University of Sussex

Imperial College London

MRC Centre for Outbreak Analysis and Modelling

Methods for Short Term Projections in epidemics (Projections Package)

Pierre Nouvellet, Anne Cori,Thibaut Jombart, Sangeeta Bhatia

pierre.nouvellet@sussex.ac.uk

University of Sussex

Imperial College London

MRC Centre for Outbreak Analysis and Modelling

Structure

- Context
  - Basic principle: from model to inference to predictions?
  - Caveats

University of Sussex

Imperial College London

MRC Centre for Outbreak Analysis and Modelling

Structure

- What do I mean by projections/forecasts/predictions?

  - Projections: short term not mechanistic – taking current trend and continuing

  - Forecasts: relies on somehow more mechanistic model but typically assumes conditions in future remain stable

  - Predictions: relies on understanding the system and making hypothesis about future conditions – closer scenario modelling

University of Sussex

Imperial College London

MRC Centre for Outbreak Analysis and Modelling

Projection/Forecasting

- Importance, especially in context of public agencies and stakeholders:
  - Advocacy and planning
  - Monitoring the situation
  - Implementation/evaluation of control strategies
- Challenges:
  - Uncertainties surrounding the data
  - Uncertainties surrounding the dynamics of transmission
- In such context, we initially focussed on projecting case incidence:
  - Pro: Robust methodology
  - Con: weak mechanistic underlying model, so limited use for modelling the impact of interventions

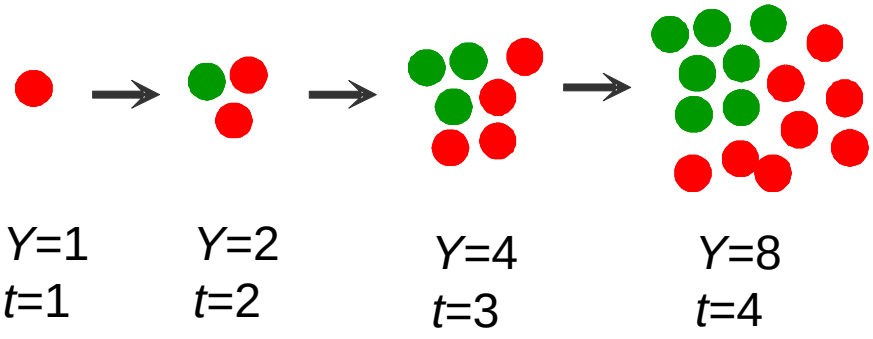
University of Sussex

Imperial College London

MRC Centre for Outbreak Analysis and Modelling

The reproduction number

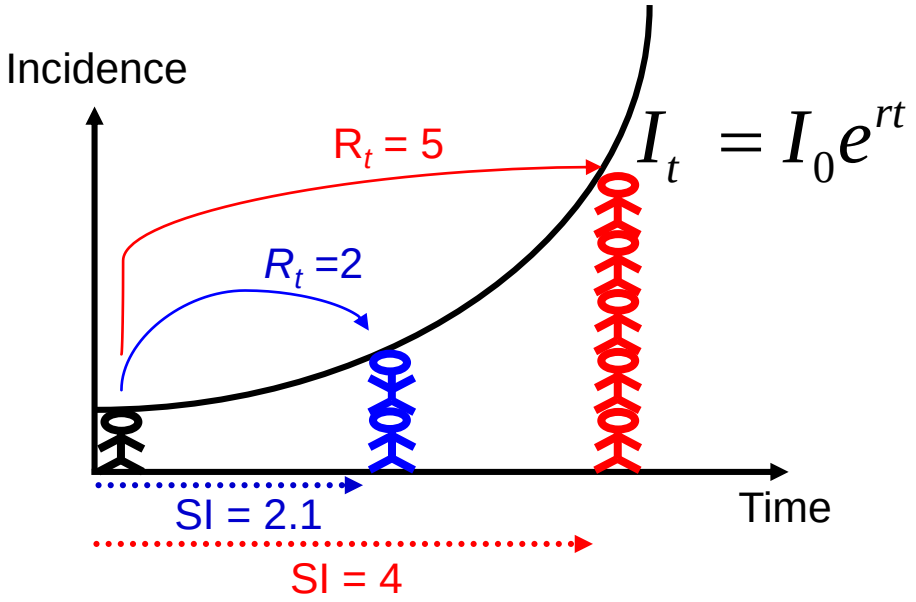
- Basic reproduction number R_0: average number of secondary cases generated by an index case in a large entirely susceptible population



Contagion

- Effective reproduction number R_t

→ equivalent at time t



University of Sussex

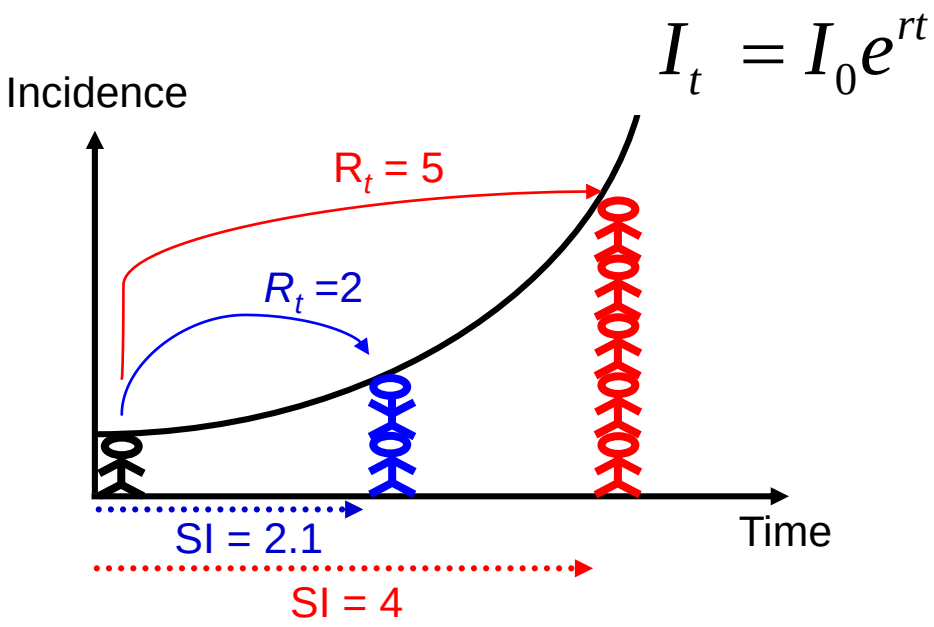
Methods

Imperial College London

MRC Centre for Outbreak Analysis and Modelling

Estimation of R0 and Rt:

As long as there is a large proportion of susceptibles in the population, the epidemic will grow exponentially R0 (later we define Rt)



The serial interval (time between symptoms onset of infector and symptoms onset of infectee), informs on the value of R_t

