Model-Based Inference and the Bigger Picture

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DAIDD 2017 – 2021

Slide Set Citation: [DOI:10.6084/m9.figshare.5687155](https://doi.org/10.6084/m9.figshare.5687155)

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Goals

- Examine examples of model-based (mechanistic) inference

- Understand differences between model-based inference and classical statistical inference

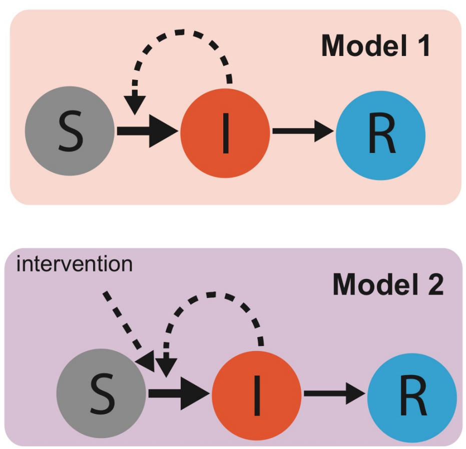
Model-Based Inference

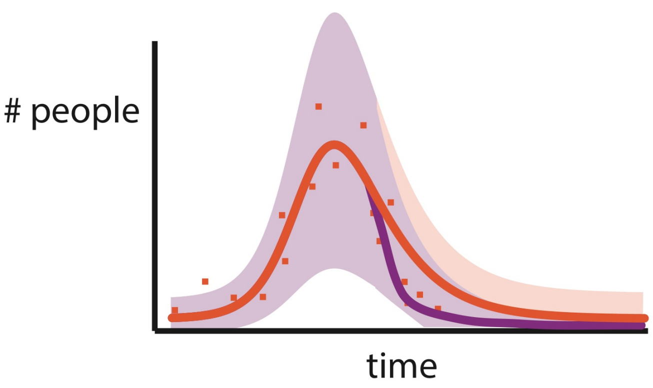
- Testing hypotheses using mechanistic models
- Requires a model!
- Can lead to strong conclusions when model captures key processes

Mechanistic Epidemiology

- Scale up from individual processes to population patterns
- "What if" scenarios not amenable to experimentation
- Estimating parameters by fitting available data
- Prediction
- Model selection

data focus emerged in last 10 years





Model-Based Inference

- Parameter estimation
- Prediction
- Model selection
- Let's learn from 2 quick examples:
  - Ebola: Evaluating interventions
  - HIV: Disentangling transmission routes

Measuring the impact of Ebola control measures in Sierra Leone

Adam Kucharski, Anton Camacho, Stefan Flasche,
Rebecca Glover, John Edmunds, Sebastian Funk

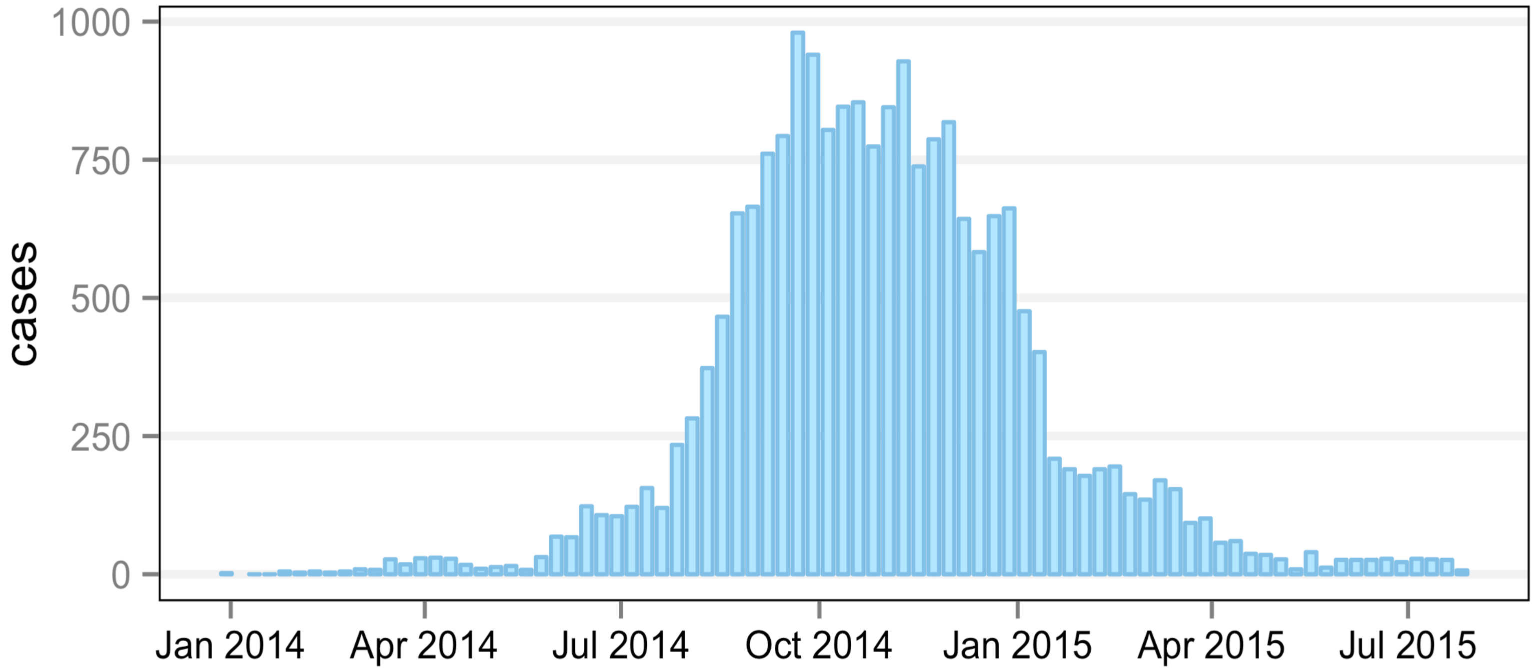
Epidemics[5]

3rd December 2015

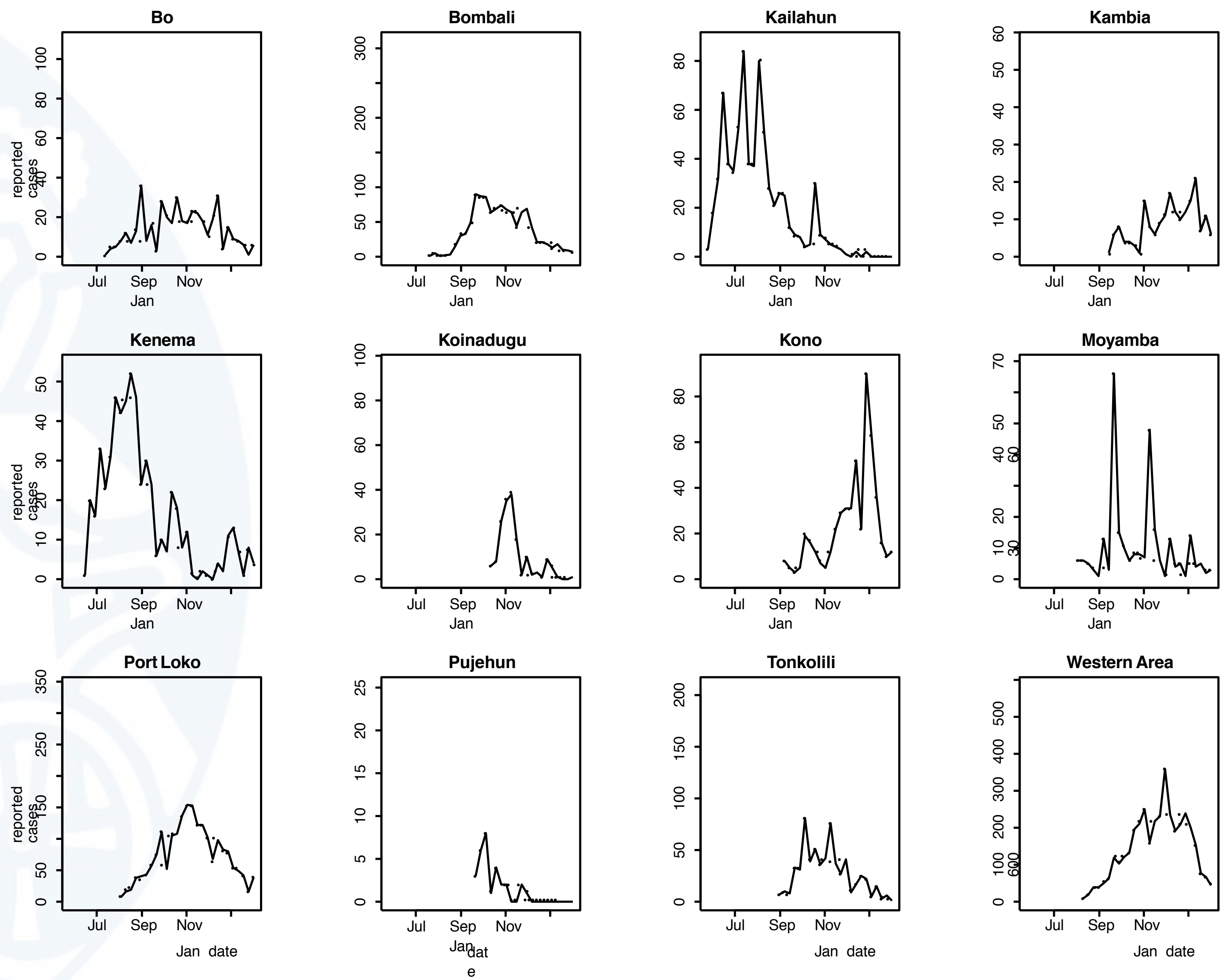
centre for the mathematical modelling of infectious diseases

LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE

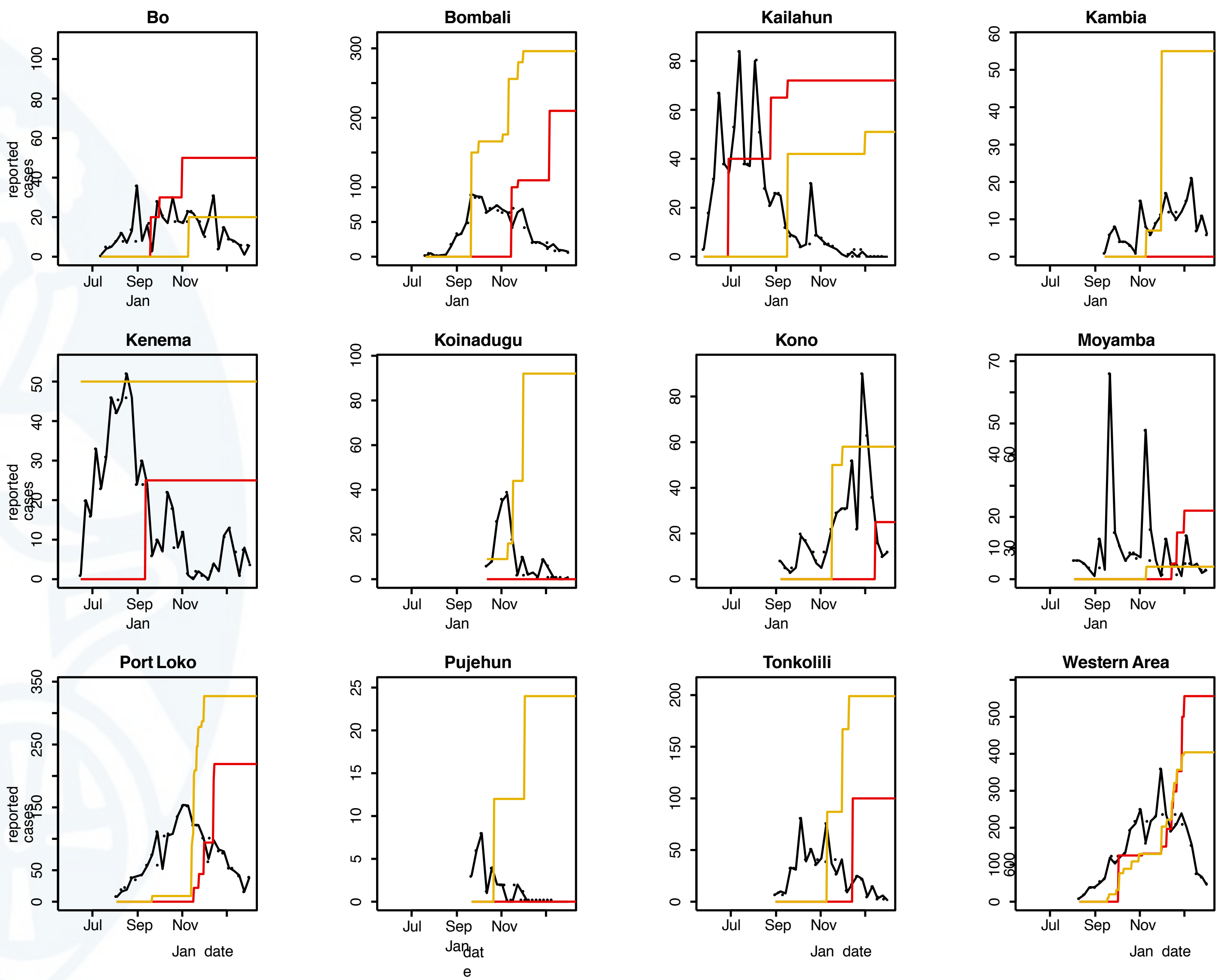
Ebola in West Africa



cmmid.lshtm.ac.uk/research/ebola



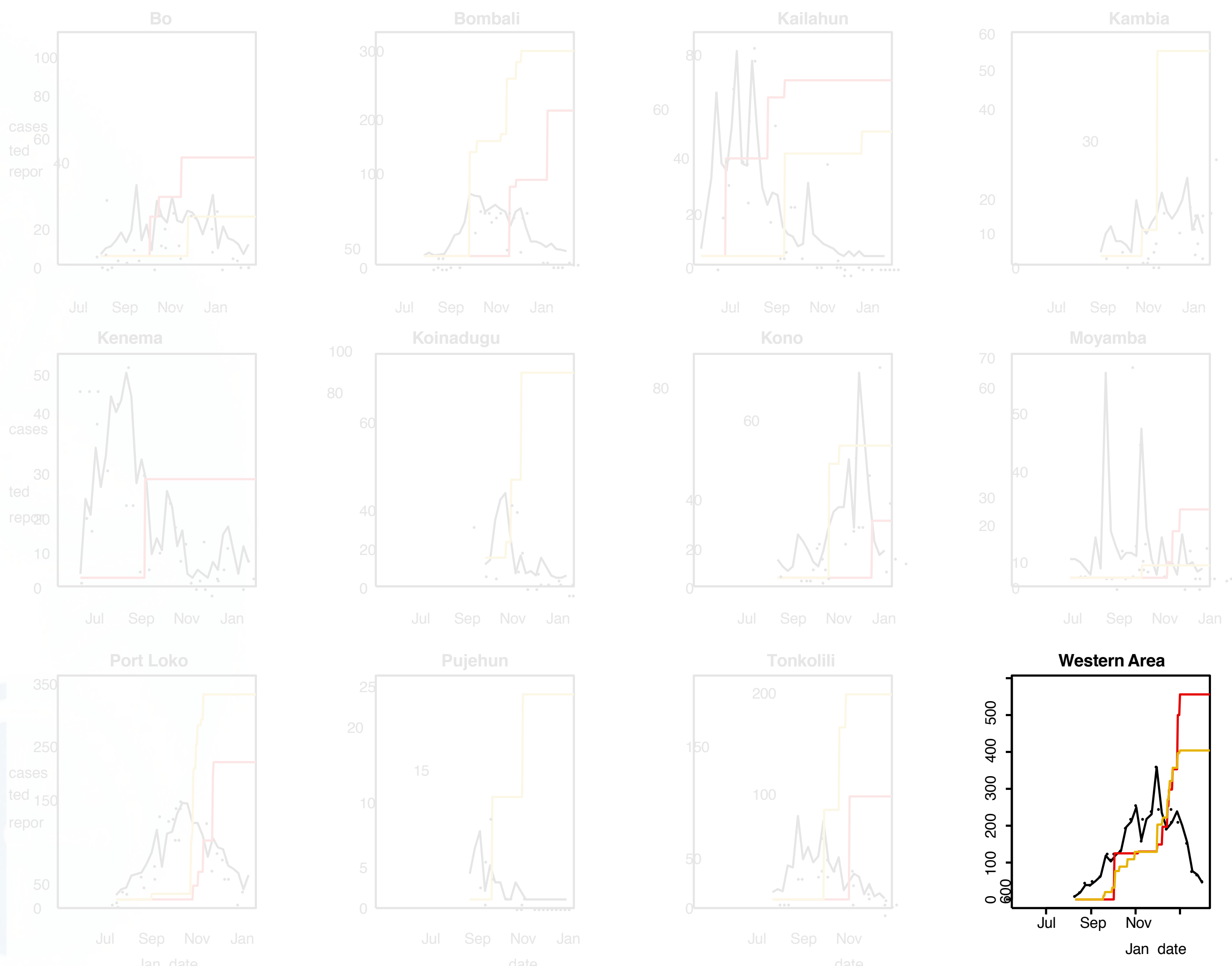
Camacho et al. (2015) *PLOS Currents*



ETU (beds)
Ebola Treatment Units

EHC/CCC (beds)
Ebola Holding Centres
Community Care Centres

Camacho et al. (2015) *PLOS Currents*



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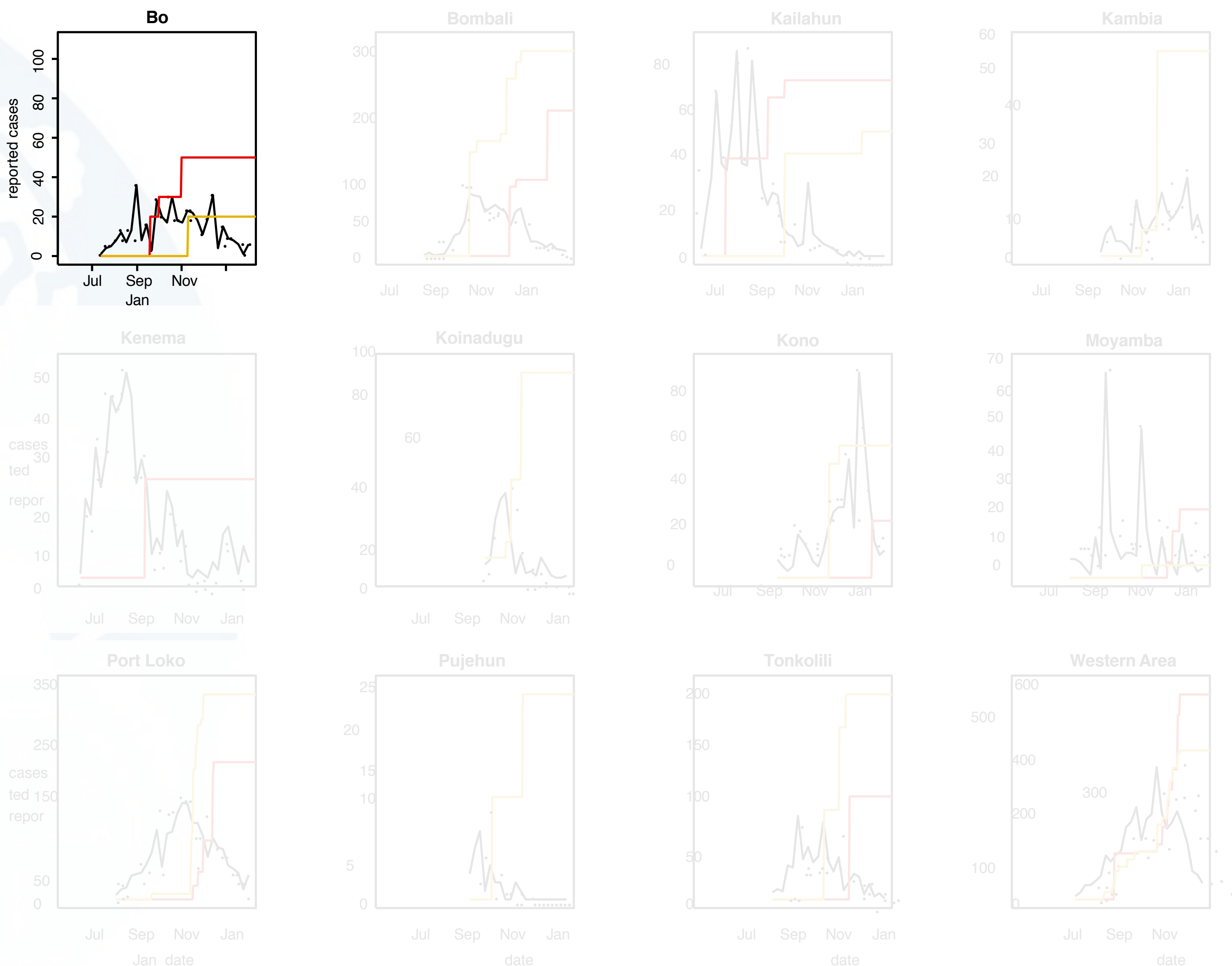

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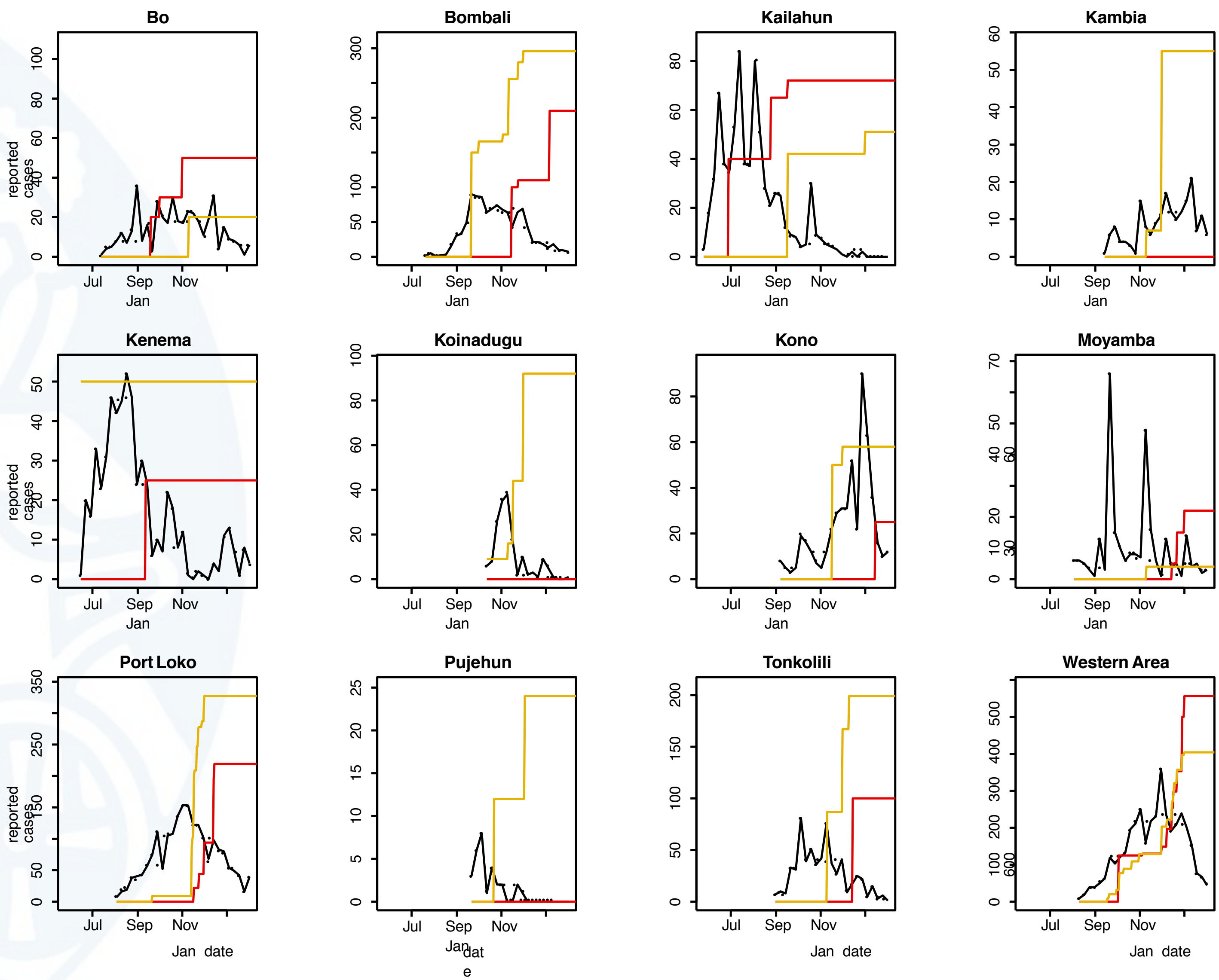

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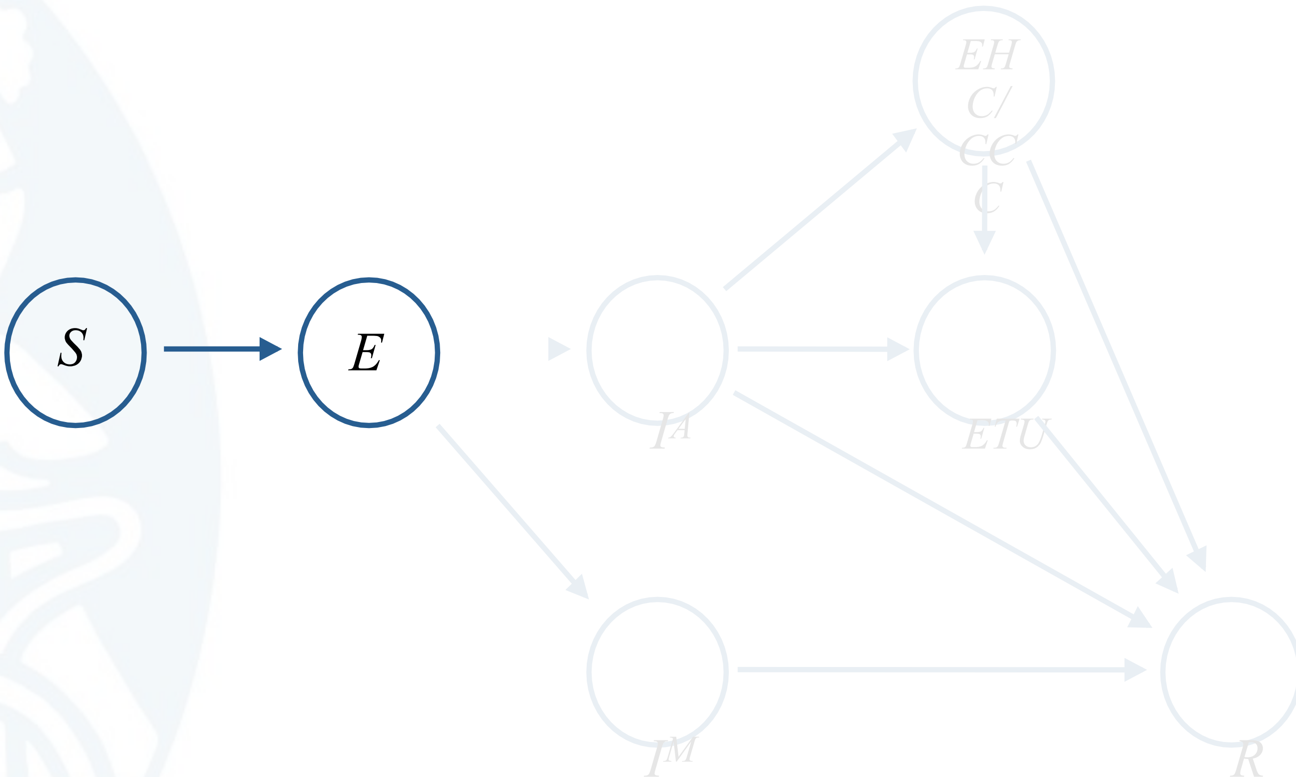
Model structure



Kucharski et al. (2015) *PNAS*

Legrand et al. (2007) *Epidemiol Infect*

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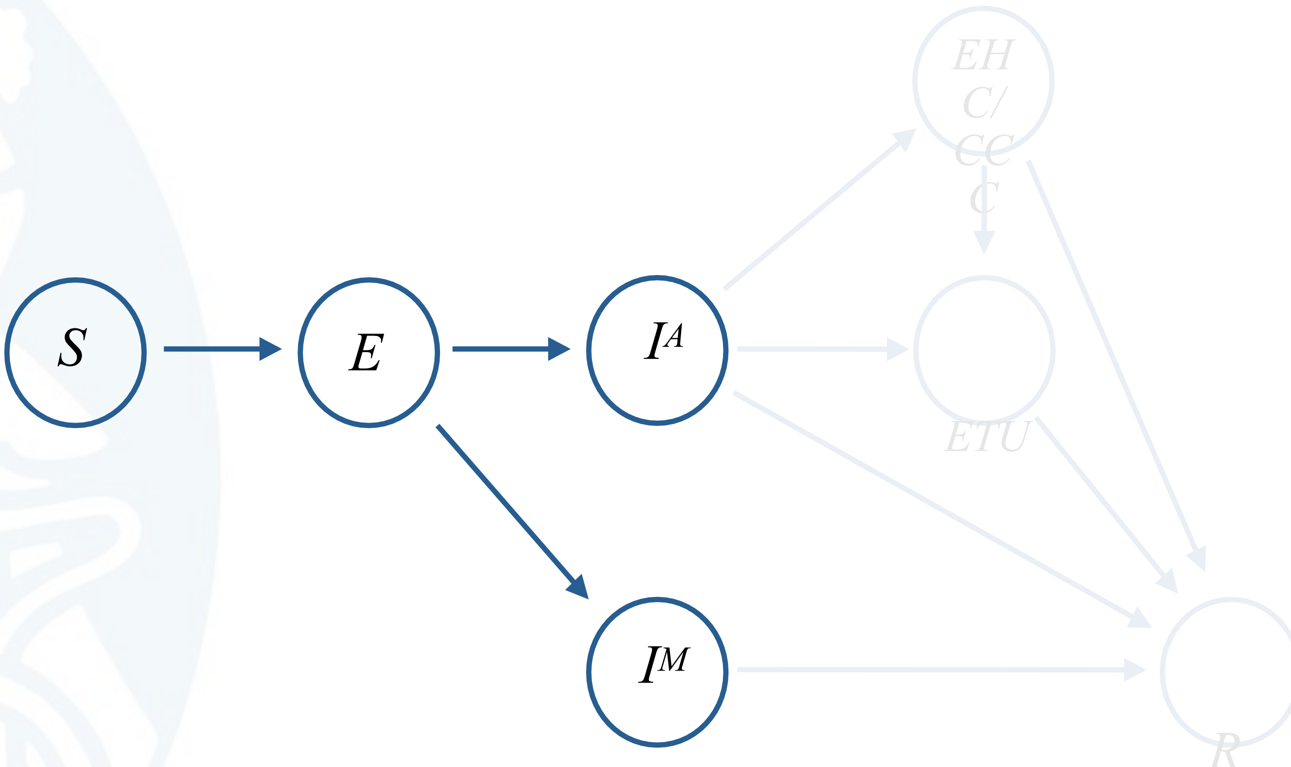

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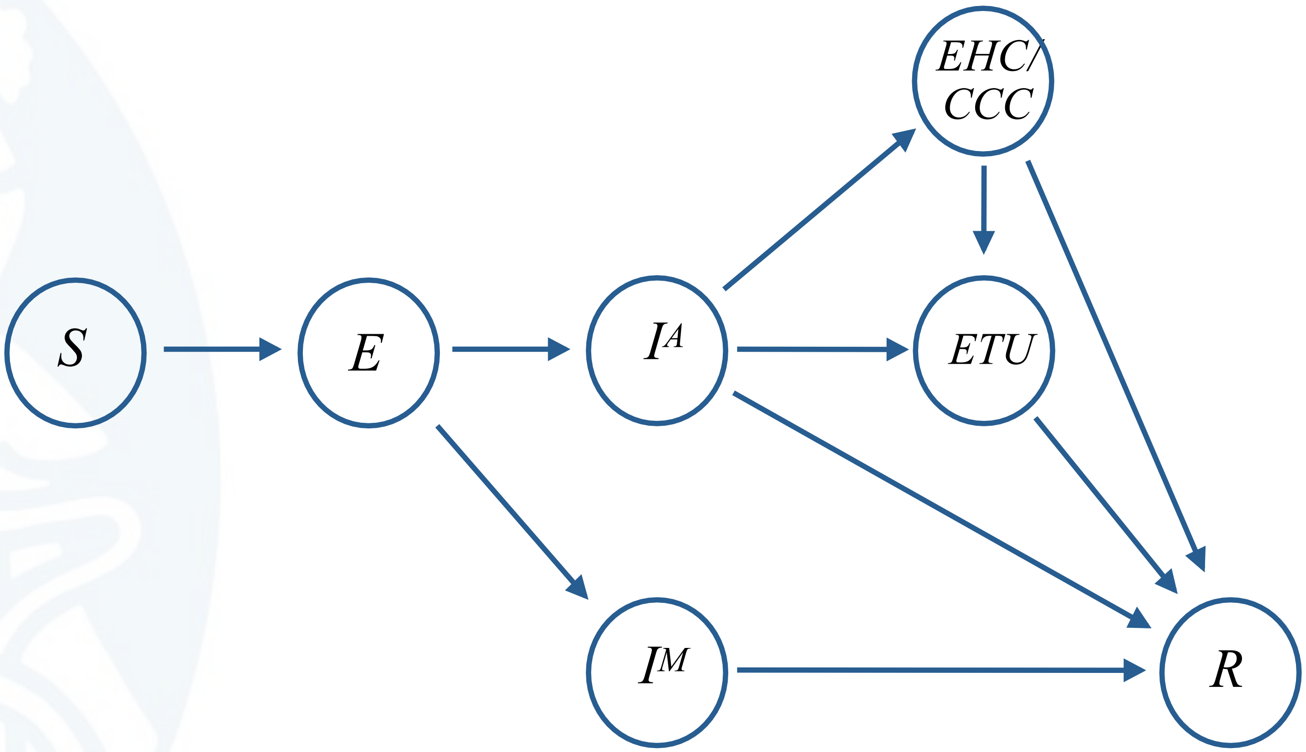

