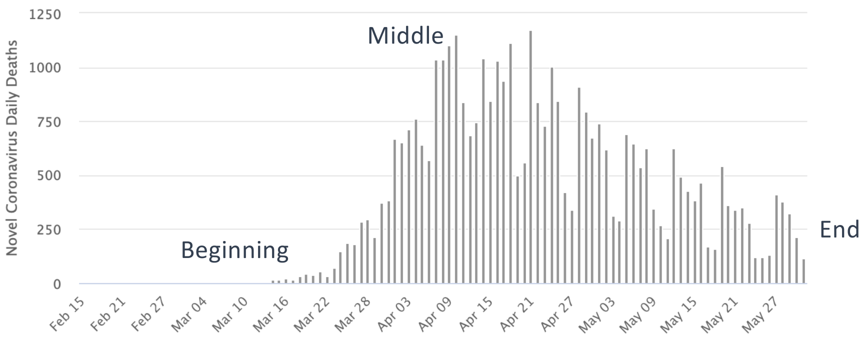
Epidemic modelling at different stages of infectious disease outbreaks

Robin Thompson

Junior Research Fellow

Christ Church, University of Oxford



Beginning

- Will initial cases lead to a major epidemic?
- Which interventions reduce the epidemic risk?

Middle

- How effective are current interventions?
- Which interventions will minimise numbers of cases?

End

- How should interventions be lifted?
- Is the epidemic over?

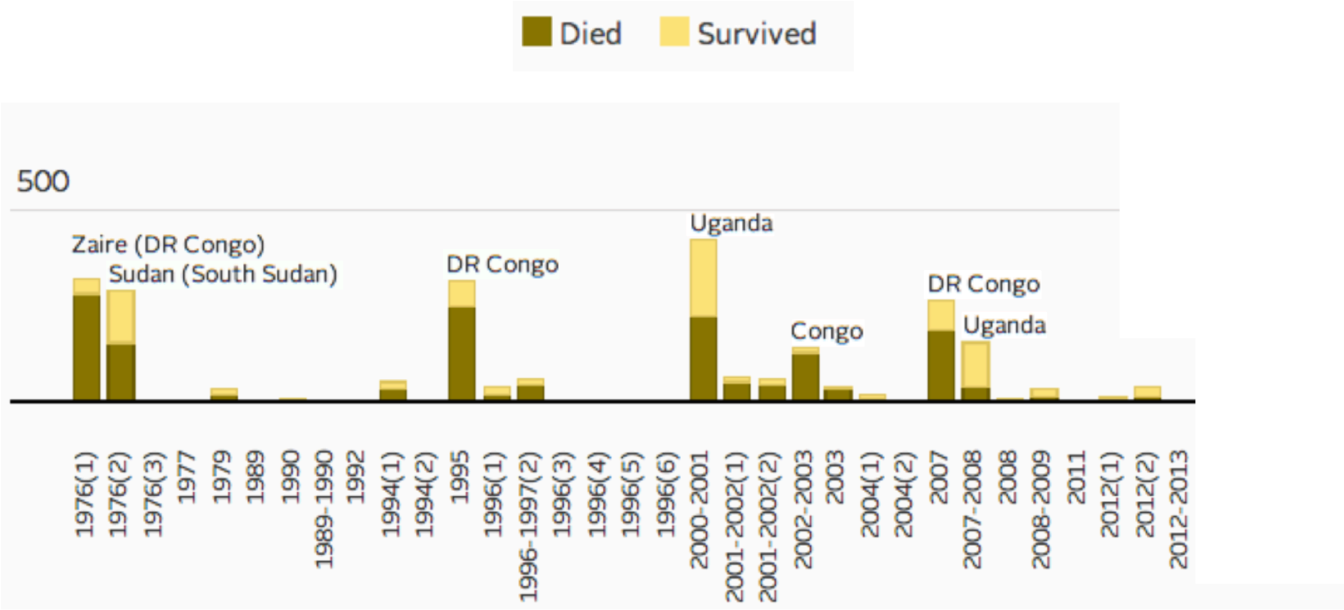
Outline

1. Assessing the risk of a major epidemic
   - Estimating the probability of a major epidemic
   - Application to COVID-19
   - More complex models: heterogeneity in reporting, age structure, time-dependence
2. Estimating changes in disease transmissibility
   - Estimation of R_t
   - Extending the basic model
   - Going forwards

Assessing the risk of a major epidemic

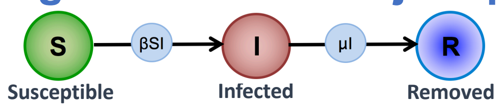
When a pathogen first arrives in a new host population, will initial cases fade out, or will they lead to a major epidemic?

Assessing the risk of a major epidemic

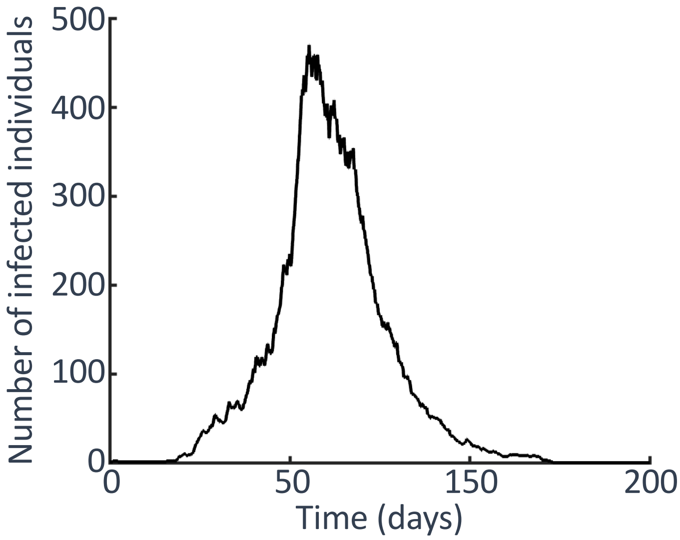


Assessing the risk of a major epidemic | Estimating changes in transmissibility
Epidemic probability | COVID-19 | Adding complexity | Estimating R_t | Extensions | Going forwards

