Infectious disease modelling

Quantifying the superspreading potential

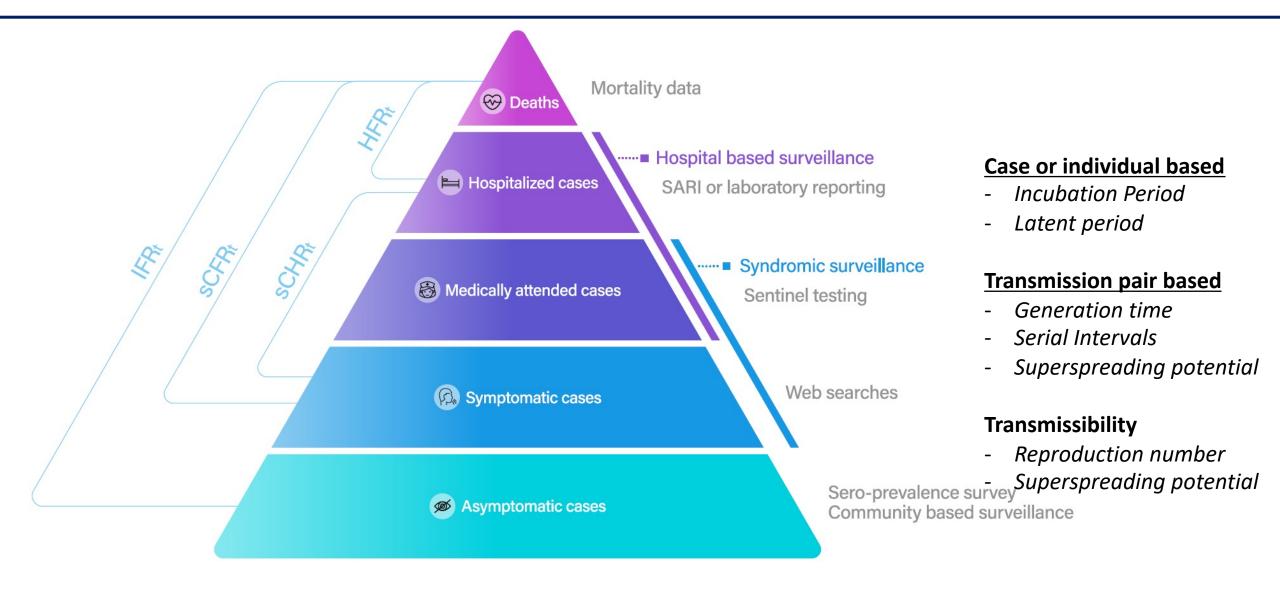
Prof. Sukhyun Ryu





After this course,

• In community epidemics, superspreading can be quantified and described.



