



Model-Based Inference and the Bigger Picture

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Goals

- Examine examples of model-based (mechanistic) inference
- Understand differences between model-based inference and classical statistical inference

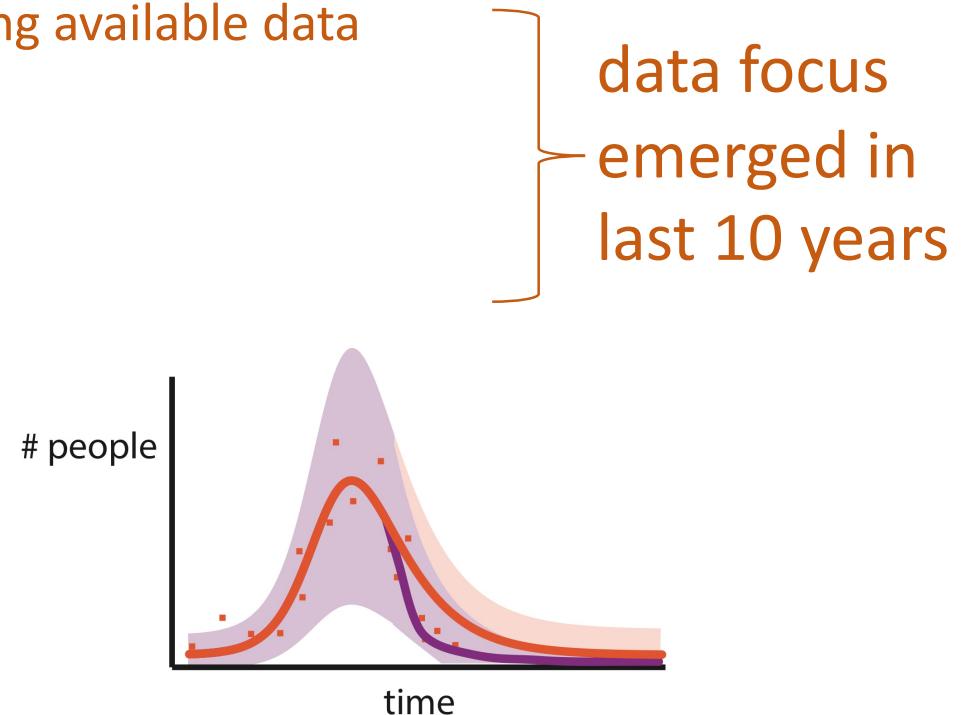
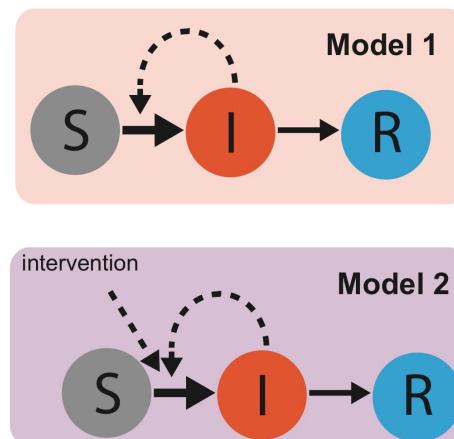
Model-Based Inference

- 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

Epidemics⁵

3rd December 2015

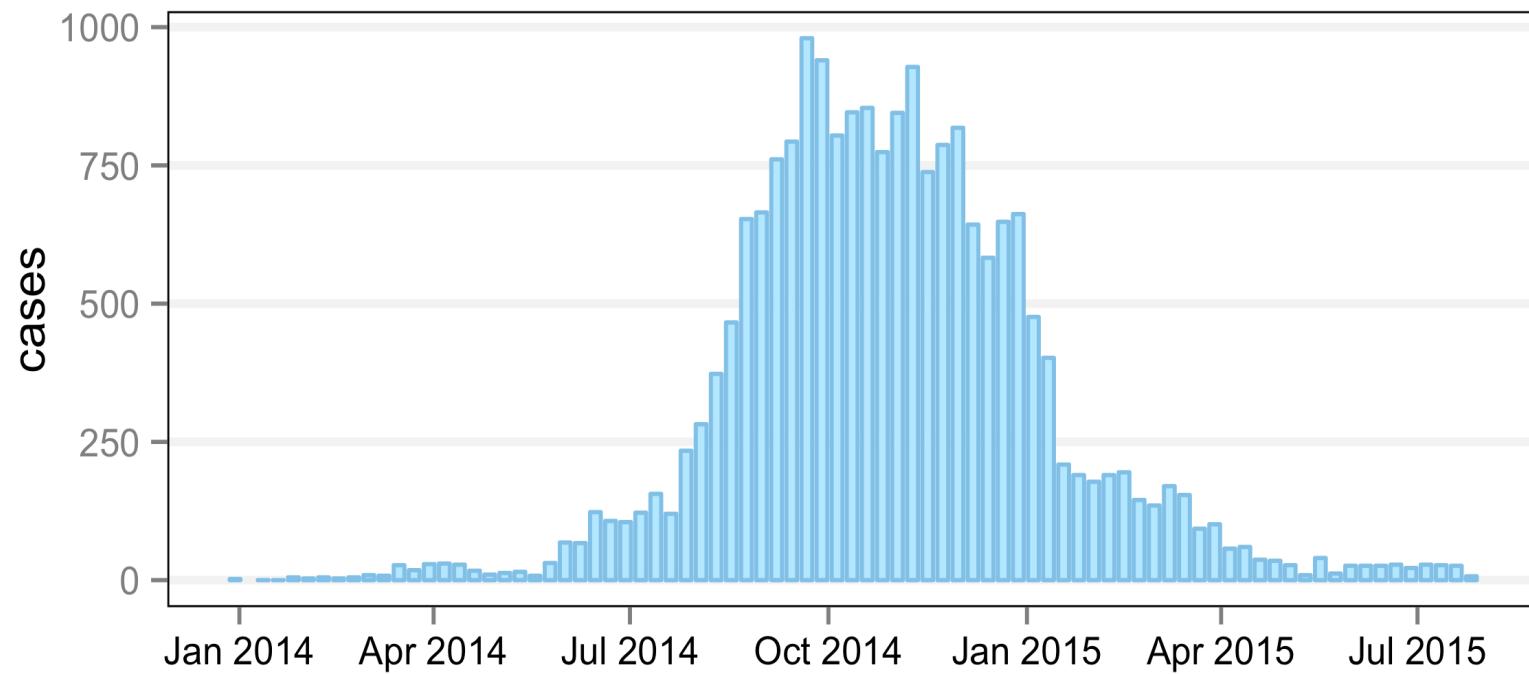


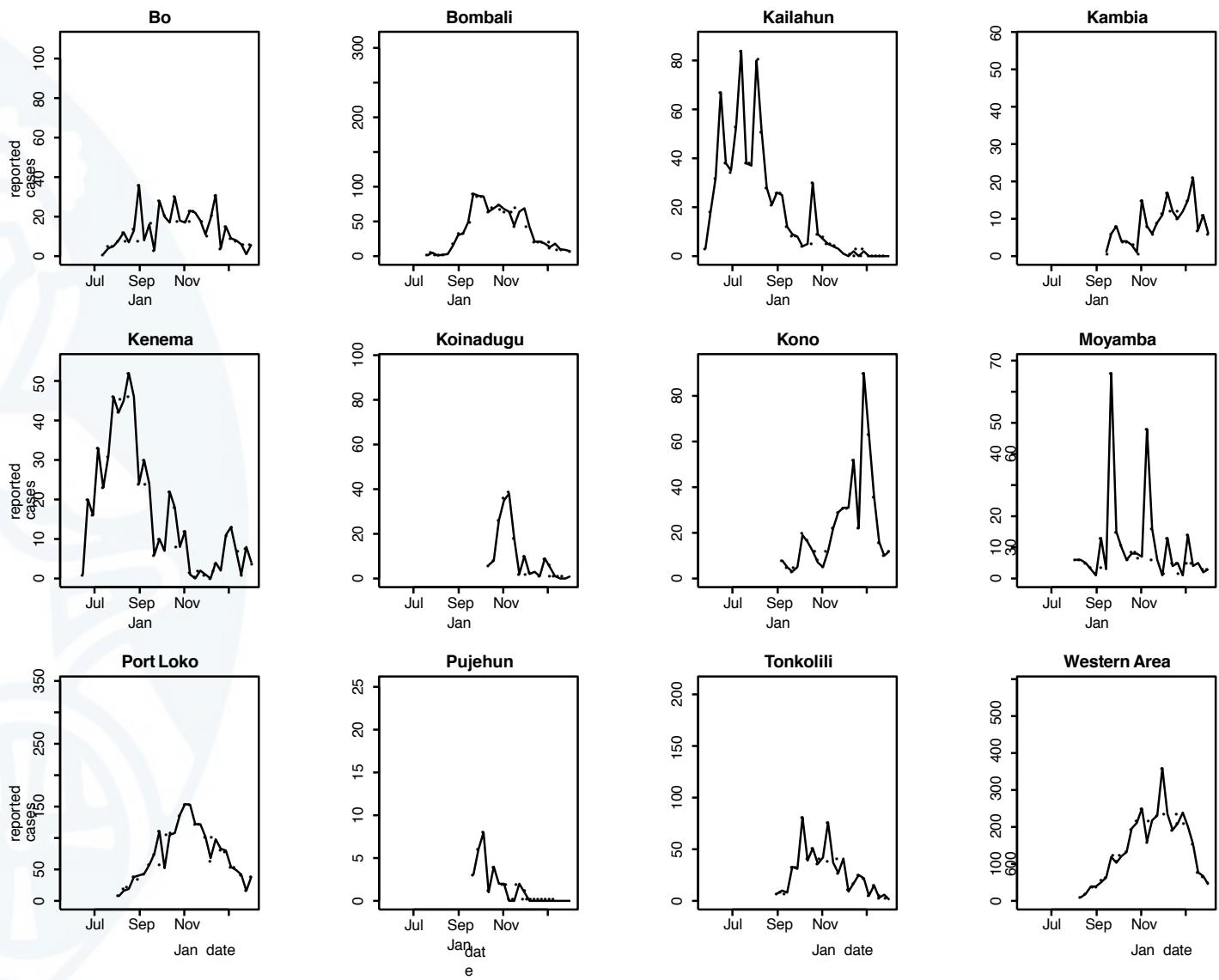
centre for the
mathematical
modelling of
infectious diseases

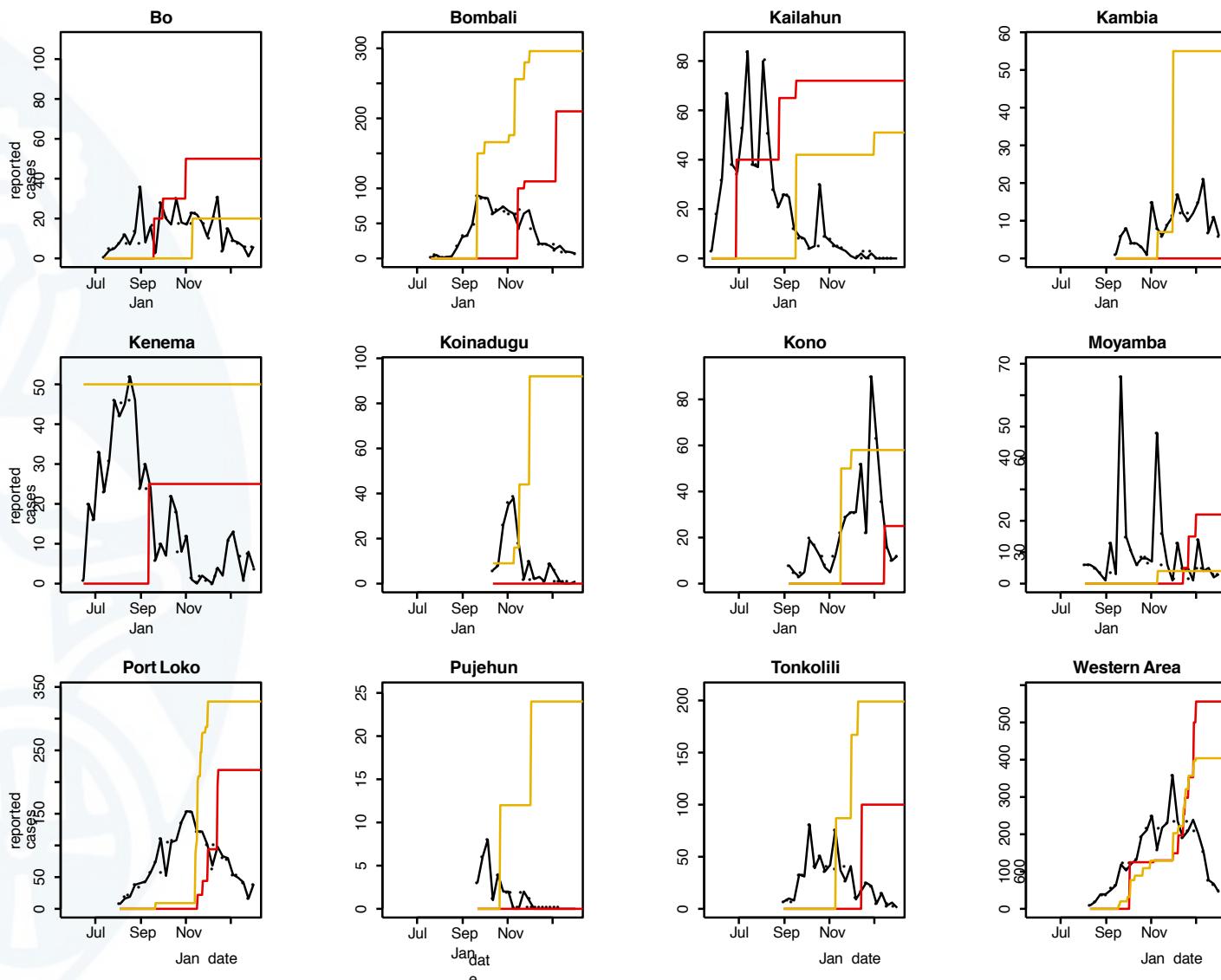
LONDON
SCHOOL of
HYGIENE
& TROPICAL
MEDICINE