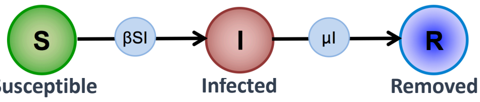
Assessing the risk of a major epidemic



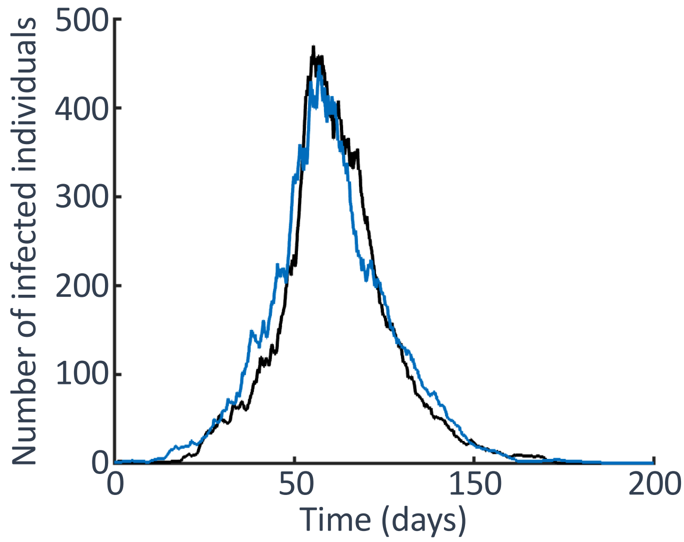
When a pathogen first arrives in a new population, there are two possibilities for what happens next



Assessing the risk of a major epidemic

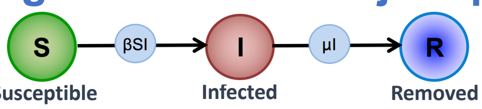


When a pathogen first arrives in a new population, there are two possibilities for what happens next

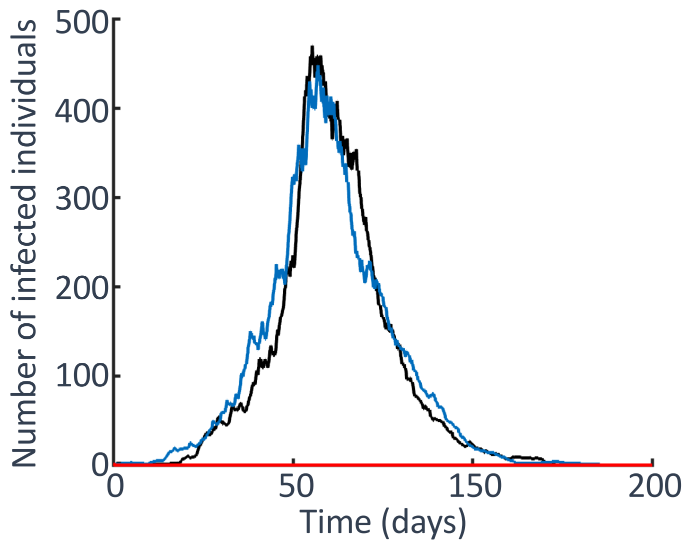


Assessing the risk of a major epidemic | Estimating changes in transmissibility
Epidemic probability | COVID-19 | Adding complexity | Estimating R_t | Extensions | Going forwards

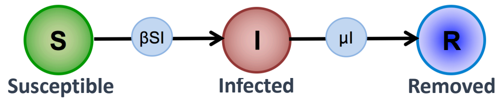
Assessing the risk of a major epidemic



When a pathogen first arrives in a new population, there are two possibilities for what happens next

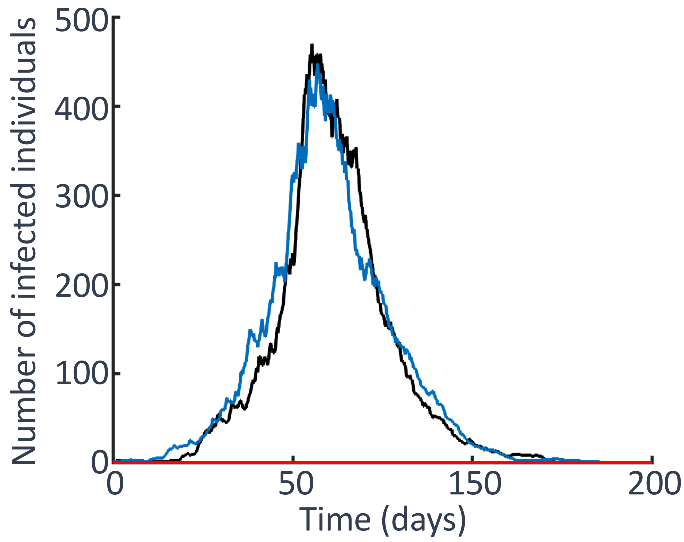


Assessing the risk of a major epidemic



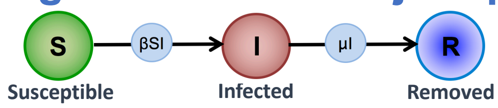
Epidemic Risk: the probability that an imported case leads to a major epidemic

If ER = 0; a major epidemic will not occur
If ER = 1; a major epidemic will definitely occur



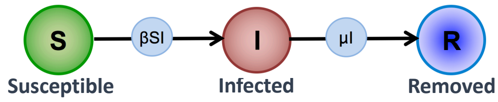
Assessing the risk of a major epidemic | Estimating changes in transmissibility
Epidemic probability | COVID-19 | Adding complexity | Estimating R_t | Extensions | Going forwards

Assessing the risk of a major epidemic



- Assume we start with one infected individual
- Denote q_i = Prob(<u>no</u> major epidemic starting from *i* infected individuals)
- Want to find $1 - q_1$

Assessing the risk of a major epidemic

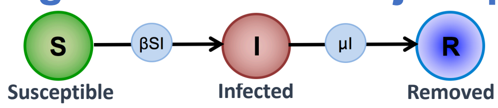


Two possibilities for the next event: infection or recovery

$$q_1 = \mathbb{P}(\text{infection}) \times q_2 + \mathbb{P}(\text{recovery}) \times q_0$$

Assessing the risk of a major epidemic | Estimating changes in transmissibility
Epidemic probability | COVID-19 | Adding complexity | Estimating R_t | Extensions | Going forwards

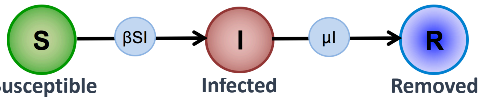
Assessing the risk of a major epidemic



Two possibilities for the next event: infection or recovery

$$q_1 \approx \mathbb{P}(\text{infection}) \times {q_1}^2 + \mathbb{P}(\text{recovery})$$

Assessing the risk of a major epidemic



Two possibilities for the next event: infection or recovery

$$q_1 \approx \mathbb{P}(\text{infection}) \times {q_1}^2 + \mathbb{P}(\text{recovery})$$

$$q_1 = \frac{1}{R_e} \text{ or } 1 \qquad ER = 1 - q_1 = 1 - \frac{1}{R_e}$$

Assessing the risk of a major epidemic | Estimating changes in transmissibility
Epidemic probability | COVID-19 | Adding complexity | Estimating R_t | Extensions | Going forwards

INTERFACE

royalsocietypublishing.org/journal/rsif

Research

Will an outbreak exceed available resources for control? Estimating the risk from invading pathogens using practical definitions of a severe epidemic