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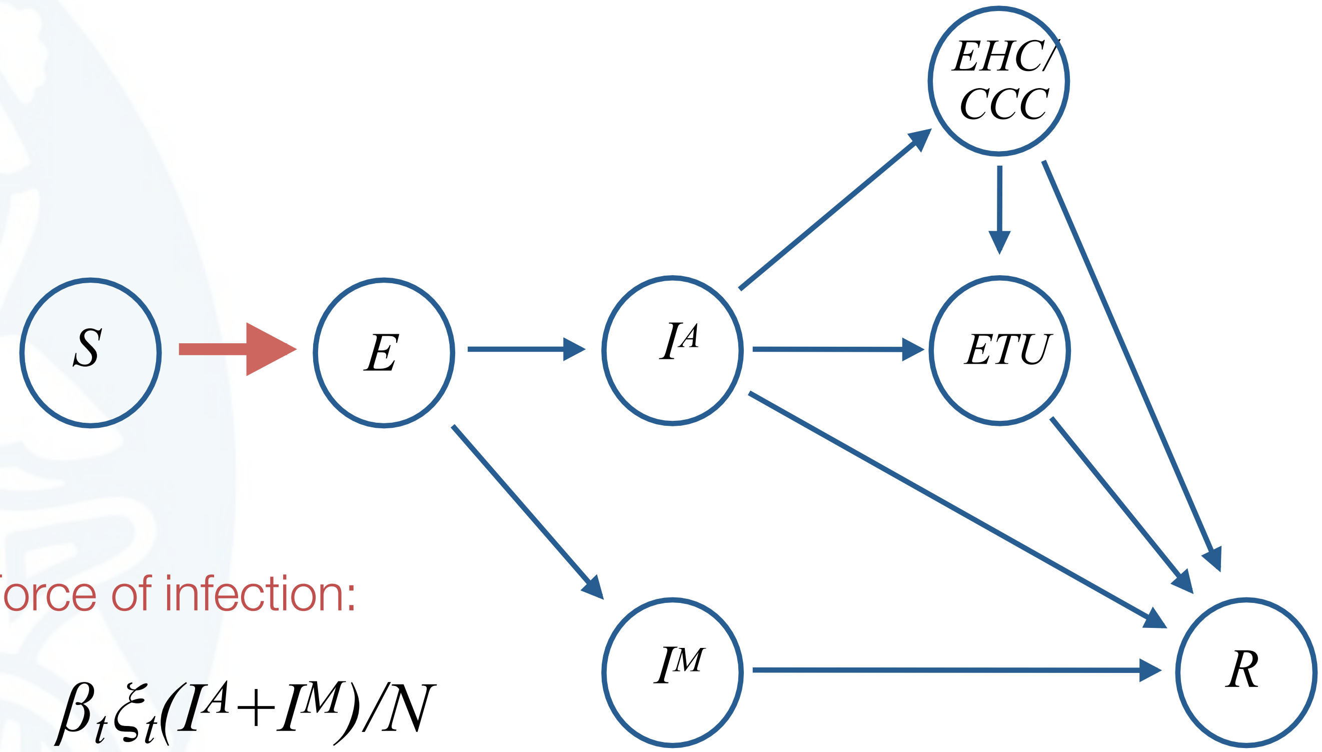


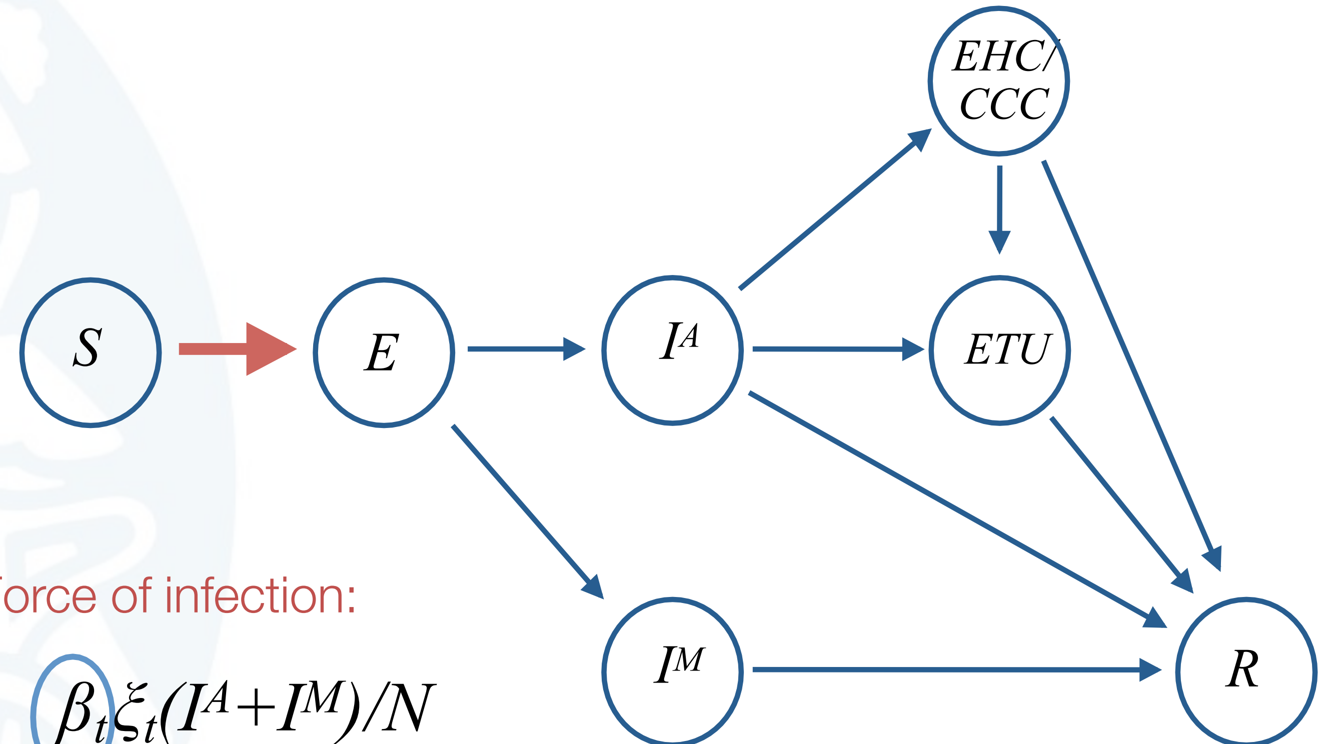
Force of infection:

$$\beta_t \xi_t (I^A + I^M)/N$$

Kucharski et al. (2015) *PNAS*

Legrand et al. (2007) *Epidemiol Infect*

Model structure



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Time varying transmission rate

Kucharski et al. (2015) *PNAS*

Legrand et al. (2007) *Epidemiol Infect*

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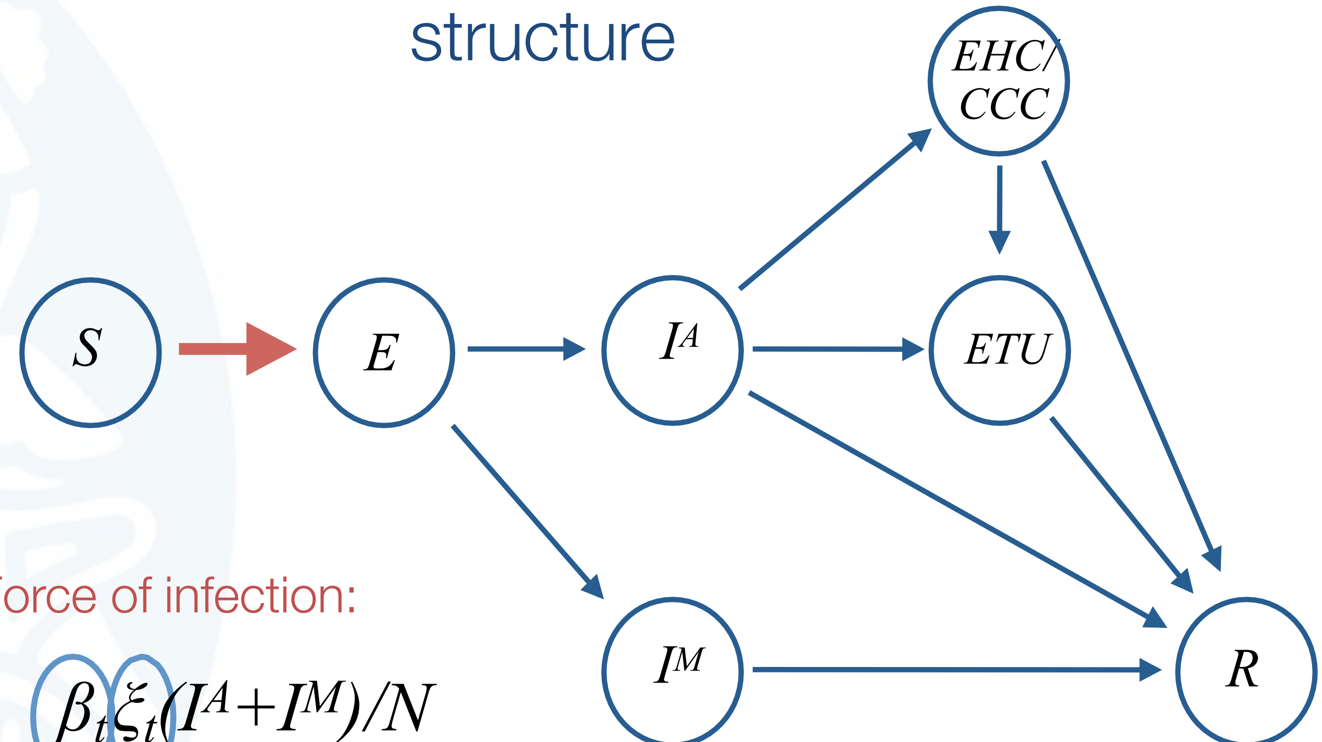

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Time varying transmission rate

Environmental noise

Kucharski et al. (2015) *PNAS*

Legrand et al. (2007) *Epidemiol Infect*

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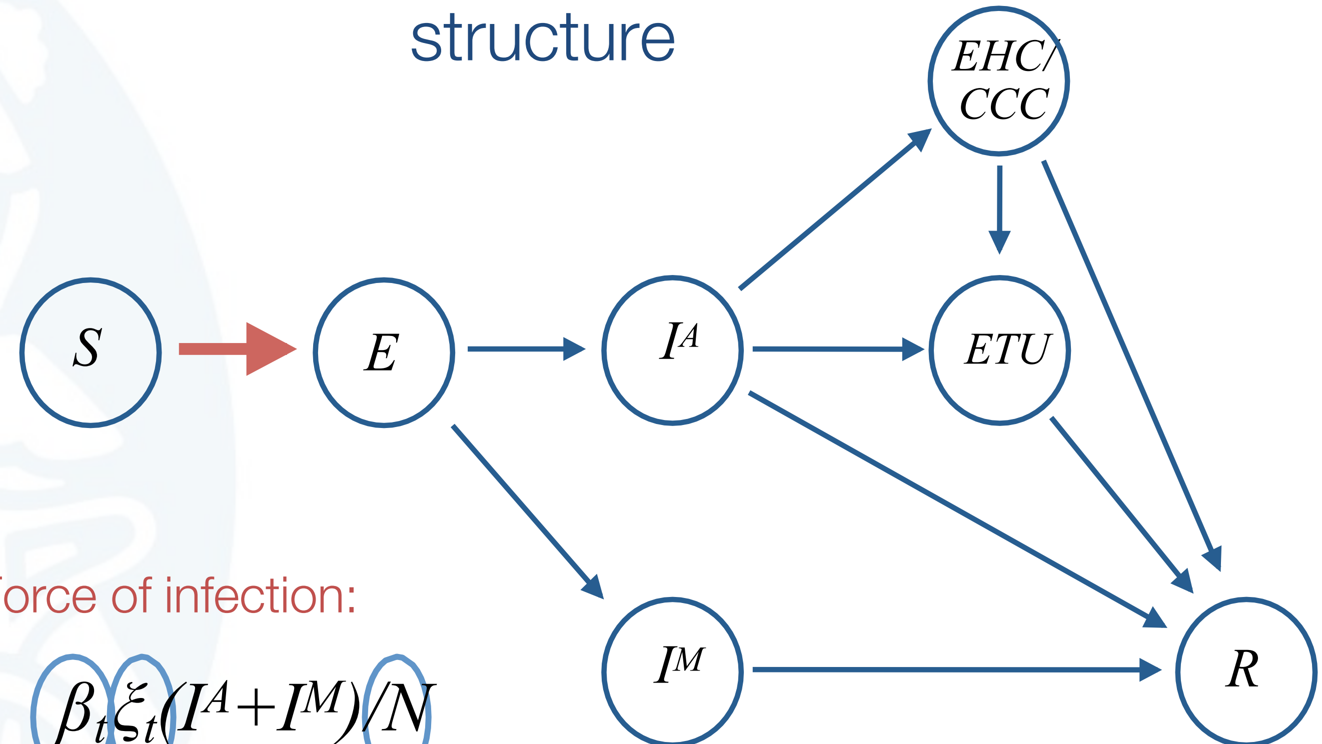

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Time varying transmission rate

Environmental noise

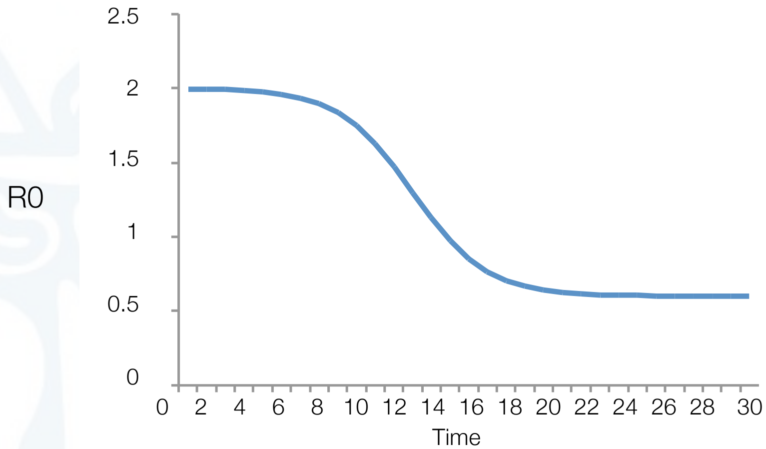
District population size

Kucharski et al. (2015) *PNAS*

Legrand et al. (2007) *Epidemiol Infect*

Parameters

- Flexible sigmoid for transmission rate:



- Natural history parameters from WHO sitreps/database
- Assume 60% cases ascertained in main analysis (sensitivity 40/80%)

Chowell et al. (2004) *J Theor Biol*

Camacho et al. (2014) *Epidemics*

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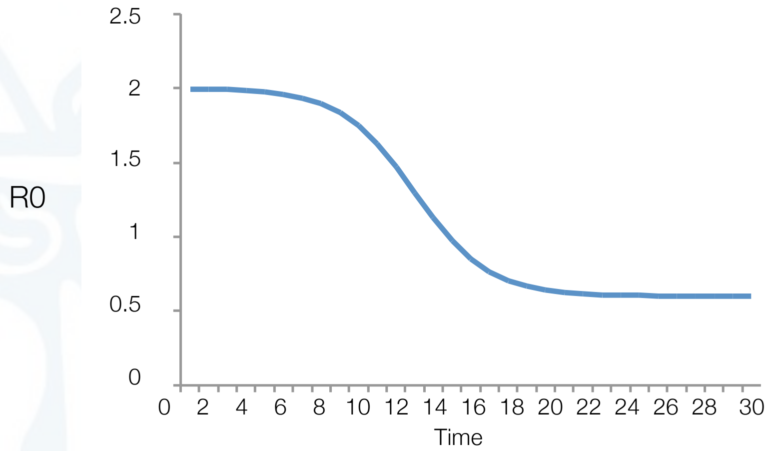

