





Methods for Short Term Projections in epidemics (Projections Package)

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Structure





Context

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



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



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

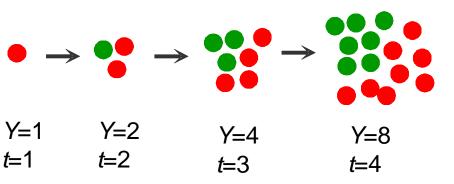


The reproduction number





 Basic reproduction number R₀: average number of secondary cases generated by an index case in a large entirely susceptible population





- Effective reproduction number R_t
 → equivalent at time t
- Incidence $R_{t} = 5$ $R_{t} = 2$ SI = 2.1 SI = 4

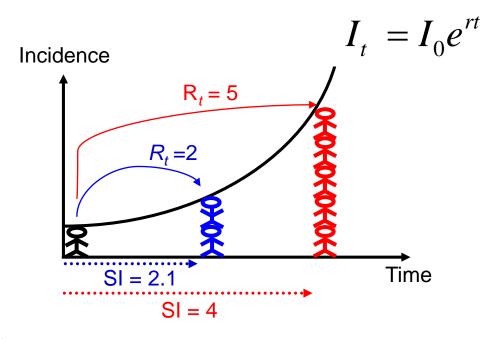






Estimation of R0 and Rt:

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

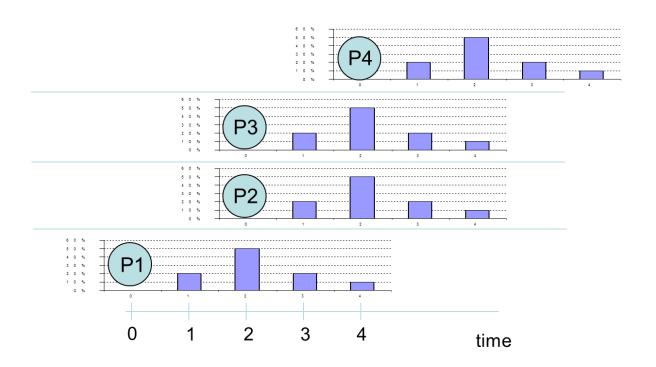






Distribution of serial interval: w_t

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





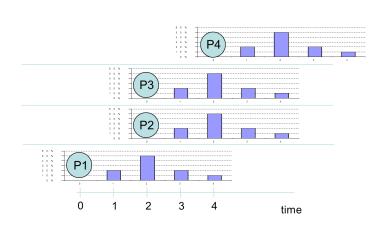




Distribution of serial interval: w_t

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)







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

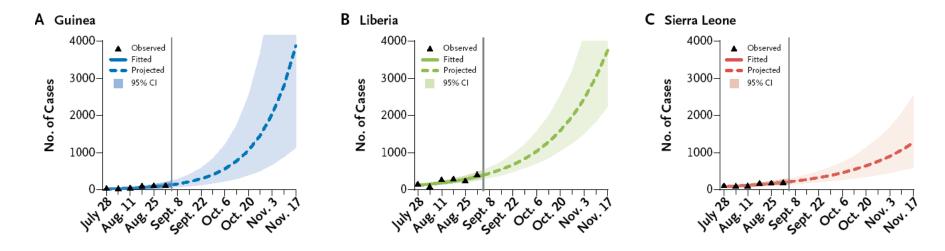
$$I_t = \mathcal{P}\left(R_t \sum_{s=1}^t I_{t-s} w_{t-s}\right)$$



How quickly was the virus spreading? Imperial College London September 2014

| | Centre for |
|-----|------------------------------------|
| MRC | Outbreak Analysis and Modelling |

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



Important for advocacy, planning

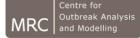


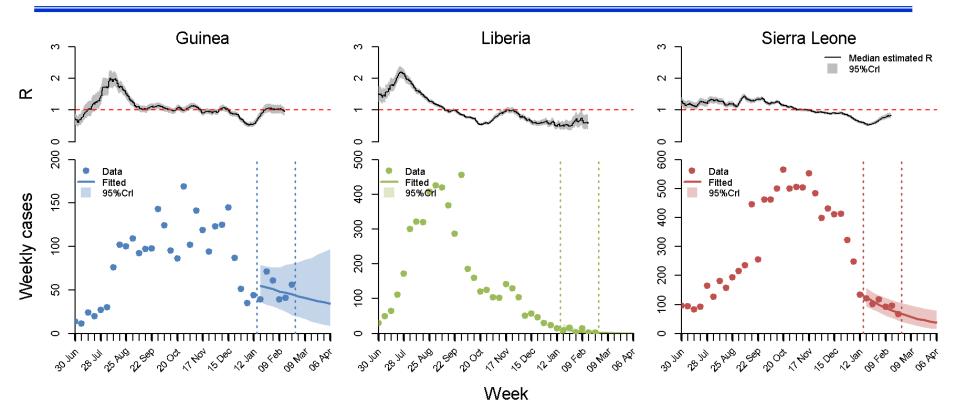
How quickly was the virus spreading? Imperial College London **March 2015**