University of Sussex

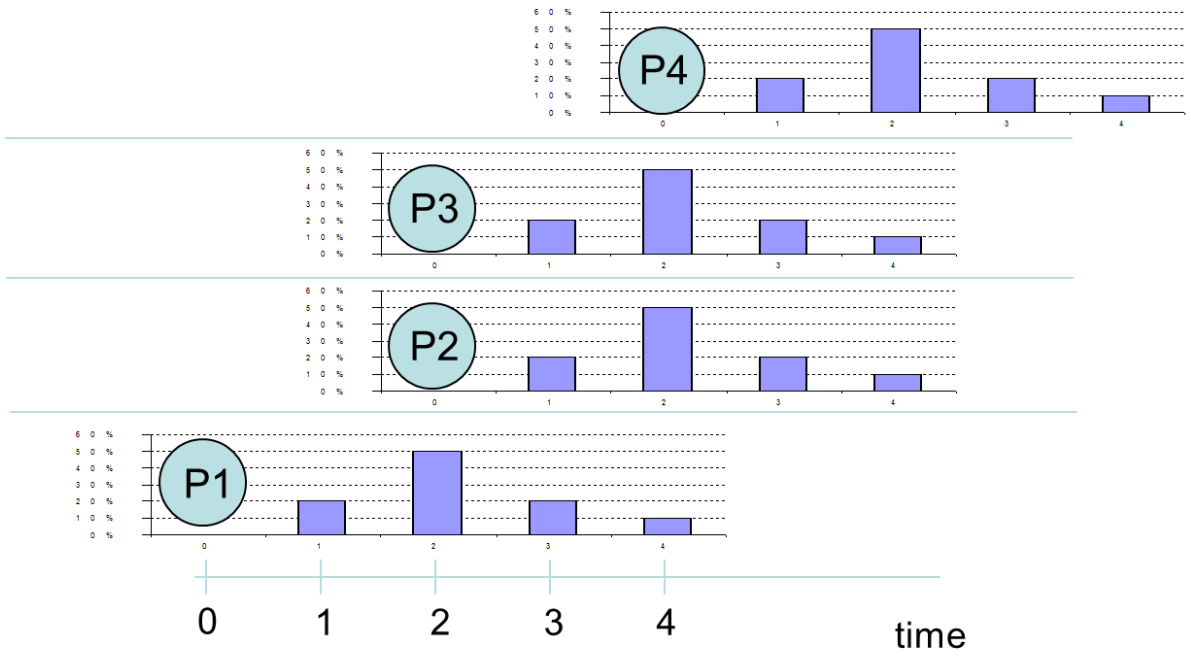
Methods

Imperial College London

MRC Centre for Outbreak Analysis and Modelling

Distribution of serial interval: w_t

proxy for infectiousness: when the R0/t new infection will occur



University of Sussex

Methods

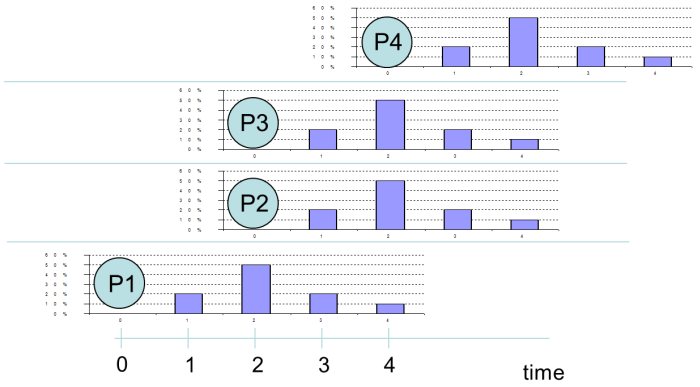
Imperial College London

MRC Centre for Outbreak Analysis and Modelling

Distribution of serial interval: w_t

proxy for infectiousness: when the R0/t new infection will occur

$$I_t = \mathcal{P}\left(R_t \sum_{s=1}^{t} I_{t-s} w_{t-s}\right)$$



Same equation used to:

– Infer R_t

– Project I_t in the future (typically assuming the last observed R_t remain constant)

University of Sussex

Methods

Imperial College London

MRC Centre for Outbreak Analysis and Modelling

Given knowledge of the serial interval distribution, we are able:

- Estimate R_t , doubling time

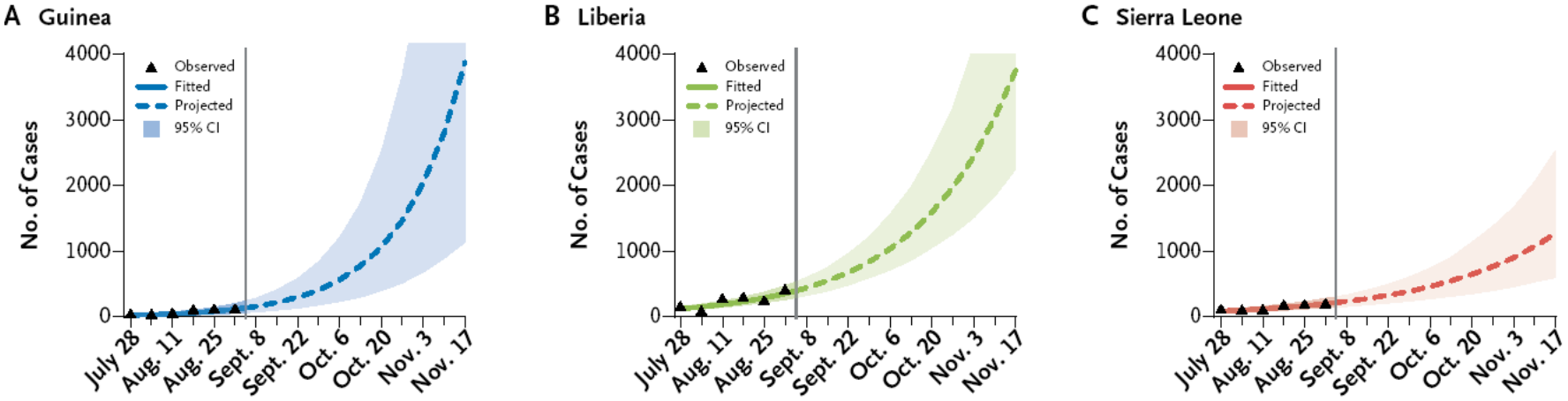
Given a time-series of incident cases and knowledge of R_t, we are able to:

- Predict the future number of cases (should the situation remains the same) - Projections

$$I_t = \mathcal{P}\left(R_t \sum_{s=1}^{t} I_{t-s} w_{t-s}\right)$$

How quickly was the virus spreading? September 2014

	Guinea	Liberia	Sierra Leone
R_t	1.81 (1.60–2.03)	1.51 (1.41–1.60)	1.38 (1.27–1.51)
Initial doubling time (days)	15.7 (12.9–20.3)	23.6 (20.2–28.2)	30.2 (23.6–42.3)



Important for advocacy, planning

[WHO Ebola Response Team. 2014, NEJM]

University of Sussex

How quickly was the virus spreading? March 2015

Imperial College London

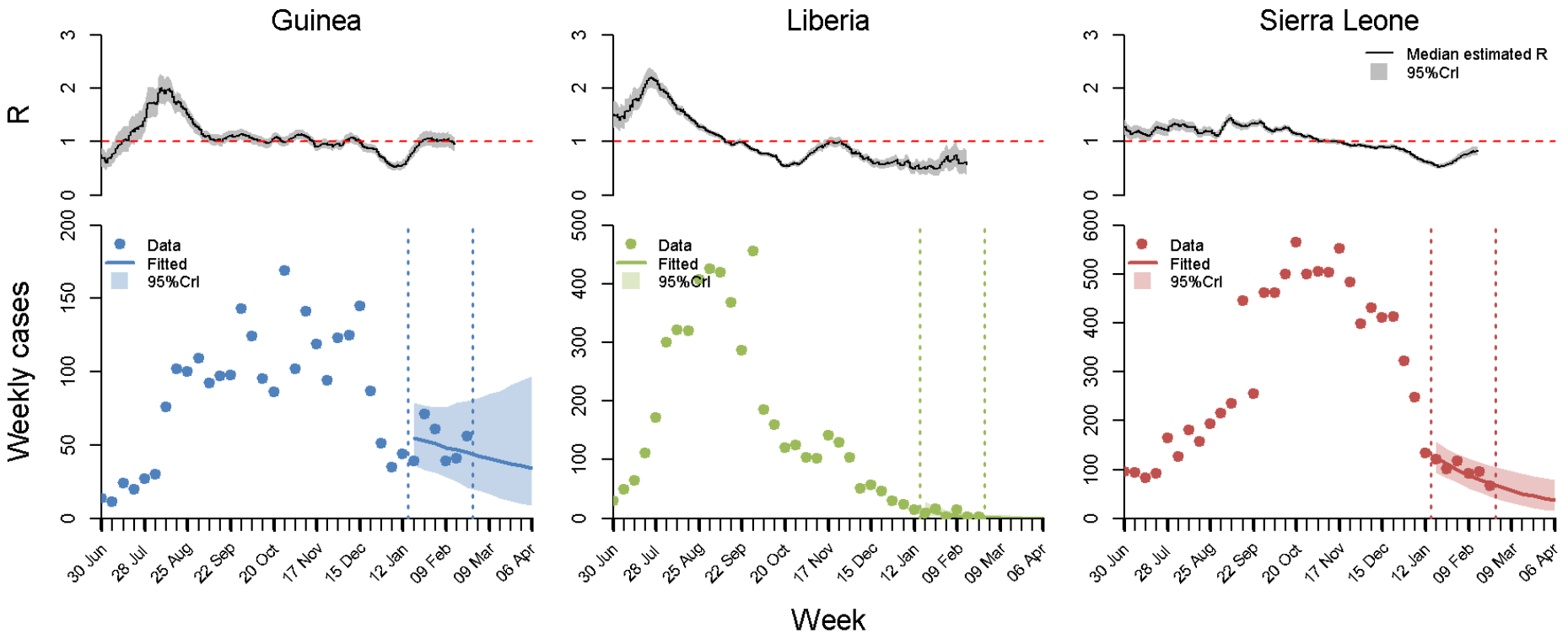
MRC Centre for Outbreak Analysis and Modelling

