

The ecology and evolution of infectious disease: Theoretical, computational and statistical approaches

- ▶ Ecology & Evolution Graduate Program Seminar Series
- ▶ Rutgers U. 15 Oct 2015
- ▶ Jonathan Dushoff
- ▶ McMaster University

Outline

Introduction

Influenza

HIV

Malaria

Ebola

Rabies

Conclusion

Rutgers



Rutgers



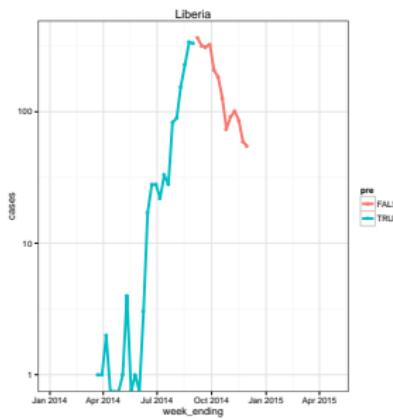
Rutgers



Rutgers



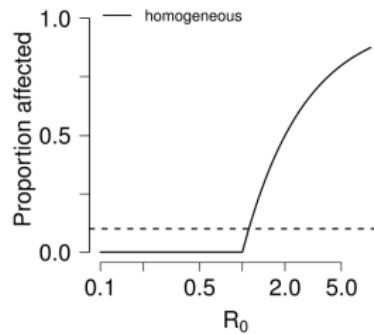
Dynamical modeling



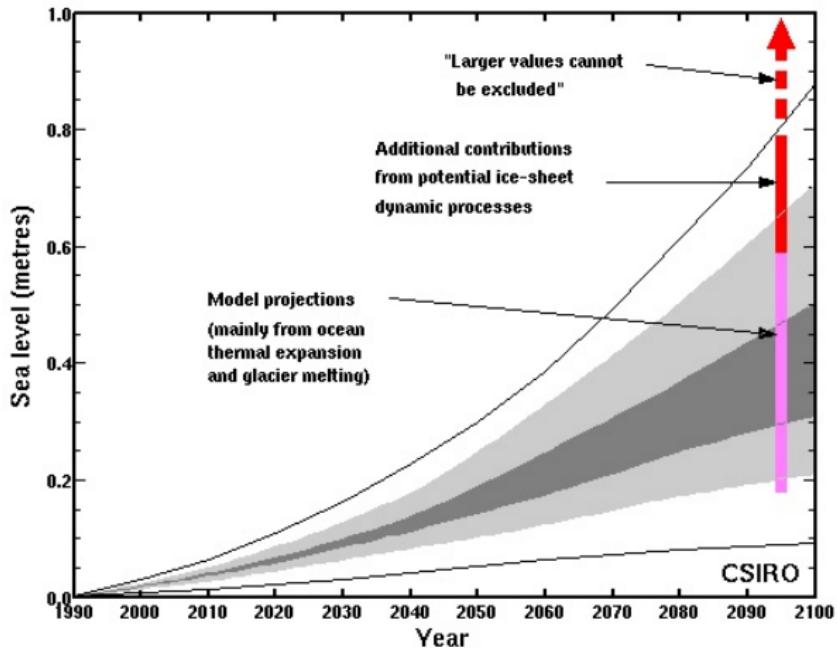
Qualitative models



endemic equilibrium



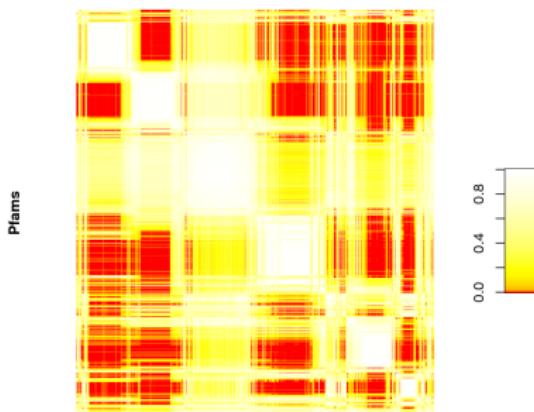
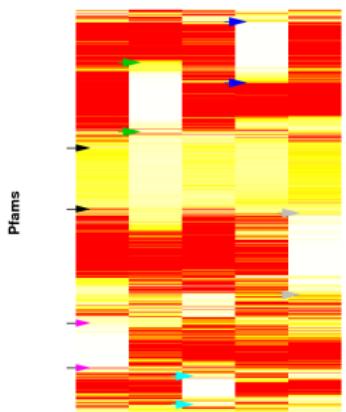
Linking dynamics and statistics



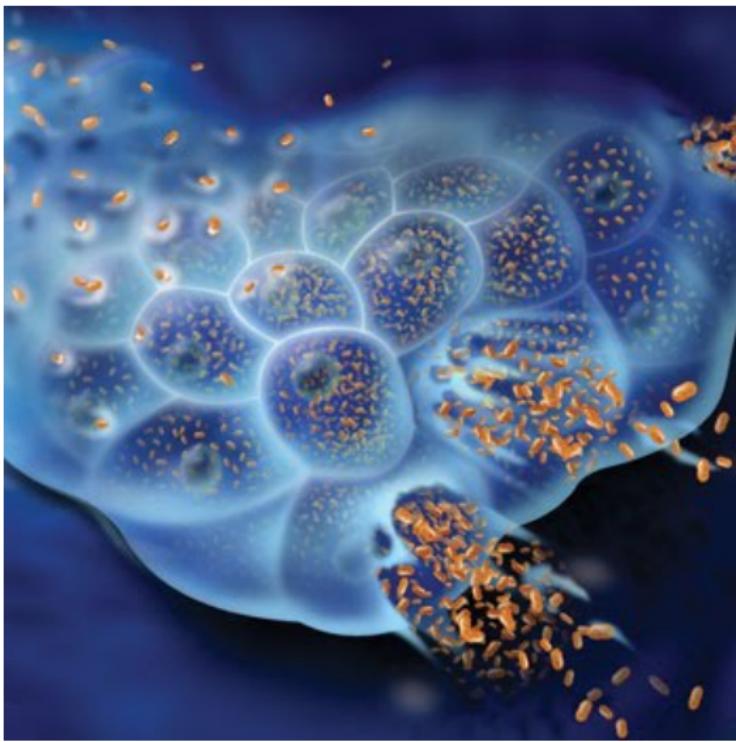
Closing the loop



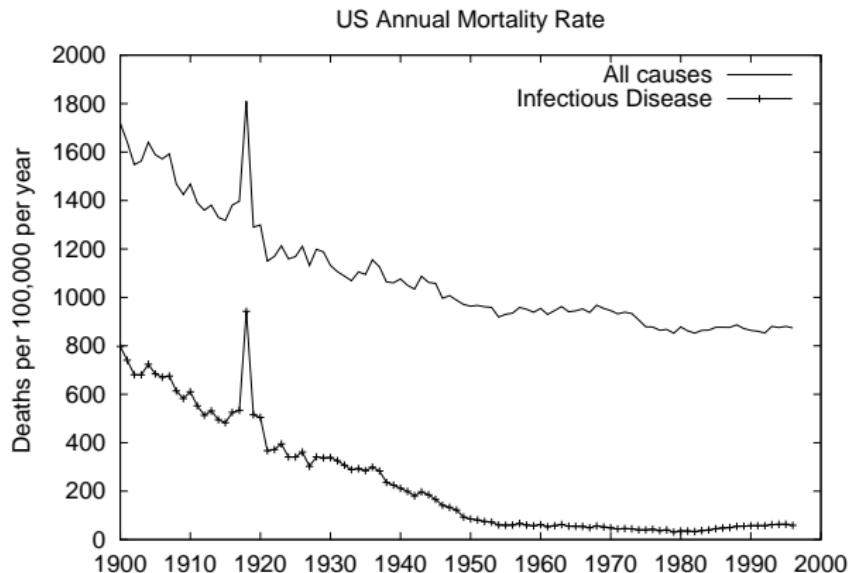
Bacterial ecology and diversity



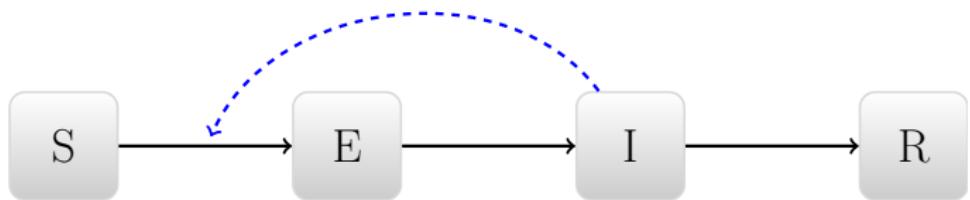
Cell dynamics



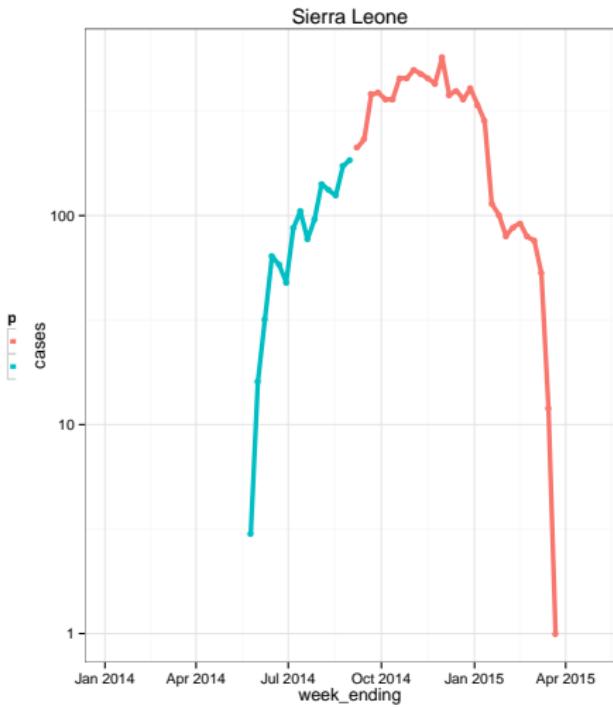
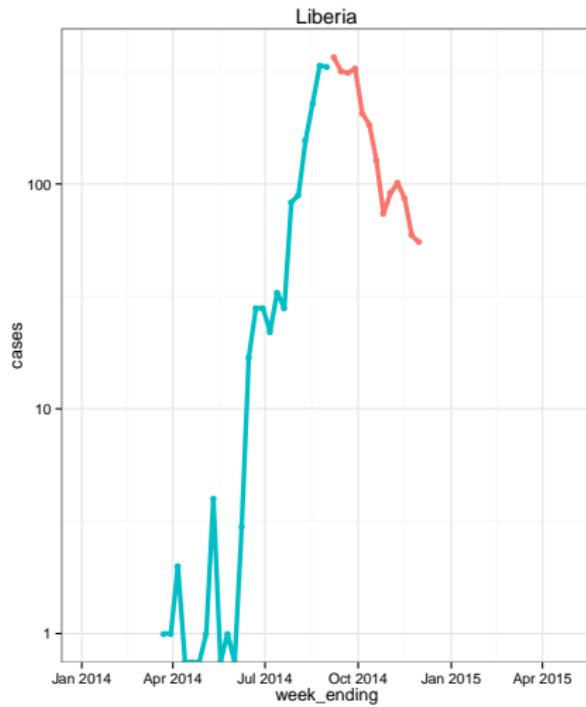
Evolution and spread of infectious disease



