When will computational epidemiologists be replaced by AI?
Planes, trains and autodidacts
COMPLEXITY
THE EMERGING SCIENCE AT THE EDGE OF ORDER AND CHAOS

M. MITCHELL WALDROP
HIV-1 Dynamics in Vivo: Virion Clearance Rate, Infected Cell Life-Span, and Viral Generation Time

Alan S. Perelson, Avidan U. Neumann, Martin Markowitz, John M. Leonard, David D. Ho*

A new mathematical model was used to analyze a detailed set of human immunodeficiency virus–type 1 (HIV-1) viral load data collected from five infected individuals after the administration of a potent inhibitor of HIV-1 protease. Productively infected cells were estimated to have, on average, a life-span of 2.2 days (half-life $t_{1/2} = 1.6$ days), and plasma virions were estimated to have a mean life-span of 0.3 days ($t_{1/2} = 0.24$ days). The estimated average total HIV-1 production was $10.3 \times 10^9$ virions per day, which is substantially greater than previous minimum estimates. The results also suggest that the
Natural History of HIV Infection

Primary infection
- Possible acute HIV syndrome
- Wide dissemination of virus
- Seeding of lymphoid organs

Clinical latency

Opportunistic diseases

Constitutional symptoms

Death

CD4+ T Cells/mm³

Weeks

Years

Plasma Viremia Titre

Try math epidemiology!

Barrier to entry low (no PhD, unlike econ)

Potential for major impact

Reusable physics skills!
From enthusiasm to emergency
Lord Robert May & Sir Roy Anderson
Epidemiological patterns

Roy M. Anderson
Parasite Epidemiology
Biology Department

Epidemiological data accumulating, but

Populace
Roy M. Anderson
Zoology Department and C
Robert M. May
Biology Department, Prince

If the host population assumed, a wider part of a two-part experiments, and a second part of the indirectly transmitted

Any contemporary ecologist devoted to predator-prey, embraces field and labor mathematical models, a prey and predator population.

In natural community evidence suggests that viruses, bacteria, protozoa, likely to play a part analog of predators or resource plant and animal population. Park's experiments in drastically reduced the Tribolium castaneum, and outcome of its competitive studies of the way the entomopathogen influences the insect Hypholoma mycetosum. The importance of infectious instabilities of wild mammal such factor in bird populations. Sheep in North America. Infection by the lungworm which then predisposes a similar

Incubation and
Most epidemiological uniform level of an incubation period onset of AIDS-1. This interval means that all cases and cohort seroconversion is k-fusion associated infection periods in activity, or indeed recent analysis of diagnosis of AIDS incubation period older than 12 yr (observation intervals which after infection, p(t) = \(1 - e^{-at}\) and a and c are constants). In

The epidermis of the viral aetiological agent of SARS in China at the end of 2003 (Paterson 2004), following the epidemic earlier in the year affecting many countries, rang alarm bells in the WHO and elsewhere. Thankfully, the epidermis of the viral aetiological agent of SARS in China at the end of 2003 (Paterson 2004), following the epidemic earlier in the year affecting many countries, rang alarm bells in the WHO and elsewhere. Thankfully, the

Ebola Virus Disease in West Africa — The First 9 Months of the Epidemic and Forward Projections

WHO Ebola Response Team

ABSTRACT

BACKGROUND
On March 23, 2014, the World Health Organization (WHO) was notified of an outbreak of the disease (EVD) in Guinea. On August 8, the WHO declared the epidemic to be a “public health emergency of international concern.”

METHODS

By September 14, 2014, a total of 4507 probable and confirmed cases, including 2296 deaths from EVD (Zaire species) had been reported from five countries in West Africa — Guinea, Liberia, Nigeria, Senegal, and Sierra Leone. We analyzed a detailed subset of data on 3343 confirmed and 667 probable Ebola cases collected in Guinea, Liberia, Nigeria, and Sierra Leone as of September 14.

devastation earlier in 2003. A clear priority is further surveillance of animals in settings where the human virus spread extensively so as to better understand the origins of the epidemic in humans and the role of animal reservoirs.
Host population
The simple SIR epidemic model

\[ S \quad I \quad R \]

Susceptible

Infected

Recovered
The simple SIR epidemic model

\[ S \xrightarrow{\lambda} I \xrightarrow{\frac{1}{d}} R \]

\( \lambda = \) force of infection

\( d = \) duration of infectiousness
2009: H1N1 influenza pandemic
Asian Lineage Avian Influenza A (H7N9) Virus

Background

Human infections with an Asian lineage avian influenza A (H7N9) virus ("Asian H7N9") were first reported in China in March 2013. Annual epidemics of sporadic human infections with Asian H7N9 viruses in China have been reported since that time. China is currently experiencing its 5th epidemic of Asian H7N9 human infections. This is the largest annual epidemic to date. As of September 13, 2017, the World Health Organization (WHO) has reported 764 human infections with Asian H7N9 virus during the 5th epidemic, making the largest epidemic to date. This brings the total cumulative number of human infections with Asian lineage H7N9 reported by WHO to 1562. Additional infections have been reported, but not yet publicly announced by WHO. During epidemics one through four, about 40 percent of people confirmed with Asian H7N9 virus infection died.
Middle East Respiratory Syndrome (MERS)

Middle East Respiratory Syndrome (MERS) is a viral respiratory illness that was recently recognized in humans. It was first reported in Saudi Arabia in 2012 and has since spread to several other countries, including the United States. Most people identified as infected with MERS-CoV developed severe acute respiratory illness, including fever, cough, and shortness of breath. Many of them have died.

ABOUT MERS
Information about MERS including symptoms and complications, how it spreads, prevention and treatment...

PEOPLE WHO MAY BE AT INCREASED RISK FOR MERS
Information for travelers from the Arabian Peninsula, contacts of ill travelers from this area, contacts of a confirmed case of MERS, healthcare personnel not using infection-control precautions, and people with exposure to camels...

