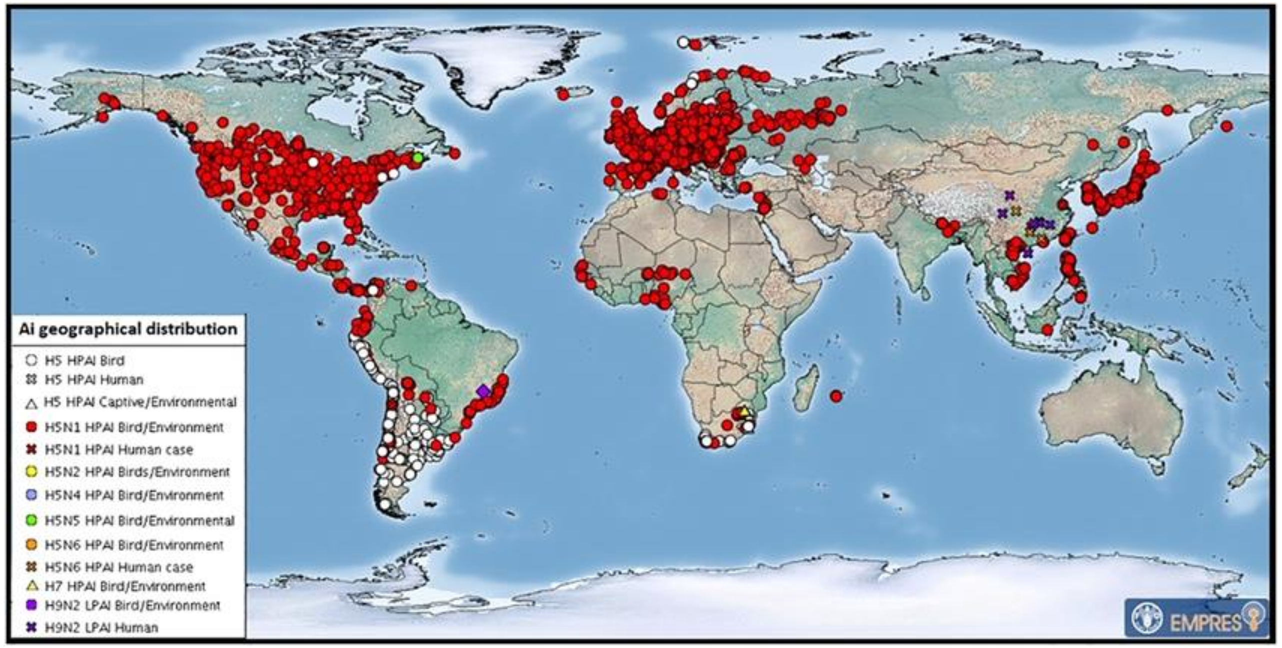
Studies Needed to Address Public Health Challenges of the 2009 H1N1 Influenza Pandemic: Insights from Modeling

Maria D. Van Kerkhove[1*], Tommi Asikainen[2], Niels G. Becker[3], Steven Bjorge[4], Jean-Claude Desenclos[5], Thais dos Santos[4], Christophe Fraser[1], Gabriel M. Leung[6], Marc Lipsitch[7], Ira M. Longini, Jr.[8,9], Emma S. McBryde[10], Cathy E. Roth[4], David K. Shay[11], Derek J. Smith[12,13,14], Jacco Wallinga[15,16], Peter J. White[1,17], Neil M. Ferguson[1], Steven Riley[18], for the WHO Informal Network for Mathematical Modelling for Pandemic Influenza H1N1 2009 (Working Group on Data Needs)

1 MRC Centre for Outbreak Analysis and Modelling, Imperial College London, United Kingdom, 2 European Centre for Disease Prevention and Control, 3 National Centre for Epidemiology and Population Health, The Australian National University, Canberra, Australia, 4 World Health Organization, 5 Institut de Veille Sanitaire, Saint Maurice, France, 6 Food and Health Bureau, Government of Hong Kong SAR, Hong Kong SAR, 7 Center for Communicable Disease Dynamics and Department of Epidemiology, Harvard School of Public Health, Boston, Massachusetts, United States of America, 8 Center for Statistics and Quantitative Infectious Disease (CSQUID), Vaccine and Infectious Diseases Institute, Hutchinson Research Center, Seattle, Washington, United States of America, 9 Department of Biostatistics, University of Washington, School of Public Health, Seattle, Washington, United States of America, 10 Victorian Infectious Diseases Service, Royal Melbourne Hospital, Melbourne, Victoria, Australia, 11 Influenza Division, US Centers for Disease Control and Prevention, Atlanta, Georgia, United States of America, 12 Department of Zoology, University of Cambridge, Cambridge, United Kingdom, 13 Erasmus Medical Center, Department of Virology, Rotterdam, The Netherlands, 14 Fogarty International Center, National Institutes of Health, Bethesda, Maryland, United States of America, 15 National Institute of Public Health and the Environment (RIVM), Centre for Infectious Disease Control, Bilthoven, The Netherlands, 16 University Medical Center Utrecht, Division Julius Center for Health Sciences and Primary Care, Utrecht, The Netherlands, 17 Modelling and Economics Unit, Health Protection Agency Centre for Infections, London, United Kingdom, 18 School of Public Health and Department of Community Medicine, The

