Imperial College London

MRC Centre for Outbreak Analysis and Modelling

Mathematical modelling and outbreak response: examples and lessons learnt from West African Ebola

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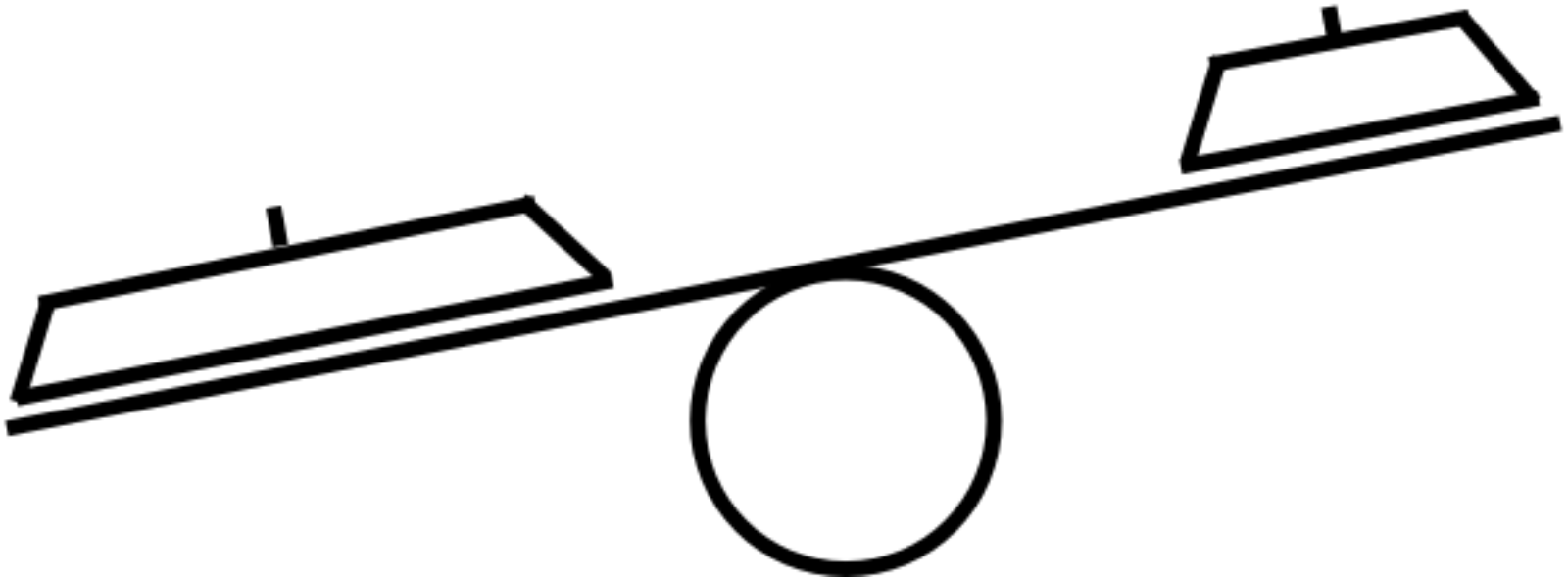
RECON meeting
22 March 2018

Mathematical modelling for outbreak response

- Theoretical mathematical work
- Ad-hoc or semi ad-hoc statistical methods to analyse epidemic data (retrospectively)

- Generic methods/tools to analyse epidemic data (in real-time)



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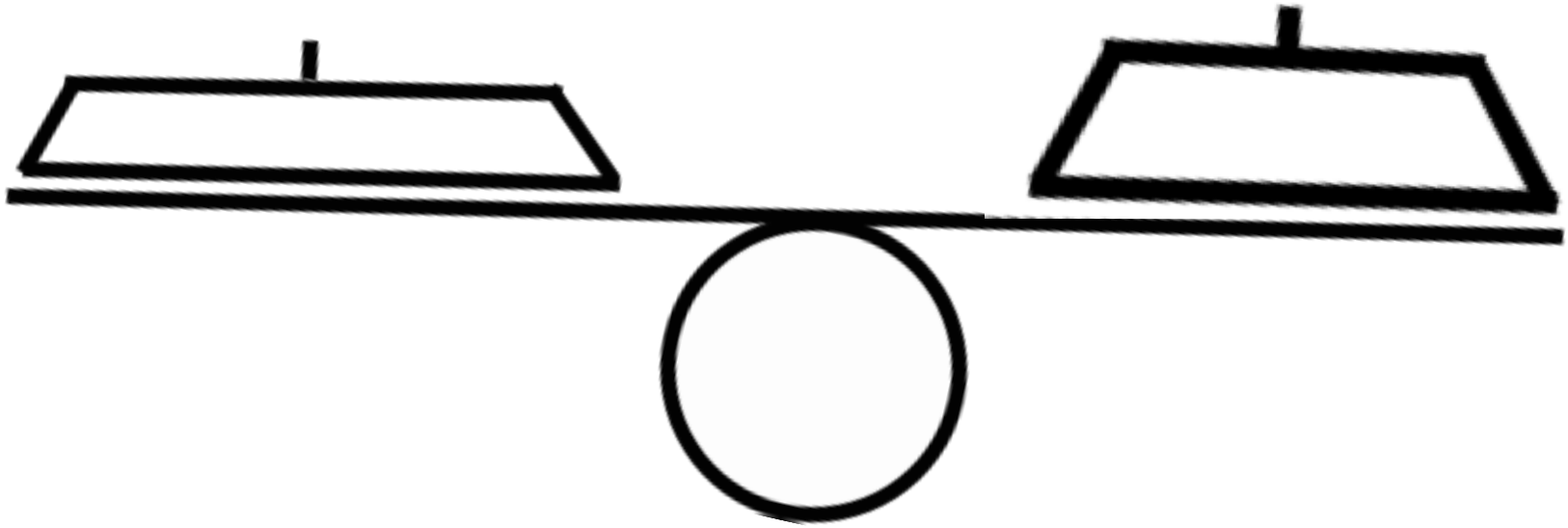

Example: the reproduction number R

The average number of secondary cases caused by each infected individual

Why should we care about R ?

