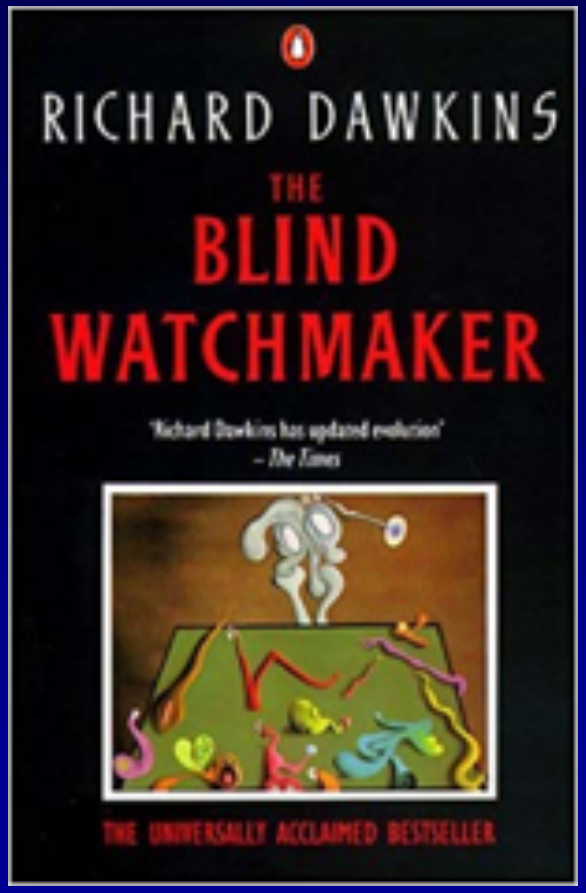
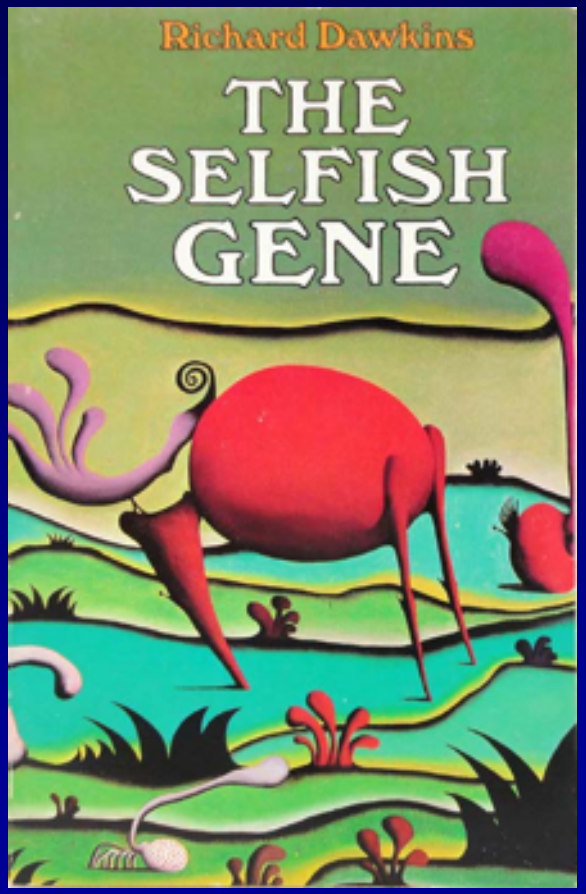
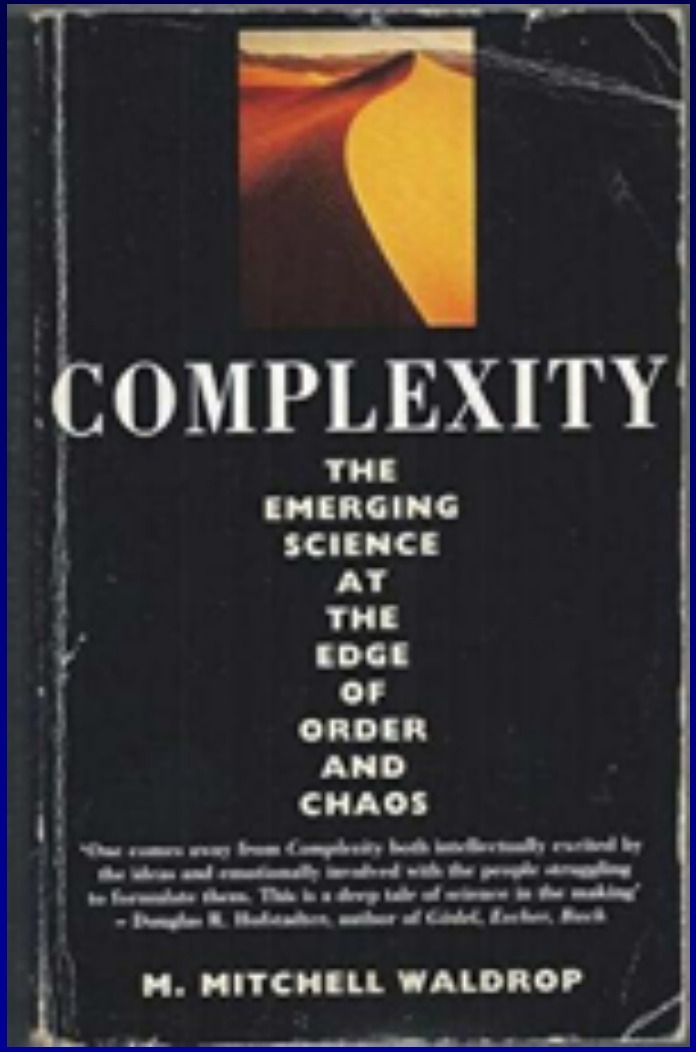
When will computational epidemiologists be replaced by AI?

Planes, trains and autodidacts


End of
front train
MARYLEBONE
InterCity

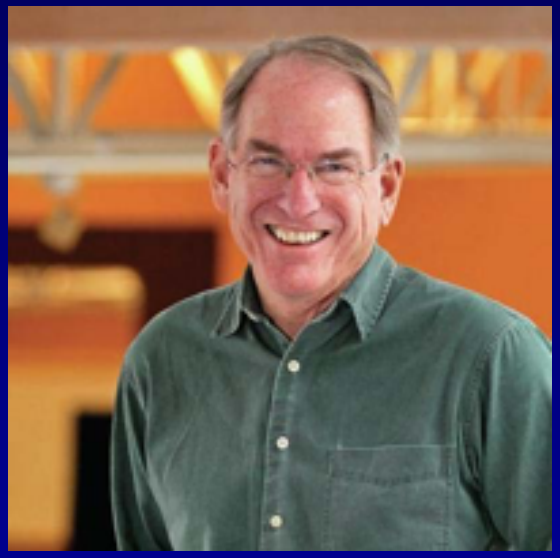

RICHARD DAWKINS
THE
BLIND
WATCHMAKER
'Richard Dawkins has updated evolution'
– The Times
THE UNIVERSALLY ACCLAIMED BESTSELLER


Richard Dawkins
THE
SELFISH
GENE

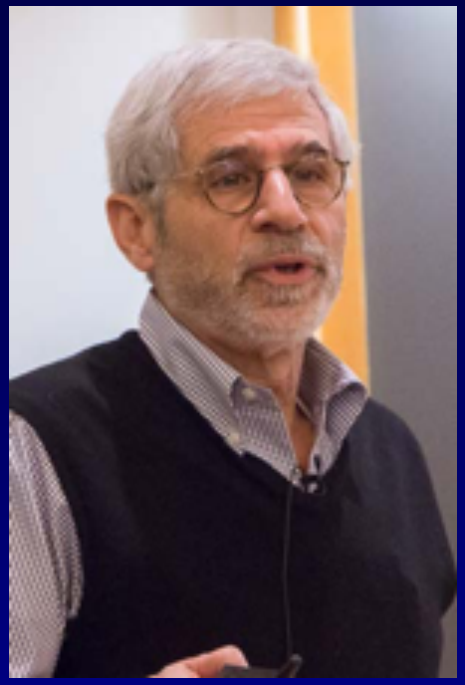

COMPLEXITY
THE EMERGING SCIENCE AT THE EDGE OF ORDER AND CHAOS
'One comes away from Complexity both intellectually excited by the ideas and emotionally involved with the people struggling to formulate them. This is a deep tale of science in the making'
– Douglas R. Hofstadter, author of Gödel, Escher, Bach
M. MITCHELL WALDROP


virgin atlantic
Virgin

Doyne Farmer



Sam Bowles



Alan Perelson

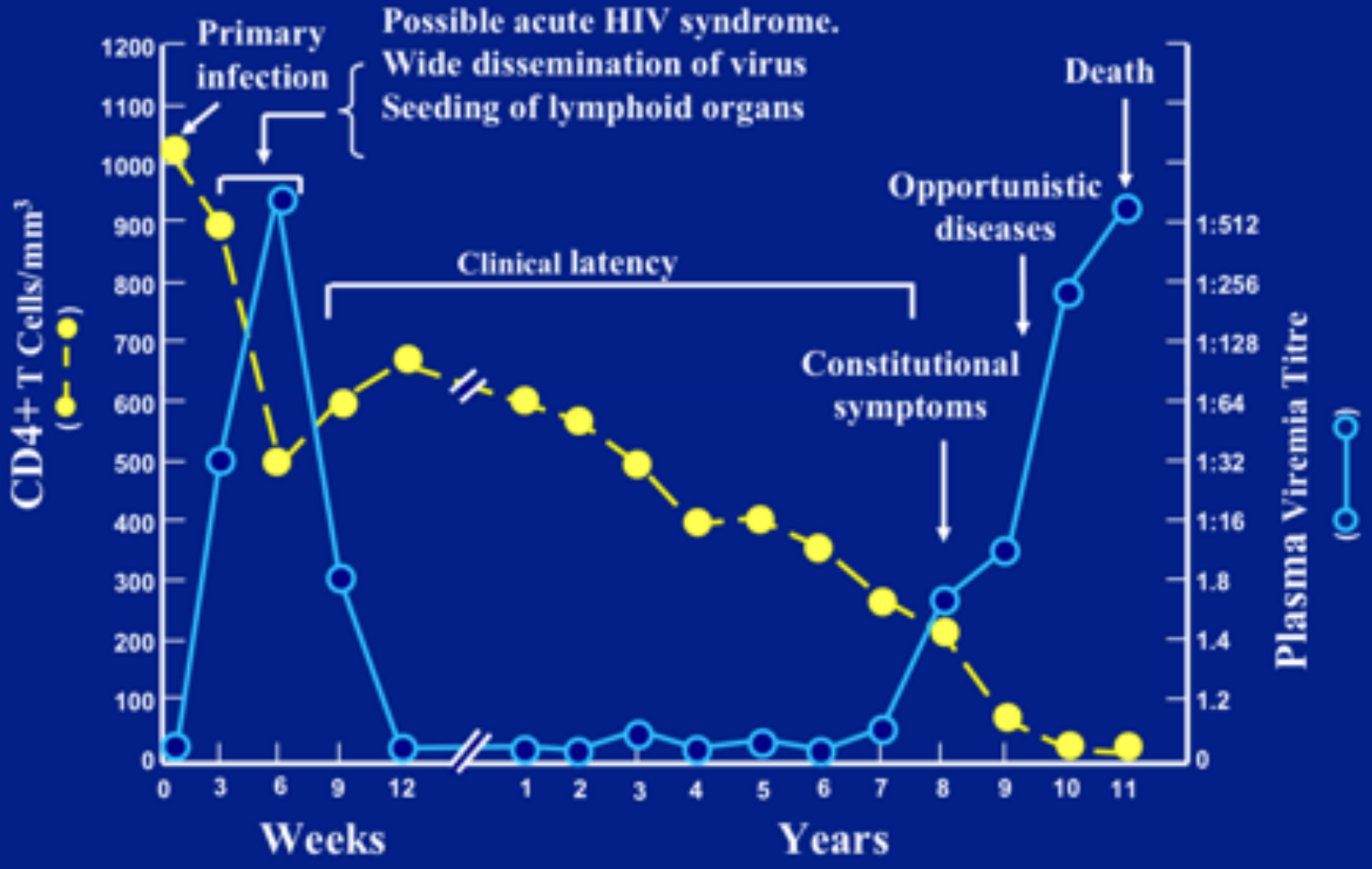
Bette Korber

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 10.3×10^9 virions per day, which is

Natural History of HIV Infection



Buchanan, C. (13 Nov. 2014). HIV & TB in children. Lecture College of William & Mary, Williamsburg,

Try math epidemiology!

Barrier to entry low (no PhD, unlike econ)

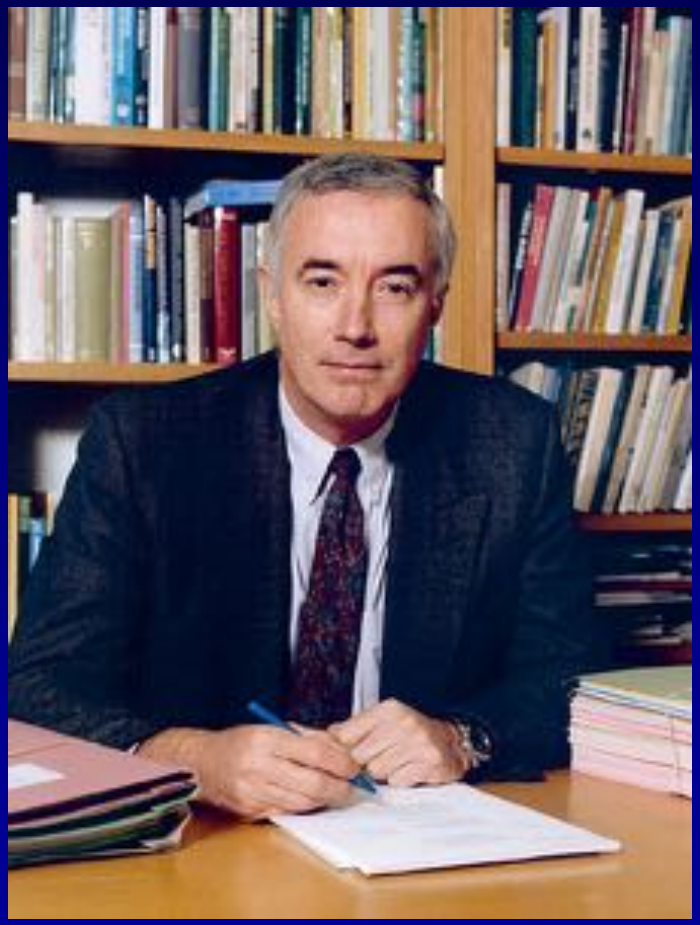
Potential for major impact

Reusable physics skills!

From enthusiasm to emergency


ST MARY'S HOSPITAL

Lord Robert May & Sir Roy Anderson



Nature Vol. 280 2 Au

review

Populatic

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

If the host populat assumed), a wider part of a two-part experiments, and u second part of the indirectly transmitt

ANY contemporary ecol devoted to predator–pre embraces field and labo mathematical models, an prey and predator popul action.

In natural communitie evidence suggests that viruses, bacteria, protoz likely to play a part analo of predators or resource plant and animal populat Park's[1] experiments in drastically reduced the *Tribolium casteneum*, an outcome of its competiti studies of the way the e *tenuabilis* influences the insect *Hydrometra myra* importance of infectious lations of wild mammal such factor in bird popul sheep in North America infection by the lungwor which then predispose t monia[8,9]. On a grand scal

Epidemiological pa transn

Roy M. And
* Parasite Epidemiolo
† Biology Departmen

Epidemiological a accumulating, bu

IT is now seven ye syndrome) was firs the etiological age type 1), was discov the National Instit throughout the wo cases reported bet and 133 countries ation in February concerning both in likely demographic extensively in the tries and why hete developing countri

The potential fo consequently AIDS magnitude of the that group[5–8]. R_0 e produced, on aver stages of the epide tible. As such, it de infected individual duration of their re partners acquired category), times the βcD. Setting aside meant by 'average' sufficient to assign components. In thi such assignments, i tainties that are en we believe can tent

Incubation and

Most epidemiologi uniform level of inf incubation period onset of AIDS[5–9]. tion intervals main cases and cohort st seroconversion is fusion associated bation periods in activity, or indeed recent analysis[12] o diagnosis of AIDS incubation periods older than 12 yr (b tion intervals whe after infection, $p(\tau) = \exp(-a\tau^c)$ and a and c are constants). In

THE RO SOCIET

Epider

Roy M. And
Steve

[1]Department o

[2]21 Sasso

This paper aetiological meters and formulation with the o make simpl tive in the be so with further und defined bio presented i

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

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 out break 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.

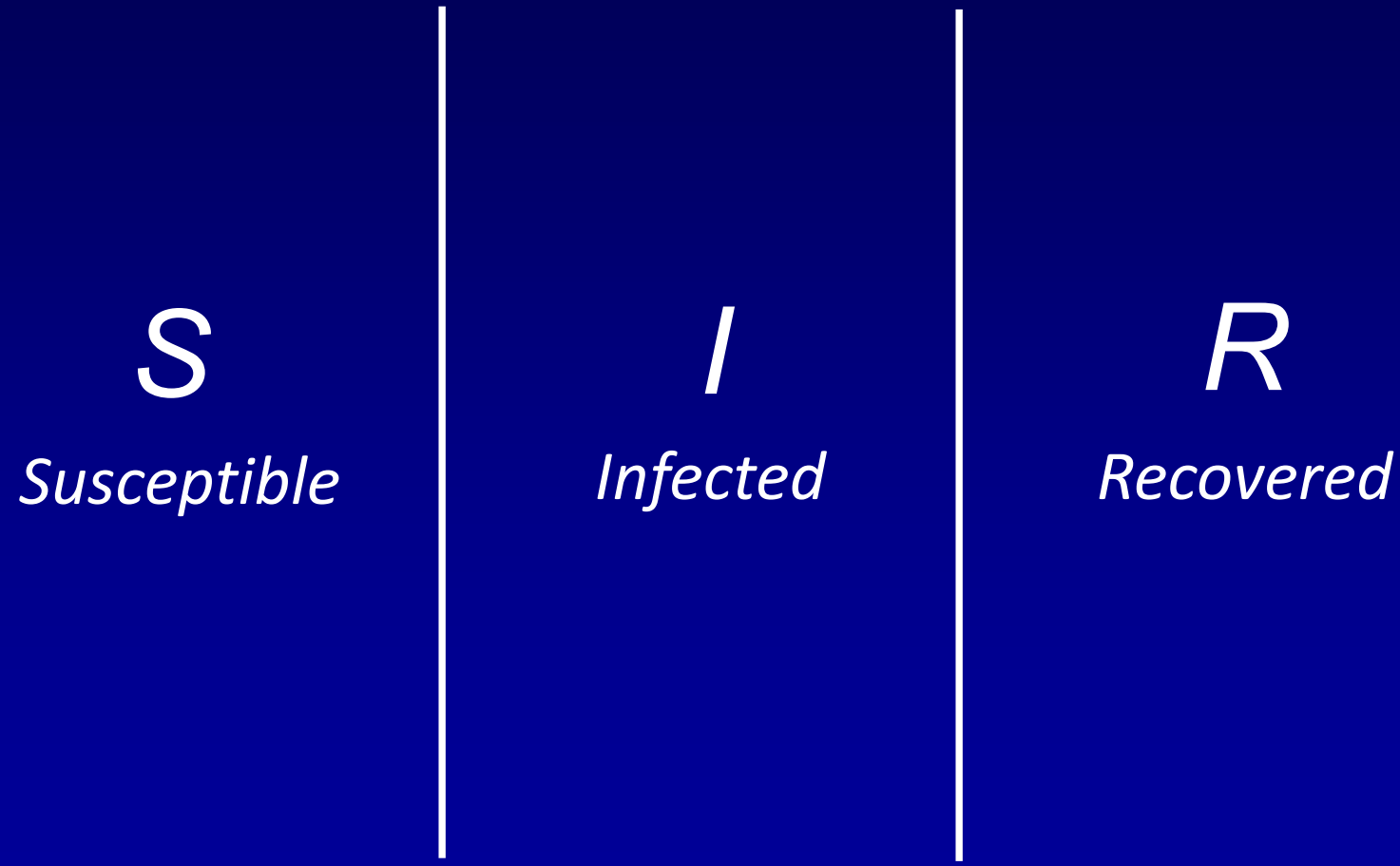
The re-emergence of the viral aetiological agent of SARS in China at the end of 2003 (Paterson 2004), following the epidemic earlier in the year affecting many countries, rang alarm bells in the WHO and elsewhere. Thankfully,

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

Male homosexual	0.60	35	48

Host population

The simple SIR epidemic model

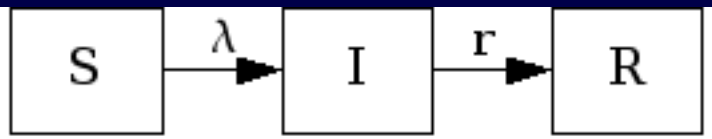


The simple SIR epidemic model

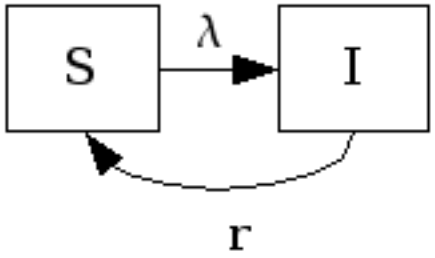
λ = force of infection

d = duration of infectiousness

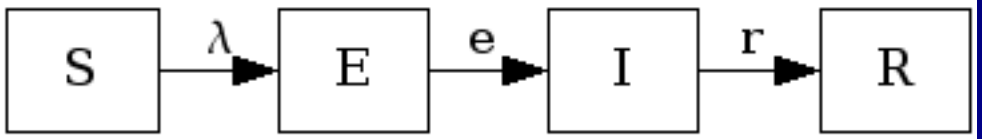
SIR



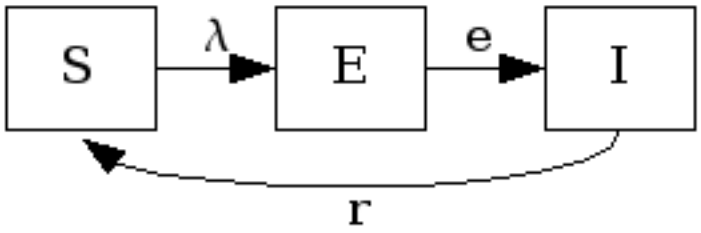
SIS

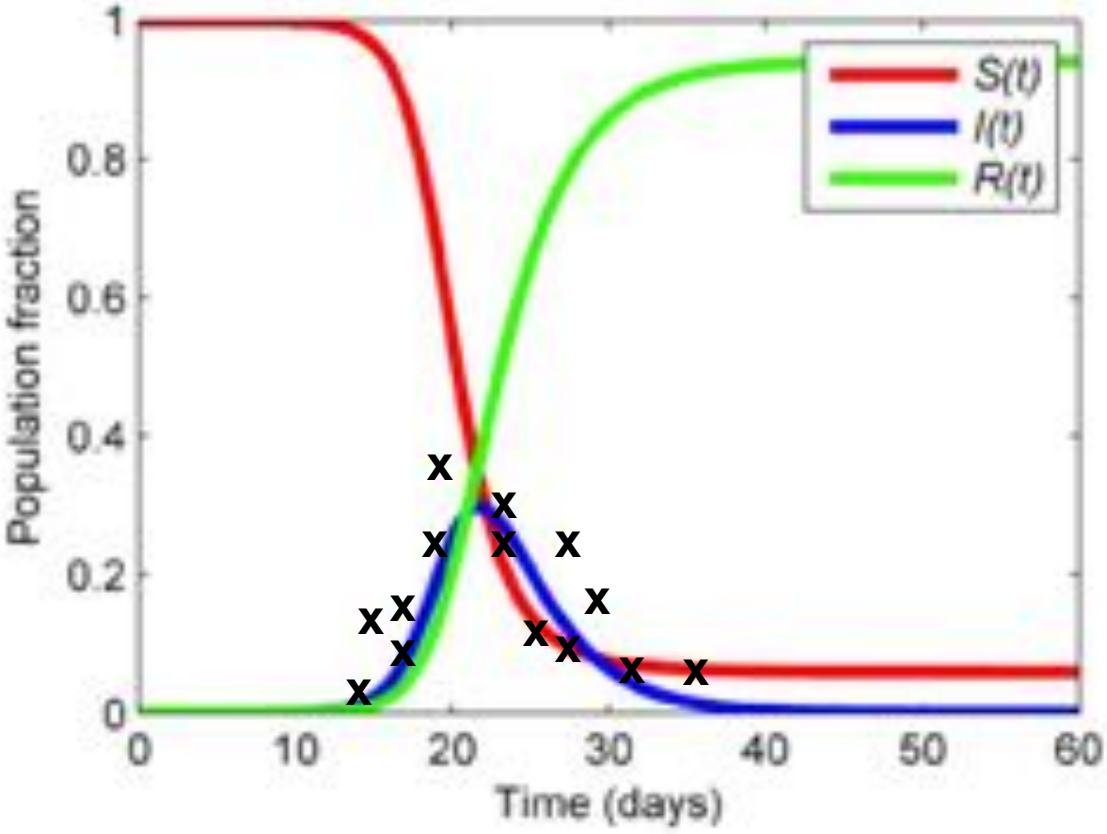


SEIR



SEIS




S(t)
I(t)
R(t)
Population fraction
Time (days)
0
0.2
0.4
0.6
0.8
1
0
10
20
30
40
50
60

2009: H1N1 influenza pandemic

Influenza (Flu)

Avian Influenza
Bird Flu Basics +
Current Situation
Specific Avian Flu Viruses −
Asian Avian Influenza A (H5N1) +
Asian Lineage Avian Influenza A (H7N9) Virus −
Additional Information
H7N9 Images
Publications & Resources
North American Lineage AI Viruses
Past Outbreaks +

Avian Influenza > Specific Avian Flu Viruses

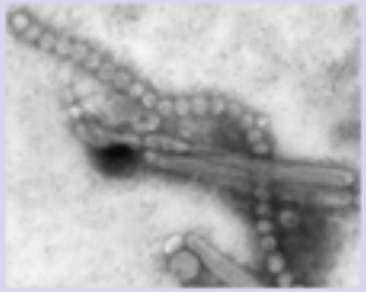
Asian Lineage Avian Influenza A (H7N9) Virus

Language: English (US)

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 publically announced by WHO. During epidemics one through four, about 40 percent of people confirmed with Asian H7N9 virus infection died.