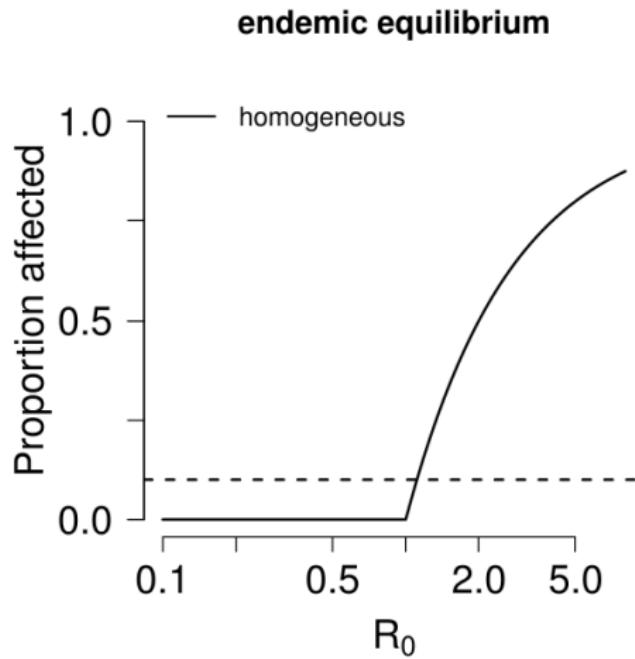
Box models of disease



r – the epidemic growth rate



\mathcal{R} – the reproductive number



\mathcal{R} – the reproductive number



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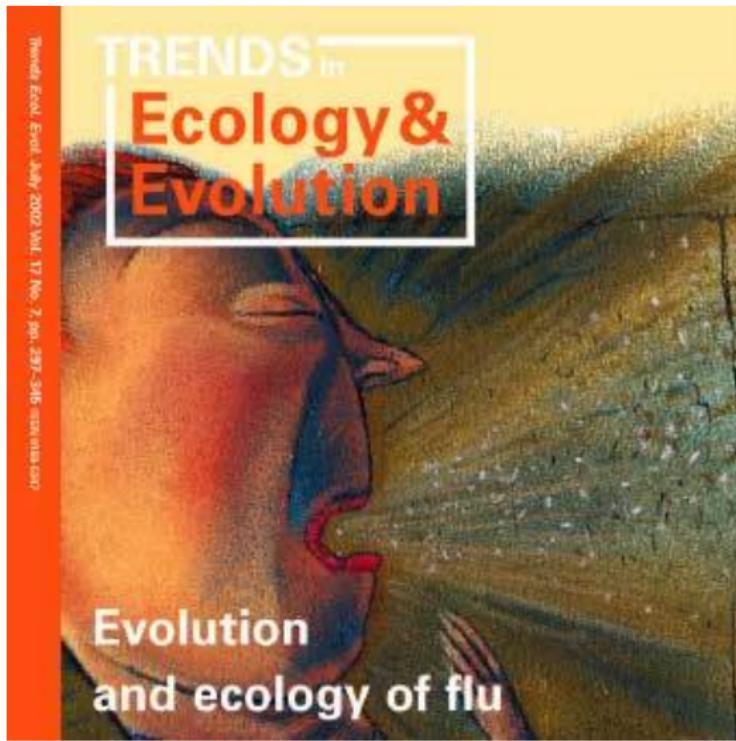
Malaria

Ebola

Rabies

Conclusion

Influenza



Clusters and vaccination strategy

Hemagglutinin sequence clusters and the antigenic evolution of influenza A virus

Joshua B. Plotkin^{*†‡}, Jonathan Dushoff*, and Simon A. Levin*

*Department of Ecology and Evolutionary Biology, Princeton University, Princeton, NJ 08540; and [†]Institute for Advanced Study, Princeton, NJ 08540

Contributed by Simon A. Levin, February 22, 2002

Continual mutations to the hemagglutinin (HA) gene of influenza A virus generate novel antigenic strains that cause annual epidemics. Using a database of 560 viral RNA sequences, we study the structure and tempo of HA evolution over the past two decades. We detect a critical length scale, in amino acid space, at which HA sequences aggregate into clusters, or swarms. We investigate the

sequences aggregate into clusters, or “swarms,” and we study their spatio-temporal patterns. We will focus on the relationships between observed cluster structure, worldwide vaccination history, and the primary antibody-combining regions of the HA protein.

genetic techniques, but we are less concerned with reconstructing the evolutionary relationships between HAI sequences. Instead, we identify natural scales at which HAI amino acid

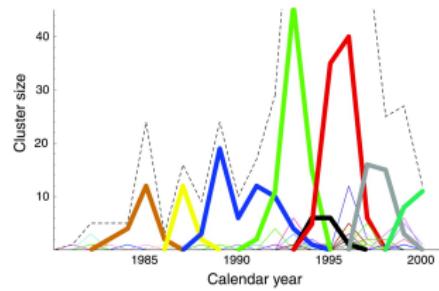
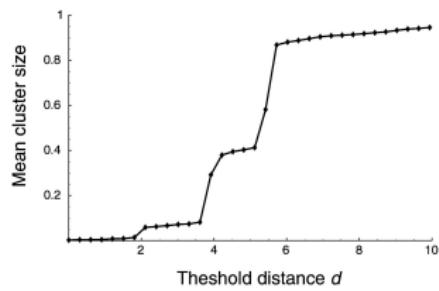
*To whom reprint requests should be addressed. E-mail: plotkin@ias.edu.

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www.pnas.org/cgi/doi/10.1073/pnas.082110799

PNAS | April 30, 2002 | vol. 99 | no. 9 | 6263–6268

Clusters and vaccination strategy



Nucleotide evolution

JOURNAL OF VIROLOGY, May 2008, p. 4938–4945
0022-538X/08/0808-00+0 doi:10.1128/JVI.02415-07
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Vol. 82, No. 10

Natural Selection for Nucleotide Usage at Synonymous and Nonsynonymous Sites in Influenza A Virus Genes[▼]

Sergey Kryazhimskiy,^{1,2*} Georgii A. Bazykin,^{3,4} and Jonathan Dushoff^{3,5}

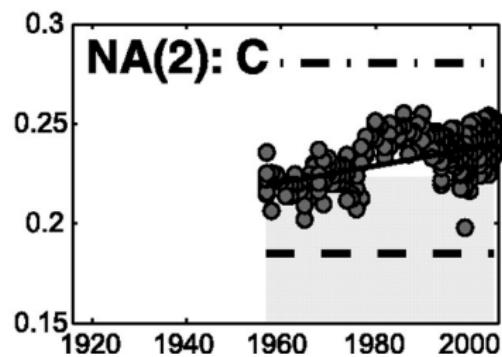
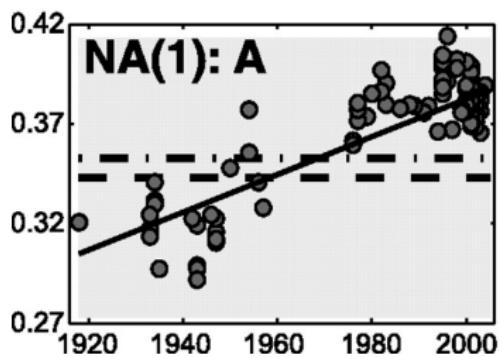
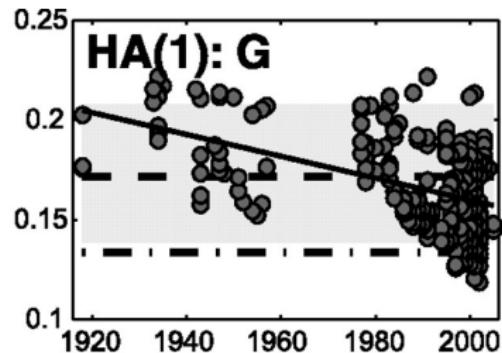
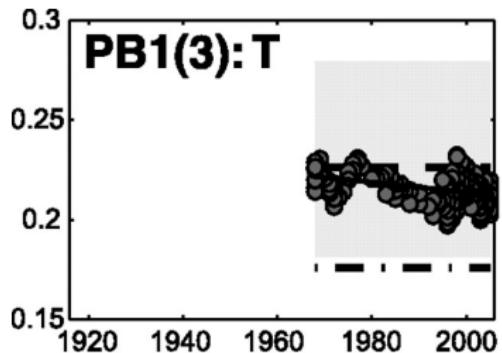
Program in Applied and Computational Mathematics, Princeton University, Princeton, New Jersey¹; Department of Biology, University of Pennsylvania, Philadelphia, Pennsylvania²; Department of Ecology and Evolutionary Biology, Princeton University, Princeton, New Jersey³; Institute for Information Transmission Problems, Russian Academy of Sciences (Kharkevich Institute), Moscow, Russia⁴; and Department of Biology, McMaster University, Hamilton, Ontario, Canada⁵

Received 8 November 2007/Accepted 26 February 2008

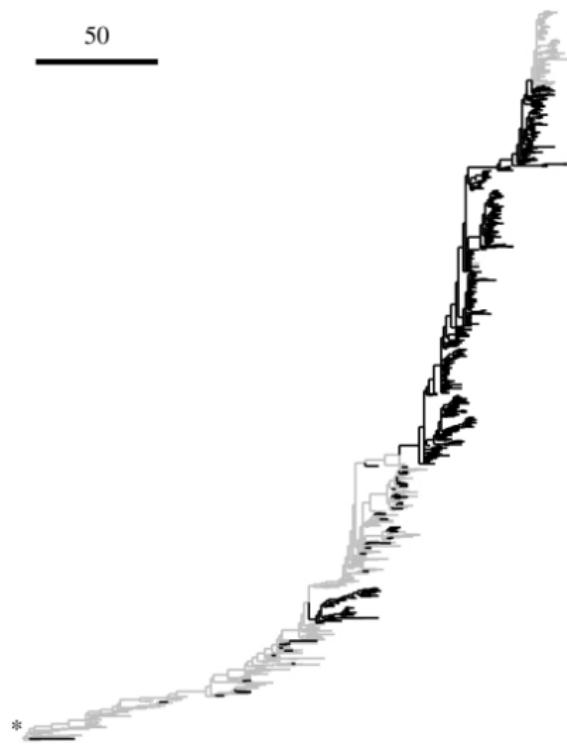
*Corresponding author. Mailing address: Department of Biology, Princeton University, Princeton, NJ 08544. Phone: (609) 258-4606; fax: (609) 258-4606; e-mail: kryazh@princeton.edu.
†Present address: Department of Biological Sciences, University of Alberta, Edmonton, Alberta, Canada T6G 2E9.

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Nucleotide evolution



Nucleotide evolution



Annualized mortality



American Journal of Epidemiology
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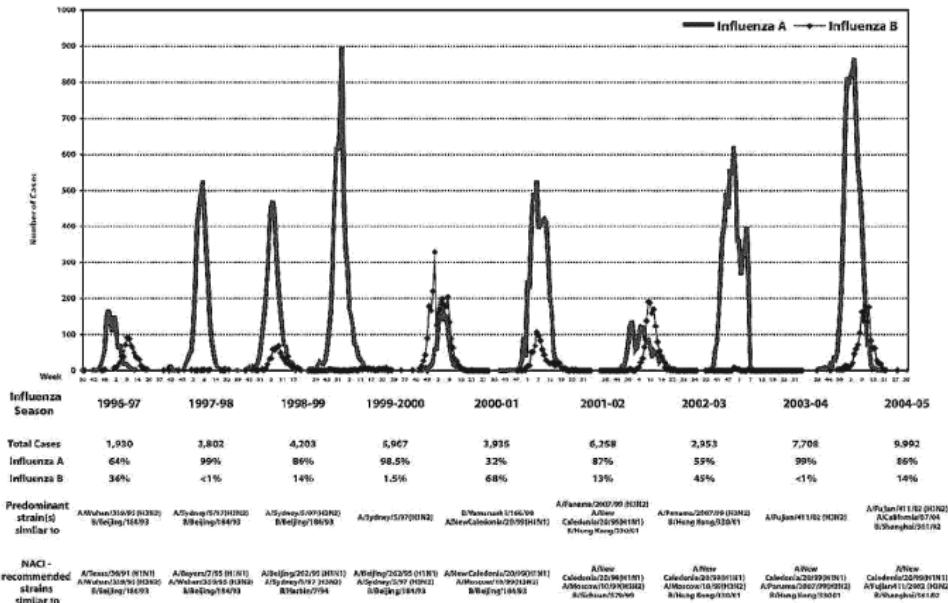
Vol. 163, No. 2
DOI: 10.1093/aje/kwz024
Advance Access publication November 30, 2005

Practice of Epidemiology

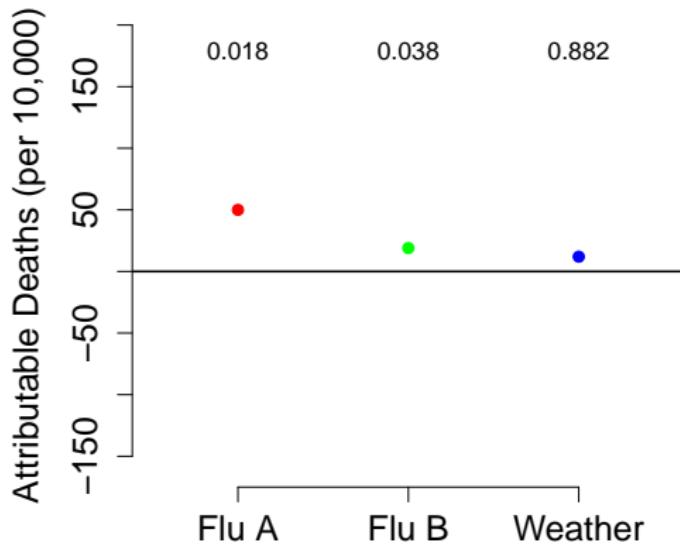
Mortality due to Influenza in the United States—An Annualized Regression Approach Using Multiple-Cause Mortality Data

Jonathan Dushoff^{1,2}, Joshua B. Plotkin³, Cecile Viboud², David J. D. Earn⁴, and Lone Simonsen⁵