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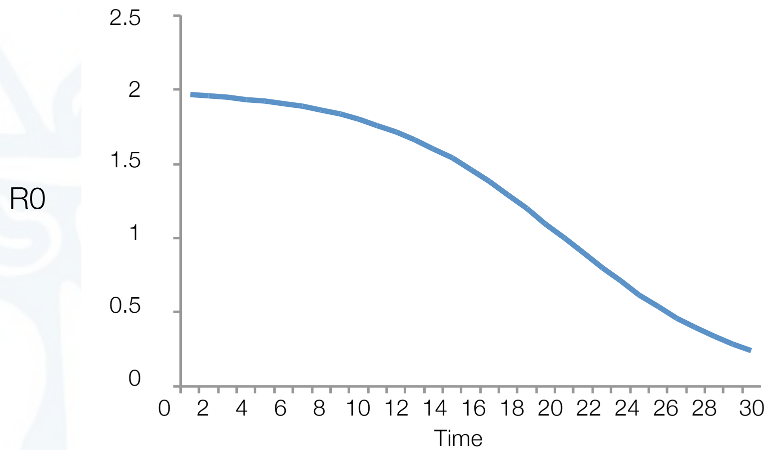

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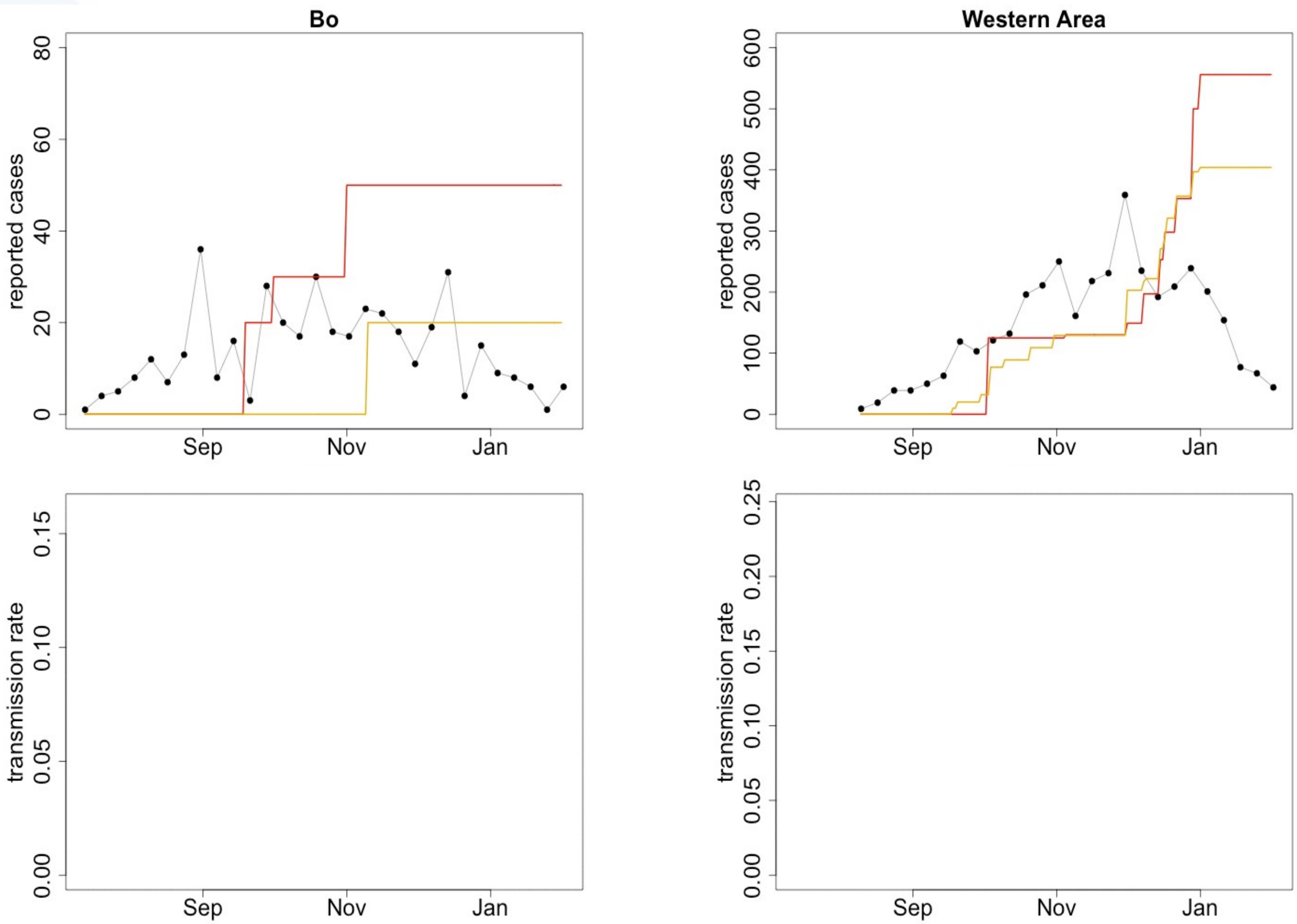

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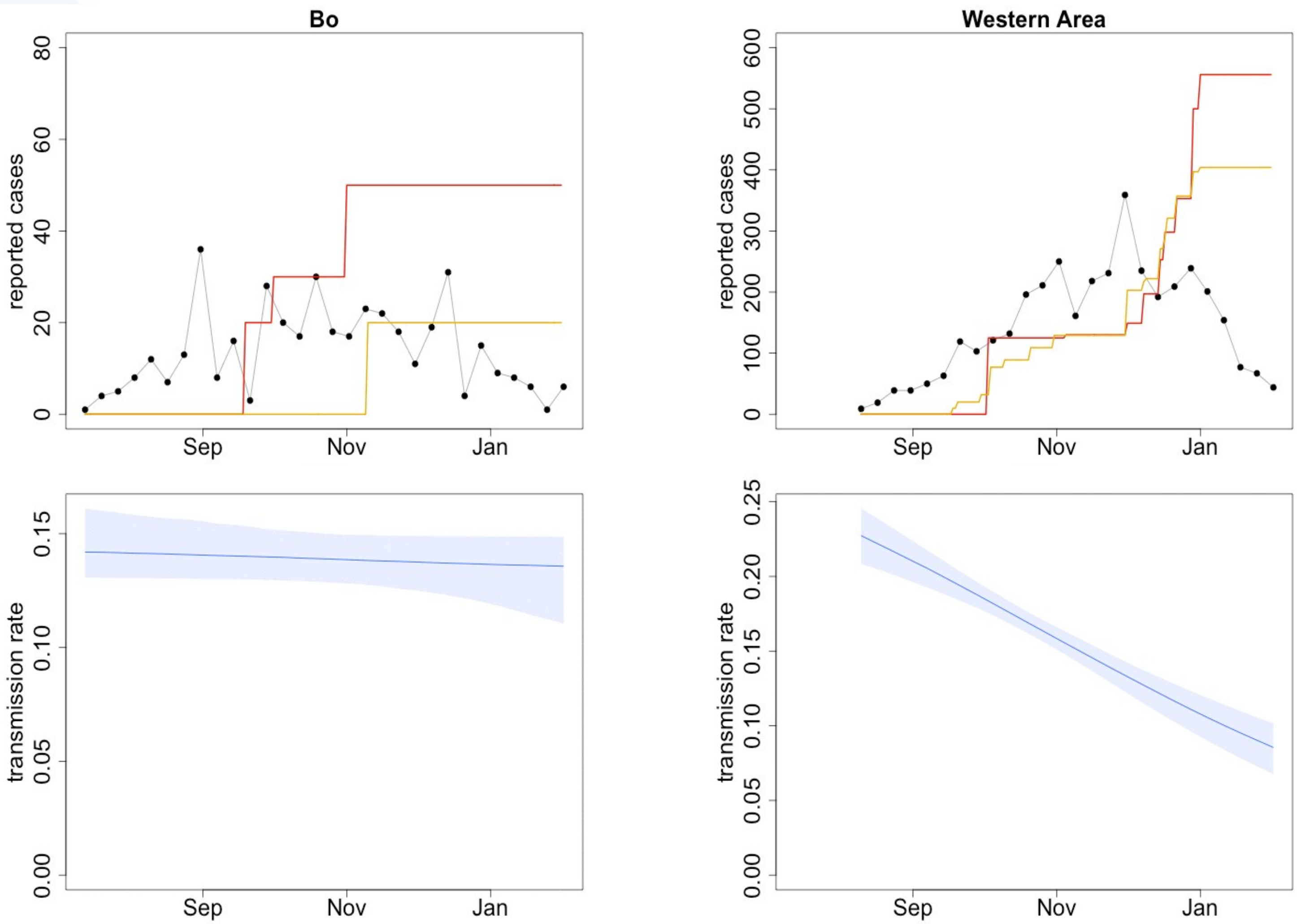

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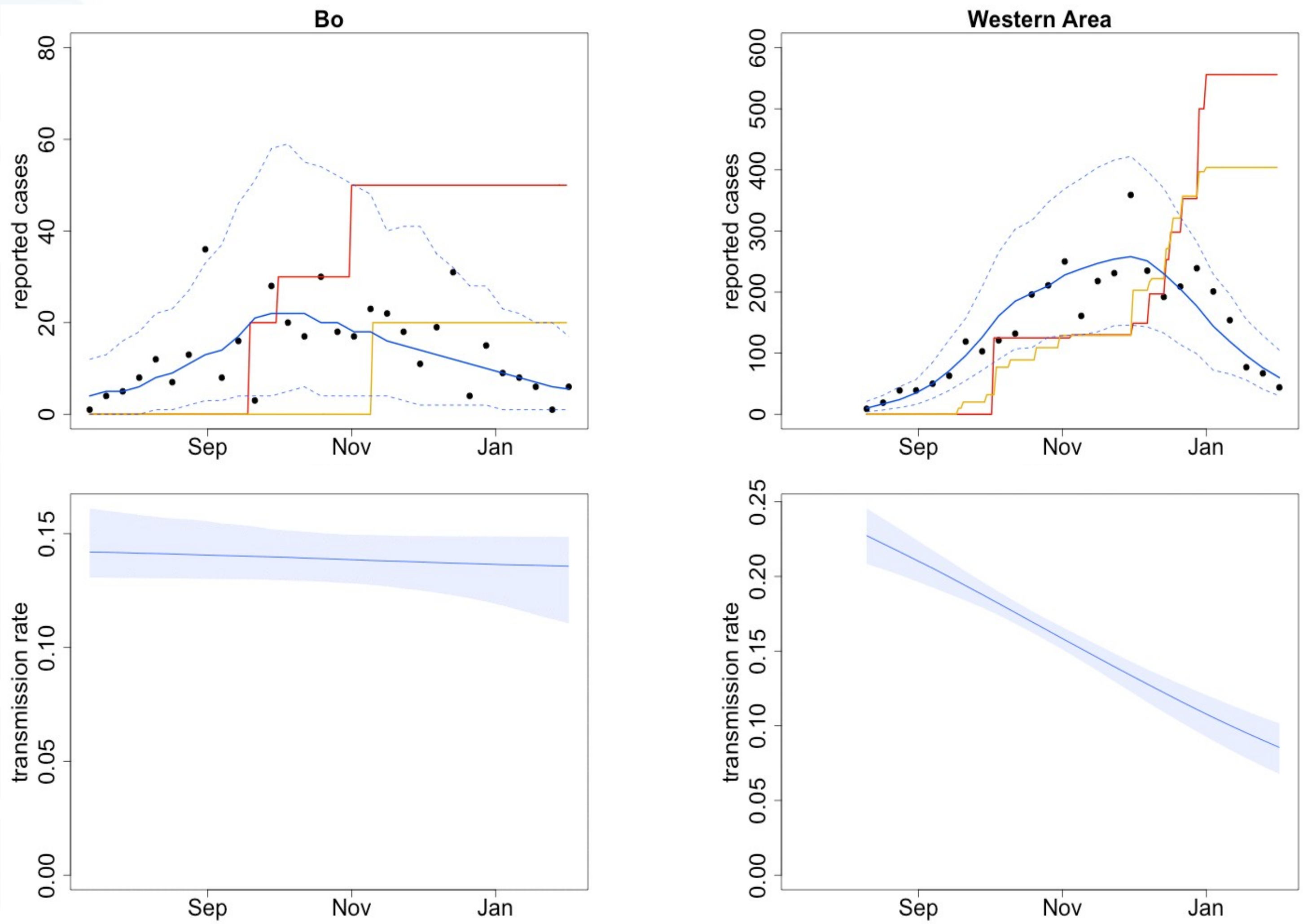

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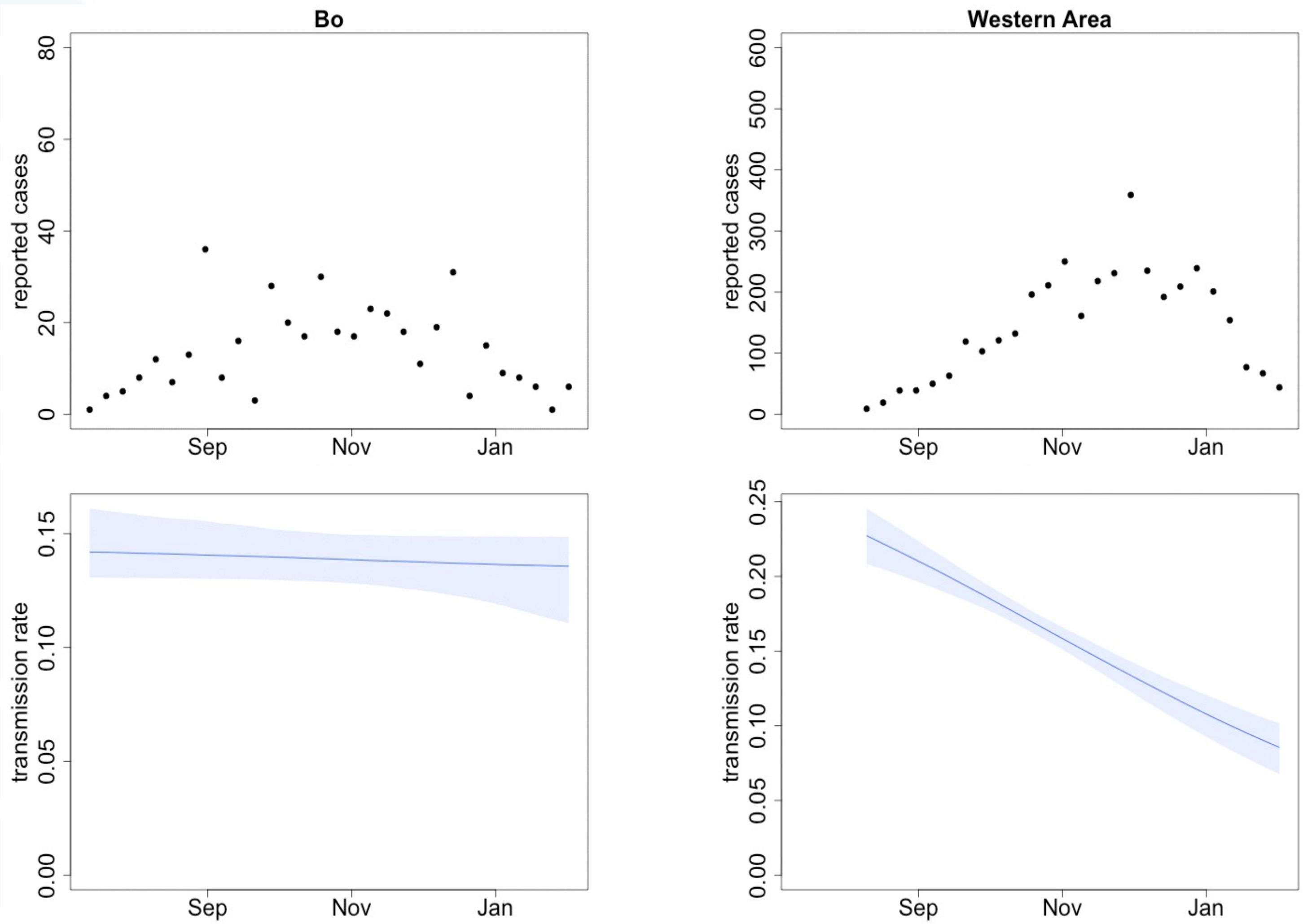