1. **Predict** the potential impact of the outbreak (R_0)
2. **Assess** the feasibility of control measures

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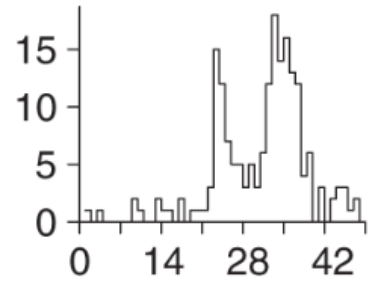
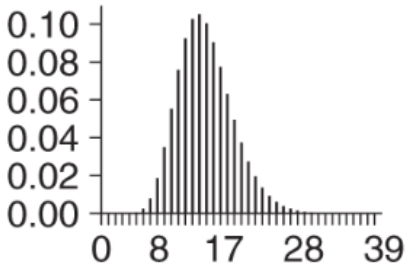
3. **Track** potential changes in transmissibility over time
4. **Evaluate** the effectiveness of control measures (R_t)

EpiEstim: an open source tool to estimate *R* in real time

Incidence time series



Serial interval distribution

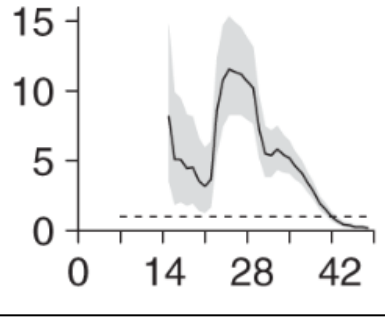


Analytical Bayesian method

Likelihood: $I_t \sim \text{Poiss}\left(R_t \sum_{s=1}^{t} I_{t-s} w_s\right)$

Prior: $R_t \sim \Gamma(a,b)$

Estimates of R_t



Seconds

http://tools.epidemiology.net/EpiEstim.xls

package https://cran.r-project.org/web/packages/EpiEstim/

https://github.com/annecori/EpiEstim

Cori et al., AJE, 2013

Using EpiEstim to quantify R for West African Ebola

(Results shown for Sierra Leone)

Early assessment of
- transmission potential
- projected impact if no further control

Evaluation/adjustment
of control measures

WHO Ebola Response team, NEJM, 2014 & 2015

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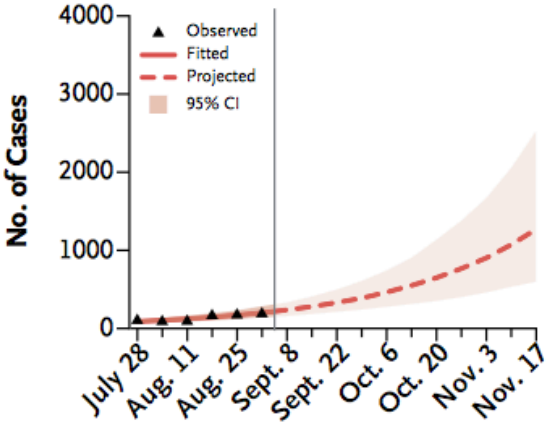
R_0 = 2.02 [1.79-2.26]
(similar to previous outbreaks)



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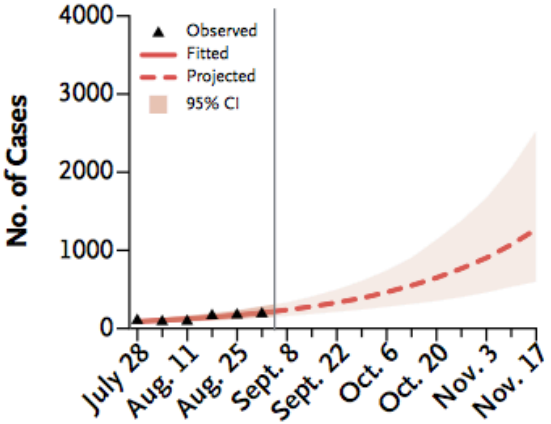

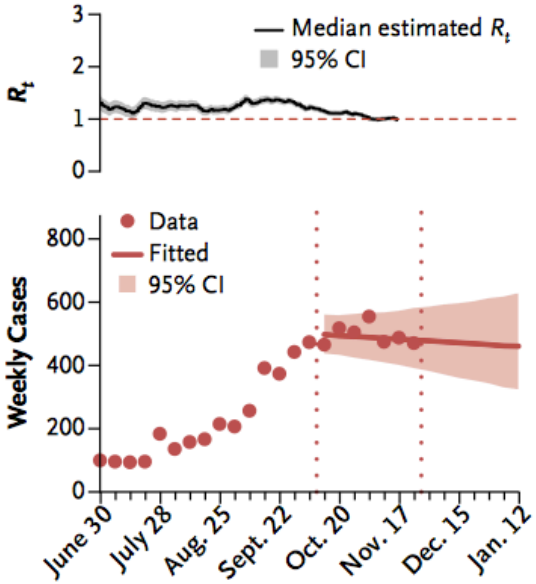

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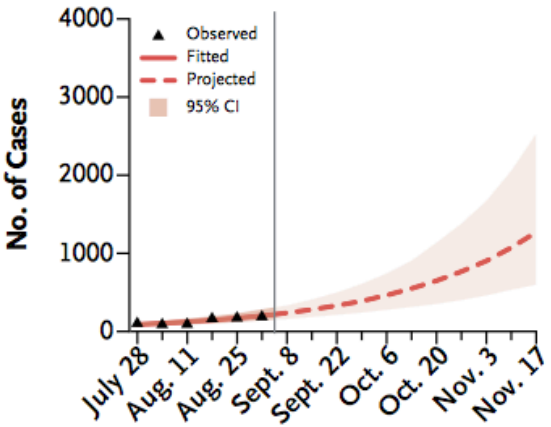
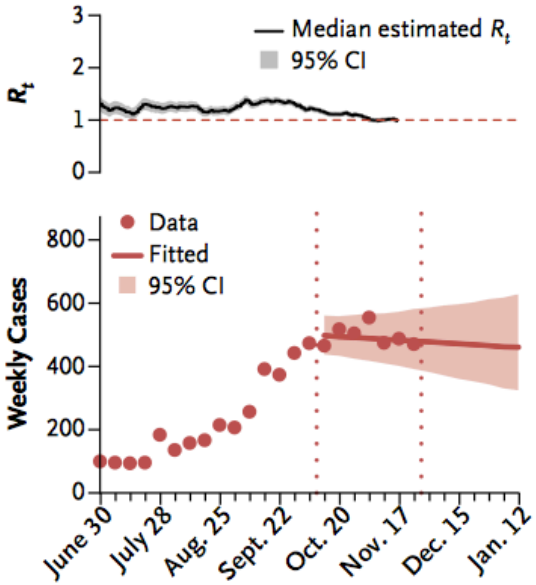
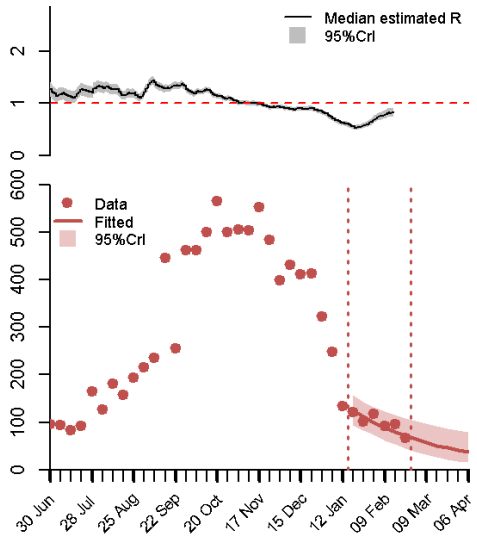