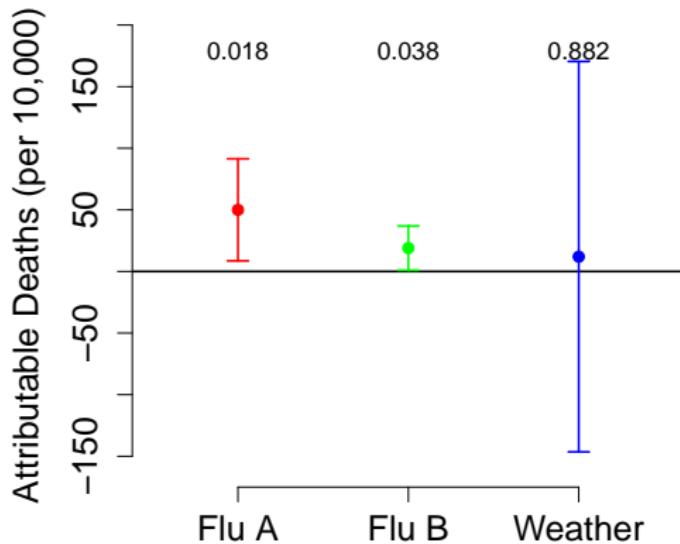
Annualized mortality



Annualized mortality



Annualized mortality



1918 pandemic in England and Wales



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Research



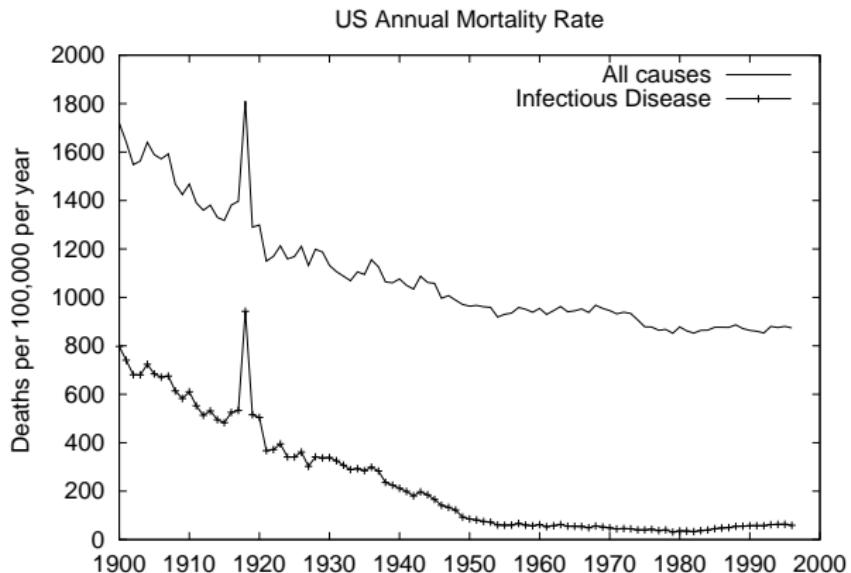
Inferring the causes of the three waves of the 1918 influenza pandemic in England and Wales

Daihai He¹, Jonathan Dushoff^{2,3}, Troy Day⁵, Junling Ma⁶
and David J. D. Earn^{3,4}

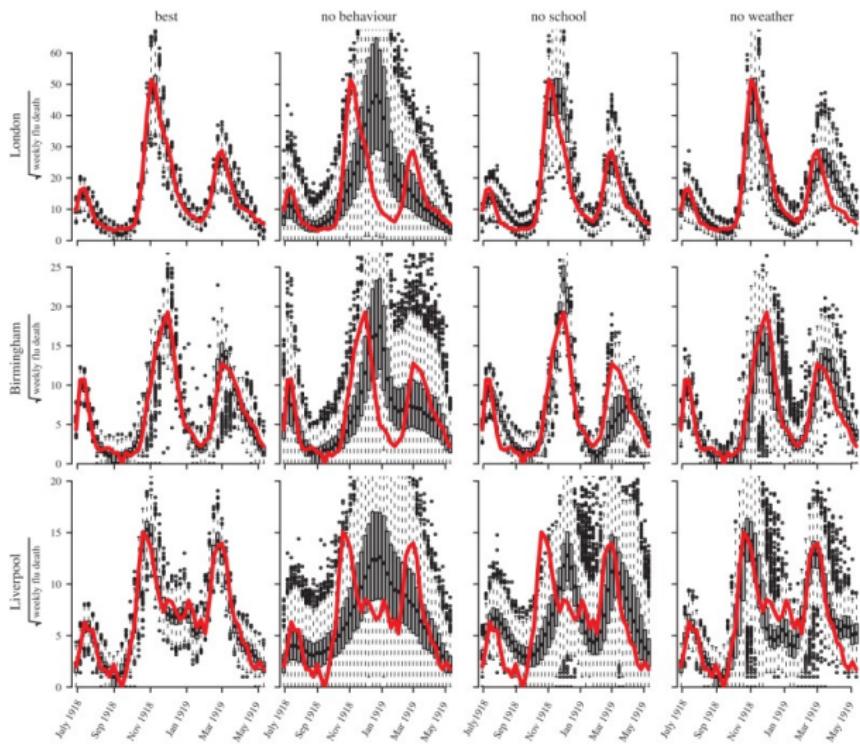
¹Department of Applied Mathematics, Hong Kong Polytechnic University Hung Hom, Kowloon, Hong Kong (SAR), People's Republic of China

²Department of Biology, ³M.G. DeGroote Institute for Infectious Disease Research, and ⁴Department of Mathematics and Statistics, McMaster University, Hamilton, Ontario, Canada

The great influenza



1918 pandemic in England and Wales



2009 pandemic Alberta

Annals of Internal Medicine

| ORIGINAL RESEARCH

Effects of School Closure on Incidence of Pandemic Influenza in Alberta, Canada

David J.D. Earn, PhD; Dalhai He, PhD; Mark B. Loeb, MD, MSc; Kevin Fonseca, PhD; Bonita E. Lee, MD, MSc; and Jonathan Dushoff, PhD

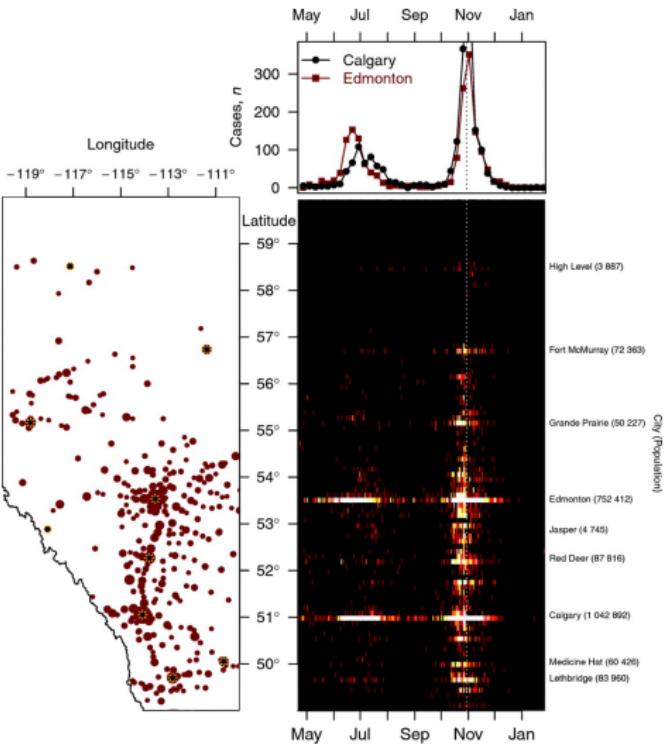
Background: Control of pandemic influenza by social-distancing measures, such as school closures, is a controversial aspect of pandemic planning. However, investigations of the extent to which these measures actually affect the progression of a pandemic have been limited.

Objective: To examine correlations between the incidence of pandemic H1N1 (pH1N1) influenza in Alberta, Canada, in 2009 and school closures or weather changes, and to estimate the effects of

pandemic influenza cases. Mathematical models suggested that school closure reduced transmission among school-age children by more than 50% and that this was a key factor in interrupting transmission. The models also indicated that seasonal changes in weather had a significant effect on the temporal pattern of the epidemic.

Limitations: Data probably represent a small sample of all viral infections. The mathematical models make simplifying assumptions

2009 pandemic Alberta



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Male circumcision and HIV transmission

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Modeling the Population-Level Effects of Male Circumcision as an HIV-Preventive Measure: A Gendered Perspective

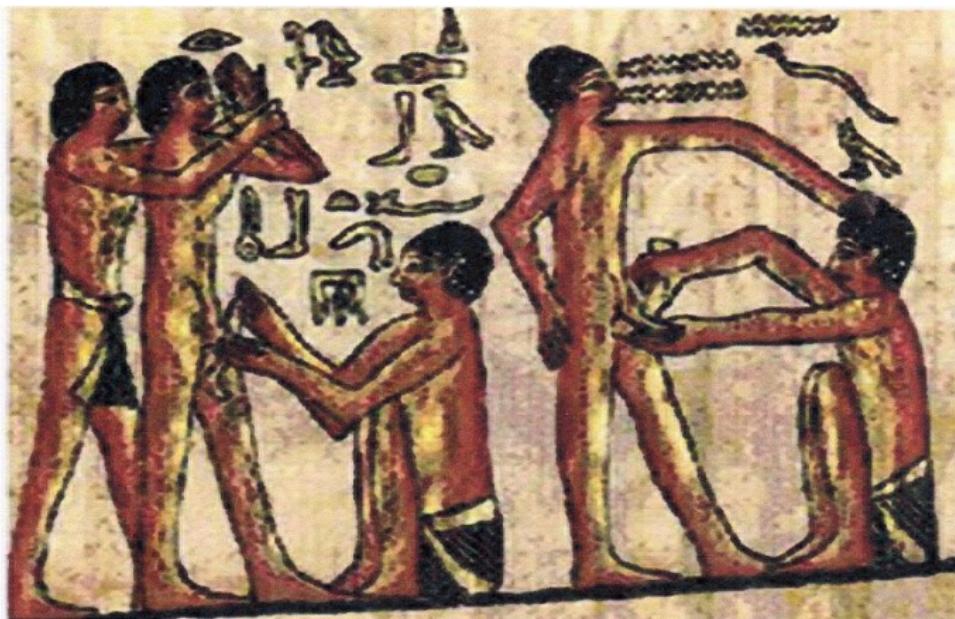
Jonathan Dushoff^a, Audrey Patocs, Chyun-Fung Shi

Department of Biology and Institute of Infectious Disease Research, McMaster University, Hamilton, Ontario, Canada

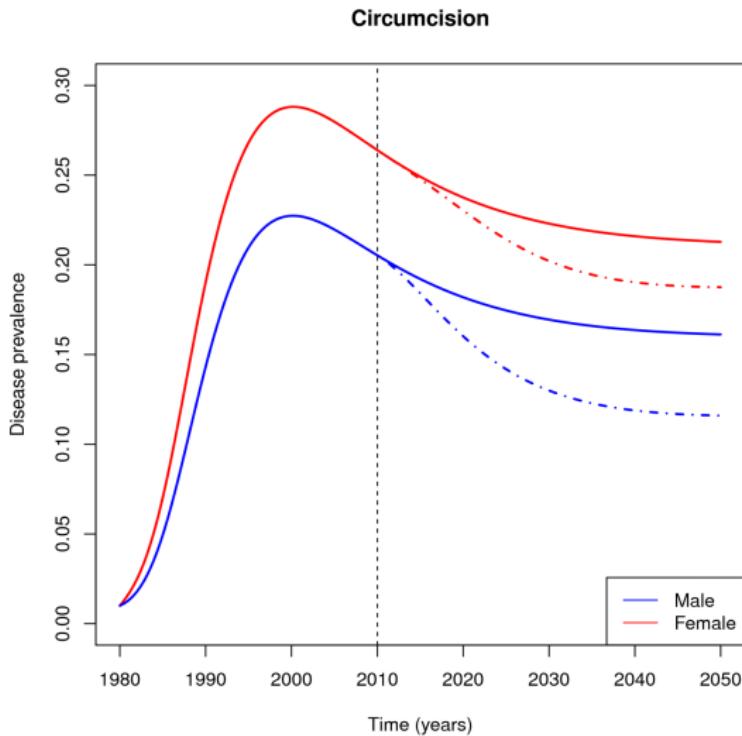
Abstract

Background: Evidence from biological, epidemiological, and controlled intervention studies has demonstrated that male