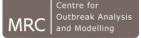
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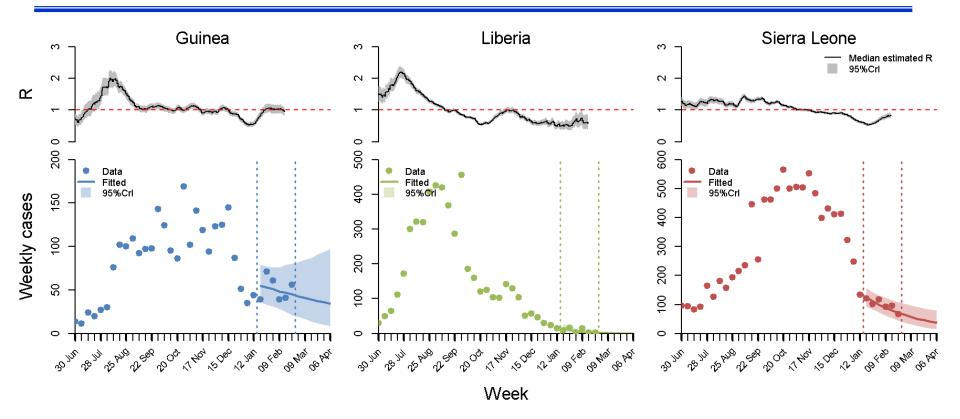






How quickly was the virus spreading? Imperial College London **March 2015**





| | 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) |



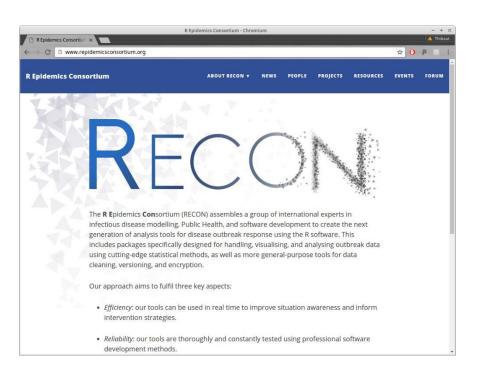
Implementation





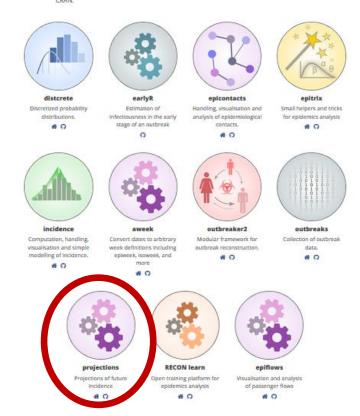
Implemented in a R package available in Recon website

(projection



Released projects and packages

These projects are in a usable form. Packages have been developed following RECON's standards, are fully functional, documented and tested, and have been released on



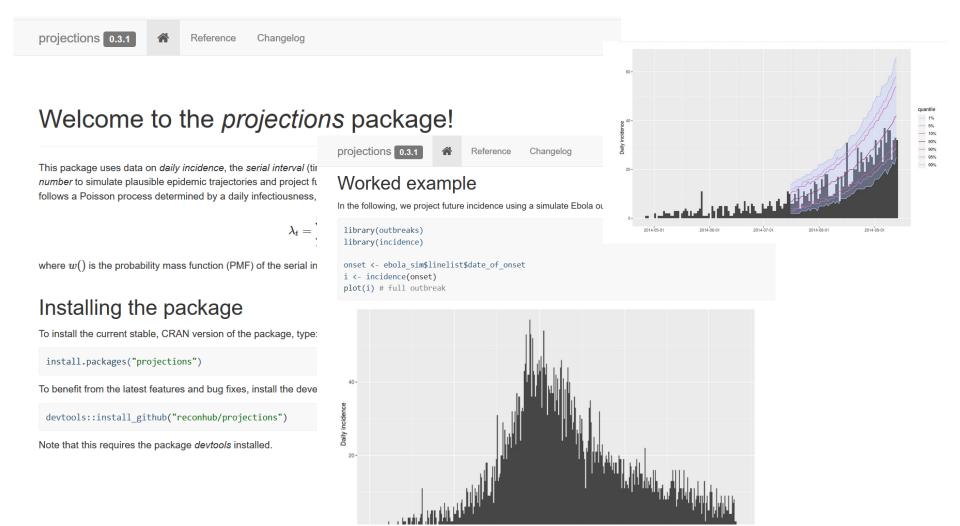


Implementation





Implemented in a R package available in Recon website





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*





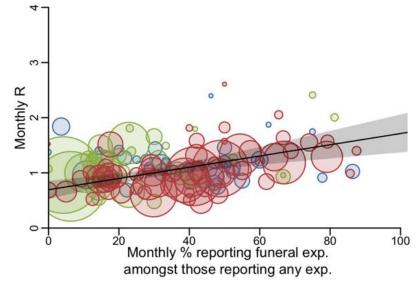
From projections to forecasting?