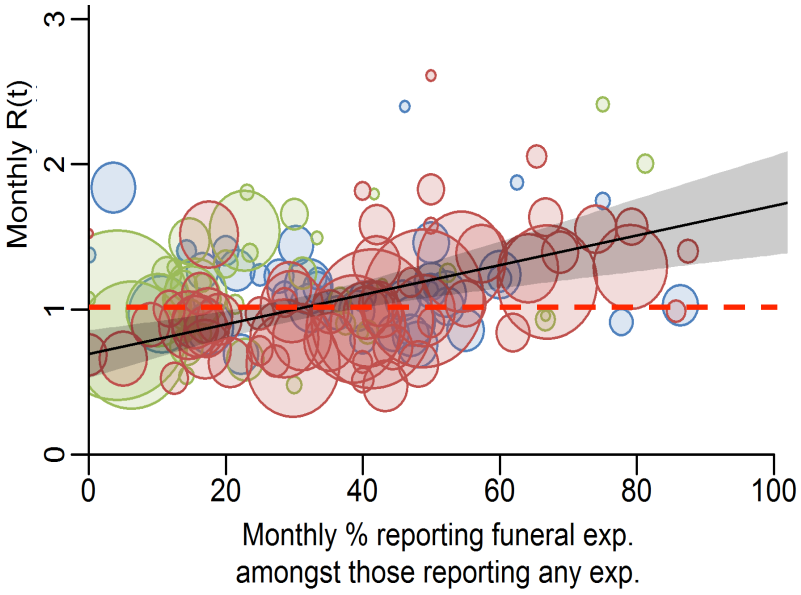


WHO Ebola Response team, NEJM, 2014 & 2015

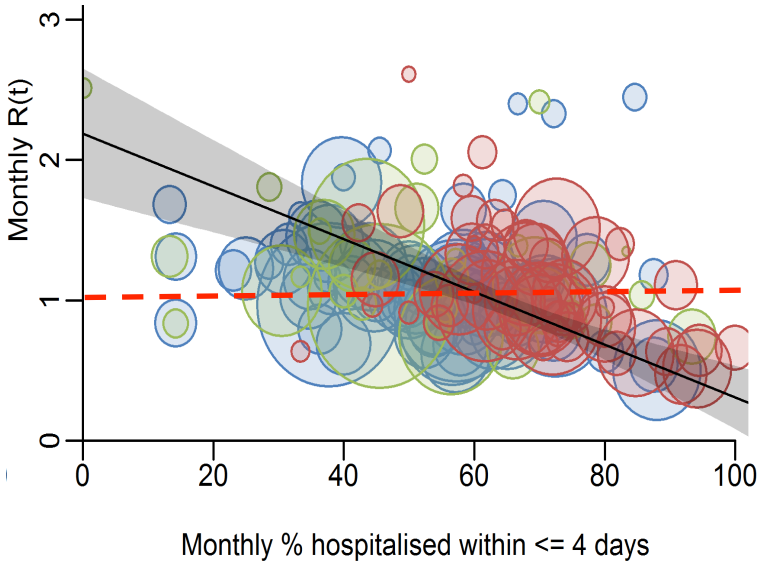
Using EpiEstim to understand drivers of transmissibility and quantify their impact

- R_t for a given district/month was correlated with…

1. Proportion of cases reporting funeral exposure



2. Proportion of cases hospitalised within 4 days of symptoms onset



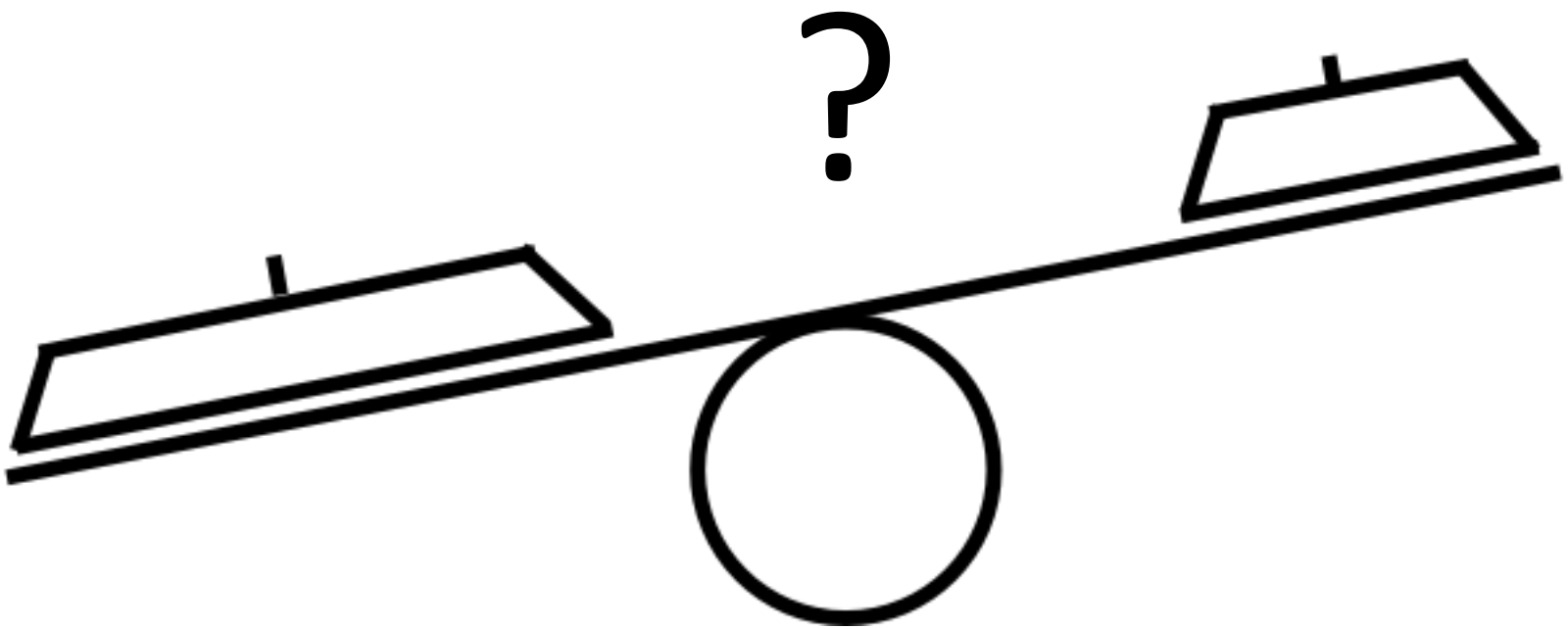
Could be used to design targets (e.g. proportion of cases to hospitalise <X days after symptoms onset) & as a first step to building more complex mechanistic models