What’s changed since 2006

- Global spread of H5N1
- Greater avian species range
- Reduced severity of human cases
- 2009 H1N1:
  - Limited use of NPIs
  - Limited use of AVs
  - Limited testing
  - Low Severity
- COVID-19:
  - Use of NPIs for suppression
  - Widespread testing (in HICs)
  - Rapid vaccine production
  - Rapid viral evolution



Strategic policy goals and drivers

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- Likely to be a perceived tension between twin goals of saving lives and minimising socioeconomic disruption
- Decisions will be driven by:
  - Severity (IFR) and predicted healthcare demand
  - How long NPIs might need to be in place (time to vaccination)
  - Politics
- COVID: keeping infection incidence low minimised health impacts at no additional economic cost
- But a politically challenging strategy in many contexts

Early questions/data needs

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- What is the true scale of the epidemic?
  - Case ascertainment, serology, testing capacity,…
- How fast is it spreading?
  - Doubling time, R_0, *Tg*
- How much of a threat does it pose?
  - CFR, HFR, IFR – by age and risk group
- What can we do?
  - Likely impact of mitigation measures

Need to be prepared for estimates to be uncertain, and for parameters to change (viral evolution)

Decision-making under uncertainty/change

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- UK 2020 response rooted in earlier crises – too much focus on one “reasonable worst case” scenario
- Key issues: decision-making under uncertainty, time horizon for costs/benefits, trust in counterfactual modelling
- In future:
  - need to plan for a range of scenarios
  - generate policy playbooks for each
  - evaluate the costs of both inaction and action
  - use accumulating data to narrow down the set of compatible scenarios

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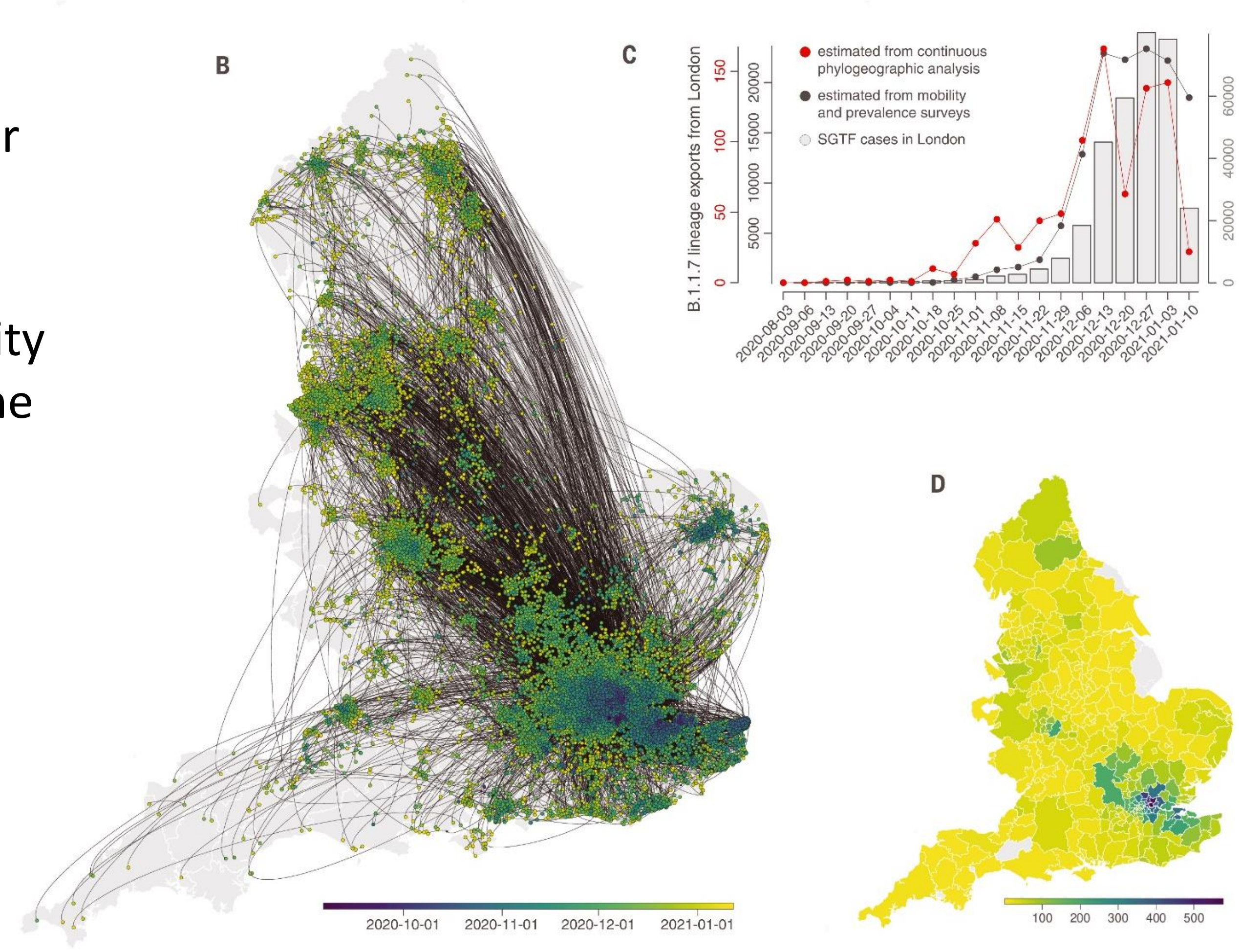
Research challenges for modelling