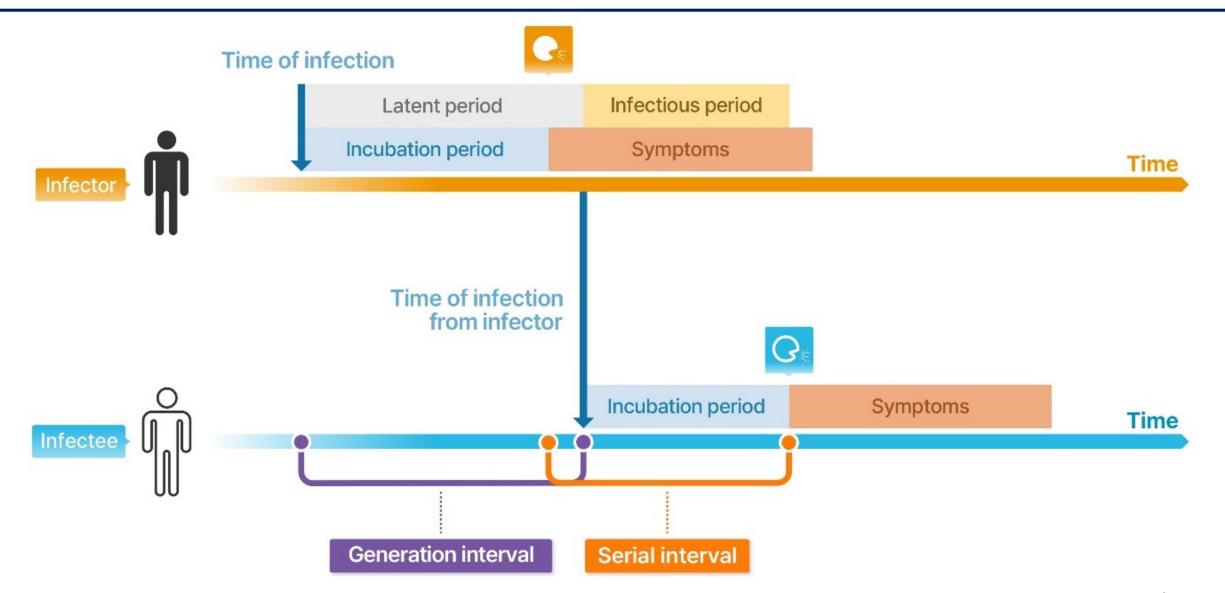
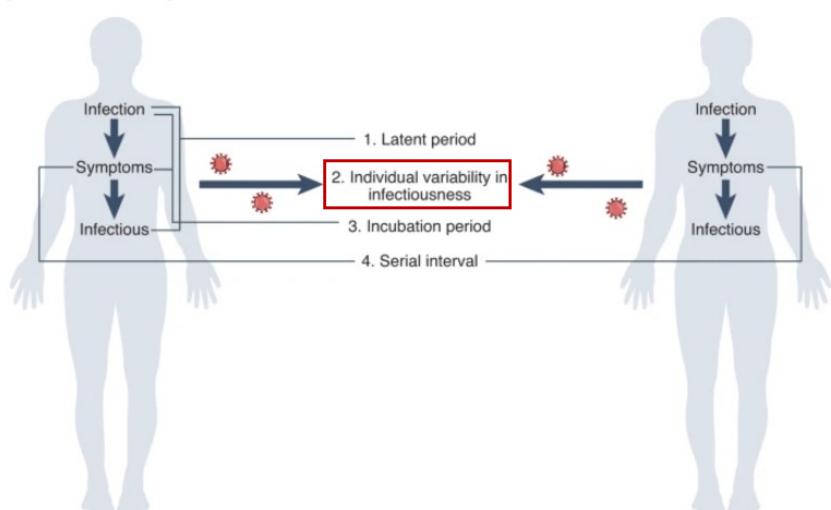


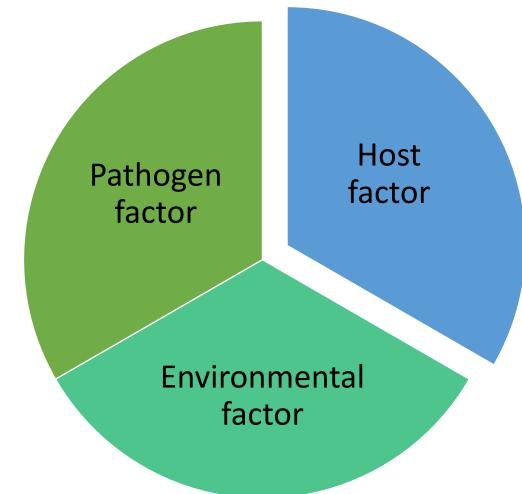
Fig. 1: Epidemiological parameters of SARS-CoV-2 transmission.



Individual variability of infectiousness

- Virulence
- Co-infectionwith another pathogen

- Crowding
- Inter-hospital transfer



- Physiological factors
- Behavioural factors
- Immunological factors

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- 1. Measures for transmissibility
- 2. Basic reproduction number
- 3. Probability distribution
- 4. Superspreading potential
- 5. Practice

Measures for transmissibility

Infection attack rate

- The proportion of a population (subgroup) infected over the course of an epidemic

$$attack\ rate = \frac{number\ of\ new\ cases\ in\ the\ population\ at\ risk}{number\ of\ persons\ at\ risk\ in\ the\ population}$$

Secondary (infection) attack rate

- The proportion of individuals infected in a semi-closed setting (e.g., households) in an outbreak caused by an index case (ideally accounting for pre-existing immunity)

Measures for transmissibility

- Basic reproductive number (R₀)
 - The average number of secondary cases generated by an index case when an epidemic begins in a completely susceptible population

Effective reproduction number (R_t)

Parameter for superspreading potential ?