University of Sussex

How quickly was the virus spreading? March 2015

Imperial College London

MRC Centre for Outbreak Analysis and Modelling

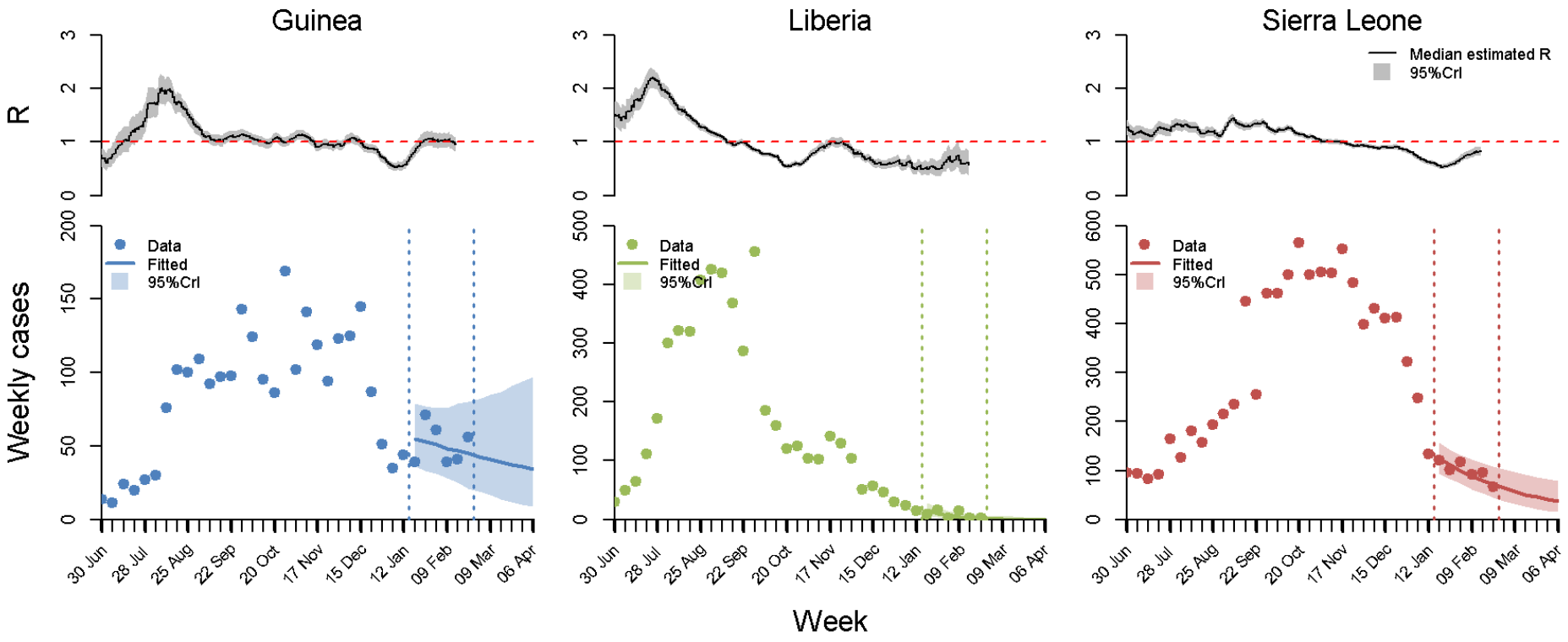


University of Sussex

How quickly was the virus spreading? March 2015

Imperial College London

MRC Centre for Outbreak Analysis and Modelling



	Guinea	Liberia	Sierra-Leone
	0.93 (0.77 ; 1.09)	0.43 (0.26 ; 0.68)	0.82 (0.74 ; 0.91)
Time to extinction	> 1 year (2015-07-16, > 1 year)	2015-03-22 (2015-02-18, 2015-06-12)	2015-11-22 (2015-07-13, > 1 year)

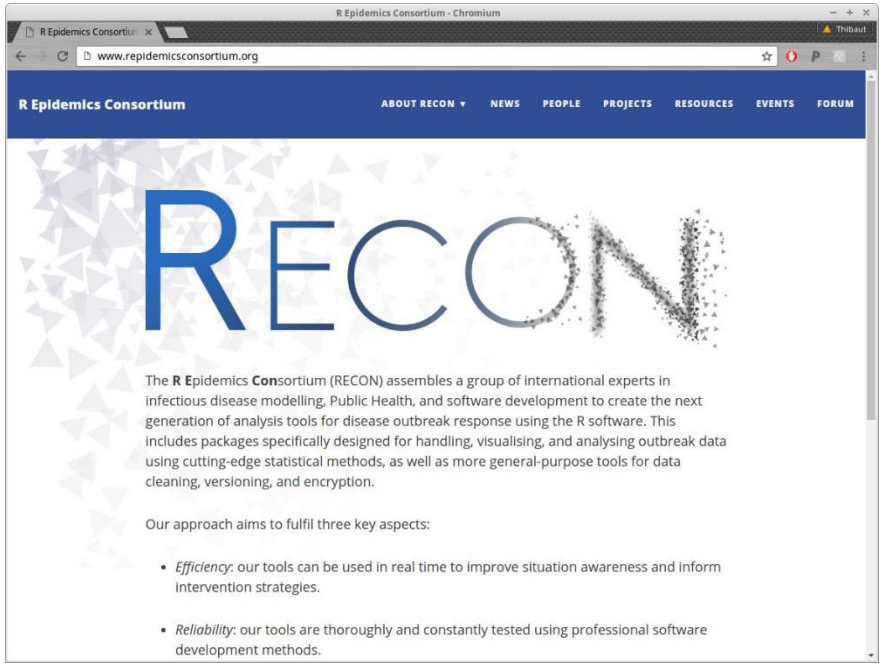
University of Sussex

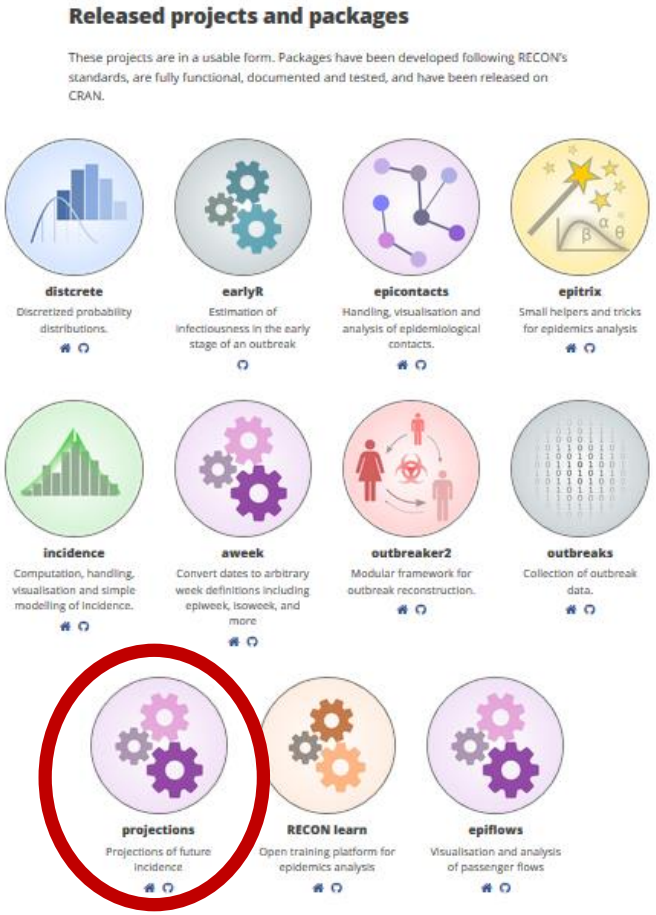
Implementation

Imperial College London

MRC Centre for Outbreak Analysis and Modelling

Implemented in a R package available in Recon website (projection





University of Sussex

Implementation

Imperial College London

MRC Centre for Outbreak Analysis and Modelling

Implemented in a R package available in Recon website

projections 0.3.1 | Reference | Changelog

Welcome to the *projections* package!

This package uses data on *daily incidence*, the *serial interval* (ti
number to simulate plausible epidemic trajectories and project fu
follows a Poisson process determined by a daily infectiousness,

$$\lambda_t =$$

where $w()$ is the probability mass function (PMF) of the serial in

Installing the package

To install the current stable, CRAN version of the package, type:

```
install.packages("projections")
```

To benefit from the latest features and bug fixes, install the deve

```
devtools::install_github("reconhub/projections")
```

Note that this requires the package *devtools* installed.