Ebola in West Africa



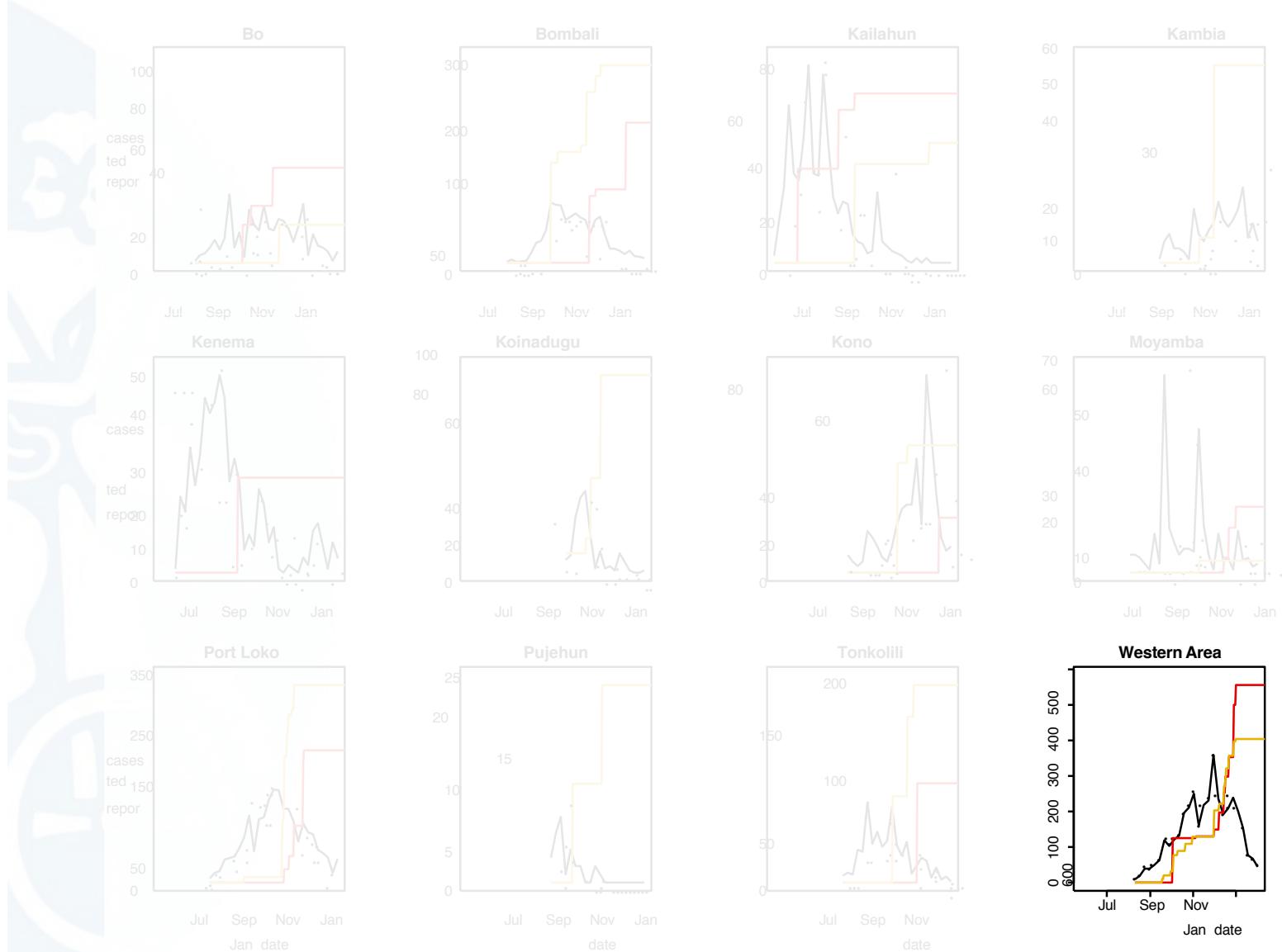




ETU (beds)
Ebola Treatment Units

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

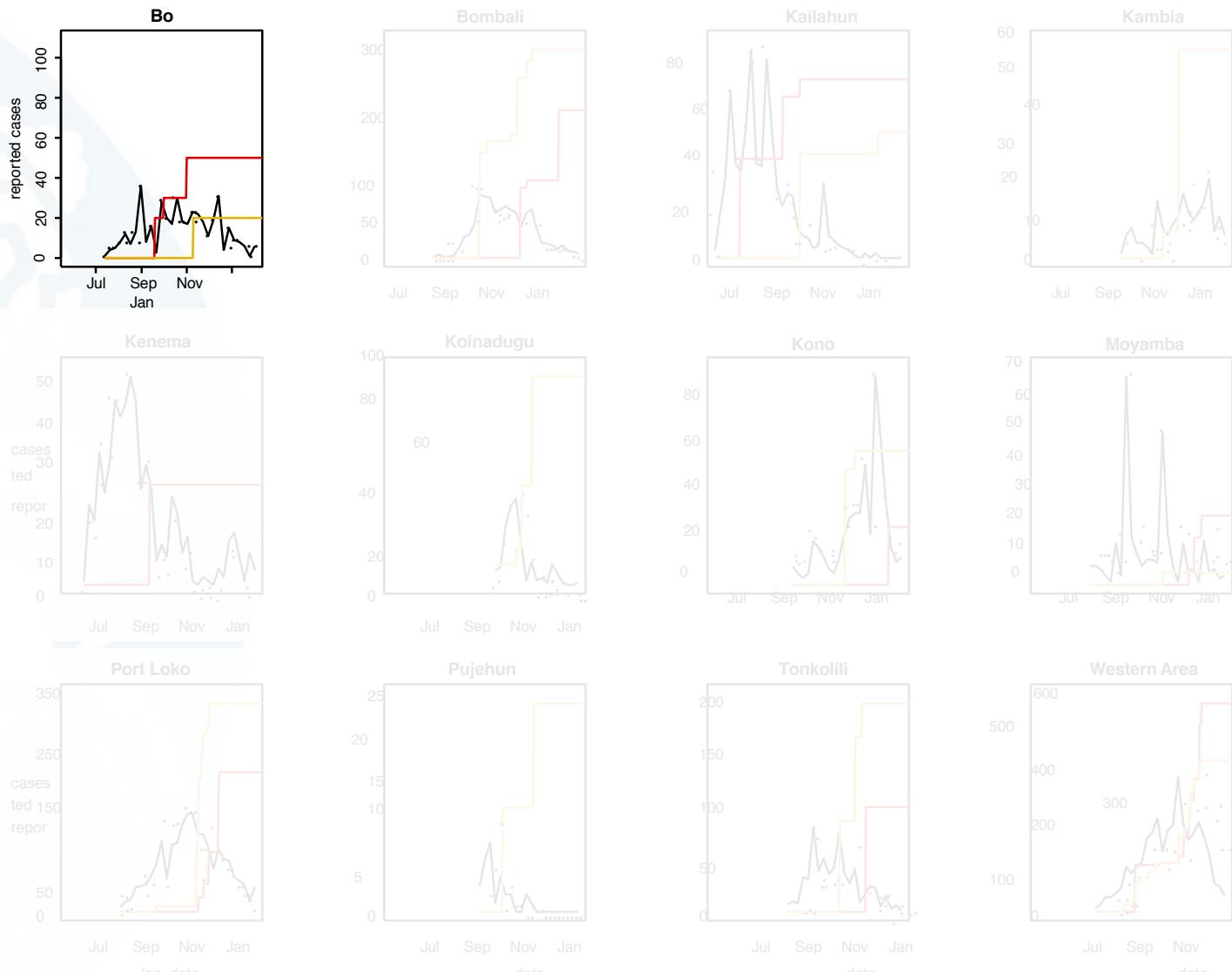
Camacho et al. (2015) *PLOS Currents*



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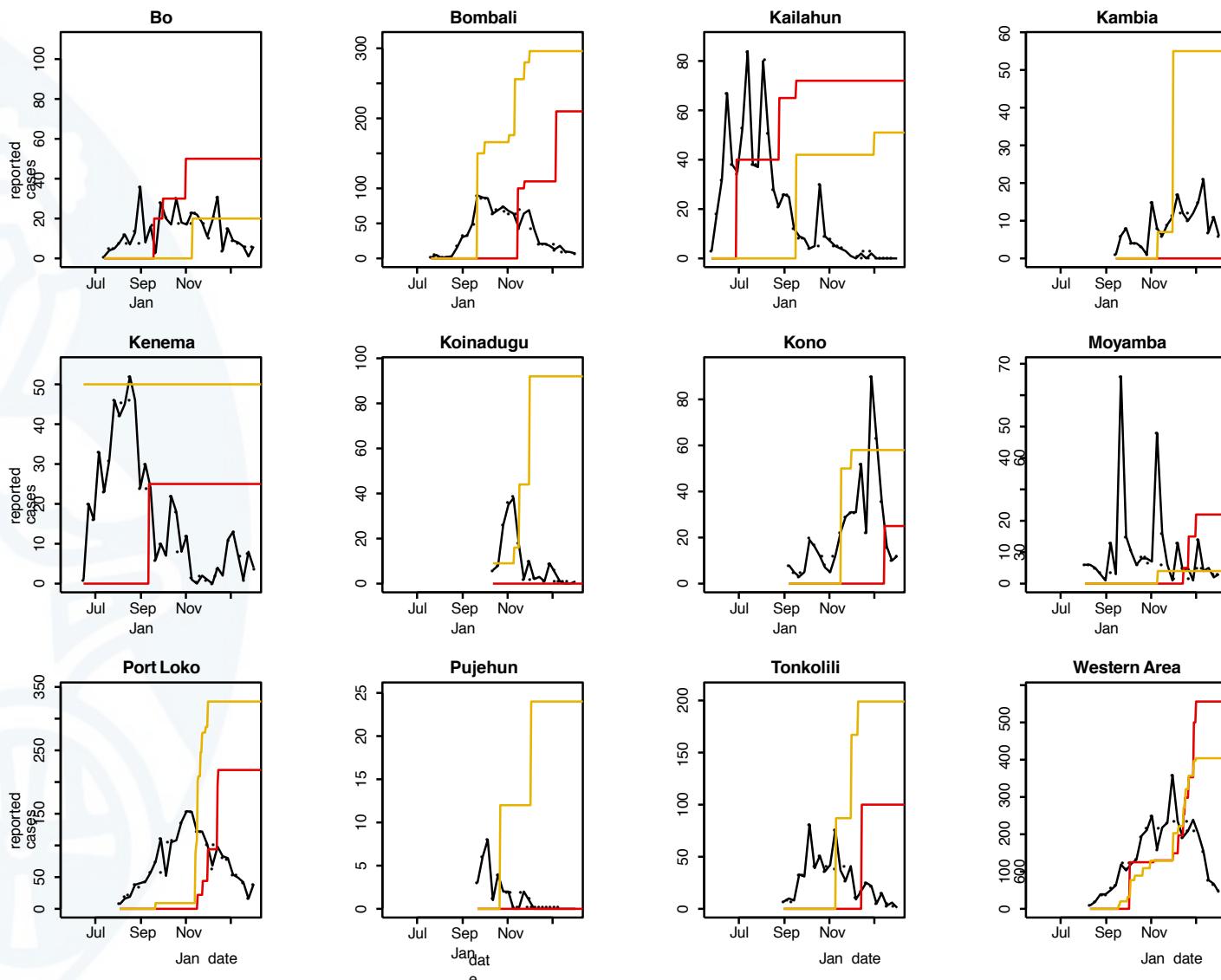
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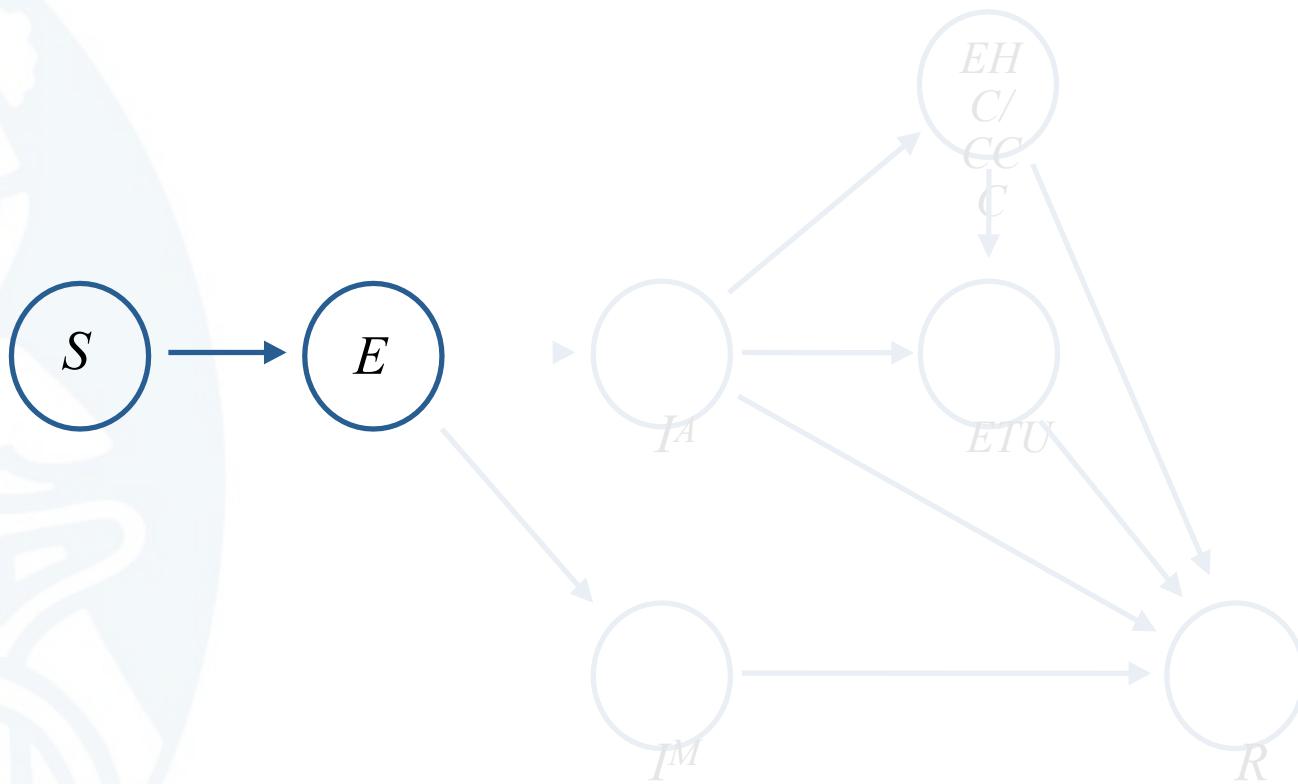


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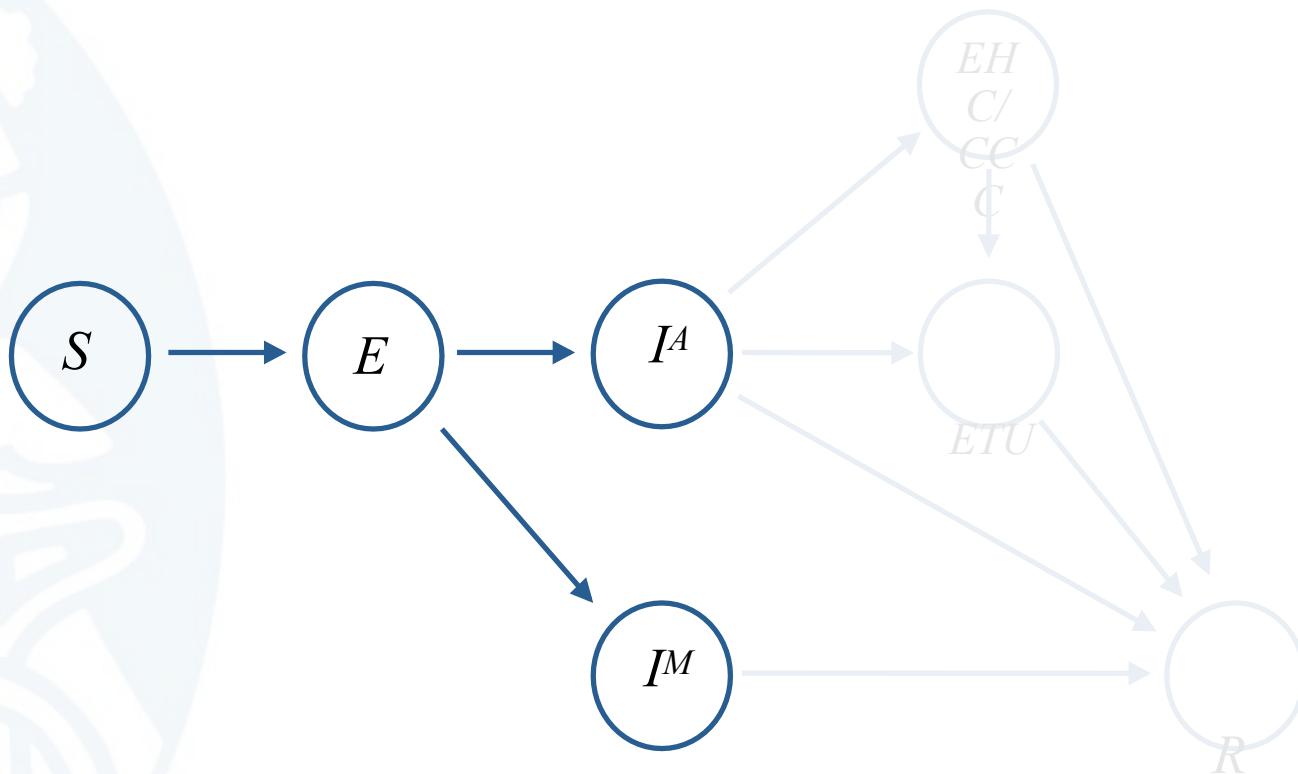
Model structure



