Quantifying superspreading for COVID-19 using Poisson mixture distributions

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Background

R_0 = average number of secondary cases by an infected individual in a completely susceptible population

- considered constant among population members or specific population groups

Transmission potential = complex combination of host, pathogen, and environmental factors
→ individual variation in disease transmission

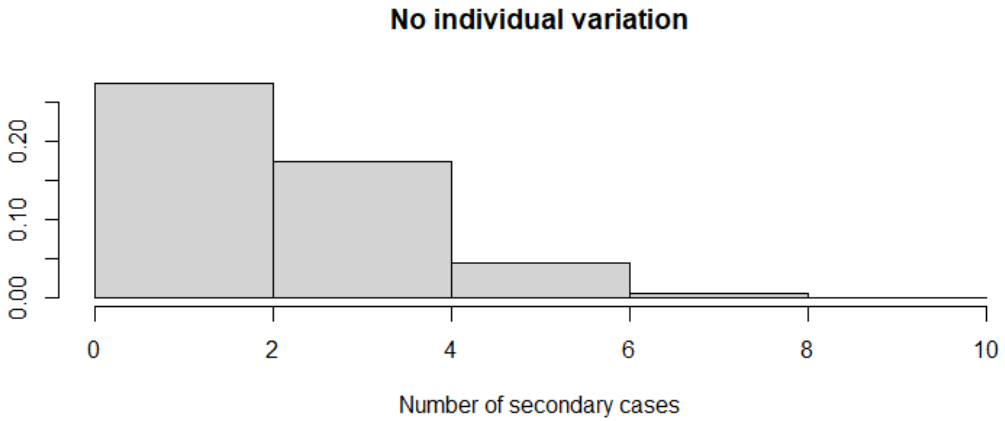
- affects outbreak probability and subsequent course

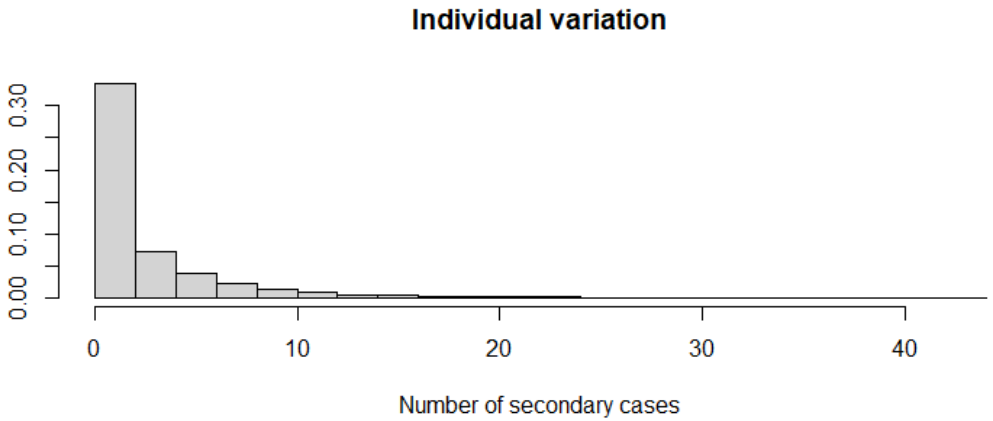
Superspreaders: infect substantially more individuals than others

- relatively small part of cases responsible for most of transmission
- many cases do not transmit disease

Population estimate of R_0 does not account for individual variation

→ Overdispersed offspring distribution with mean R_0





Lloyd-Smith *et al.* (2005): individual reproduction number ν as a random variable that represents the **expected** number of secondary cases

- Distribution with population mean R_0
  - encodes all variation in infectiousness
  - $\rightarrow$ SSE are realizations from the right-hand tail of the distribution of ν
- Stochastic effects in transmission modelled using a Poisson process
  - Most studies have assumed the rate $\nu \sim$ Gamma
  - $=$ negative binomial offspring distribution $\rightarrow$ heterogeneity quantified by dispersion parameter k
    - $k < 1$: substantial superspreading
    - lower k = increased heterogeneity
    - $\rightarrow$ easy comparison between studies

Individual variation in SARS-CoV-2 transmission

* (almost) all studies assume a negative binomial distribution
* k ranging from 0.1 to 0.6
* $p_{80\%}$ = proportion of cases responsible for 80% of transmission; ranging from 9% to 20%

$\rightarrow$ indicates important role of SSE in transmission

Other distributions?