Measures for transmissibility

- Basic reproductive number (R₀)
 - The average number of secondary cases generated by an index case when an epidemic begins in a completely susceptible population

• Effective reproduction number (R_t)

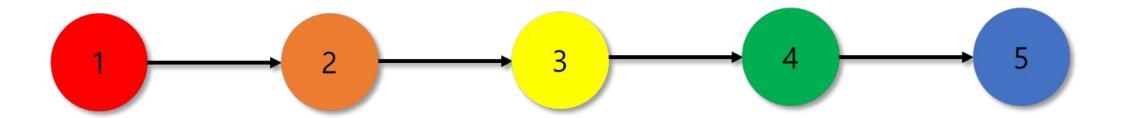
Overdispersion parameter (K)

Contents

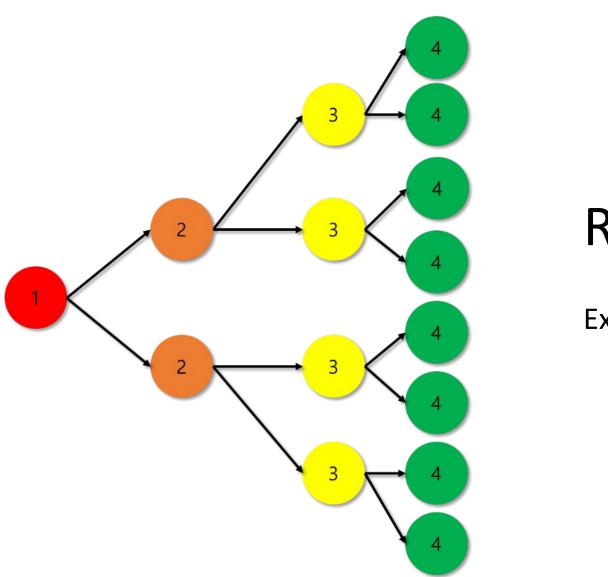
- 1. Measures for transmissibility
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Basic reproductive number

- The <u>average number</u> of secondary cases generated by an index case when an epidemic begins in a completely susceptible population.



$$R_0 = 1$$



$$R_0 > 1$$

Ex)
$$R_0 = 2$$

- R₀ < 1 → the disease will eventually disappear
- $R_0 = 1 \rightarrow$ the disease will become endemic
- $R_0 > 1 \rightarrow$ there will be endemic

Info. of parameters, susceptible populations, etc

Compartment model with differential equations

Info. of offspring distribution

Likelihood model based on the probability distribution



$$R_0 = \frac{\beta S(0)}{\gamma N} \approx R_0 = \frac{\beta}{\gamma}$$

$$R_0 = \frac{\beta S(0)}{\gamma N} \approx R_0 = \frac{\beta}{\gamma} \qquad R = -\frac{\log\left(\frac{1-AR}{S_0}\right)}{AR - (1-S_0)}$$