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)







From projections to forecasting?

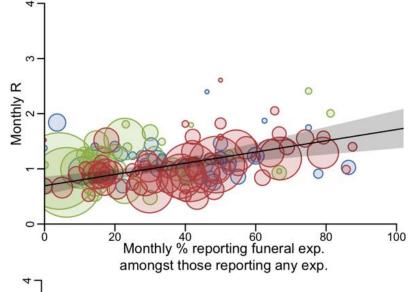


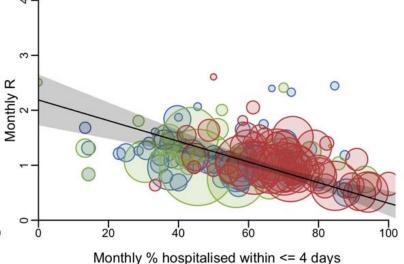
Can we say more about the determinants of Ebola dynamics?

Reproduction number for a given month was correlated with:

 % of individuals reporting funeral exposure (positive correlation)

 % of individuals hospitalised within 4 days (negative correlation)









From projections to predictions?



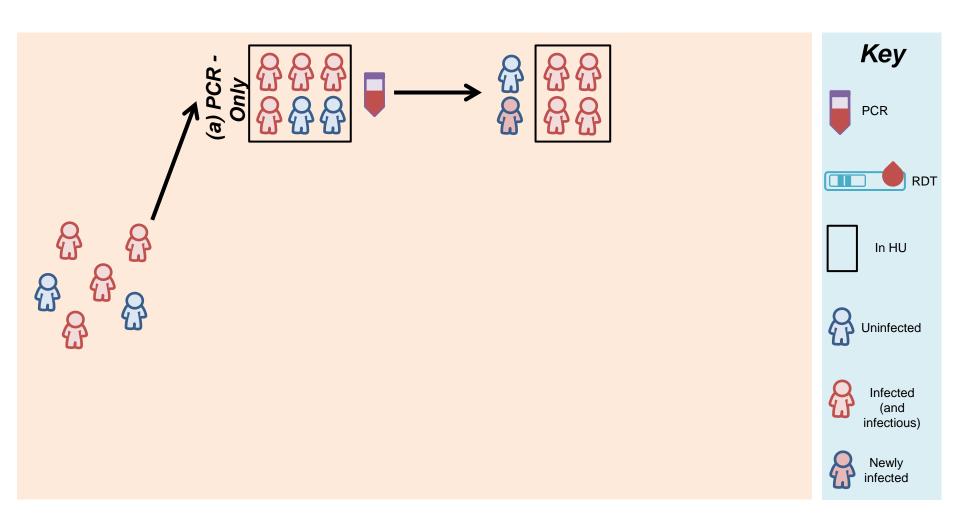
Can we make predictions if conditions were different?



From projections to predictions?