Kucharski et al. (2015) PNAS

Legrand et al. (2007) Epidemiol Infect

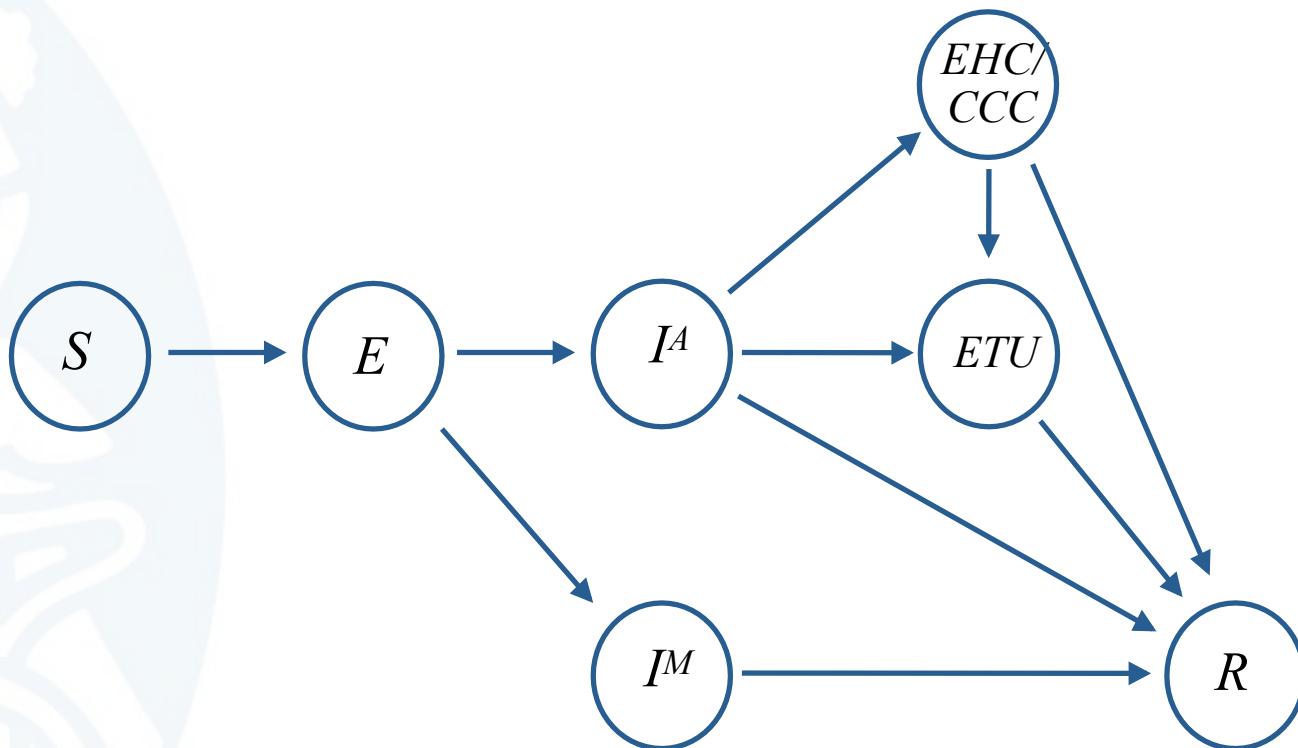
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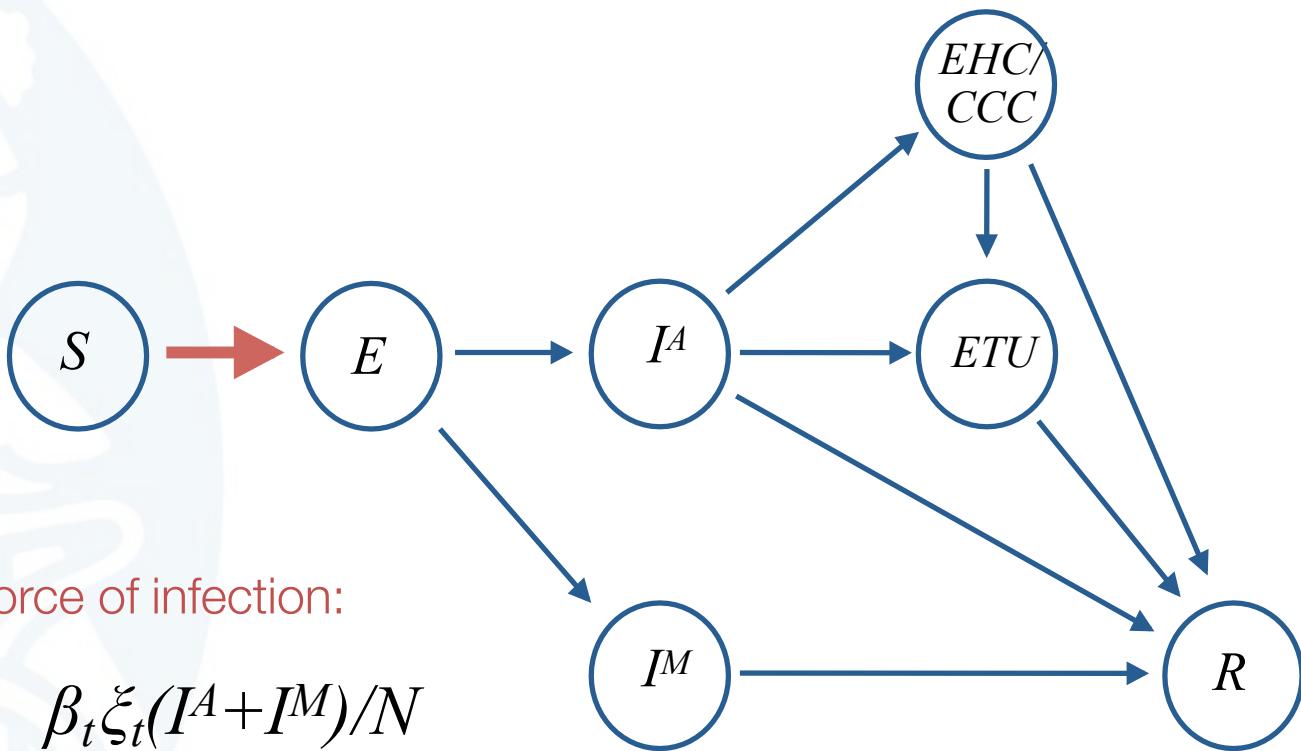
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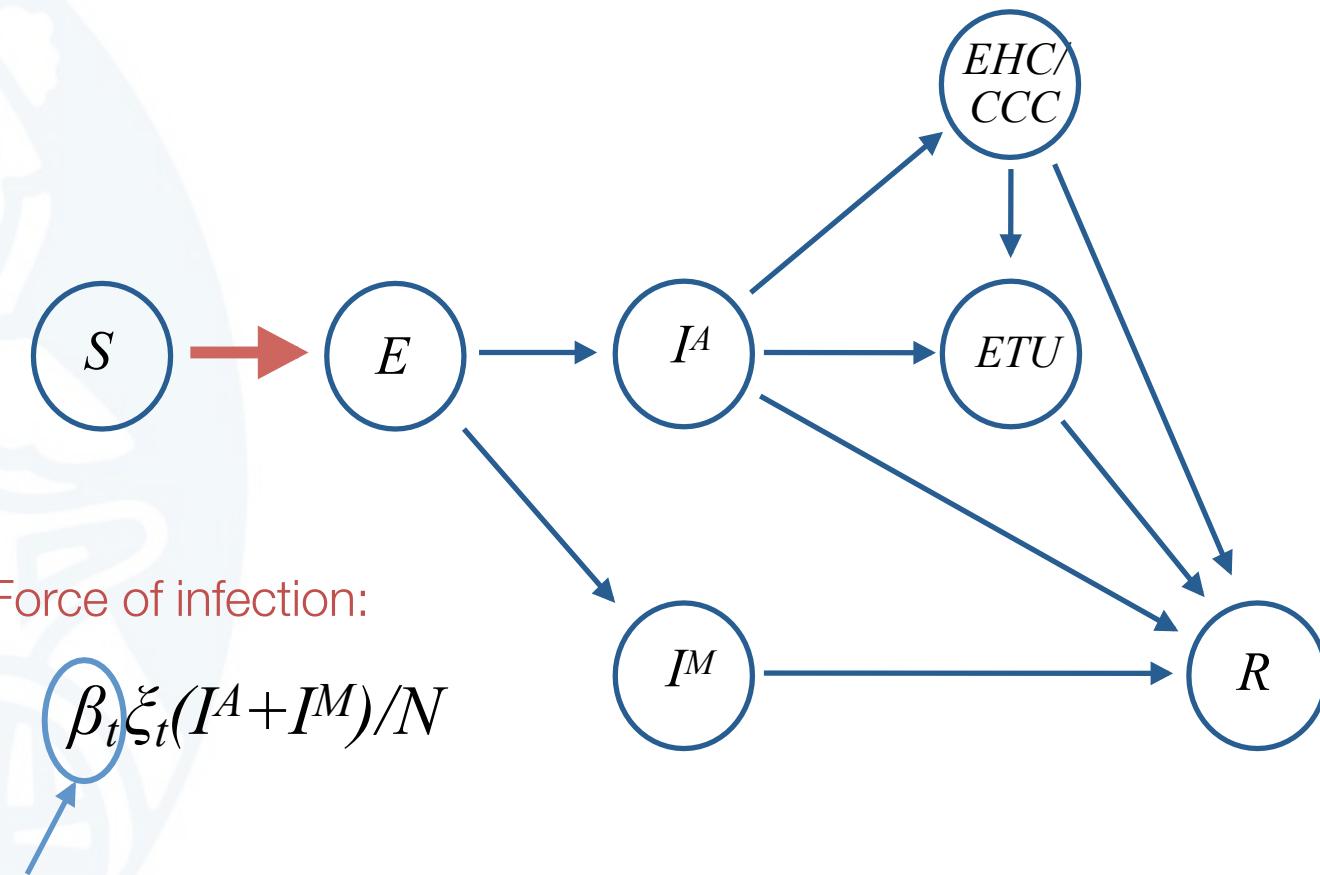
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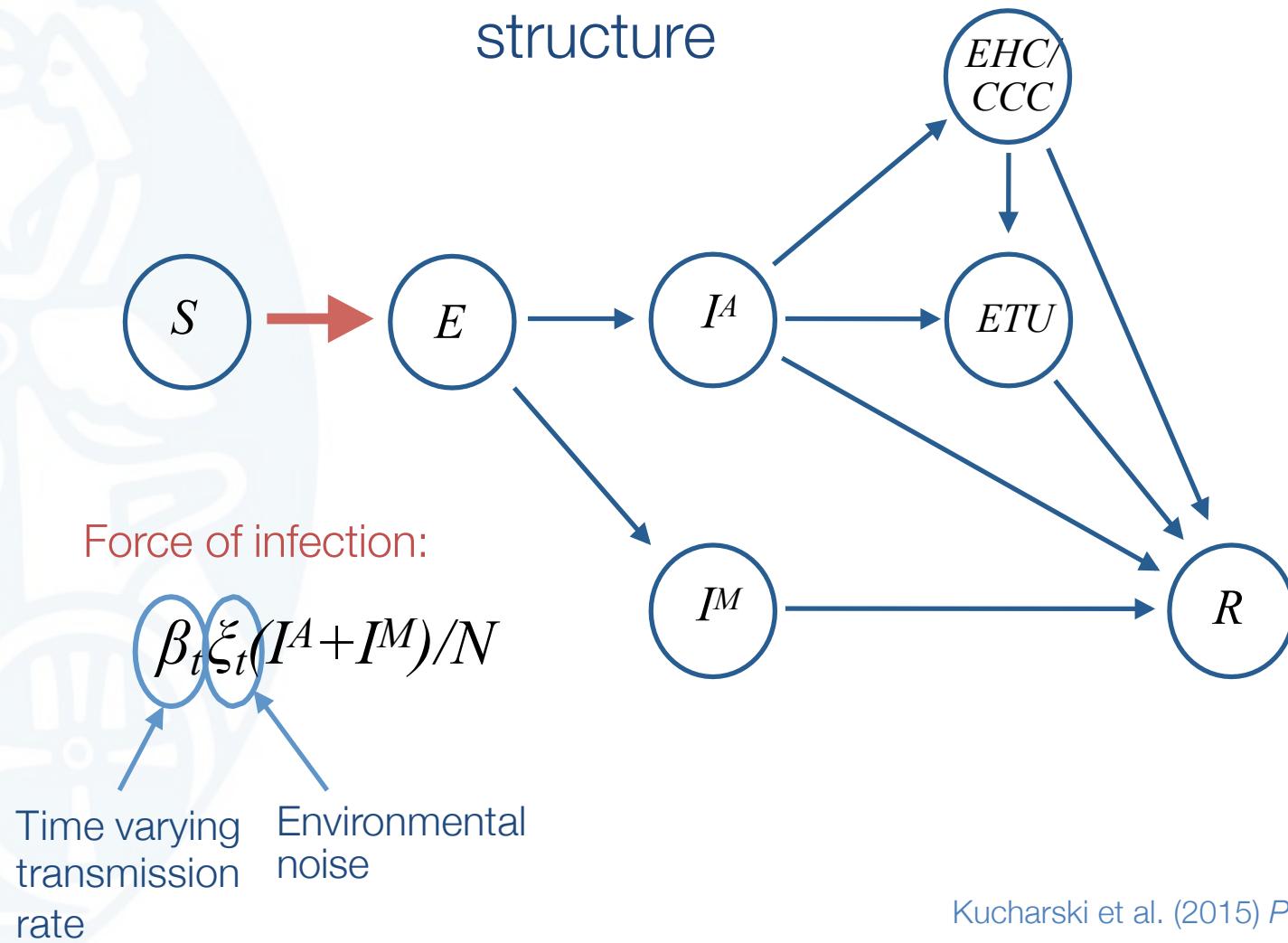
Model structure



Time varying
transmission
rate

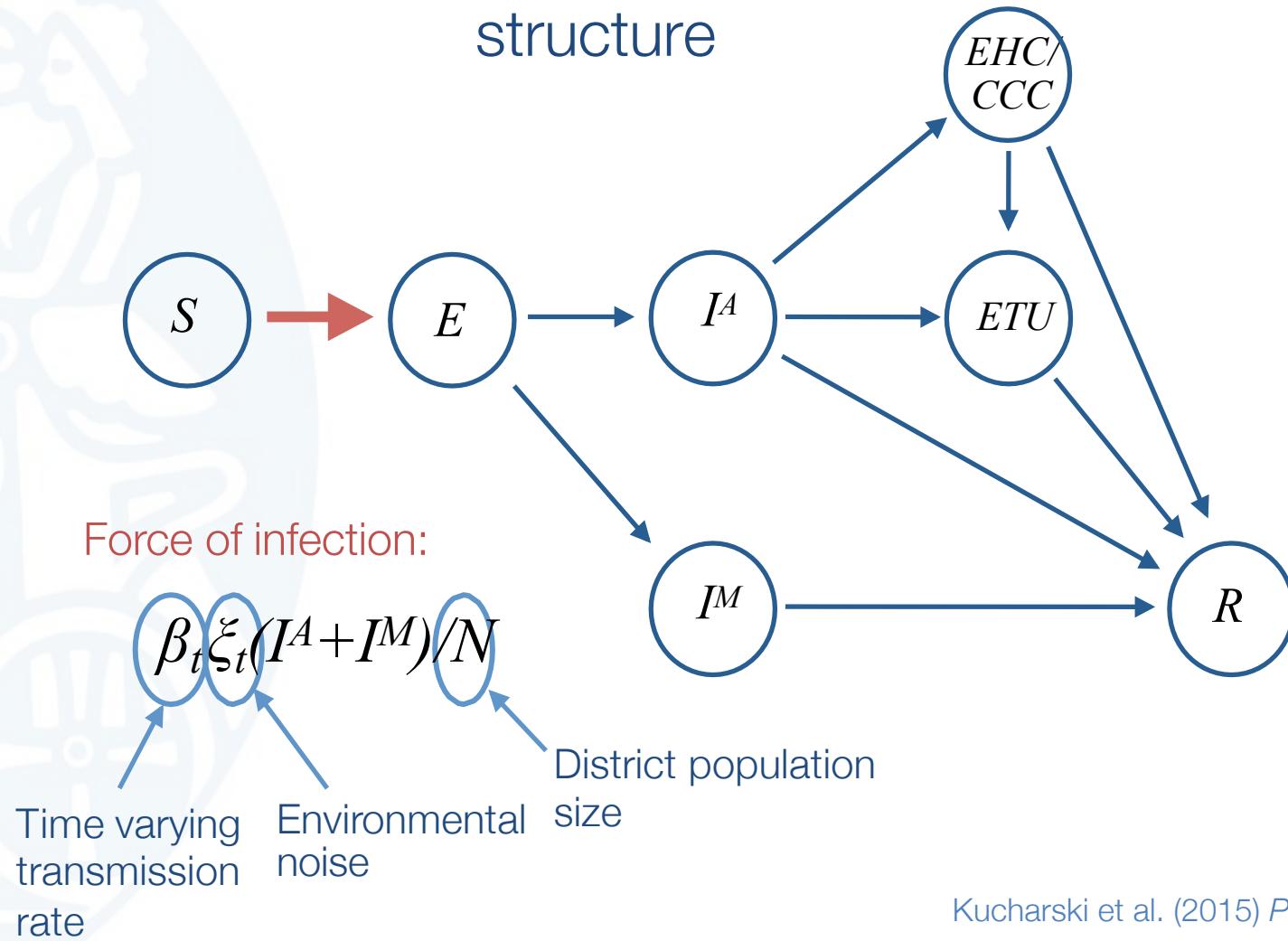
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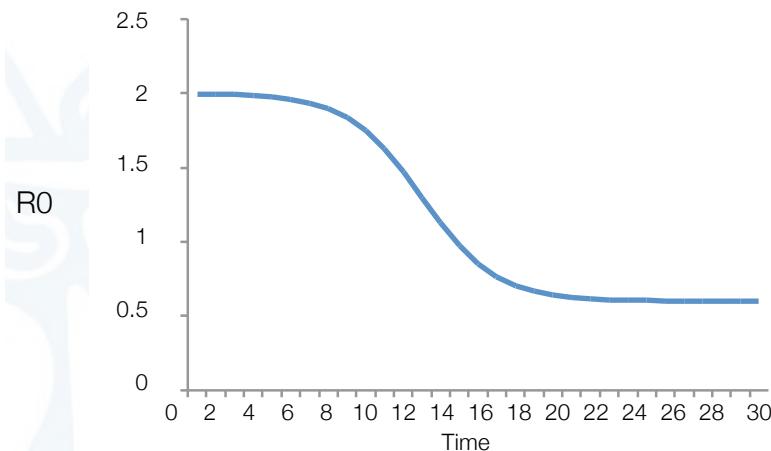
Model structure



Kucharski et al. (2015) PNAS
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Parameters

- Flexible sigmoid for transmission rate:

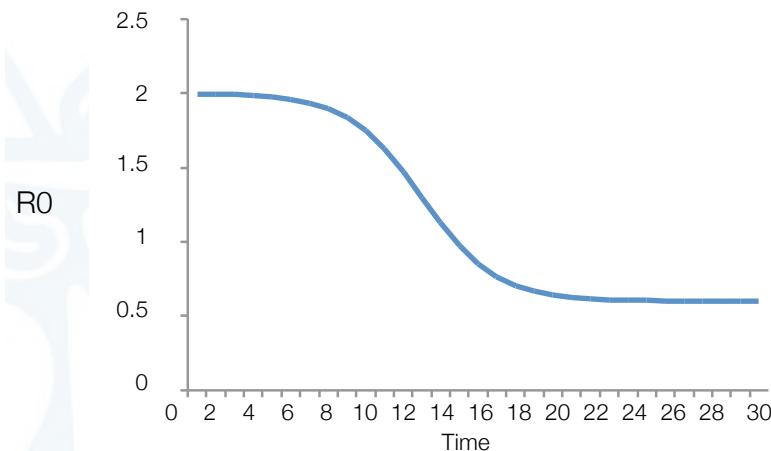


- Natural history parameters from WHO sitreps/database
- Assume 60% cases ascertained in main analysis (sensitivity 40/80%)

Chowell et al. (2004) *J Theor Biol*
Camacho et al. (2014) *Epidemics*

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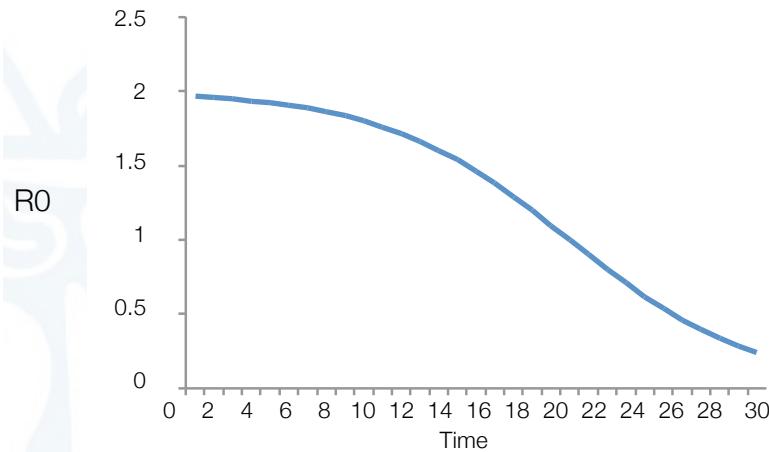