- Brooks-Pollock *et al.* (2020): model the distribution of cluster sizes for TBC in the UK and NL
  - Poisson-lognormal better fit to UK data

→ importance of comparing different assumptions

What if the assumption of a negative binomial offspring distribution is not the best one?
→ Impact on estimates of heterogeneity?

Poisson mixtures

Number of secondary infections caused by each case is described by an offspring distribution

- Poisson contact process
- Rate following a continuous probability distribution
  - individual reproduction number ν

$\rightarrow$ Poisson mixture distribution: $Y \sim \text{Poisson}(\nu)$

Distribution for ν	Offspring distribution	Mean R	Variance σ^2
$\nu \sim \text{GG}(a,d,p)$	$Y \sim \text{PoGG}(a,d,p)$	$a\frac{\Gamma(\frac{d+1}{p})}{\Gamma(\frac{d}{p})}$	$a\frac{\Gamma(\frac{d+1}{p})}{\Gamma(\frac{d}{p})} + a^2\left[\frac{\Gamma(\frac{d+2}{p})}{\Gamma(\frac{d}{p})} - \left(\frac{\Gamma(\frac{d+1}{p})}{\Gamma(\frac{d}{p})}\right)^2\right]$
$\nu \sim \text{Ga}(\alpha,\beta)$	$Y \sim \text{NB}(\mu,k)$	$\mu = \frac{\alpha}{\beta}$	$\mu(1+\frac{\mu}{k}) = \frac{\alpha}{\beta}(1+\frac{1}{\beta})$
$\nu \sim \text{LogN}(\mu_{log},\sigma_{log})$	$Y \sim \text{PoLN}(\mu_{log},\sigma_{log})$	$e^{\mu_{log}+\frac{\sigma^2_{log}}{2}}$	$e^{\mu_{log}+\frac{\sigma^2_{log}}{2}} + \left[(e^{\sigma^2_{log}}-1)e^{2\mu_{log}+\sigma^2_{log}}\right]$
$\nu \sim \text{Weibull}(p,l)$	$Y \sim \text{PoWB}(p,l)$	$l\Gamma(1+\frac{1}{p})$	$l\Gamma(1+\frac{1}{p}) + l^2\left[\Gamma(1+\frac{2}{p}) - \left(\Gamma(1+\frac{1}{p})\right)^2\right]$

Simulation study

Objective: assess bias in estimates of R and its overdispersion

* generate data from each proposed mixture
  * varying levels of overdispersion
* estimate parameters using MLE
* obtain $\hat{R}_i$ and $\hat{\sigma}_i$

$\rightarrow$ Impact of assumed offspring distribution on proportion of cases responsible for certain proportion of transmission?

* i.e. importance of superspreading

Expected vs. realized proportions of transmission

Two methods:

1. **Lloyd-Smith et al. (2005):** calculate proportion responsible based on the distribution of ν $\rightarrow$ **expected** proportion of transmission based on inherent transmission potential
    * only depends on level of overdispersion, not R
2. **Endo et al. (2020):** take into account additional variation from Poisson process $\rightarrow$ **realized** proportion of transmission
    * depends on level of overdispersion as well as R

Same reasoning $\rightarrow$ CDF for disease transmission, $1 - F_{trans}(x)$ gives proportion of transmission due to cases with # secondary $> x$

1. Define proportion p of transmission we are interested in
2. x such that $1 - F_{trans}(x) = p$
3. Proportion responsible are those with # secondary $> x$

When based on discrete Poisson mixture $\rightarrow$ unlikely that there exists an integer x such that $1 - F_{trans}(x) = p$

- **Endo et al. (2020):** continuous approximation of discrete distribution
- Account for uncertainty around proportions
  - define x_1,x_2 such that $1 - F_{trans}(x_2) < p < 1 - F_{trans}(x_1)$
  - proportion responsible given by a range

Data examples

Fit Poisson mixtures to three **COVID-19 datasets** using MLE

- Empirical offspring distribution for
  - 290 cases in Hong Kong Adam et al. (2020)
  - 84 965 cases in India Laxminarayan et al. (2020)
  - 795 cases in Rwanda