Asian H7N9 Outbreak Characterization



- Asian H7N9 virus infections in poultry in China
- Sporadic infections in people; most with poultry exposure

CDC Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™

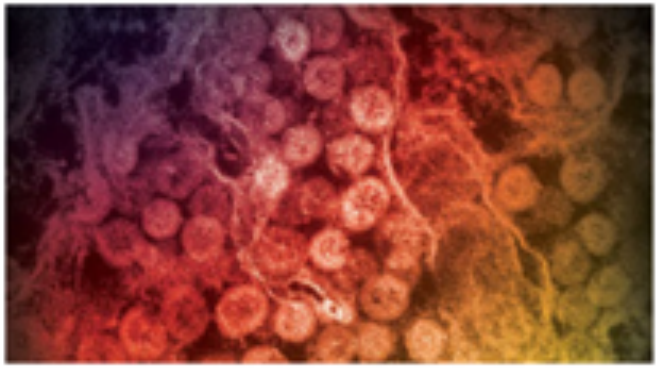
SEARCH

CDC A-Z INDEX

Middle East Respiratory Syndrome (MERS)

Middle East Respiratory Syndrome (MERS) is 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.

More >



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.

SUPPLEMENT ARTICLE

Infectious Disease Modeling Methods as Tools for Informing Response to Novel Influenza Viruses of Unknown Pandemic Potential

Manoj Gambhir,[1,2,3,a] Catherine Bozio,[4,a] Justin J. O'Hagan,[2,3,a] Anna Uricanin,[5] Lucinda E. Johnson,[6] Matthew Biggerstaff,[6] and David L. Swerdlow[7]

[1]Epidemiological Modelling Unit, 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), [3]IHRC Inc, [4]Graduate Program in Epidemiology and Molecules to Mankind, Laney Graduate School, Emory University, [5]Division of Global Migration and Quarantine, National Center for Emerging and Zoonotic Infectious Diseases, [6]Influenza Division, and [7]Modeling 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?

Table 1. Key Questions Related to Pandemic Preparedness and Response That Infectious Disease Modeling Methods Address

Questions	Pandemic Stage			Method			
	P	E	L	Sim	Stat	Analysis Time Commitment	Method
Epidemiology							
What is the basic reproduction number (R_0) and the current value, or the time course, of the effective reproduction number (Re)?		X	X		✓	<1 mo	Growth rate of case incidence curve
		X	X		✓	<1 mo	Infection tree reconstruction
		X	X		✓	<1 mo	Richards population growth model
		X			✓	<1 mo	Chain binomial model
		X	X		✓	<1 mo	Case renewal process
		X			✓	<1 mo	Influenza genetic sequence analysis
		X	X	✓		<1 mo	Age-structured SEIR model
		X	X		✓	<1 wk	Maximum likelihood estimation
		X		✓	✓	<1 mo	Coalescent analysis
		X		✓		<1 wk	Next generation matrix
What is the predicted peak number of cases and time? What is the predicted cumulative number of cases over the epidemic (ie, final attack rate)?		X		✓		<1 mo	Age-structured SEIR model
				✓	✓	<1 mo	Digital surveillance methods
What are the possible spatiotemporal patterns of spread of the infection?		X		✓		>>1 mo	Individual-based model
				✓		<1 mo	Metapopulation model
What was the likely sequence of spatiotemporal spread of infection since the outbreak began?		X			✓	<1 mo	Infection tree reconstruction & travel pattern modeling
What is the severity of the virus(es) (ie, case-hospitalization/death-rate) accounting for ascertainment biases (eg, more likely to detect severe cases)?		X	X	✓		>>1 mo	Individual-based model
					✓	<1 mo	Bayesian evidence synthesis
					✓	<1 wk	Incidence curve backcalculation

Table 2. Description of the Modeling Methods Listed in Table 1

Method	Description	Data Needed
Age-structured SEIR model	A compartmental model in which hosts are grouped into population compartments composed of their age-group and their infection status, eg, 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].	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).
Antigenic cartography	A method for quantifying and visualizing the antigenic evolution of the influenza virus according to antigenic distances [13].	Influenza virus genetic sequences, antigenic distances between subtypes (using eg, hemagluttination inhibition assay).
Antigenic distance	Antigenic distances of proposed vaccine strains from predicted dominant circulating strain(s) are correlated with prior years' vaccine effectiveness estimates [14].	Hemagluttination 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
Bayesian evidence synthesis	Prior knowledge and distinct surveillance data sources are combined to estimate epidemiologic quantities (eg number infected, case-hospitalization rate) [9].	Repeated cross-sectional serosurveys, numbers and dates of onset of confirmed cases, symptomatic cases, hospitalizations, intensive care admissions, dates of severe outcomes.
Branching process analysis	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.	Contact tracing data, surveillance datasets, R_0 population distribution (ie, the probability associated with an individual in the population generating R_0 secondary cases at the start of the epidemic).
Case renewal process	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].	Case incidence time series (infection/hospitalization/death).
Chain binomial model	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].	Case incidence time series (infection/hospitalization/death).
Coalescent analysis	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	Influenza genetic sequences and sampling times.

PHILOSOPHICAL TRANSACTIONS B

rstb.royalsocietypublishing.org

Opinion piece

Cite this article: Cori A *et al.* 2017 Key data for outbreak evaluation: building on the Ebola experience. *Phil. Trans. R. Soc. B* **372**: 20160371.
http://dx.doi.org/10.1098/rstb.2016.0371

Accepted: 11 November 2016

One contribution of 17 to a theme issue 'The 2013–2016 West African Ebola epidemic: data, decision-making and disease control'.

Subject Areas:
health and disease and epidemiology

Key data for outbreak evaluation: building on the Ebola experience

Anne Cori[1,†], Christl A. Donnelly[1], Ilaria Dorigatti[1], Neil M. Ferguson[1], Christophe Fraser[2], Tini Garske[1], Thibaut Jombart[1], Gemma Nedjati-Gilani[1], Pierre Nouvellet[1], Steven Riley[1], Maria D. Van Kerkhove[3], Harriet L. Mills[1,4,5,†] and Isobel M. Blake[1,†]

[1]Medical Research Council Centre for Outbreak Analysis and Modelling, Department of Infectious Disease Epidemiology, School of Public Health, Imperial College London, London W2 1PG, UK
[2]Oxford Big Data Institute, Li Ka Shing Centre for Health Information and Discovery, Nuffield Department of Medicine, University of Oxford, Oxford OX3 7FZ, UK
[3]Centre for Global Health, Institut Pasteur, 25-28 Rue du Dr Roux, 75015 Paris, France
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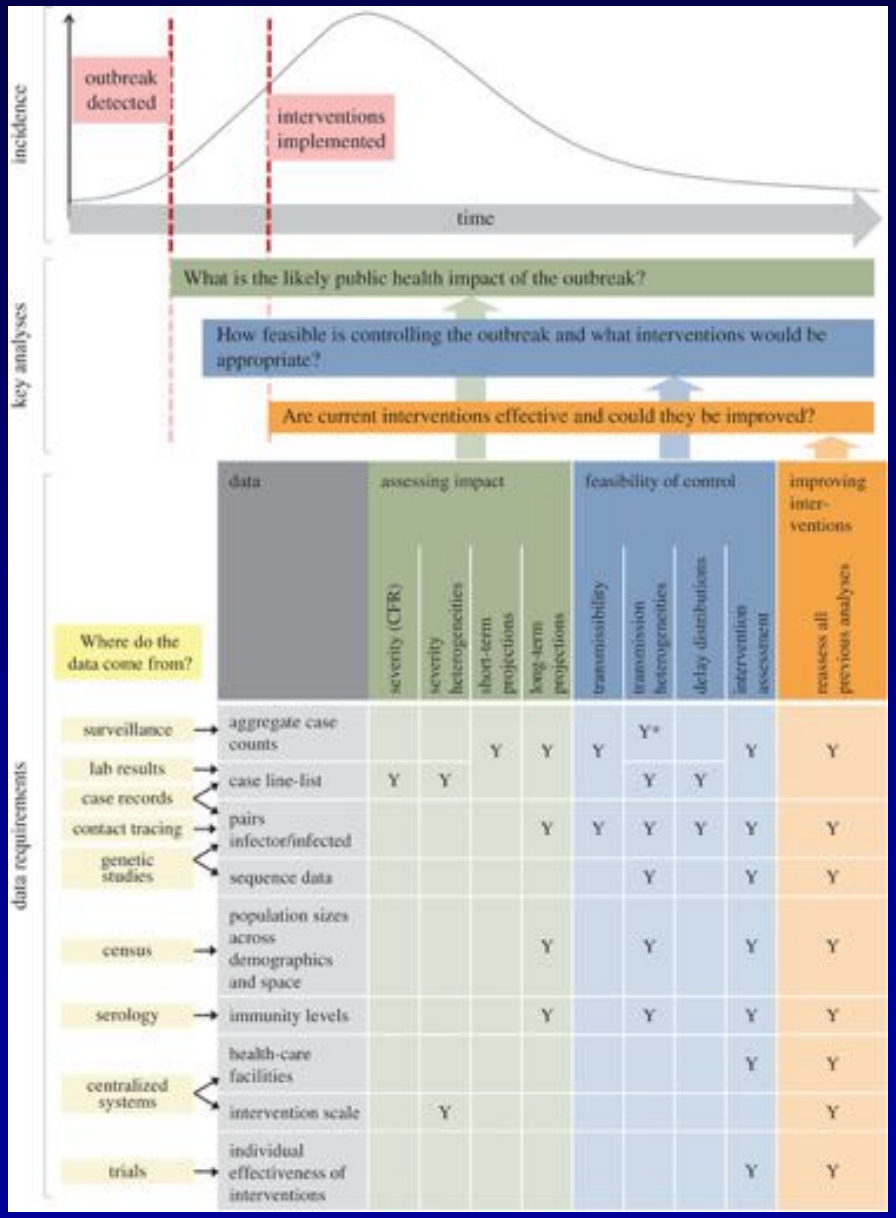
[5]School of Veterinary Sciences, University of Bristol, Bristol BS40 5DU, UK

AC, 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

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.



Anne Cori et al. Phil. Trans. R. Soc. B 2017;372:20160371

fectious disease modelling using data from

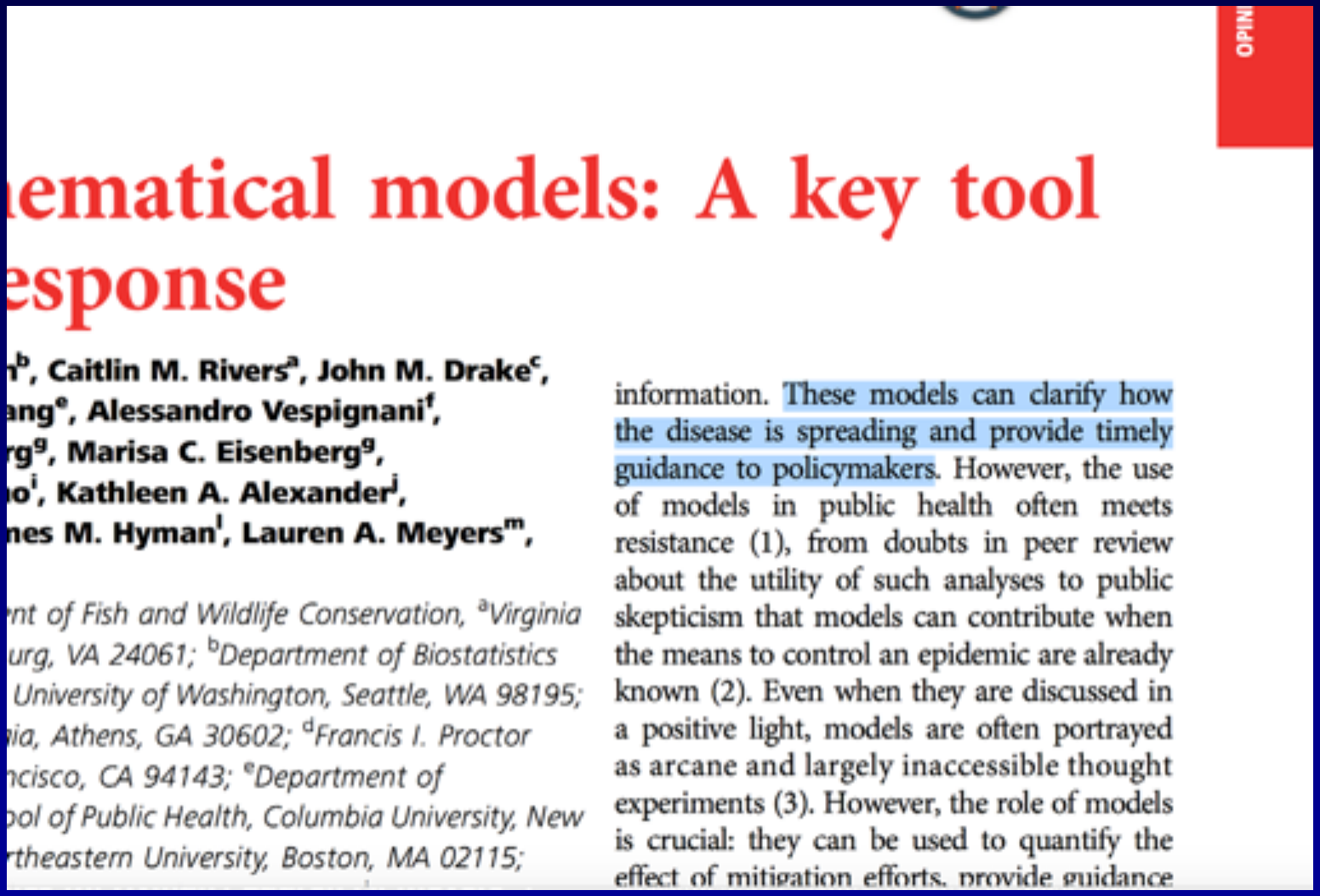
Presanis [a], Paul J. Birrell [a], Gianpaolo Scalia Tomba [c],

ealth, Robinson Way, Cambridge CB2 0SR, UK
W9 5HT, UK
ergata, Rome, Italy
k, Coventry CV4 7AL, UK

ABSTRACT

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.

Daniela De Angelis et al. Epidemics 2015;10: PP83-87, Four key challenges in infectious disease modelling using data from multiple sources



ematical models: A key tool esponse

h[b], Caitlin M. Rivers[a], John M. Drake[c], ang[e], Alessandro Vespignani[f], rg[g], Marisa C. Eisenberg[g], o[i], Kathleen A. Alexander[j], nes M. Hyman[l], Lauren A. Meyers[m],

nt of Fish and Wildlife Conservation, [a]Virginia urg, VA 24061; [b]Department of Biostatistics University of Washington, Seattle, WA 98195; ia, Athens, GA 30602; [d]Francis I. Proctor ncisco, CA 94143; [e]Department of ol of Public Health, Columbia University, New rtheastern University, Boston, MA 02115;

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

Eric Lofgren et al. PNAS 2014;v111: 51, Mathematical models: A key tool for outbreak response

MAY 15, 2017

TIME

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

time.com

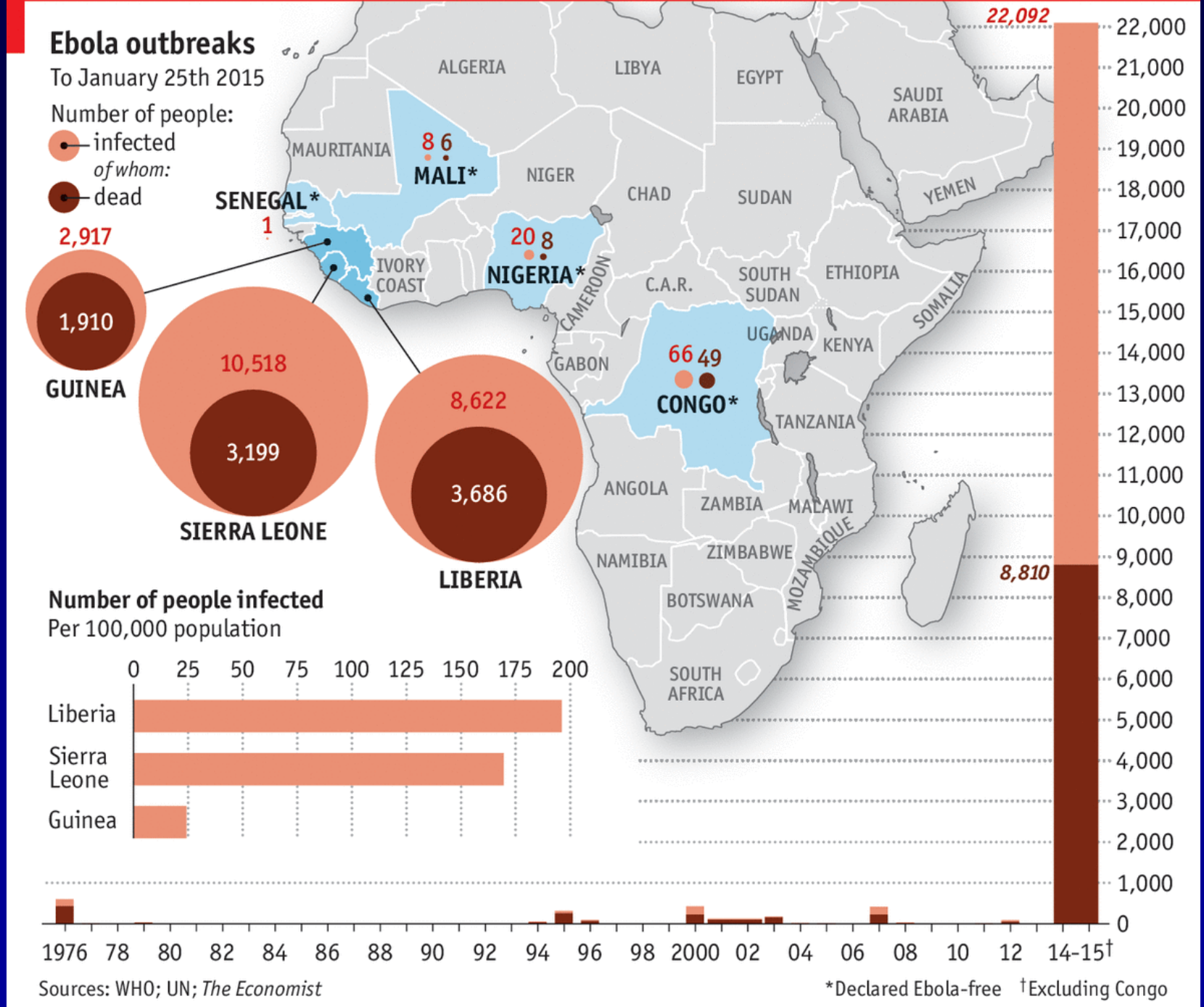
However, this isn't working

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



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Ebola Virus Disease
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Activations
Ebola: 2014 West Africa Outbreak
Polio Eradication
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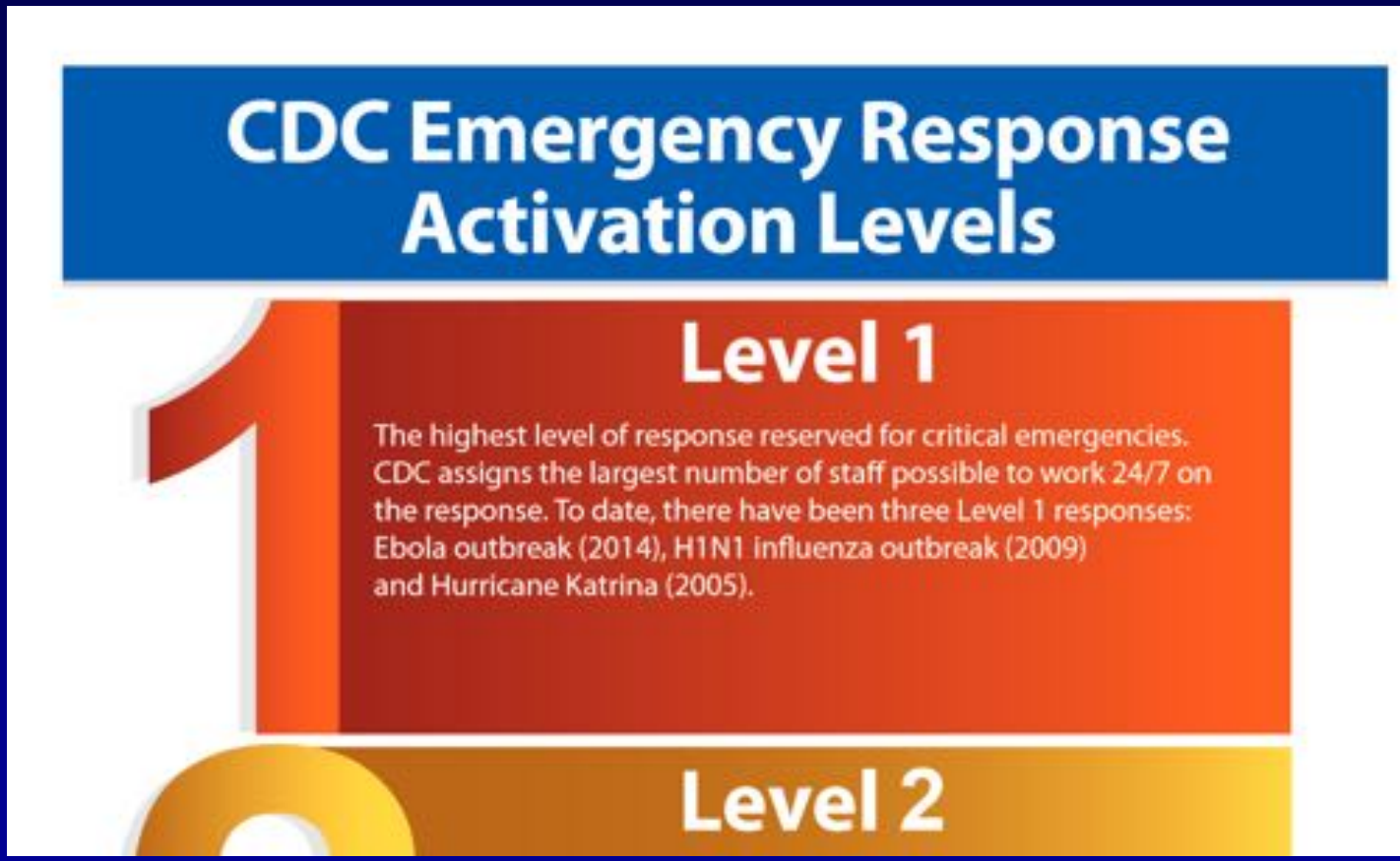
Business Pulse: 2014-2015 Flu Season
NATURAL DISASTERS
Wildfires, Floods, Hurricanes & more
RECENT INCIDENTS
Ebola, Chikungunya & more
Tweets
Follow
CDC Flu
@CDCFlu
15 Oct


CDC Emergency Response Activation Levels
1
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).
2
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.
3
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
CDC


CDC Emergency Response Activation Levels
1
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?

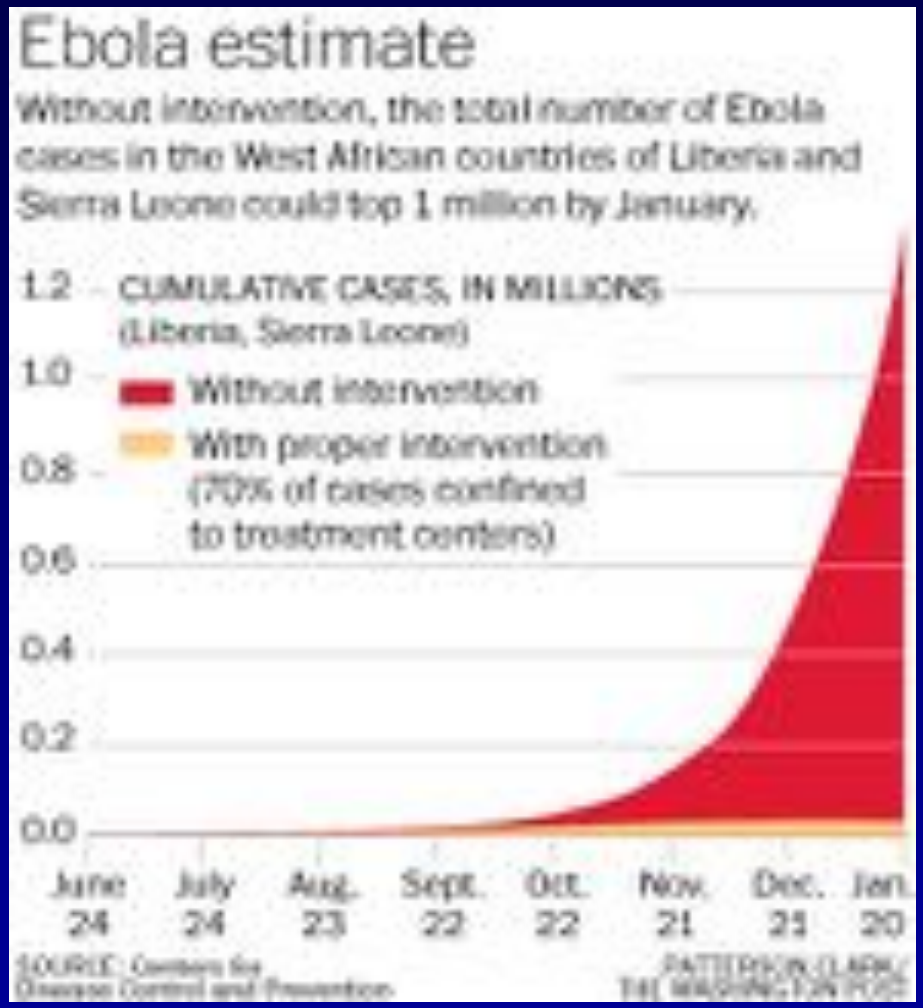
When will the epidemic end?

What will it take to end the epidemic?

Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Supplement / Vol. 63 / No. 3
September 26, 2014

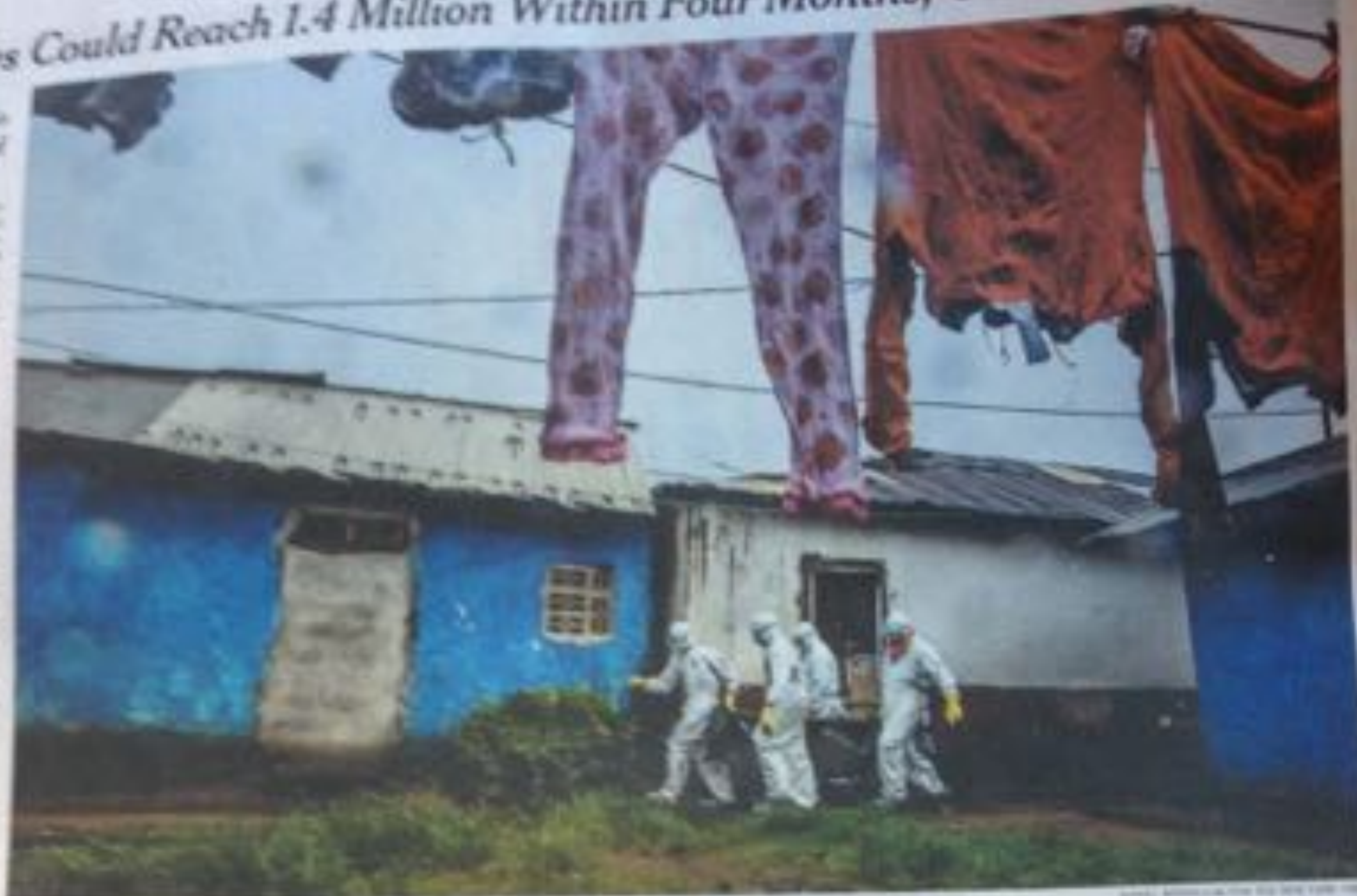
Estimating the Future Number of Cases in the Ebola Epidemic — Liberia and Sierra Leone, 2014–2015

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention


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
1.0
0.8
0.6
0.4
0.2
0.0
CUMULATIVE CASES, IN MILLIONS
(Liberia, Sierra Leone)
Without intervention
With proper intervention
(70% of cases confined
to treatment centers)
June 24
July 24
Aug. 23
Sept. 22
Oct. 22
Nov. 21
Dec. 21
Jan. 20

Ebola Cases Could Reach 1.4 Million Within Four Months, C.D.C. Estimates

Worst-Case Scenario Can Still Be Avoided



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.

Job creation/destruction

So, why is it so hard to get traction?

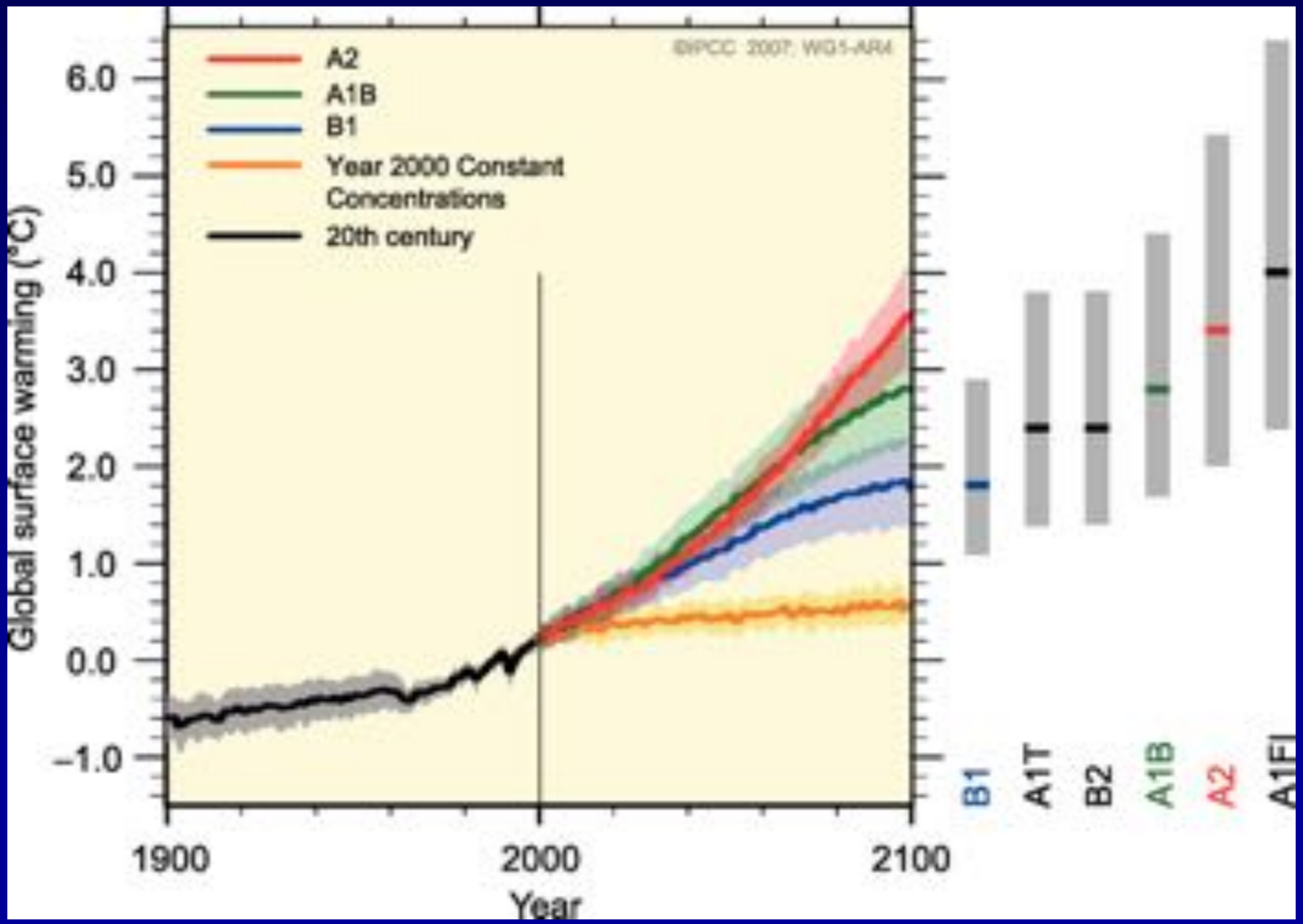
Policymakers don't trust the model(s), they trust the person presenting the model

They don't trust single models, they need ensembles

They're comfortable with statistics but not mechanistic modelling

Multi-model ensembles

IPCC report (AR4)

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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?

Epidemics 18 (2017) 48–55

Contents lists available at ScienceDirect

Epidemics

journal homepage: www.elsevier.com/locate/epidemics

Probabilistic forecasts of trachoma transmission at the district level: A statistical model comparison

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

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

ARTICLE INFO

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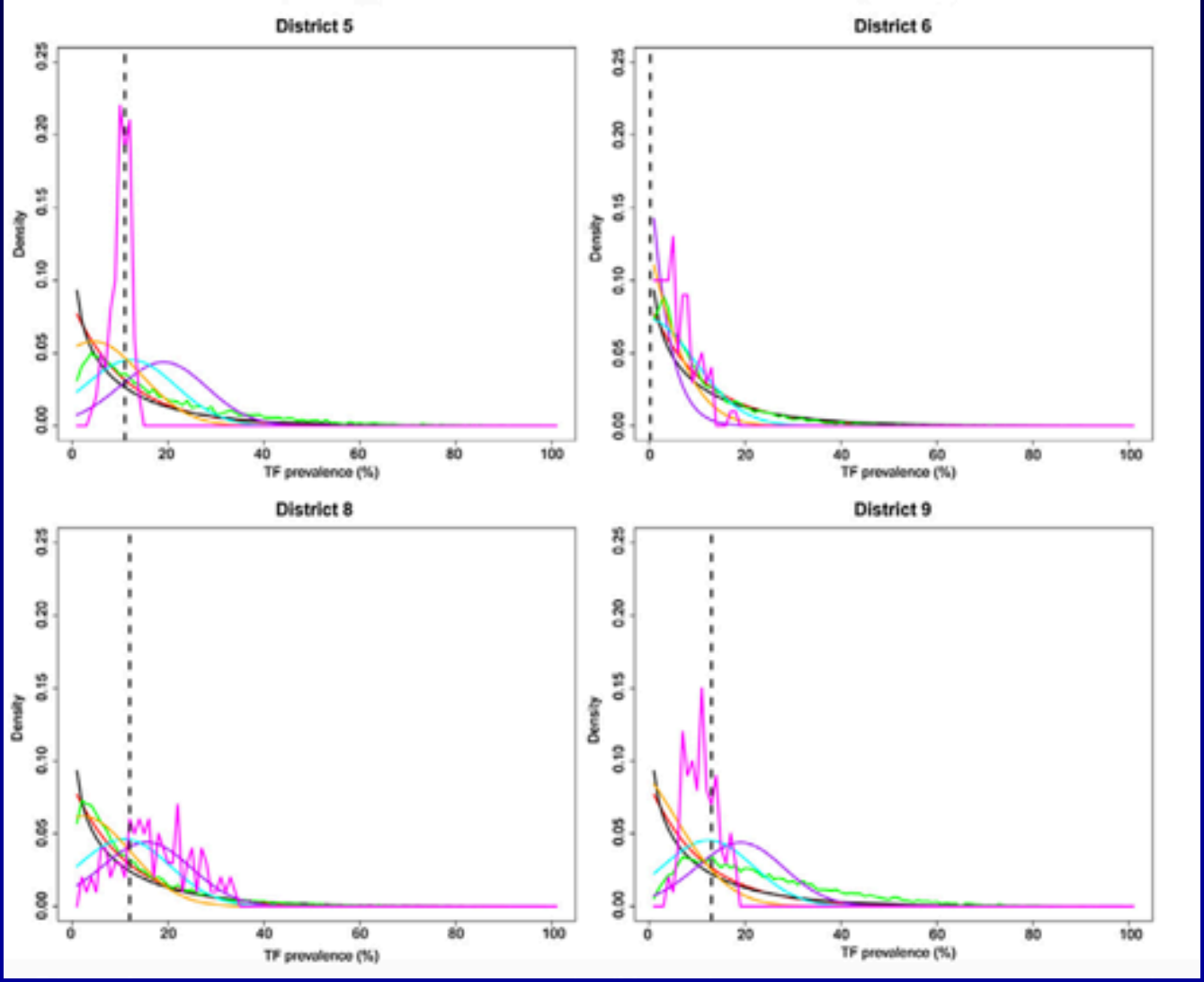
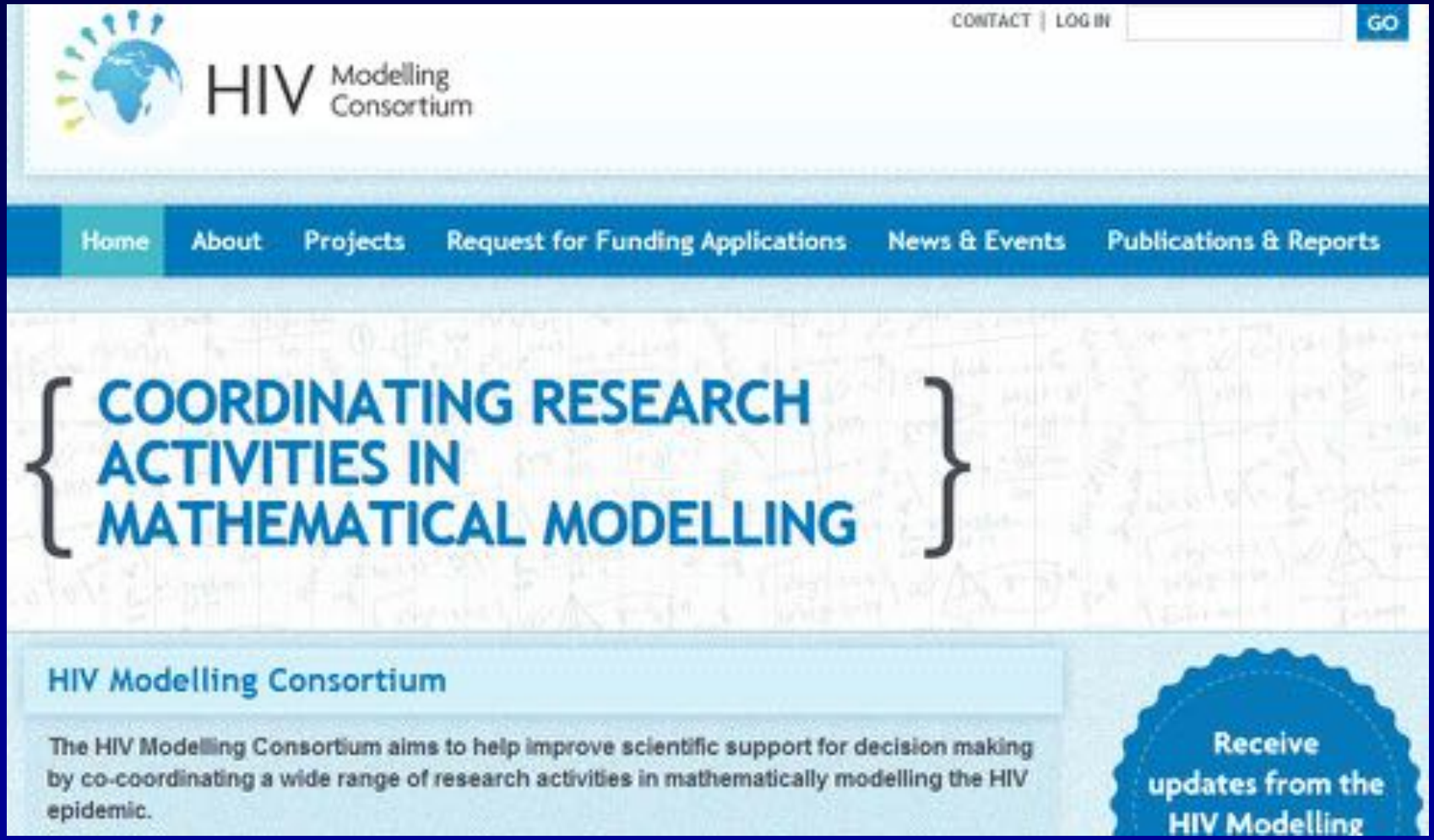
Keywords:
Trachoma
Elimination

ABSTRACT

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


District 5
District 6
District 8
District 9
Density
TF prevalence (%)
0.00
0.05
0.10
0.15
0.20
0.25
0
20
40
60
80
100
Model 1
Model 2.1
Model 2.2
Model 2.3
Model 3.1
Model 3.1
Model 4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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.
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PLoS MEDICINE

HIV Treatment as Prevention: Systematic Comparison of Mathematical Models of the Potential Impact of Antiretroviral Ther

Jeffrey W. Eaton[1*], Leigh F. Johns
Anna Bershteyn[4], David E. Bloom[
Salal Humair[3,11], Daniel J. Klein[4], E
Edward A. Wenger[5], Brian G. Willi

1 Department of Infectious Disease Epidemiology, Imperia
Cape Town, Cape Town, South Africa, 2 Harvard School o
University of KwaZulu-Natal, Mtubatuba, South Africa, 3
Laboratory, Bellevue, Washington, United States of Ameri
4 Medical Research Council Centre for Outbreak Analysis
9 Erasmus University, Rotterdam, Netherlands, 10 Depa
11 School of Science and Engineering, Lahore University
12 Futures Institute, Glastonbury, Connecticut, United St

Abstract

Background Many mathematical mode
on new HIV infections. Comparing resu
slightly different questions and have n
mathematical models simulating the sa
about the epidemiological impact of e

Methods and Findings Twelve indep
scenarios in South Africa and reported a
threshold for treatment eligibility, access
individuals start treatment on average 1
3 y, the models projected that HIV incid
counterfactual scenario in which there
incidence. The impact of optimistic inter
substantial uncertainty about the theore
next four decades. The number of pe

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

Summary

Background New WHO guidelines recommend 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 (generalised epidemic, moderate antiretroviral therapy coverage), Zambia (generalised epidemic, high antiretroviral therapy coverage), India (concentrated epidemic, moderate antiretroviral therapy coverage), and Vietnam (concentrated 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, with results projected over 20 years. Analyses assessed the extension 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 initiation with CD4 counts of 350 cells per μL or less. We assessed costs from a health-system perspective, and calculated the incremental cost (in US$) 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-head gross domestic product (GDP; South Africa $8040; Zambia $1625; India $1489; Vietnam $1687) and cost effective if the cost per DALY averted was less than three times the per-head GDP.

Findings In South Africa, the cost per DALY averted of extending eligibility for antiretroviral therapy to adult patients with CD4 counts of 500 cells per μL or less ranged from $237 to $6691 per DALY averted compared with 2010 guidelines. In Zambia, expansion of eligibility to adults with a CD4 count threshold of 500 cells per μL ranged from improving 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 where substantially expanded

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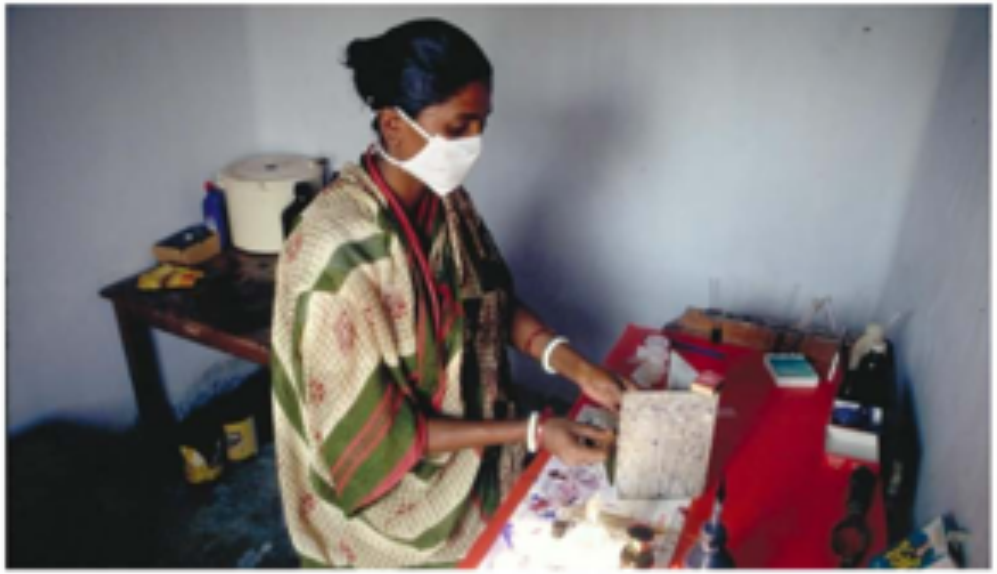
TB diagnosis

The practical process of preparing sputum samples for TB diagnosis.



News

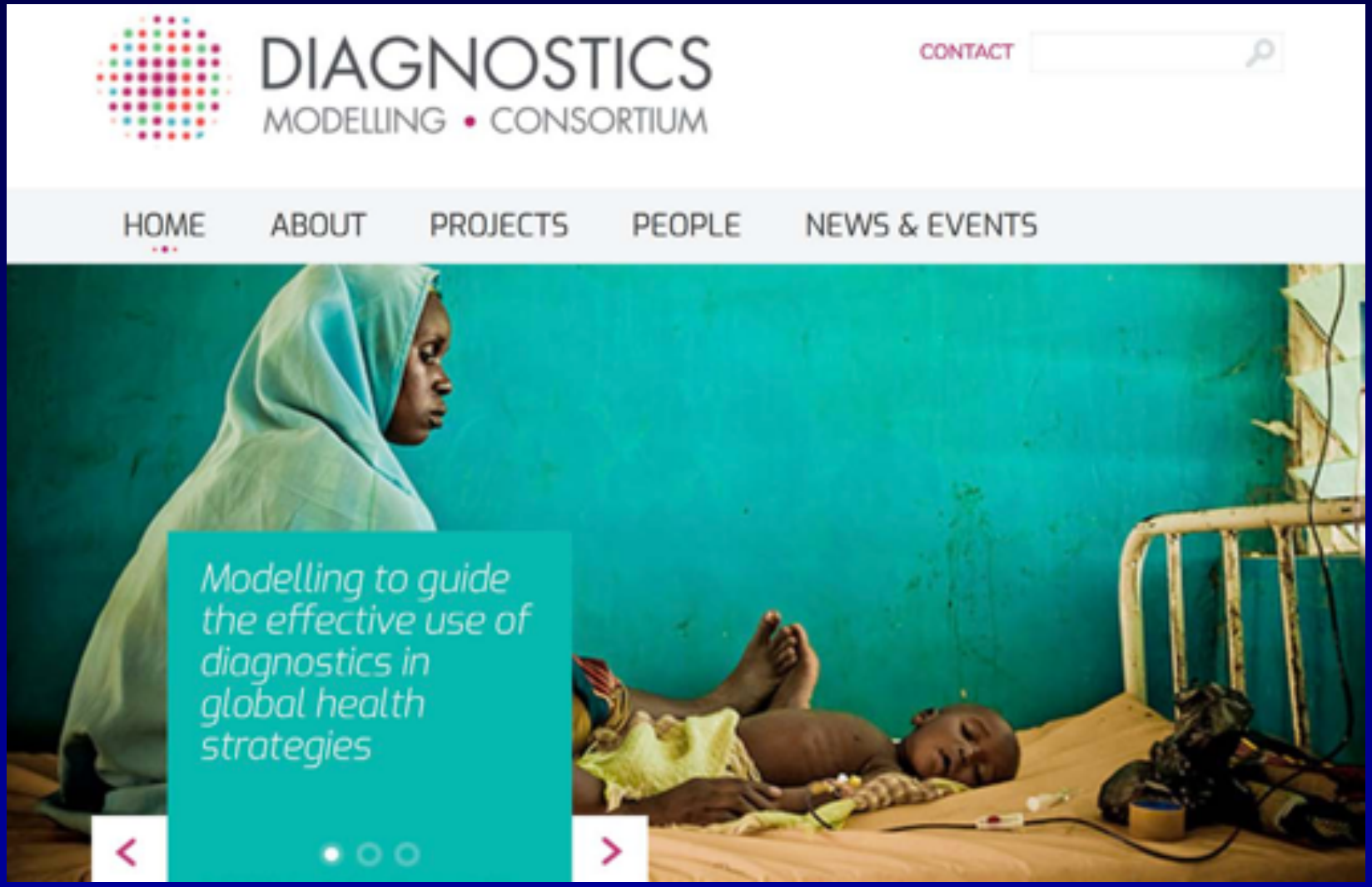
- Lit review mathematical and economic TB modelling
- Annual meeting report 2017
- Intro to TB modelling PG course
- TB MAC Symposium at Union 2017 conference
- TB MAC / WHO first annual meeting
- TB MAC Stakeholder meeting
- TB MAC and GHCC
- Modelling socio-economic determinants report
- Post 2015 Global TB

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,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Modelling to guide the effective use of diagnostics in global health strategies

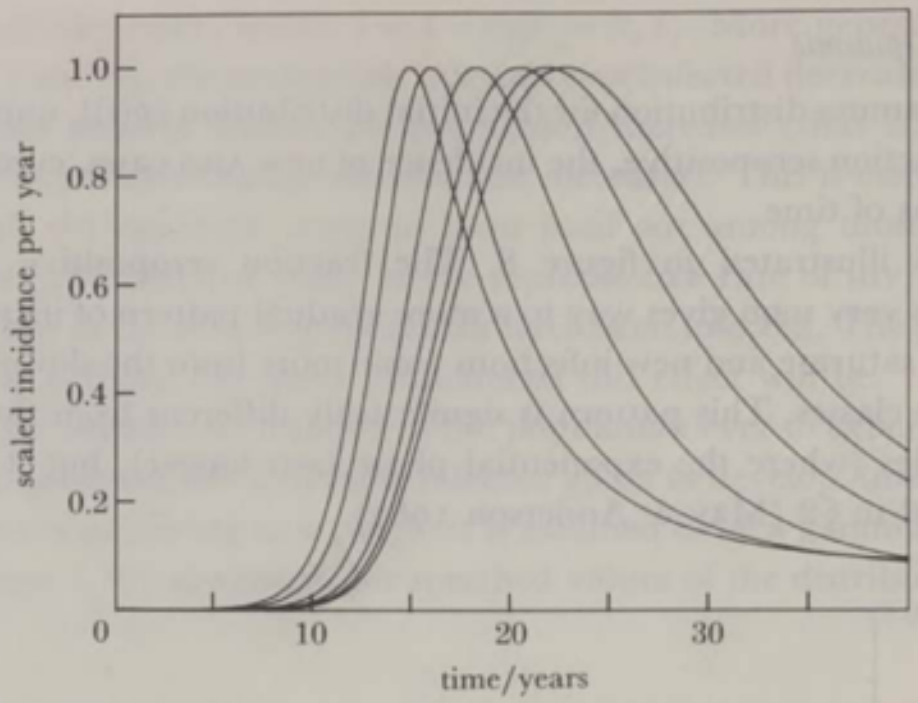
Improved training to data

Phil. Trans. R. Soc. Lond. B **321**, 565–607 (1988)
Printed in Great Britain

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.*



THE ROYAL SOCIETY

Published online 15 June 2004

Epidemiology, transmission dynamics and control of SARS: the 2002–2003 epidemic

Roy M. Anderson[1*], Christophe Fraser[1], Azra C. Ghani[1], Christl A. Donnelly[1], Steven Riley[1], Neil M. Ferguson[1], Gabriel M. Leung[2], T. H. Lam[2] and Anthony J. Hedley[2]

[1]*Department of Infectious Disease Epidemiology, Faculty of Medicine, Imperial College London, St Mary's Campus, Norfolk Place, London W2 1PG, UK*

[2]*21 Sassoon Road, Faculty of Medicine Building, University of Hong Kong, Pokfulam, Hong Kong, China*

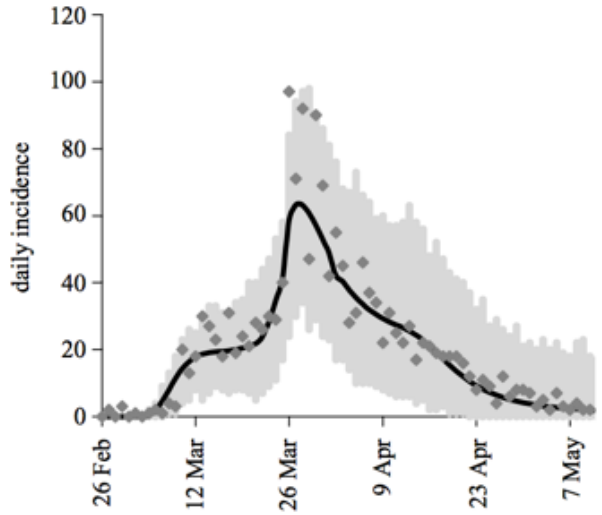


Figure 12. The SARS epidemic in Hong Kong and the fit of a multi-compartment meta-population stochastic model (from Riley *et al.* 2003). The dots are reported SARS cases and the solid line is the best fit model. The vertical grey bars denote 95% prediction intervals.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

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.