Countries with Lab-Confirmed MERS Cases
Countries in or near the Arabian Peninsula with MERS cases: Bahrain, Iran, Jordan, Kuwait, Lebanon, Oman, Qatar, Saudi Arabia, United Arab Emirates (UAE), and Yemen.
Infectious Disease Modeling Methods as Tools for Informing Response to Novel Influenza Viruses of Unknown Pandemic Potential

Manoj Gambhir, 1,2,5,8 Catherine Bozio, 5,6 Justin J. O'Hagan, 2,5,8 Amra Uzicanin, 5,8 Lucinda E. Johnson, 5,8 Matthew Biggerstaff, 5,8 and David L. Swerdlow 7

1Epidemiological Modelling Unit, Department of Epidemiology and Preventive Medicine, Monash University, Melbourne, Australia; 2Modeling Unit, National Center for Immunization and Respiratory Diseases (NCIRD), Centers for Disease Control and Prevention (CDC); 3HRG Inc; 4Graduate Program in Epidemiology and Molecules to Mankind, Laney Graduate School, Emory University; 5Division of Global Migration and Quarantine, National Center for Emerging and Zoonotic Infectious Diseases; 6Influenza Division, and 7Modeling Unit and Office of the Director, NCIRD, CDC, Atlanta, Georgia

The rising importance of infectious disease modeling makes this an appropriate time for a guide for public health practitioners tasked with preparing for, and responding to, an influenza pandemic. We list several questions that public health practitioners commonly ask about pandemic influenza and match these with analytical methods, giving details on when during a pandemic the methods can be used, how long it might take to implement them, and what data are required. Although software to perform these tasks is available, care needs to be taken to understand: (1) the type of data needed, (2) the implementation of the methods, and (3) the interpretation of results in terms of model uncertainty and sensitivity. Public health leaders can use this article to evaluate the modeling literature, determine which methods can provide appropriate evidence for decision-making, and to help them request modeling work from in-house teams or academic groups.

The 2009 influenza A (H1N1) pandemic was one of the most closely tracked and studied epidemics in history. Traditional epidemiological methods, such as outbreak investigations and laboratory-based surveillance, were rapidly used to inform policy decisions [1–4]. These methods were enhanced by newer computational techniques such as bioinformatics and digital surveillance methods [5]. Simultaneously, substantial contributions

During an outbreak of influenza with pandemic potential, public health leaders ask a range of questions to inform situational awareness, help assess severity [11] and guide decisions that aim to control the spread and impact of disease. Critical questions include:

• What is the case-fatality ratio?
• What is the case-hospitalization ratio?
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<th>Questions</th>
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<td>Age-structured SEIR model</td>
<td>A compartmental model in which hosts are grouped into population compartments composed of their age-group and their infection status, e.g., an SEIR model. These models can be deterministic or stochastic, and the transitions between infection states are governed by contact and recovery rates [10, 12].</td>
<td>Case incidence stratified by age, contact matrix by age, cross-sectional serosurveys, physician visit/hospitalization rates to calculate symptomatic proportion/disease reporting rate/proportion immune, severity of infection across risk groups, initial number of infected individuals (or date on which the first infected individual was introduced into the population).</td>
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<td>Antigenic cartography</td>
<td>A method for quantifying and visualizing the antigenic evolution of the influenza virus according to antigenic distances [13].</td>
<td>Influenza virus genetic sequences, antigenic distances between subtypes (using e.g., hemagglutination inhibition assay).</td>
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<td>Antigenic distance</td>
<td>Antigenic distances of proposed vaccine strains from predicted dominant circulating strain(s) are correlated with prior years’ vaccine effectiveness estimates [14].</td>
<td>Hemagglutination inhibition assay distances of potential circulating strain(s) and record of vaccine effectiveness from prior years with amino acid sequences of past vaccine strains and dominant seasonal strains</td>
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<td>Bayesian evidence synthesis</td>
<td>Prior knowledge and distinct surveillance data sources are combined to estimate epidemiologic quantities (e.g., number infected, case-hospitalization rate) [9].</td>
<td>Repeated cross-sectional serosurveys, numbers and dates of onset of confirmed cases, symptomatic cases, hospitalizations, intensive care admissions, dates of severe outcomes.</td>
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<td>Branching process analysis</td>
<td>Branching process theory is used to estimate the number of offspring of primary cases [15]. The generation time distribution between households and incidence of infection of households [16] is estimated.</td>
<td>Contact tracing data, surveillance datasets, R0 population distribution (i.e., the probability associated with an individual in the population generating R0 secondary cases at the start of the epidemic).</td>
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<td>Case renewal process</td>
<td>Initial cases are modeled as a renewal process, which is a generalization of the Poisson process in which the time between cases is random and arbitrary, but independent and identically distributed [8, 17].</td>
<td>Case incidence time series (infection/hospitalization/death).</td>
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<td>Chain binomial model</td>
<td>Initial cases are modeled as a discrete time chain of infections from one individual to another with probability of infection, or escape from infection, calculated using the binomial probability distribution [18].</td>
<td>Case incidence time series (infection/hospitalization/death).</td>
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<td>Coalescent analysis</td>
<td>A Bayesian phylogenetic “coalescent” model is fitted to genetic sequence data obtained from isolates sampled from the infected population [19]. Growth rates of the epidemic are inferred.</td>
<td>Influenza genetic sequences and sampling times.</td>
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Key data for outbreak evaluation: building on the Ebola experience

Anne Cori¹, Christl A. Donnelly¹, Ilaria Dorigatti¹, Neil M. Ferguson¹, Christophe Fraser², Tini Garske¹, Thibaut Jombart¹, Gemma Nedjati-Gilani¹, Pierre Nouvellet¹, Steven Riley¹, Maria D. Van Kerkhove³, Harriet L. Mills¹,⁴,⁵,⁶ and Isobel M. Blake¹,⁷