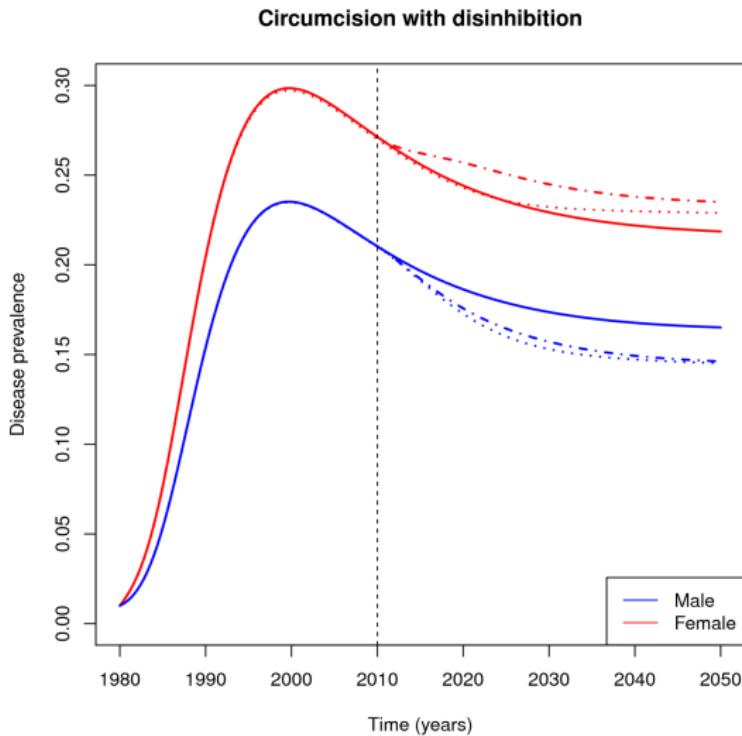
Male circumcision and HIV transmission



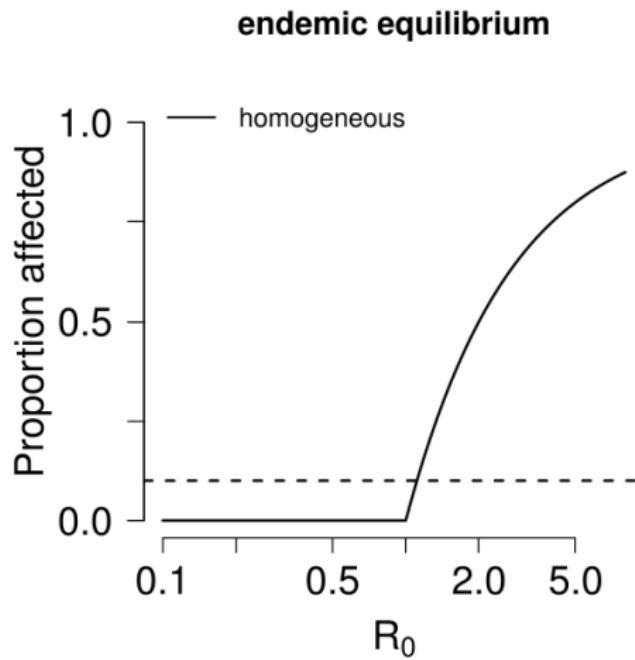
Male circumcision and HIV transmission



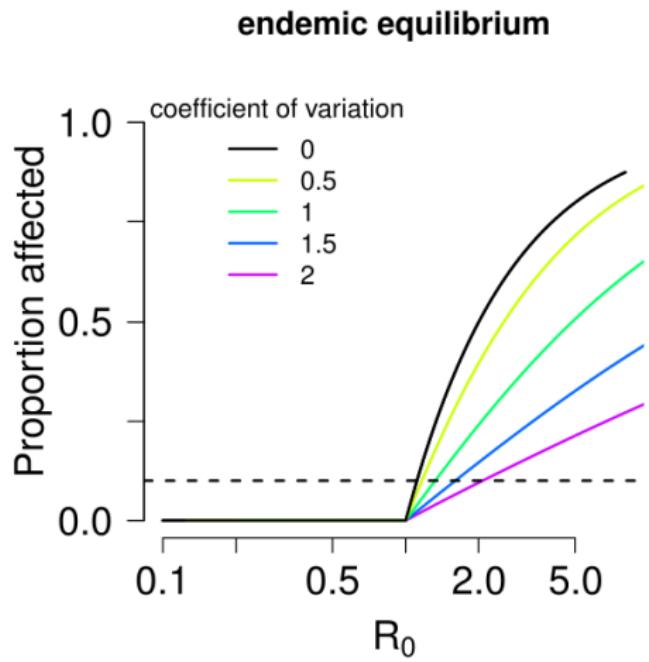
Male circumcision and HIV transmission



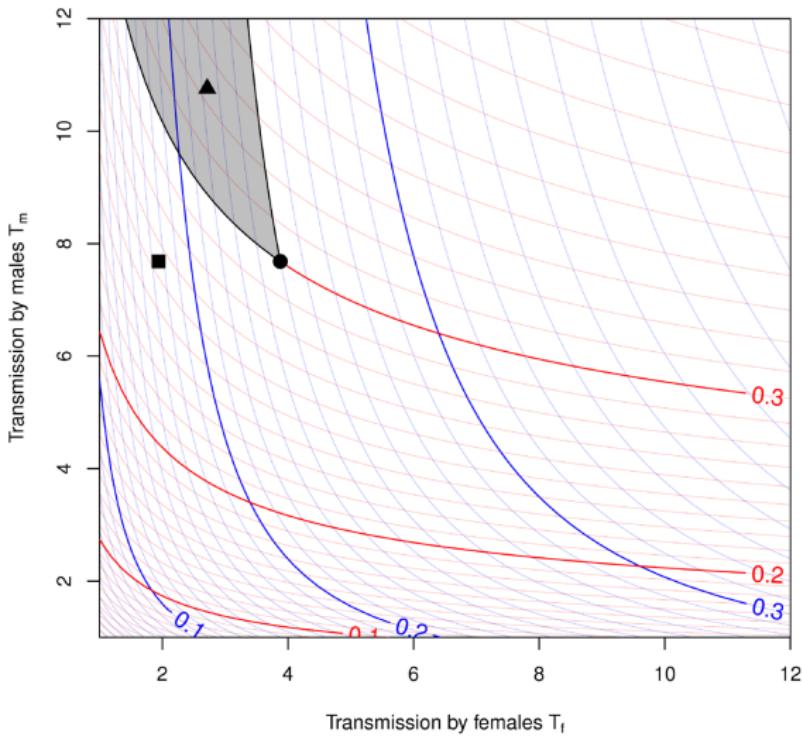
Transmission and prevalence



Transmission and prevalence



Heterosexual transmission and prevalence



HIV treatment as prevention



Cohort transmission



RESEARCH ARTICLE

Reassessment of HIV-1 Acute Phase Infectivity: Accounting for Heterogeneity and Study Design with Simulated Cohorts

Steve E. Bellan^{1*}, Jonathan Dushoff², Alison P. Galvani^{3,4}, Lauren Ancel Meyers^{5,6}

1 Center for Computational Biology and Bioinformatics, The University of Texas at Austin, Austin, Texas, United States of America, **2** Department of Biology, McMaster University, Hamilton, Ontario, Canada, **3** Yale School of Public Health, Yale University, New Haven, Connecticut, United States of America, **4** Department of Ecology and Evolution, Yale University, New Haven, Connecticut, United States of America, **5** Department of Integrative Biology, The University of Texas at Austin, Austin, Texas, United States of America, **6** The Santa Fe Institute, Santa Fe, New Mexico, United States of America



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Extra-couple HIV transmission in sub-Saharan Africa: a mathematical modelling study of survey data



Steve E Bellan, Kathryn J Fiorella, Dessalegn Y Melesse, Wayne M Getz, Brian G Williams, Jonathan Dushoff

Summary

Background The proportion of heterosexual HIV transmission in sub-Saharan Africa that occurs within cohabiting partnerships compared with that in single people or extra-couple relationships is widely debated. We estimated the

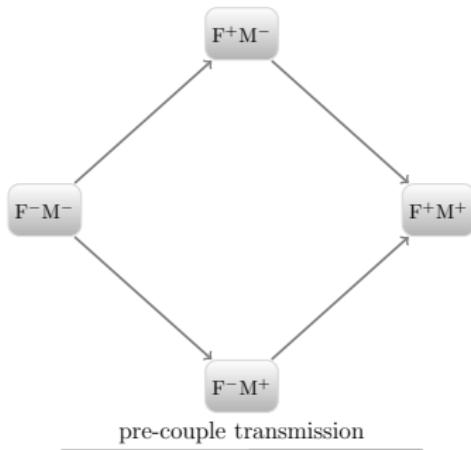
Lancet 2013; 381: 1561-69

routes of transmission and intervention efficacy. We used mathematical modelling to estimate rates attributable to extra-couple intercourse, and rates within serodiscordant couples, to assess the proportional contribution of different routes of transmission to new HIV infections. Because the probability that an