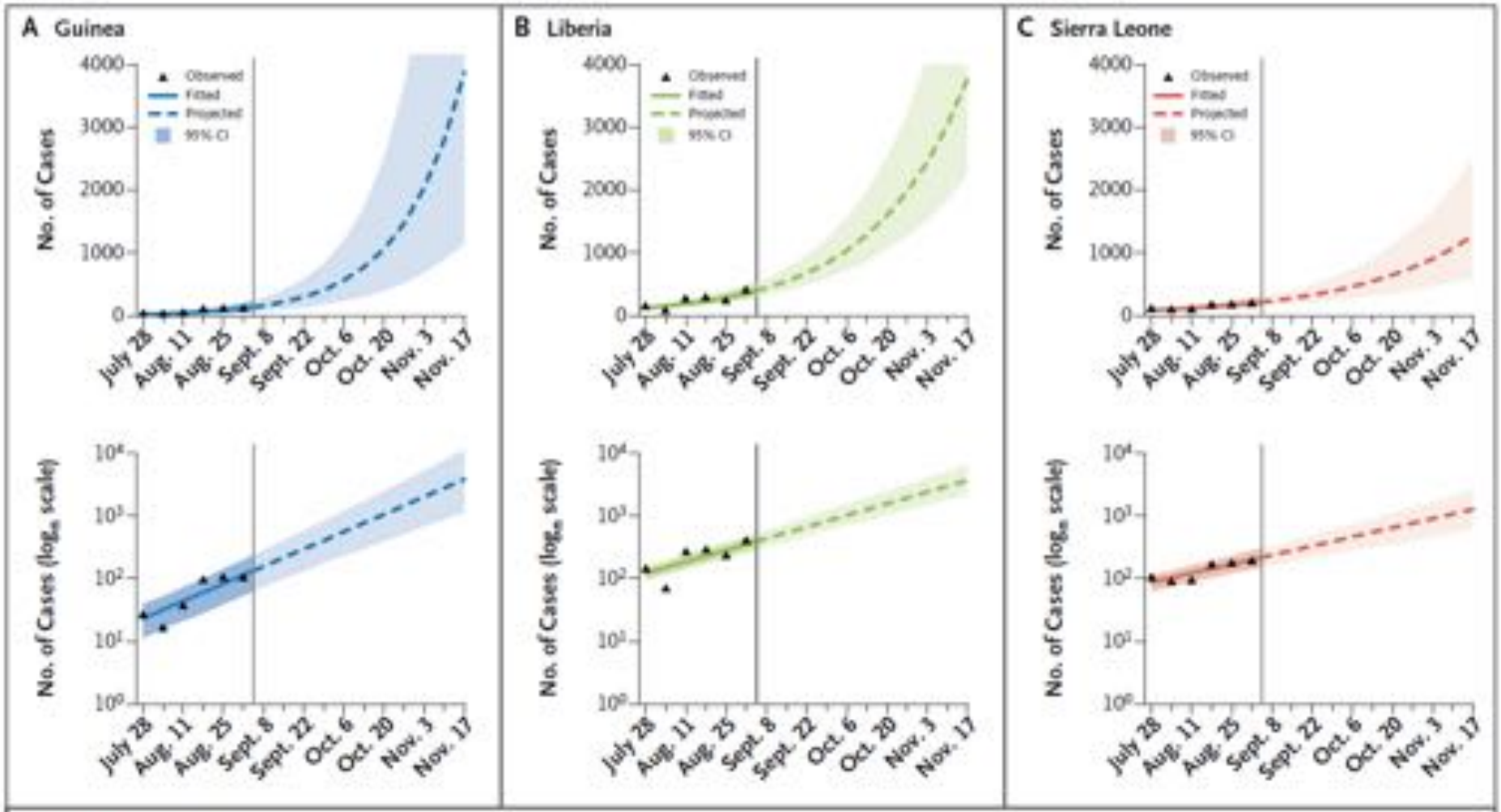


Figure 4. Observed and Projected Case Incidence.

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

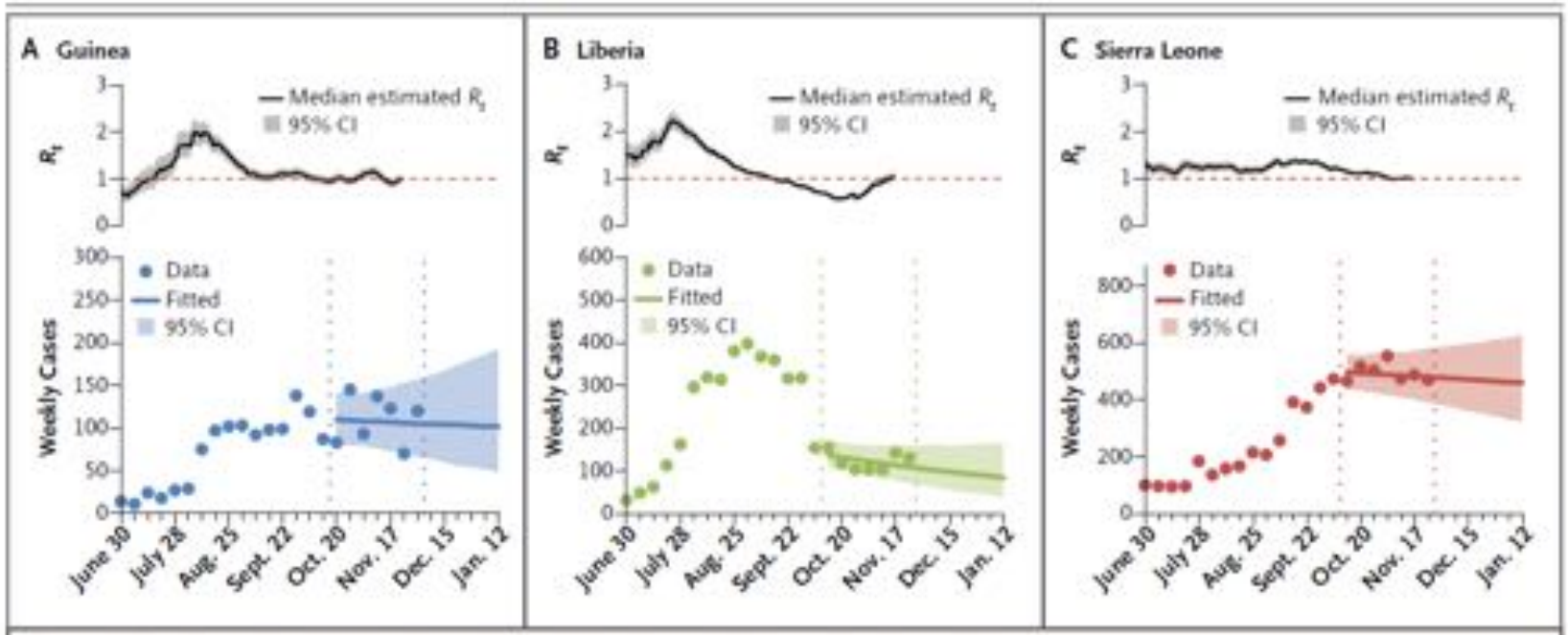
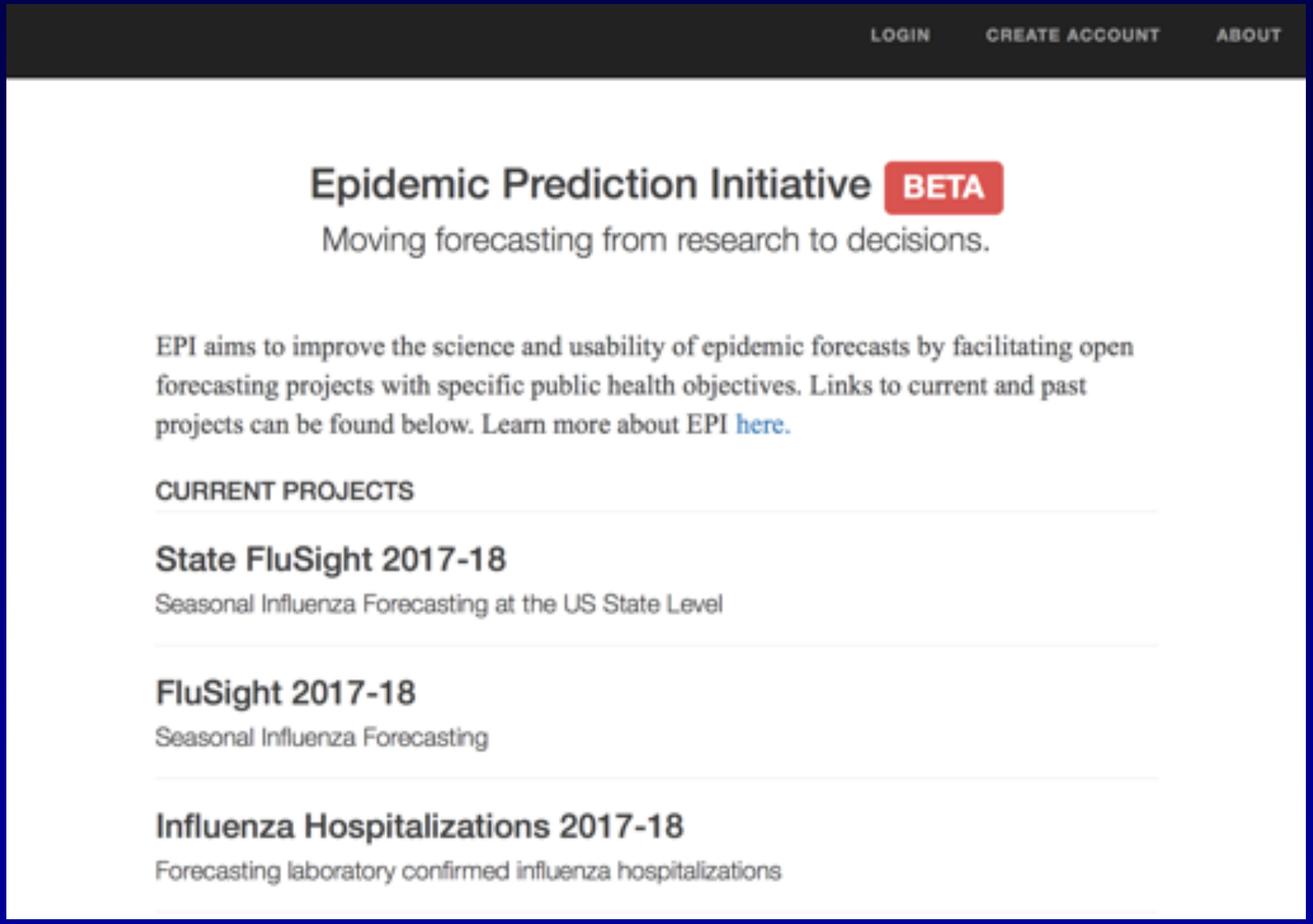


Figure 1. Case Reproduction Numbers and Weekly Incidence in Guinea, Liberia, and Sierra Leone.

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).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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.
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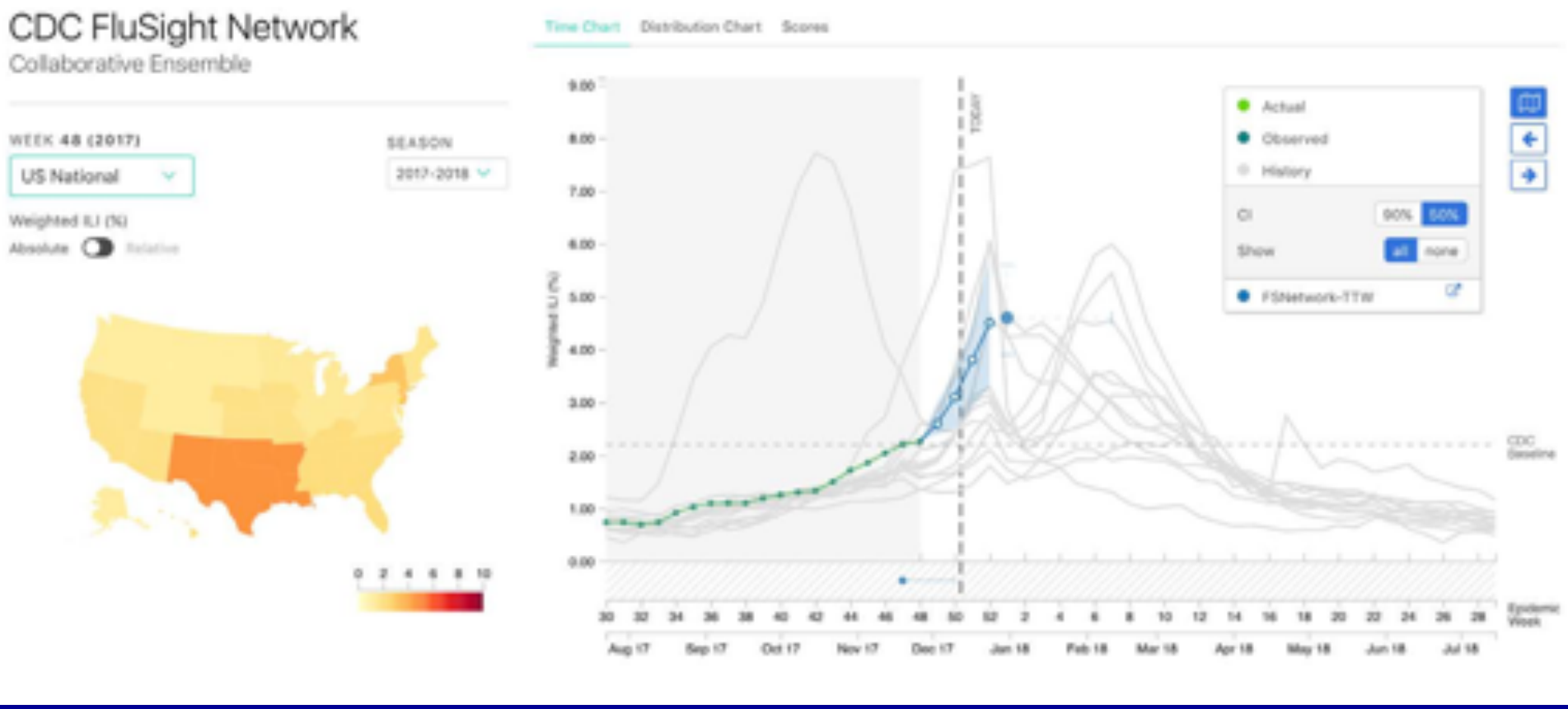
FluSight 2017-18
Seasonal Influenza Forecasting
Influenza Hospitalizations 2017-18
Forecasting laboratory confirmed influenza hospitalizations



Prof Nicholas Reich: http://flusightnetwork.io

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

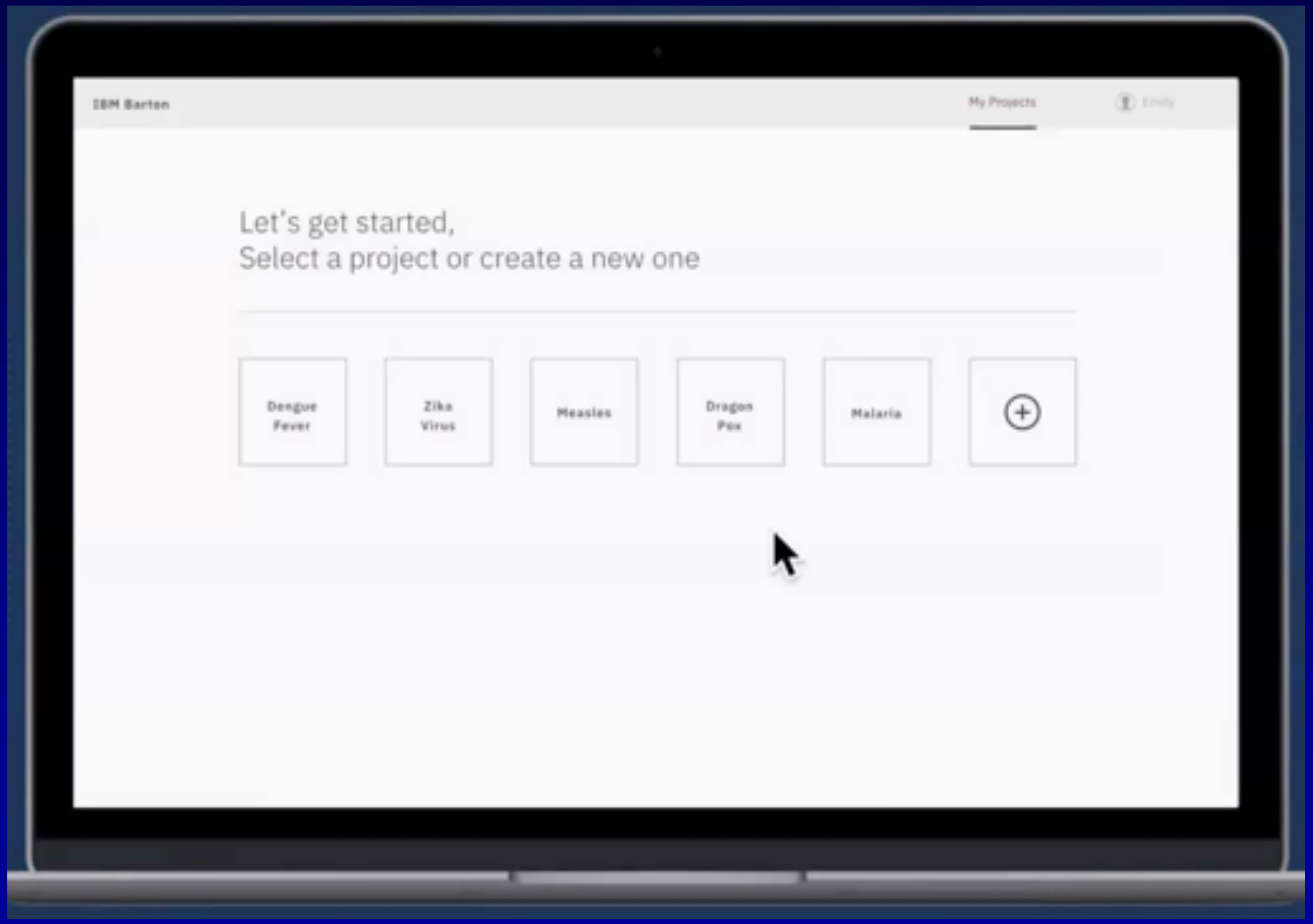
However, things are changing

- ✓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’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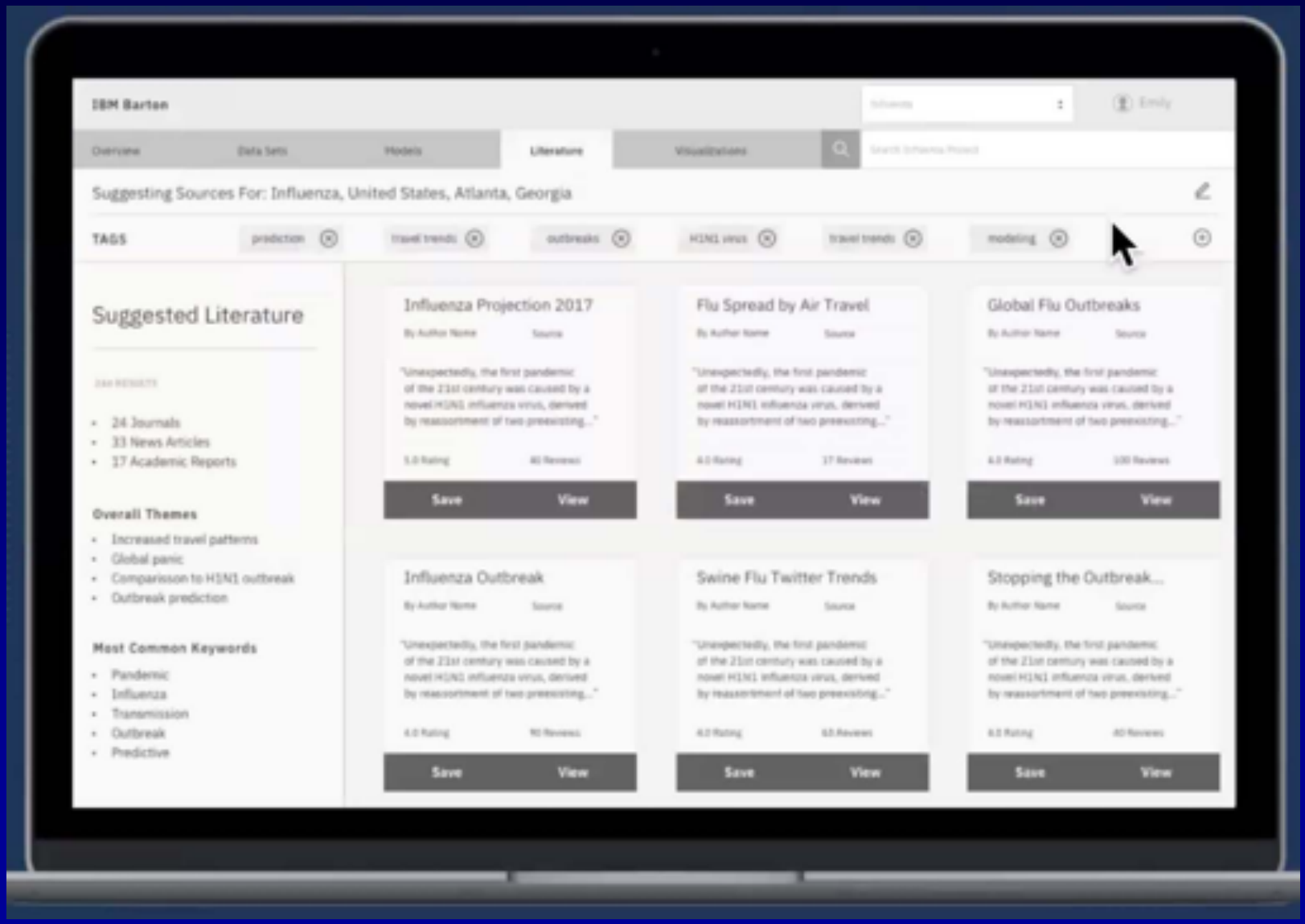
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Whooping C
Epidemic

By JESSE McKINLEY
Published: June 23, 2010

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often is mistaken f
told, 910 cases hav
under investigatio
largest in the state

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Whooping-cough booster may soon be added The CDC advisory panel, however, rejected adding chicken pox, a setback for vaccine-maker Merck.
July 1, 2005

Chemical In Child Vaccines Stirs Debate
July 8, 1999

Web Site Makes Case For Vaccines Children's Hospital Of Phila. Aims To Ease Fears About The Growing Number Of Shots Required.
October 16, 2000

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Cases of whooping cough in United States highest since 1959

December 12, 2012 | By Don Sapatkin, Inquirer Staff Writer

With pertussis at its highest level nationally in a half-century, the Philadelphia region has been weathering a spike that in some places is more than triple the previous record set two years ago.

"We're sort of way off the scale this year," said Stephen Ostroff, Pennsylvania's acting physician general. "It really started picking up in the summer, and once kids got back to school, the [pertussis] was already there."

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.

Story continues below

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THE WEEKEND AUSTRALIAN MAGAZINE

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How worried should we be about the whooping cough epidemic?