→ Compare distributions in terms of AIC and GOF

- Akaike weights to quantify model selection uncertainty

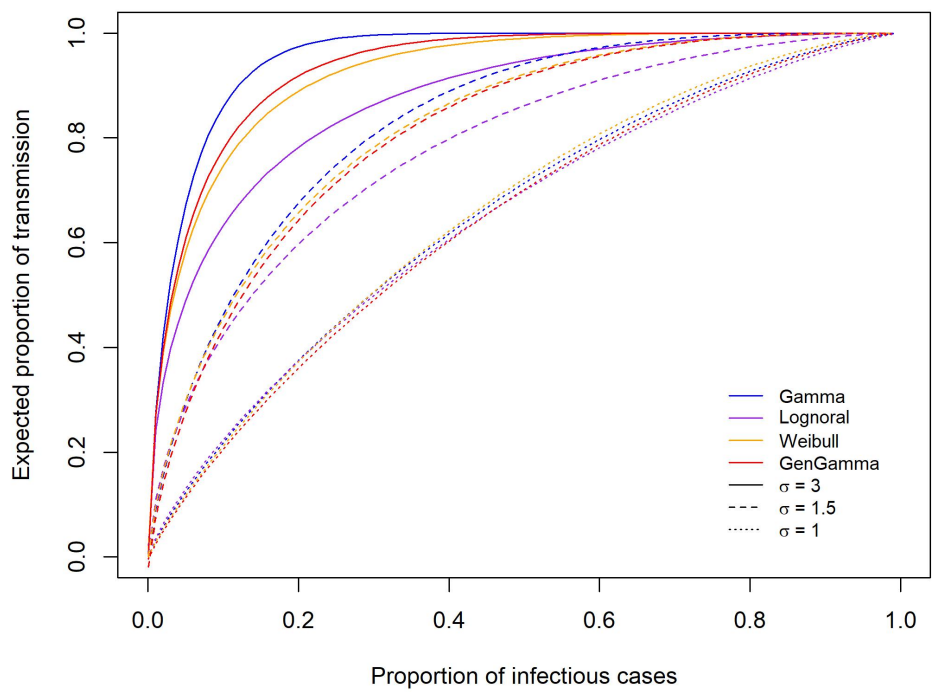
→ Different conclusions regarding superspreading potential, based on $p_{80\%}$?

Simulation study

As overdispersion ↗

- bias in variance estimates increases
- substantial difference between distributions