¹Medical Research Council Centre for Outbreak Analysis and Modelling, Department of Infectious Disease Epidemiology, School of Public Health, Imperial College London, London W2 1PG, UK
²Oxford Big Data Institute, Li Ka Shing Centre for Health Information and Discovery, Nuffield Department of Medicine, University of Oxford, Oxford OX3 7FZ, UK
³Centre for Global Health, Institut Pasteur, 25-28 Rue du Dr Roux, 75015 Paris, France
⁴MRC Integrative Epidemiology Unit, School of Social and Community Medicine, University of Bristol, Bristol BS8 2BN, UK
⁵School of Veterinary Sciences, University of Bristol, Bristol BS40 5DU, UK
⁶AC, 0000-0002-8443-9162; CAD, 0000-0002-0195-2463; TG, 0000-0002-8952-4710; GN G, 0000-0001-5723-5028; IMB, 0000-0002-3977-1318


Subject Areas:
health and disease and epidemiology

Following the detection of an infectious disease outbreak, rapid epidemiological assessment is critical for guiding an effective public health response. To understand the transmission dynamics and potential impact of an outbreak, several types of data are necessary. Here we build on experience gained in the West African Ebola epidemic and prior emerging infectious disease outbreaks to set out a checklist of data needed to: (1) quantify severity and transmissibility; (2) characterize heterogeneities in transmission and their determinants; and (3)
Schematic illustrating the data needed to answer questions at different stages of the epidemic to inform the response.

Where do the data come from?

- surveillance
- lab results
- case records
- contact tracing
- genetic studies
- census
- serology
- centralized systems

What is the likely public health impact of the outbreak?

- severity (CFR)
- transmission characteristics
- short-term projections
- long-term projections

How feasible is controlling the outbreak and what interventions would be appropriate?

- transmissibility
- transmission characteristics
- delays in distribution
- intervention effectiveness
- intervention impact

Are current interventions effective and could they be improved?

- aggregate case counts
- case line-list
- pairs infected/infected
- sequence data
- population sizes across demographics and space
- immunity levels
- health-care facilities
- intervention scale
- individual effectiveness of interventions

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Four key challenges in infectious disease modelling using data from multiple sources

Presanis a, Paul J. Birrell a, Gianpaolo Scalia Tomba c,

A B S T R A C T

Public health-related decision-making on policies aimed at controlling epidemics is increasingly evidence-based, exploiting multiple sources of data. Policy makers rely on complex models that are required to be robust, realistically approximating epidemics and consistent with all relevant data. Meeting these requirements in a statistically rigorous and defendable manner poses a number of challenging problems. How to weight evidence from different datasets and handle dependence between them, efficiently estimate and critically assess complex models are key challenges that we expound in this paper, using examples from influenza modelling.

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Mathematical models: A key tool for outbreak response

...information. These models can clarify how the disease is spreading and provide timely guidance to policymakers. However, the use of models in public health often meets resistance (1), from doubts in peer review about the utility of such analyses to public skepticism that models can contribute when the means to control an epidemic are already known (2). Even when they are discussed in a positive light, models are often portrayed as arcane and largely inaccessible thought experiments (3). However, the role of models is crucial: they can be used to quantify the effect of mitigation efforts, provide guidance...
WARNING:
WE ARE NOT READY FOR THE NEXT PANDEMIC

SCIENCE KNOWS HOW TO FIGHT AN OUTBREAK—BUT POLICY STILL GETS IN THE WAY
BY BRYAN WALSH

HOW TO KEEP THE WORLD SAFE
BY BILL GATES
However, this isn’t working

At least not on a reasonable timescale

Math epi has been around for 5 decades but it’s barely used in public health agencies, unless...
The sky is falling down

Ebola
Level 1
The highest level of response reserved for critical emergencies. CDC assigns the largest number of staff possible to work 24/7 on the response. To date, there have been three Level 1 responses: Ebola outbreak (2014), H1N1 influenza outbreak (2009) and Hurricane Katrina (2005).

Level 2
The CDC experts in the particular disease lead the response with a large number of other staff from the program area. A large number of staff from CDC’s Emergency Operations Center may assist with the response.

Level 3
The CDC experts in the particular disease lead the response with some of their own staff. Some staff from CDC’s Emergency Operations Center may assist in the response. CDC decides when a different level of response is needed.
CDC Emergency Response Activation Levels

Level 1

The highest level of response reserved for critical emergencies. CDC assigns the largest number of staff possible to work 24/7 on the response. To date, there have been three Level 1 responses: Ebola outbreak (2014), H1N1 influenza outbreak (2009) and Hurricane Katrina (2005).

Level 2
CDC leaders integral to the Ebola response, including epidemiologists, laboratorians, logistics, and more, assemble in agency’s command center to discuss next steps in directing the response at CDC Emergency Operations Center in Atlanta, August 8. Spencer Lowell for TIME magazine
Questions from leadership

How many cases might there be?

When will the epidemic end?

What will it take to end the epidemic?
Ebola estimate

Without intervention, the total number of Ebola cases in the West African countries of Liberia and Sierra Leone could top 1 million by January.

- **1.2** – CUMULATIVE CASES, IN MILLIONS (Liberia, Sierra Leone)
  - **Without intervention**
  - **0.8** – With proper intervention (70% of cases confined to treatment centers)

**SOURCE:** Centers for Disease Control and Prevention

**PATTerson CLARK/ THE WASHINGTON POST**
Worst-Case Scenario Can Still Be Avoided

By DENISE GRADY

The other day, a World Health Organization report on the Ebola outbreak in West Africa was released. It estimated that the number of cases could reach 25,000 cases by the end of September, with a possible 600,000 cases by the end of the year. However, the report also estimated that it is possible to prevent the outbreak from escalating to that level if effective measures are taken immediately.