R. N. Thompson[1,2], C. A. Gilligan[3] and N. J. Cunniffe[3]

PLOS | COMPUTATIONAL BIOLOGY

RESEARCH ARTICLE

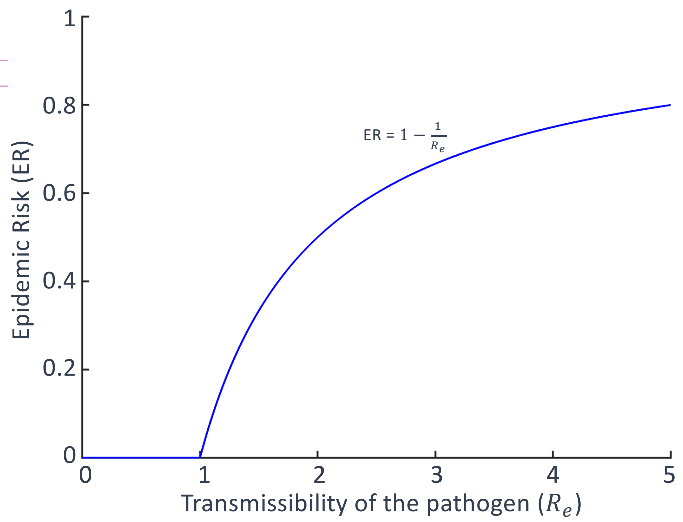
Detecting Presymptomatic Infection Is Necessary to Forecast Major Epidemics in the Earliest Stages of Infectious Disease Outbreaks

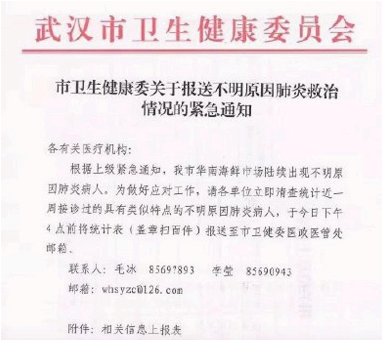
Robin N. Thompson*, Christopher A. Gilligan, Nik J. Cunniffe

Sustained transmission of Ebola in new locations: more likely than previously thought

THE LANCET Infectious Diseases

*Robin N Thompson, Katri Jalava, *Uri Obolski*




武汉市卫生健康委员会

市卫生健康委关于报送不明原因肺炎救治情况的紧急通知

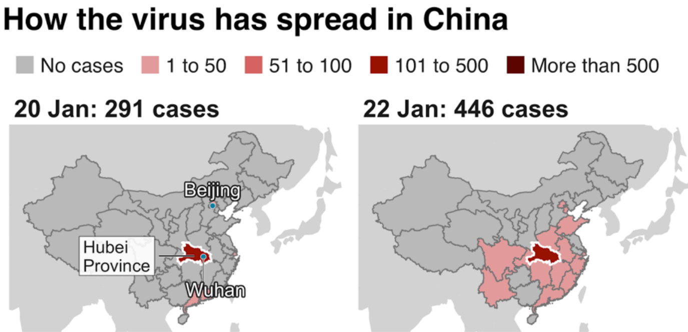
各有关医疗机构：

根据上级紧急通知，我市华南海鲜市场陆续出现不明原因肺炎病人。为做好应对工作，请各单位立即清查统计近一周接诊过的具有类似特点的不明原因肺炎病人，于今日下午4点前将统计表（盖章扫面件）报送至市卫健委医政医管处邮箱。

联系人：毛冰 85697893 李莹 85690943

邮箱：whsyzc@126.com

附件：相关信息上报表

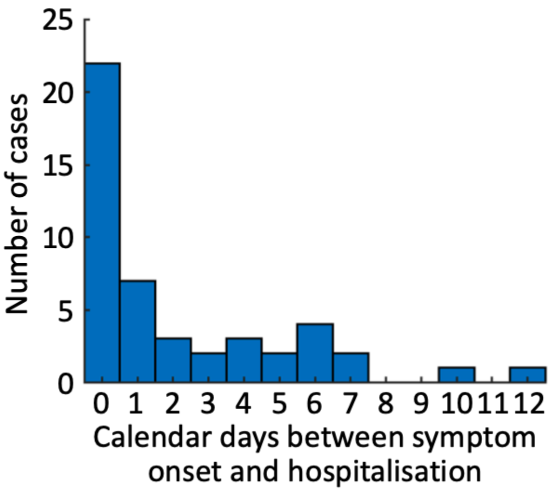


23 Jan: Line lists released (approx. 70 patients, incomplete data)

What is the epidemic risk outside of China?

Assessing the risk of a major epidemic | Estimating changes in transmissibility
Epidemic probability | COVID-19 | Adding complexity | Estimating R_t | Extensions | Going forwards

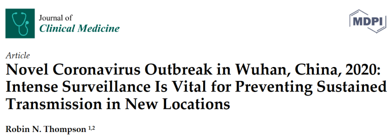
$$R_e = \text{Infection rate} \times \text{Duration of infection}$$



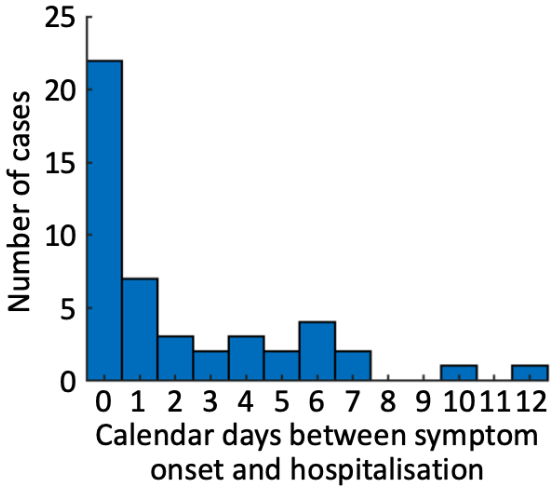
Interval-censored data

E.g. Symptoms – 10 Jan
Hospitalisation – 11 Jan

Symptom onset to hospitalisation lies in the range 0 – 2 days



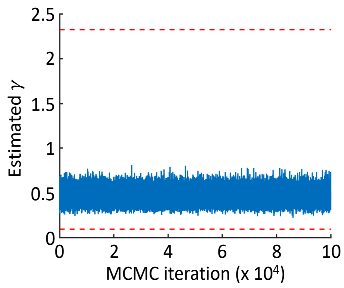
$$R_e = \text{Infection rate} \times \text{Duration of infection}$$