1. Forecasting – lots of progress on short-medium term, but quantitative accuracy rapidly fell off
2. Limited use of agent-based models
3. Fitting spatiotemporal models (easy to fit space or time, not both) – models typically represented spatial heterogeneity as disconnected areas
4. Curse of dimensionality meant social heterogeneity (beyond age) rarely included – including by income group, ethnicity etc…
5. Most current models underestimate heterogeneity/over-dispersion
6. Integrating large numbers of data sources into models (including sequence data)
7. Estimating/disentangling effects of different NPIs
8. Adding dynamical representations of behaviour, economics into epidemic models



Kraemer et al., Science, 2021

Interdisciplinary challenges

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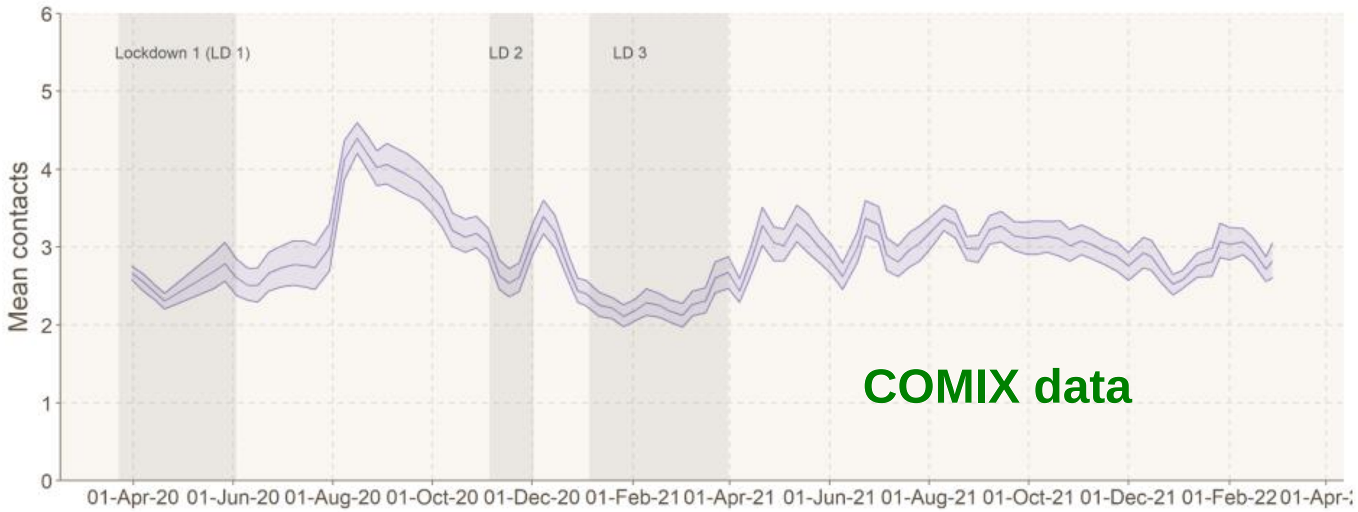
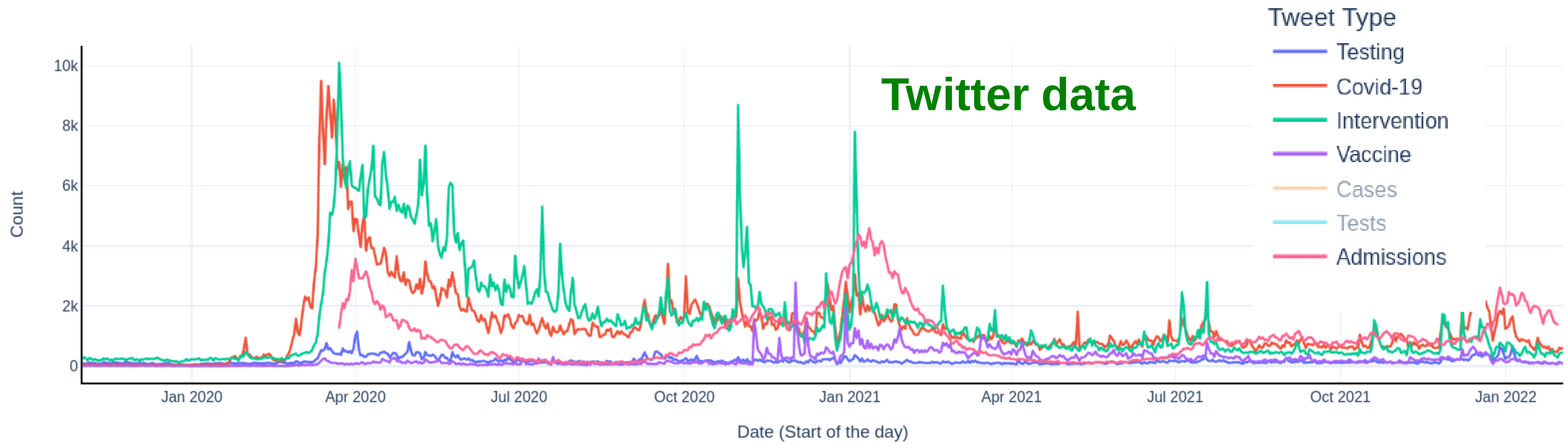
- Optimising measurement of behaviours relevant to transmission (e.g. COMIX)
- Validating proxy data sources – Google mobility, social media etc
- Mechanistic behavioural modelling – responses to mandatory/voluntary measures, risk avoidance, vaccination
- What measures were most effective, and what messaging?
- Role of social heterogeneity (income, ethnicity, politics, social networks/cliques)
- Minimising economic impacts while controlling transmission