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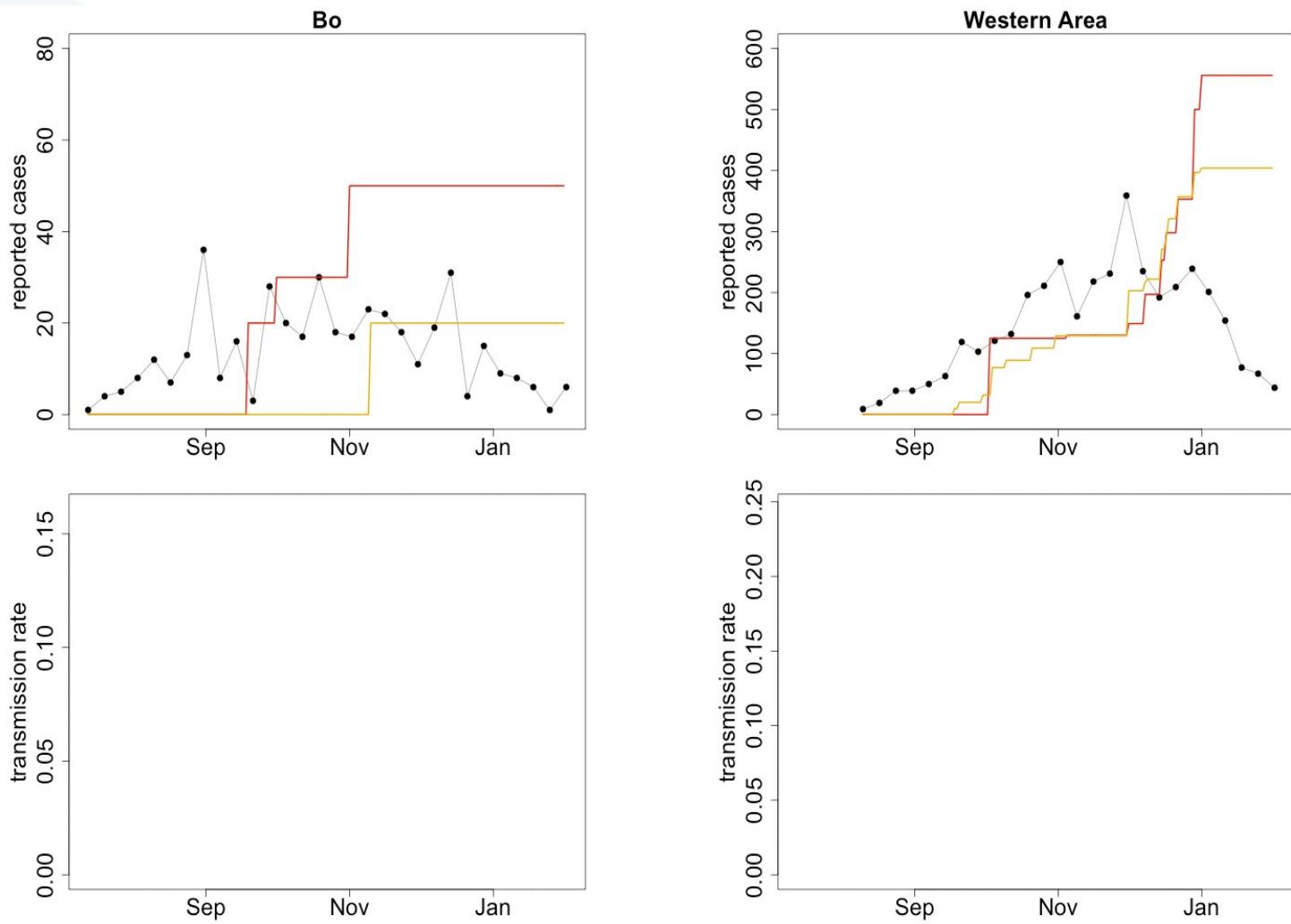
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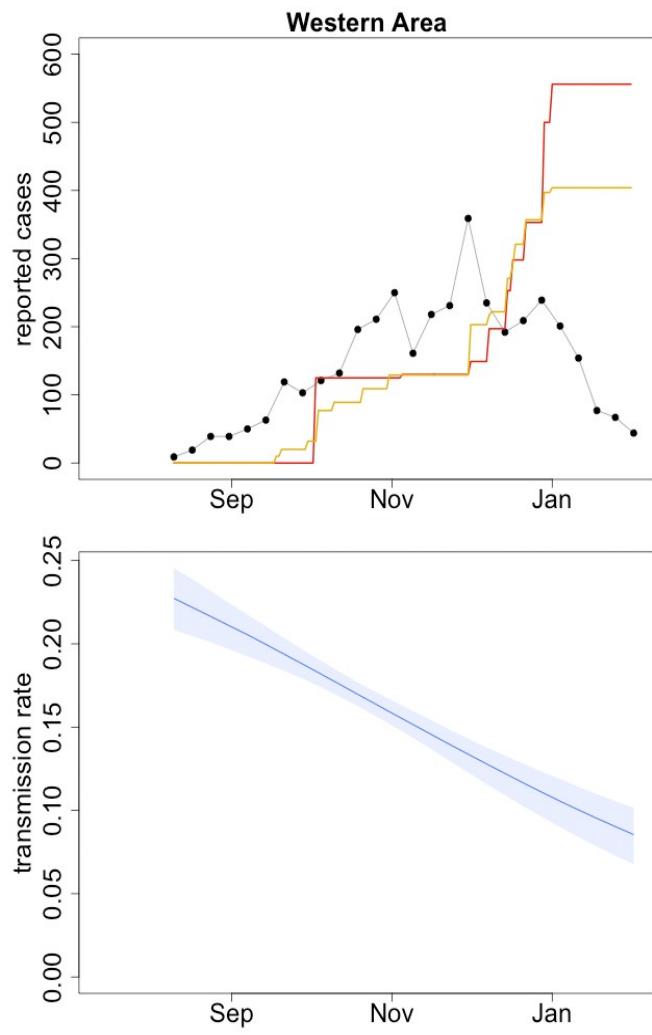
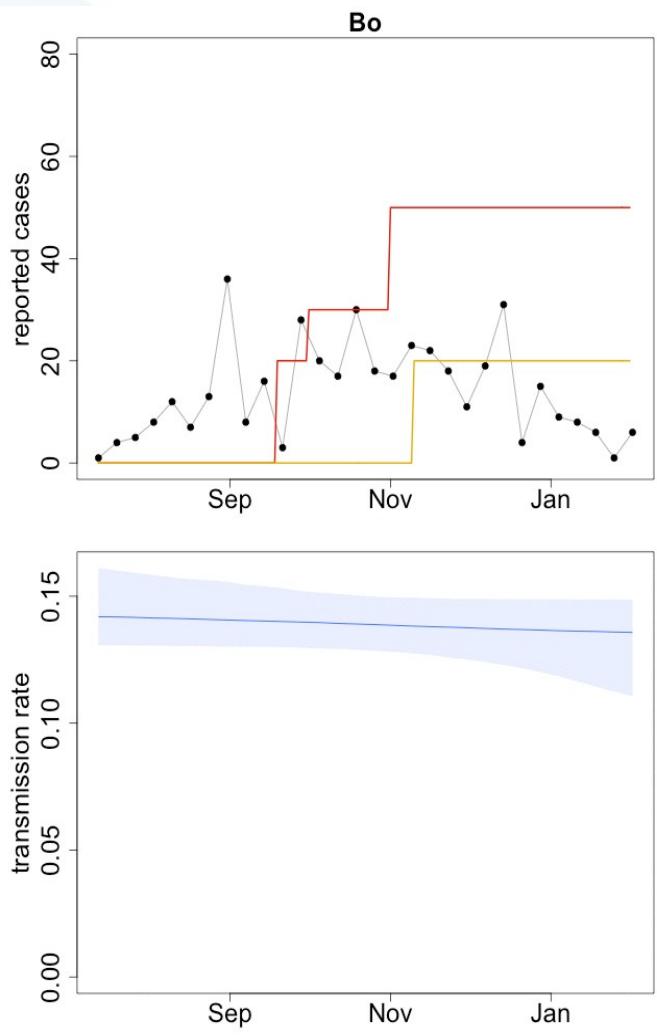
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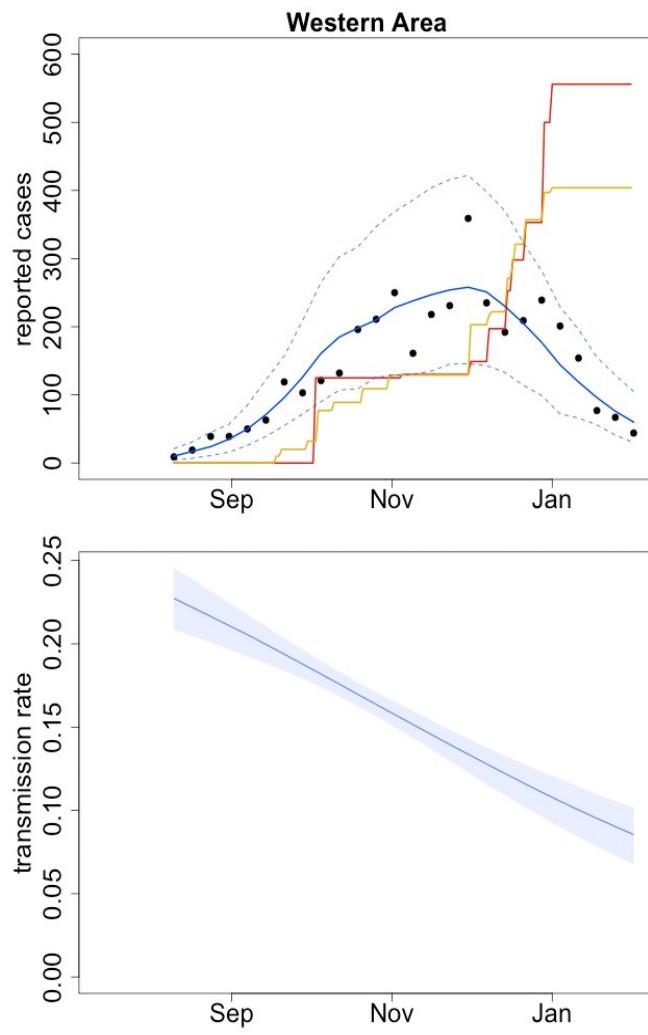
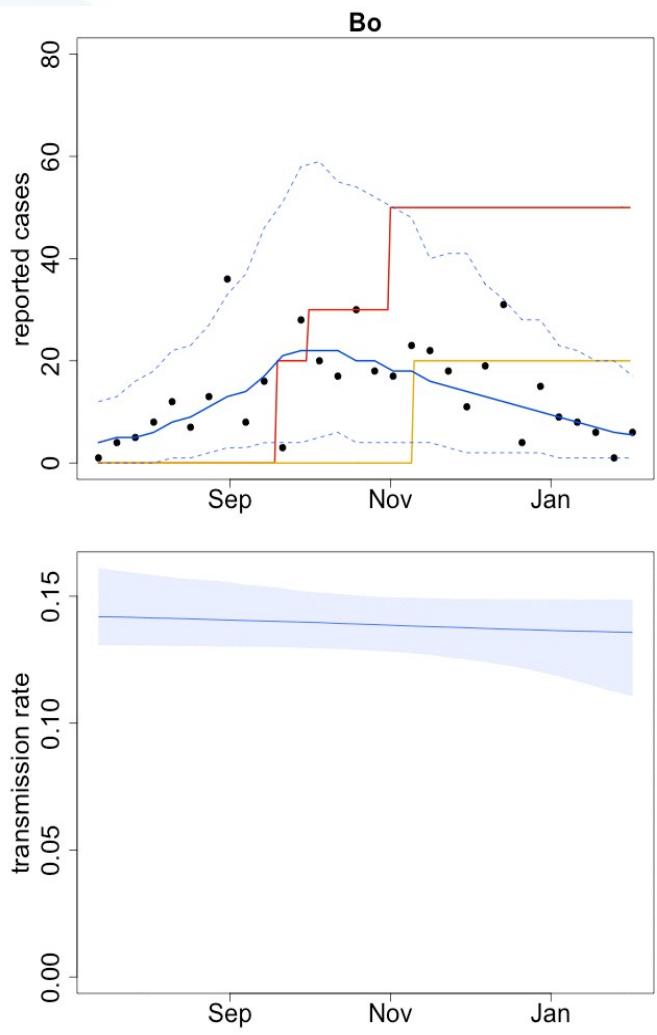