Interval-censored data

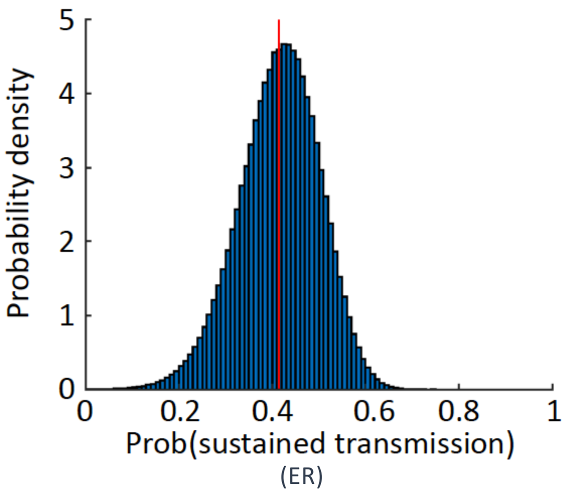
E.g. Symptoms – 10 Jan
Hospitalisation – 11 Jan

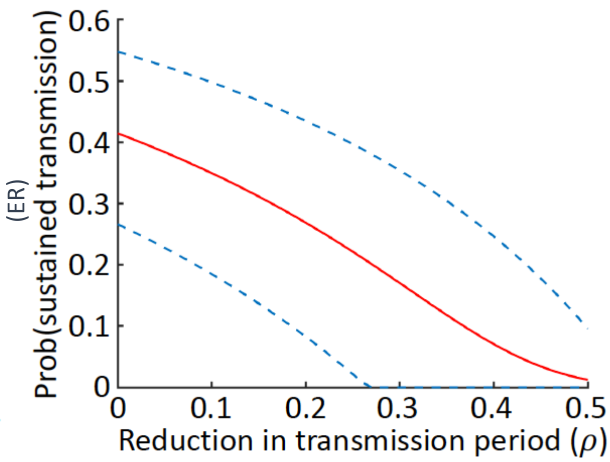
Symptom onset to hospitalisation lies in the range 0 – 2 days



Journal of Clinical Medicine
MDPI
Article
Novel Coronavirus Outbreak in Wuhan, China, 2020: Intense Surveillance Is Vital for Preventing Sustained Transmission in New Locations
Robin N. Thompson [1,2]

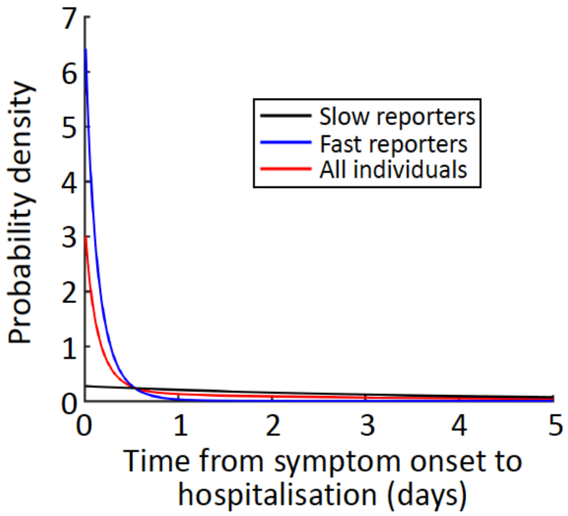
$$R_e = \text{Infection rate} \times \text{Duration of infection}$$

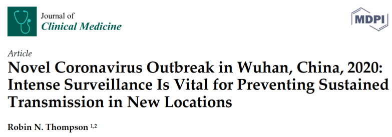




Journal of Clinical Medicine
MDPI
Article
Novel Coronavirus Outbreak in Wuhan, China, 2020: Intense Surveillance Is Vital for Preventing Sustained Transmission in New Locations
Robin N. Thompson [1,2]

Heterogeneity in reporting rates



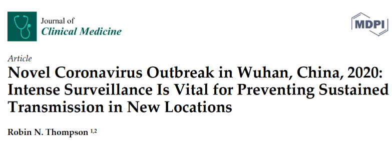

Journal of Clinical Medicine
MDPI
Article
Novel Coronavirus Outbreak in Wuhan, China, 2020: Intense Surveillance Is Vital for Preventing Sustained Transmission in New Locations
Robin N. Thompson [1,2]

Heterogeneity in reporting rates

$$q_{i,j} = \text{Prob}(\text{no major epidemic} \mid i \text{ fast reporters}, j \text{ slow reporters})$$

$$q_{1,0} = \frac{\alpha\beta}{\beta + \gamma^{(1)}} q_{2,0} + \frac{(1-\alpha)\beta}{\beta + \gamma^{(1)}} q_{1,1} + \frac{\gamma^{(1)}}{\beta + \gamma^{(1)}} q_{0,0},$$

$$q_{0,1} = \frac{\alpha\beta}{\beta + \gamma^{(2)}} q_{1,1} + \frac{(1-\alpha)\beta}{\beta + \gamma^{(2)}} q_{0,2} + \frac{\gamma^{(2)}}{\beta + \gamma^{(2)}} q_{0,0}.$$


Journal of Clinical Medicine
MDPI
Article
Novel Coronavirus Outbreak in Wuhan, China, 2020: Intense Surveillance Is Vital for Preventing Sustained Transmission in New Locations
Robin N. Thompson [1,2]

Heterogeneity in reporting rates

$q_{i,j}$ = Prob(no major epidemic | i fast reporters, j slow reporters)

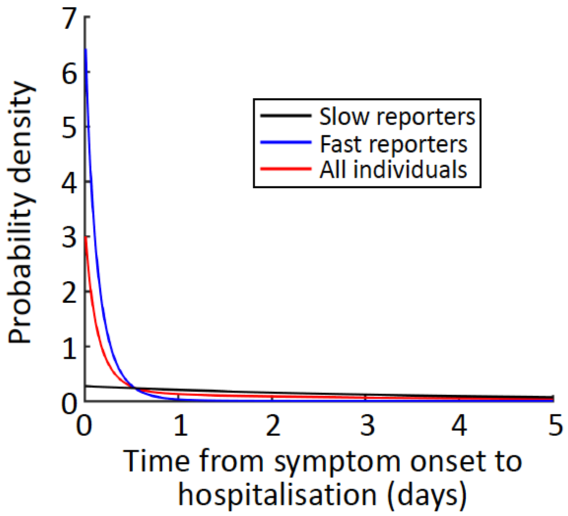
$$q_{1,0} = \frac{\alpha\beta}{\beta+\gamma^{(1)}} {q_{1,0}}^2 + \frac{(1-\alpha)\beta}{\beta+\gamma^{(1)}} q_{1,0}q_{0,1} + \frac{\gamma^{(1)}}{\beta+\gamma^{(1)}},$$