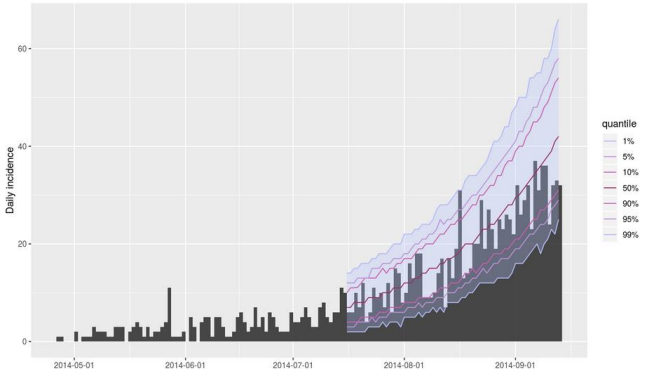
projections 0.3.1 | Reference | Changelog

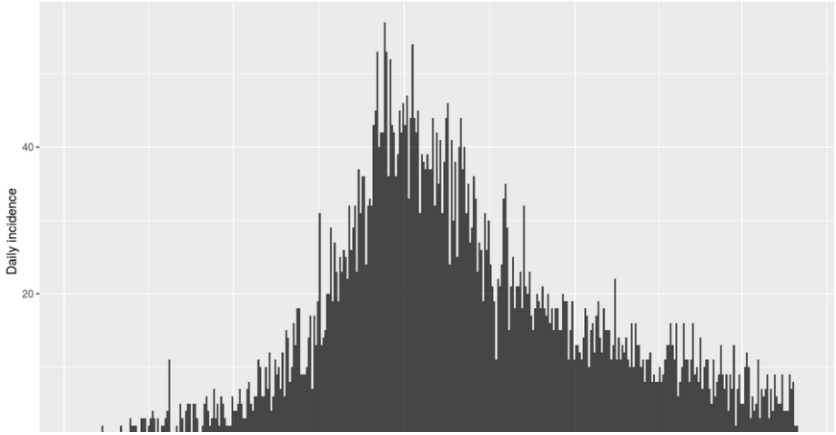
Worked example

In the following, we project future incidence using a simulate Ebola ou

```
library(outbreaks)
library(incidence)

onset <- ebola_sim$linelist$date_of_onset
i <- incidence(onset)
plot(i) # full outbreak
```





University of Sussex

Imperial College London

MRC Centre for Outbreak Analysis and Modelling

From projections to forecasting?

Can we say more about the determinants of Ebola dynamics?

Exposure patterns driving Ebola transmission in West Africa

International Ebola Response Team (2016), *PLoS Medicine*

University of Sussex

Imperial College London

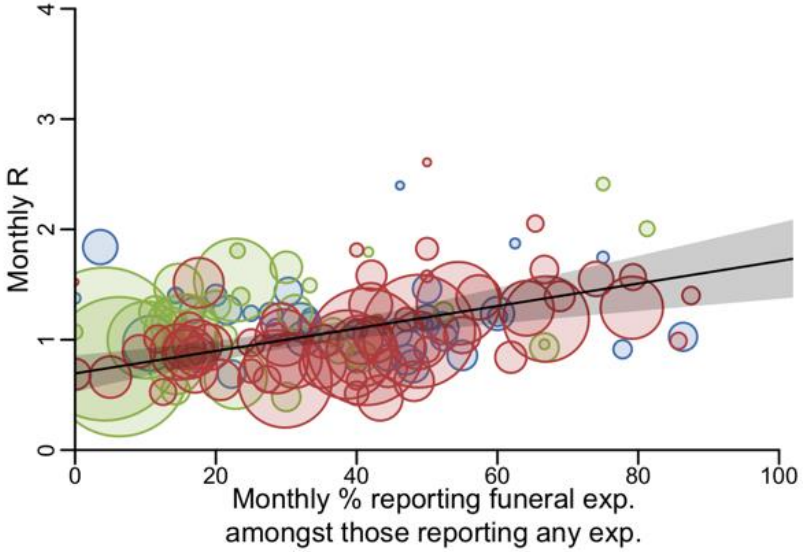
MRC Centre for Outbreak Analysis and Modelling

From projections to forecasting?

Can we say more about the determinants of Ebola dynamics?

Reproduction number for a given month was correlated with:

- % of individuals reporting funeral exposure (positive correlation)



University of Sussex

Imperial College London

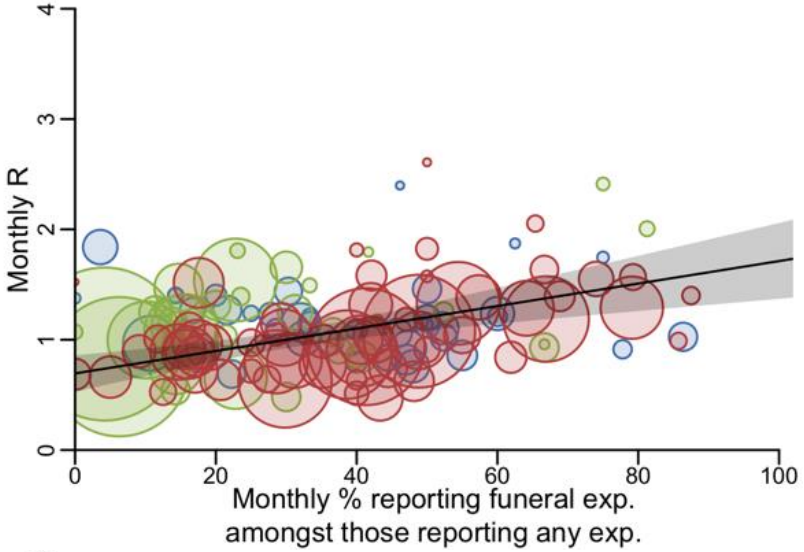
MRC Centre for Outbreak Analysis and Modelling

From projections to forecasting?

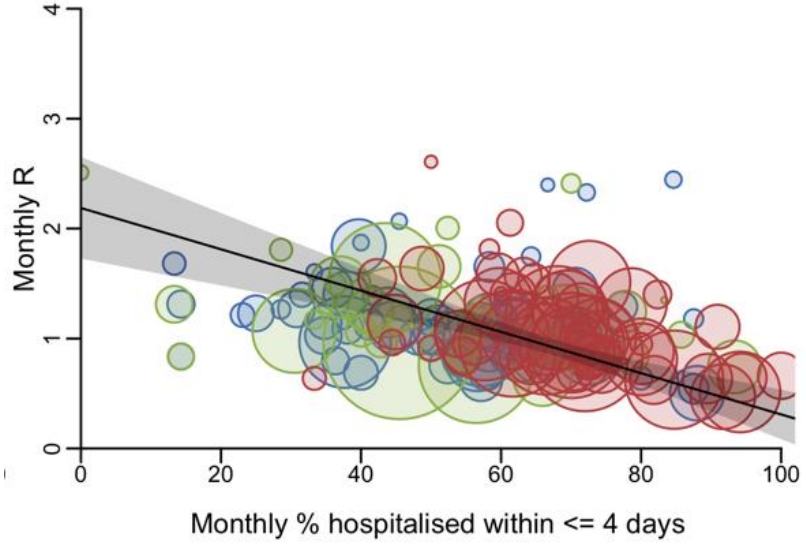
Can we say more about the determinants of Ebola dynamics?

Reproduction number for a given month was correlated with:

- % of individuals reporting funeral exposure (positive correlation)



- % of individuals hospitalised within 4 days (negative correlation)



University of Sussex

Imperial College London

MRC Centre for Outbreak Analysis and Modelling

From projections to predictions?

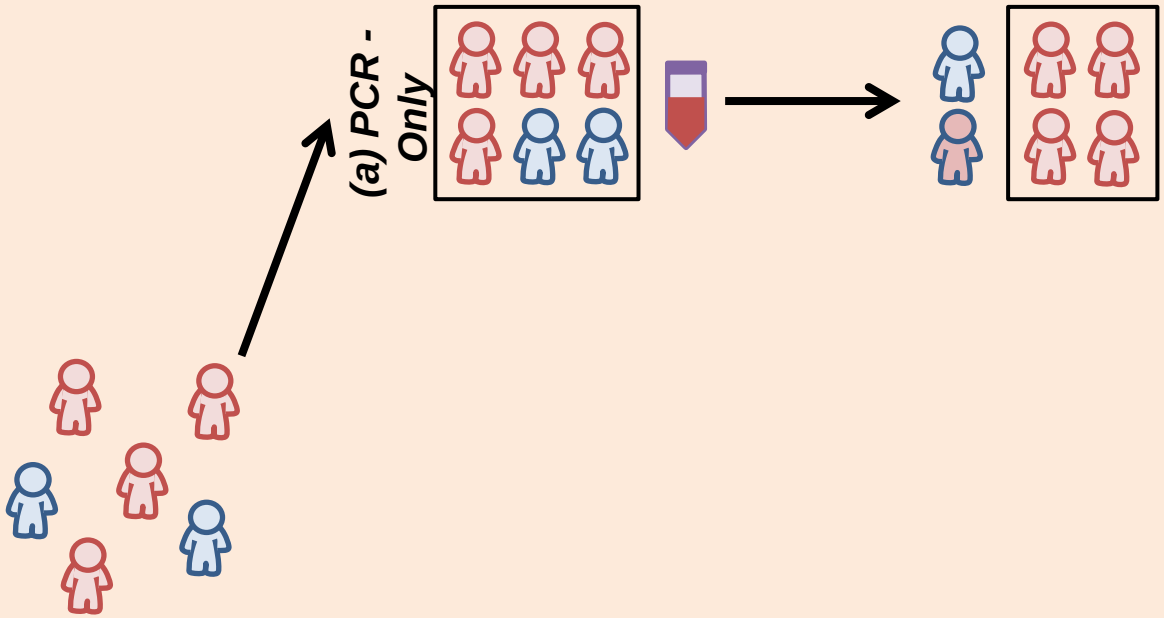
Can we make predictions if conditions were different?