In the worst-case scenario, the number of cases could reach 1.4 million within four months, according to the report. This would be a significant increase from the current number of cases, which is estimated to be around 1,000.

The report also stated that the current response to the outbreak is not enough to contain the spread of the virus. It emphasized the need for increased resources and coordination among the affected countries.

A Red Cross team removed the body of a woman believed to have died of Ebola in Monrovia, Liberia, last week. Officials urge caution in handling victims' bodies.

He added, “If the case comes to pass, with, say, 700,000 cases by January, the epidemic will quickly overwhelm the capabilities that the U.S. plans to send.”

The W.H.O. report also raised the possibility that hospitals would be ready or who would staff them.

Dr. Frieden said the Defense Department had already delivered parts of a 25-bed unit that would soon be set up to treat health workers who become infected, a safety measure he said was important to help encourage health professionals to volunteer. He said that more aid groups

“Where are they going to go?” he said.

Though providing home-care kits may seem like a pragmatic approach, some public health authorities said they found no substitute for beds in isolation or containment wards.

But Dr. Frieden said that home care kits had been used to help stamp out smallpox in Africa in the 1960s. The containers were often
Job creation/destruction
So, why is it so hard to get traction?

Policymakers don’t trust the model(s), they trust the person presenting the model.

They don’t trust single models, they need ensembles.

They’re comfortable with statistics but not mechanistic modelling.
Multi-model ensembles
Neglected Tropical Disease Modelling Consortium

- **9 universities**: Warwick, Yale, Erasmus, Notre Dame, Imperial College London, Case Western Reserve, Monash, London and Liverpool Schools of Hygiene

- **9 diseases** incl: schistosomiasis, lymphatic filariasis, trachoma, soil transmitted helminths
2 questions from BMGF

Are we on target for the 2020 goals with current strategies?
If not, what other strategies will be required, and where?
Probabilistic forecasts of trachoma transmission at the district level: A statistical model comparison

Amy Pinsent\textsuperscript{a, *}, Fengchen Liu\textsuperscript{b}, Michael Deiner\textsuperscript{b, e}, Paul Emerson\textsuperscript{c, d}, Ana Bhaktiari\textsuperscript{c}, Travis C. Porco\textsuperscript{b, e, f}, Thomas Lietman\textsuperscript{b, e, f, g}, Manoj Gambhir\textsuperscript{a}

\textsuperscript{a} Department of Public Health and Preventative Medicine, Monash University, Melbourne, Australia
\textsuperscript{b} F.J. Proctor Foundation, University of California San Francisco, San Francisco, CA, USA
\textsuperscript{c} International Trachoma Initiative, Atlanta, GA, USA
\textsuperscript{d} School of Public Health, Emory University, Atlanta, GA, USA
\textsuperscript{e} Department of Ophthalmology, University of California San Francisco, San Francisco, CA, USA
\textsuperscript{f} Department of Epidemiology and Biostatistics, University of California San Francisco, San Francisco, CA, USA
\textsuperscript{g} Global Health Sciences, University of California San Francisco, San Francisco, CA, USA

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The World Health Organization and its partners are aiming to eliminate trachoma as a public health problem by 2020. In this study, we compare forecasts of TF prevalence in 2011 for 7 different statistical and mechanistic models across 9 de-identified trachoma endemic districts, representing 4 unique trachoma endemic countries. We forecast TF prevalence between 1–6 years ahead in time and compare the 7 different models to the observed 2011 data using a log-likelihood score. An SIS model, including a district-specific random effect for the district-specific transmission coefficient, had the highest log-likelihood score across all 9 districts and was therefore the best performing model. While overall the deterministic transmission model was the least well-performing model, although it did comparably well to the other
COORDINATING RESEARCH ACTIVITIES IN MATHEMATICAL MODELLING

HIV Modelling Consortium

The HIV Modelling Consortium aims to help improve scientific support for decision making by co-coordinating a wide range of research activities in mathematically modelling the HIV epidemic.
HIV Treatment as Prevention: Systematic Comparison of Mathematical Models of the Potential Impact of Antiretroviral Therapy

Jeffrey W. Eaton, Leigh F. Johnson, Anna Bershtein, David E. Bloom, Salal Humair, Daniel J. Klein, Brian G. Williams

1 Department of Infectious Disease Epidemiology, Imperial College London, London, United Kingdom
2 Harvard School of Public Health, Boston, Massachusetts, United States
3 University of KwaZulu-Natal, Durban, South Africa
4 Mount Sinai School of Medicine, New York, New York, United States
5 Medical Research Council, London, United Kingdom
6 London School of Hygiene & Tropical Medicine, London, United Kingdom
7 Imperial College London, London, United Kingdom
8 Department of Epidemiology, London School of Hygiene & Tropical Medicine, London, United Kingdom
9 School of Policy Sciences and Health, University of the West of England, Bristol, United Kingdom
10 Institute for Global Health, University College London, London, United Kingdom
11 School of Science and Engineering, Lahore University of Management Sciences, Lahore, Pakistan
12 Future Institute, Glastonbury, Connecticut, United States

Health benefits, costs, and cost-effectiveness of earlier eligibility for adult antiretroviral therapy and expanded treatment coverage: a combined analysis of 12 mathematical models


Abstract

Background: Many mathematical models have been developed to explore the potential impact of future health strategies on new HIV infections. Comparing results from these models can be difficult because they are built on slightly different assumptions and have been used to inform policy through various mathematical models simulating the same target population. We aimed to systematically compare the predictions of existing models related to the epidemiological impact of expanded antiretroviral therapy (ART) coverage.