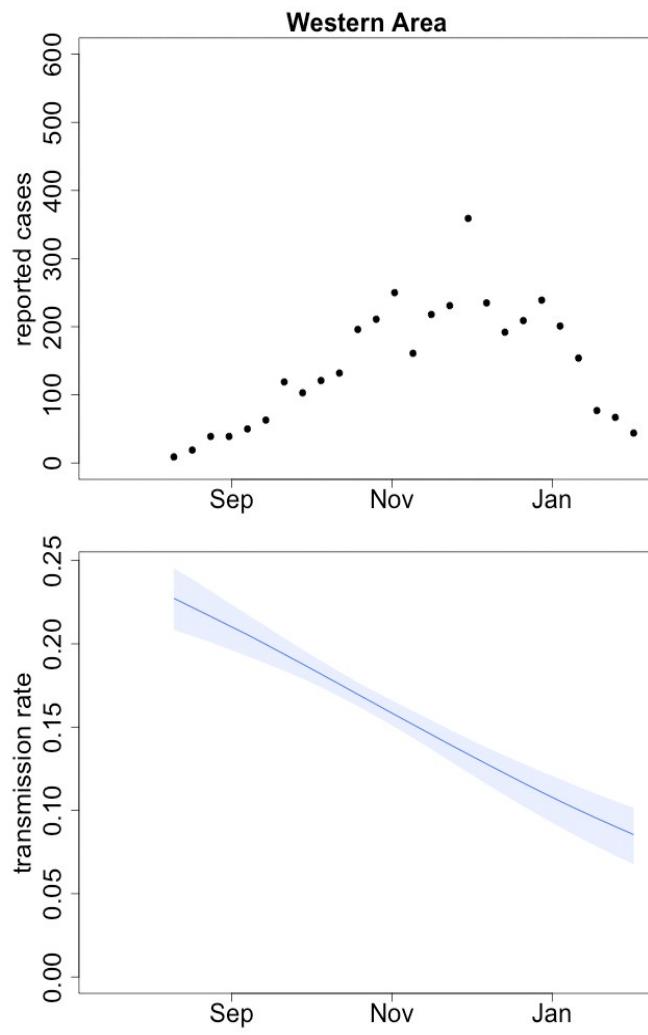
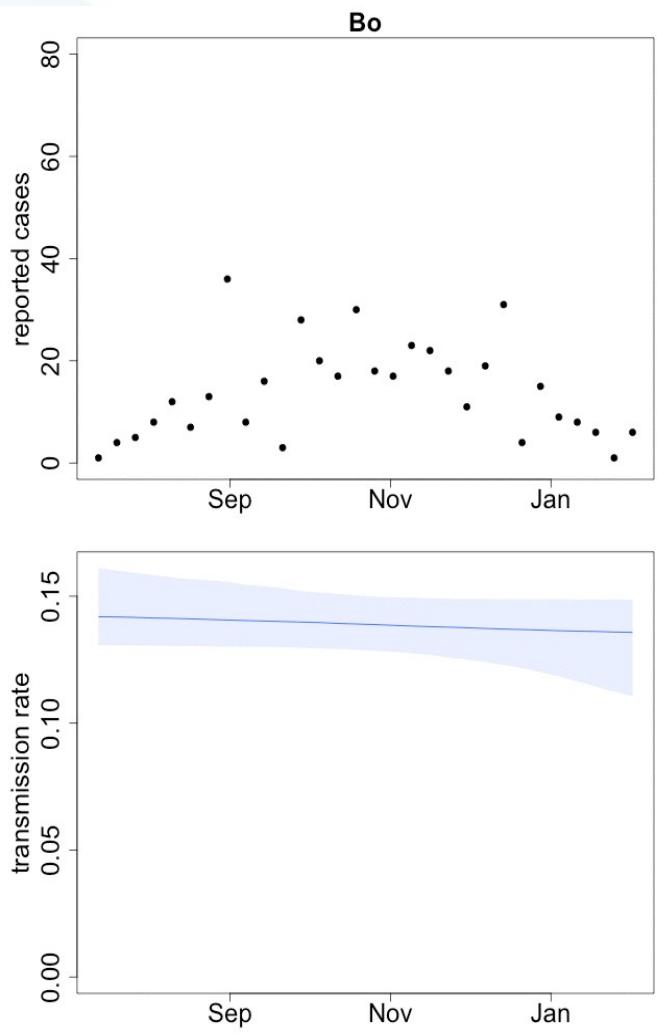
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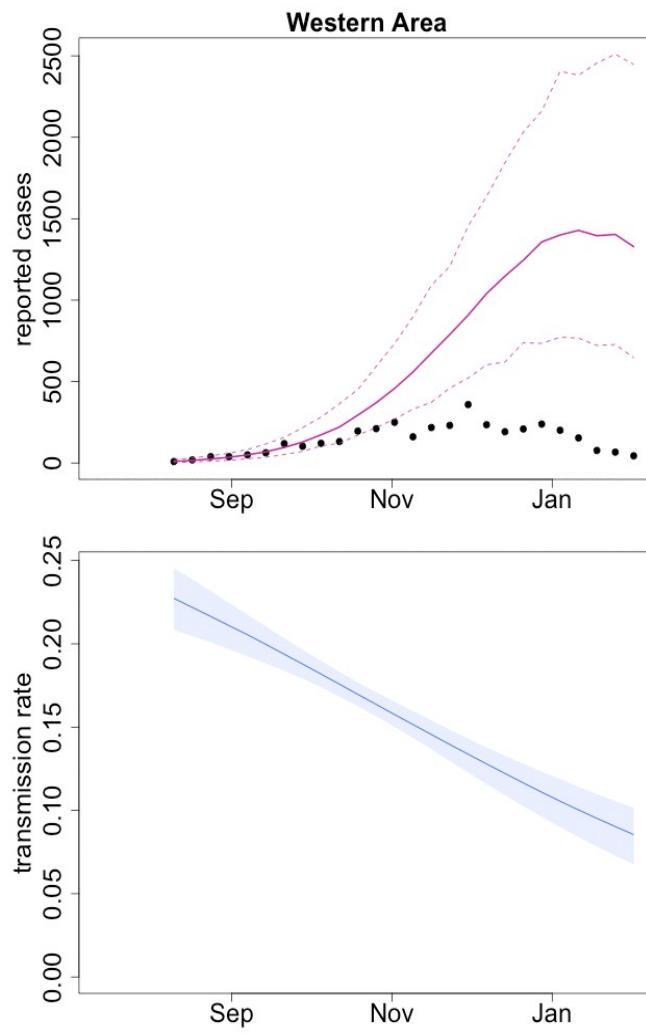
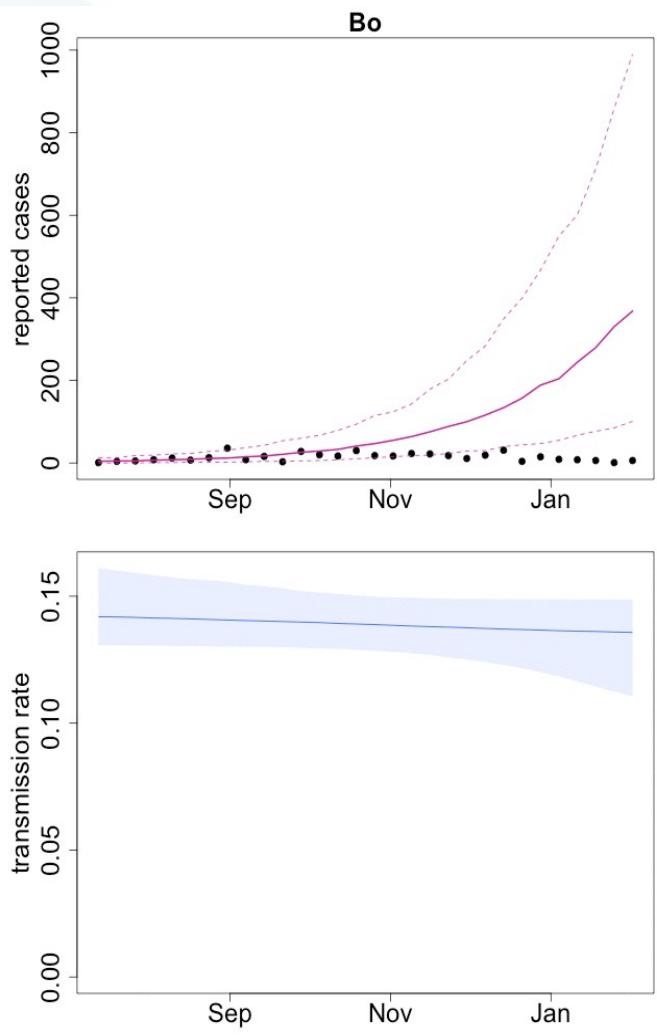
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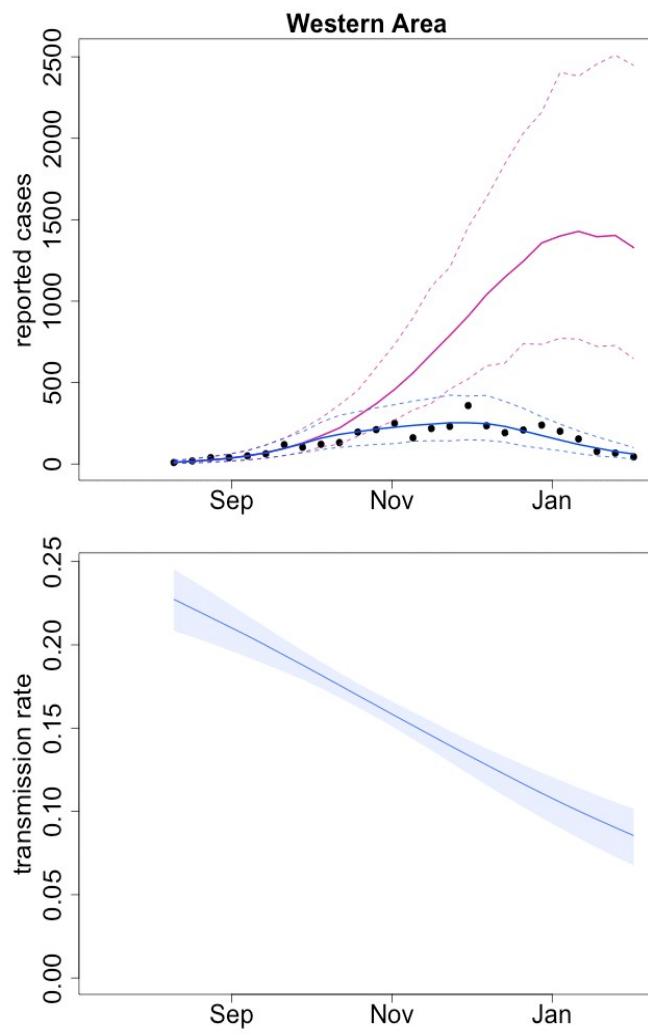
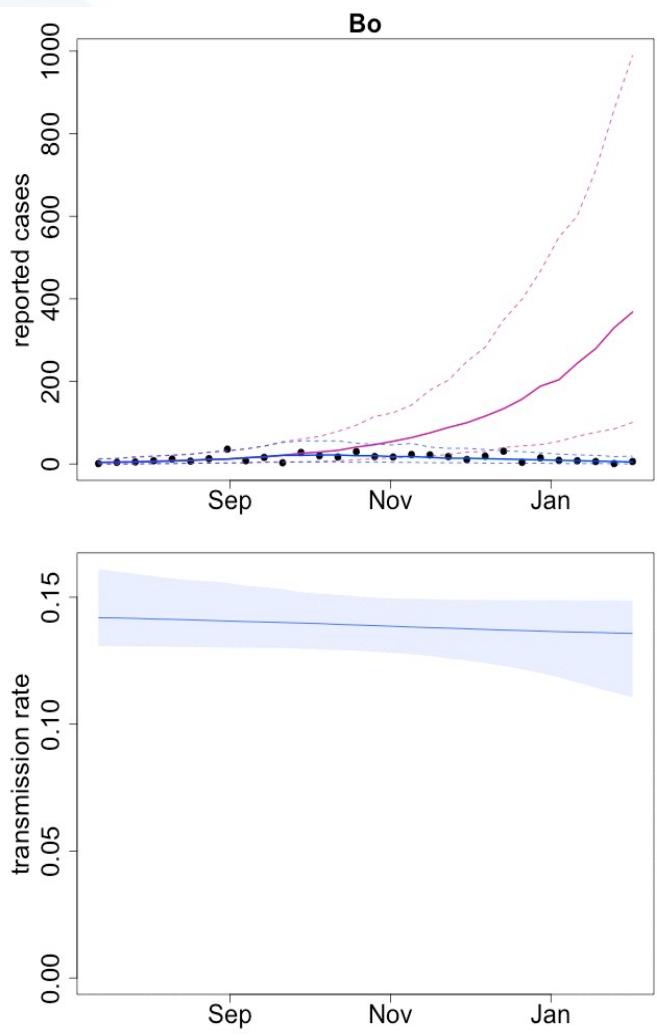












Difference in cases

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)

Kucharski et al. (2015) PNAS

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Cases averted

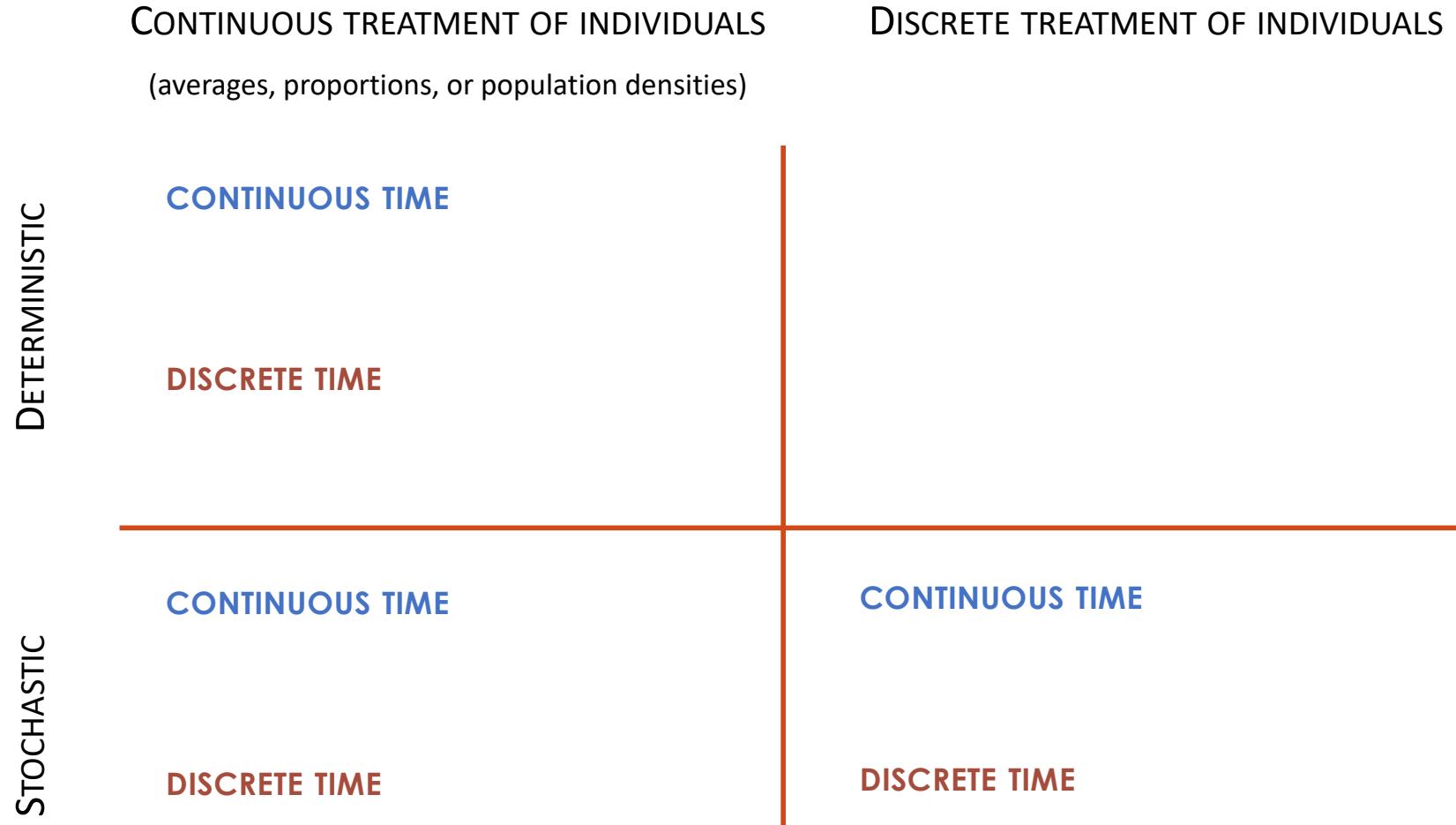
District	Addition of beds	4 weeks earlier
Bo	6,310 (4,150–9,040)	6,820 (4,730–9,620)
Western Area	32,600 (25,500–40,200)	39,200 (32,100–47,100)
Total	56,600 (48,300–84,500)	69,100 (59,500–122,000)

Summary

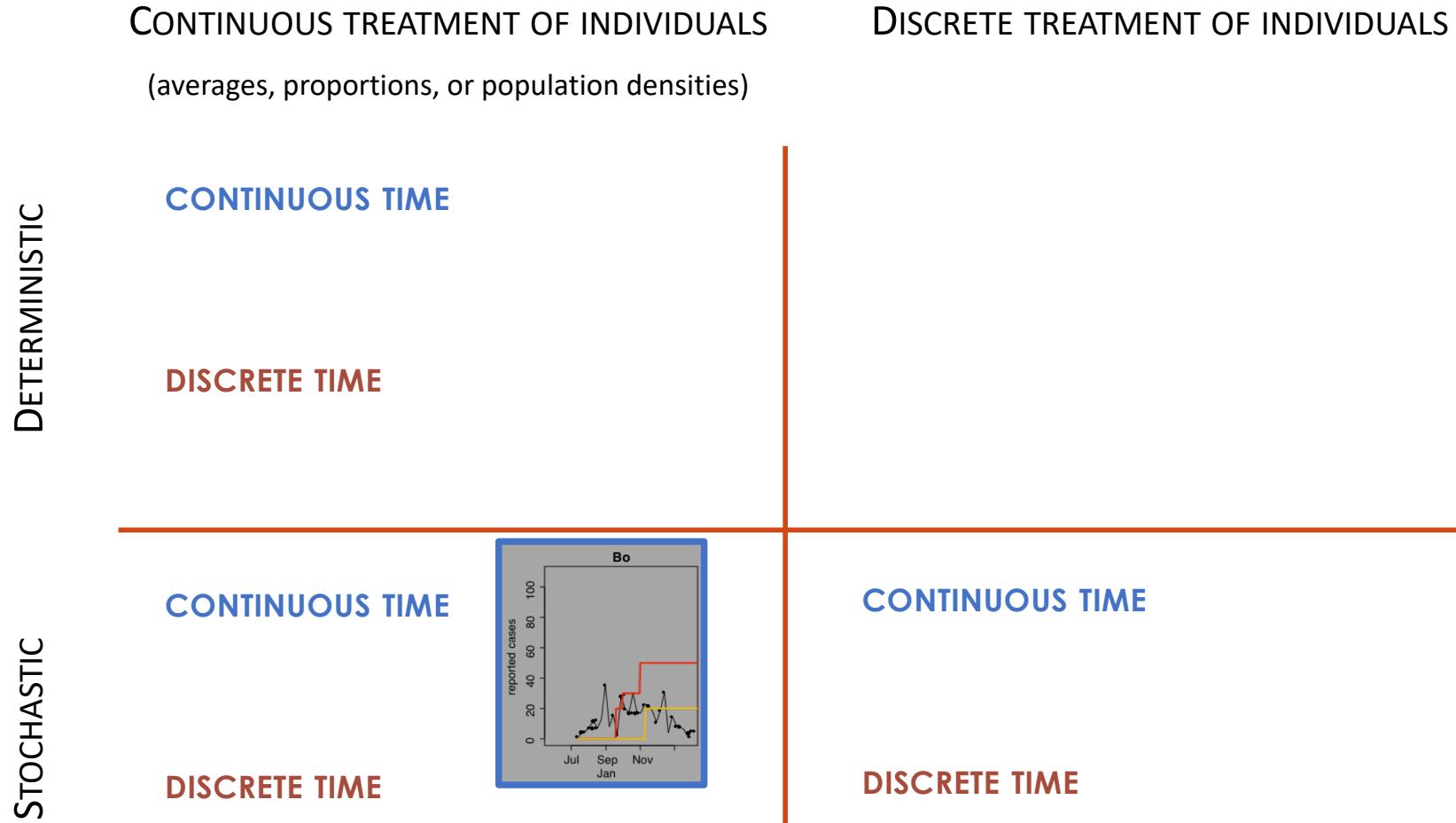
- Introduction of beds prevented around 57,000 cases in Sierra Leone between June 2014 and February 2015.
- Cases averted would have been even higher with earlier response.
- Reduction in community transmission occurred alongside introduction of beds.