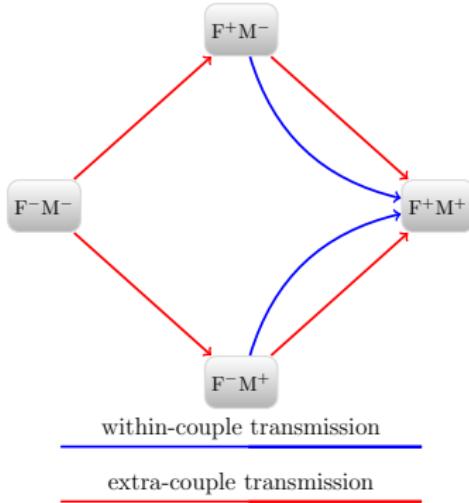
Routes of HIV transmission



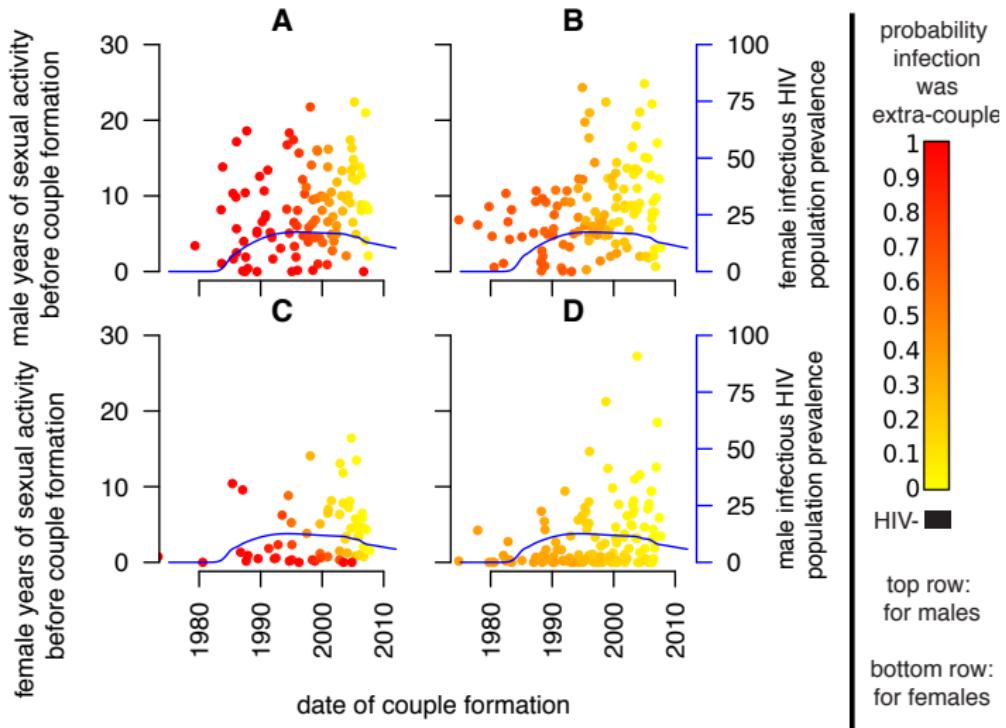
Routes of HIV transmission



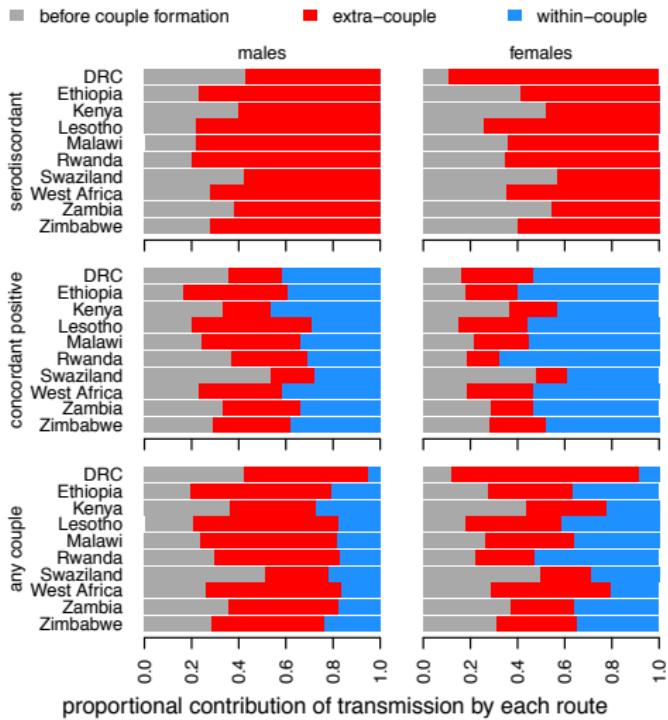
Routes of HIV transmission



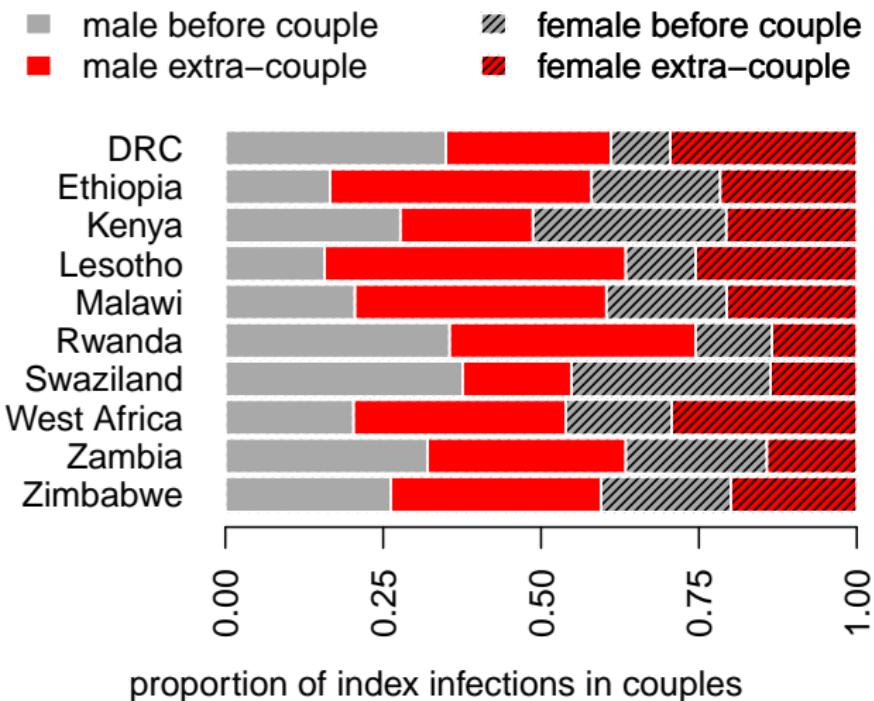
Routes of HIV transmission



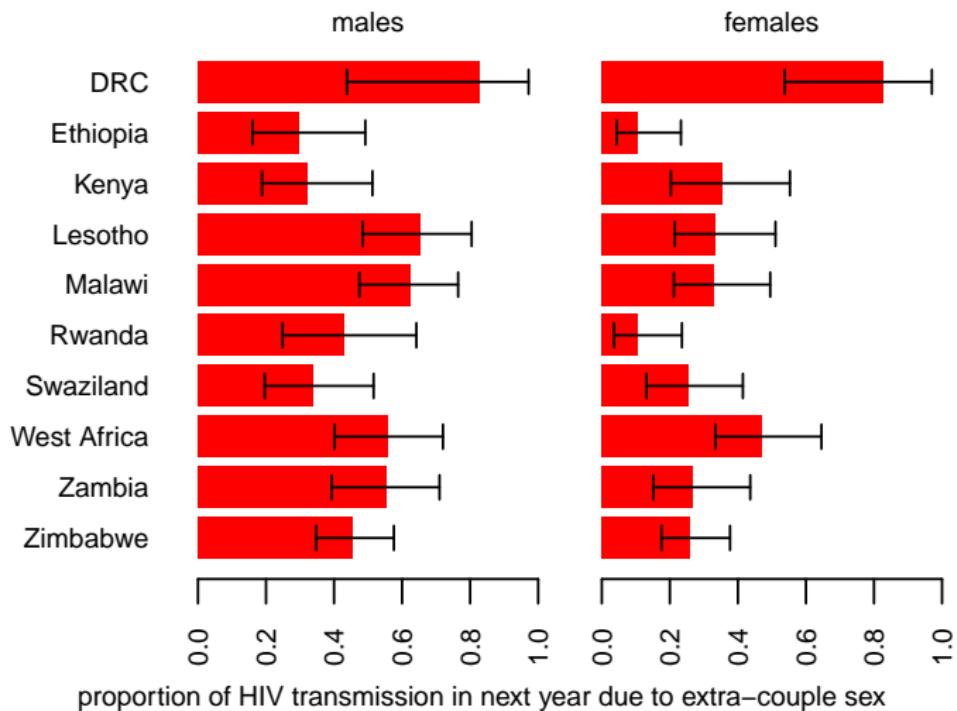
Routes of HIV transmission



Routes of HIV transmission



Routes of HIV transmission



Time scales



Why the proportion of transmission during early-stage HIV infection does not predict the long-term impact of treatment on HIV incidence

Jeffrey W. Eaton¹ and Timothy B. Hallett

Department of Infectious Disease Epidemiology, Imperial College London, St Mary's Hospital, London W2 1PG, United Kingdom

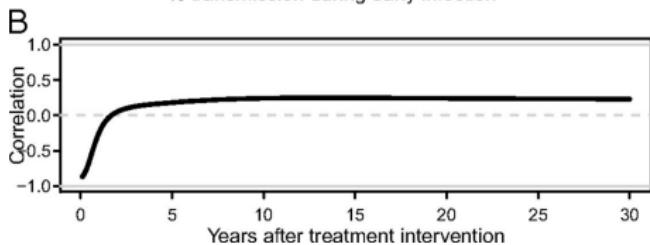
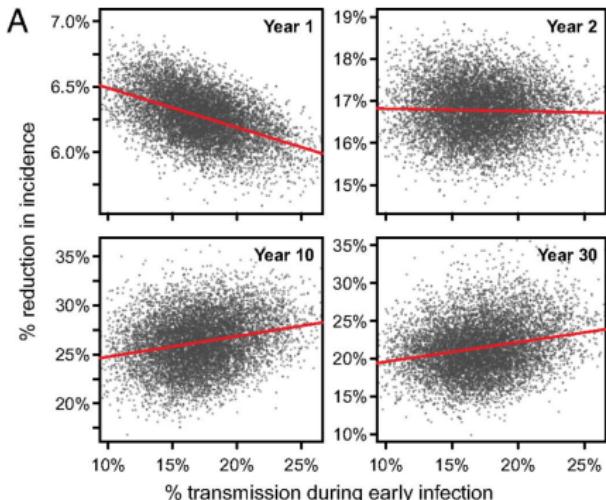
Edited by Alan S. Perelson, Los Alamos National Laboratory, Los Alamos, NM, and accepted by the Editorial Board September 5, 2014 (received for review December 23, 2013)

Antiretroviral therapy (ART) reduces the infectiousness of HIV-infected persons, but only after testing, linkage to care, and successful viral suppression. Thus, a large proportion of HIV transmission during a period of high infectiousness in the first few months after infection ("early transmission") is perceived as a threat to the impact of HIV "treatment-as-prevention" strategies. We created a mathematical model of a heterosexual HIV epidemic to investigate how the proportion of early transmission affects the impact of ART on reducing HIV incidence. The model includes stages of HIV infection, flexible sexual mixing, and changes in risk behavior over the epidemic. The model was calibrated to HIV prevalence data from South Africa using a Bayesian framework. Immediately after ART was in-

been infected recently affects the impact of treatment scale-up on HIV incidence. The model is calibrated to longitudinal HIV prevalence data from South Africa using a Bayesian framework. Thus, the model accounts for not only the early epidemic growth rate highlighted in previous research (5, 9, 18), but also the heterogeneity and sexual behavior change to explain the peak and decline in HIV incidence observed in sub-Saharan African HIV epidemics (32, 33).

The model calibration allows uncertainty about factors that determine the amount of early transmission, including the relative infectiousness during early infection, heterogeneity in propensity for sexual risk behavior, assortativity in sexual partner selection,

Time scales



Success!



GUIDELINES



GUIDELINE ON WHEN
TO START ANTIRETROVIRAL
THERAPY AND
ON PRE-EXPOSURE
PROPHYLAXIS FOR HIV

SEPTEMBER 2015

Going forward



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Population-level effects of clinical immunity

Keegan and Dushoff *BMC Infectious Diseases* 2013, **13**:428
<http://www.biomedcentral.com/1471-2334/13/428>



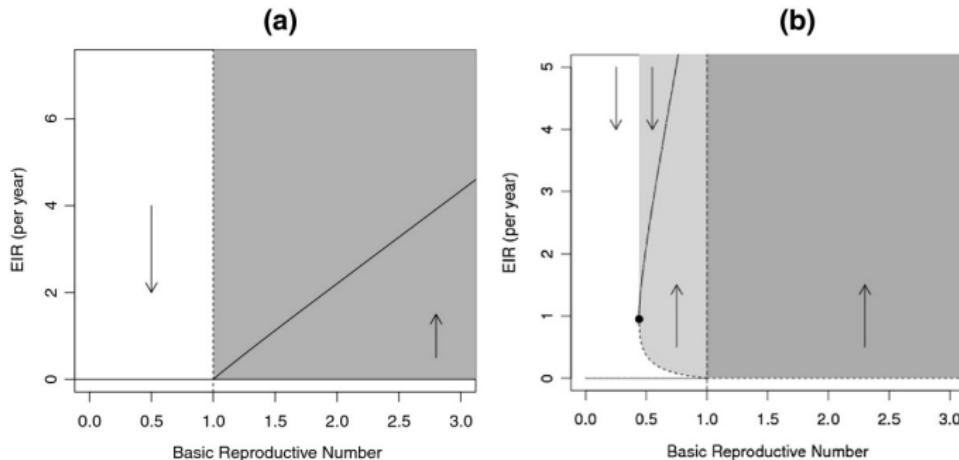
RESEARCH ARTICLE

Open Access

Population-level effects of clinical immunity to malaria

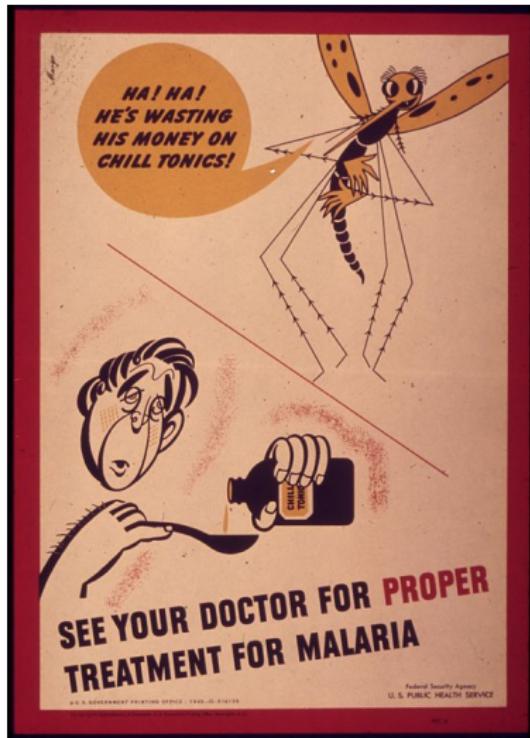
Lindsay T. Keegan* and Jonathan Dushoff

Population-level effects of clinical immunity



$$\mathcal{R}_{CC}/\mathcal{R}_{NN} > 1 + D/(\pi L)$$

Population-level effects of clinical immunity



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Asymptomatic infection

Correspondence

Ebola control: effect of asymptomatic infection and acquired immunity

Evidence suggests that many Ebola infections are asymptomatic,^{1,2} a factor overlooked by recent outbreak

when planning intervention strategies. For instance, should a safe and effective vaccine become available, the vaccination coverage needed for elimination will depend on pre-existing immunity in the population (appendix). Immunity resulting from asymptomatic

ill and infectious patients, minimising disease spread to susceptible health-care workers.