University of Sussex

Imperial College London

MRC Centre for Outbreak Analysis and Modelling

From projections to predictions?



Key

PCR

RDT

In HU

Uninfected

Infected (and infectious)

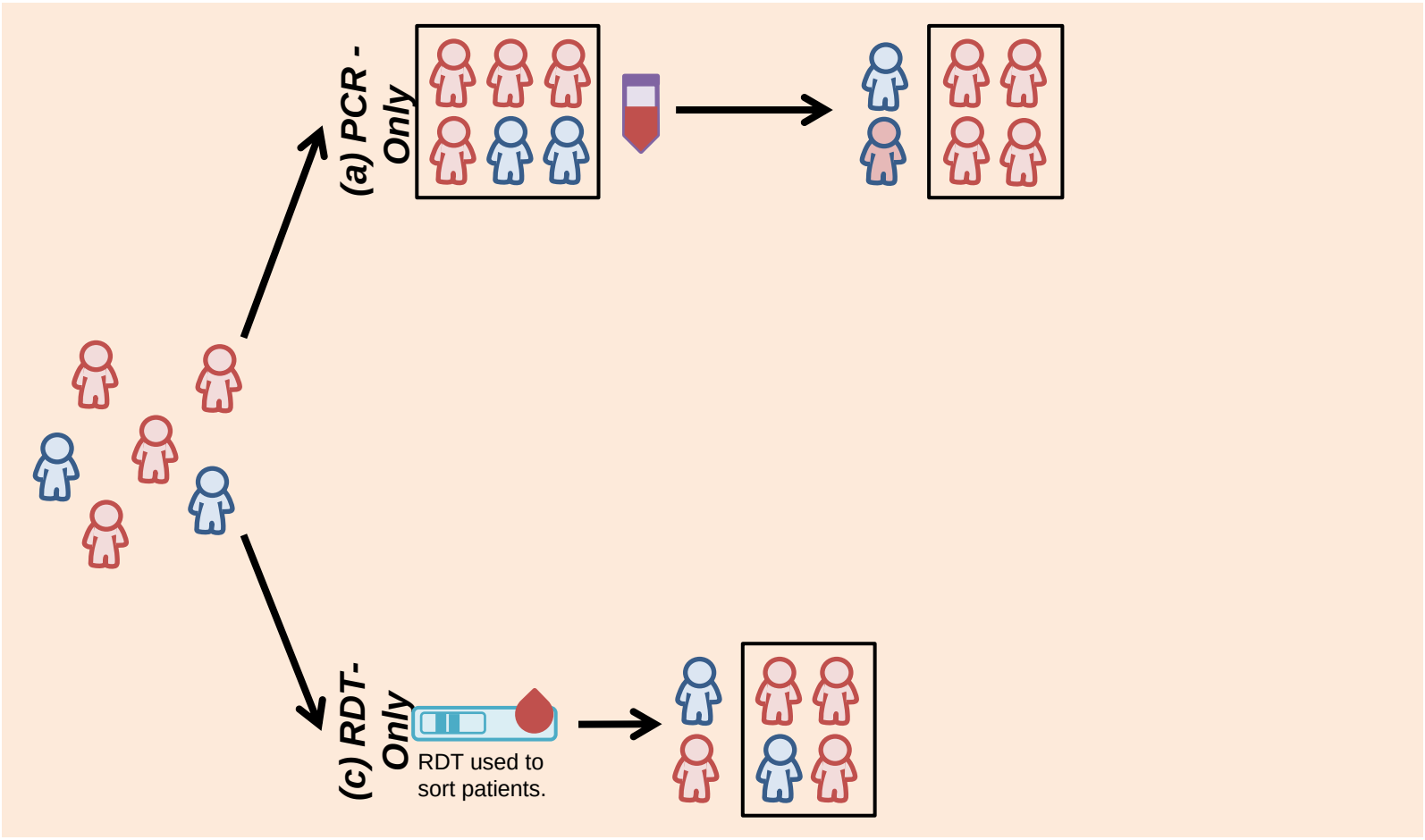
Newly infected

University of Sussex

Imperial College London

MRC Centre for Outbreak Analysis and Modelling

From projections to predictions?

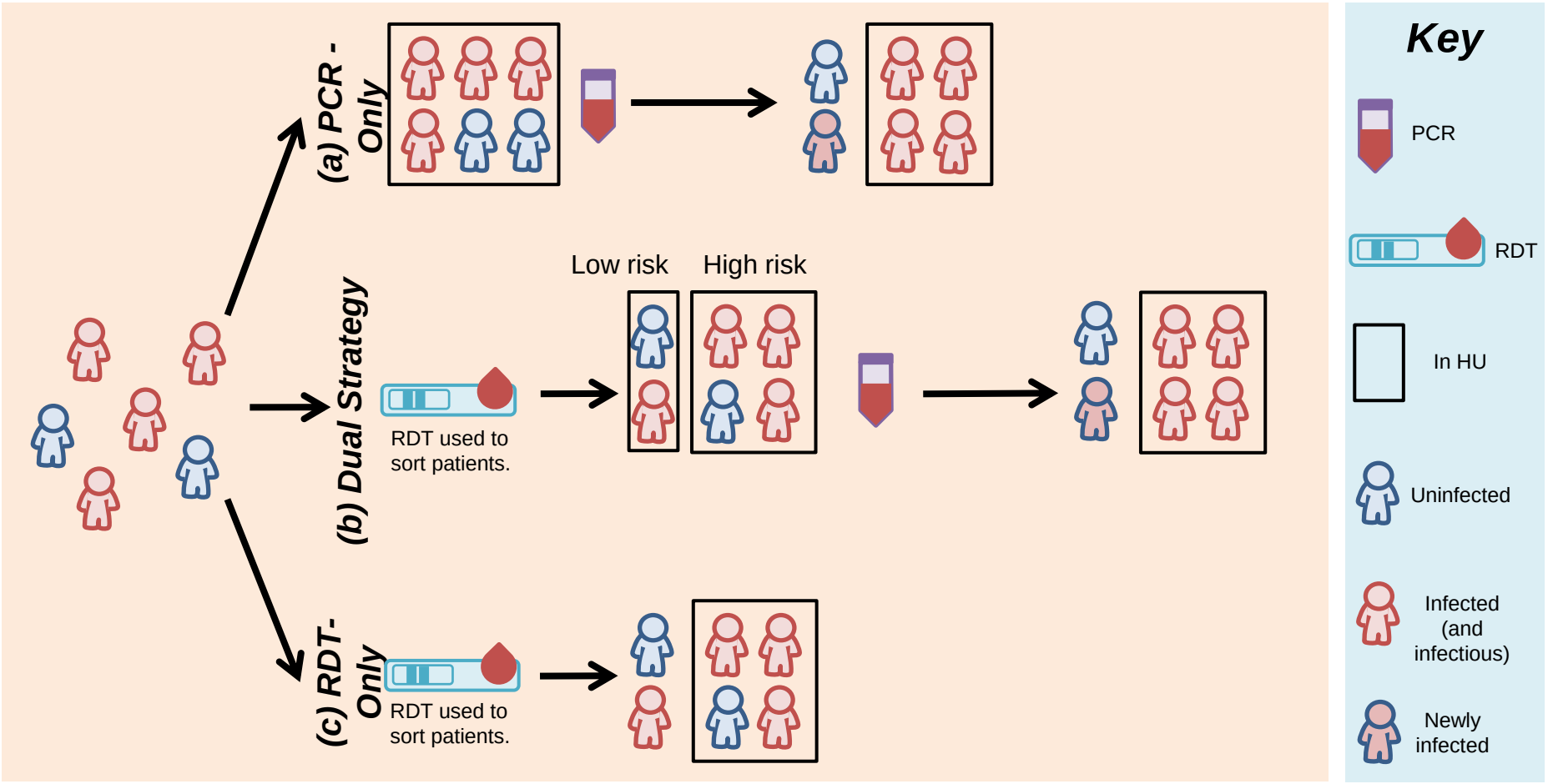


University of Sussex

Imperial College London

MRC Centre for Outbreak Analysis and Modelling

From projections to predictions?