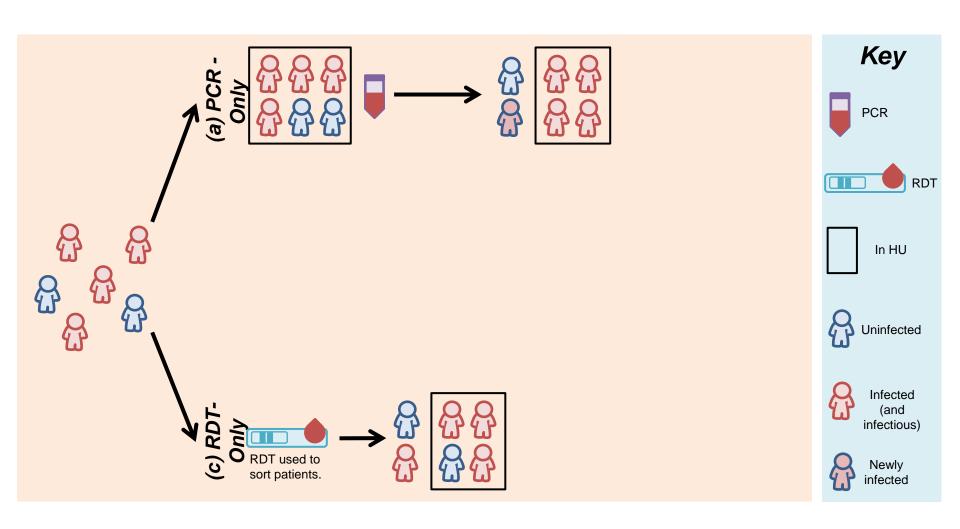
Imperial College London





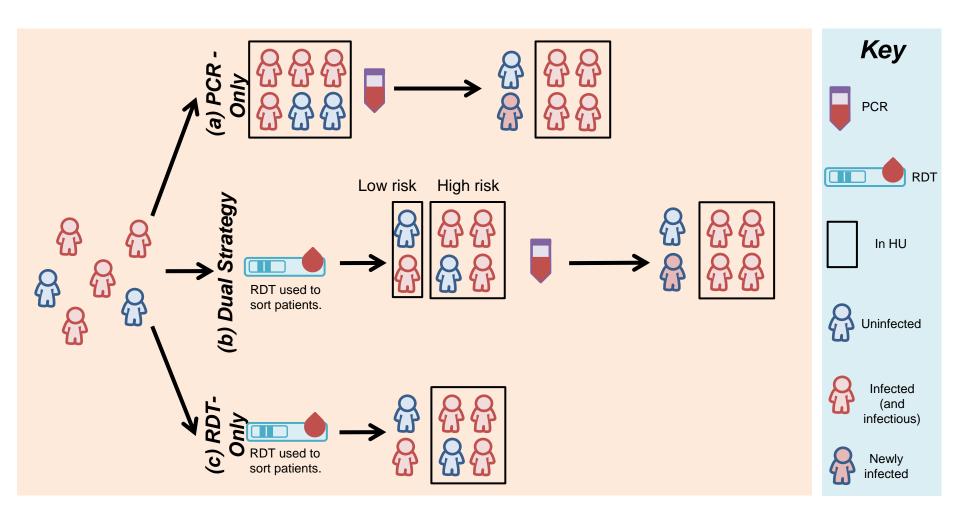




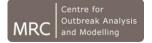


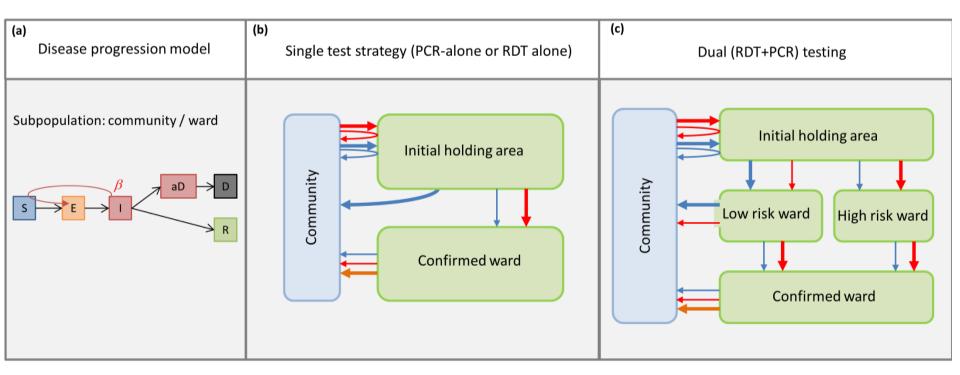








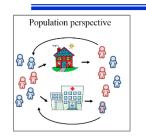


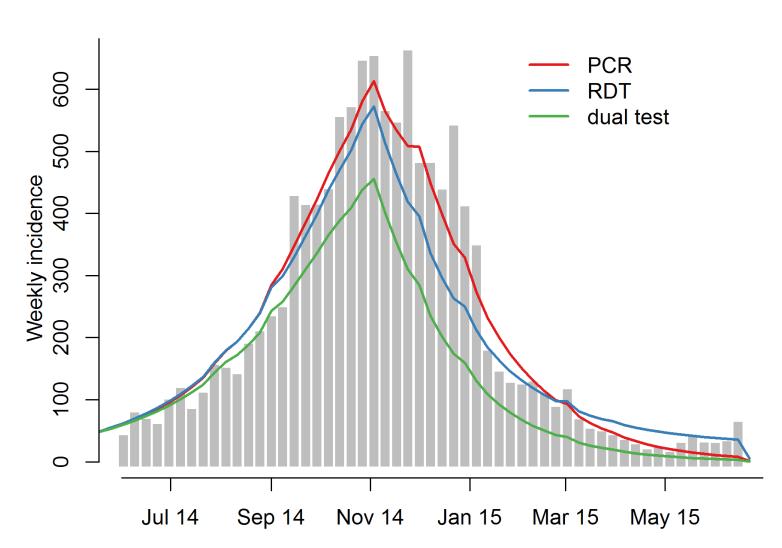










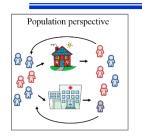


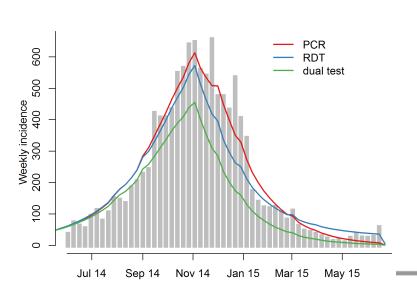


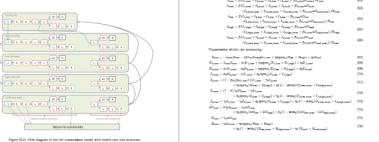
From projections to predictions?

Imperial College London









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

| Transmission within the initial holding ward, infection within a health-care unit: | | | |
|---|-----------|--|--|
| $\dot{S}_{hold} = -\lambda_{hold}S_{hold} + \kappa D_{hol}S_{non}p_{RU,nor} - \eta_1S_{hold}$ | (77) | | |
| $E_{1,\text{hold}} = \lambda_{\text{hold}} S_{\text{hold}} - (a_1 + \eta_1) E_{1,\text{hold}}$ | (79) | | |
| $E_{2,\text{hold}} = \alpha_2 E_{1,\text{hold}} - (\alpha_2 + \eta_1) E_{2,\text{max}}$ | (79) | | |
| $I_{1,hold} = \alpha_0 H_{2,hold} - (\gamma_1 + \eta_1) I_{1,hold}$ | (80) | | |
| $I_{2,\mathrm{bold}} = \gamma_1 I_{1,\mathrm{bold}} - (\gamma_2 + \eta_1) I_{3,\mathrm{bold}}$ | (RI) | | |
| $I_{3,hold} = (1 - \pi) \gamma_0 I_{3,hold} - (\gamma_3 + \eta_1) I_{3,hold}$ | (R2) | | |
| $I_{4,\text{hold}} = \gamma_5 I_{3,\text{hold}} - (\gamma_4 + \eta_1) I_{4,\text{hold}}$ | (903) | | |
| $aD_{hold} = \pi \gamma_0 I_{3,hold} - (\gamma_D + \eta_1) aD_{hold}$ | (84) | | |