Last thoughts

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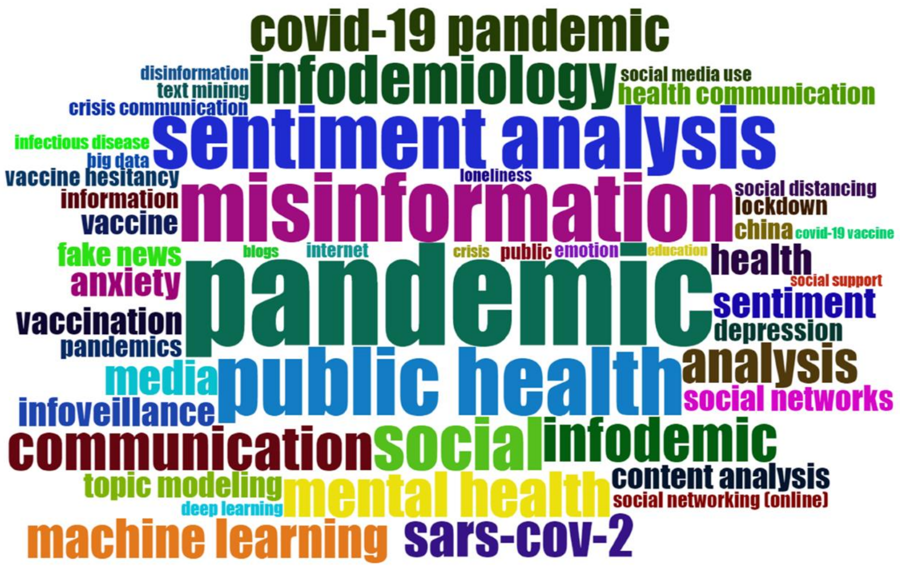
- COVID led to a paradigm shift in pandemic response: suppression policies, testing, accelerated vaccine production
- Still a lot of research to do comparing countries' COVID experience – some did much better than others
- Need innovation in transmission models: haven't evolved much in 20 years
- Given its role in informing policy, need to expect and prepare for modelling being emmeshed in politics
- Data-sharing can't be relied upon – intrinsically political, and requires incentives
- Need to build global capacity, especially in LMICs – all countries used modelling in 2020, but major HIC centres had limited capacity
- Better pre-packaged software tools will help, but skilled and experienced analysts still essential



Michailidis et al., Information, 2022