Ripley and Thompson, Analyst 1987; R package *deming;* WHO Ebola Response team, PLoS Med 2016

Using modelling to assess the role of rapid diagnostic tools for Ebola

PCR
Slow
Sensitive and specific

RDT
Fast
Less sensitive and specific



Nouvellet et al. Nature 2015

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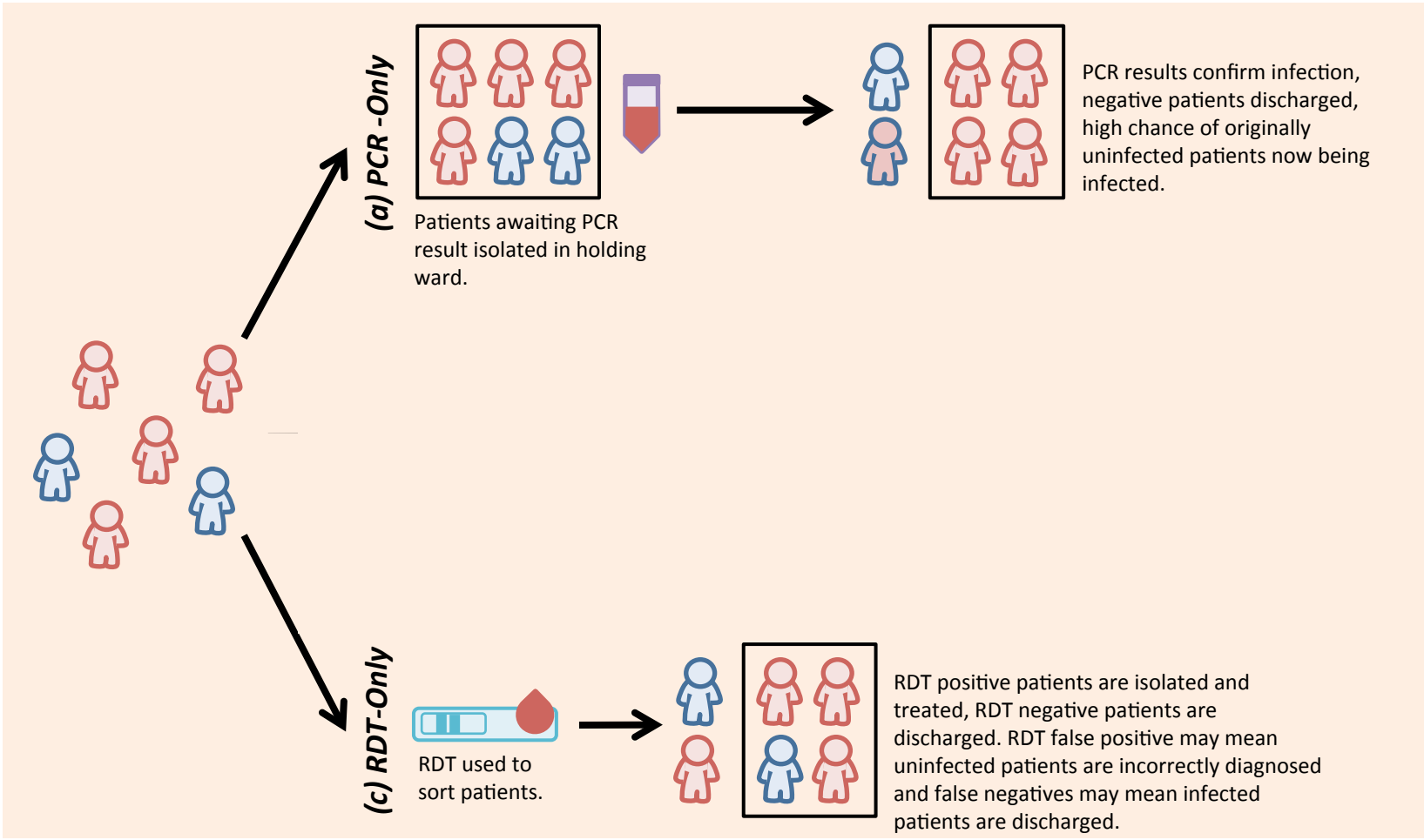

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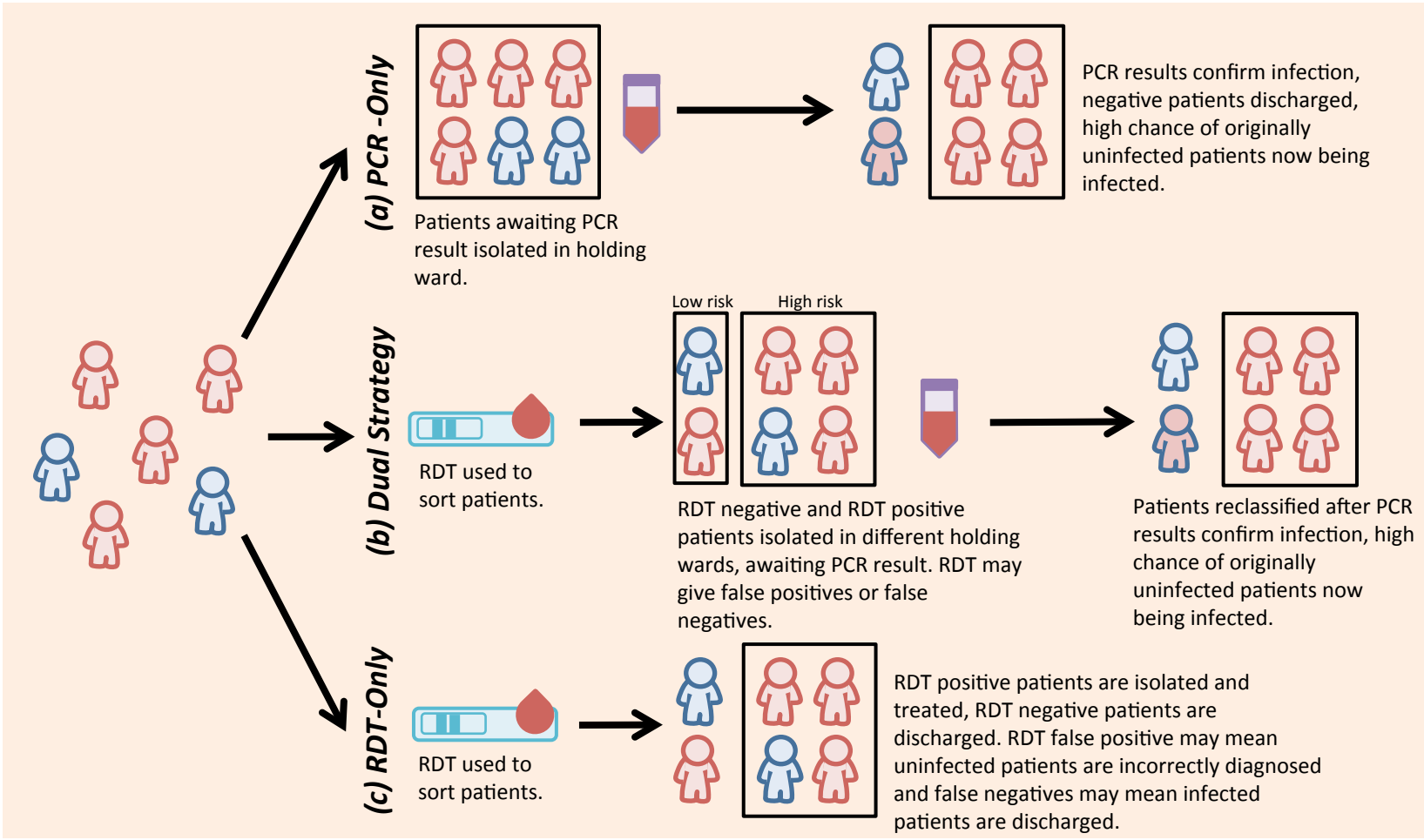