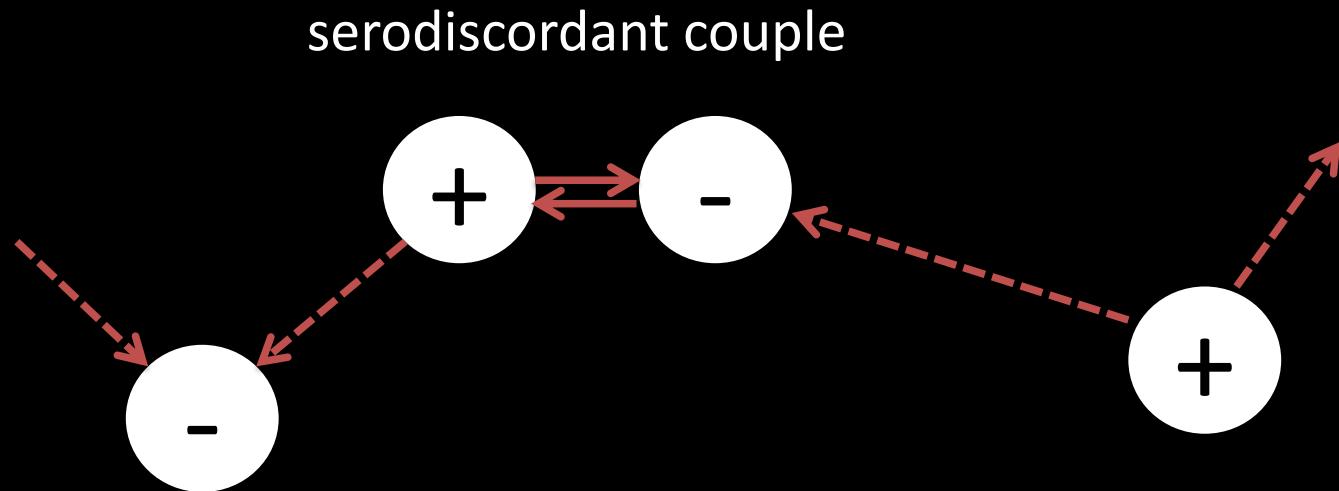
Model Taxonomy



Model Taxonomy



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

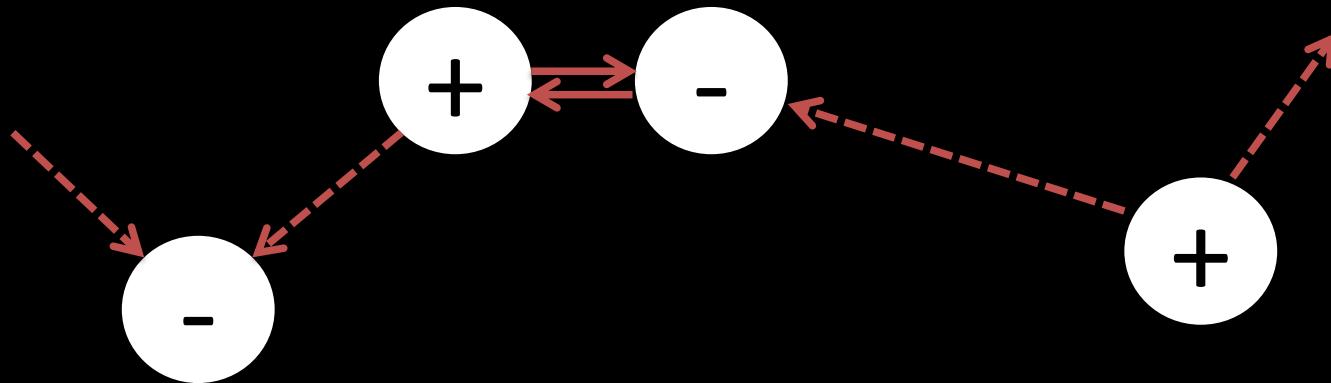
- M+ F+
- M+ F-
- M- F+
- M- F-



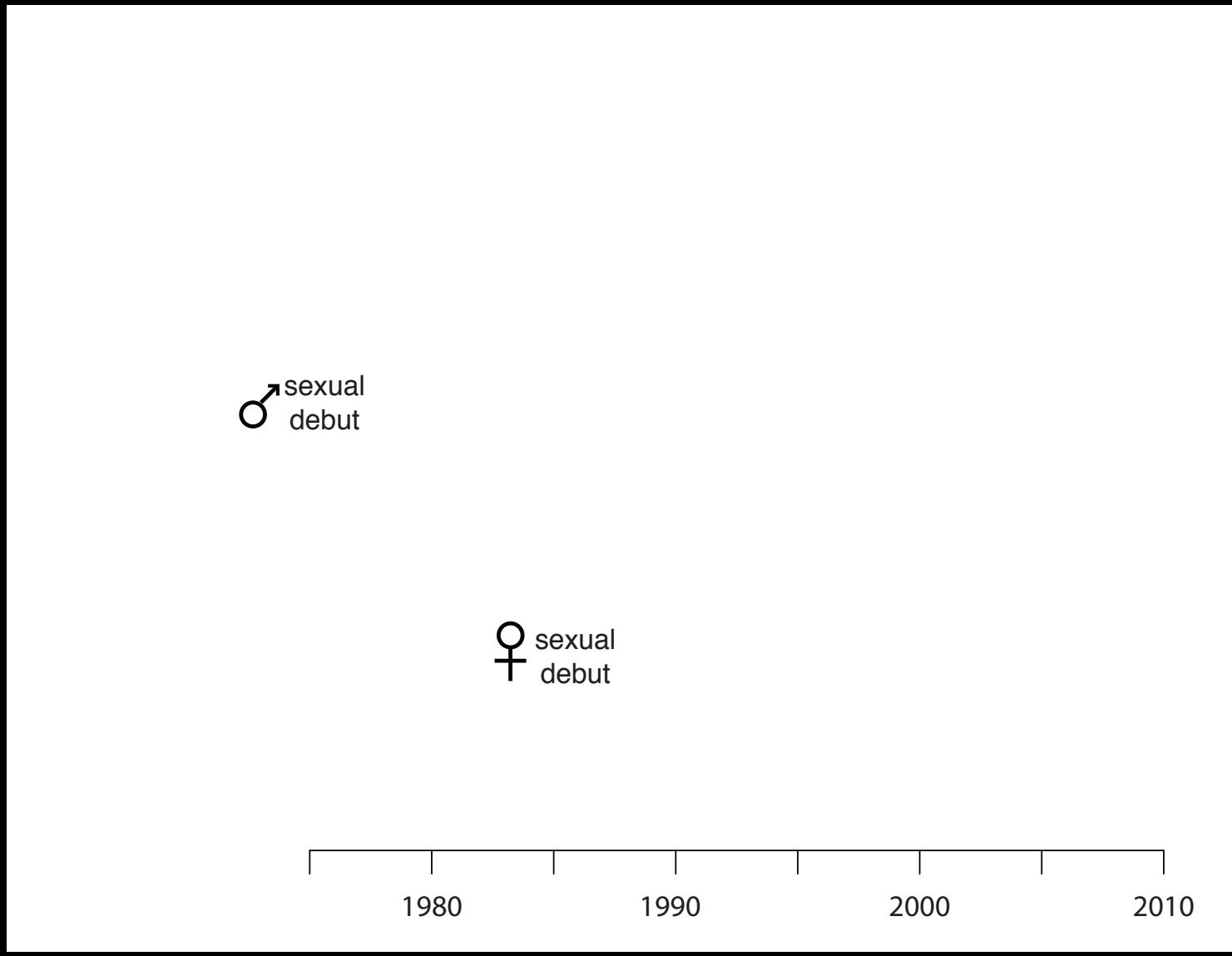
proportion of couples in serogroup

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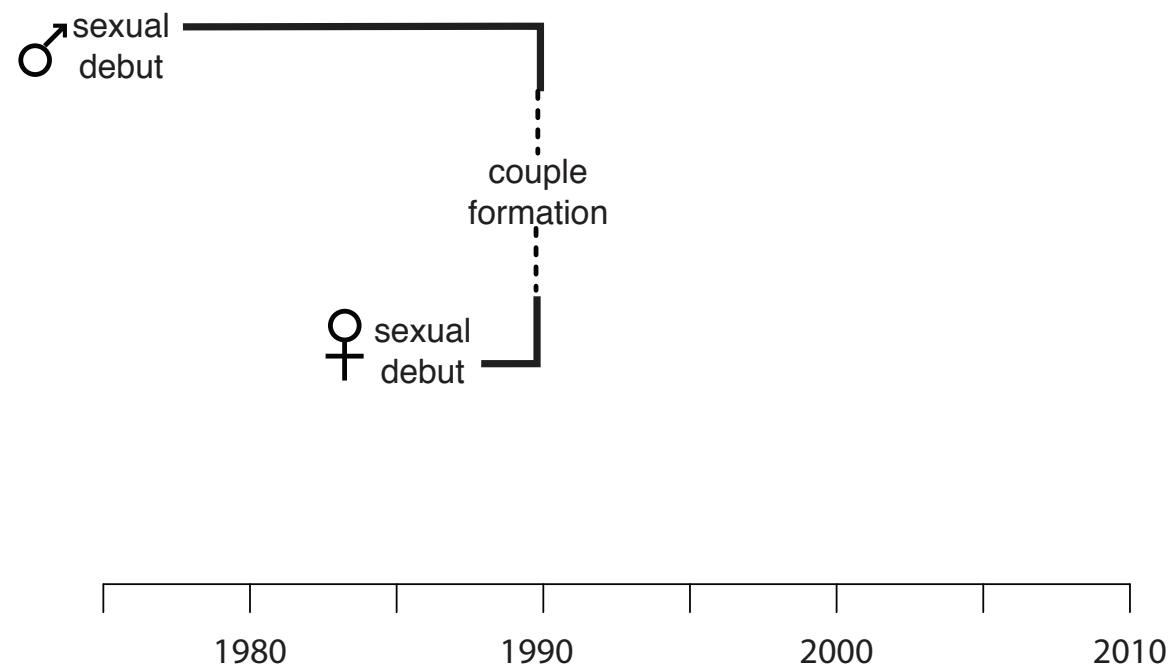
serodiscordant couple