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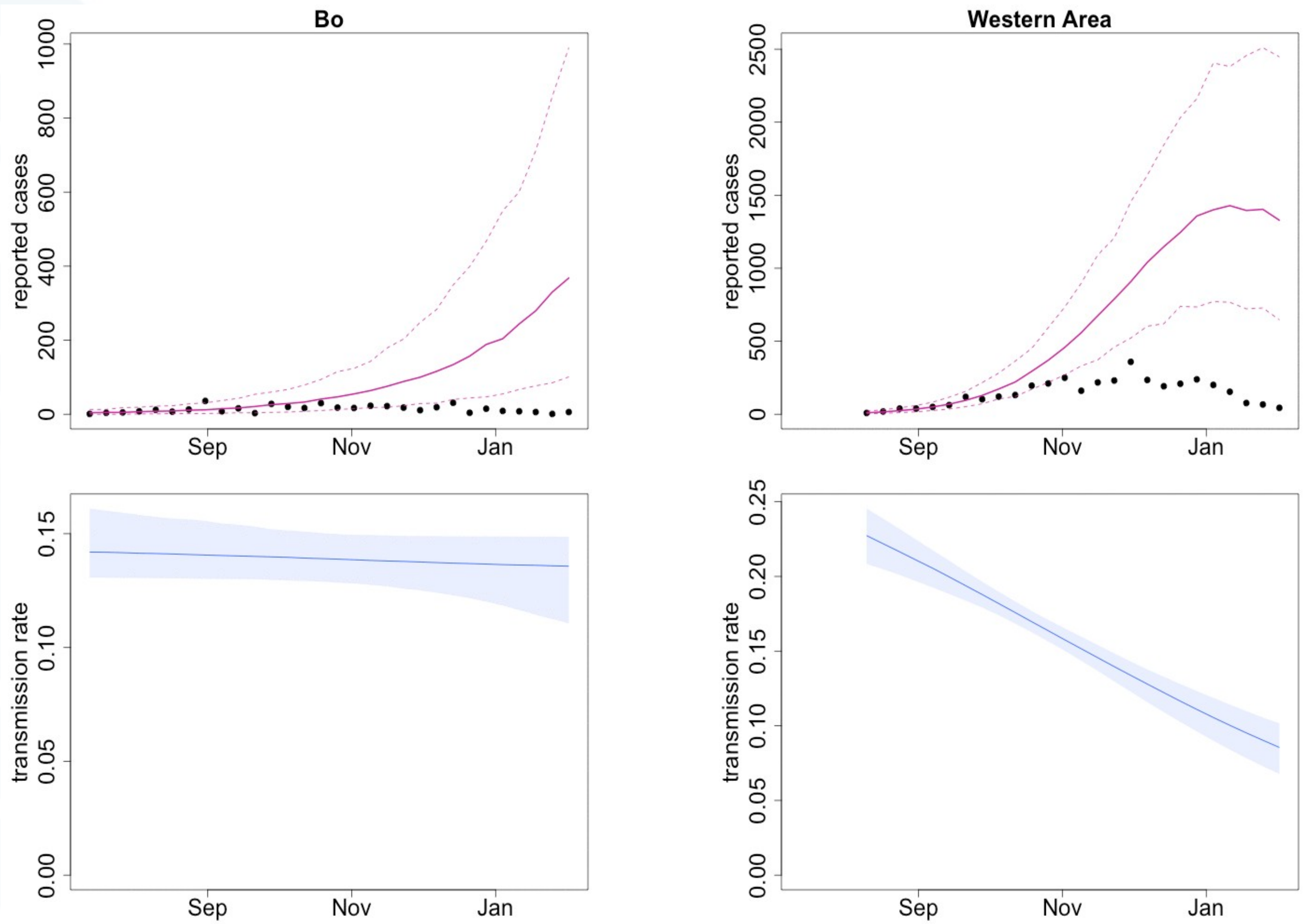

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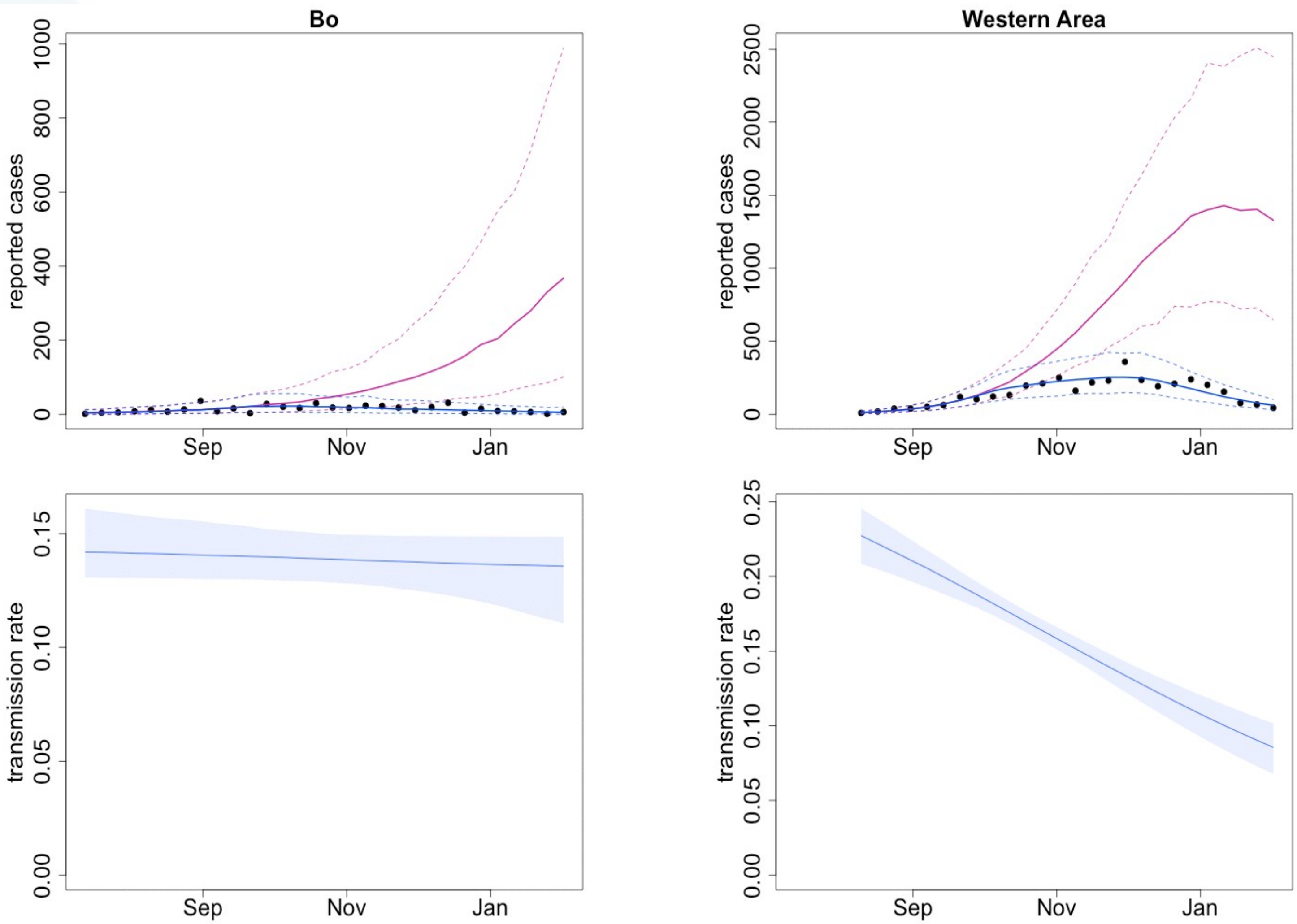

Kucharski et al. (2015) *PNAS*

Difference in cases

District	Total beds	Cases averted
Bo	124	6,310 (4,150–9,040)
Western Area	960	32,600 (25,500–40,200)
Bombali	506	6,480 (1,800–22,900)
Kailahun	123	3,650 (2,250–6,750)
Kambia	55	545 (2–4,430)
Kenema	75	1 (0–10,500)
Koinadugu	92	35 (11–104)
Kono	83	1,570 (928–2,430)
Moyamba	34	130 (77–197)
Port Loko	546	3,850 (853–13,400)
Pujehun	24	11 (2–34)
Tonkolili	349	568 (140–2,900)
Total	2971	56,600 (48,300–84,500)

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Kucharski et al. (2015) *PNAS*

Cases averted

District	**Addition of beds**	**4 weeks earlier**
Bo	6,310 (4,150–9,040)	6,820 (4,730–9,620)
Western Area	32,600 (25,500–40,200)	39,200 (32,100–47,100)
Total	56,600 (48,300–84,500)	69,100 (59,500–122,000)

Kucharski et al. (2015) *PNAS*

Summary

- Introduction of beds prevented around 57,000 cases in Sierra Leone between June 2014 and February 2015.

- Cases averted would have been even higher with earlier response.

- Reduction in community transmission occurred alongside introduction of beds.

wellcome trust

r2hc research for health in humanitarian crises

UK aid from the British people

Model Taxonomy

	Continuous treatment of individuals (averages, proportions, or population densities)	Discrete treatment of individuals
Deterministic	**Continuous time** **Discrete time**	
Stochastic	**Continuous time** **Discrete time**	**Continuous time** **Discrete time**

Model Taxonomy

CONTINUOUS TREATMENT OF INDIVIDUALS

(averages, proportions, or population densities)

DISCRETE TREATMENT OF INDIVIDUALS

DETERMINISTIC

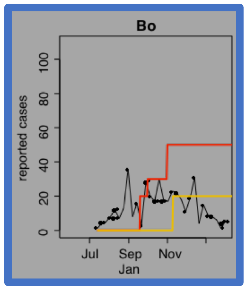
CONTINUOUS TIME

DISCRETE TIME

STOCHASTIC

CONTINUOUS TIME

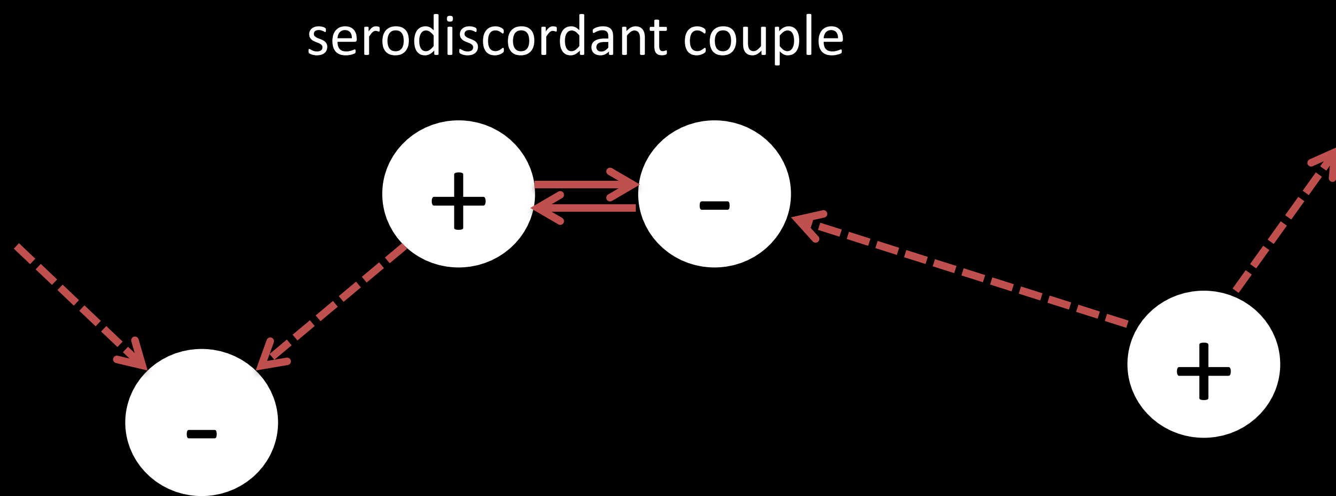
DISCRETE TIME



CONTINUOUS TIME

DISCRETE TIME

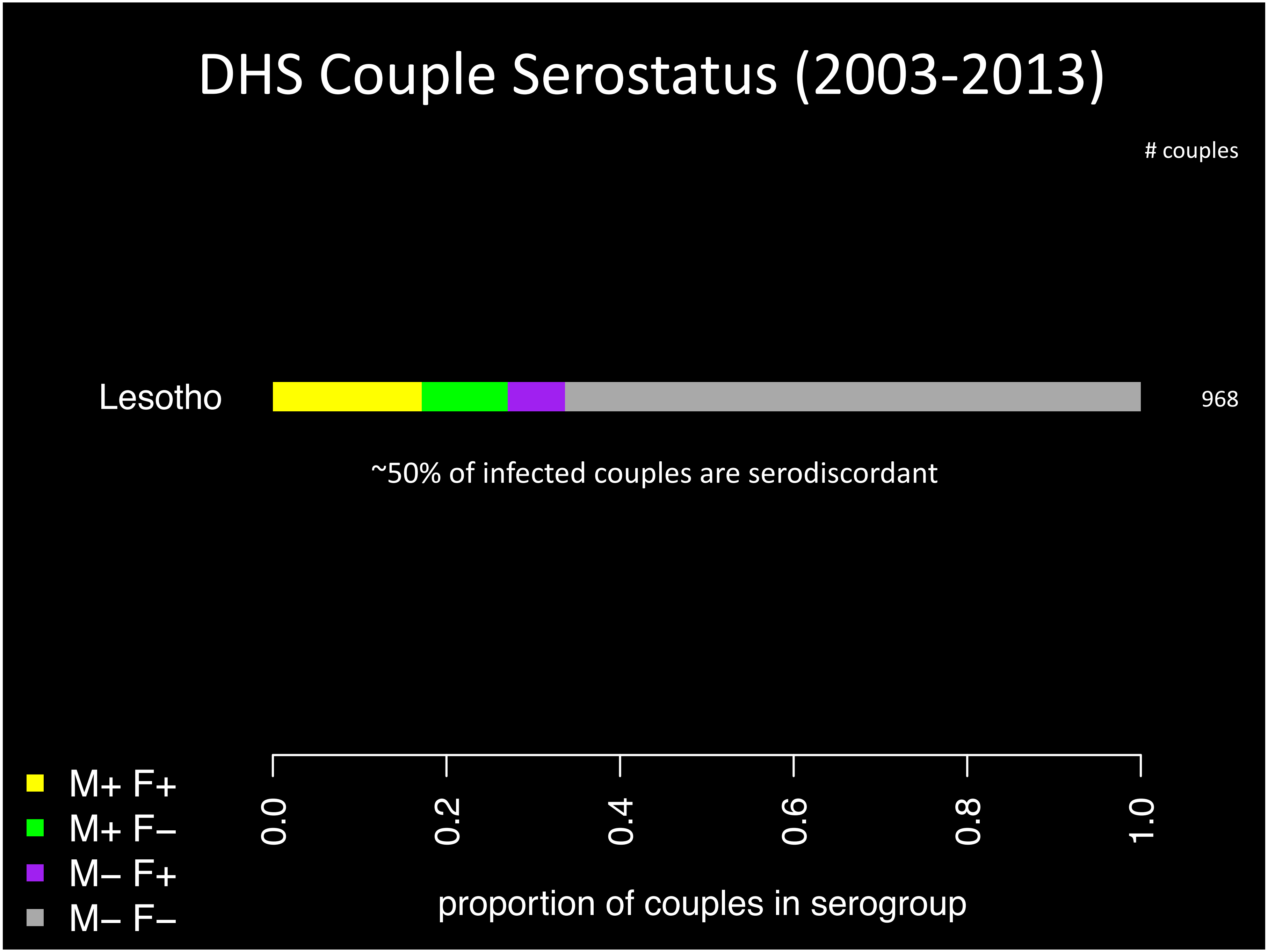
What proportion of HIV incidence is driven by transmission inside VS. outside of stable partnerships?