Methods and Findings: Twelve independent models were included in this study. Twelve models were developed using different methods and were used to explore the potential impact of antiretroviral therapy on new HIV infections. The models were developed using different methods and were used to explore the potential impact of antiretroviral therapy on new HIV infections. The models were developed using different methods and were used to explore the potential impact of antiretroviral therapy on new HIV infections. The models were developed using different methods and were used to explore the potential impact of antiretroviral therapy on new HIV infections. The models were developed using different methods and were used to explore the potential impact of antiretroviral therapy on new HIV infections. The models were developed using different methods and were used to explore the potential impact of antiretroviral therapy on new HIV infections.

Summary

Background: New WHO guidelines recommend the initiation of antiretroviral therapy for HIV-positive adults with CD4 counts of 500 cells per µL or less, a higher threshold than was previously recommended. Country decision makers have to decide whether to further expand eligibility for antiretroviral therapy accordingly. We aimed to assess the potential health benefits, costs, and cost-effectiveness of various eligibility criteria for adult antiretroviral therapy and expanded treatment coverage.

Methods: We used several independent mathematical models in four settings—South Africa, generalized epidemic models, moderate antiretroviral therapy coverage, Zambia (generalized epidemic, high antiretroviral therapy coverage), India (generalized epidemic, moderate antiretroviral therapy coverage), and Vietnam (generalized epidemic, low antiretroviral therapy coverage)—to assess the potential health benefits, costs, and cost-effectiveness of various eligibility criteria for adult antiretroviral therapy under scenarios of existing and expanded treatment coverage. Results were projected over 20 years. Analyses assessed the extent of eligibility to include individuals with CD4 counts of 500 cells per µL or less, or all HIV-positive adults, compared with the previous (2010) recommendation of initiating therapy with CD4 counts of 350 cells per µL or less. We assessed costs from a health-system perspective, and calculated the incremental cost (in USS per disability-adjusted life-year (DALY) averted to compare competing strategies. Strategies were regarded very cost effective if the cost per DALY averted was less than the country’s 2012 per capita gross domestic product (GDP, South Africa: $30,409; Zambia: $1,425; India: $1,489; Vietnam: $1,407) and cost effective if the cost per DALY averted was less than three times the per capita GDP.

Findings: In South Africa, the per capita DALY averted of expanded eligibility for antiretroviral therapy to adult patients with CD4 counts of 500 cells per µL or less ranged from $237 to $1,691 per DALY averted compared with 2010 guidelines. In Zambia, expansion of eligibility to adults with a CD4 count threshold of 500 cells per µL resulted in improved health outcomes while reducing costs (ie, dominating the previous guidelines) to $749 per DALY averted. In both countries results were similar for expansion of eligibility to all HIV-positive adults, and when substantially expanded treatment coverage was assumed. Expansion of treatment coverage in the general population was also cost-effective. In
TB diagnosis

The practical process of preparing sputum samples for TB diagnosis.

Mission Statement

TB MAC aims to increase the effectiveness and efficiency of TB control policy and practice at global and country level.

We will do this by:

- building stronger and more effective links between decision makers, modellers and practitioners.
Modelling to guide the effective use of diagnostics in global health strategies
Improved training to data
The transmission dynamics of human immunodeficiency virus (HIV)

By R. M. May,¹ F.R.S., and R. M. Anderson,² F.R.S.

¹ Department of Biology, Princeton University, Princeton, N.J. 08544, U.S.A.
² Department of Pure and Applied Biology, Imperial College, London University, London SW7 2BB, U.K.
Epidemiology, transmission dynamics and control of SARS: the 2002–2003 epidemic

Roy M. Anderson¹*, Christophe Fraser¹, Azra C. Ghani¹, Christl A. Donnelly¹,
Steven Riley¹, Neil M. Ferguson¹, Gabriel M. Leung², T. H. Lam²
and Anthony J. Hedley²

¹Department of Infectious Disease Epidemiology, Faculty of Medicine, Imperial College London, St Mary’s Campus,
Norfolk Place, London W2 1PG, UK
²21 Sassoon Road, Faculty of Medicine Building, University of Hong Kong, Pokfulam, Hong Kong, China

Figure 12. The SARS epidemic in Hong Kong and the fit of a multi-compartment meta-population stochastic model (from Riley et al. 2003). The dots are reported SARS cases and the solid line is the best fit model. The vertical grey bars denote 95% prediction intervals.
Ebola Virus Disease in West Africa — The First 9 Months of the Epidemic and Forward Projections

WHO Ebola Response Team*

ABSTRACT

BACKGROUND
On March 23, 2014, the World Health Organization (WHO) was notified of an outbreak of Ebola virus disease (EVD) in Guinea. On August 8, the WHO declared the epidemic to be a “public health emergency of international concern.”

METHODS
By September 14, 2014, a total of 4507 probable and confirmed cases, including 2296 deaths from EVD (Zaire species) had been reported from five countries in West Africa — Guinea, Liberia, Nigeria, Senegal, and Sierra Leone. We analyzed a detailed subset of data on 3343 confirmed and 667 probable Ebola cases collected in Guinea, Liberia, Nigeria, and Sierra Leone as of September 14.
Figure 4. Observed and Projected Case Incidence.
Observed and projected weekly case incidence in Guinea (Panel A), Liberia (Panel B), and Sierra Leone (Panel C) are shown on linear (upper panels) and logarithmic (lower panels) scales.
Figure 1. Case Reproduction Numbers and Weekly Incidence in Guinea, Liberia, and Sierra Leone.

Shown are the estimated case reproduction number ($R_t$) over time (upper panels) and the observed and projected weekly incidence (lower panels) of confirmed and probable cases of Ebola virus disease (EVD), according to the date of symptom onset, from the week beginning June 30, 2014, until the week beginning January 12, 2015, on the basis of data reported through December 7 for Guinea and November 30 for Liberia and Sierra Leone. The projections shown in the lower panels were generated from $R_t$ estimates derived from data on case incidence (daily situation reports) for the 7 weeks through December 7 for Guinea and November 30 for Liberia and Sierra Leone (the time period delineated by the vertical dotted lines).
Epidemic Prediction Initiative BETA
Moving forecasting from research to decisions.