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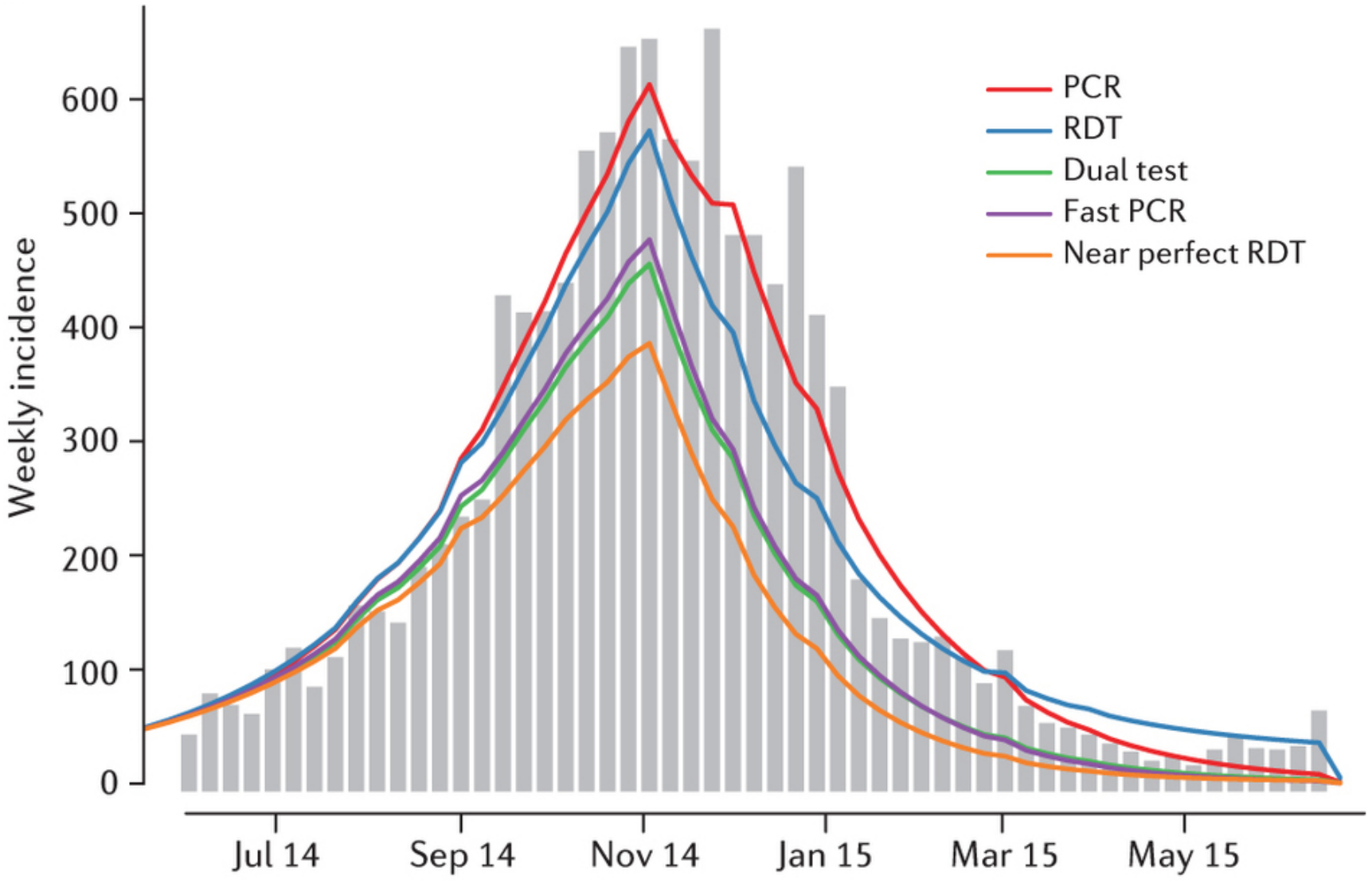
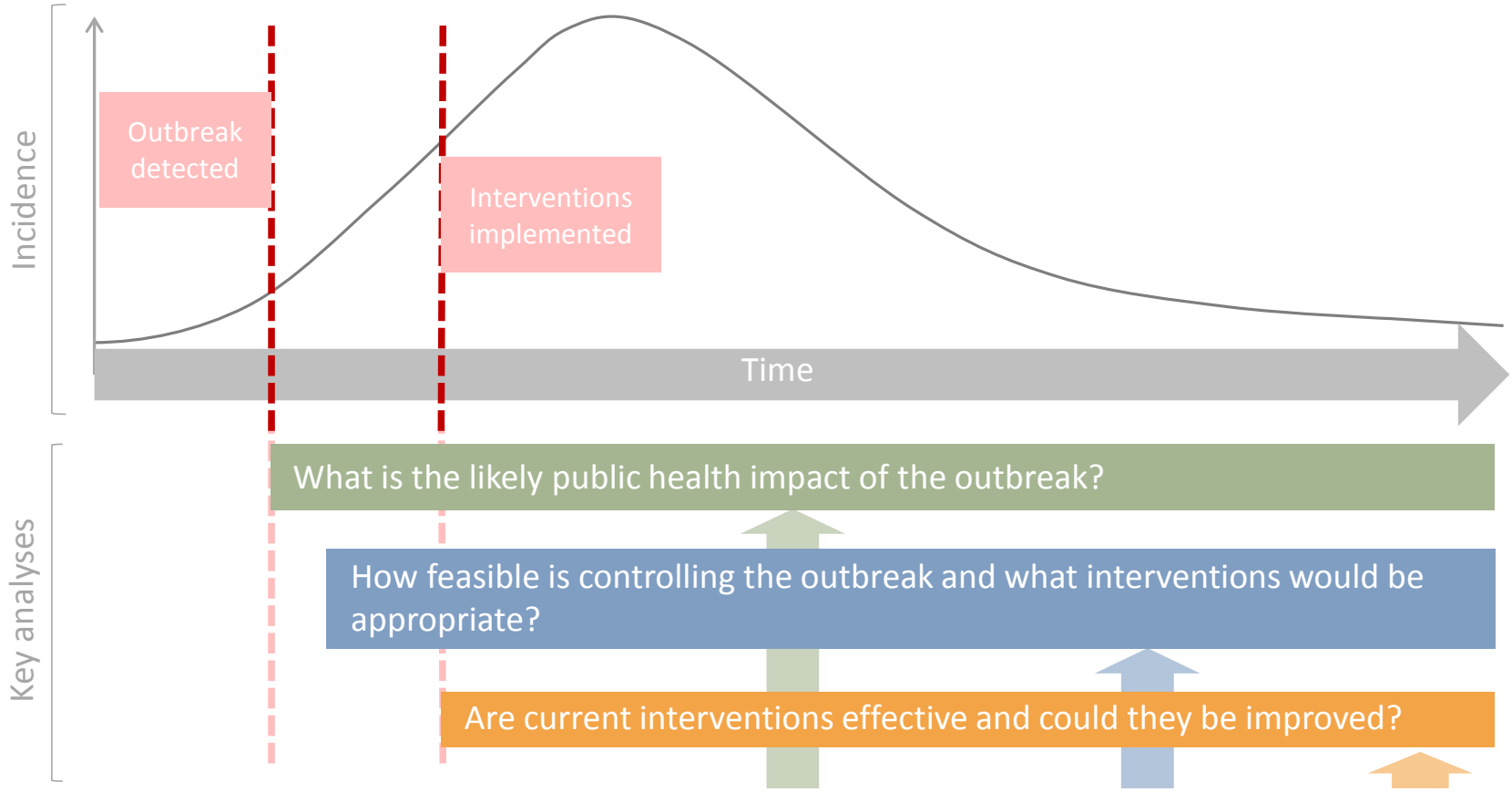