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

THE LANCET
Volume 381, Issue 9877, 4–10 May 2013, Pages 1561–1569


DHS Couple Serostatus (2003-2013)
couples
Lesotho
968
~50% of infected couples are serodiscordant
M+ F+
M+ F−
M− F+
M− F−
0.0
0.2
0.4
0.6
0.8
1.0
proportion of couples in serogroup

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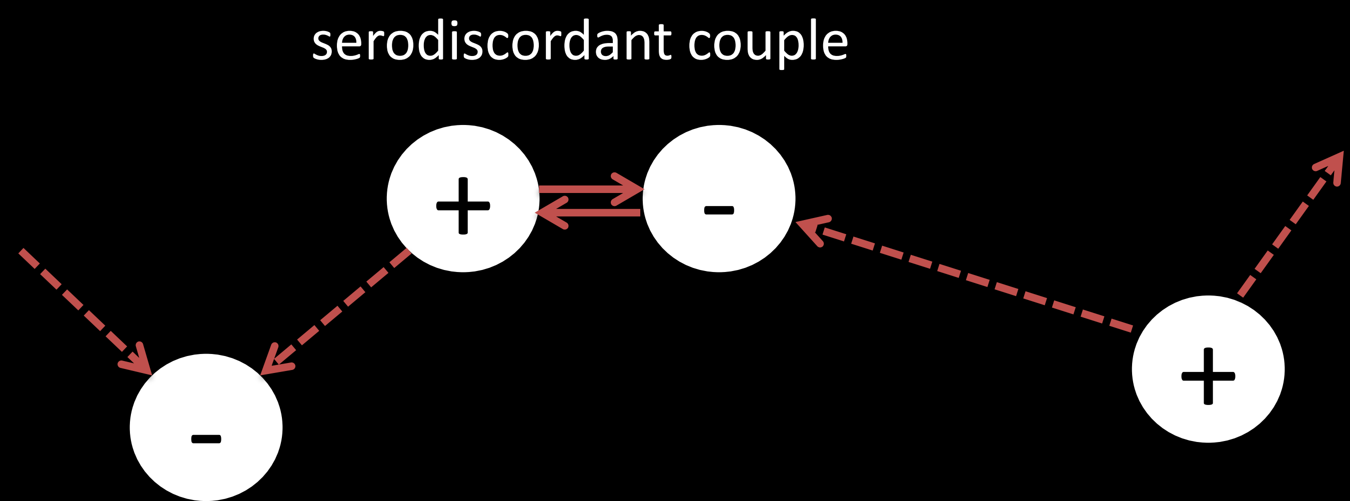
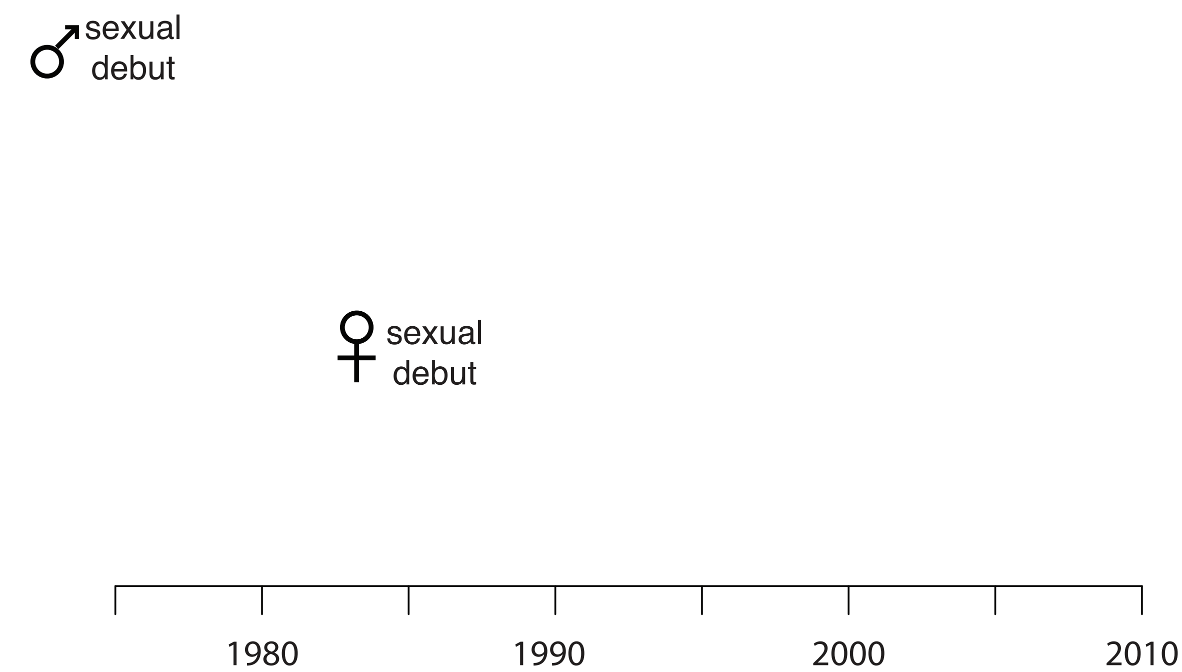


Example Relationship History



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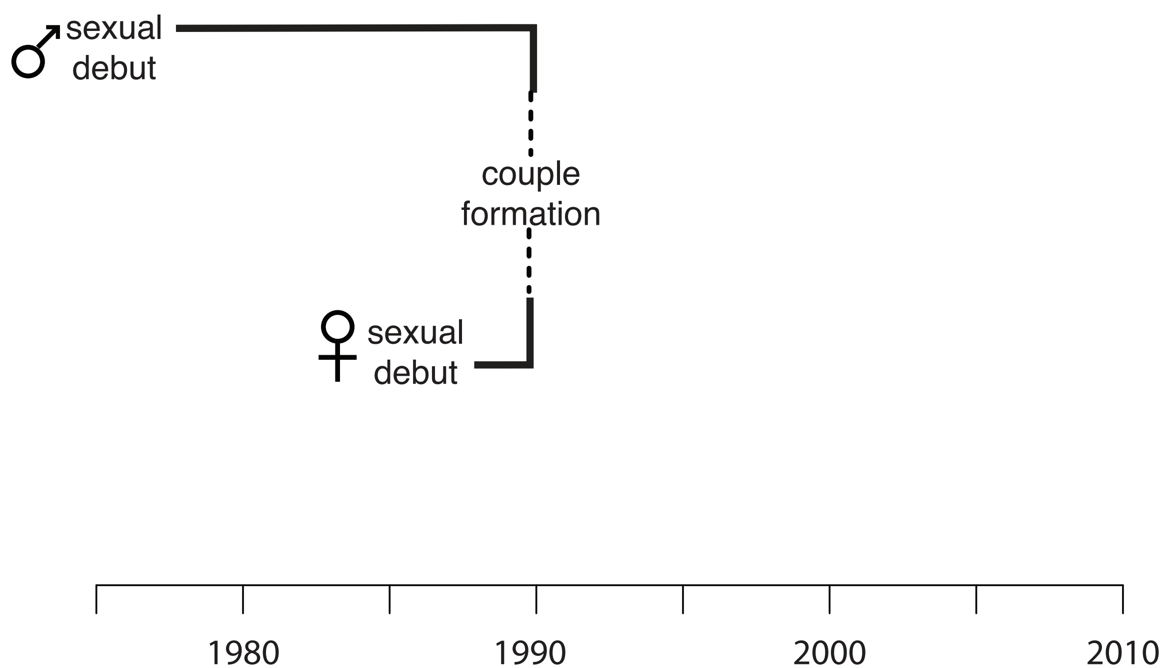

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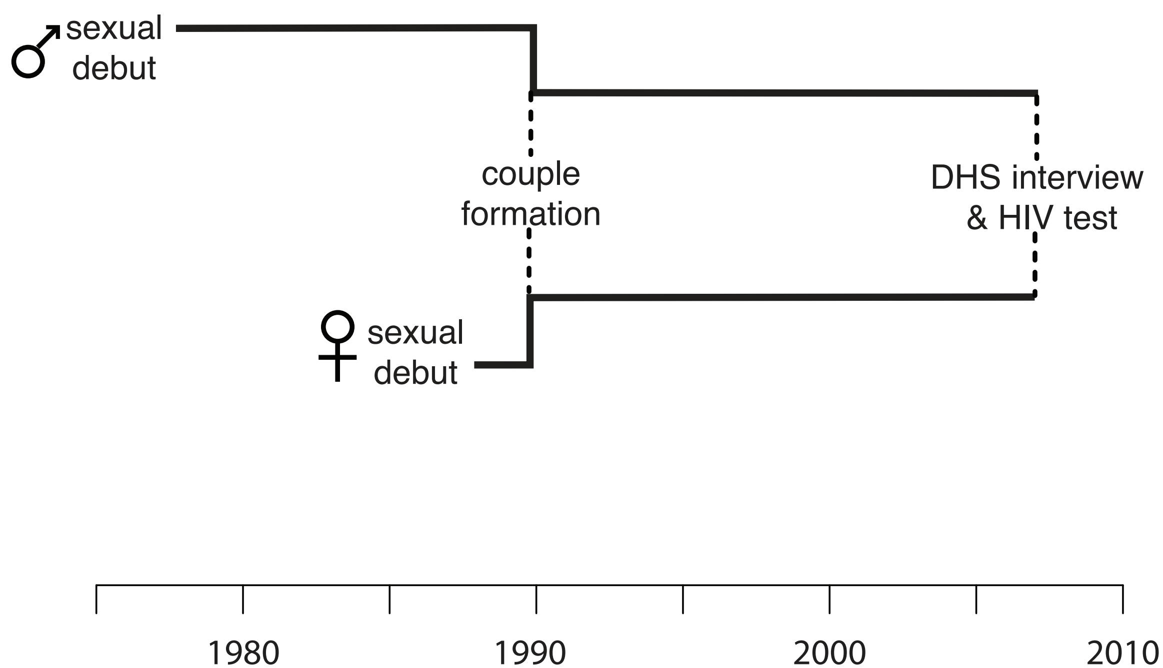

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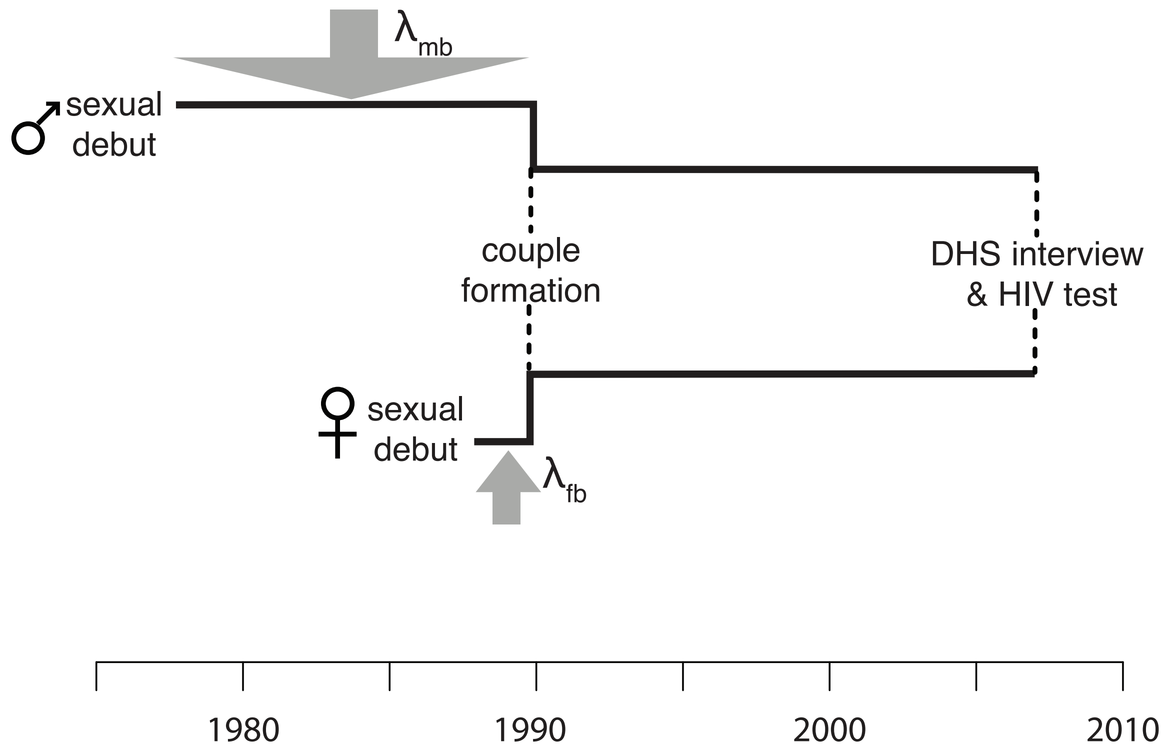

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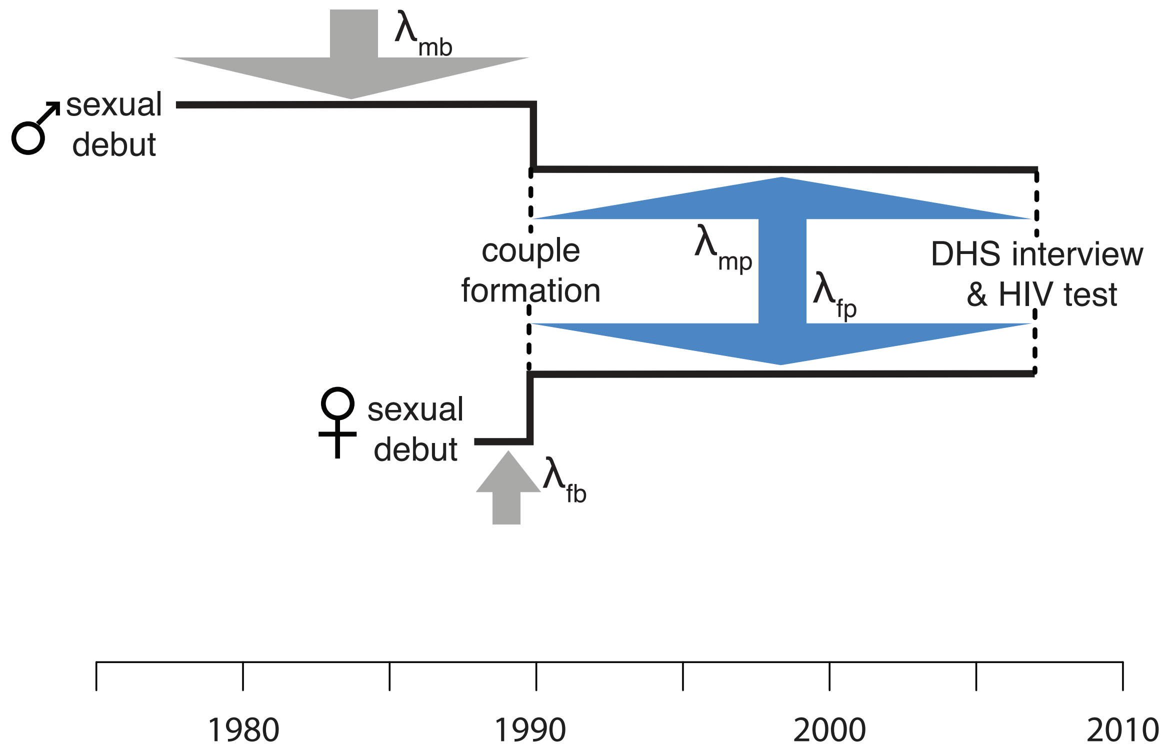

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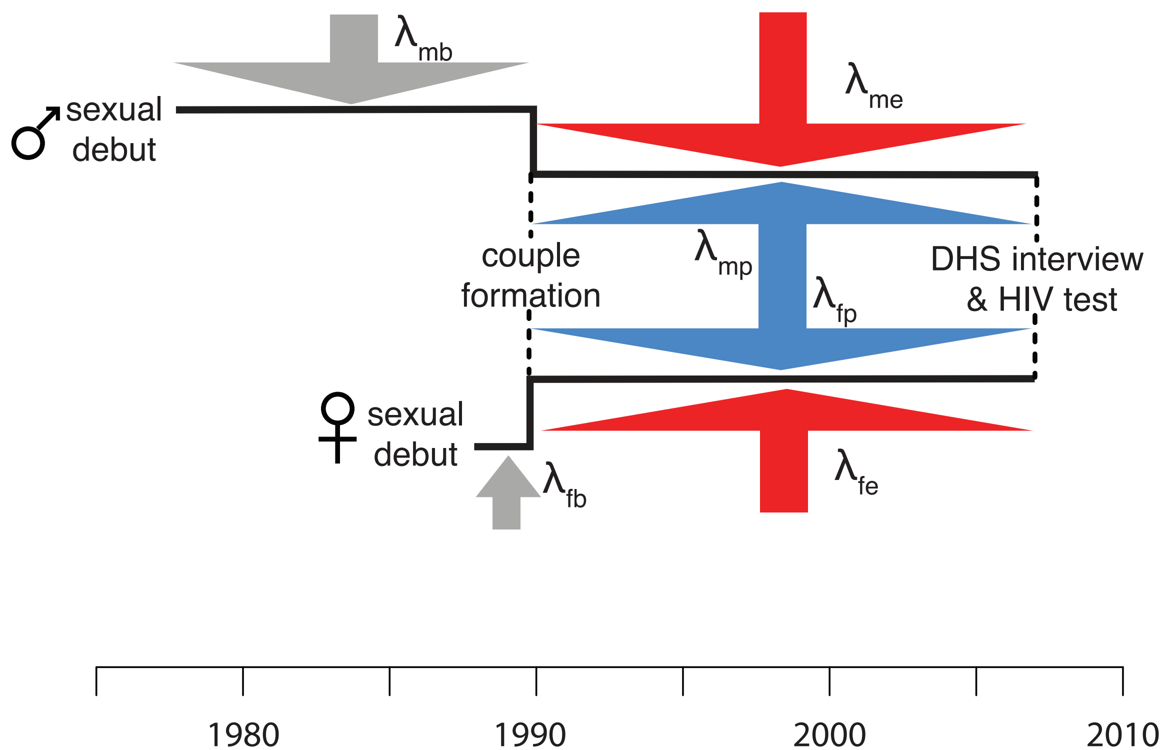