| $\hat{D}_{hold} = \gamma m D_{hold}$ | (RG) | | |
| $\dot{R}_{\rm bold} = \gamma_0 I_{\rm Ljoid} - \gamma_1 R_{\rm bold}$ | (86) | | |
| Transmission within the initial holding ward, infletion within the community: | | | |
| $I_{2,\text{local},\text{incom}} = p_{\text{BH2}}p_{\text{BH2},\text{mere}}\gamma_1I_{1,\text{meas}} - (\gamma_2 + \eta_1)I_{2,\text{local},\text{incom}}$ | (87) | | |
| $I_{3,\text{lockl,jerom}} = (1 - \pi) \gamma_3 I_{3,\text{lockl,jerom}} - (\gamma_3 + \eta_1) I_{3,\text{lockl,jerom}}$ | (989) | | |
| $I_{4,\text{bolt,inom}} = \gamma n I_{3,\text{bolt,inom}} - (\gamma t + \eta t) I_{4,\text{bolt,inom}}$ | (86) | | |
| $aD_{bull,loom} = \pi \gamma_0 I_{0,bull,loom} - (\gamma_D + \eta_1) aD_{bull,loom}$ | (90) | | |
| $\hat{D}_{hold,journ} = \gamma_D a D_{hold,journ}$ | (91) | | |
| $R_{\text{bridd,jerom}} = \gamma_0 I_{\text{d,bridd,jerom}} - \eta_1 R_{\text{bridd,jerom}}$ | (92) | | |
| Transmission within the low-risk ward, infection within a health-ears unit: | | | |
| $\hat{S}_{loc} = -\lambda_{loc}S_{loc} - \eta_2S_{loc} + \eta_1 spec_1S_{local}$ | (90) | | |
| $\hat{E}_{1,low} = \lambda_{low} S_{low} - (\alpha_1 + \eta_1) E_{1,low} + \eta_1 spec_1 E_{1,look}$ | (1941) | | |
| $E_{1,loc} = arE_{1,loc} - (au + \eta u)E_{1,loc} + \eta uspec_1E_{1,loc}$ | (DC) | | |
| $I_{1,low} = \alpha_2 E_{2,low} - (\gamma_1 + \eta_2) I_{1,low} + \eta_1 exc_1 I_{1,look}$ | (DG) | | |