The conclusions above depend on whether asymptomatic infections are common, and protective against future infection. Further, strategies to leverage protective immunity



Published Online
October 14, 2014
<http://dx.doi.org/10.1016/j.laneuro.2014.09.020>

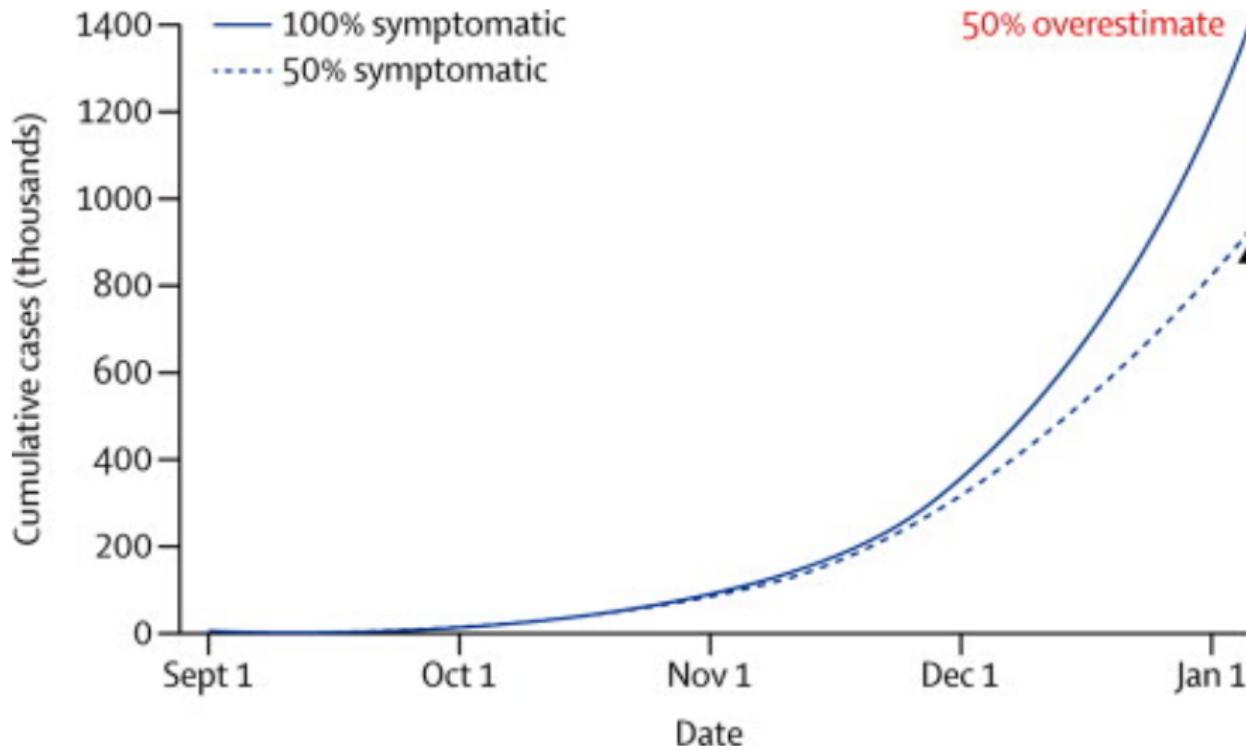
See Online for appendix

¹Steve E Bellan, Juliet R C Pulliam,
Jonathan Dushoff, Lauren Ancel Meyers
steve.bellan@gmail.com

27 countries in the world with a high burden of multidrug-resistant (MDR) tuberculosis and in 2012, there were an estimated 6800 new cases in the

and care, including a legal framework for tuberculosis cross-border collaboration.⁶ Programmes to screen for latent and active tuberculosis should

Asymptomatic infection



Post-death transmission



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SUBJECT AREAS:
INFECTIOUS DISEASES
COMPUTATIONAL MODELS
POPULATION DYNAMICS

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9 December 2014

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2 February 2015

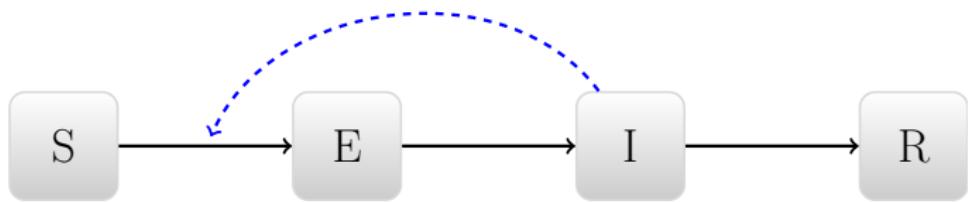
Modeling Post-death Transmission of Ebola: Challenges for Inference and Opportunities for Control

Joshua S. Weitz^{1,2} & Jonathan Dushoff^{3,4}

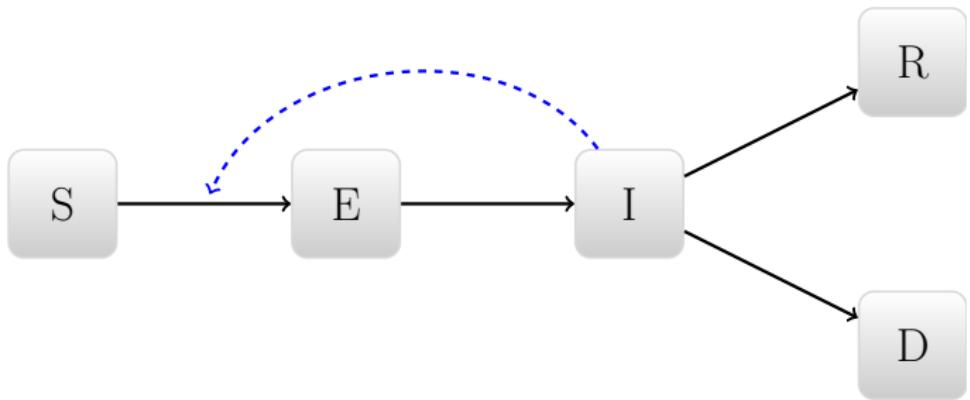
¹School of Biology, Georgia Institute of Technology, Atlanta, GA, USA, ²School of Physics, Georgia Institute of Technology, Atlanta, GA, USA, ³Department of Biology, McMaster University, Hamilton, ON, Canada, ⁴Institute of Infectious Disease Research, McMaster University, Hamilton, ON, Canada.

Multiple epidemiological models have been proposed to predict the spread of Ebola in West Africa. These

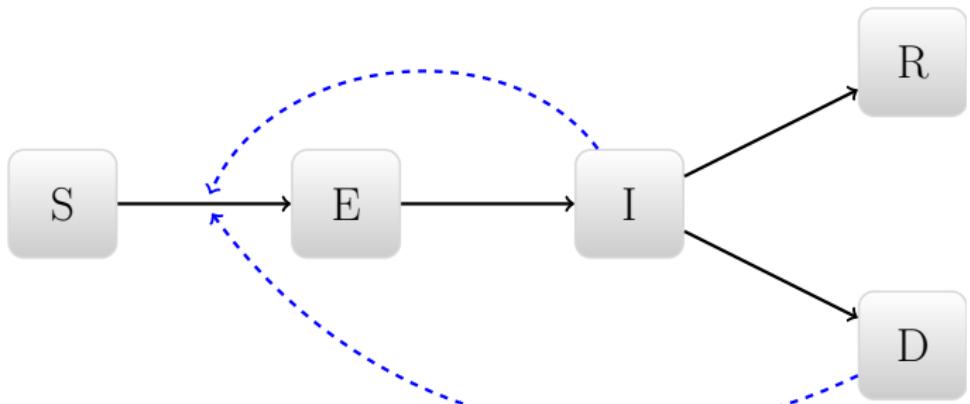
Standard model again



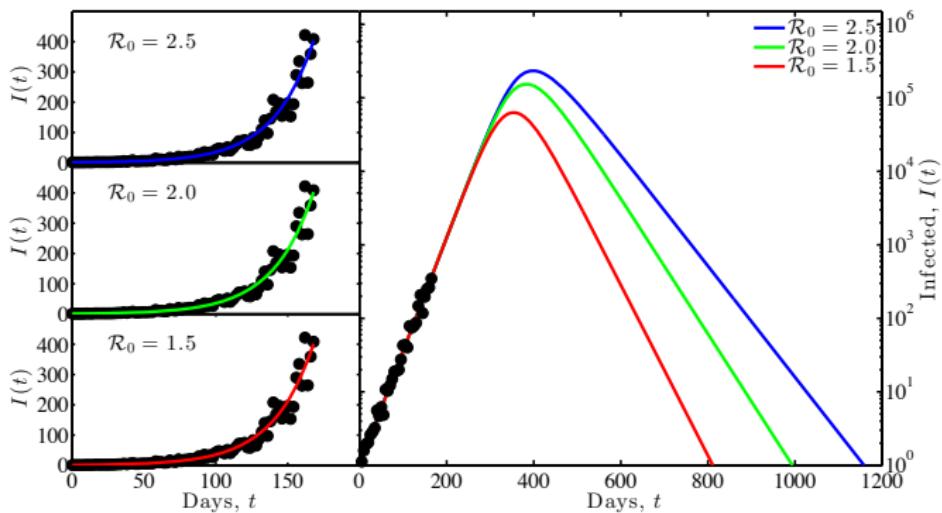
Keep track of dead people



Consider transmission from dead people

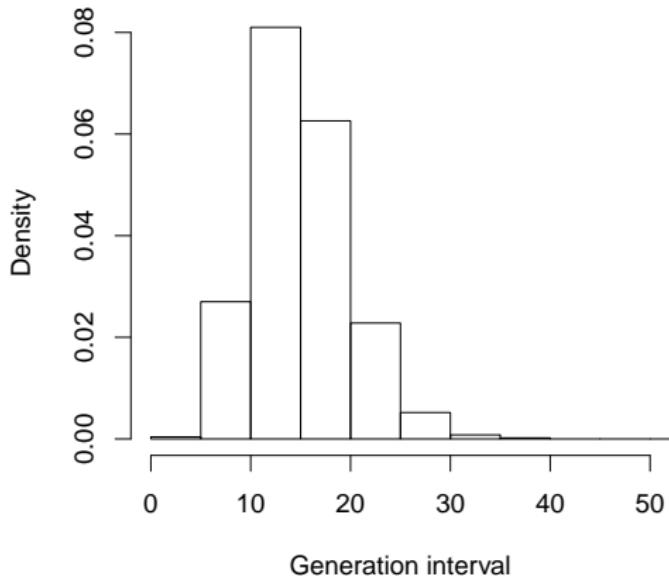


Scenarios

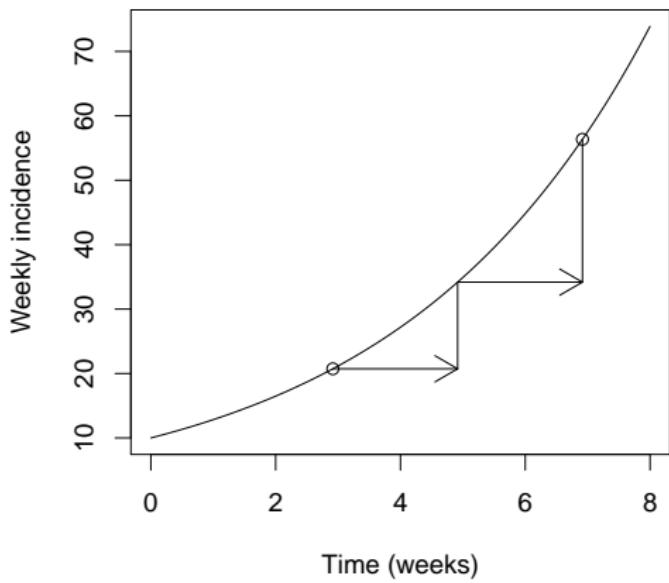


Generation intervals

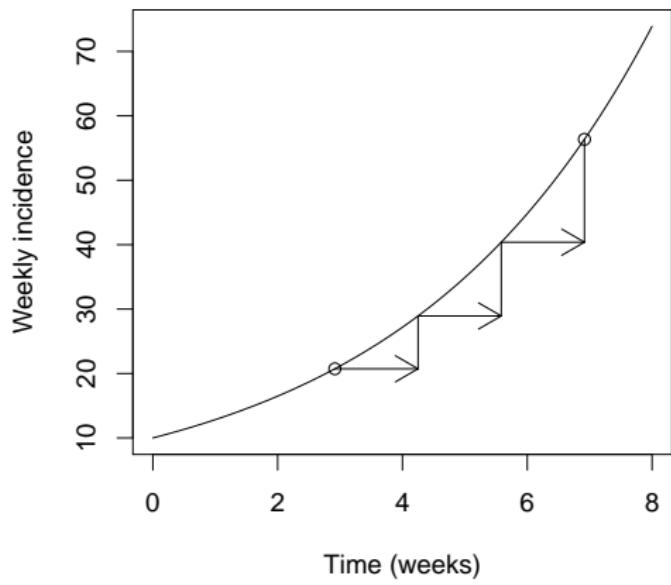
Approximate generation intervals



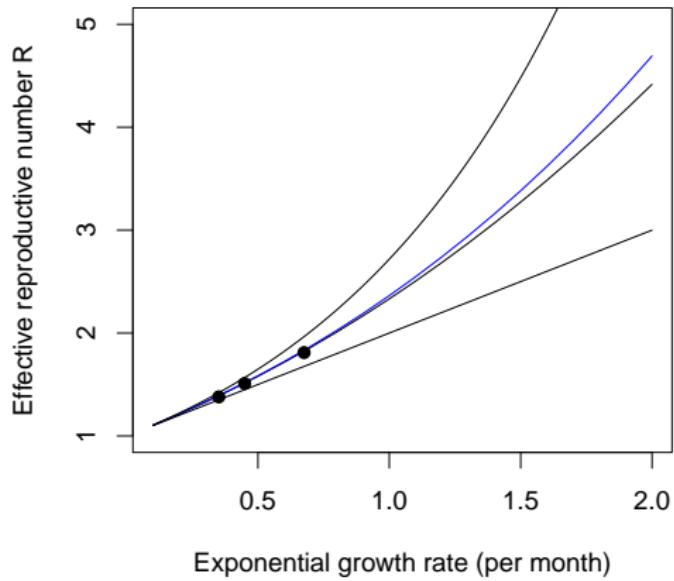
Time scales



Time scales



Moment approximations



Vaccine trials



BMJ 2014;349:g7518 doi: 10.1136/bmj.g7518 (Published 10 December 2014)