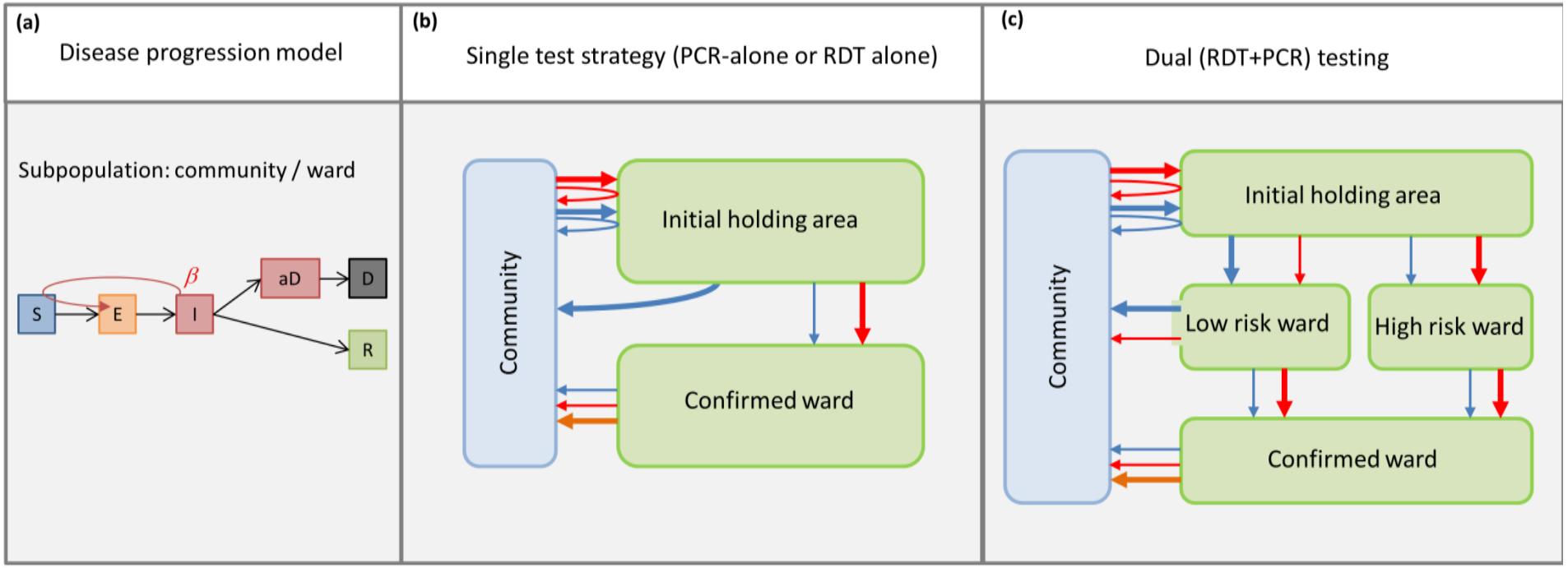


University of Sussex

Imperial College London

MRC Centre for Outbreak Analysis and Modelling

From projections to predictions?

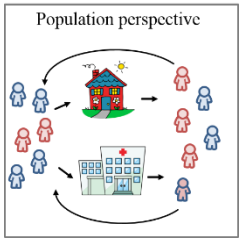


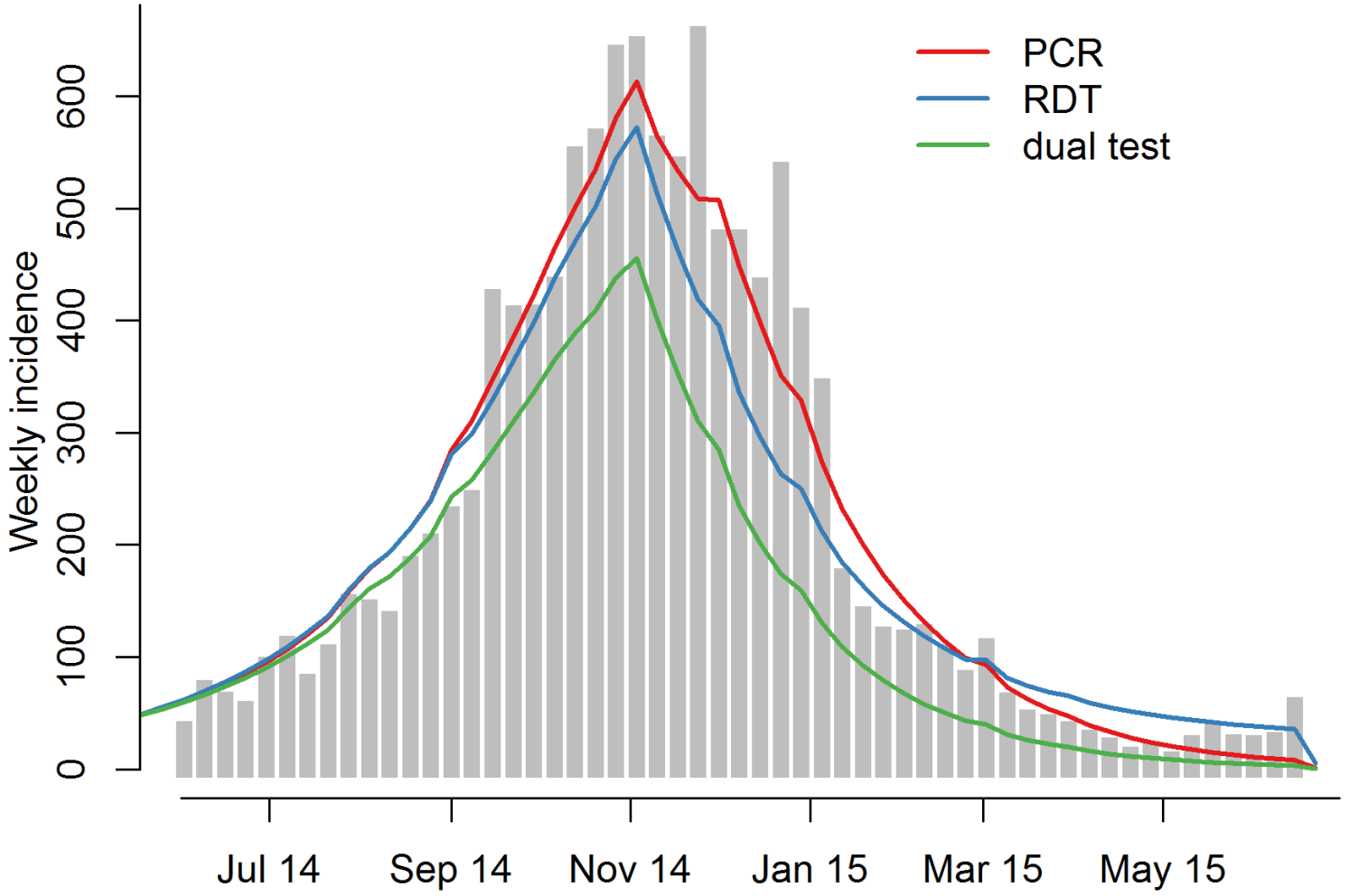
University of Sussex

Imperial College London

MRC Centre for Outbreak Analysis and Modelling

From projections to predictions?



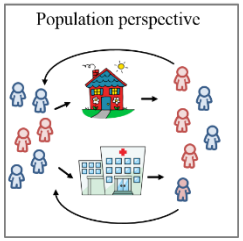


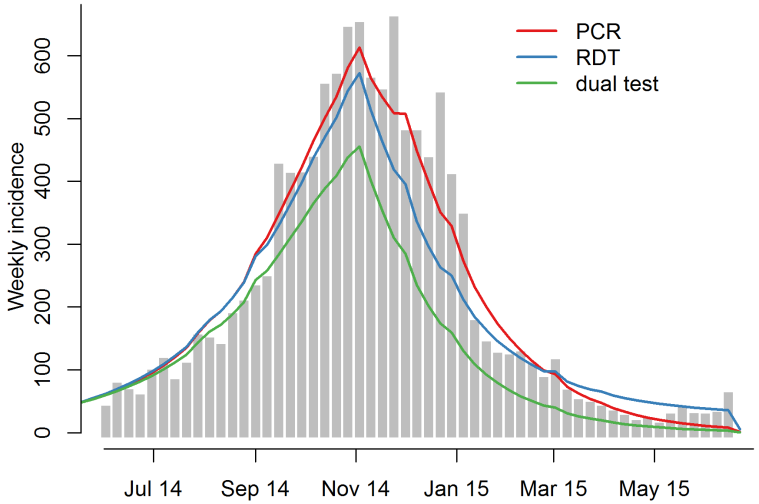
University of Sussex

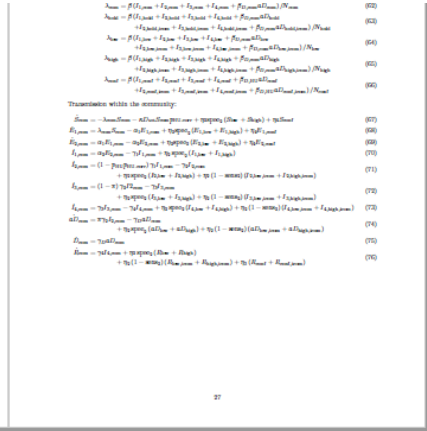
Imperial College London

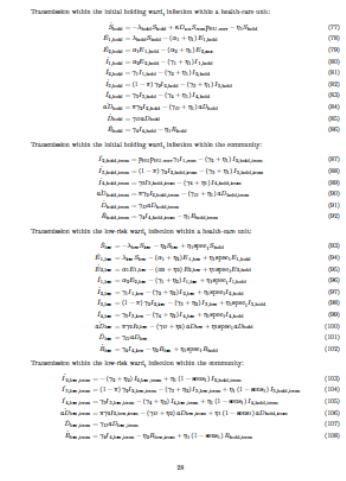
MRC Centre for Outbreak Analysis and Modelling