| $\hat{I}_{2,loc} = \gamma_1 I_{1,loc} - (\gamma_2 + \eta_2) I_{2,loc} + \eta_1 \text{spec}_1 I_{2,lock}$ | (DT) | | |
| $I_{3,low} = (1 - \pi) \gamma_2 I_{3,low} - (\gamma_1 + \eta_2) I_{3,low} + \eta_1 spec_1 I_{3,loid}$ | (1961) | | |
| $I_{4,low} = \gamma_5 I_{3,low} - (\gamma_4 + \eta_5) I_{4,low} + \eta_5 spec_5 I_{4,look}$ | (1961) | | |
| $aD_{loc} = \pi \gamma a D_{loc} - (\gamma v + \eta s) aD_{loc} + \eta s s p s c_1 aD_{loc}$ | (100) | | |
| $D_{bw} = \gamma_D a D_{bw}$ | (101) | | |
| $\hat{\Pi}_{low} = \gamma_0 I_{4,low} - \eta_0 \Pi_{low} + \eta_1 \text{space}_1 \Pi_{look}$ | (102) | | |
| Transmission within the low-risk ward, inflorion within the community: | | | |
| $\hat{I}_{0,low,jerm} = -(\gamma_0 + \eta_0) I_{0,low,jerm} + \eta_1 (1 - mess_1) I_{0,lodd,jerm}$ | (100) | | |
| $I_{2,\mathrm{low},\mathrm{jeam}} = (1-\pi)\gamma_2 I_{2,\mathrm{low},\mathrm{jeam}} - (\gamma_2 + \eta_2)I_{2,\mathrm{low},\mathrm{jeam}} + \eta_1(1-\mathrm{wes}_1)I_{2,\mathrm{lodd},\mathrm{jeam}}$ | (104) | | |
| $I_{4,\text{low},\text{low}} = \gamma_2 I_{3,\text{low},\text{low}} - (\gamma_4 + \eta_2) I_{4,\text{low},\text{low}} + \eta_1 (1 - \text{sens}_1) I_{4,\text{look},\text{low}}$ | (105) | | |
| $aD_{\text{total joins}} = \pi \gamma aB_{\text{joins, joins}} - (\gamma v + \eta v) aD_{\text{total joins}} + \eta v (1 - \text{security}) aD_{\text{total joins}}$ | (106) | | |
| $D_{low,jerm} = \gamma_D a D_{low,jerm}$ | (107) | | |
| i | d topoli. | | |