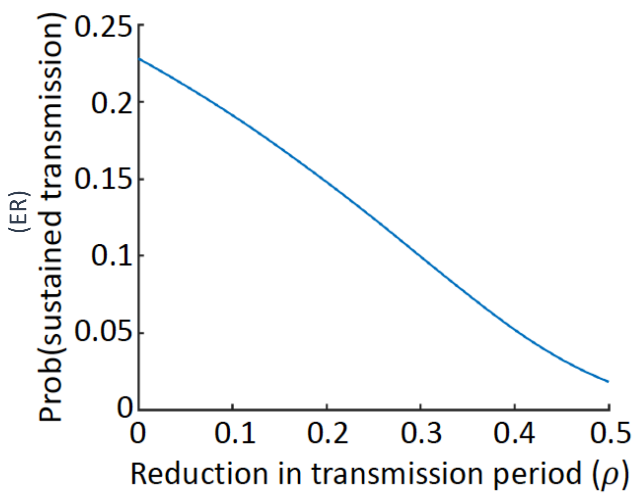
$$q_{0,1} = \frac{\alpha\beta}{\beta+\gamma^{(2)}} q_{1,0}q_{0,1} + \frac{(1-\alpha)\beta}{\beta+\gamma^{(2)}} {q_{0,1}}^2 + \frac{\gamma^{(2)}}{\beta+\gamma^{(2)}}.$$

Journal of Clinical Medicine
MDPI
Article
Novel Coronavirus Outbreak in Wuhan, China, 2020: Intense Surveillance Is Vital for Preventing Sustained Transmission in New Locations
Robin N. Thompson [1,2]

Assessing the risk of a major epidemic | Estimating changes in transmissibility
Epidemic probability | COVID-19 | Adding complexity | Estimating R_t | Extensions | Going forwards

Heterogeneity in reporting rates

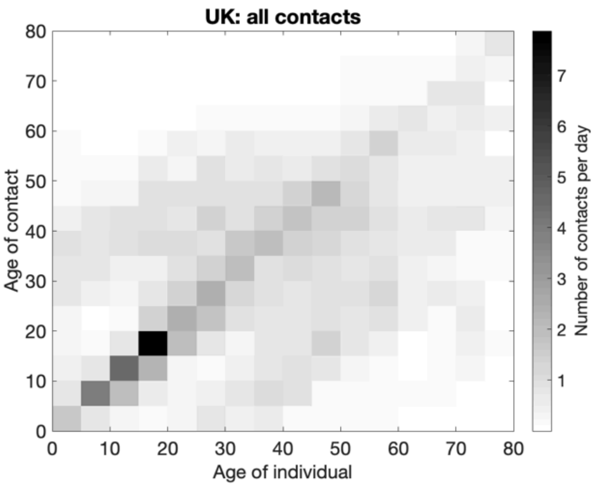


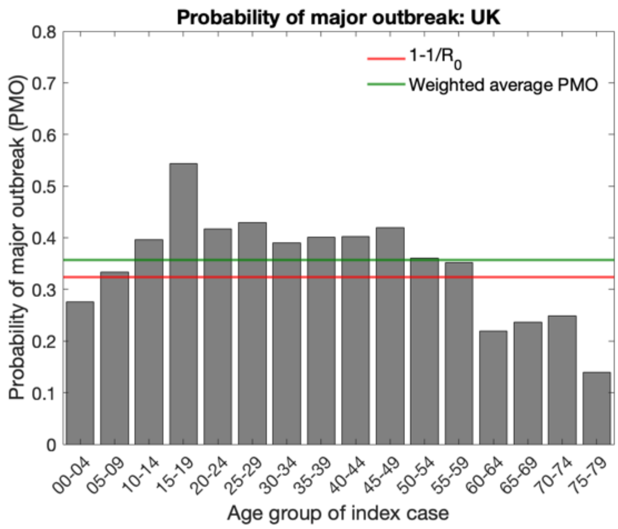


Journal of Clinical Medicine
MDPI
Article
Novel Coronavirus Outbreak in Wuhan, China, 2020: Intense Surveillance Is Vital for Preventing Sustained Transmission in New Locations
Robin N. Thompson [1,2]

Age structure

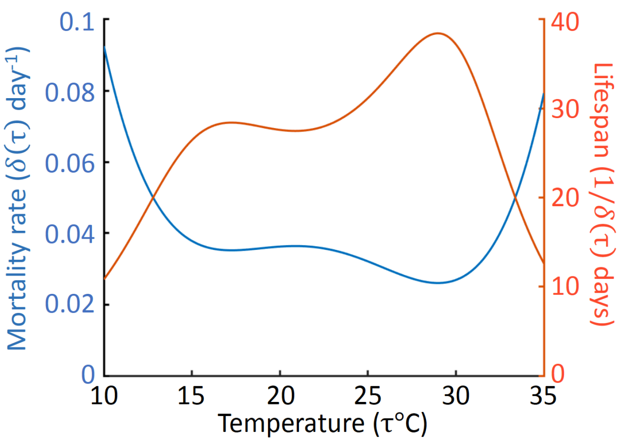
$$q_{i,j,k,\ldots} = \text{Prob}(\text{no major epidemic} \mid i \text{ in age group } 1, j \text{ in age group } 2, k \text{ in age group } 3, \ldots.)$$

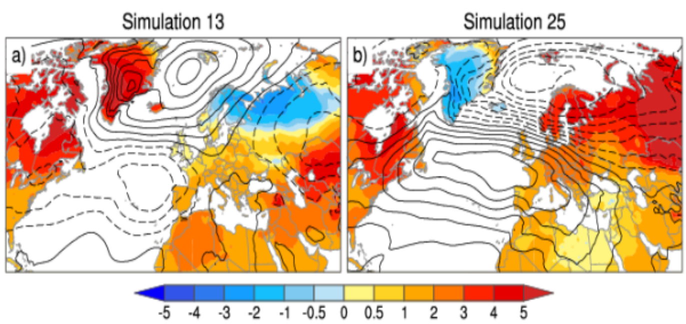




Time-dependence

$$q(1,t) = q(2,t+\Delta t)\beta(t)N\Delta t + q(0,t+\Delta t)\mu\Delta t + q(1,t+\Delta t)(1-\beta(t)N\Delta t - \mu\Delta t).$$





Climate forecast → Vector population forecast → Epidemic Risk forecast

Thompson *et al., Astrophys Space Sci Proc* (2020)

Assessing Epidemic Risks – Summary

Stochastic compartmental models can be **used to estimate the Epidemic Risk** (the probability that an imported case leads to a major epidemic)

Epidemic Risk estimates can be **generated analytically**, informed by using outbreak data, and **adjusted in real-time**

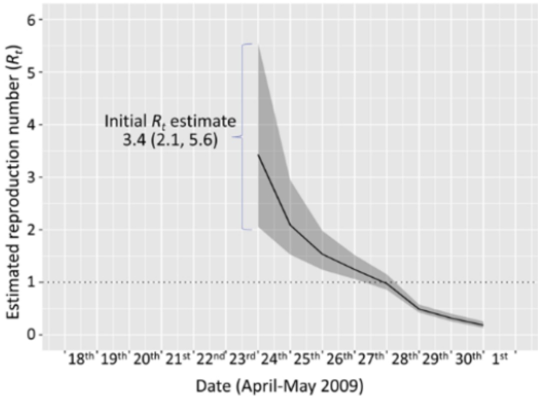
Estimates can be extended to include a range of features, **including heterogeneity in reporting rates, age structure and temporal heterogeneity**