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LETTERS

EBOLA

Ebola virus vaccine trials: the ethical mandate for a therapeutic safety net

Steve E Bellan *postdoctoral fellow*¹, Juliet R C Pulliam *assistant professor*², Jonathan Dushoff *associate professor*³, Lauren Ancel Meyers *professor*⁴



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

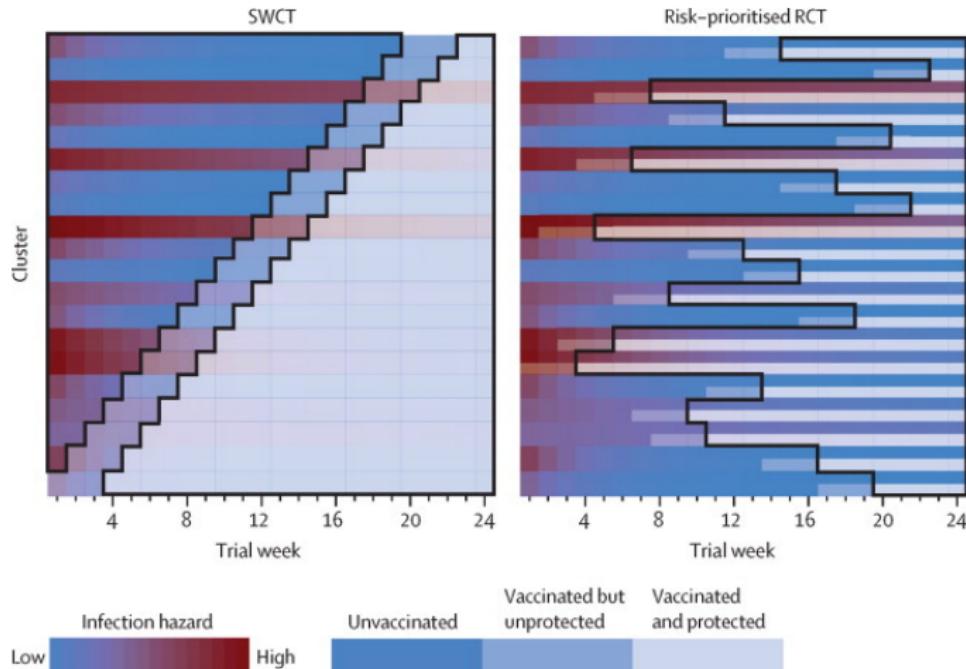
Background Safe and effective vaccines could help to end the ongoing Ebola virus disease epidemic in west Africa.

In the proposed ring vaccination trial design, contacts of incident Ebola virus disease cases are randomly assigned to be vaccinated either immediately (as in traditional ring vaccination strategies) or after some delay.¹ Although the

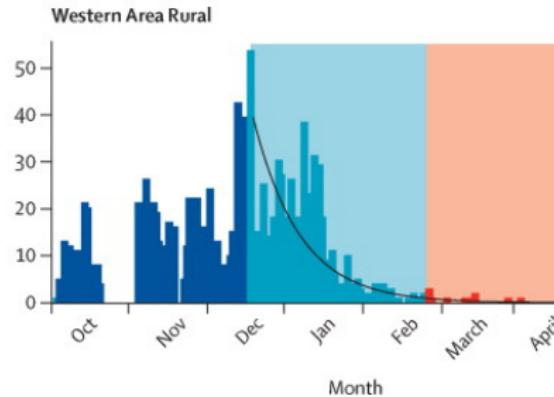
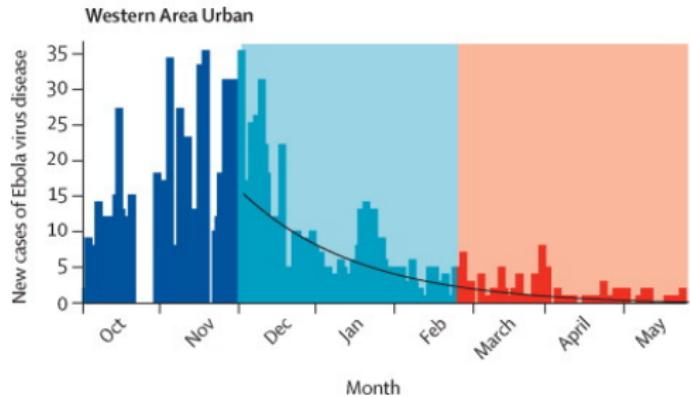
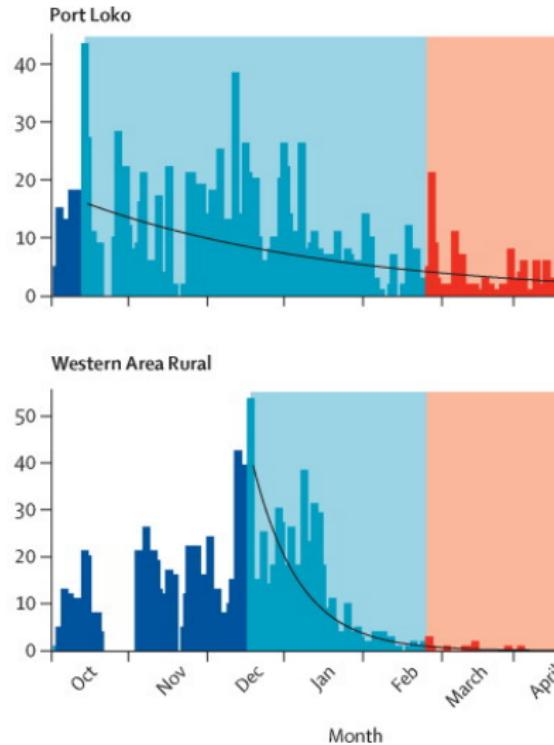
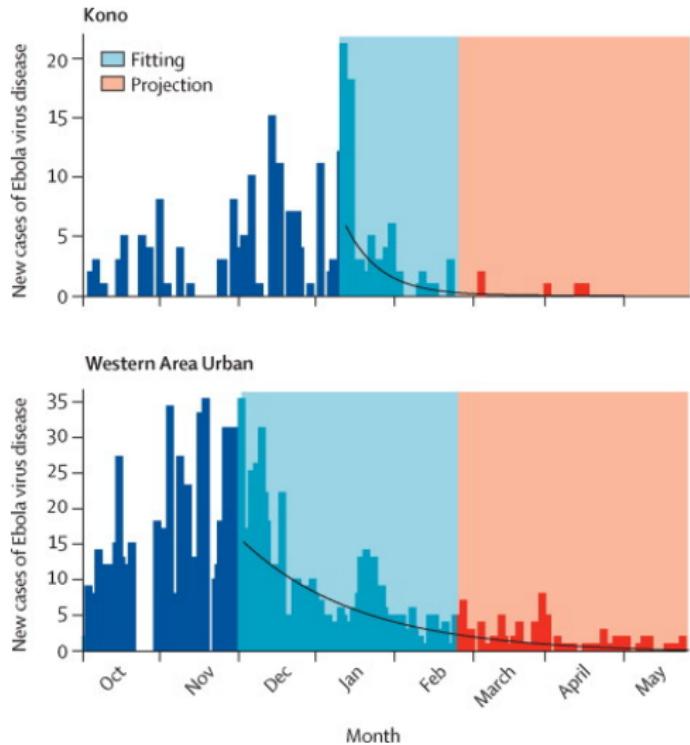
In October, 2014, when the incidence of Ebola virus disease was still rising in west Africa, the US Centers for Disease Control and Prevention (CDC) proposed an SWCT in view of these concerns. In theory, SWCTs

(Prof T C Porco PhD),
Department of Ophthalmology
(Prof T C Porco), and
Department of Epidemiology &
Biostatistics (Prof T C Porco).

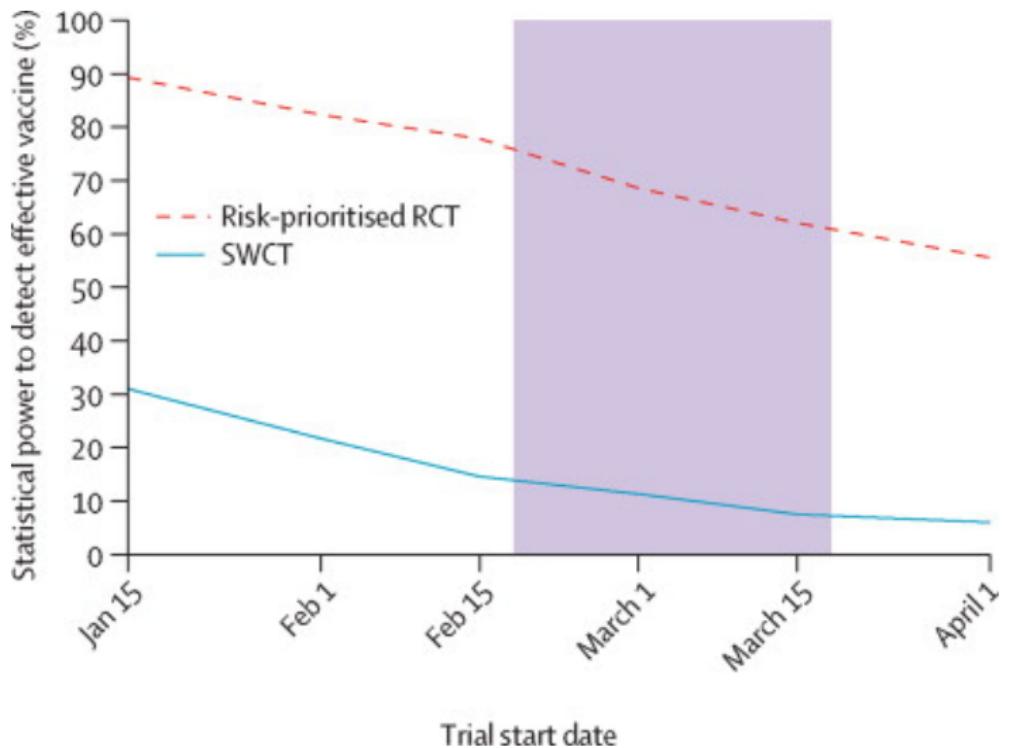
Vaccine trials



Vaccine trials



Vaccine trials



Outline

Introduction

Influenza

HIV

Malaria

Ebola

Rabies

Conclusion

Cycles and Synchrony in Africa

Synchronous cycles of domestic dog rabies in sub-Saharan Africa and the impact of control efforts

Katie Hampson^{†*}, Jonathan Dushoff^{‡‡}, John Bingham[§], Gideon Brückner[¶], Y. H. Ali^{||}, and Andy Dobson^{*}

^{*}Department of Ecology and Evolutionary Biology, Princeton University, Princeton, NJ 08544; [†]Fogarty International Center, National Institutes of Health, Bethesda, MD 20892; [‡]Australian Animal Health Laboratory, Commonwealth Scientific and Industrial Research Organization, Geelong, Victoria 3220, Australia; ^{||}Department of Agriculture, Chief Directorate Veterinary Services, Private Bag X1, Elsenburg 7607, South Africa; and [§]Virology Department, Central Veterinary Research Laboratory, P.O. Box 8067, Khartoum, Sudan

Edited by Bruce Levin, Emory University, Atlanta, GA, and accepted by the Editorial Board March 13, 2007 (received for review October 16, 2006)

Rabies is a fatal neurological pathogen that is a persistent problem throughout the developing world where it is spread primarily by domestic dogs. Although the disease has been extensively studied in wildlife populations in Europe and North America, the dynamics of rabies in domestic dog populations have been almost entirely

little has been published on the spatial and temporal dynamics of rabies in domestic dogs, which we might expect to be different. Surveillance data for rabies in domestic dog populations are scant compared with comprehensive data sets of rabies in

most other developing countries. Because rabies in developing countries have been well documented for the spread of rabies in Europe and North America (15–18). In contrast, very

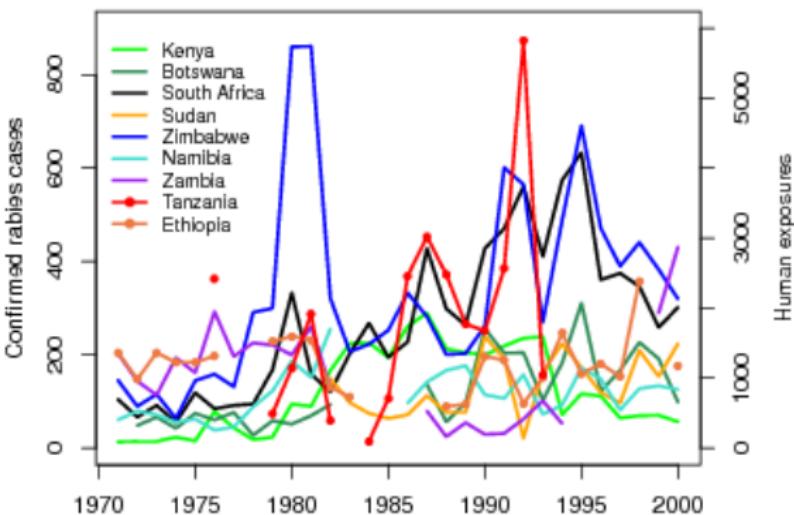
This article contains supporting information online at [www.pnas.org/lookup/doi/10.1073/pnas.0609122104/DC1](http://www.pnas.org/lookup/doi/10.1073/pnas.0609122104).