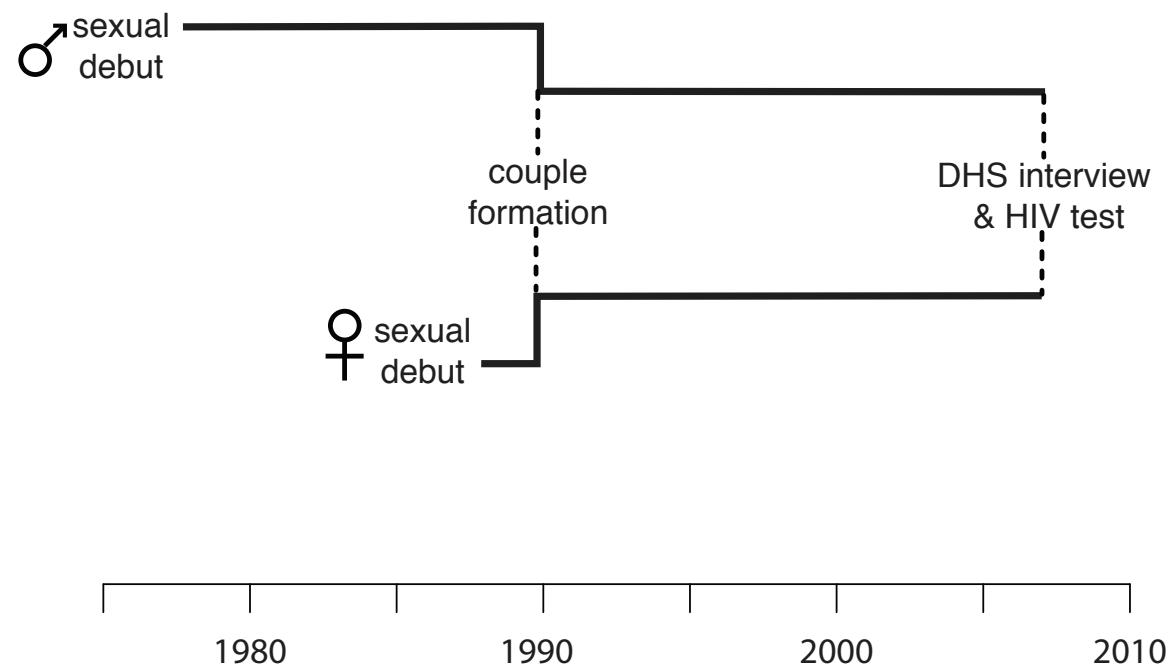
Example Relationship History



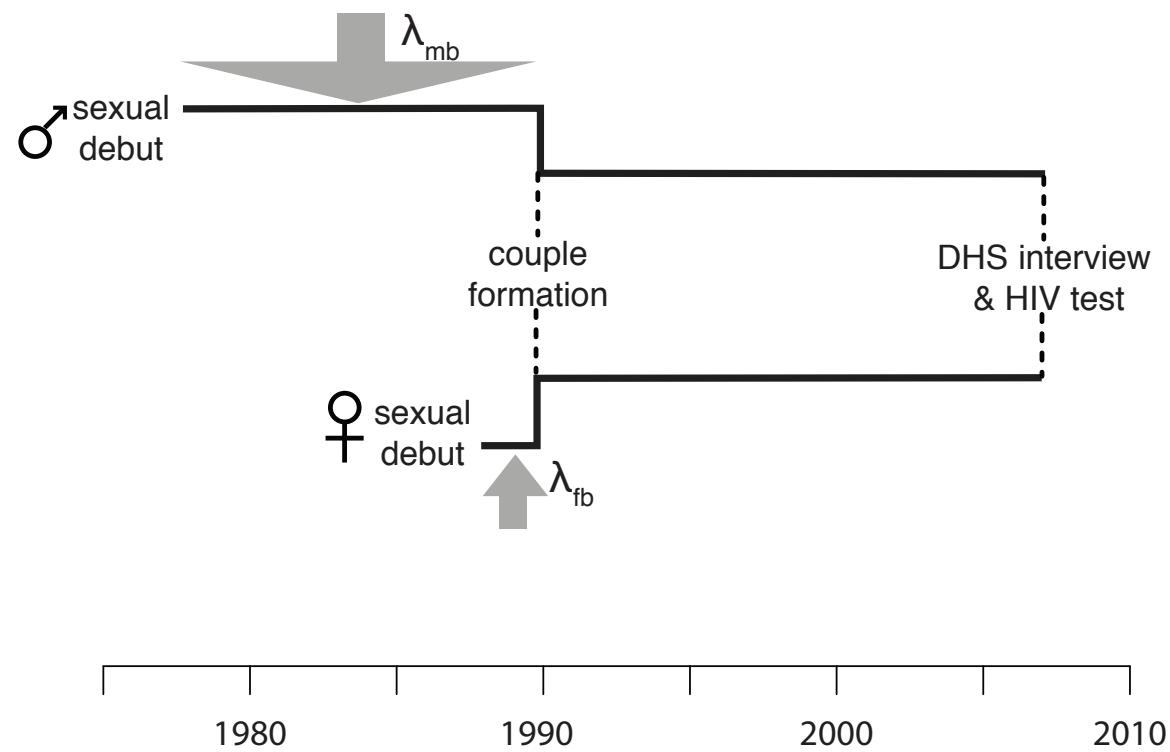
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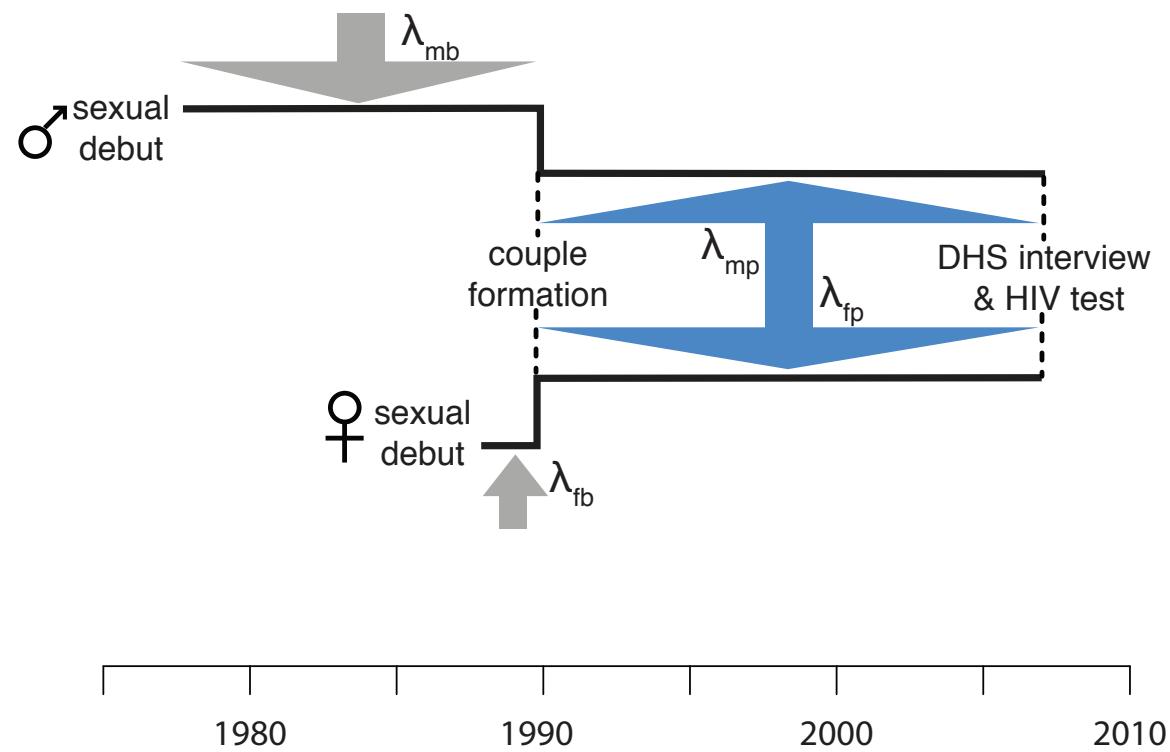
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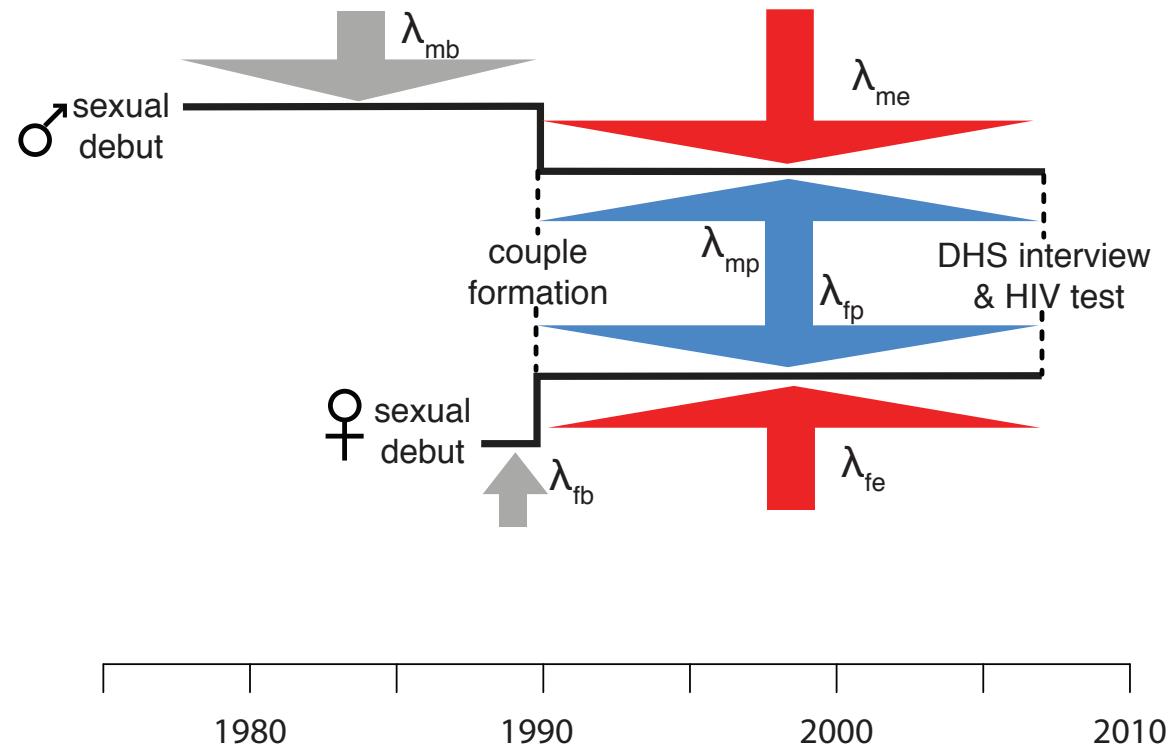
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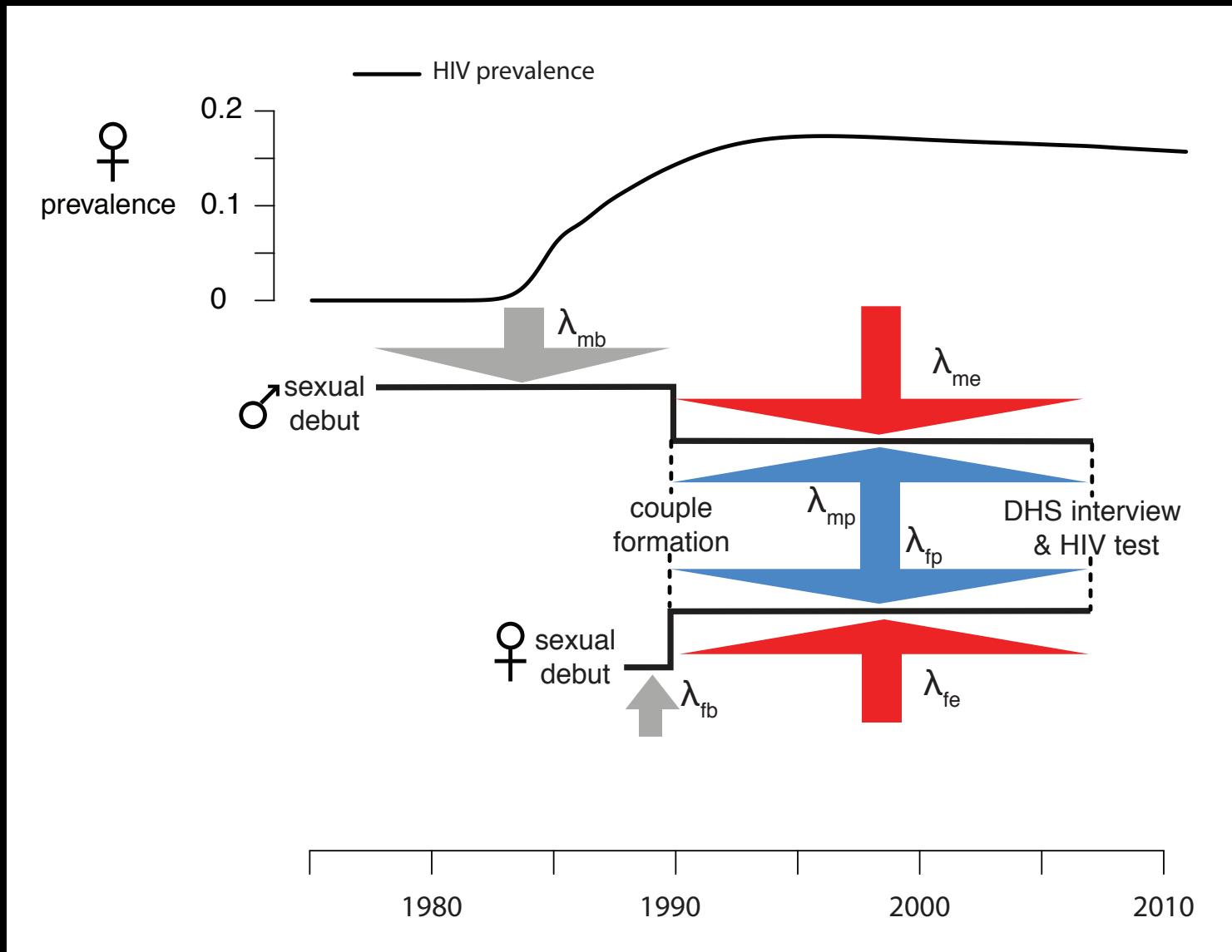
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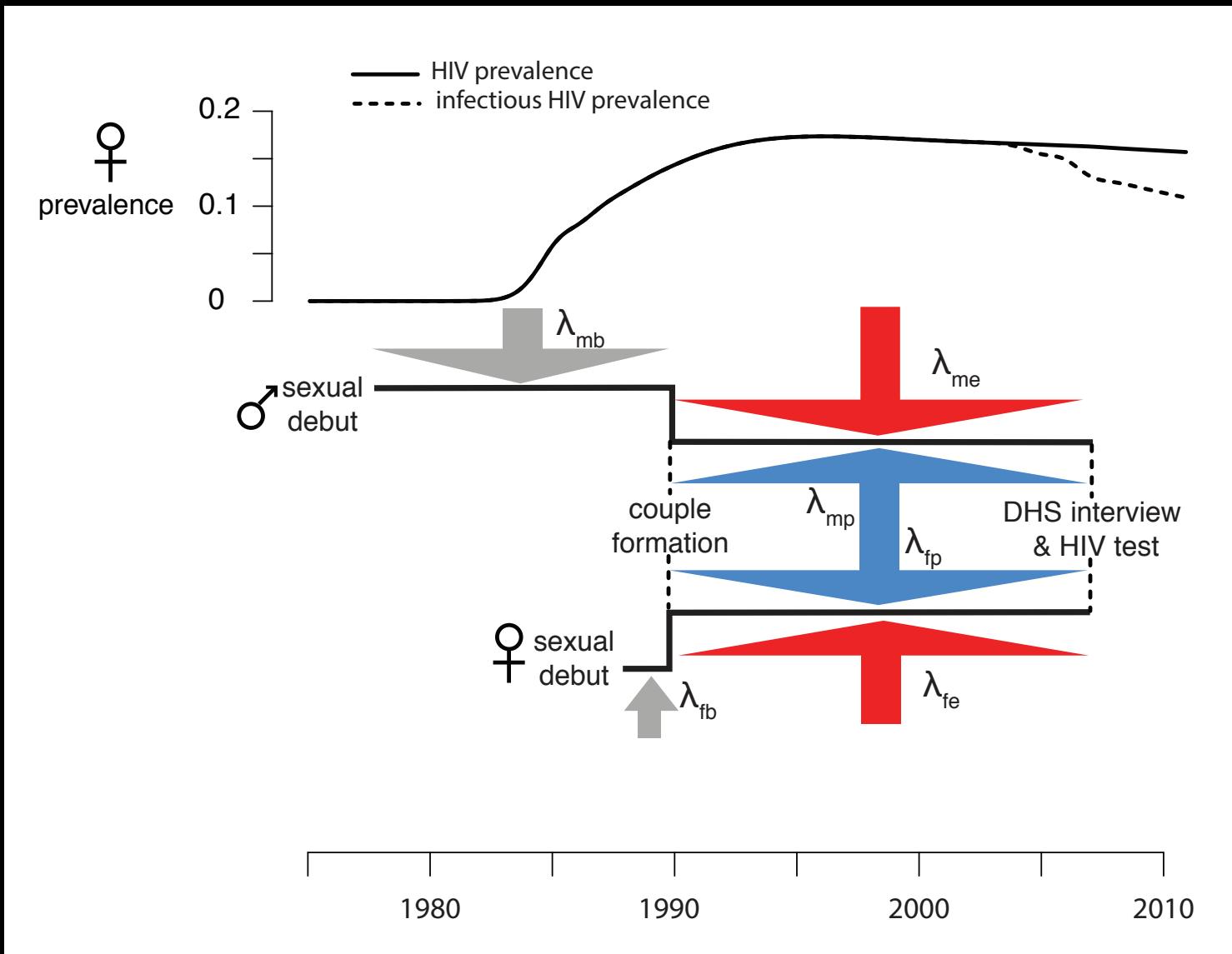
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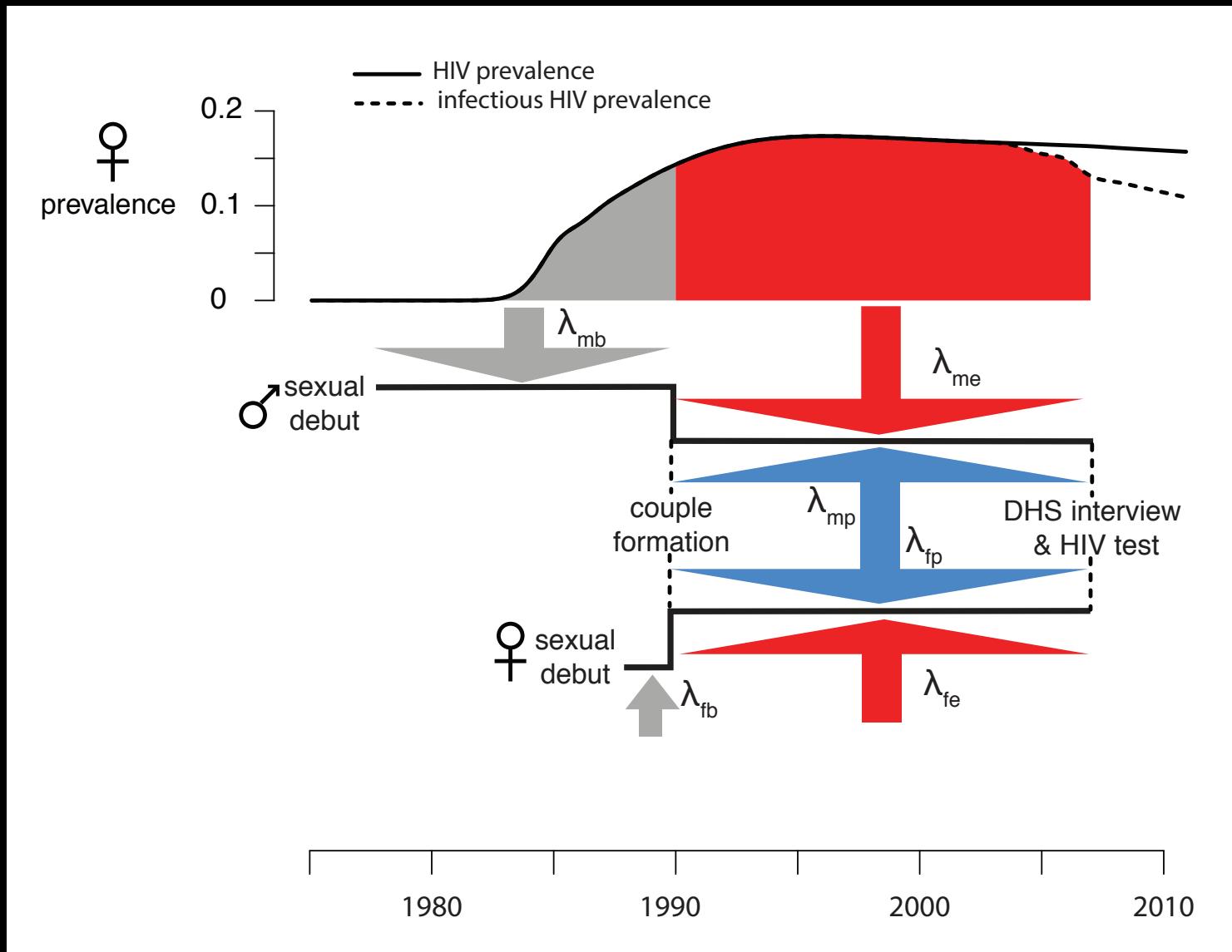
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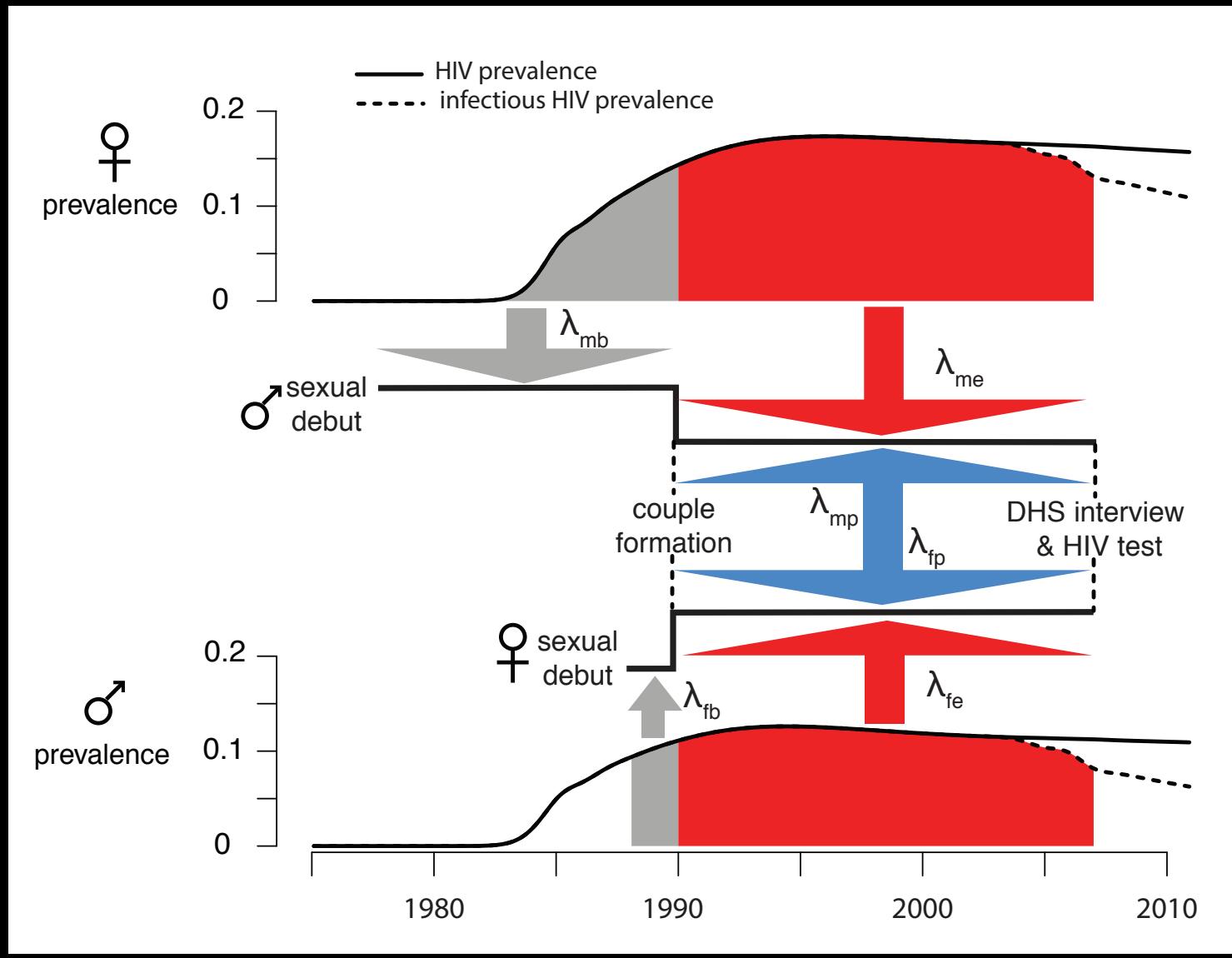
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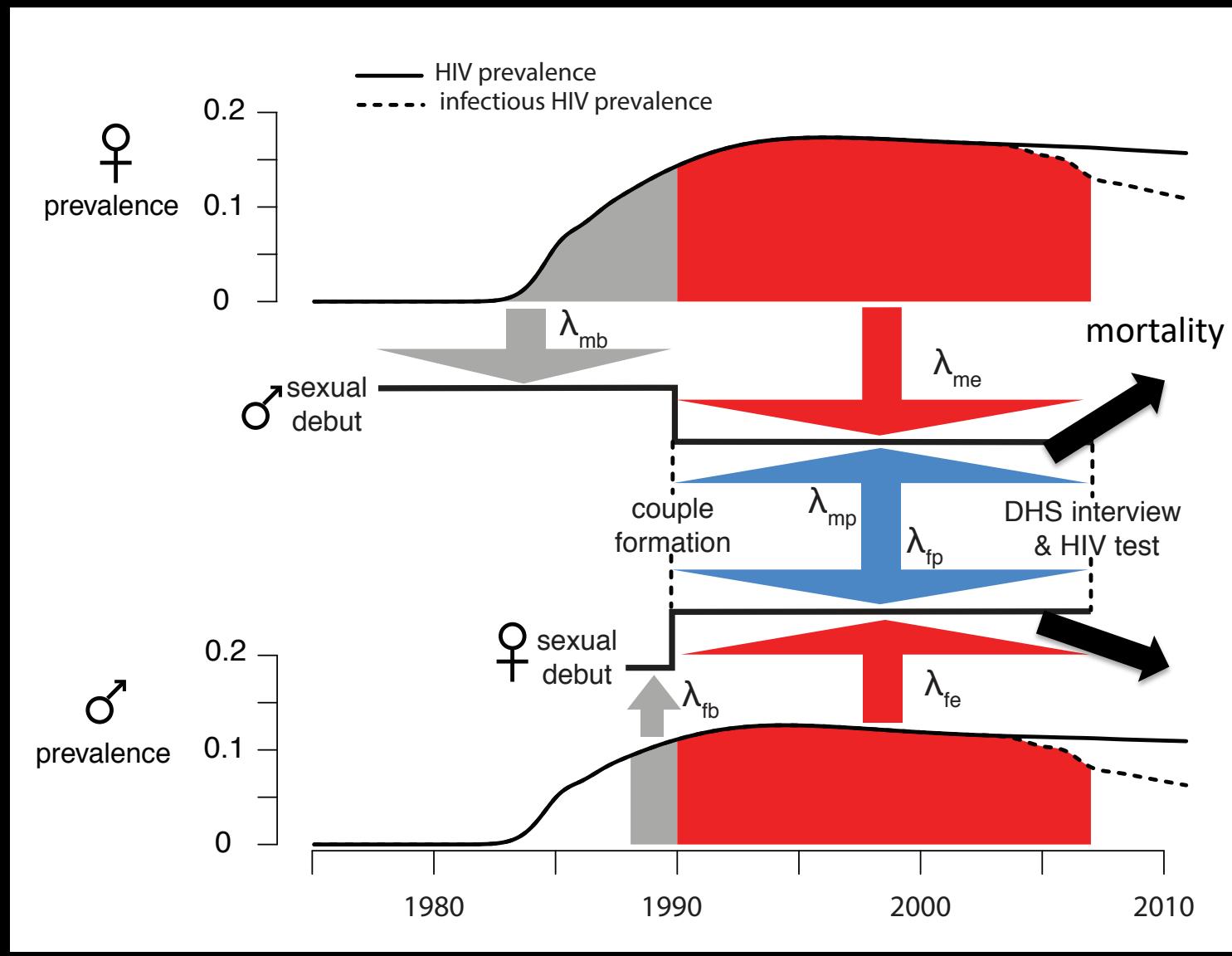
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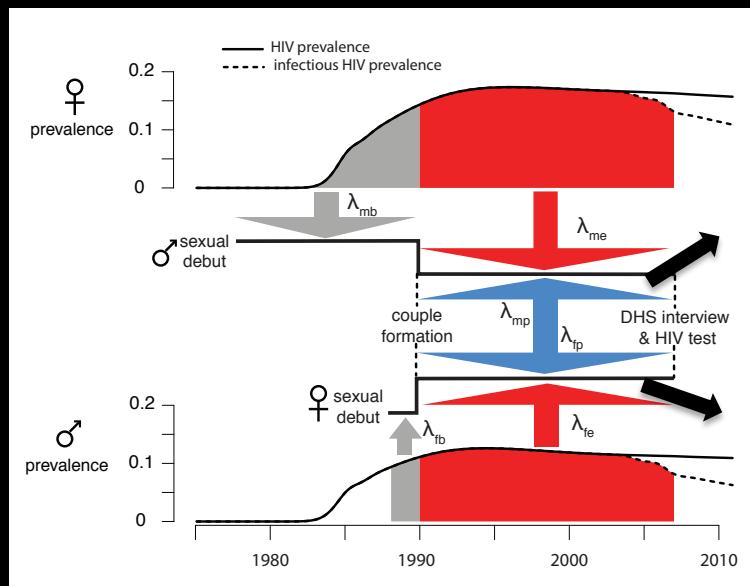
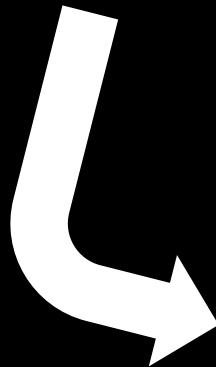
Example Relationship History