Nouvellet et al. Nature 2015

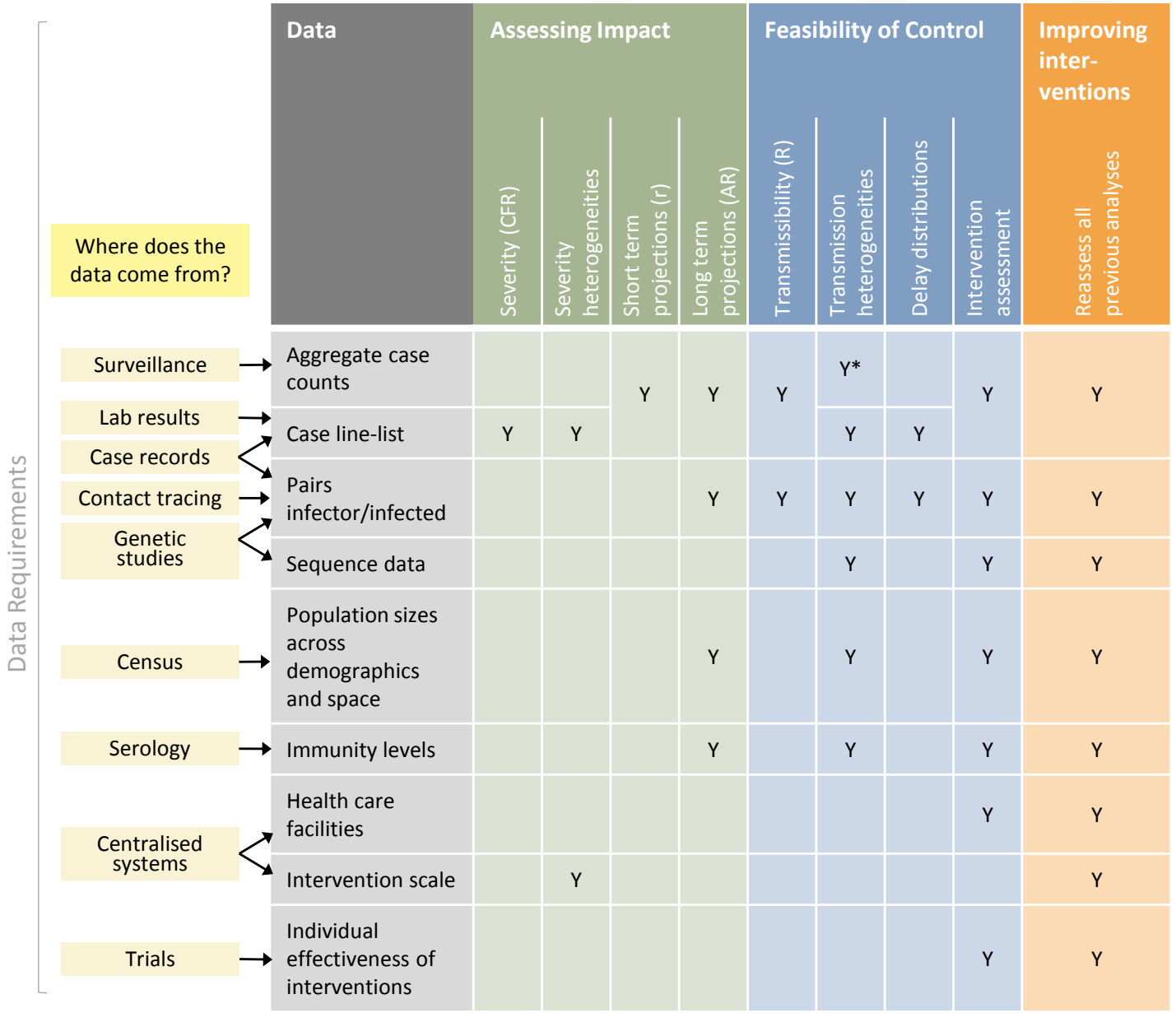
Learning from the Ebola experience: Formalising the questions modellers can help answering



- Other recurring questions of interest in the field?

Cori et al. Phil Trans R Soc B, in press

Clarifying what data are needed to answer each question



Data Requirements

Where does the data come from?