→ Inference of heterogeneity based on the 'wrong' distribution may be biased

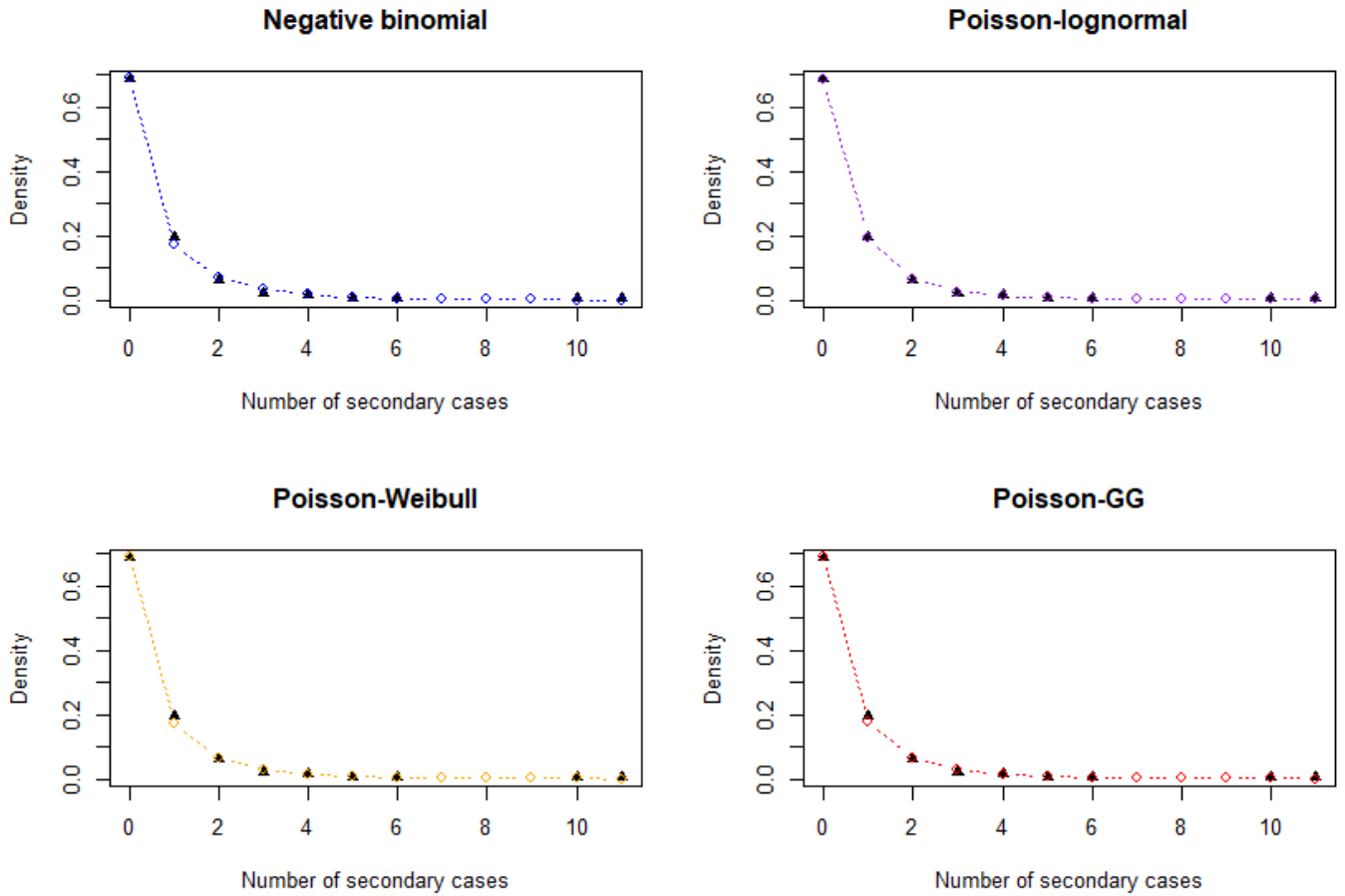


Data examples

Dataset	Distribution	R (95%CI)	$p_{80\%}$ (95%CI)	AIC	w_i
Hong Kong	NB	0.583 (0.448 - 0.718)	0.288 (0.208 - 0.345)	593.925	0.078
	POLN	0.587 (0.456 - 0.779)	0.332 (0.236 - 0.438)	590.009	0.551
	POWB	0.580 (0.445 - 0.745)	0.294 (0.223 - 0.358)	591.747	0.231
	POGG	0.580 (0.3789 - 0.724)	0.303 (0.279 - 0.325)	592.738	0.141
India	NB	0.484 (0.480 - 0.494)	0.319 (0.314 - 0.324)	163974.5	0.000
	POLN	0.484 (0.477 - 0.491)	0.373 (0.367 - 0.379)	162980.6	1.000
	POWB	0.483 (0.476 - 0.489)	0.322 (0.318 - 0.327)	163530.8	0.000
	POGG	0.484 (0.477 - 0.490)	0.333 (0.332 - 0.335)	163286.5	0.000
Rwanda	NB	0.259 (0.216 - 0.302)	0.323 (0.223 - 0.390)	1015.261	0.157
	POLN	0.260 (0.219 - 0.311)	0.389 (0.318 - 0.459)	1013.073	0.468
	POWB	0.259 (0.217 - 0.311)	0.331 (0.241 - 0.394)	1014.350	0.247
	POGG	0.259 (0.216 - 0.301)	0.344 (0.337 - 0.350)	1015.667	0.128

* Poisson-lognormal best fit based on AIC
* Considerable differences in expected $p_{80\%}$ when based on distribution of ν, compared to NB
    * ranges mostly overlapping when based on complete offspring distribution

Hong Kong data: NB, POGG, (POWB) don't adequately capture proportion of cases generating one secondary case → overestimating superspreading potential



Conclusions

Importance of model comparison

- NB often underestimates proportion of cases with only 1 secondary case
  - → overestimates importance of SSEs

- Studies can also be compared by $p_{80\%}$ instead of k
  - can be obtained for any distribution
  - more intuitive interpretation
  - be aware of the two different approaches!

Importance of correctly quantifying heterogeneity

- 'Superspreading potential' needs to be taken in account when modeling disease control / planning control strategies
  - In case of high overdispersion (i.e. low $p_{80\%}$), control measures should focus on limiting potential SSE
    - restricting large events, avoid crowding, ...
  - For higher $p_{80\%}$, additional control measures needed focusing on regular contacts

Future work

- Inference from final size data
- Disentangle heterogeneity coming from variation in contact rates vs. variation in viral shedding, to improve control measures
- Other distributions to describe contact process
  - Poisson process is likely a simplification

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