Outline

1. Assessing the risk of a major epidemic
   - Estimating the probability of a major epidemic
   - Application to COVID-19
   - More complex models: heterogeneity in reporting, age structure
2. Estimating changes in disease transmissibility
   - Estimation of R_t
   - Extending the basic model
   - Going forwards

Middle

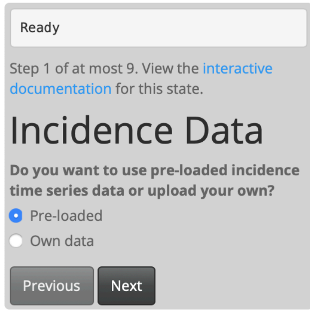
- How effective are current interventions?
- Which interventions will minimise numbers of cases?



$$\mathbf{P}(I_{t-\tau}^{\text{local}}, I_{t-\tau+1}^{\text{local}}, \ldots, I_t^{\text{local}} \mid I_0, \ldots, I_{t-\tau-1}, w_s, R_t) = \prod_{k=t-\tau}^{t} \frac{(R_t \Lambda_k(w_s))^{I_k^{\text{local}}} \exp(-R_t \Lambda_k(w_s))}{I_k^{\text{local}}!}$$

$$\mathbf{P}(R_t \mid I_0, I_1, I_2, \ldots, I_{t-\tau-1}, I_{t-\tau}^{\text{local}}, I_{t-\tau+1}^{\text{local}}, \ldots, I_t^{\text{local}}, w_s)$$

$$\propto \mathbf{P}(I_{t-\tau}^{\text{local}}, I_{t-\tau+1}^{\text{local}}, \ldots, I_t^{\text{local}} \mid I_0, \ldots, I_{t-\tau-1}, w_s, R_t)\mathbf{P}(R_t)$$



- **Estimating changes in disease transmissibility**

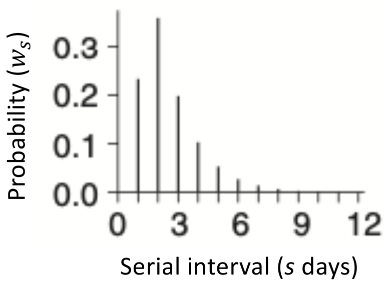
Thompson *et al.*, Epidemics, 2019

Assessing the risk of a major epidemic | Estimating changes in transmissibility
Epidemic probability | COVID-19 | Adding complexity | Estimating R_t | Extensions | Going forwards

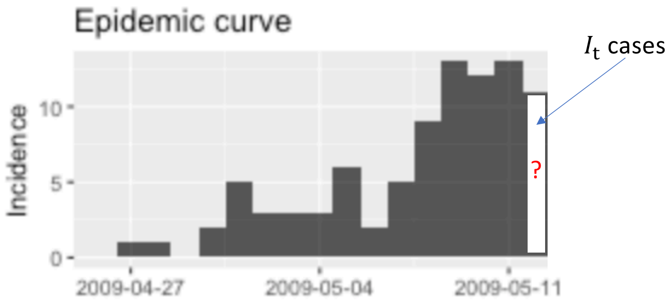
Two important quantities

Time dependent reproduction number — R_t — Definition / Threshold

Serial interval

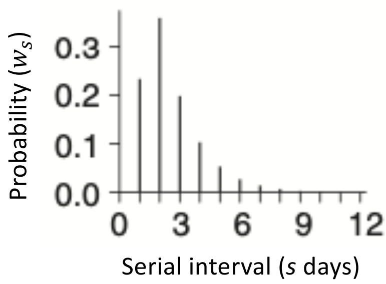


Basic simulation model



Know

R_t &

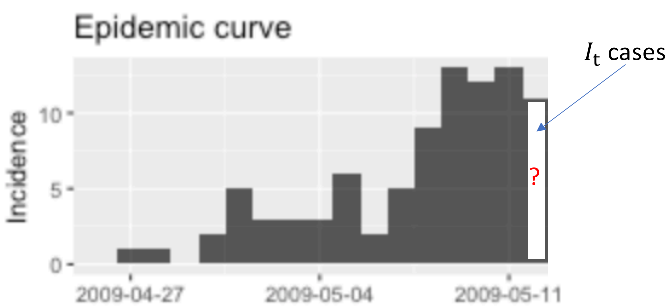


Basic model

$$\mathrm{E}(I_t \mid R_t, \{w_s\}, \{I_0, I_1, I_2, \dots, I_{t-1}\}) = R_t \sum_{s=1}^{t} I_{t-s} w_s$$

$$\mathrm{P}(I_t = x \mid R_t, \{w_s\}, \{I_0, I_1, I_2, \dots, I_{t-1}\}) = \frac{(\mathrm{E}(I_t))^x \exp(-\mathrm{E}(I_t))}{x!}$$

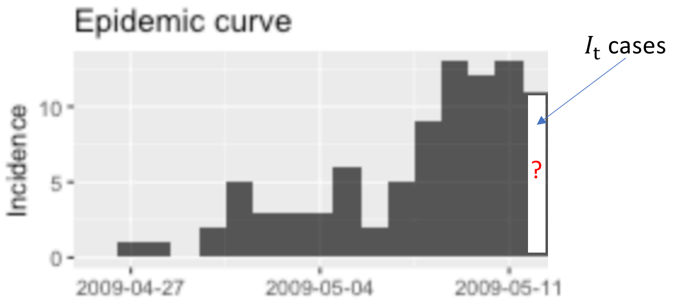
Cori *et al.*, Am. J. Epi., 2013



$$\text{Bayes' rule:}\ \ \mathrm{P}(A \mid B) = \frac{\mathrm{P}(B \mid A) P(A)}{P(B)}$$

$$\mathrm{P}(I_t = x \mid R_t, \{w_s\}, \{I_0, I_1, I_2, \dots, I_{t-1}\}) \quad \Rightarrow \quad \mathrm{P}(R_t \mid I_t = x, \{w_s\}, \{I_0, I_1, I_2, \dots, I_{t-1}\})$$