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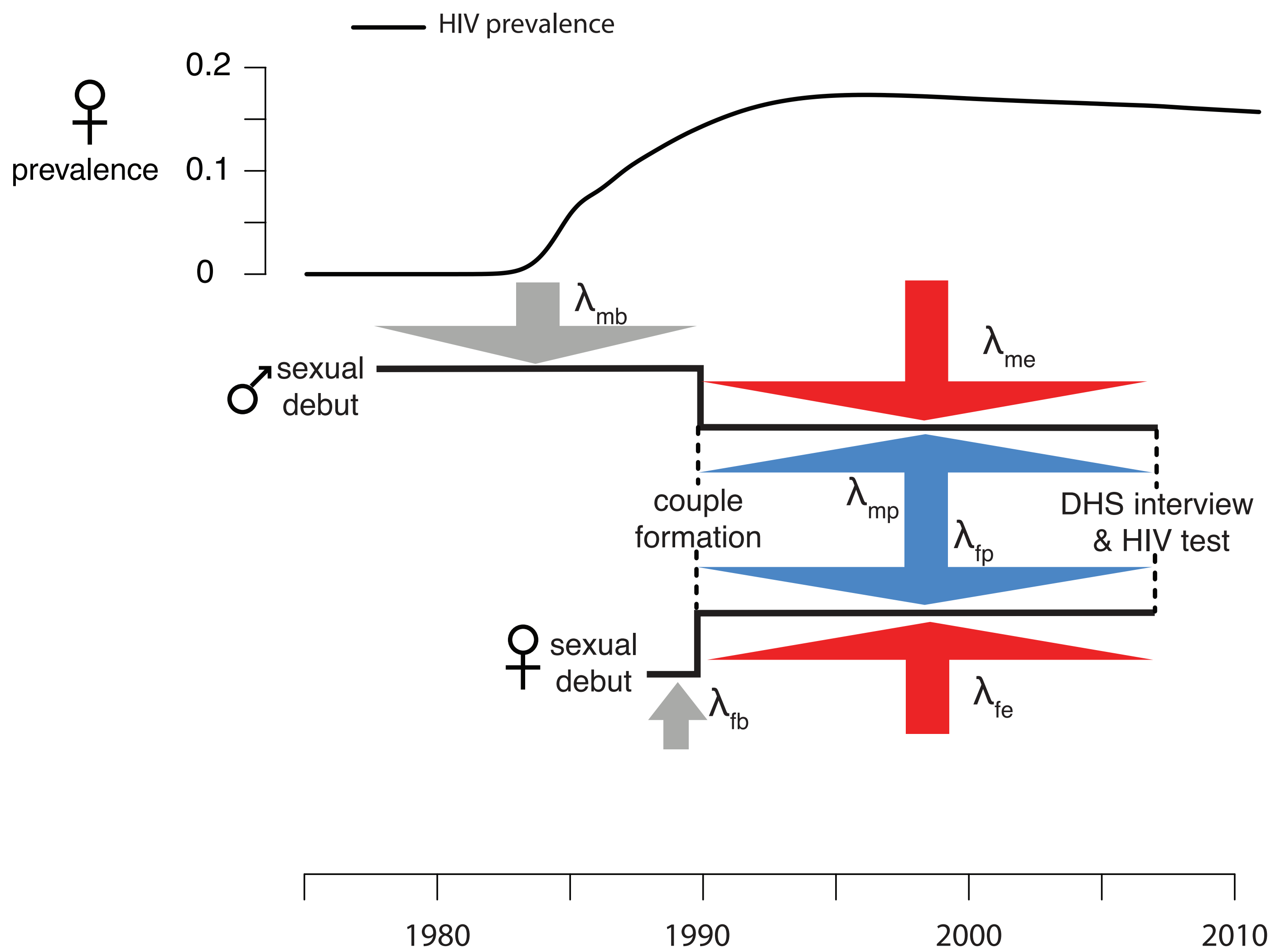

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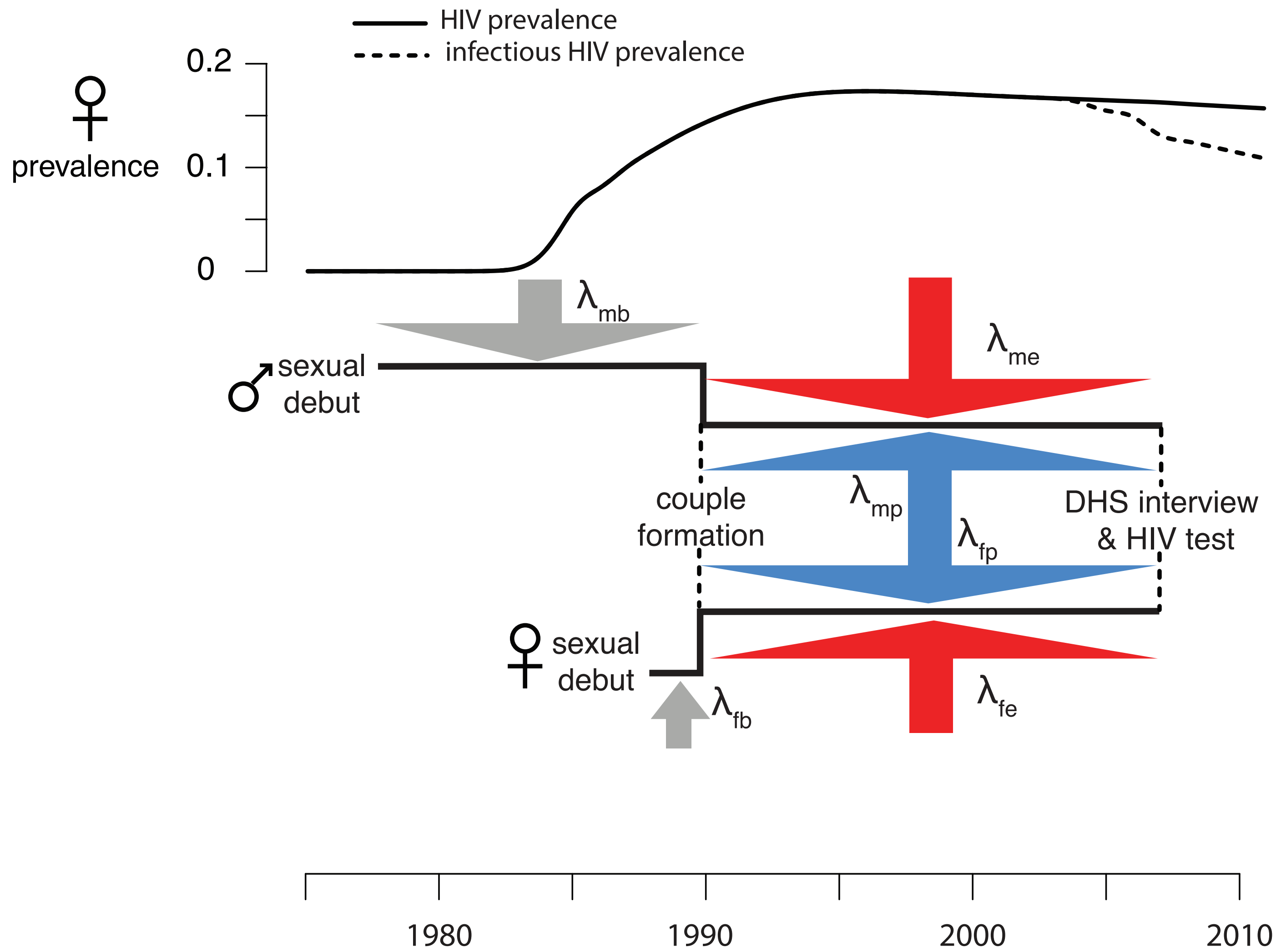

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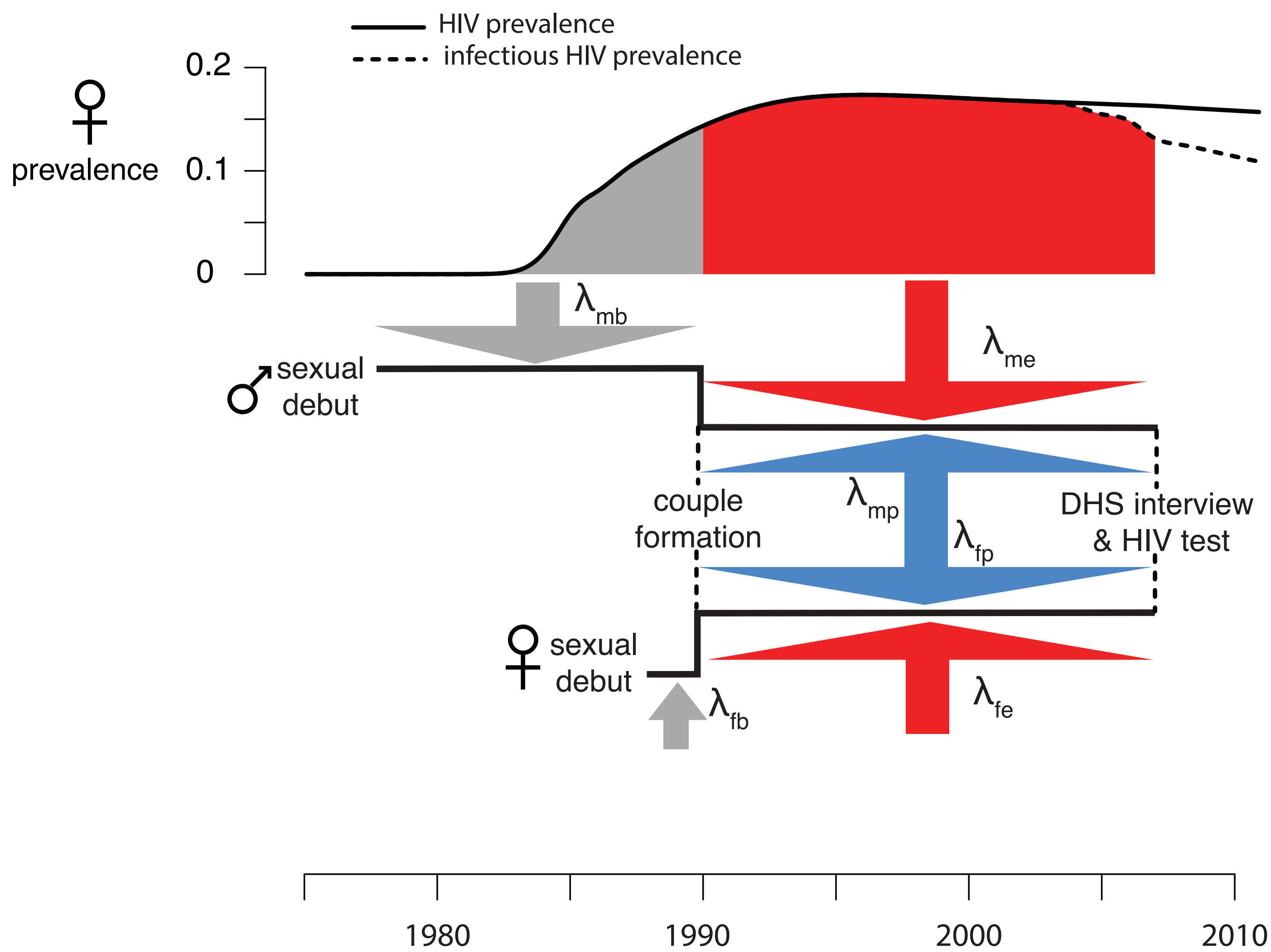

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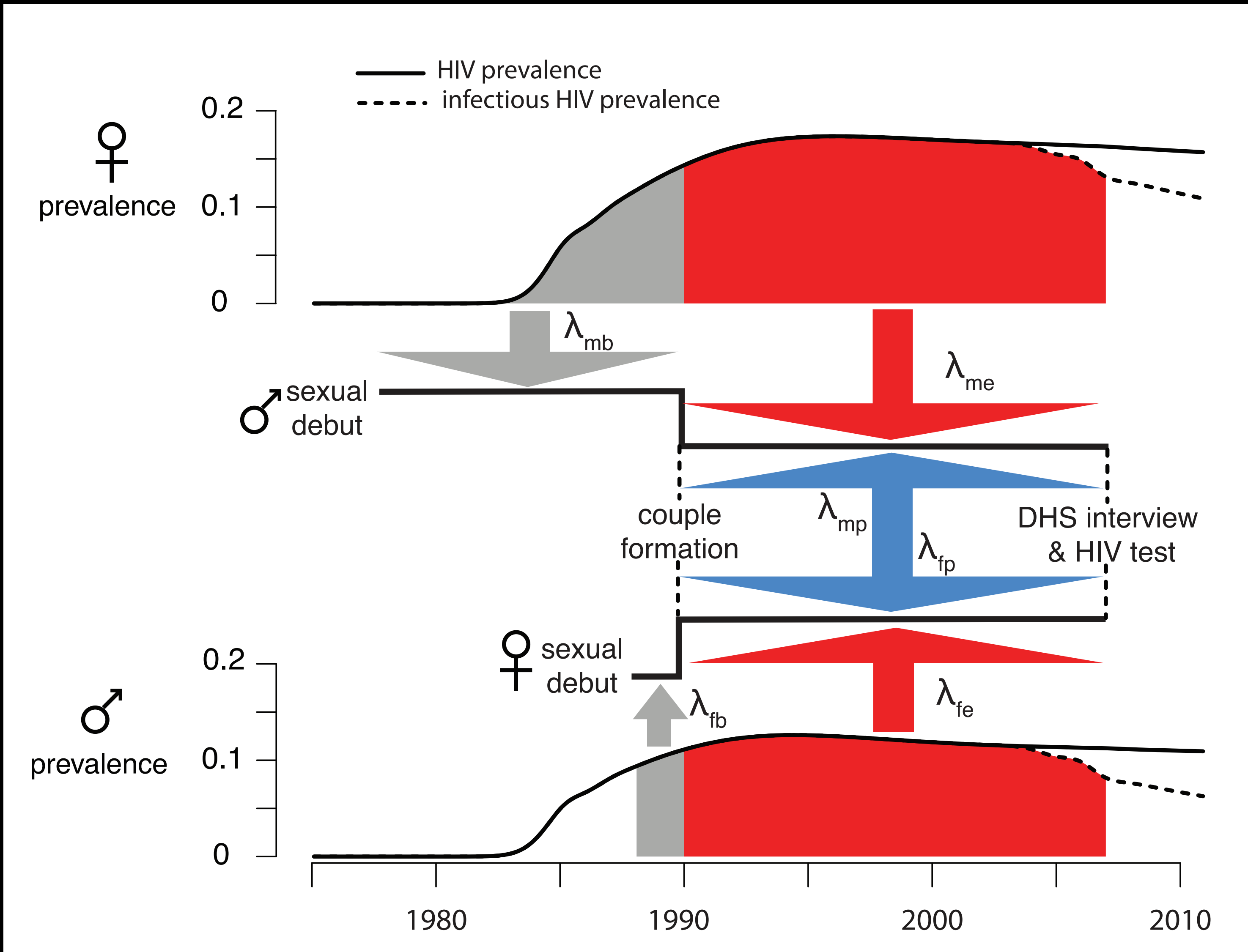