EPI aims to improve the science and usability of epidemic forecasts by facilitating open forecasting projects with specific public health objectives. Links to current and past projects can be found below. Learn more about EPI here.

CURRENT PROJECTS

State FluSight 2017-18
Seasonal Influenza Forecasting at the US State Level

FluSight 2017-18
Seasonal Influenza Forecasting

Influenza Hospitalizations 2017-18
Forecasting laboratory confirmed influenza hospitalizations
Automation
So, what does a mathematical epidemiologist do?

✓ Devises (and performs) data collection
✓ Cleans the data
✓ Selects appropriate mathematical models
✓ Trains those models on the data
✓ Forecasts/Nowcasts/Scenario Analyses
✓ Communicates results to leadership
Which of these can be automated?

- Devises (and performs) data collection
- Cleans the data
- Selects appropriate mathematical models
- Trains those models on the data
- Forecasts/Nowcasts/Scenario Analyses
- Communicates results to leadership
However, things are changing

- New data types
- New mathematical models
- New training methods
- New visualisation of data/results

So, the AI epidemiologist would need to be upgraded frequently
In addition...

- Open sourcing code and data (when possible): reproducibility
- Breakthrough in model training needed
- ML methods are flexible to adding in new data types
- ML models can be reusable: ‘transfer learning’
Let’s get started,
Select a project or create a new one
Workspace

\[ C'_{k} = \frac{\sum_{i=1}^{T-h} \left( R(T + h) - F(T + h) \right)^2}{\sum_{j=1}^{T} \left( R(T + h) - F \right)^2} \]

Change
```
Click variable to change
```

to
```
Enter new value
```

Activity Log

Calibrate Model

- **Influence**

*TIME, IN WEEKS RELATIVE TO OCTOBER 3, 2015*
Thank you
San Francisco health authorities were investigating a whooping cough epidemic in the city on Wednesday, the latest sign of a nationwide outbreak that has come under investigation by federal health authorities.

The announcement by city health authorities comes as the state of California has seen reports of pertussis, which is often mistaken for the milder form of whooping cough, and which can be more severe in children.

The state's largest city, San Francisco, has had 910 cases of whooping cough in the city as of November 21, 2012, according to the San Francisco Department of Public Health. The city's public health department said it was the highest number of cases in the city in more than a half-century.

“Whooping cough is highly contagious and can cause severe illness, particularly in children under the age of two,” said Dr. Philovia L. Almoguera, San Francisco's director of public health.

Whooping cough, also known as pertussis, is a highly contagious respiratory illness that can cause severe and even fatal complications in young children. The illness is characterized by a hacking cough that can last for weeks or even months. It can be prevented with a series of vaccines, but a lack of vaccination among children has led to a rise in cases nationwide.

The illness is typically spread through droplets from coughing or sneezing, and can be prevented with a series of vaccines. The first round of shots is given at 2 months of age, with a second round at 4 months and a third at 6 months. A fourth shot is recommended for children at 12 months of age or older.

The rise in cases has been particularly concerning in California, where the state's public health department has seen a sharp increase in the number of cases this year. As of November 21, 2012, the state had reported 5,405 cases of pertussis, the highest number of cases in the state since 1959.

Cases of pertussis, also known as whooping cough, often decline in late fall into early winter. In Philadelphia, which recorded 50 cases for August - more typical of an entire year - infections plummeted last month. But there has been no major decrease statewide, Ostroff said.
How worried should we be about the whooping cough epidemic?

MARY-ROSE MACCOLL  The Australian  April 28, 2012  12:00AM

Newborn babies are most at risk of death from the disease.
Reported pertussis cases – 1922-2010

Number of cases

Year


SOURCE: CDC, National Notifiable Diseases Surveillance System and Supplemental Pertussis Surveillance System and 1922-1949, passive reports to the Public Health Service
Questions from leadership

Is the effectiveness and duration of protection of the new vaccine different to the old?
\[ S \xrightarrow{\lambda(t)} I_1 \xrightarrow{\tau} R \]

- **Loss of immunity**: \( \alpha \)
- **Force of infection**: \( \lambda(t) \)
- **Recovery from infection**: \( \tau \)
- **Recovery from reinfection**: \( \sigma \lambda(t) \)

Diagram:

- States: \( S, I_1, R, I_2 \)
- Transitions:
  - \( S \rightarrow I_1 \)
  - \( I_1 \rightarrow R \)
  - \( R \rightarrow I_2 \)

- Labels:
  - \( \alpha \): Loss of immunity
  - \( \lambda(t) \): Force of infection
  - \( \sigma \lambda(t) \): Force of reinfection
  - \( \tau \): Recovery from infection
Table 1. Descriptions of the nested models that were fitted to the NNDSS incidence data.

<table>
<thead>
<tr>
<th>Model</th>
<th>Description</th>
<th>DIC</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Protection duration of whole cell vaccine same as natural infection; aacellular vaccine same as whole-cell</td>
<td>-9720</td>
</tr>
<tr>
<td>2</td>
<td>Protection duration of whole cell vaccine same as natural infection; different efficacy for aacellular vaccine</td>
<td>-9570</td>
</tr>
<tr>
<td>3</td>
<td>Protection duration of whole cell vaccine same as natural infection; different protection duration for aacellular vaccine;</td>
<td>-9250</td>
</tr>
<tr>
<td>4</td>
<td>Protection duration of whole cell vaccine different from natural infection; aacellular vaccine same as whole-cell</td>
<td>-9800</td>
</tr>
<tr>
<td>5</td>
<td>Protection duration of whole cell vaccine same as natural infection; protection duration and efficacy different for aacellular vaccine</td>
<td>-8422</td>
</tr>
<tr>
<td>6</td>
<td>Whole cell vaccine protection duration different from natural infection; different efficacy for aacellular vaccine</td>
<td>-9183</td>
</tr>
<tr>
<td>7</td>
<td>Whole cell vaccine protection duration different from natural infection; different protection duration for aacellular vaccine</td>
<td>-9230</td>
</tr>
<tr>
<td>8</td>
<td>Whole cell vaccine protection duration different from natural infection; protection duration and efficacy different for aacellular vaccine</td>
<td>-8417</td>
</tr>
</tbody>
</table>