Cori *et al.*, Am. J. Epi., 2013



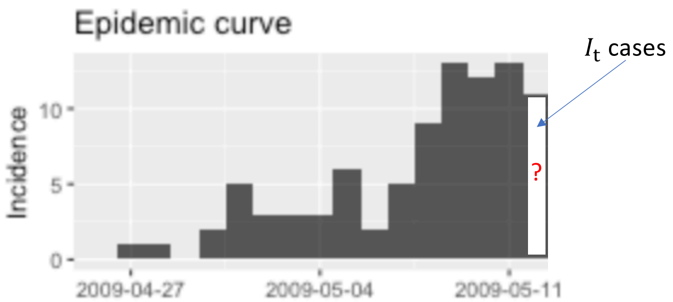
$$\text{Bayes'rule:} \quad P(A \mid B) = \frac{P(B \mid A)P(A)}{P(B)}$$

$$P(I_t = x \mid R_t, \{w_s\}, \{I_0, I_1, I_2, \dots, I_{t-1}\}) \quad \Rightarrow \quad P(R_t \mid I_t = x, \{w_s\}, \{I_0, I_1, I_2, \dots, I_{t-1}\})$$

Generates estimates of R_t that are highly sensitive to randomness in I_t
Solution: Consider constant R_t over a window $\{t-\tau, t-\tau+1, \dots t\}$

Cori *et al.*, Am. J. Epi., 2013

Assessing the risk of a major epidemic | Estimating changes in transmissibility
Epidemic probability | COVID-19 | Adding complexity | Estimating R_t | Extensions | Going forwards

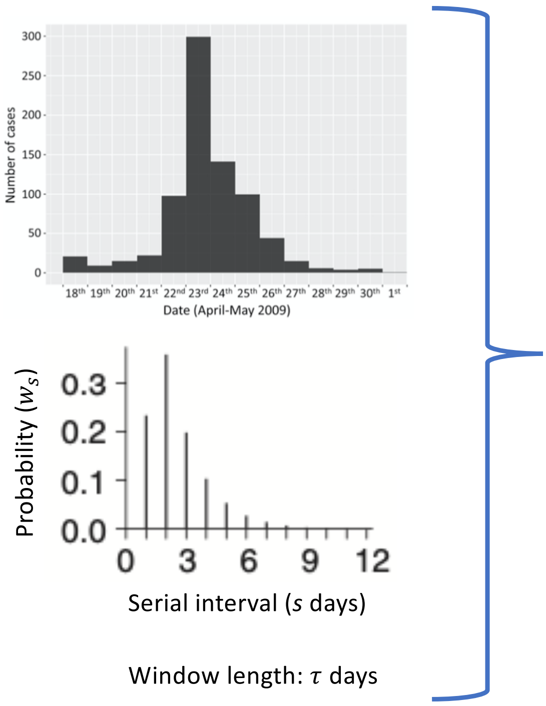


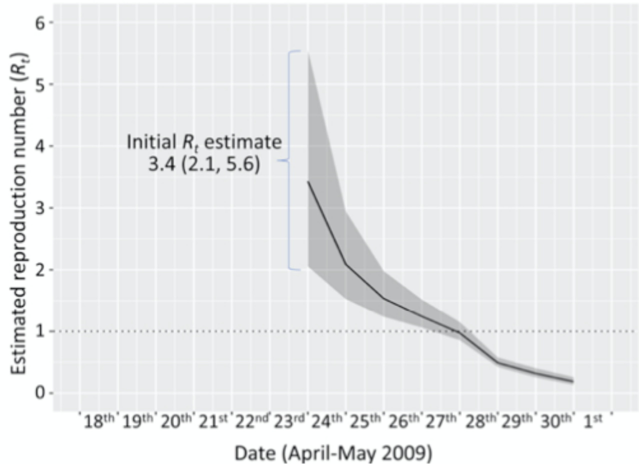
$$\text{Bayes'rule:} \quad P(A \mid B) = \frac{P(B \mid A)P(A)}{P(B)}$$

$$P(I_{t-\tau} = x_{t-\tau}, \dots, I_t = x_t \mid R_t, \{w_s\}, \{I_0, I_1, I_2, \dots, I_{t-\tau-1}\}) \quad \Rightarrow \quad P(R_t \mid I_{t-\tau} = x_{t-\tau}, \dots I_t = x_t, \{w_s\}, \{I_0, I_1, I_2, \dots, I_{t-\tau-1}\})$$

