

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

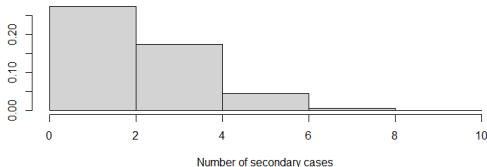
Superspreaders: infect substantially more individuals than others

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

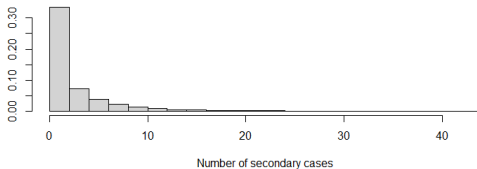
Population estimate of R_0 does not account for individual variation

→ Overdispersed offspring distribution with mean R_0

No individual variation



Individual variation



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
 - 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 $\nu \sim \text{Gamma}$
 - = **negative binomial offspring distribution** → heterogeneity quantified by dispersion parameter k
 - * $k < 1$: substantial superspreading
 - * lower k = increased heterogeneity
 - 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%
- 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

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

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

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 $\hat{\sigma}_i$

→ 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 $\nu \rightarrow$ **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

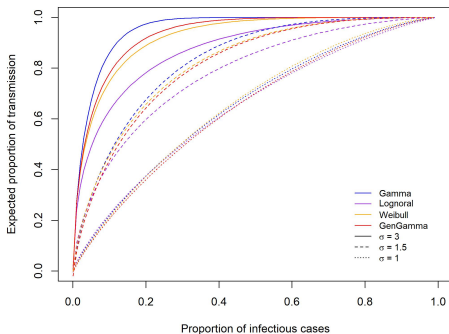
- * Empirical offspring distribution for
 - * 290 cases in Hong Kong Adam et al. (2020)
 - * 84 965 cases in India Laxminarayan et al. (2020)
 - * 795 cases in Rwanda
- Compare distributions in terms of AIC and GOF
 - * Akaike weights to quantify model selection uncertainty
- Different conclusions regarding 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

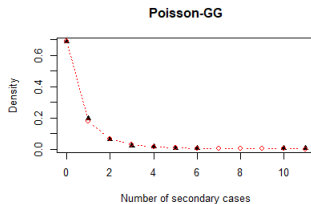
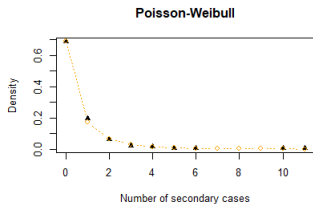
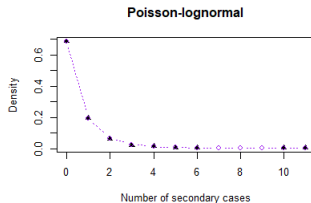
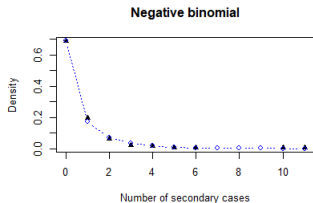


Data examples

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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