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

NAVIGATE TO A SECTION | 0 SAVED STORIES

Newborn babies are most at risk of death from the disease

Babies are offered a whooping cough vaccine at two, three and four months of age

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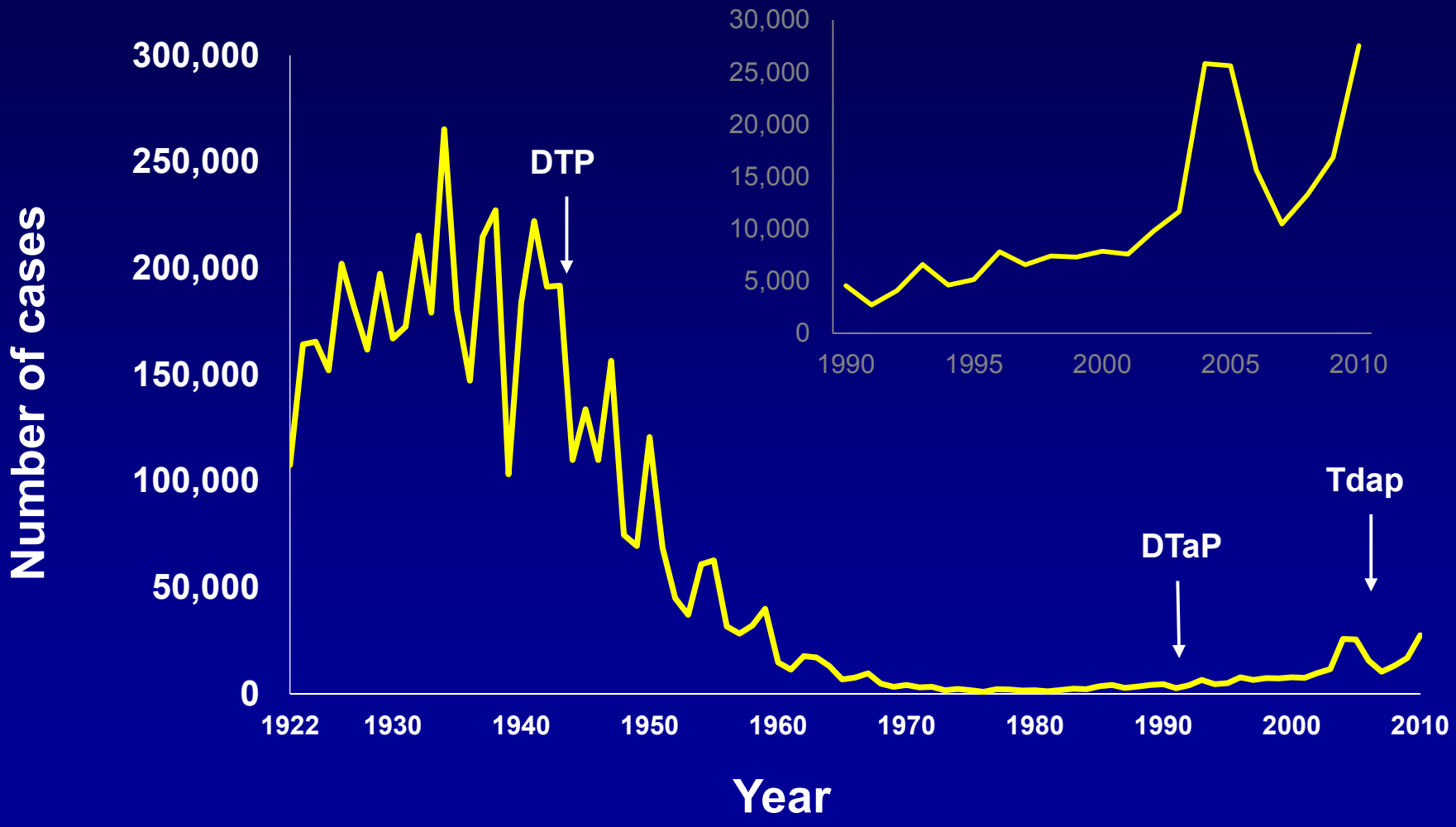
Reported pertussis cases – 1922-2010



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?

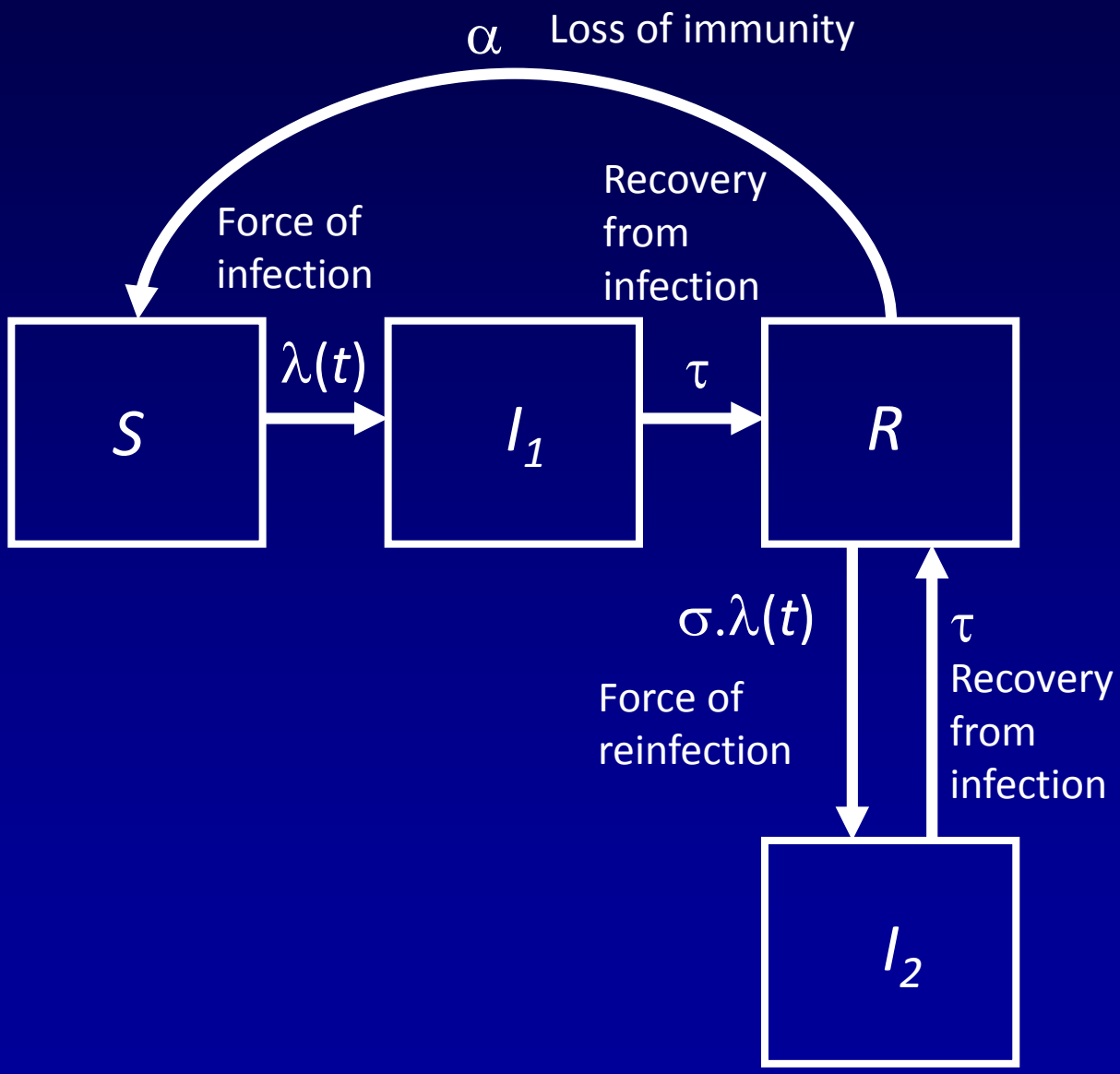

α
Loss of immunity
Force of infection
Recovery from infection
λ(t)
τ
S
I1
R
σ.λ(t)
Force of reinfection
τ
Recovery from infection
I2

Table 1. Descriptions of the nested models that were fitted to the NNDSS incidence data.

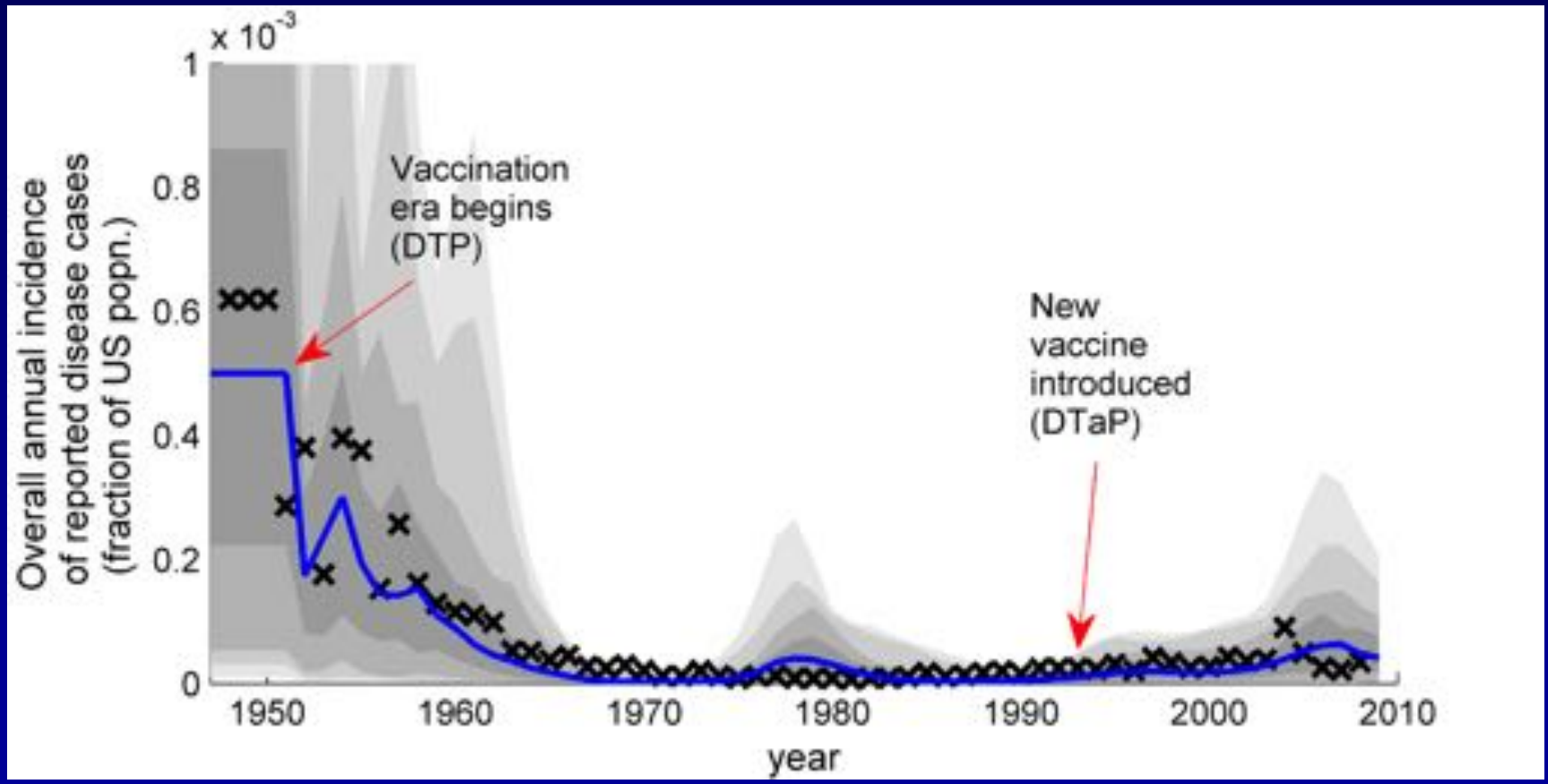
Model	Description	DIC
1	Protection duration of whole cell vaccine same as natural infection; acellular vaccine same as whole-cell	-9720
2	Protection duration of whole cell vaccine same as natural infection; different efficacy for acellular vaccine	-9570
3	Protection duration of whole cell vaccine same as natural infection; different protection duration for acellular vaccine;	-9250
4	Protection duration of whole cell vaccine different from natural infection; acellular vaccine same as whole-cell	-9800
5	Protection duration of whole cell vaccine same as natural infection; protection duration and efficacy different for acellular vaccine	-8422
6	Whole cell vaccine protection duration different from natural infection; different efficacy for acellular vaccine	-9183
7	Whole cell vaccine protection duration different from natural infection; different protection duration for acellular vaccine	-9230
8	Whole cell vaccine protection duration different from natural infection; protection duration and efficacy different for acellular vaccine	-8417

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

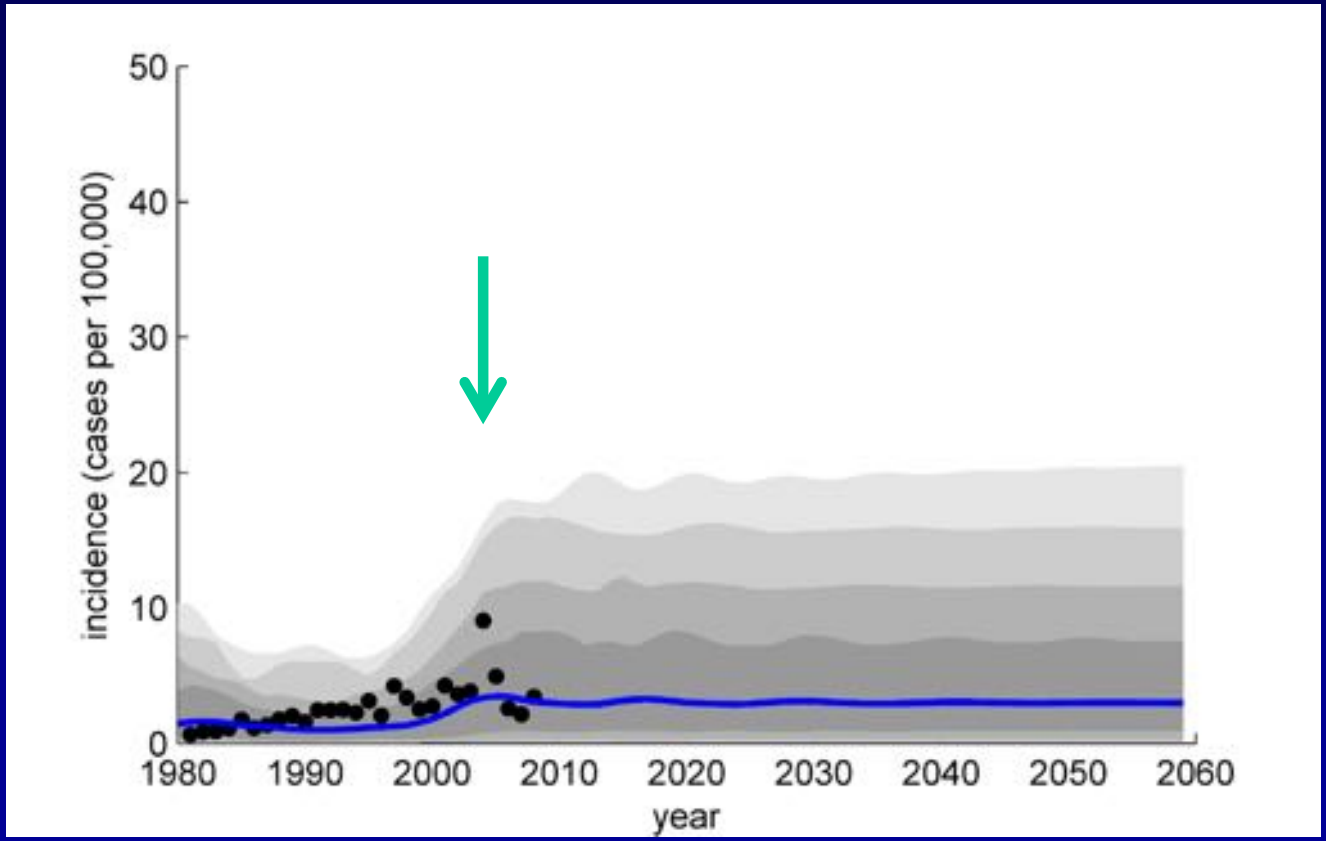
doi:10.1371/journal.pcbi.1004138.t001

Gambhir M, Clark TA, Cauchemez S, Tartof SY, Swerdlow DL, et al. (2015) A Change in Vaccine Efficacy and Duration of Protection Explains Recent Rises in Pertussis Incidence in the United States. PLoS Comput Biol 11(4): e1004138. doi:10.1371/journal.pcbi.1004138
http://journals.plos.org/ploscompbiol/article?id=info:doi/10.1371/journal.pcbi.1004138

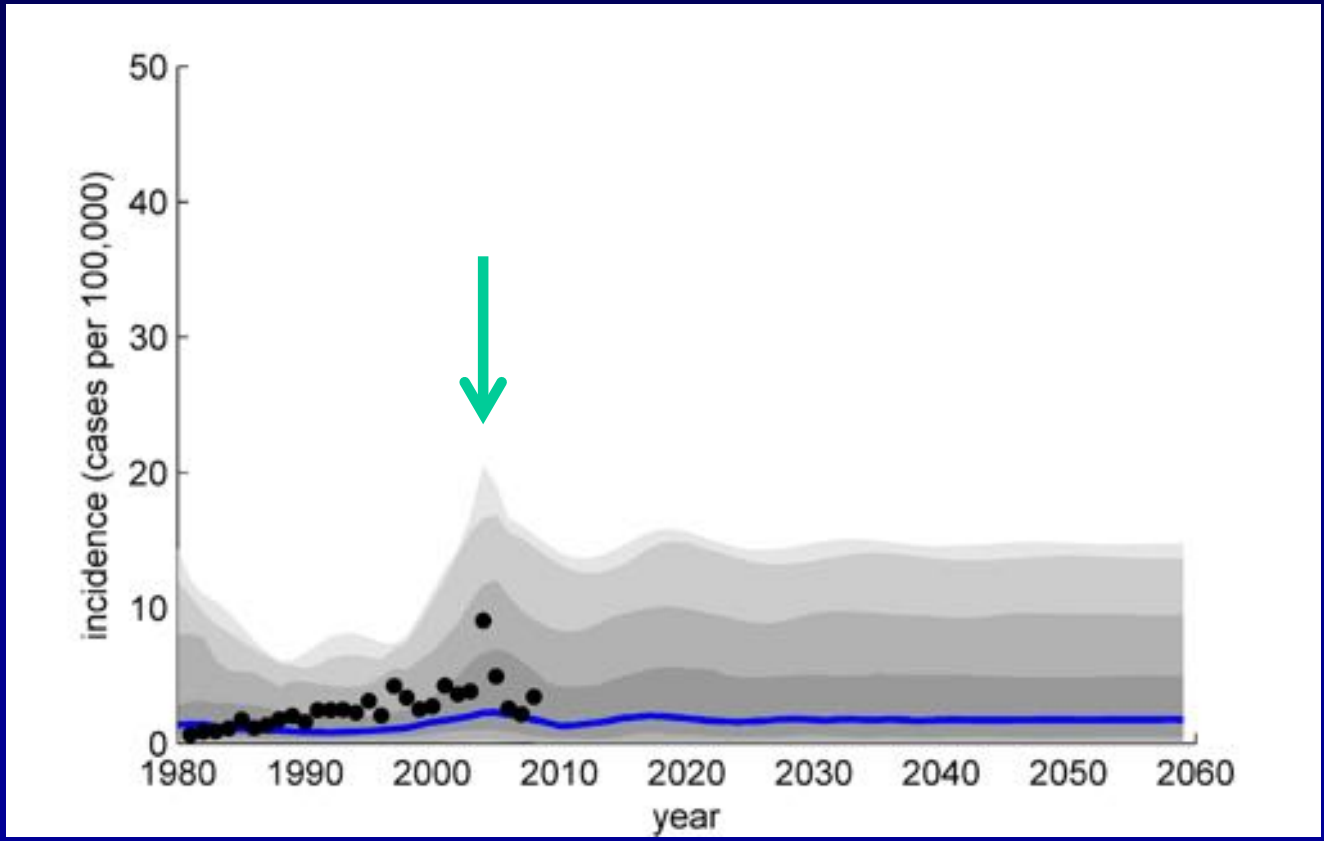
Total incidence since vaccination began: model vs. data



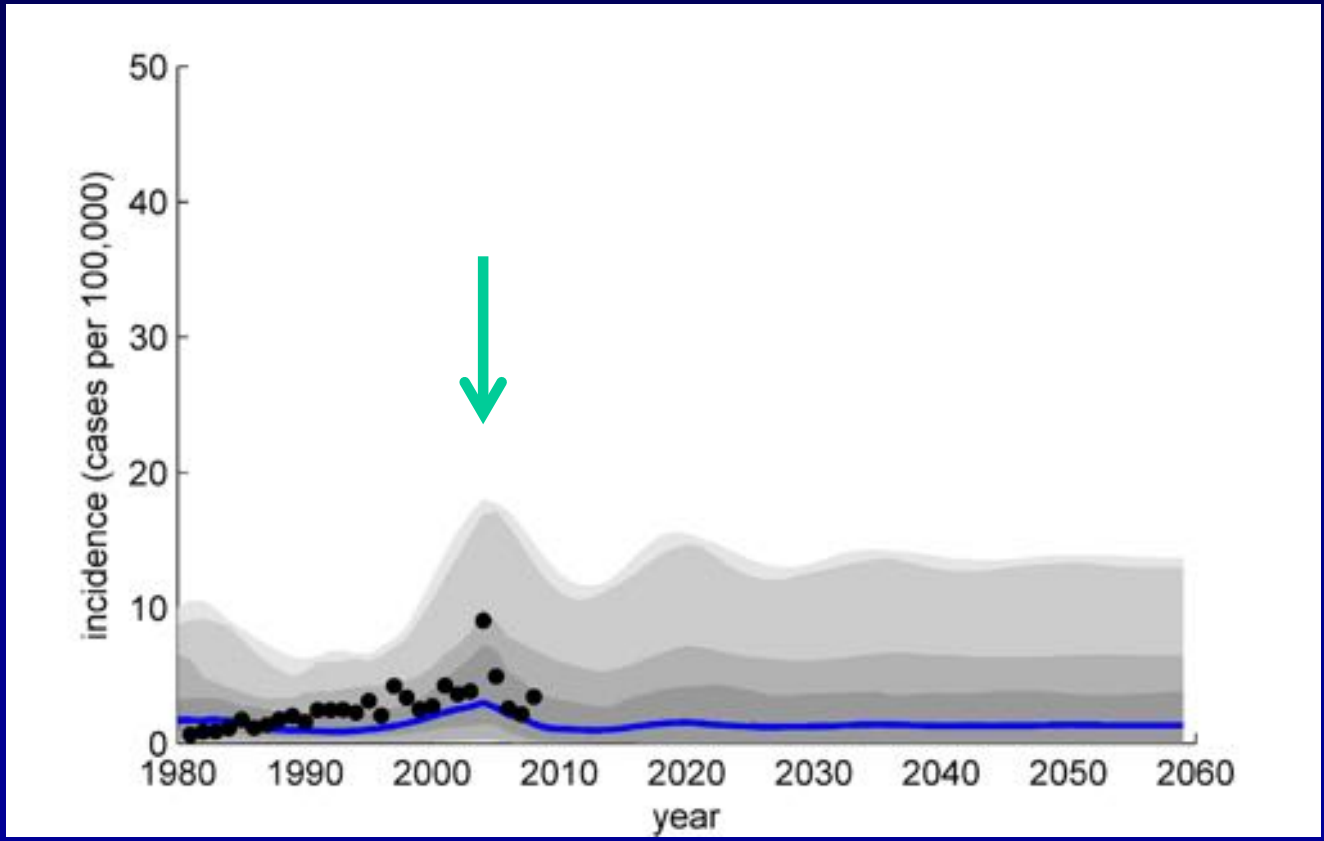
Projecting forward in time



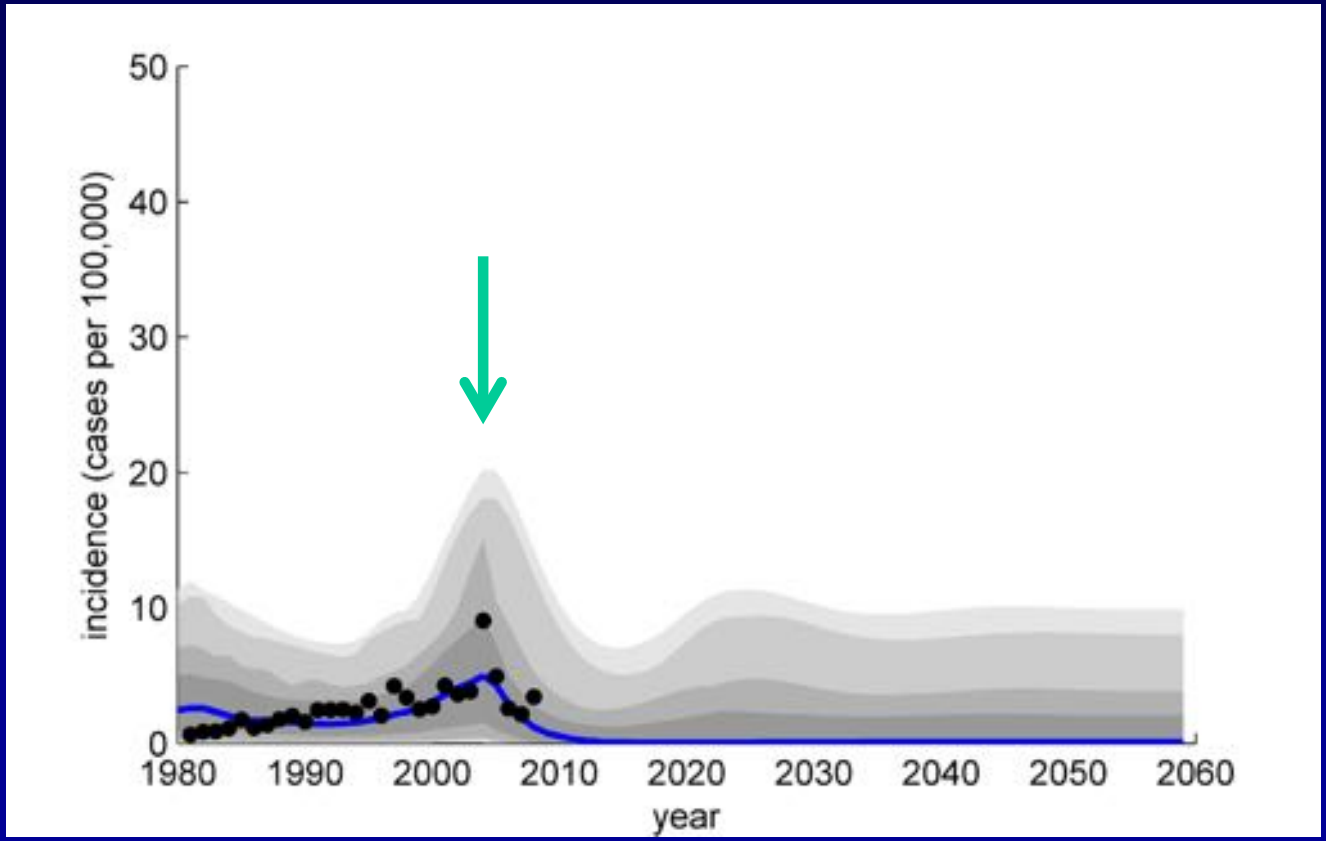
*VE*coverage*=10%



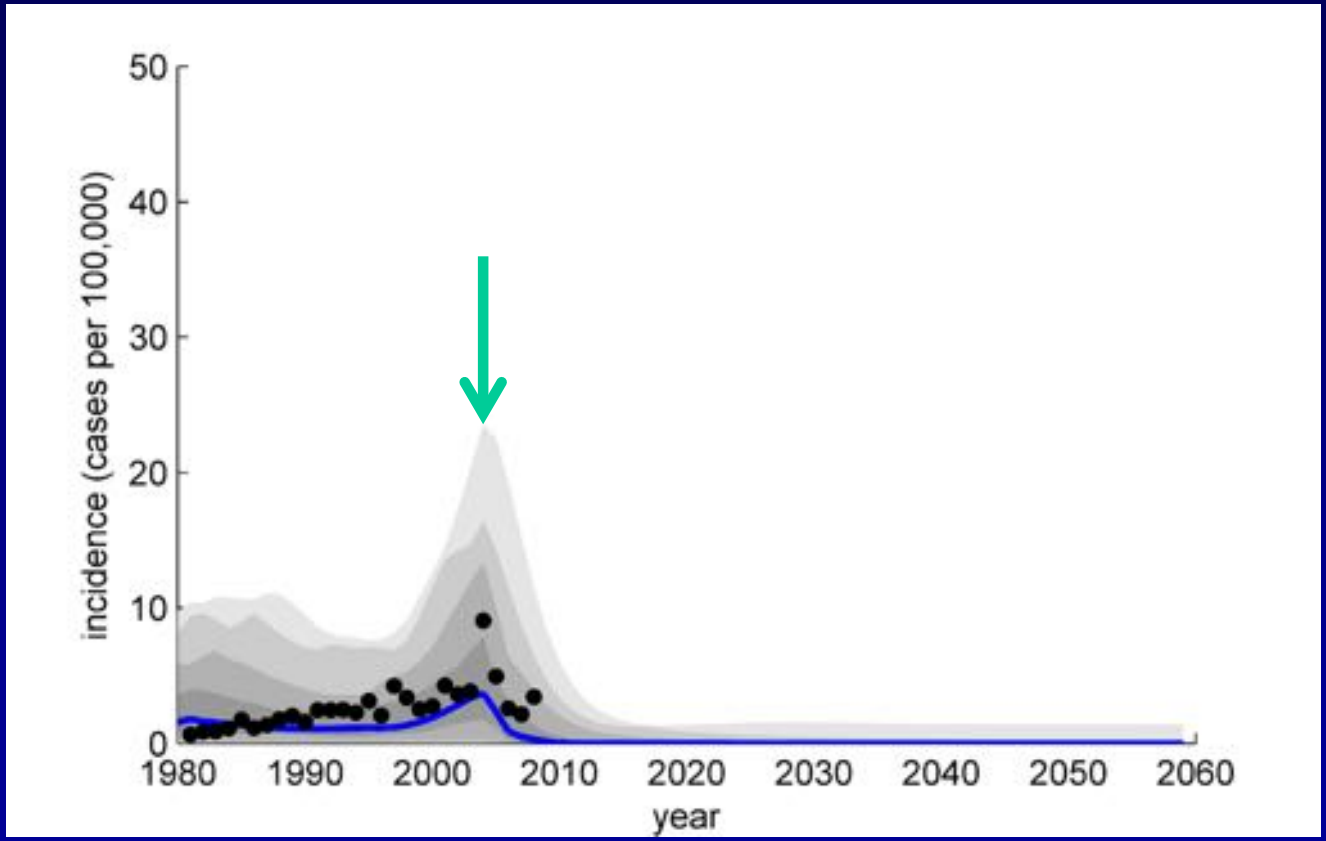
40%


incidence (cases per 100,000)
50
40
30
20
10
0
1980
1990
2000
2010
2020
2030
2040
2050
2060
year