The mean posterior values of the Deviance Information Criterion (DIC) of the models are given in the rightmost column.

doi:10.1371/journal.pcbi.1004138.t001

http://journals.plos.org/ploscompbiol/article?id=info:doi/10.1371/journal.pcbi.1004138
Total incidence since vaccination began: model vs. data
Projecting forward in time
VE*coverage=10%
70%
90%
RESEARCH ARTICLE

A Change in Vaccine Efficacy and Duration of Protection Explains Recent Rises in Pertussis Incidence in the United States

Manoj Gambhir¹,²,³*, Thomas A. Clark⁴, Simon Cauchemez⁵,⁶, Sara Y. Tartof⁷, David L. Swerdlow²,⁸, Neil M. Ferguson⁵

1 Department of Epidemiology and Preventive Medicine, Monash University, Melbourne, Australia, 2 Modeling Unit, National Center for Immunization and Respiratory Diseases (NCIRD), Centers for Disease Control and Prevention (CDC), Atlanta, Georgia, United States of America, 3 IHRC, Inc., Atlanta, Georgia, United States of America, 4 Meningitis and Vaccine Preventable Diseases Branch, Division of Bacterial Diseases, NCIRD, CDC, Atlanta, Georgia, United States of America, 5 Medical Research Council Centre for Outbreak Analysis and Modelling, Imperial College London, London, United Kingdom, 6 Mathematical Modelling of Infectious Diseases Unit, Institut Pasteur, Paris, France, 7 Kaiser Permanente Southern California, Kaiser Permanente Research, Department of Research & Evaluation, Pasadena, California, United States of America, 8 Office of Science and Integrative Programs, NCIRD, CDC, Atlanta, Georgia, United States of America

* manoj.gambhir@monash.edu

OPEN ACCESS
http://journals.plos.org/ploscompbiol/article?id=info:doi/10.1371/journal.pcbi.1004138
Projects throughout CDC

**Pertussis** Explaining the recent upsurge in cases in 7-10 yos and rise in overall cases

**Ebola** 2014-2015 West African epidemic
Lessons
Modelling’s major contribution comes very early (when sit. awareness is poor)

Embed within a public health agency

Academic publication often isn’t useful during an emergency (but is afterward)
Thank you for your time!

Special thanks to:

David Swerdlow
Lyn Finelli
Carrie Reed
Matt Biggerstaff
Cristina Carias
Martin Meltzer
Rebekah Borse
Isaac Fung
Neil Ferguson
Simon Cauchemez
Christl Donnelly
Tom Clark
Ben Lopman
Amy Pinsent

+ many others
Figure: Temporal trends on Twitter and Google about Ebola and influenza (flu) before, during, and after Ebola cases in the USA, September to November, 2014

*Numbers are relative to the highest number of searches done on Google (for Ebola on Oct 16).
Table 2. Parameter estimates for the best-fitting model, Model 8 (models outlined in Table 1).

<table>
<thead>
<tr>
<th>Parameter description</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaccine efficacies &amp; waning</td>
<td></td>
</tr>
<tr>
<td>Whole-cell</td>
<td></td>
</tr>
<tr>
<td>Vaccine efficacy of 1st 3 doses/4th/5th dose</td>
<td>90% [87%, 94%]</td>
</tr>
<tr>
<td>Rate of loss of whole-cell vaccine immunity</td>
<td>$3 \times 10^{-5} \text{yr}^{-1}$ [2x10$^{-6}$, 2x10$^{-4}$] i.e. essentially lifelong</td>
</tr>
<tr>
<td>Acellular</td>
<td></td>
</tr>
<tr>
<td>Vaccine efficacy of 1st 3 doses/4th/5th dose</td>
<td>80% [78%,82%]</td>
</tr>
<tr>
<td>Rate of loss of acellular vaccine immunity</td>
<td>$0.018 \text{yr}^{-1}$ [0.015, 0.020] i.e. average of approx. 50 yrs protection</td>
</tr>
<tr>
<td>Tdap</td>
<td></td>
</tr>
<tr>
<td>Vaccine efficacy</td>
<td>As acellular</td>
</tr>
<tr>
<td>Epidemiological Parameters</td>
<td></td>
</tr>
<tr>
<td>Basic reproduction number, $R_0$</td>
<td>11.0 [9.9, 11.5]</td>
</tr>
<tr>
<td>Rate of loss of natural immunity</td>
<td>$3 \times 10^{-5} \text{yr}^{-1}$ [2x10$^{-6}$, 2x10$^{-4}$] i.e. essentially lifelong (as for whole-cell)</td>
</tr>
<tr>
<td>Relative susceptibility of individuals to subsequent infection (with reference to naïve individuals)</td>
<td>32% [29%, 35%]</td>
</tr>
<tr>
<td>Relative infectiousness of individuals with subsequent infection (with reference to primary-infected individuals)</td>
<td>17% [14%, 23%]</td>
</tr>
<tr>
<td>Year of reporting rate change</td>
<td>None</td>
</tr>
<tr>
<td>Mean reporting rate prior to change</td>
<td>6.0% [0.1%, 22%]</td>
</tr>
<tr>
<td>Mean reporting rate after change</td>
<td>n/a</td>
</tr>
</tbody>
</table>

doi:10.1371/journal.pcbi.1004138
http://journals.plos.org/ploscompbiol/article?id=info:doi/10.1371/journal.pcbi.1004138
Fig 3. Cross-sectional incidence of disease over age of population.