Example Relationship History



Estimated: 6 sex-route transmission coefficients
Given: couple relationship histories & serostatuses



$p(\text{observed couple serostatus} \& \text{both partners alive at sampling})$

Fit via Bayesian MCMC

(M+ F-) Couples in Zambia

years sexually active prior (M)

30

20

10

0

1980

1990

2000

2010

date of couple formation

% prevalence (F)

100

75

50

25

probability male infected extracouply

1

0.9

0.8

0.7

0.6

0.5

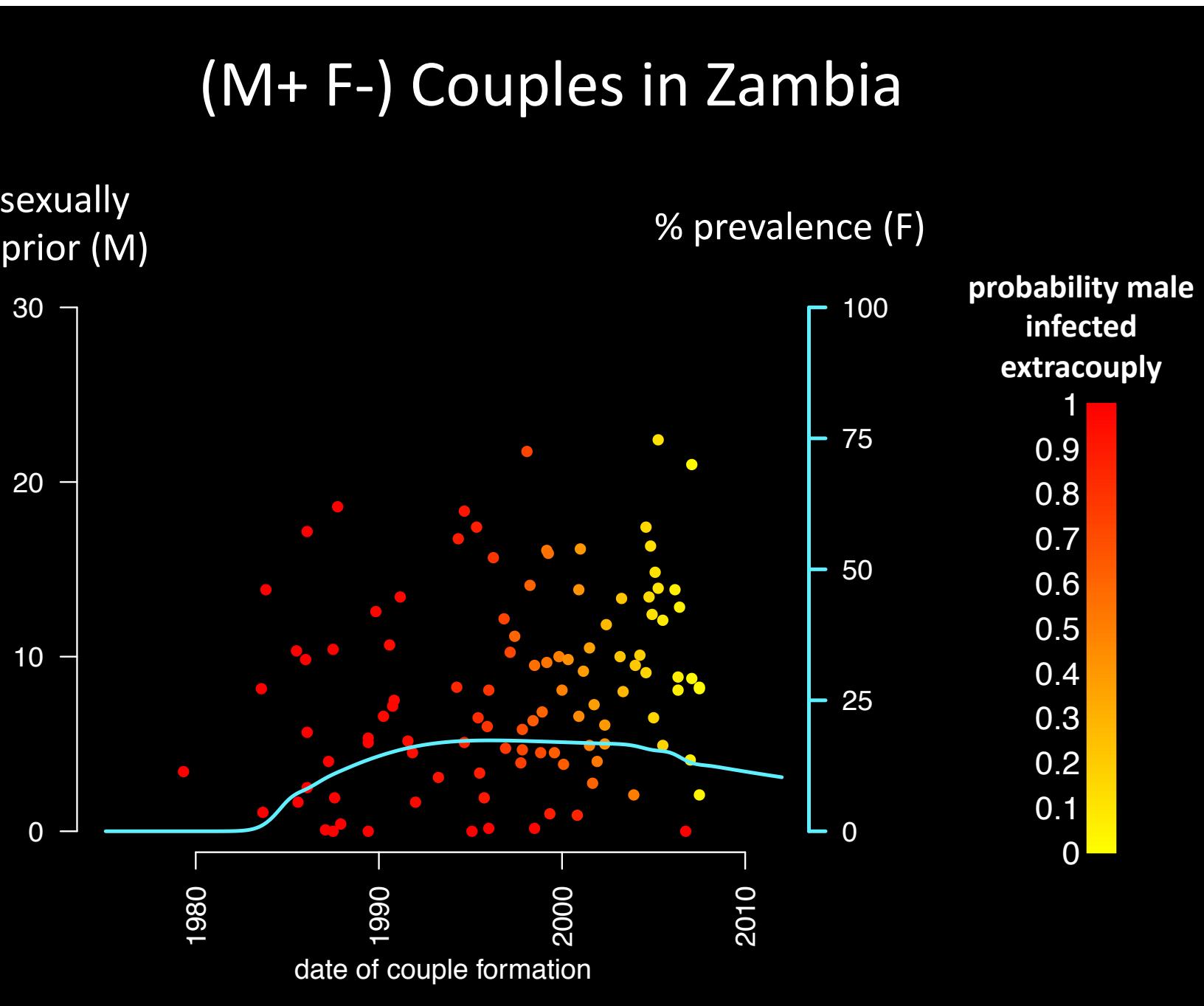
0.4

0.3

0.2

0.1

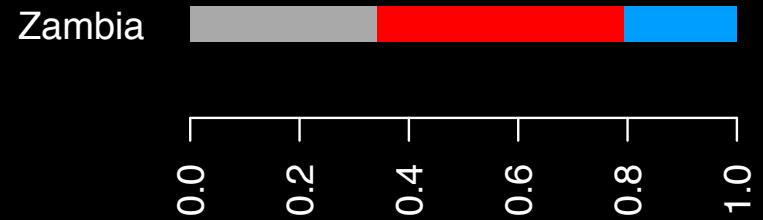
0



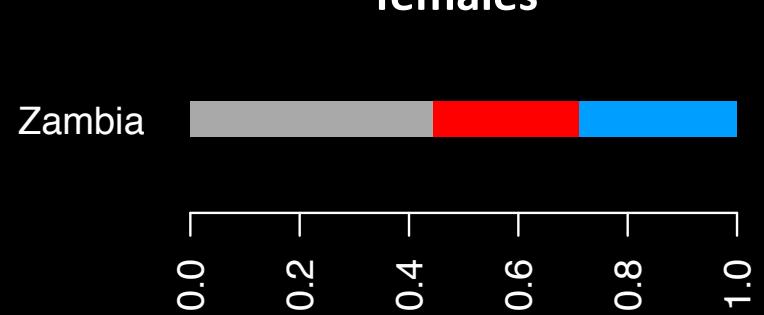
Is HIV incidence driven by transmission inside or outside of stable partnerships?

- pre-couple
- extra-couple
- within-couple

males



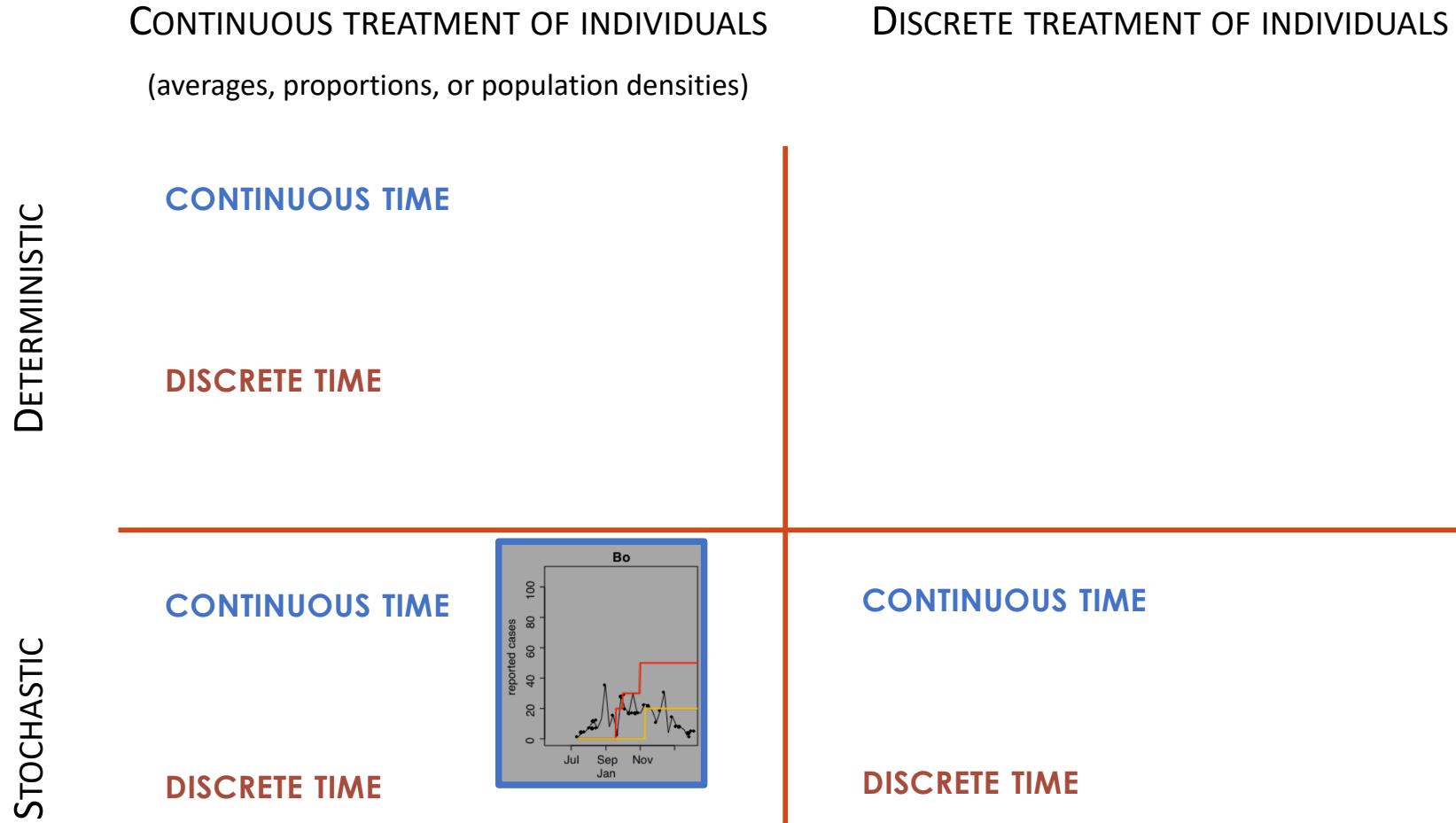
females



0.0 0.2 0.4 0.6 0.8 1.0

proportion of infected individuals

Model Taxonomy



Model Taxonomy

CONTINUOUS TREATMENT OF INDIVIDUALS

(averages, proportions, or population densities)

DISCRETE TREATMENT OF INDIVIDUALS

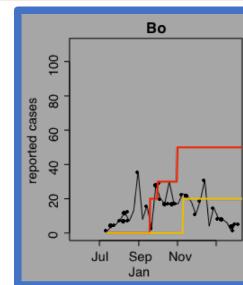
DETERMINISTIC

CONTINUOUS TIME

DISCRETE TIME

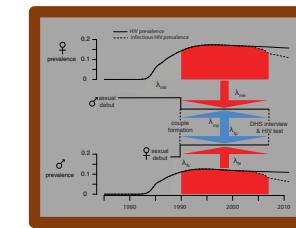
CONTINUOUS TIME

DISCRETE TIME



CONTINUOUS TIME

DISCRETE TIME

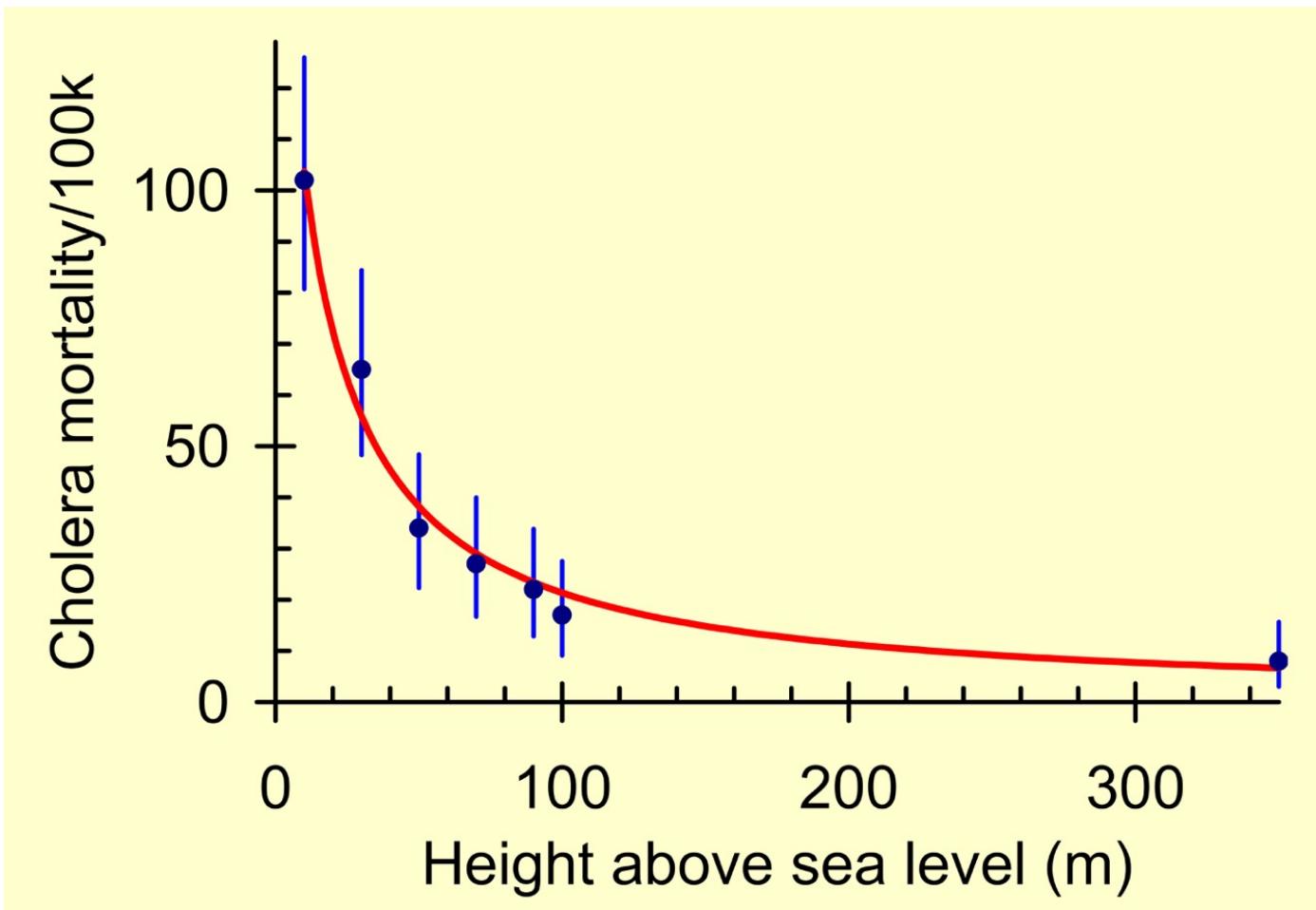


Model-Based Inference

- 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!



62

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!



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[Bellan SE. “Model-based inference and the bigger picture” Clinic on Dynamical Approaches to Infectious Disease Data. DOI:10.6084/m9.figshare.5687155.](#)

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