70%


incidence (cases per 100,000)
50
40
30
20
10
0
1980
1990
2000
2010
2020
2030
2040
2050
2060
year

90%


incidence (cases per 100,000)
50
40
30
20
10
0
1980
1990
2000
2010
2020
2030
2040
2050
2060
year

PLOS | COMPUTATIONAL BIOLOGY

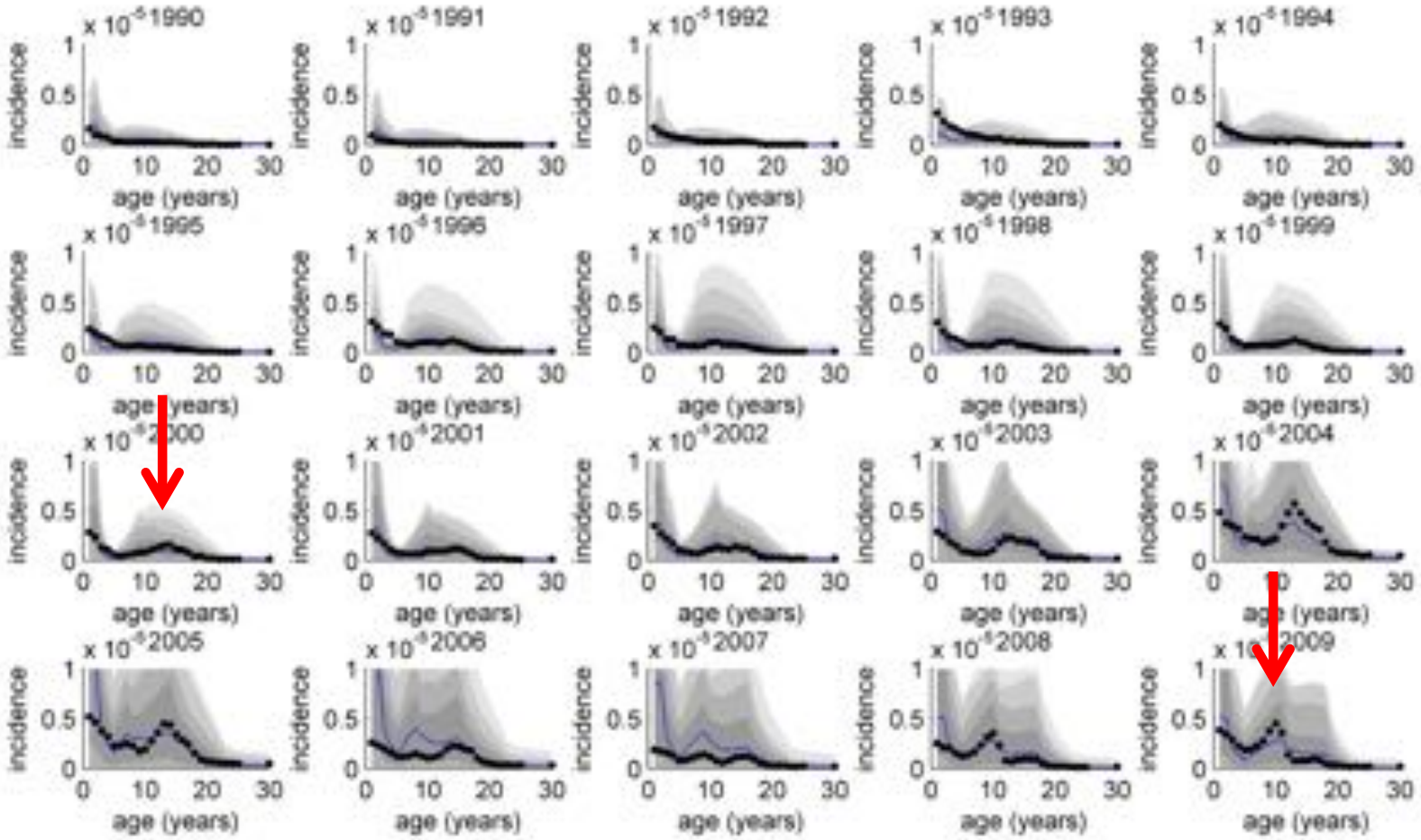
RESEARCH ARTICLE

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

Manoj Gambhir[1,2,3]*, Thomas A. Clark[4], Simon Cauchemez[5,6], Sara Y. Tartof[7], David L. Swerdlow[2,8], Neil M. Ferguson[5]

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



Gambhir M, Clark TA, Cauchemez S, Tartof SY, Swerdlow DL, et al. (2015) A Change in Vaccine Efficacy and Duration of Protection Explains Recent Rises in Pertussis Incidence in the United States. PLoS Comput Biol 11(4): e1004138. doi:10.1371/journal.pcbi.1004138
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

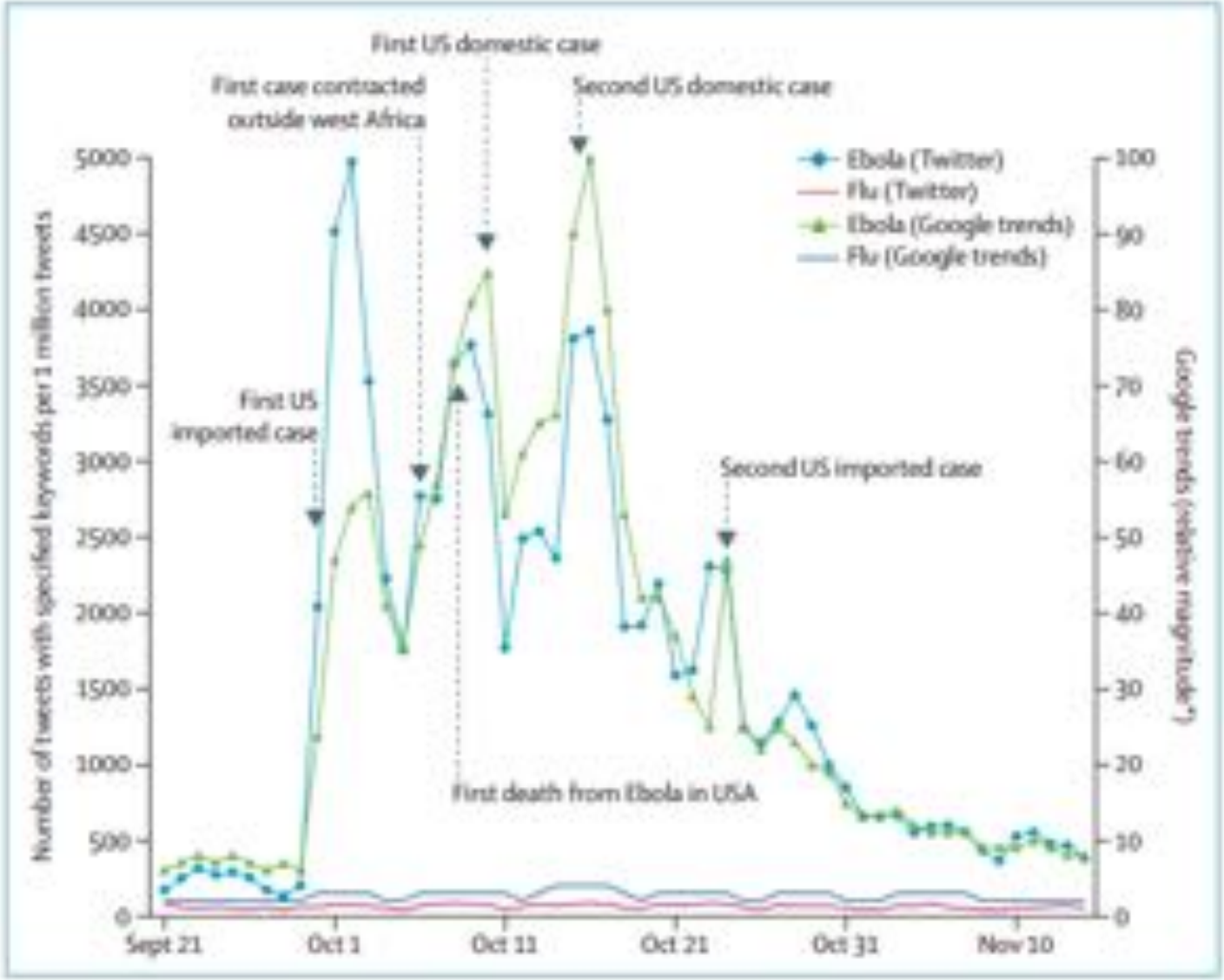
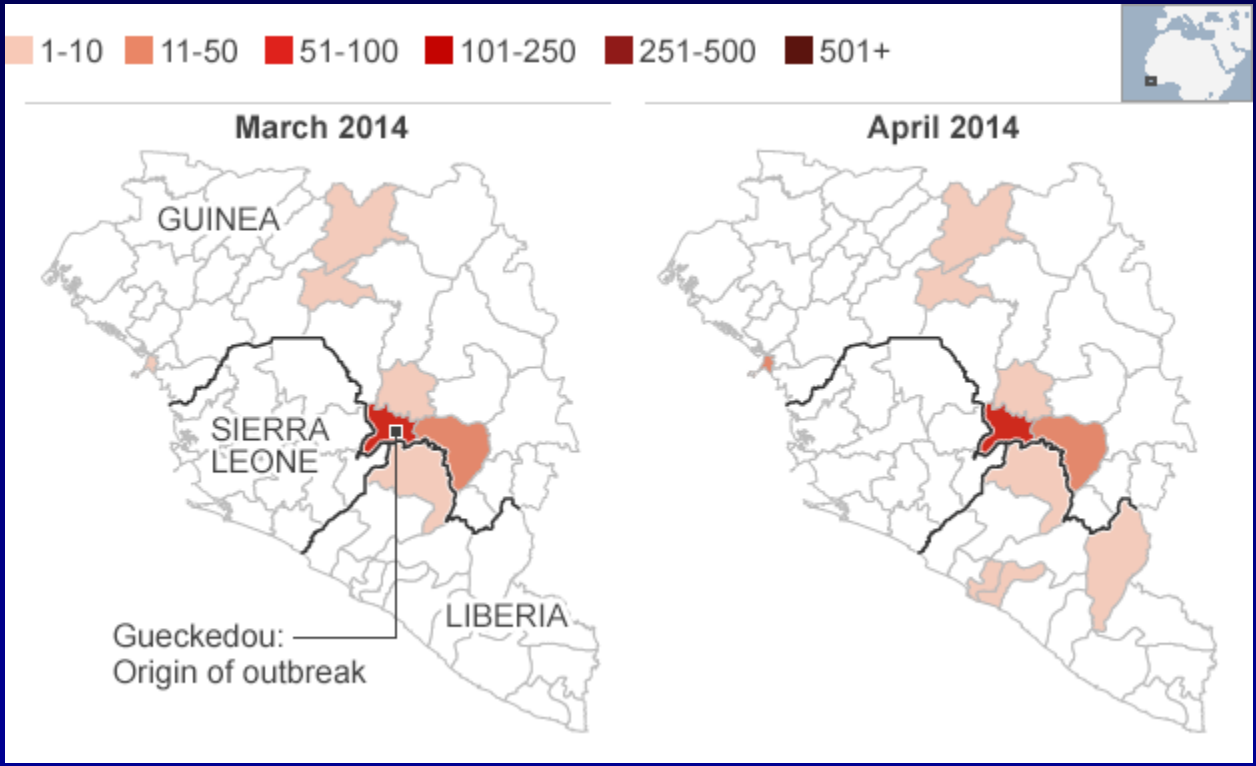
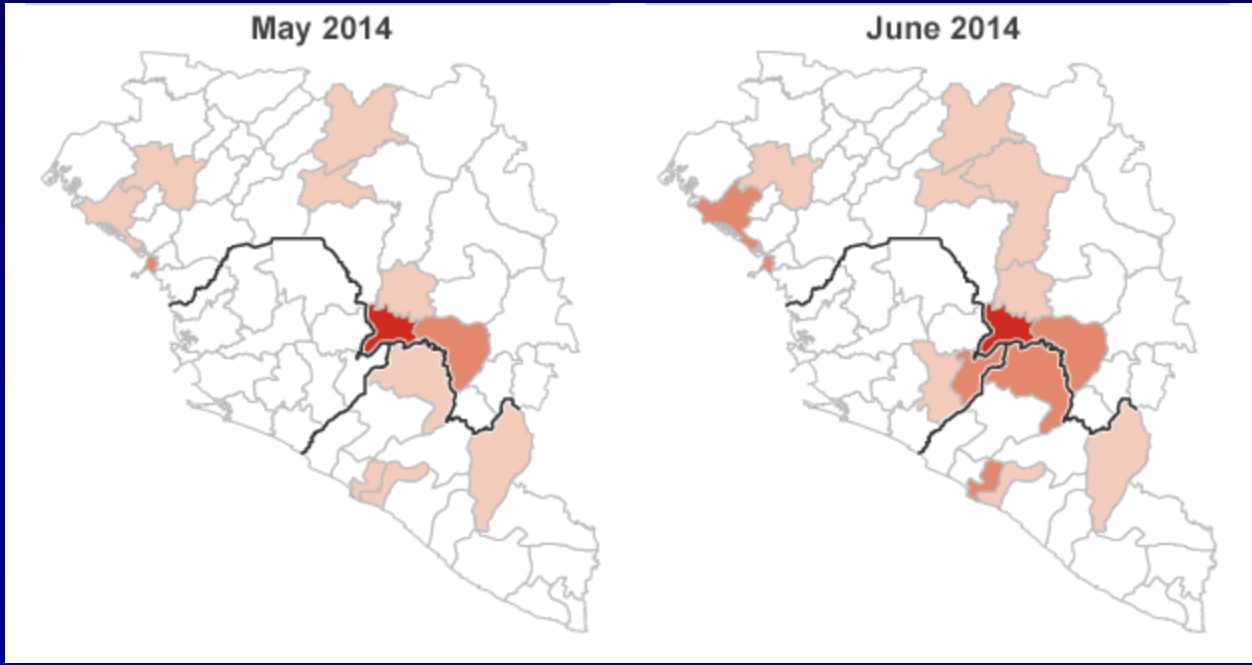
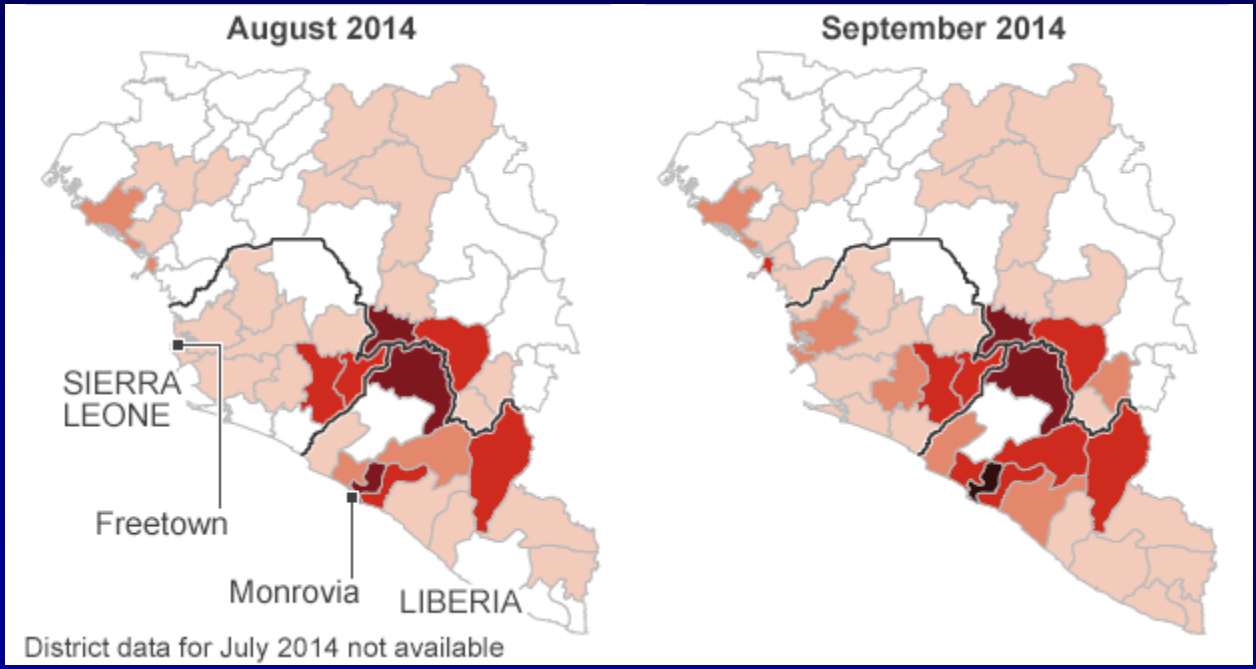


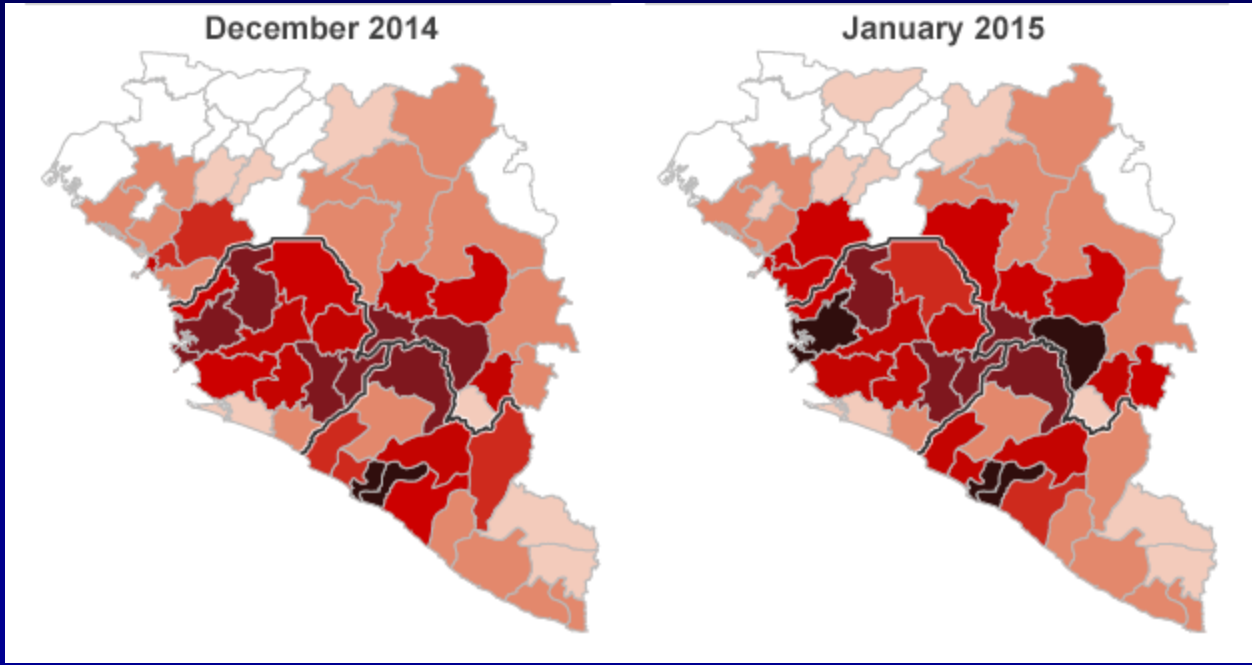
Figure: Temporal trends on Twitter and Google about Ebola and influenza (flu) before, during, and after Ebola cases in the USA, September to November, 2014

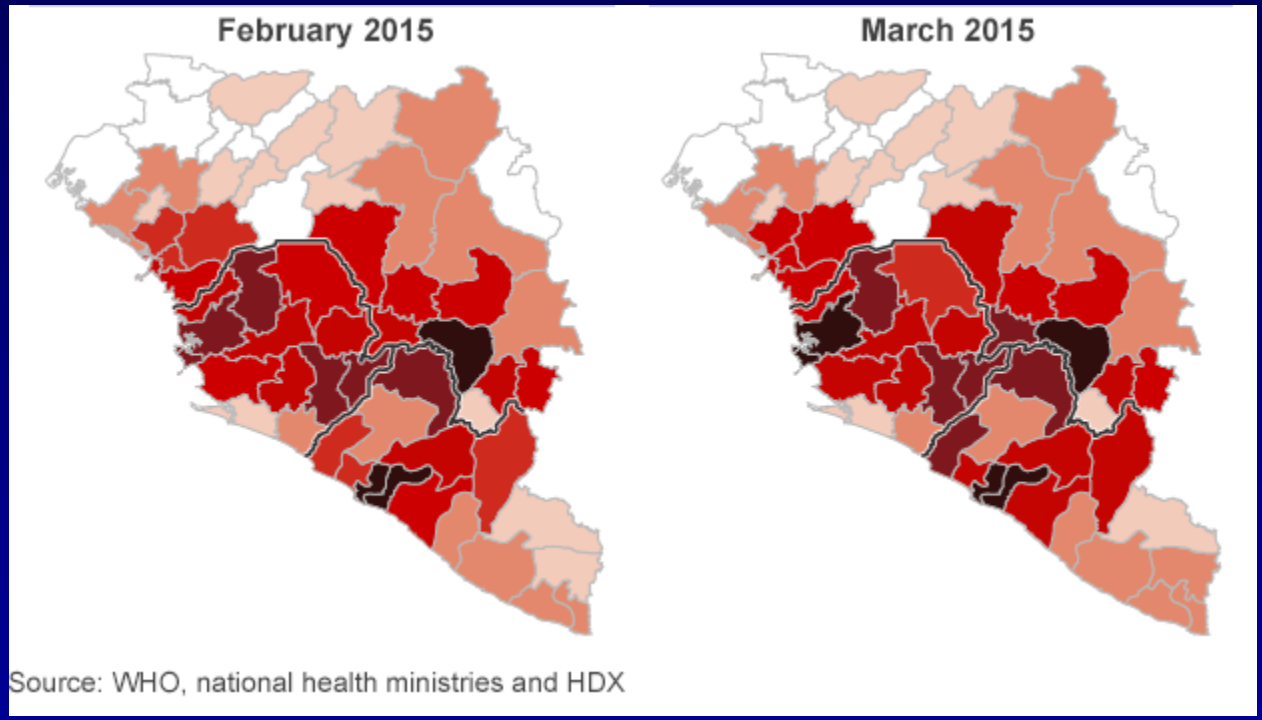
*Numbers are relative to the highest number of searches done on Google (for Ebola on Oct 16).