http://journals.plos.org/ploscompbiol/article?id=info:doi/10.1371/journal.pcbi.1004138
Disease modelers use math to try to provide a more precise picture of a certain situation or to predict how the situation will change, and have become critical in the world of infectious diseases. But the accuracy — or inaccuracy — of such models is increasingly a talking point.
Model equations

\[
\frac{dS}{dt} \quad \text{Susceptible}
\]

\[
\frac{dI}{dt} \quad \text{Infected}
\]

\[
\frac{dR}{dt} \quad \text{Recovered}
\]
Inflow & outflow

\[
\frac{dS}{dt} = -\beta S I \\
\frac{dI}{dt} = \beta S I - \frac{1}{\delta} I \\
\frac{dR}{dt} = \frac{1}{\delta} I
\]

- Susceptible
- Infected
- Recovered
As infecteds increase, *rate* increases
Assessing the International Spreading Risk Associated with the 2014 West African Ebola Outbreak

September 2, 2014 • Research

This article is either a revised version or has previous revisions
Edition 1 - September 2, 2014

Authors

Marcelo F. C. Gomes, Ana Pastore y Piontti, Luca Rossi, Dennis Chao, Ira Longini, M. Elizabeth Halloran, Alessandro Vespignani

Abstract

Background: The 2014 West African Ebola Outbreak is so far the largest and deadliest recorded in history. The affected countries, Sierra Leone, Guinea, Liberia, and Nigeria, have been struggling to contain and to mitigate the outbreak. The ongoing rise in confirmed and suspected cases, 2615 as of 20 August 2014, is considered to increase the risk of international dissemination, especially because the epidemic is now affecting cities with major commercial airports.

Method: We use the Global Epidemic and Mobility Model to generate stochastic, individual-based simulation
CENTERS FOR DISEASE CONTROL & PREVENTION (CDC)

Sierra Leone EbolaResponse (ER)
Modeling the spread of disease impact & intervention
Version 3.0

Contributors: Michael Washington, Charisma Atkins, Martin Meltzer

Division of Preparedness & Emerging Infections
Health Economics & Modeling Unit (HEMU)
December 4, 2014
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**Intermediate Results**

% Patients by category over time

User may enter data into any of the white cells. When user selects a cell to input data, a short description of the cell and details explaining the data and how it should be entered will upload.
Questions from leadership

What’s a viable vaccine trial design during the outbreak?
Example Vaccination Groups: (1) facility HCW such as doctors, nurses, phlebotomists (2) facility support such as cooking and food delivery, housekeeping, sanitation (3) ambulance teams (4) burial teams. Each of 3 shifts is a treated as a different Vaccination Group. Vaccination Groups and shifts are distributed evenly across Vaccination Weeks, with a vaccination weeks assigned at random.
Specific questions

Will an e.g. Cox Proportional Hazards approach be able to account for:

- Declining background disease risk
- Clustering of disease risk
- Healthy vaccinee effect
Example simulation (single model run):

Nelson-Aalen cumulative hazard estimates

Unvaccinated: 43 cases
0.81 cases/person-month

Vaccinated: 27 cases
0.51 cases/person-month

No cases included until first vaccinee reaches end of seroconversion period

Longer lag to accrue vaccinated cases

Hazard ratio:
0.55 (0.32 – 0.96)

Vaccine Efficacy:
45% (4% - 68%)
No bias: Predicted VE
1000 runs at each VE input (range 50% to 90%)
Statistical power and validity of Ebola vaccine trials in Sierra Leone: a simulation study of trial design and analysis

Steven E Bellan, Juliet R C Pulliam, Carl A B Pearson, David Champredon, Spencer J Fox, Laura Skrip, Alison P Galvani, Manoj Gambhir, Ben A Lopman, Travis C Porco, Lauren Ancel Meyers, Jonathan Dushoff

Summary
Background Safe and effective vaccines could help to end the ongoing Ebola virus disease epidemic in parts of west Africa, and mitigate future outbreaks of the virus. We assess the statistical validity and power of randomised controlled trial (RCT) and stepped-wedge cluster trial (SWCT) designs in Sierra Leone, where the incidence of Ebola virus disease is spatiotemporally heterogeneous, and is decreasing rapidly.

Methods We projected district-level Ebola virus disease incidence for the next 6 months, using a stochastic model fitted to data from Sierra Leone. We then simulated RCT and SWCT designs in trial populations comprising geographically distinct clusters at high risk, taking into account realistic logistical constraints, and both individual-level and cluster-level variations in risk. We assessed false-positive rates and power for parametric and non-parametric analyses of simulated trial data, across a range of vaccine efficacies and trial start dates.

Findings For an SWCT, regional variation in Ebola virus disease incidence trends produced increased false-positive rates (up to 0.15 at α=0.05) under standard statistical models, but not when analysed by a permutation test, whereas analyses of RCTs remained statistically valid under all models. With the assumption of a 6-month trial starting on Feb 18, 2015, we estimate the power to detect a 90% effective vaccine to be between 49% and 89% for an RCT, and between 6% and 26% for an SWCT, depending on the Ebola virus disease incidence within the trial population. We estimate that a 1-month delay in trial initiation will reduce the power of the RCT by 20% and that of the SWCT by 49%.

Interpretation Spatiotemporal variation in infection risk undermines the statistical power of the SWCT. This variation also undercuts the SWCT’s expected ethical advantages over the RCT, because an RCT, but not an SWCT, can prioritise vaccination of high-risk clusters.
Questions from leadership

Where should ETUs be constructed next?

Which neighboring countries are at the highest risk?
Can we learn from the business/start-up world too?

Research: do it once

Development: can it be done many times?

Product/Service: do it many, many times