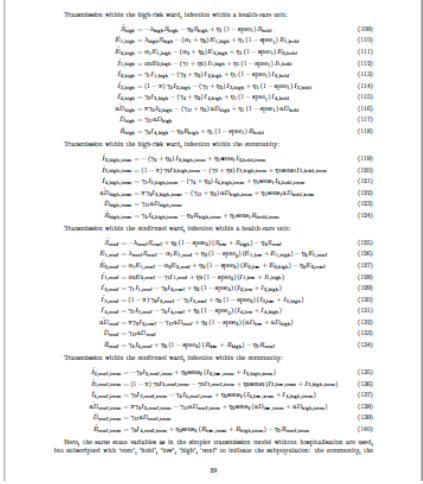
From projections to predictions?











- But requires even better understanding of the dynamics:
  - Easy to construct,
  - Hard to parameterise,
  - Can be hard to interpret results.

University of Sussex

Imperial College London

MRC Centre for Outbreak Analysis and Modelling

Caveats for projections

- When using projections, things to consider:
  - Caveats linked to estimation of transmissibility (e.g. epiestim issues if level reporting changes or delay in reporting)
  - Assume constant transmissibility in the future – to be used for short term projections (few serial intervals)
  - Be aware of the importance of accounting for
    - Delay in reporting
    - Uncertainty in current situation before projecting in the future (nowcasting)
  - Heterogeneity in transmission

University of Sussex

Imperial College London

MRC Centre for Outbreak Analysis and Modelling

Caveats for projections

- Heterogeneity in transmission

University of Sussex

Imperial College London

MRC Centre for Outbreak Analysis and Modelling

SARS and heterogeneity in transmission

The cases of Amoy garden:

- over 300 cases
- Concentrated in 4 blocks
- Required quarantine
- Linked to drainage system

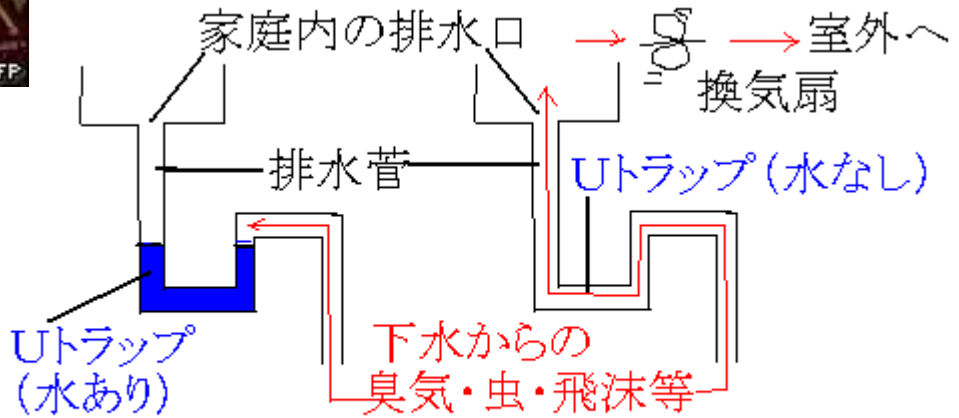


図3. Uトラップ（水なし）からの下水飛沫の侵入

SARS and heterogeneity in transmission

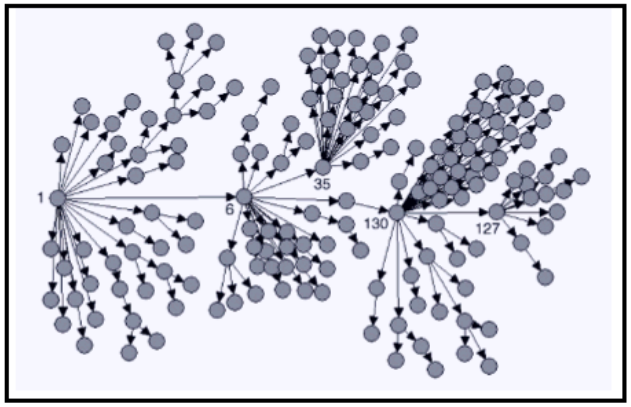
SARS and heterogeneity in transmission

Reproduction number:

The number of cases one case generates on average over the course of its infectious period

Contagion

FIGURE 2. Probable cases of severe acute respiratory syndrome, by reported source of infection* — Singapore, February 25–April 30, 2003



Typically require detailed investigation

University of Sussex

SARS and heterogeneity in transmission

Imperial College London

MRC Centre for Outbreak Analysis and Modelling

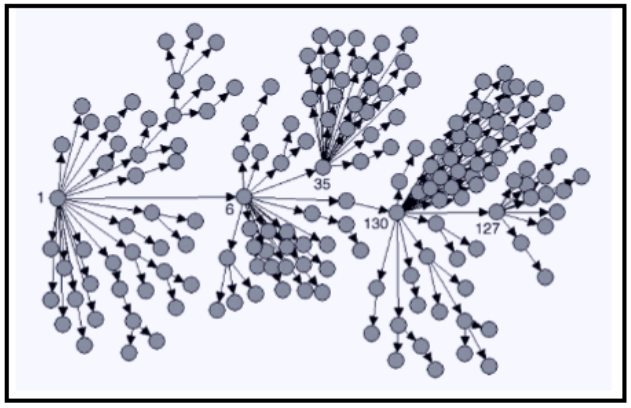
SARS and heterogeneity in transmission

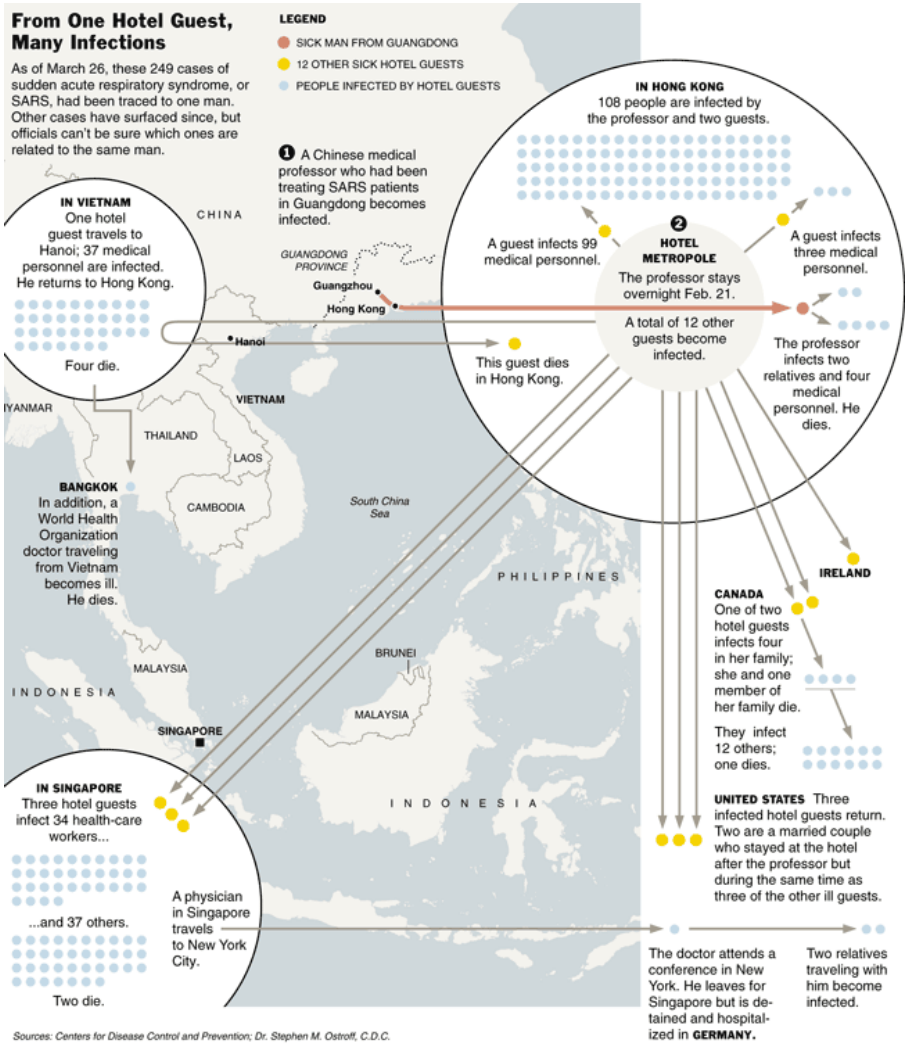
Reproduction number:

The number of cases one case generates on average over the course of its infectious period,

BUT…

FIGURE 2. Probable cases of severe acute respiratory syndrome, by reported source of infection* — Singapore, February 25–April 30, 2003





SARS and heterogeneity in transmission

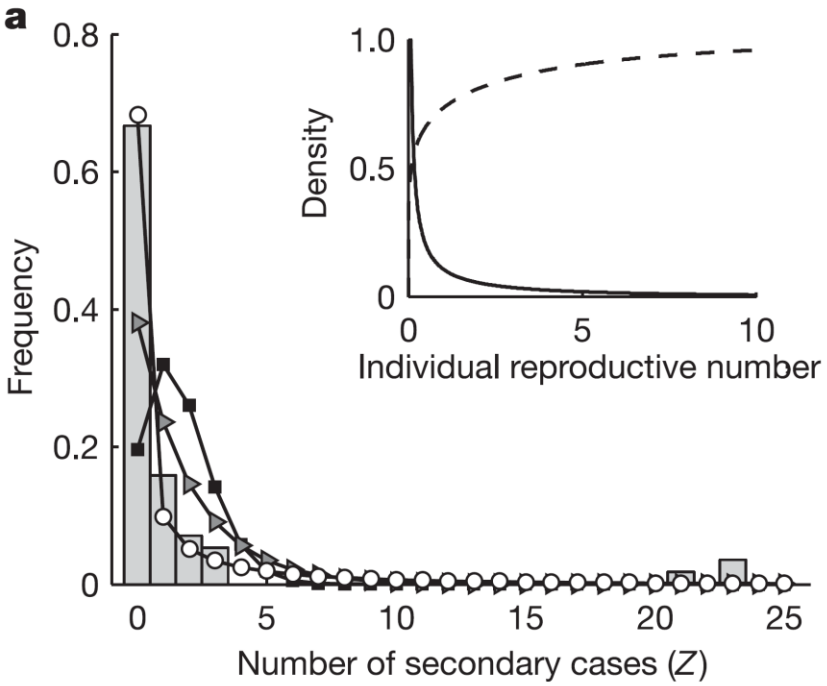
Simplest case, assumes:

- Number of secondary cases for each infectious individual follows a Poisson distribution (offspring distribution)
- Same mean for everyone (R)

Increased heterogeneity, assumes:

- Individual 'offspring distribution' is still Poisson
- Individual R is gamma distributed (not the same for everyone)

➢ Negative binomial offspring distribution for the population



Vol 438|17 November 2005|doi:10.1038/nature04153 nature

LETTERS

Superspreading and the effect of individual variation on disease emergence

J. O. Lloyd-Smith[1,2], S. J. Schreiber[3], P. E. Kopp[4] & W. M. Getz[1]

University of Sussex

Imperial College London

MRC Centre for Outbreak Analysis and Modelling

SARS and heterogeneity in transmission

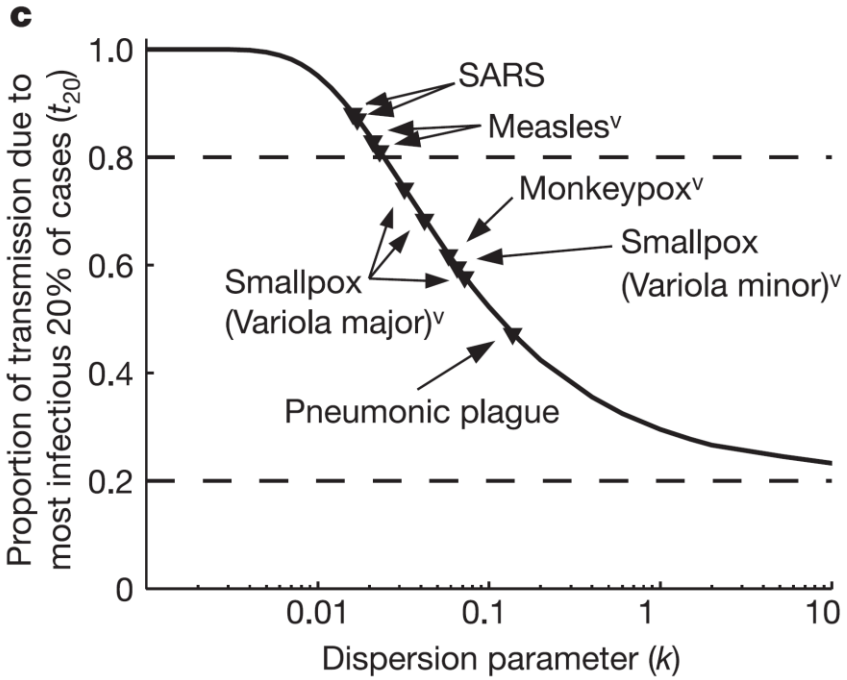
Simplest case, assumes:

- Number of secondary cases for each infectious individual follows a Poisson distribution (offspring distribution)
- Same mean for everyone (R)

Increased heterogeneity, assumes

- Individual 'offspring distribution' is still Poisson
- Individual R is gamma distributed (not the same for everyone)

➢ Negative binomial offspring distribution for the population



Vol 438|17 November 2005|doi:10.1038/nature04153 nature

LETTERS

Superspreading and the effect of individual variation on disease emergence

J. O. Lloyd-Smith[1,2], S. J. Schreiber[3], P. E. Kopp[4] & W. M. Getz[1]

University of Sussex

Imperial College London

MRC Centre for Outbreak Analysis and Modelling

SARS and heterogeneity in transmission

Simplest case, assumes:

- Number of secondary cases for each infectious individual follows a Poisson distribution (offspring distribution)
- Same mean for everyone (R)

Implications for Projections

$$I_t = \mathcal{P}\left(R_t \sum_{s=1}^{t} I_{t-s} w_{t-s}\right)$$

Increased heterogeneity, assumes:

- Individual 'offspring distribution' is still Poisson
- Individual R is gamma distributed (not the same for everyone)

➢ Negative binomial offspring distribution for the population

$$I_t = NB\left(R_t \sum_{s=1}^{t} I_{t-s} w_{t-s}, \delta\right)$$

SARS and heterogeneity in transmission

Simplest case, assumes:

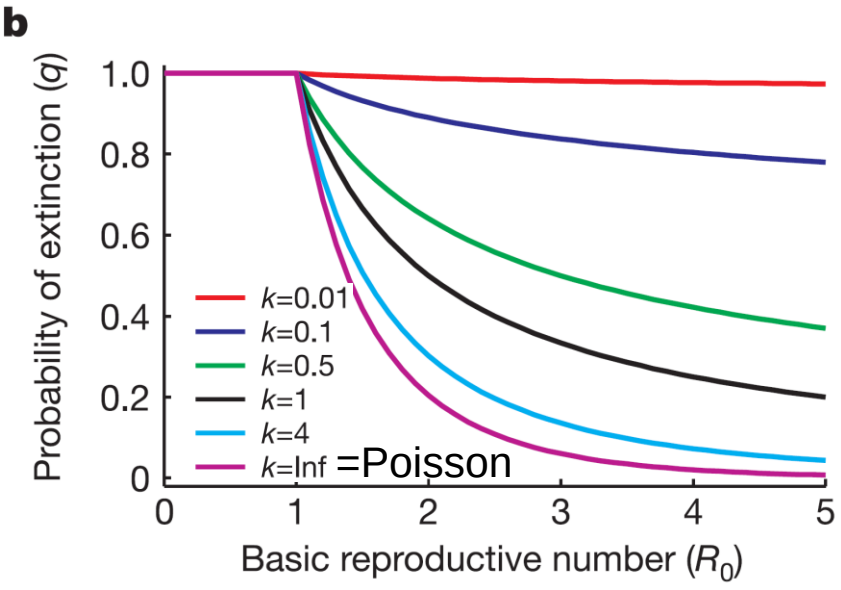
- Number of secondary cases for each infectious individual follows a Poisson distribution (offspring distribution)
- Same mean for everyone (R)

Increased heterogeneity, assumes:

- Individual 'offspring distribution' is still Poisson
- Individual R is gamma distributed (not the same for everyone)

➢ Negative binomial offspring distribution for the population

Implications for outbreak extinctions



Vol 438|17 November 2005|doi:10.1038/nature04153 nature

LETTERS

Superspreading and the effect of individual variation on disease emergence

J. O. Lloyd-Smith[1,2], S. J. Schreiber[3], P. E. Kopp[4] & W. M. Getz[1]

University of Sussex

Imperial College London

MRC Centre for Outbreak Analysis and Modelling

Thank you!