1-10
11-50
51-100
101-250
251-500
501+
March 2014
April 2014
GUINEA
SIERRA LEONE
LIBERIA
Gueckedou:
Origin of outbreak

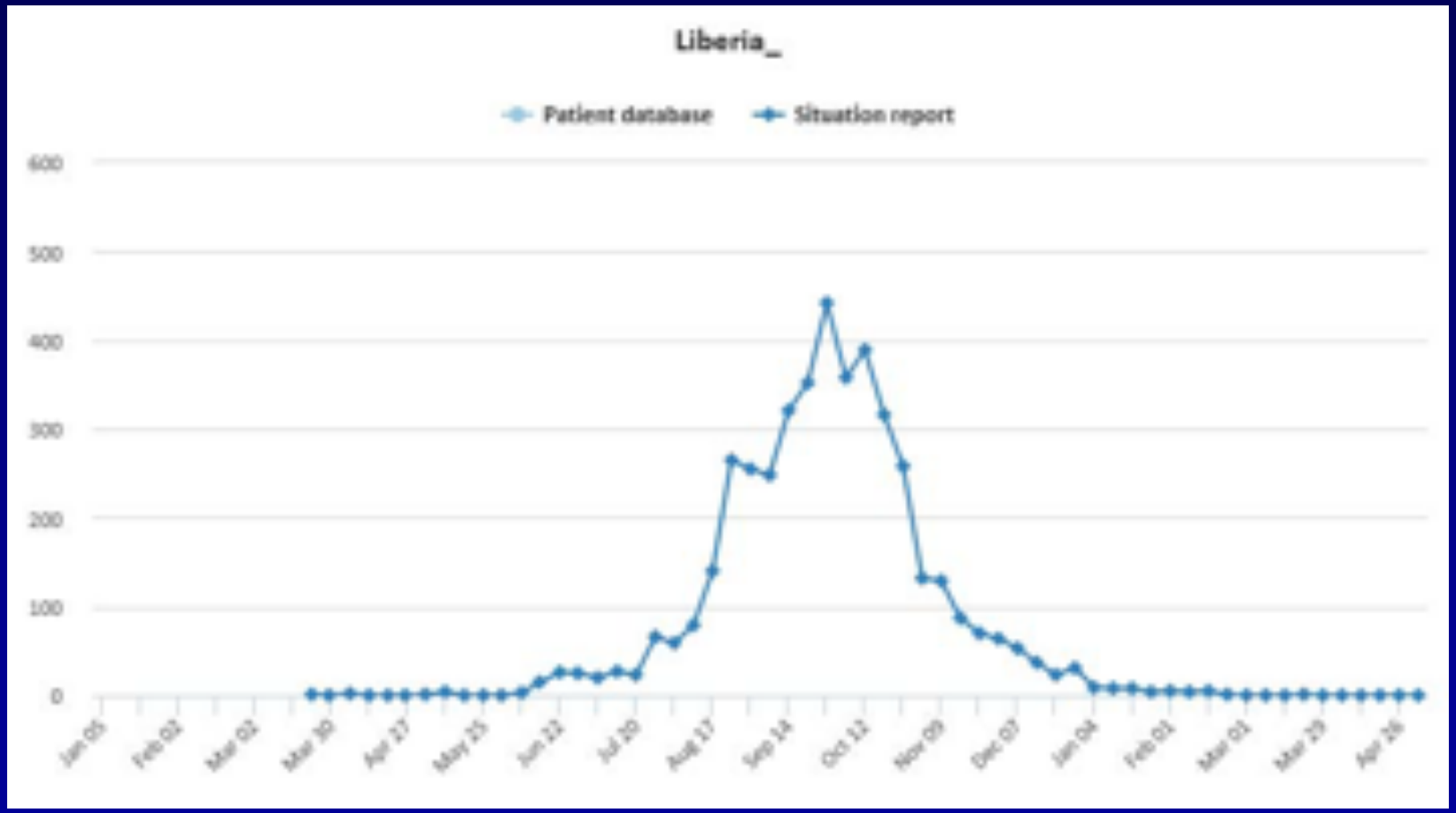

May 2014
June 2014


August 2014
September 2014
SIERRA LEONE
Freetown
Monrovia
LIBERIA
District data for July 2014 not available

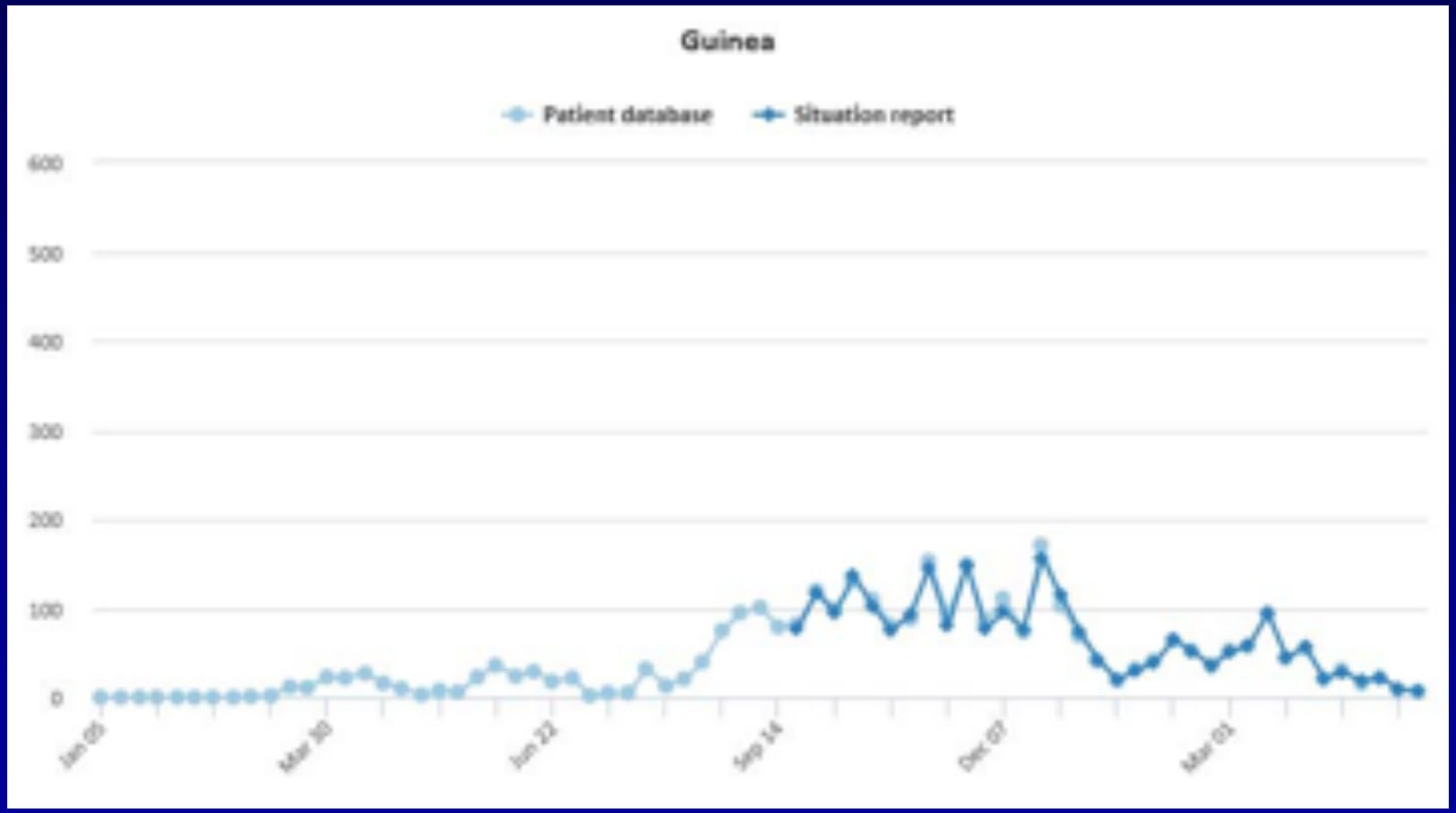

December 2014
January 2015

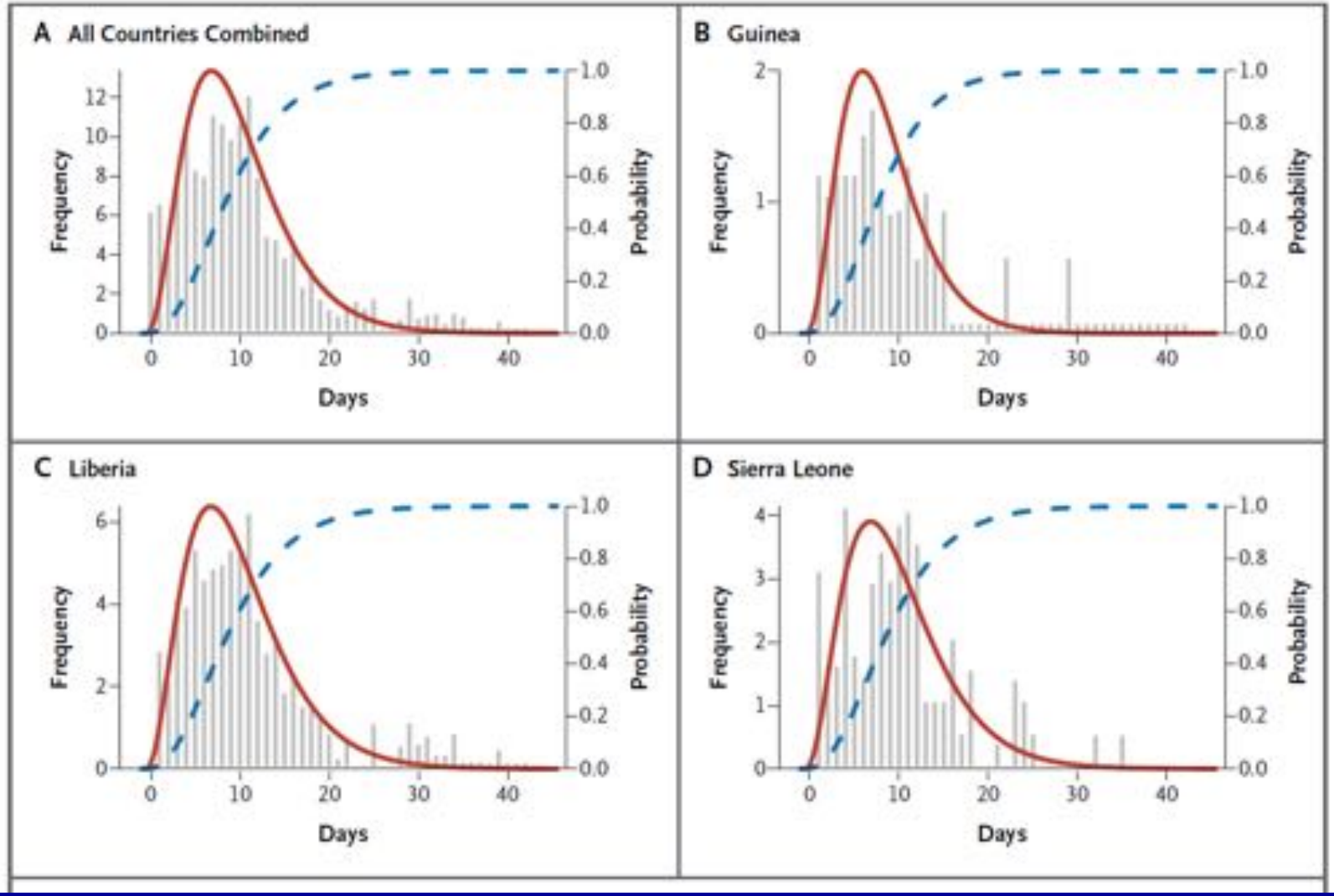


Source: WHO, national health ministries and HDX


Liberia_
Patient database
Situation report
600
500
400
300
200
100
0
Jan 05
Feb 02
Mar 02
Mar 30
Apr 27
May 25
Jun 22
Jul 20
Aug 17
Sep 14
Oct 13
Nov 09
Dec 07
Jan 04
Feb 01
Mar 01
Mar 29
Apr 26


Sierra Leone
Patient database
Situation report
600
500
400
300
200
100
0
Jan 05
Mar 30
Jun 22
Sep 14
Dec 07
Mar 01


Guinea
Patient database
Situation report
600
500
400
300
200
100
0
Jan 05
Mar 30
Jun 22
Sep 14
Dec 07
Mar 01


A All Countries Combined
B Guinea
C Liberia
D Sierra Leone
Frequency
Probability
Days
0
10
20
30
40
0.0
0.2
0.4
0.6
0.8
1.0

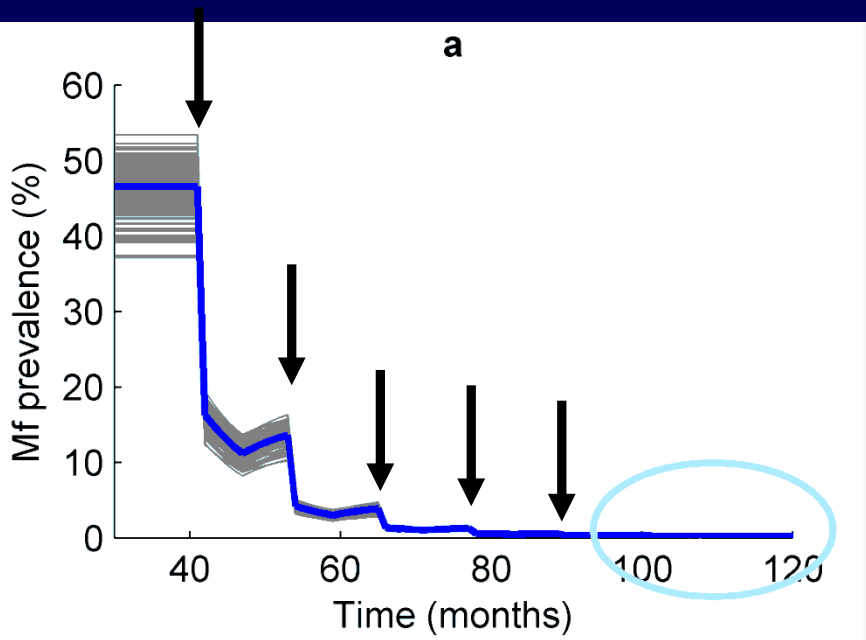

a
60
50
40
30
20
10
0
Mf prevalence (%)
40
60
80
100
120
Time (months)

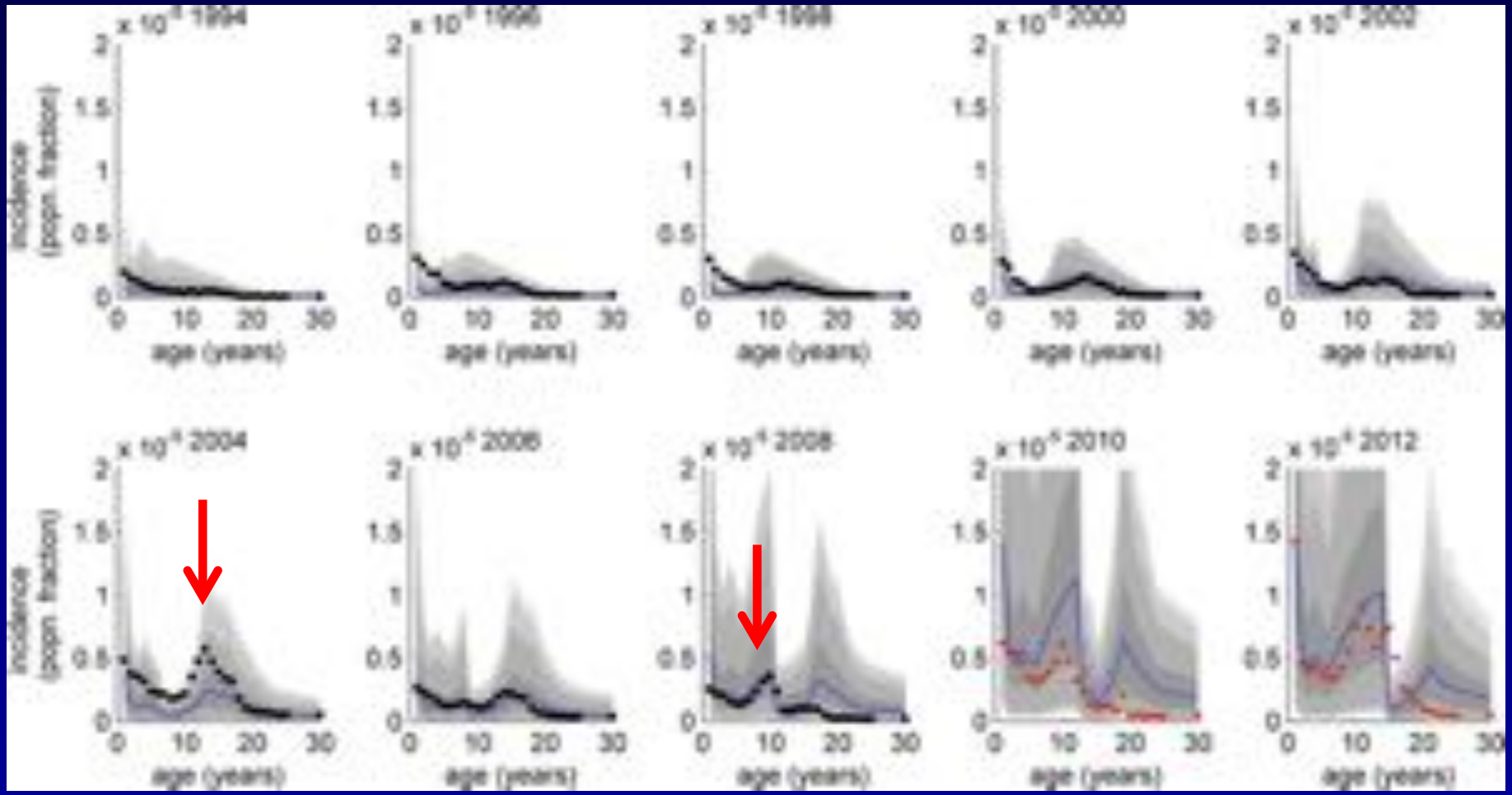
Table 2. Parameter estimates for the best-fitting model, Model 8 (models outlined in Table 1).

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

doi:10.1371/journal.pcbi.1004138.t002

Gambhir M, Clark TA, Cauchemez S, Tartof SY, Swerdlow DL, et al. (2015) A Change in Vaccine Efficacy and Duration of Protection Explains Recent Rises in Pertussis Incidence in the United States. PLoS Comput Biol 11(4): e1004138. 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.



Gambhir M, Clark TA, Cauchemez S, Tartof SY, Swerdlow DL, et al. (2015) A Change in Vaccine Efficacy and Duration of Protection Explains Recent Rises in Pertussis Incidence in the United States. PLoS Comput Biol 11(4): e1004138. doi:10.1371/journal.pcbi.1004138
http://journals.plos.org/ploscompbiol/article?id=info:doi/10.1371/journal.pcbi.1004138

Health | Nation | Nation & World

CDC's overblown estimate of Ebola outbreak draws criticism

Originally published August 1, 2015 at 2:24 pm | *Updated August 1, 2015 at 5:51 pm*

Martin Meltzer, standing in the Emergency Operations Center at the Centers for Disease Control and Prevention in Atlanta, is a disease modeler for the agency. (David Goldman/AP)

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

$$\frac{dS}{dt}$$ *Susceptible*

$$\frac{dI}{dt}$$ *Infected*

$$\frac{dR}{dt}$$ *Recovered*

Inflow & outflow

$$\frac{dS}{dt} = \square \; \boxed{-\beta S.I}$$

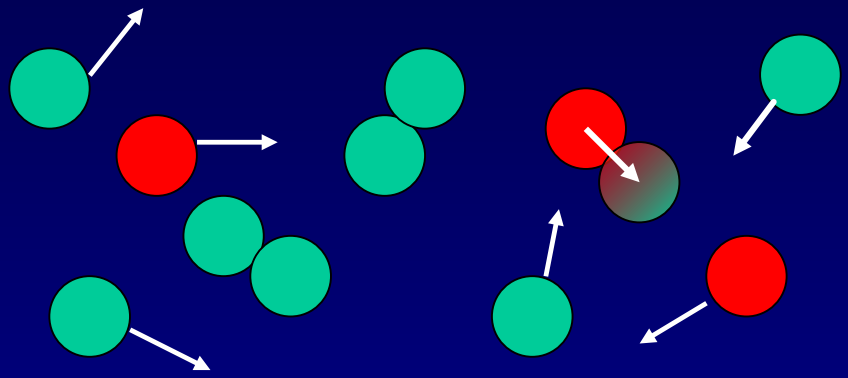
Susceptible

$$\frac{dI}{dt} = \boxed{\beta S.I} \; \boxed{-\frac{1}{d}.I}$$

Infected

$$\frac{dR}{dt} = \boxed{\frac{1}{d}.I} \; \square$$

Recovered



As infecteds increase, *rate* increases

PLOS | CURRENTS OUTBREAKS

Assessing the International Spreading Risk Associated with the 2014 West African Ebola Outbreak

SEPTEMBER 2, 2014 - RESEARCH

REVISIONS

This article is either a revised version or has previous revisions

Edition 1 - September 2, 2014

AUTHORS

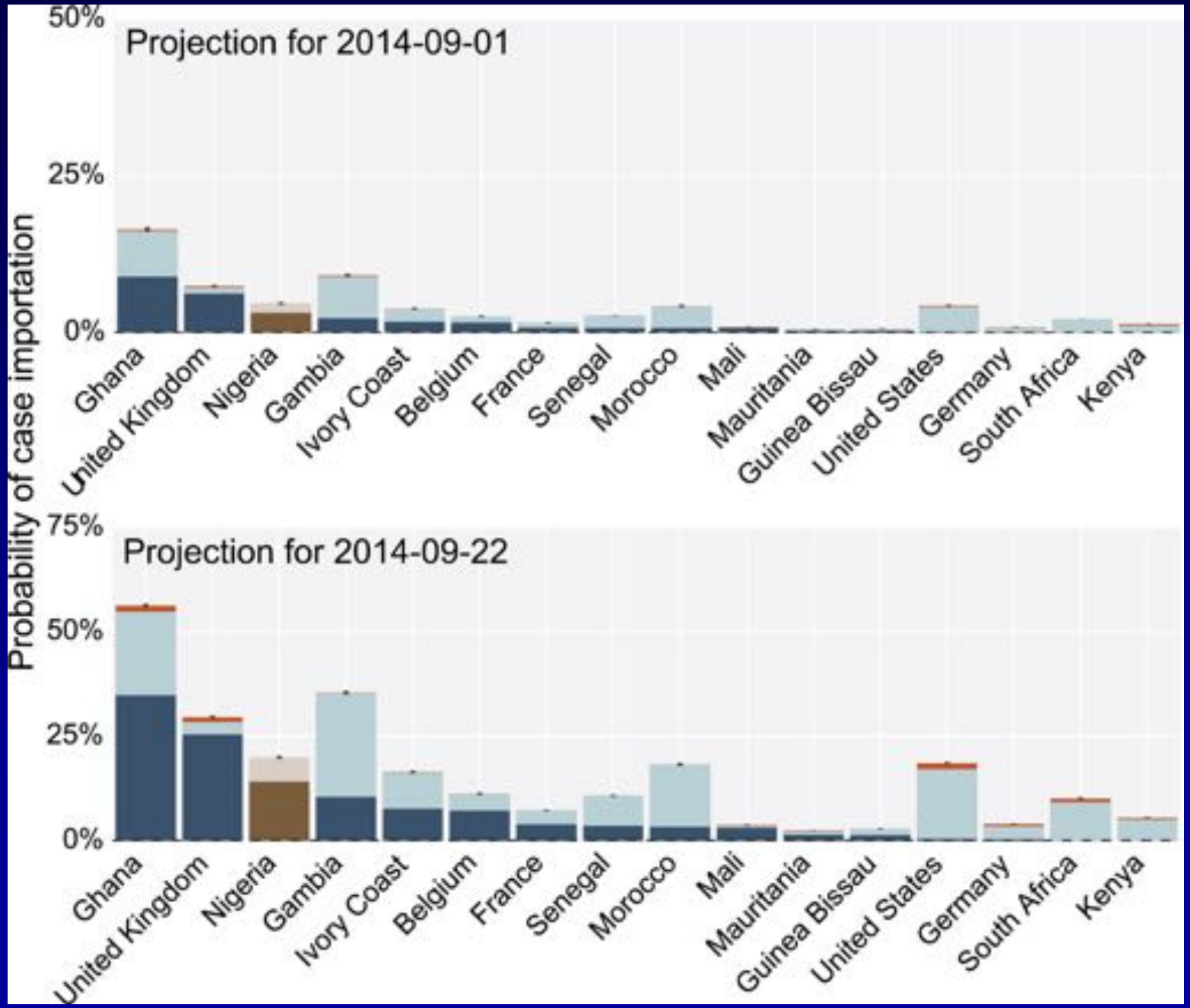
Marcelo F. C. Gomes Ana Pastore y Piontti Luca Rossi Dennis Chao Ira Longini M. Elizabeth Halloran Alessandro Vespignani