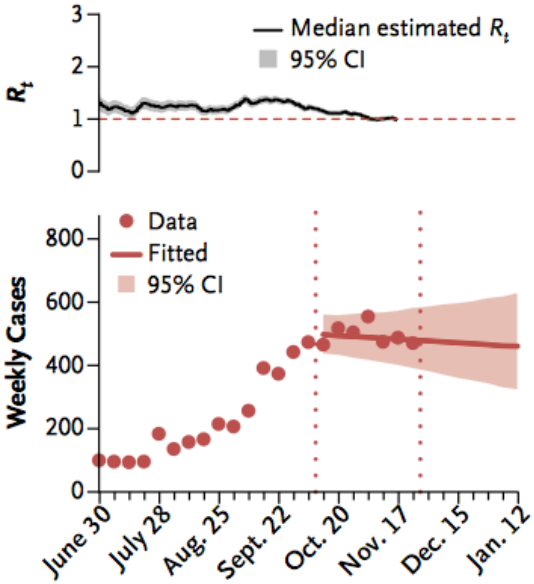
Data	Assessing Impact				Feasibility of Control				Improving inter-ventions
	Severity (CFR)	Severity heterogeneities	Short term projections (r)	Long term projections (AR)	Transmissibility (R)	Transmission heterogeneities	Delay distributions	Intervention assessment	Reassess all previous analyses
Surveillance → Aggregate case counts			Y	Y	Y	Y*		Y	Y
Lab results → Case line-list	Y	Y				Y	Y		
Case records → Contact tracing → Genetic studies → Pairs infector/infected				Y	Y	Y	Y	Y	Y
Genetic studies → Sequence data						Y		Y	Y
Census → Population sizes across demographics and space				Y		Y		Y	Y
Serology → Immunity levels				Y		Y		Y	Y
Centralised systems → Health care facilities								Y	Y
Centralised systems → Intervention scale		Y							Y
Trials → Individual effectiveness of interventions								Y	Y

Cori et al. Phil Trans R Soc B, in press

Some ongoing work since Ebola:

Developing automated frameworks for incidence forecasting

Incidence forecasting: how did we do?



Epidemics xxx (xxxx) xxx–xxx

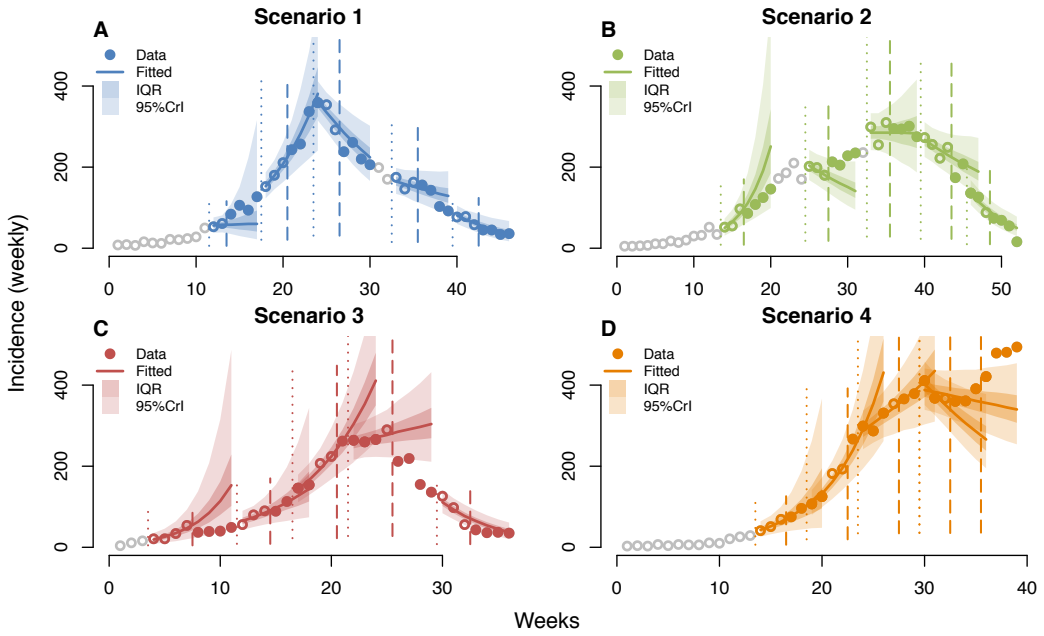
Contents lists available at ScienceDirect

Epidemics

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

Editorial

The RAPIDD Ebola forecasting challenge special issue: Preface



WHO Ebola Response team, NEJM, 2014 & 2015; Nouvellet et al., Epidemics, 2017

Towards real-time, automated, spatially explicit incidence forecasting?