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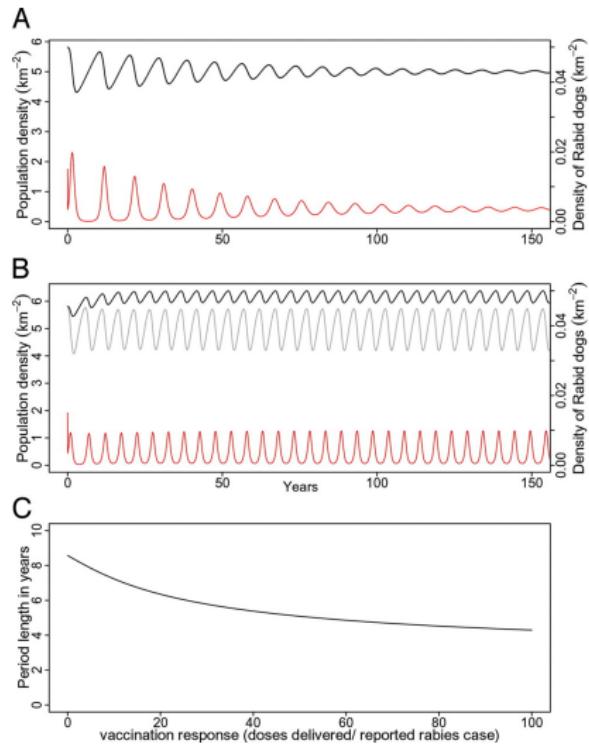
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Cycles and Synchrony in Africa



Cycles and Synchrony in Africa



Rabies transmission in Tanzania

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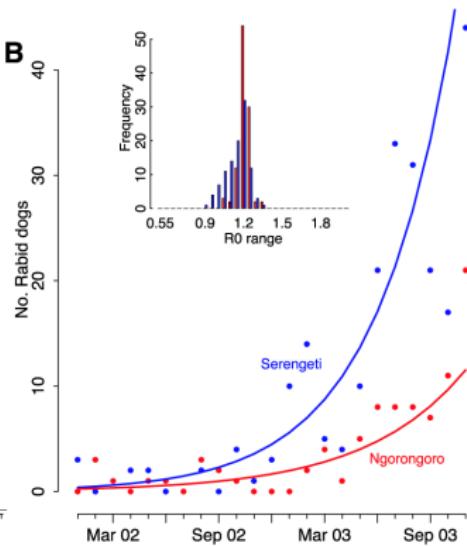
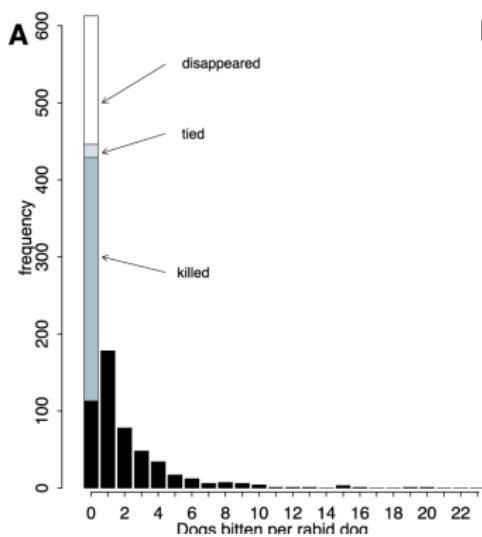
Transmission Dynamics and Prospects for the Elimination of Canine Rabies

Katie Hampson^{1,2*}, Jonathan Dushoff³, Sarah Cleaveland^{4,5}, Daniel T Haydon⁵, Magai Kaare⁶, Craig Packer⁷,
Andy Dobson¹

1 Department of Ecology and Evolutionary Biology, Princeton University, Princeton, New Jersey, United States of America, **2** Department of Animal and Plant Sciences, University of Sheffield, Western Bank, Sheffield, United Kingdom, **3** Department of Biology, McMaster University, Hamilton, Ontario, Canada, **4** The Roslin Institute/Royal (Dick) School of Veterinary Studies, University of Edinburgh, Easter Bush, Roslin, Midlothian, United Kingdom, **5** Boyd Orr Centre for Population and Ecosystem Health, University of Glasgow, Glasgow, United Kingdom, **6** Centre for Infectious Diseases, School of Biological Sciences, University of Edinburgh, Edinburgh, Midlothian, United Kingdom, **7** Department of Ecology, Evolution and Behavior, University of Minnesota, St. Paul, Minnesota, United States of America

Rabies has been eliminated from domestic dog populations in Western Europe and North America, but continues to kill

Rabies transmission in Tanzania



Global rabies burden



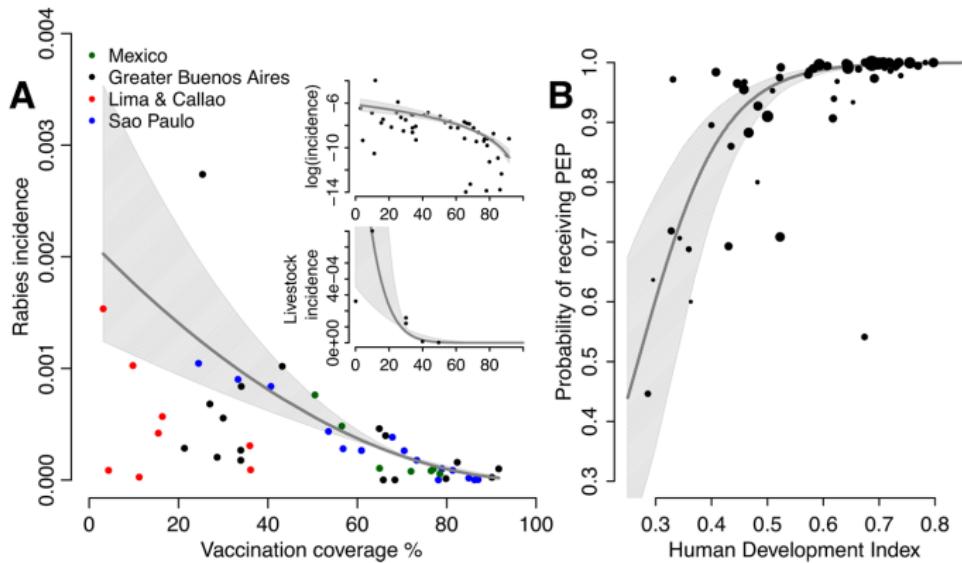
RESEARCH ARTICLE

Estimating the Global Burden of Endemic Canine Rabies

Katie Hampson^{1*}, Laurent Coudeville², Tiziana Lembo¹, Maganga Sambo³,
Alexia Kieffer², Michaël Attlan², Jacques Barrat⁴, Jesse D. Blanton⁵, Deborah J. Briggs⁶,
Sarah Cleaveland¹, Peter Costa⁶, Conrad M. Freuling⁷, Elly Hiby⁸, Lea Knopf⁹,
Fernando Leanes⁹, François-Xavier Meslin¹⁰, Artem Metlin¹¹, Mary Elizabeth Miranda⁶,
Thomas Müller⁷, Louis H. Nel¹², Sergio Recuenco⁶, Charles E. Rupprecht^{6,13},
Carolin Schumacher¹⁴, Louise Taylor⁶, Marco Antonio Natal Vigilato⁹, Jakob Zinsstag¹⁵,
Jonathan Dushoff¹⁶, on behalf of the Global Alliance for Rabies Control Partners for
Rabies Prevention



Global rabies burden



Outline

Introduction

Influenza

HIV

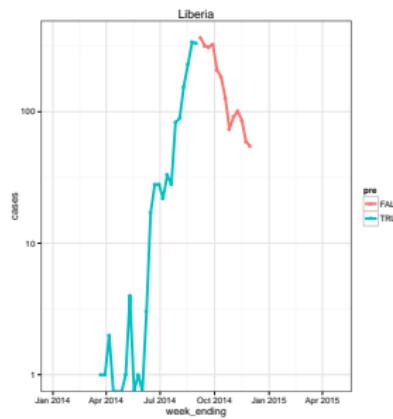
Malaria

Ebola

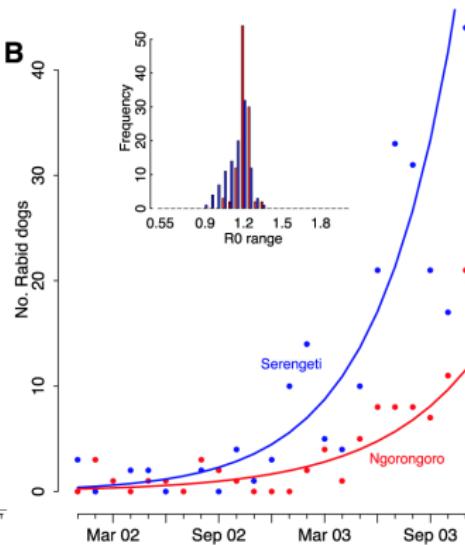
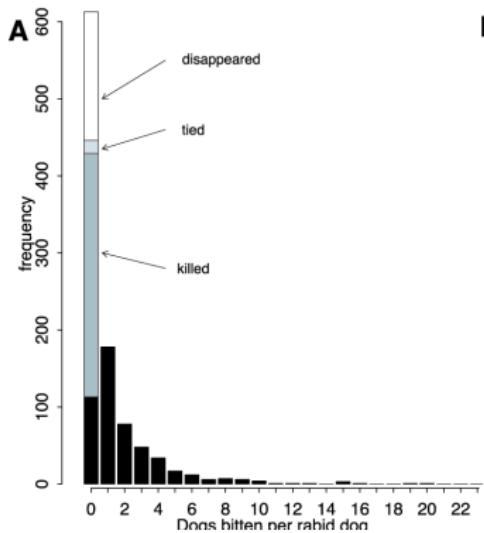
Rabies

Conclusion

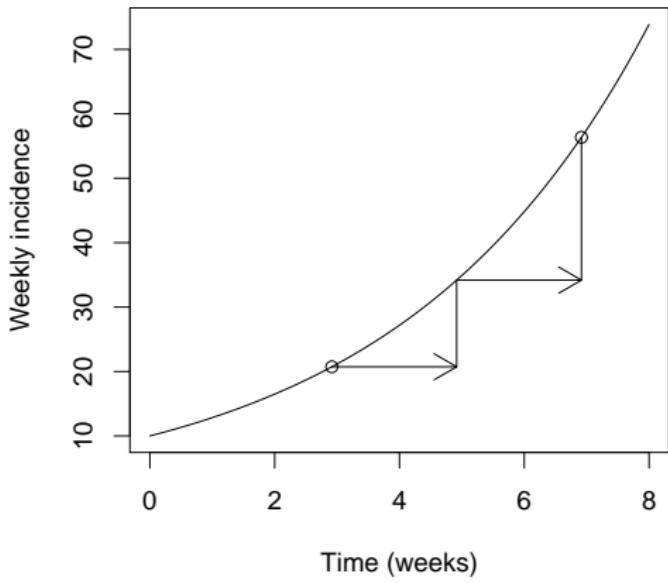
Dynamical models link scales



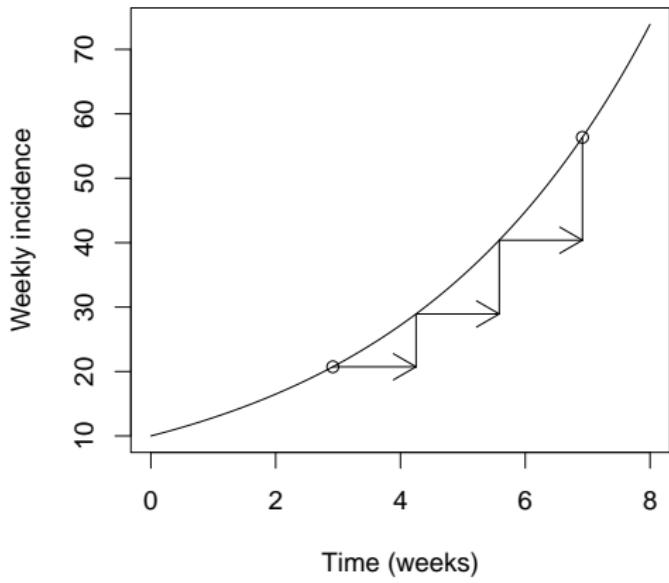
Linking dynamics and statistics



Bridge between strength and speed of epidemics



Bridge between strength and speed of epidemics



Close the loop



Thanks

- ▶ Organizers
- ▶ Audience
- ▶ Collaborators
- ▶ Funders: NSERC,
CIHR