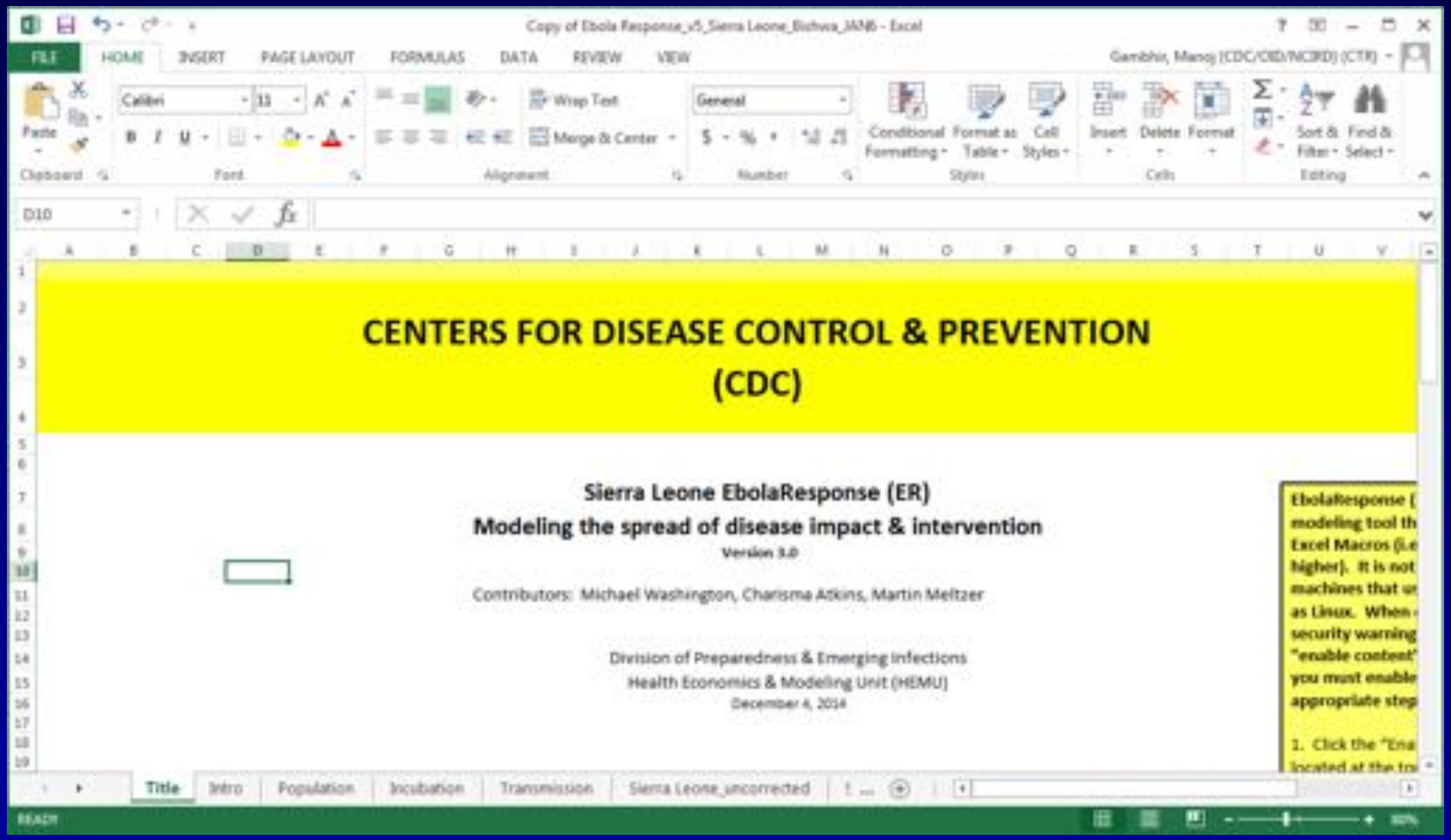
ABSTRACT

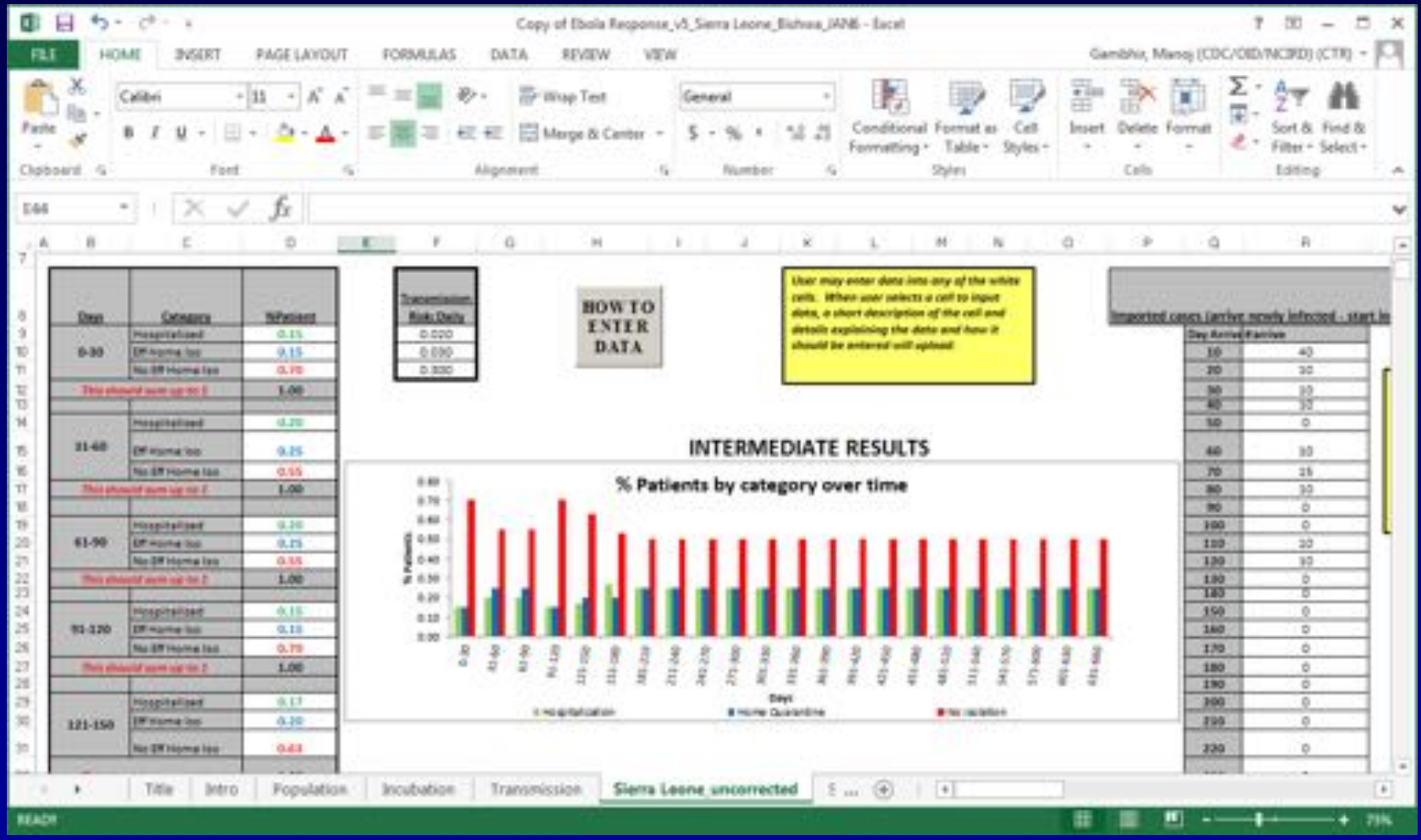
Background: The 2014 West African Ebola Outbreak is so far the largest and deadliest recorded in history. The affected countries, Sierra Leone, Guinea, Liberia, and Nigeria, have been struggling to contain and to mitigate the outbreak. The ongoing rise in confirmed and suspected cases, 2615 as of 20 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


UK
GERMANY
FRANCE
ITALY
SPAIN
CANADA
USA
MOROCCO
TURKEY
LEBANON
EGYPT
UNITED ARAB EMIRATES
SAUDI ARABIA
CHINA
INDIA
NIGER
SENEGAL
GAMBIA
GUINEA
SIERRA LEONE
LIBERIA
COTE D'IVOIRE
GHANA
NIGERIA
CAMEROON
KENYA
SOUTH AFRICA
TOP PASSENGER FLOWS:
Number of passengers (weekly)
6000-
3000-6000
1500-3000
300-1500


Projection for 2014-09-01
50%
25%
0%
Probability of case importation
Ghana
United Kingdom
Nigeria
Gambia
Ivory Coast
Belgium
France
Senegal
Morocco
Mali
Mauritania
Guinea Bissau
United States
Germany
South Africa
Kenya
Projection for 2014-09-22
75%
50%
25%
0%
Ghana
United Kingdom
Nigeria
Gambia
Ivory Coast
Belgium
France
Senegal
Morocco
Mali
Mauritania
Guinea Bissau
United States
Germany
South Africa
Kenya

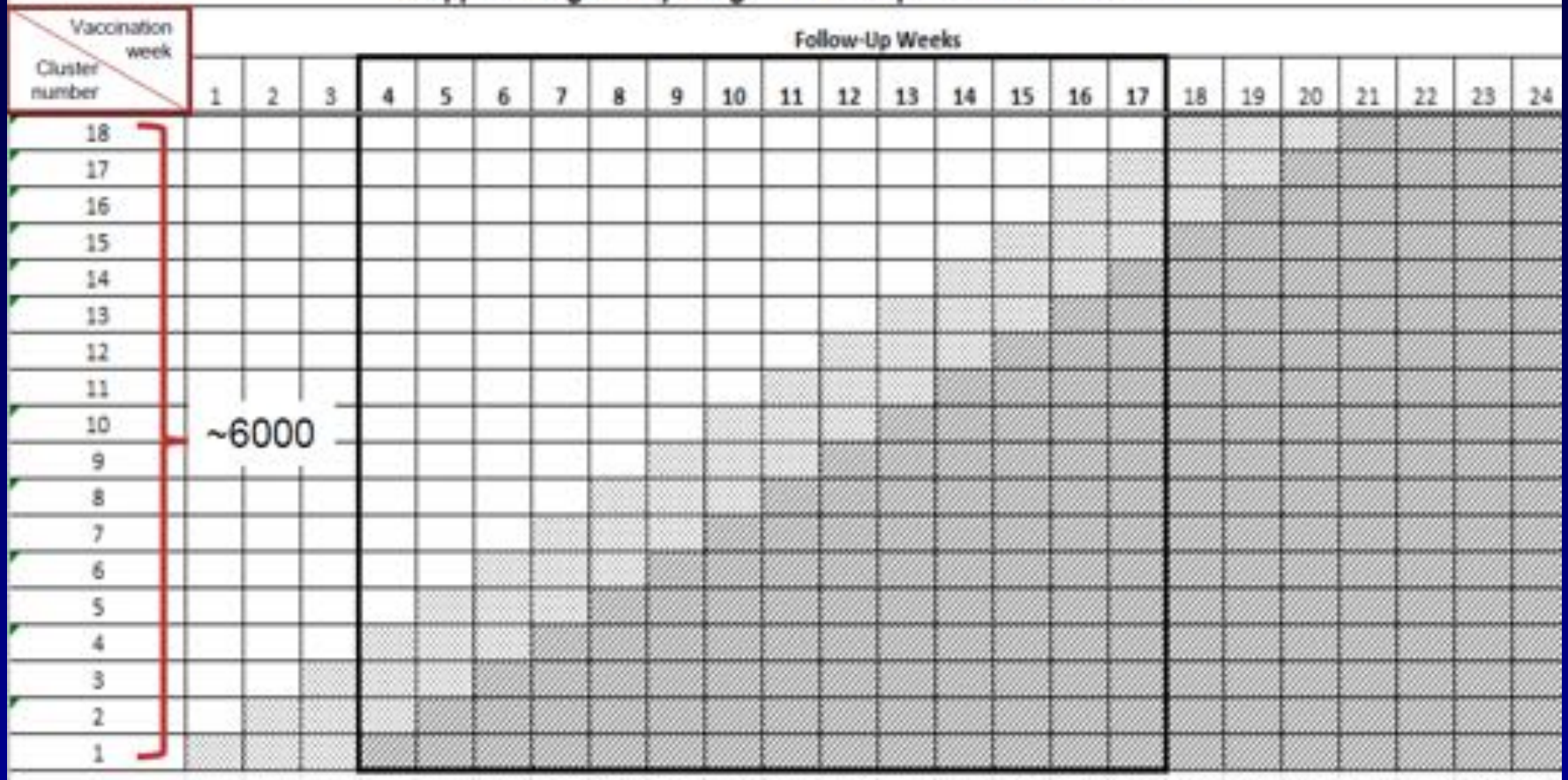

Copy of Ebola Response_v5_Sierra Leone_Bichwa_JAN6 - Excel
FILE
HOME
INSERT
PAGE LAYOUT
FORMULAS
DATA
REVIEW
VIEW
Gambhir, Manoj (CDC/OID/NCIRD) (CTR)
Paste
Calibri
11
Wrap Text
Merge & Center
General
Conditional Formatting
Format as Table
Cell Styles
Insert
Delete
Format
Sort & Filter
Find & Select
Clipboard
Font
Alignment
Number
Styles
Cells
Editing
D10
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
EbolaResponse (
modeling tool th
Excel Macros (i.e
higher). It is not
machines that u
as Linux. When
security warning
"enable content"
you must enable
appropriate step
1. Click the "Ena
located at the to
Title
Intro
Population
Incubation
Transmission
Sierra Leone_uncorrected
READY


Copy of Ebola Response_v5_Sierra Leone_Bishwa_JANB - Excel
HOME
INSERT
PAGE LAYOUT
FORMULAS
DATA
REVIEW
VIEW
Day
Category
%Patient
0-30
31-60
61-90
91-120
121-150
Transmission Risk: Daily
0.020
0.030
0.030
HOW TO ENTER DATA
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
Imported cases (arrive newly infected - start in
Day Arrive
arrive
INTERMEDIATE RESULTS
% Patients by category over time
% Patients
Days
Title
Intro
Population
Incubation
Transmission
Sierra Leone uncorrected
READY

Questions from leadership

What's a viable vaccine trial design during the outbreak?

Stepped wedge study design - 18 week phase-in of vaccination



type of person-time		proportions
unvaccinated		0.50
vaccinated, seroconverting		n/a
vaccinated, seroconvered		0.50

Bolded square highlights follow-up time usable for efficacy analyses, excluding 21 day sero-conversion time. Usable follow-up weeks contain both unvaccinated and vaccinated cohort time.

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

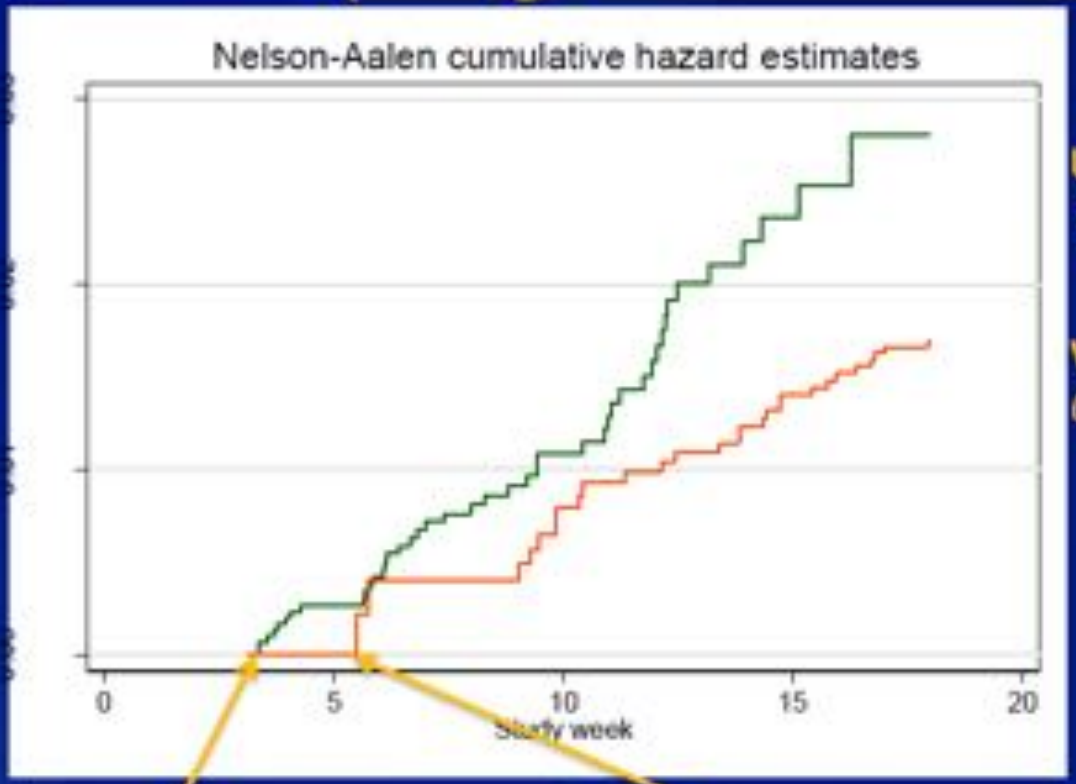
Will an e.g. Cox Proportional Hazards approach be able to account for:

-Declining background disease risk

-Clustering of disease risk

-Healthy vaccinee effect

Example simulation (single model run):



Unvaccinated: 43 cases
0.81 cases/person-month

Vaccinated: 27 cases
0.51 cases/person-month

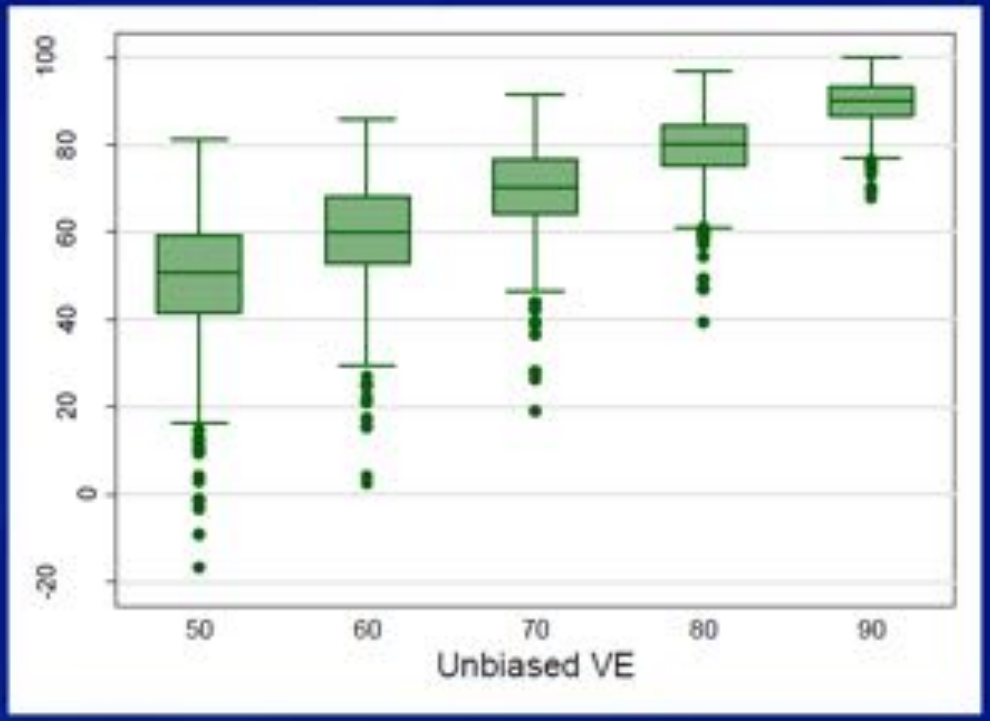
No cases included until first vaccinee reaches end of seroconversion period

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%.

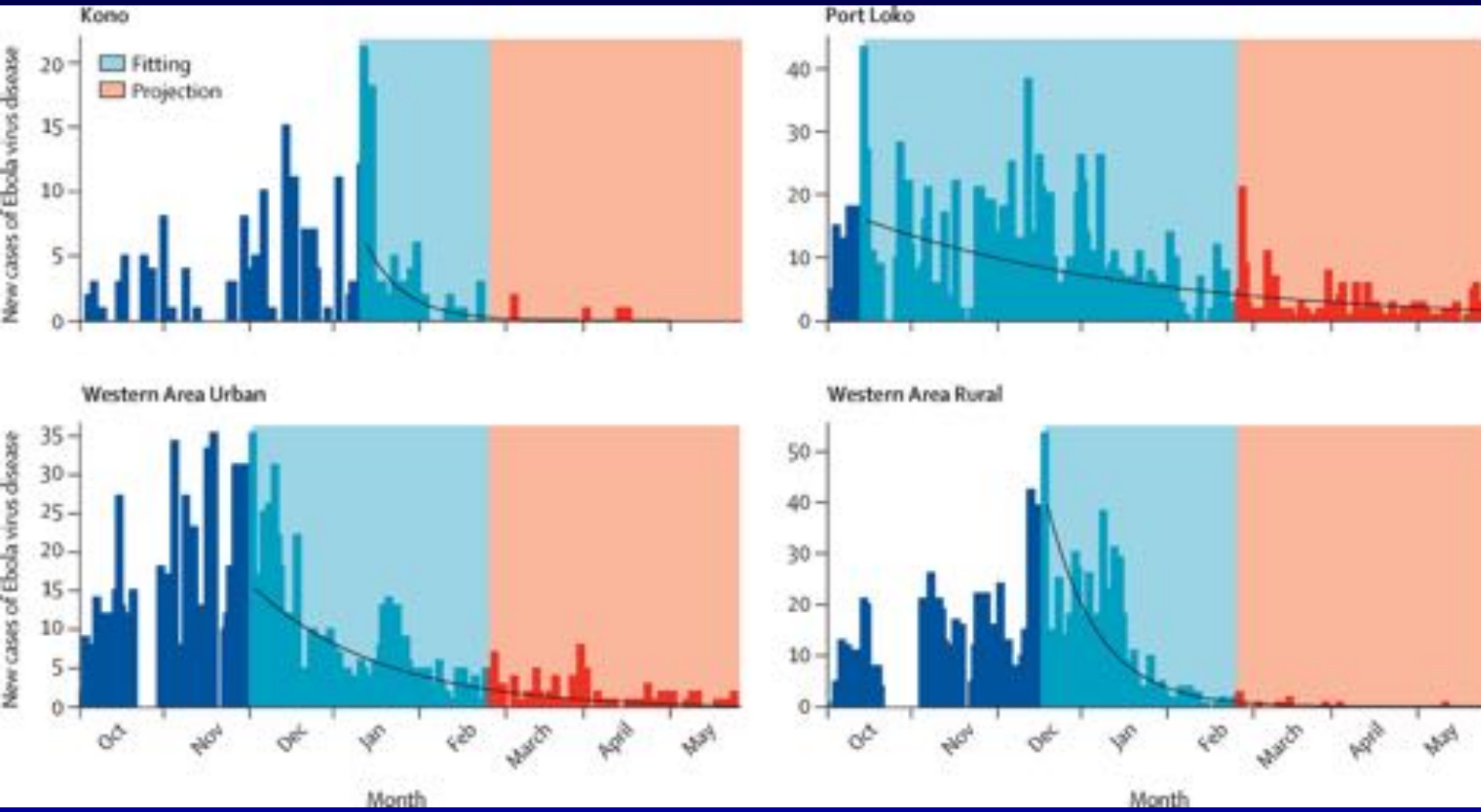
Interpretation Spatiotemporal variation in infection risk undermines the statistical power of the SWCT. This variation also undercuts the SWCT's expected ethical advantages over the RCT, because an RCT, but not an SWCT, can prioritise vaccination of high-risk clusters.

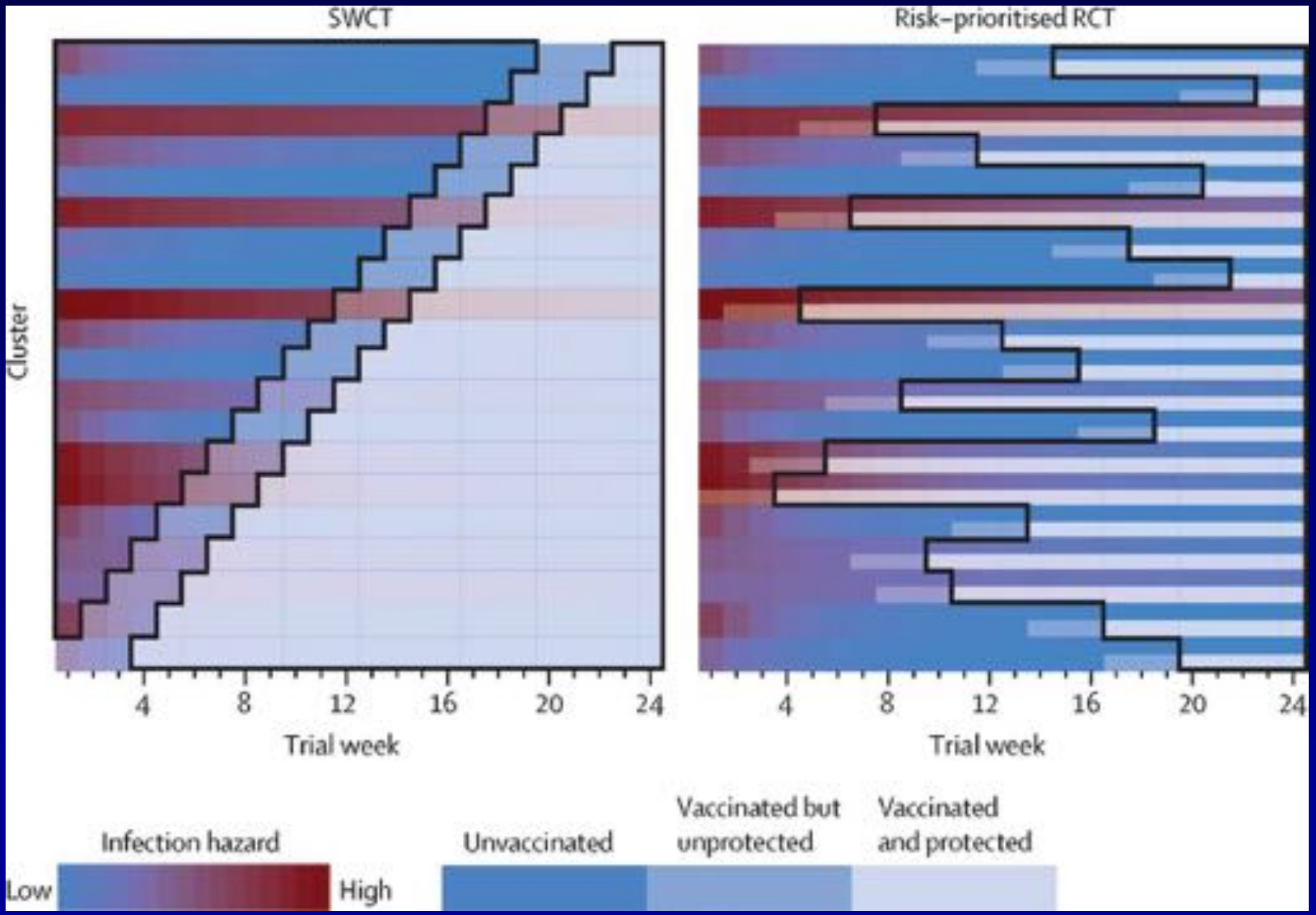
Lancet Infect Dis 2015

Published Online
April 15, 2015
http://dx.doi.org/10.1016/S1473-3099(15)70139-8

See Online/Comment
http://dx.doi.org/10.1016/S1473-3099(15)70159-3

Center for Computational Biology and Bioinformatics (S E Bellan PhD) **and Department of Integrative Biology** (S J Fox BS, Prof L A Meyers PhD), **The University of Texas at Austin, Austin, TX, USA**; **Department of Biology** (J R C Pulliam PhD) **and Emerging Pathogens Institute** (J R C Pulliam, C A B Pearson PhD), **University of Florida, Gainesville, FL, USA**; **School of Computational Science and Engineering** (D Champredon MSc) **and Department of Biology** (J Dushoff PhD), **McMaster**


Konso
Fitting
Projection
New cases of Ebola virus disease
Port Loko
Western Area Urban
Western Area Rural
Oct
Nov
Dec
Jan
Feb
March
April
May
Month


SWCT
Risk–prioritised RCT
Cluster
4
8
12
16
20
24
Trial week
Infection hazard
Low
High
Unvaccinated
Vaccinated but unprotected
Vaccinated and protected

Questions from leadership

Where should ETUs be constructed next?

Which neighboring countries are at the highest risk?


SENEGAL
THE GAMBIA
GUINEA-BISSAU
MALI
GUINEA
SIERRA LEONE
LIBERIA
COTE D'IVOIRE
BURKINA FASO
Probability of becoming affected
National boundary
District with reported cases

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