MRIIDS
Mapping the Risk of International Infectious Disease Spread

ProMED mail

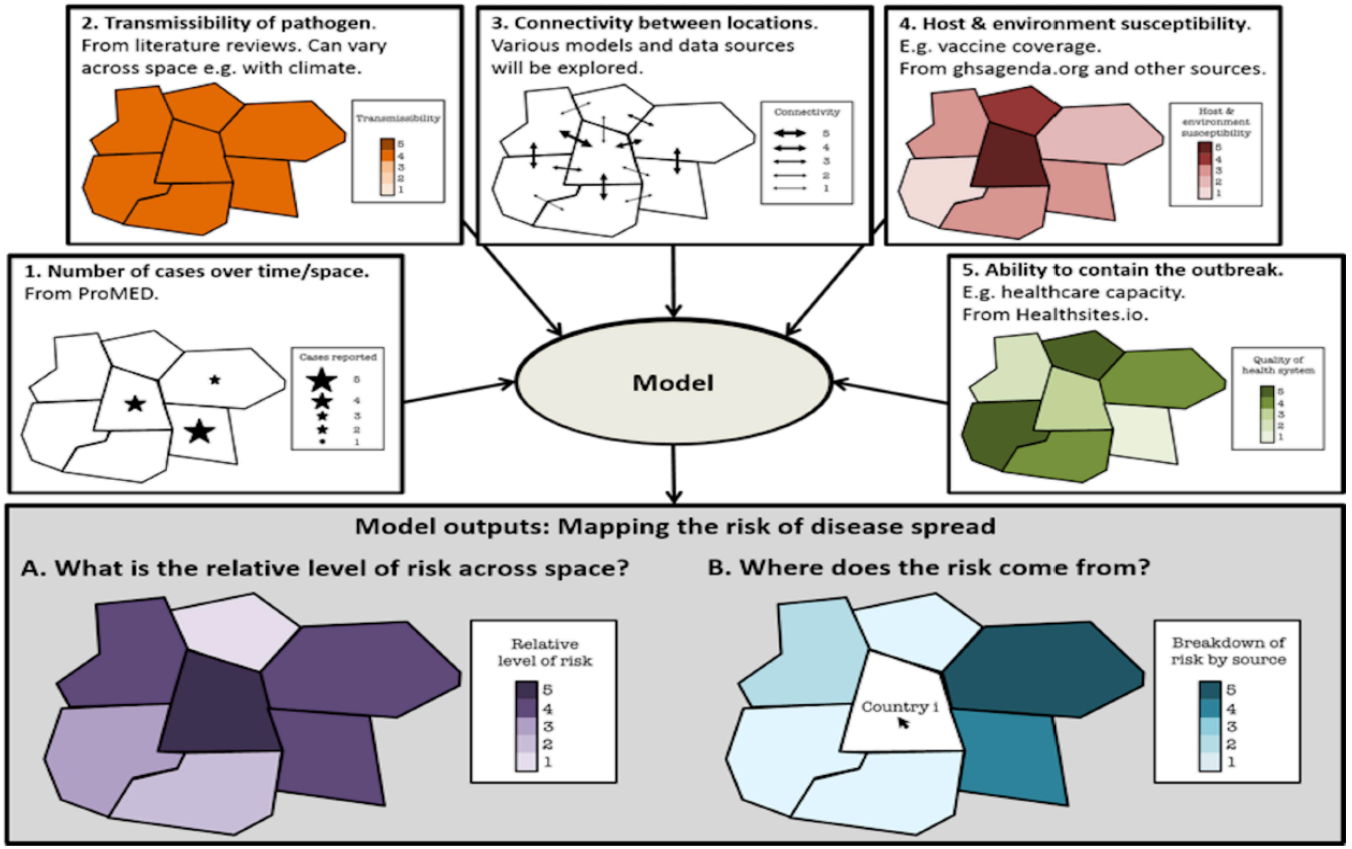
HealthMap

Imperial College London

MRC Centre for Outbreak Analysis and Modelling

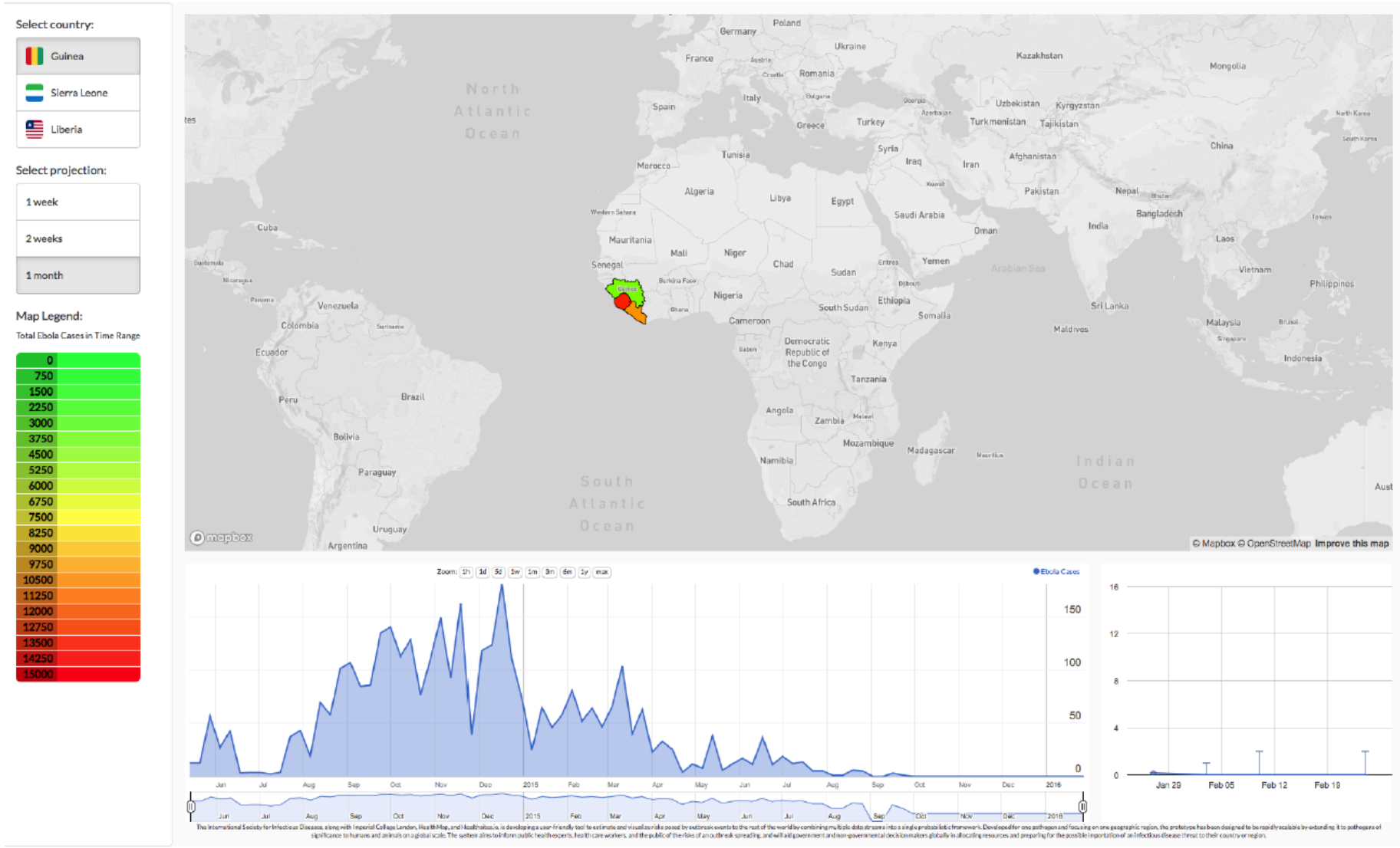
International Society for Infectious Diseases

healthsites.io



https://github.com/healthsites/mRIIDS

MRIIDS prototype for Ebola in West Africa in progress



Conclusions

More and more tools available to assist modelling during outbreaks

They should be flexible, tested & documented, and freely available

They need to talk to one another

They need to answer questions that are useful to contain outbreaks in practice

BUT: realistically we cannot rely ONLY on such tools; sometimes need to expand to answer more specific questions in a given context

Acknowledgements

- **The WHO Ebola Response team**
  - **Imperial College**: Isobel Blake, Christl A Donnelly, Ilaria Dorigatti, Neil M Ferguson, Christophe Fraser, Tini Garske, Gemma Nedjati Gilani, Wes Hinsley, Thibaut Jombart, Harriet Mills, Pierre Nouvellet, Steven Riley, Maria D Van Kerkhove
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  - **MoH of Guinea, Liberia and Sierra Leone**
  - *Thanks to the hundreds of medical staff, lab technicians, volunteers and personnel treating patients, testing samples, and working to contain this epidemic*
- **The "parameter estimation" team at Hackout 3**
  - Robin Thompson, Alex Demarsh, Rolina van Gaalen, Jonathan Polonsky, Elisabeth Dahlqwist, Shikun Li, Isabel Rodriguez, Justin Lessler, Simon Cauchemez, Jake Stockwin
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Thank you for your attention!