| The state of the s | |
|--|-----------------------|
| $\dot{S}_{high} = -\lambda_{high} S_{high} - \eta_2 S_{high} + \eta_1 (1 - spec_1) S_{hold}$ | (109) |
| $\hat{E}_{1,high} = \lambda_{high} S_{high} - (\alpha_1 + \eta_2) E_{1,high} + \eta_1 (1 - spec_1) E_{1,hold}$ | (110) |
| $\dot{E}_{2,high} = \alpha_1 E_{1,high} - (\alpha_2 + \eta_2) E_{2,high} + \eta_1 (1 - spec_1) E_{2,hold}$ | (111) |
| $\hat{B}_{1,\text{begin}} = \text{craffe}_{1,\text{begin}} - (\gamma v + \eta v) B_{1,\text{begin}} + \eta v (1 - \text{spec}_1) B_{1,\text{begin}}$ | (112) |
| $I_{2,high} = \gamma_1 I_{1,high} - (\gamma_2 + \eta_2) I_{2,high} + \eta_1 (1 - spec_1) I_{2,held}$ | (113) |
| $\hat{I}_{3,high} = (1 - \pi) \gamma_0 I_{2,high} - (\gamma_2 + \eta_2) I_{3,high} + \eta_1 (1 - \pi \rho c c_1) I_{3,held}$ | (114) |
| $I_{4,high} = \gamma_5 I_{3,high} - (\gamma_4 + \eta_2) I_{4,high} + \eta_1 (1 - spec_1) I_{4,hold}$ | (115) |
| $aD_{high} = \pi \gamma_0 I_{0,high} - (\gamma_D + \eta_0) aD_{high} + \eta_1 (1 - \pi pos_1) aD_{hold}$ | (116) |
| $\hat{D}_{high} = \gamma_D a D_{high}$ | (117) |
| $R_{high} = \gamma_0 I_{A,high} - \gamma_0 R_{high} + \gamma_1 (1 - spec_1) R_{hold}$ | (118) |
| Transmission within the high-risk ward, infection within the community: | |
| $\hat{I}_{2,\text{high,loom}} = -\left(\gamma_1 + \eta_2\right)I_{2,\text{high,loom}} + \eta_1 \text{sens}_1 I_{2,\text{hold,loom}}$ | (119) |
| $\hat{I}_{2,\text{high,imm}} = (1 - \pi) \gamma_{1} I_{2,\text{high,imm}} - (\gamma_{1} + \eta_{2}) I_{2,\text{high,imm}} + \eta_{1} \pi \pi \pi I_{2,\text{hold,imm}}$ | (120) |
| $I_{4,\mathrm{high,imm}} = \gamma_2 I_{2,\mathrm{high,imm}} - (\gamma_4 + \eta_2) I_{4,\mathrm{high,imm}} + \eta_1 \mathrm{secus}_1 I_{4,\mathrm{hold,imm}}$ | (121) |
| $aD_{\text{high,loom}} = \pi \gamma_2 I_{2,\text{high,loom}} - (\gamma_D + \eta_2) aD_{\text{high,loom}} + \eta_1 \text{sects}_1 aD_{\text{hidd,loom}}$ | (122) |
| $\hat{D}_{high,imm} = \gamma_D a D_{high,imm}$ | (122) |
| $\hat{H}_{high,imm} = \gamma_1 I_{h,high,imm} - \eta_2 R_{high,imm} + \eta_1 mm_1 R_{hold,imm}$ | (124) |
| Transmission within the confirmed ward, infection within a health-care unit: | |
| $\dot{S}_{mad} = -\lambda_{mad}S_{mad} + \eta_2 (1 - spec_2)(S_{low} + S_{high}) - \eta_4S_{mad}$ | (125) |
| $\hat{E}_{1,mad} = \lambda_{mad} S_{mad} - \alpha_1 E_{1,mad} + \eta_2 (1 - \text{spec}_2) (E_{1,low} + E_{1,loigh}) - \eta_k E_{1,mad}$ | (126) |
| $\dot{E}_{2,mad} = a_1 E_{1,mad} - a_2 E_{2,mad} + \eta_2 (1 - spec_2) (E_{2,loc} + E_{2,high}) - \eta_2 E_{2,mad}$ | (127) |
| $\hat{I}_{1,\text{mod}} = \text{ort}(1,\text{mod} - \gamma_1 I_{1,\text{mod}} + \gamma_2 I_{1} - \text{spec}_2)(I_{1,\text{mod}} + I_{1,\text{log}_1})$ | (128) |
| $I_{2,mad} = \gamma_1 I_{1,mad} - \gamma_2 I_{2,mad} + \eta_2 (1 - s_2^{max}) (I_{2,low} + I_{2,logk})$ | (129) |
| $\hat{I}_{2,mad} = (1 - \pi) \gamma_2 I_{2,mad} - \gamma_2 I_{2,mad} + \eta_2 (1 - \text{xpec}_2) (I_{2,low} + I_{2,logh})$ | (130) |
| $I_{4,\text{read}} = \gamma_2 I_{2,\text{read}} - \gamma_4 I_{4,\text{read}} + \gamma_5 (1 - \text{space}_0) (I_{4,\text{low}} + I_{4,\text{high}})$ | (131) |
| $aD_{mad} = \pi \gamma_2 I_{2,mad} - \gamma_D aD_{mad} + \eta_2 (1 - \operatorname{spec}_2) (aD_{hor} + aD_{high})$ | (132) |
| $D_{mad} = \gamma_D a D_{mad}$ | (130) |
| $R_{mad} = \gamma_k I_{k,mad} + \eta_k \left(1 - \operatorname{spac}_k\right) \left(R_{kw} + R_{high}\right) - \eta_k R_{mad}$ | (134) |
| Transmission within the confirmed ward, infection within the community: | |
| $I_{2,mat,loom} = -\gamma_2 I_{2,mat,loom} + \gamma_2 \text{nesses}_2 \left(I_{2,low,loom} + I_{2,high,loom} \right)$ | (135) |
| $\hat{B}_{ijml,loom} = (1 - \pi) \gamma_{i} f_{1jml,loom} - \gamma_{i} f_{2jml,loom} + \gamma_{i} m_{i} r_{i} r_{i}$ | (136) |
| $I_{4,mat,loom} = \gamma_0 I_{3,mat,loom} - \gamma_4 I_{4,mat,loom} + \eta_4 accs_1 (I_{4,loo,loom} + I_{4,bigh,loom})$ | (1317) |
| $aD_{mal,inm} = \pi \gamma_0 I_{2,mal,inm} - \gamma_D aD_{mal,inm} + \eta_0 mn_0 (aD_{lw,inm} + aD_{high,inm})$ | (128) |
| $D_{mal,loom} = \gamma_D a D_{mal,loom}$ | (139) |
| $\dot{R}_{mat,loom} = \gamma_0 I_{4,mat,loom} + \eta_0 m c s_0 (R_{low,loom} + R_{high,loom}) - \eta_0 R_{mat,loom}$ | (140) |
| Here, the same state variables as in the simpler transmission model without hospitalisation a but subscripted with 'com', 'hold', 'low', 'high', 'cont' to indicate the subpopulation: the commu | no used, nity, the |