Solution: Consider constant R_t over a window $\{t-\tau, t-\tau+1, \dots t\}$

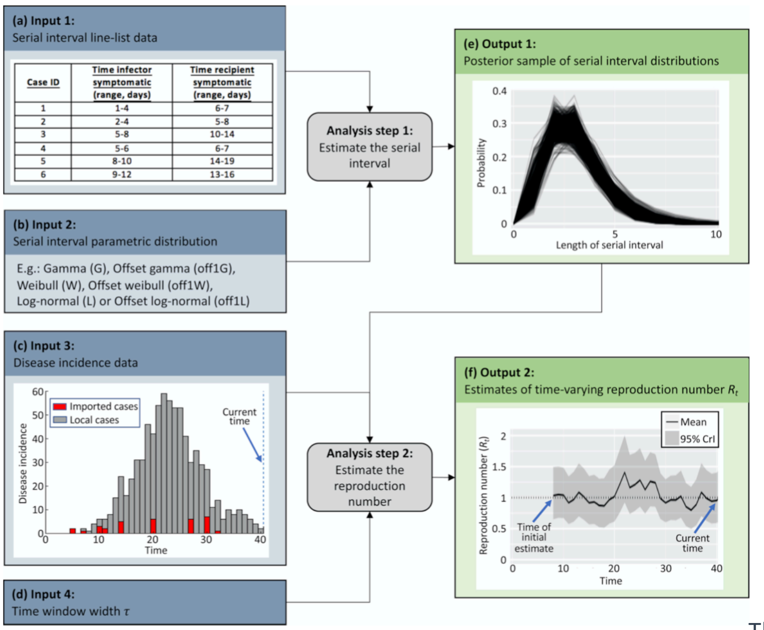
Cori *et al.*, Am. J. Epi., 2013

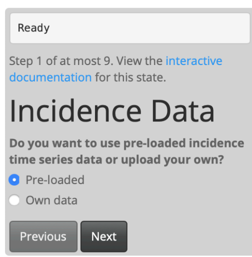




Cori *et al.*, Am. J. Epi., 2013
Thompson *et al.*, Epidemics, 2019

Uncertainty in the serial interval, imported cases

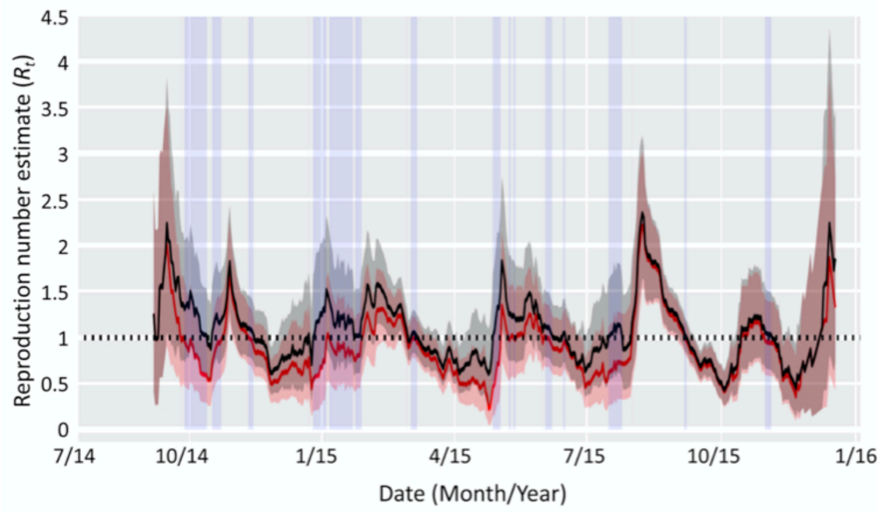




Thompson *et al.*, Epidemics, 2019

Imported cases

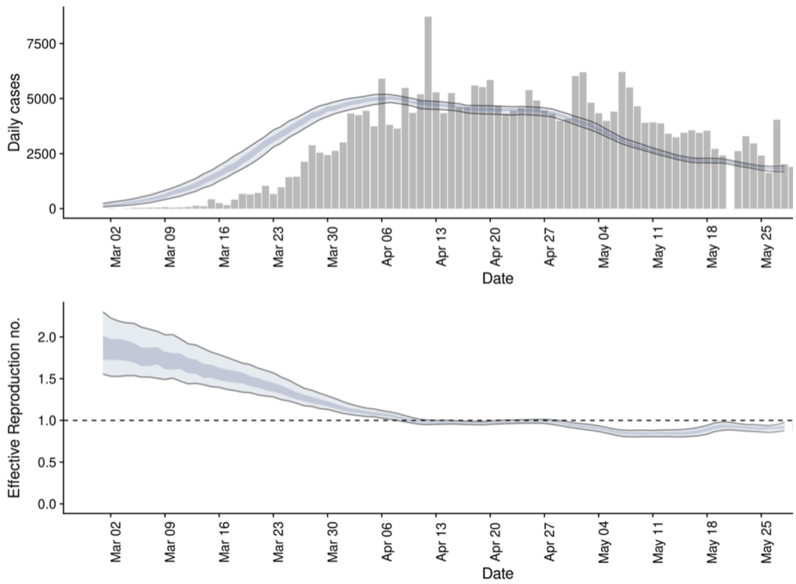
Imported cases have not been infected locally



Thompson *et al.*, Epidemics, 2019

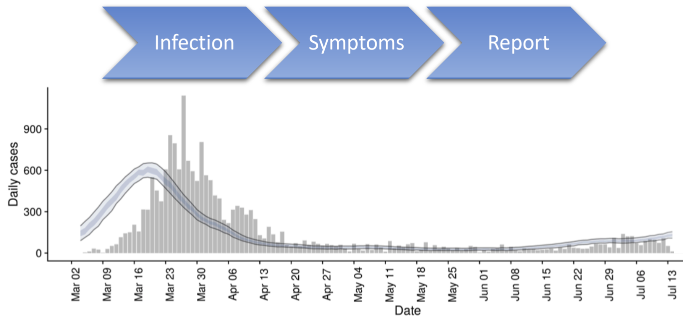
Conclusions – Estimating changes in transmissibility

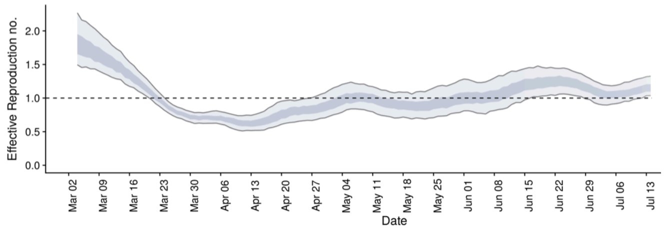
- Parameter inference can be used to estimate reproduction numbers in real-time during epidemics
- This approach has been used worldwide for COVID-19
- Population heterogeneity is important (e.g. local cases may have different characteristics compared to imported cases)



Six challenges - Estimation of R_t

1. Unpicking effects of different measures
2. Reporting delays
3. Estimation when case numbers are low



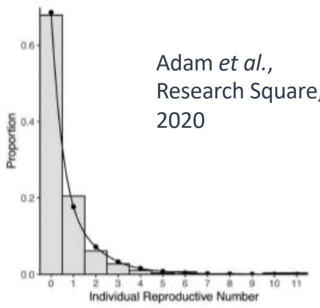


PROCEEDINGS B
royalsocietypublishing.org/journal/rspb

Key questions for modelling COVID-19 exit strategies

Thompson *et al.*, Proc Roy Soc B, 2020

Six challenges - Estimation of R_t



Adam *et al.*, Research Square, 2020

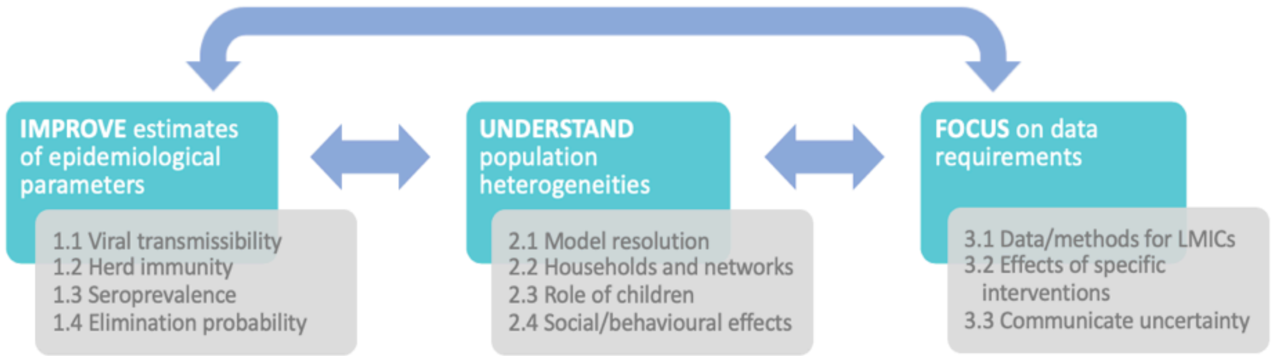
4. Effect of heterogeneity within populations: i) different groups; ii) super-spreading
5. Asymptomatic transmission
6. Temporal changes in serial interval

PROCEEDINGS B
royalsocietypublishing.org/journal/rspb

Key questions for modelling COVID-19 exit strategies

Thompson *et al.*, Proc Roy Soc B, 2020

Challenges going forwards



PROCEEDINGS B
royalsocietypublishing.org/journal/rspb
Key questions for modelling COVID-19 exit strategies

Thompson *et al.*, Proc Roy Soc B, 2020

Thanks!

@RobinNThompson