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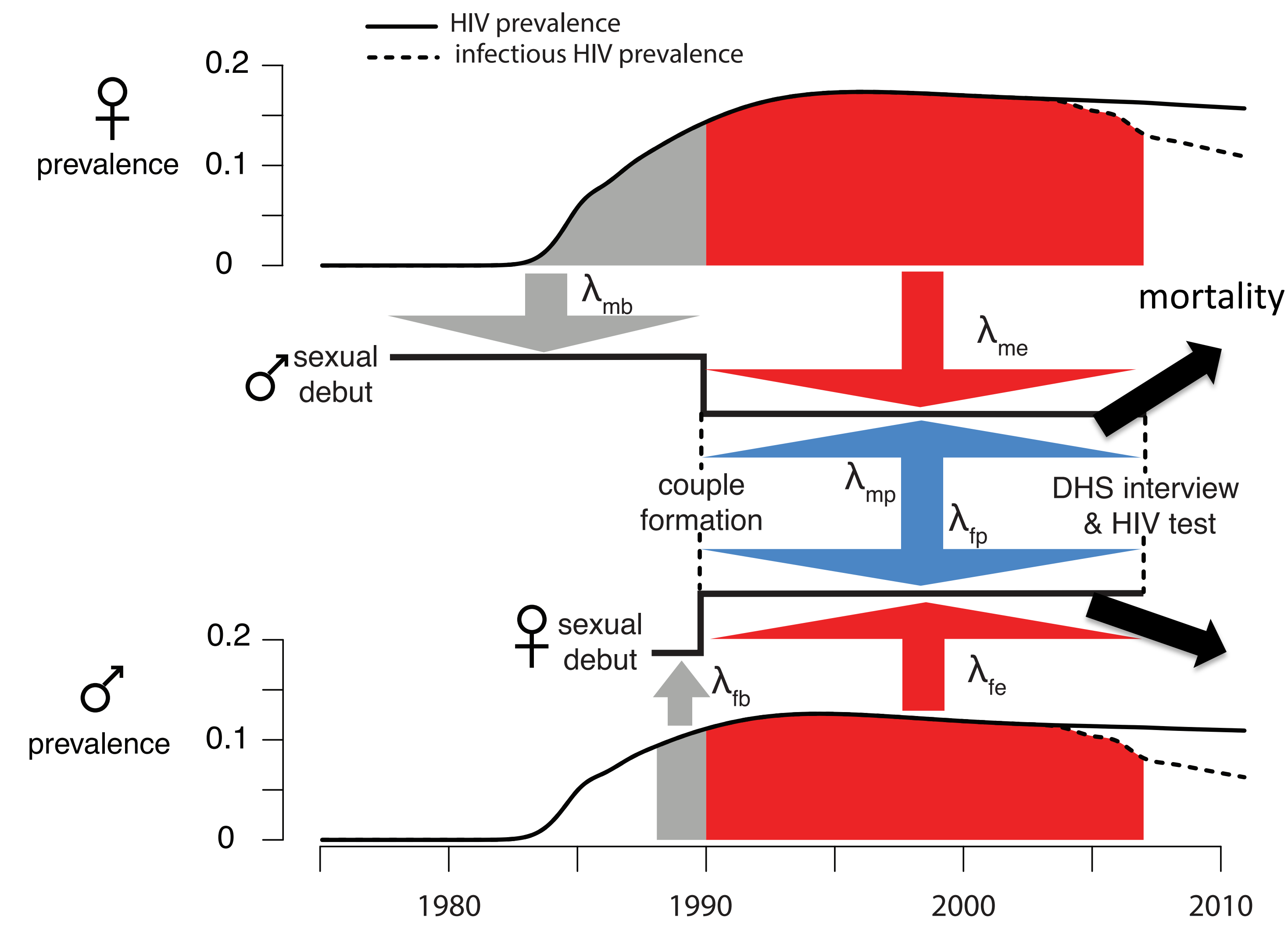
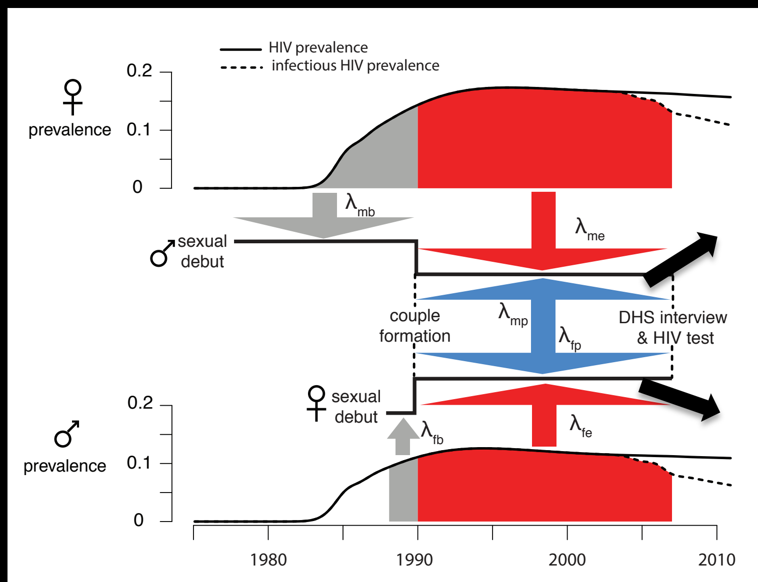


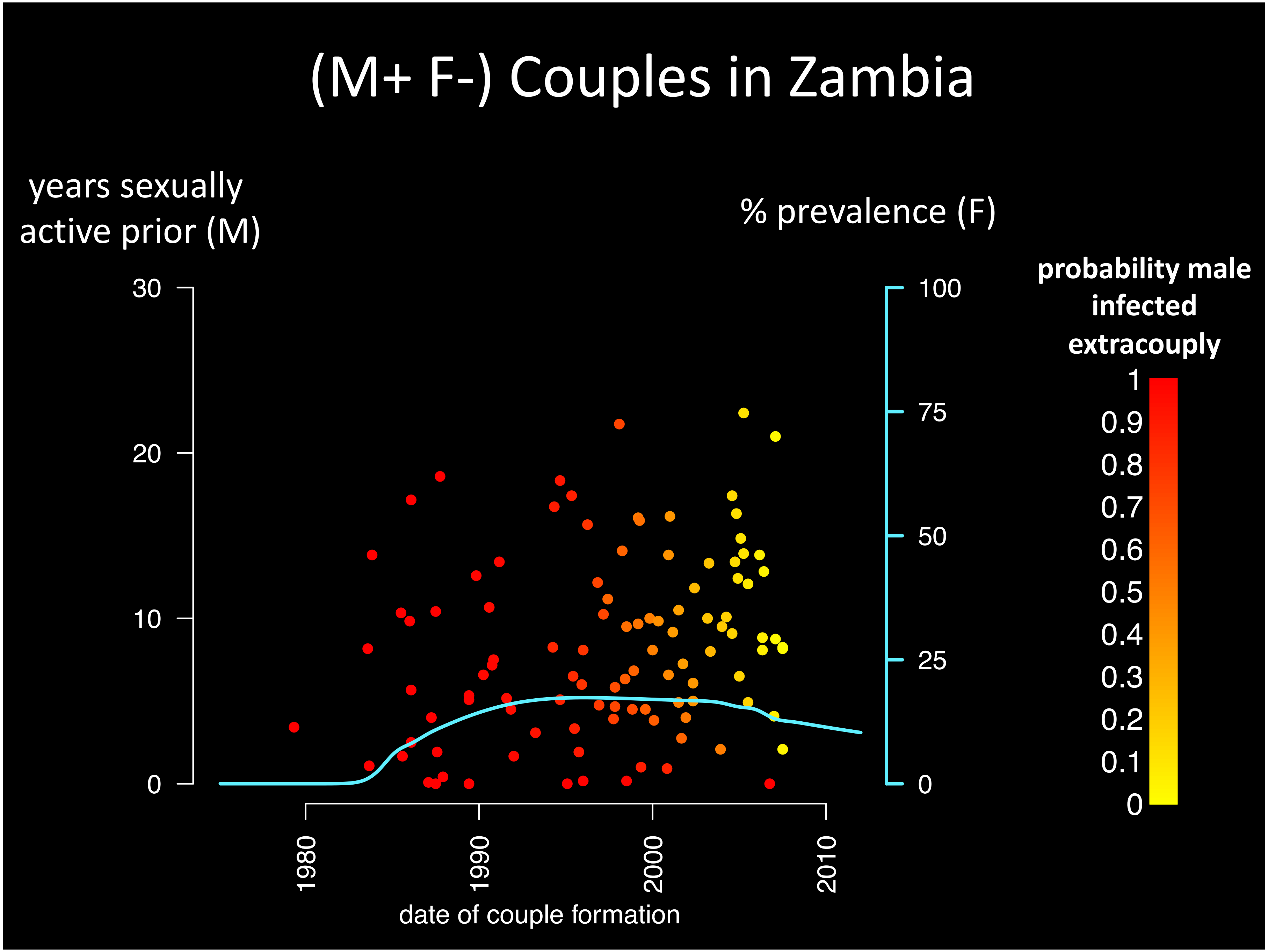
<u>Estimated</u>: 6 sex-route transmission coefficients

<u>Given</u>: couple relationship histories & serostatuses

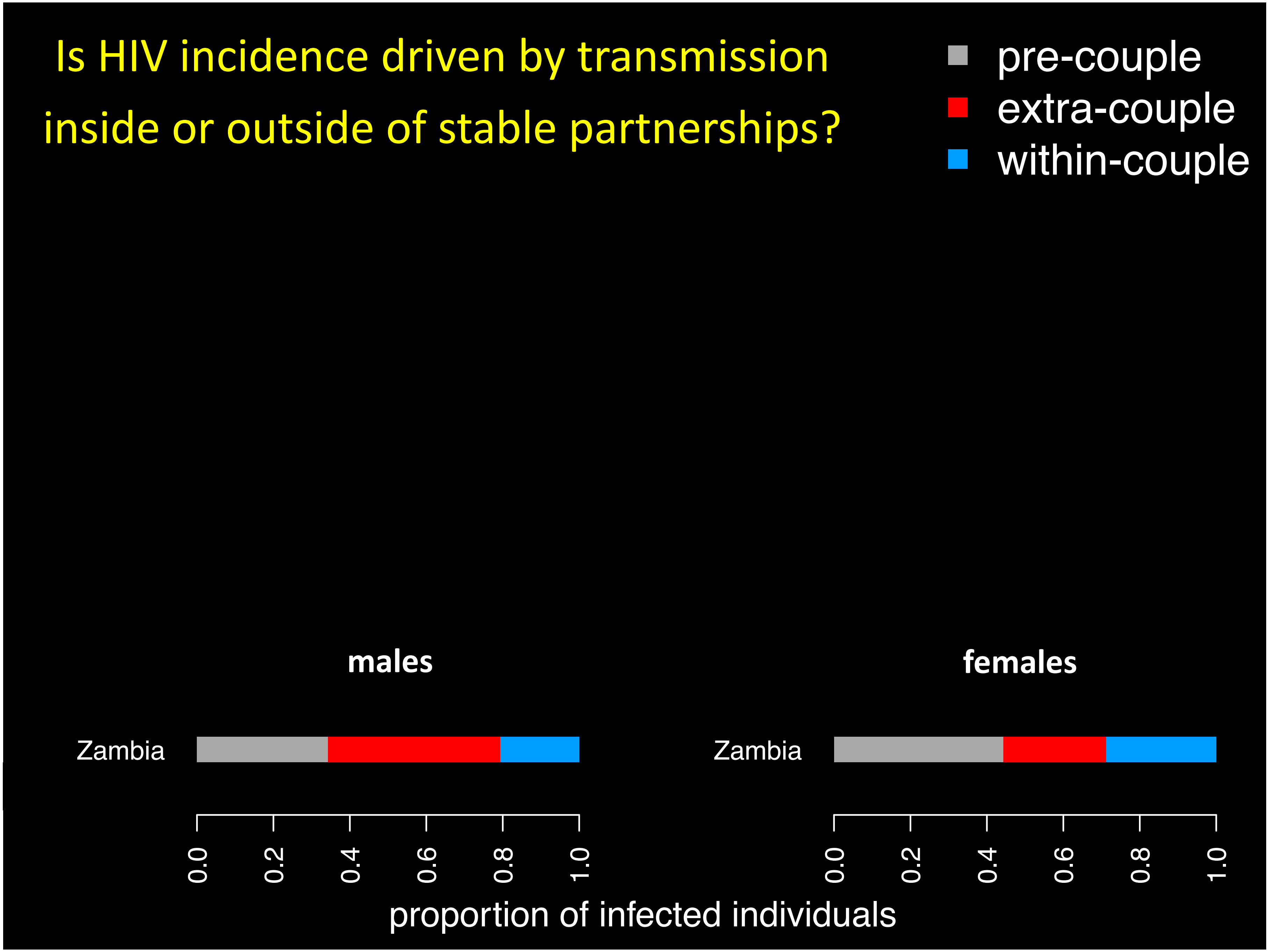


p(observed couple serostatus & both partners alive at sampling)

Fit via Bayesian MCMC

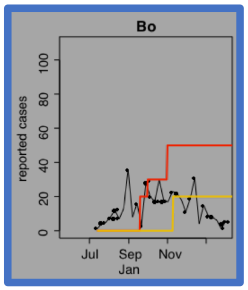


(M+ F-) Couples in Zambia
years sexually active prior (M)
% prevalence (F)
probability male infected extracouply
30
20
10
0
100
75
50
25
0
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
1980
1990
2000
2010
date of couple formation


Is HIV incidence driven by transmission
inside or outside of stable partnerships?
pre-couple
extra-couple
within-couple
males
females
Zambia
Zambia
0.0
0.2
0.4
0.6
0.8
1.0
0.0
0.2
0.4
0.6
0.8
1.0
proportion of infected individuals

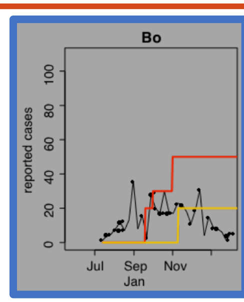
Model Taxonomy

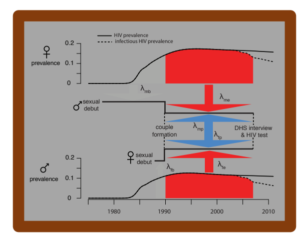
	CONTINUOUS TREATMENT OF INDIVIDUALS (averages, proportions, or population densities)	DISCRETE TREATMENT OF INDIVIDUALS
DETERMINISTIC	CONTINUOUS TIME DISCRETE TIME	
STOCHASTIC	CONTINUOUS TIME DISCRETE TIME	CONTINUOUS TIME DISCRETE TIME



Model Taxonomy

	Continuous treatment of individuals (averages, proportions, or population densities)	Discrete treatment of individuals
Deterministic	**CONTINUOUS TIME** **DISCRETE TIME**	
Stochastic	**CONTINUOUS TIME** **DISCRETE TIME**	**CONTINUOUS TIME** **DISCRETE TIME**



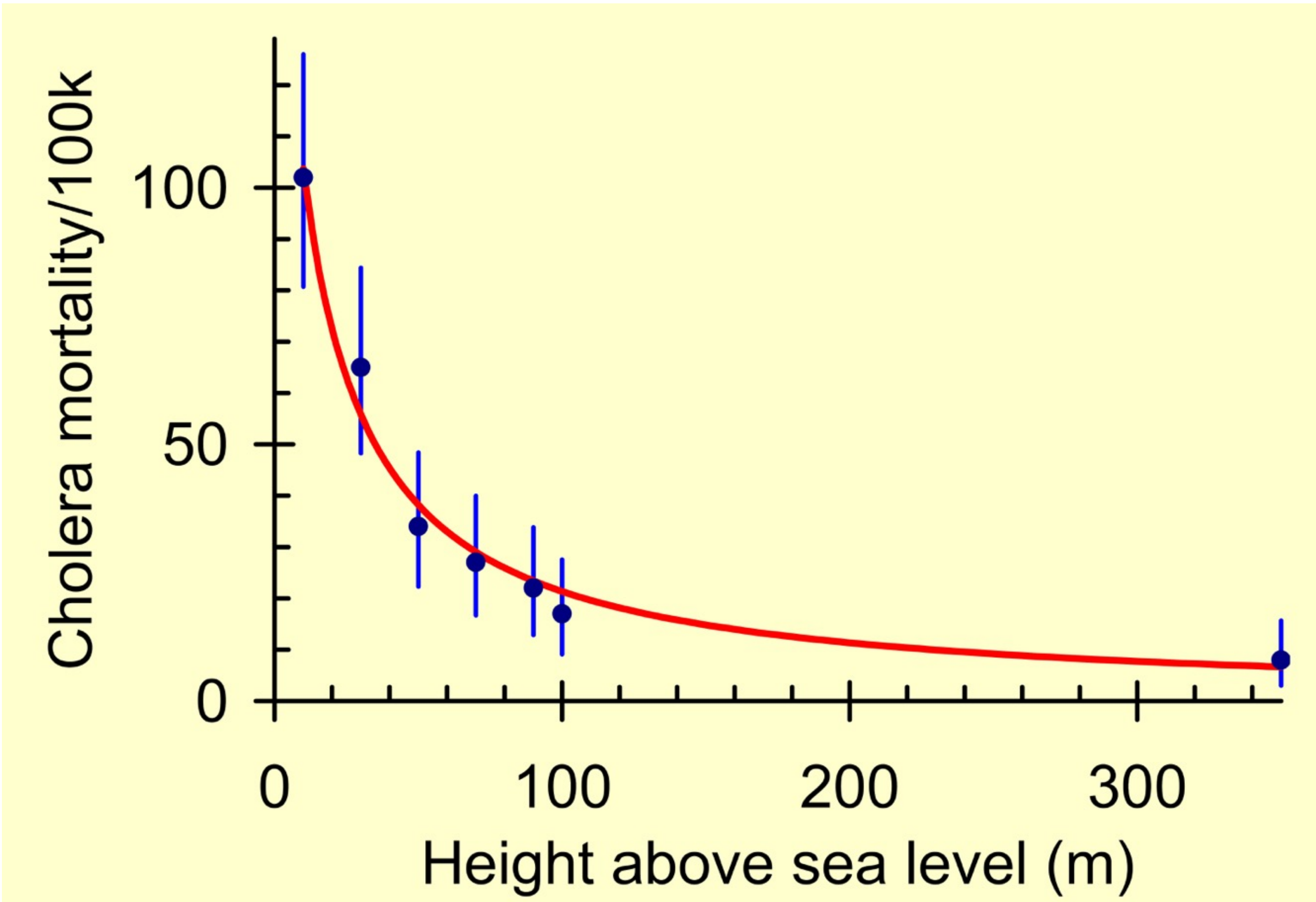


Model-Based Inference

- Uses mechanistic thinking to infer from data
- Inferences can be very strong if the model is reasonable
- Contrasts with machine learning methods
  - Find the most predictive model
  - No focus on whether model is mechanistically understandable

Farr & Cholera

Beware good fits you don't understand!



Summary

- Mechanistic inference can (sometimes) be used to tease more information out of data than possible with other methods

  - Detectable signal that ETUs averted cases of Ebola

  - Large proportion of HIV transmission occurs pre-, extra-, and within-couple

- Must explain the inference–don't trust black boxes!