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



Caveats for projections





Heterogeneity in transmission



SARS and heterogeneity in transmission







The cases of Amoy garden:

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

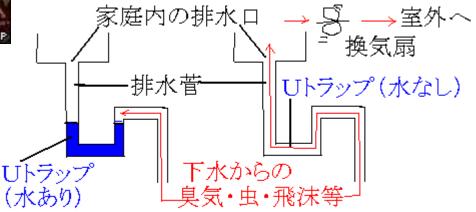


図3. Uトラップ(水なし)からの下水飛沫の侵入



SARS and heterogeneity in transmission





SARS and heterogeneity in transmission

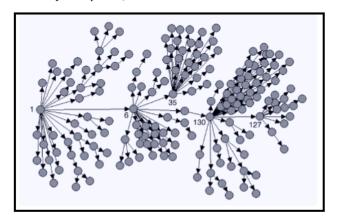
Reproduction number:

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



SARS and heterogeneity in transmission



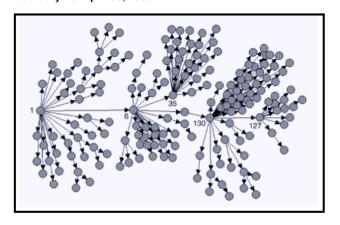


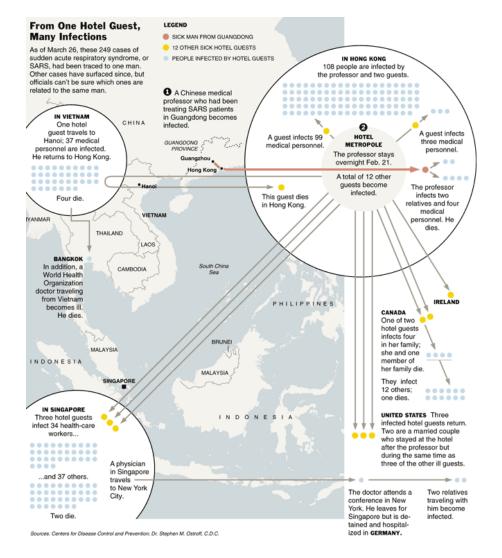
SARS and heterogeneity in transmission

Reproduction number:

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

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







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and heterogeneity in transmission

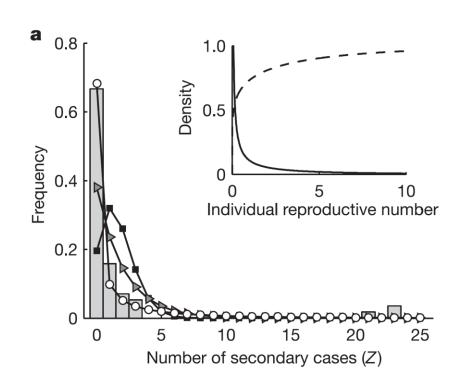


Simplest case, assumes:

- 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. Schreiber³, P. E. Kopp⁴ & W. M. Getz¹



Imperial College London

and heterogeneity in transmission

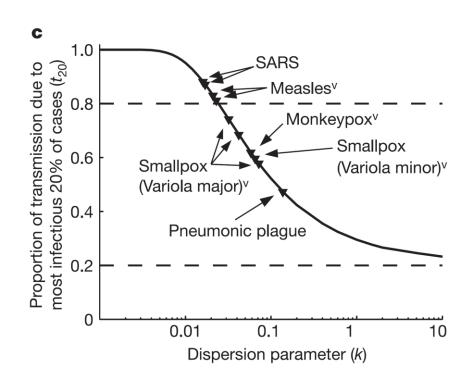


Simplest case, assumes:

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Increased heterogeneity, assumes

- Individual 'offspring distribution' is still Poisson
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LETTERS

Superspreading and the effect of individual variation on disease emergence

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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

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



Imperial College London

and heterogeneity in transmission



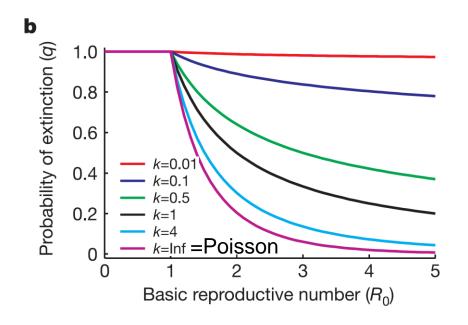
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Implications for outbreak extinctions



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Thank you!