$$Y \sim Poisson(\lambda)$$

Poisson distribution

Article Talk

From Wikipedia, the free encyclopedia

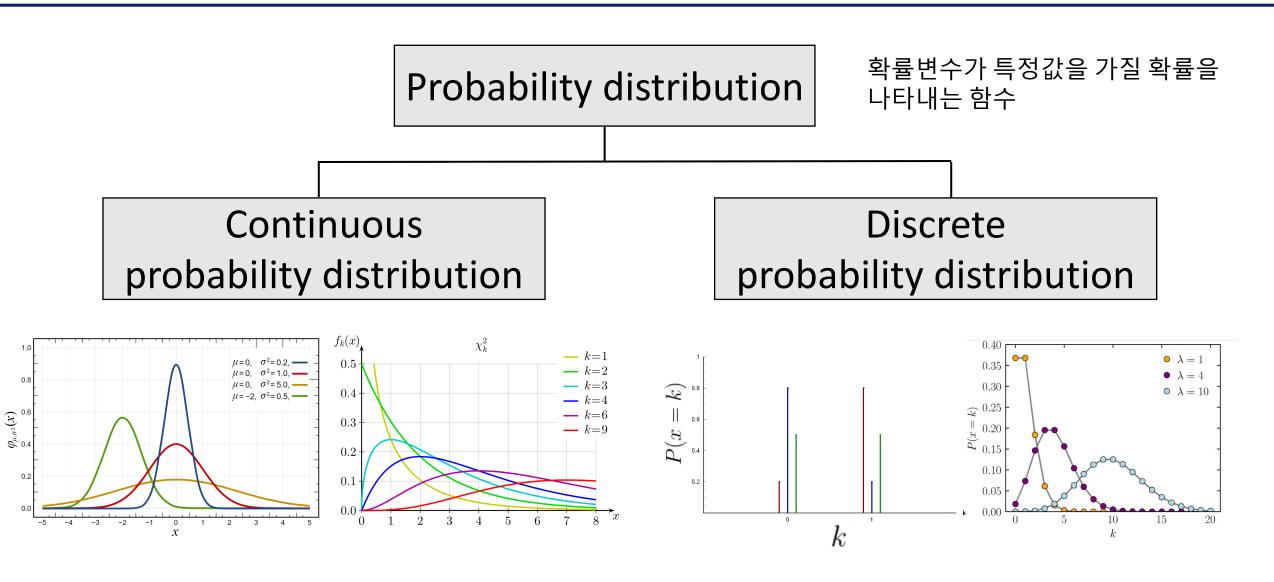
In probability theory and statistics, the **Poisson distribution** (/pwasson/) is a discrete probability distribution that expresses the probability of a given number of events occurring in a fixed interval of time if these events occur with a known constant mean rate and independently of the time since the last event.^[1] It can



Siméon Denis Poisson (1781-1840)

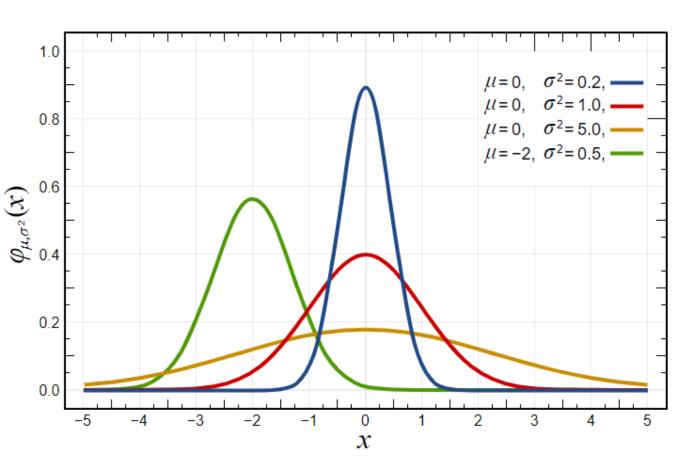
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https://en.wikipedia.org/wiki/Probability_distributioff

Normal distribution

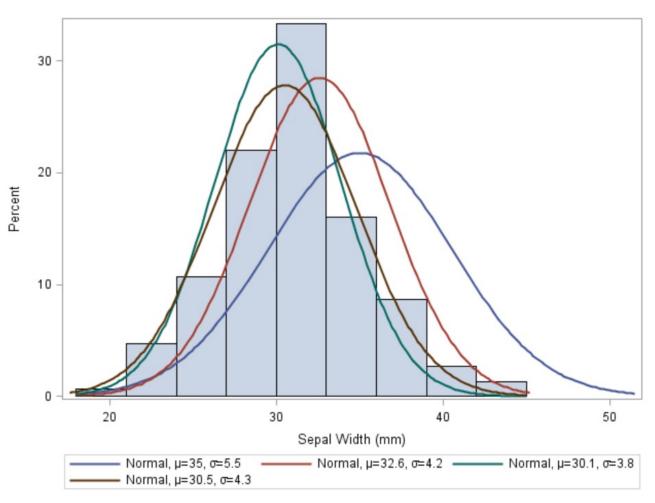


- Continuous probability distribution
- General form of its probability density function(PDF):

$$f(x_i|\theta) = \frac{1}{\sqrt{2\pi\sigma^2}} e^{\frac{-(x-\mu)^2}{2\sigma^2}}$$

Mean: µ

Standard deviation: σ



- Maximum likelihood estimation (MLE)
- Estimate the most appropriate parameters among the assumed probability distribution forms.

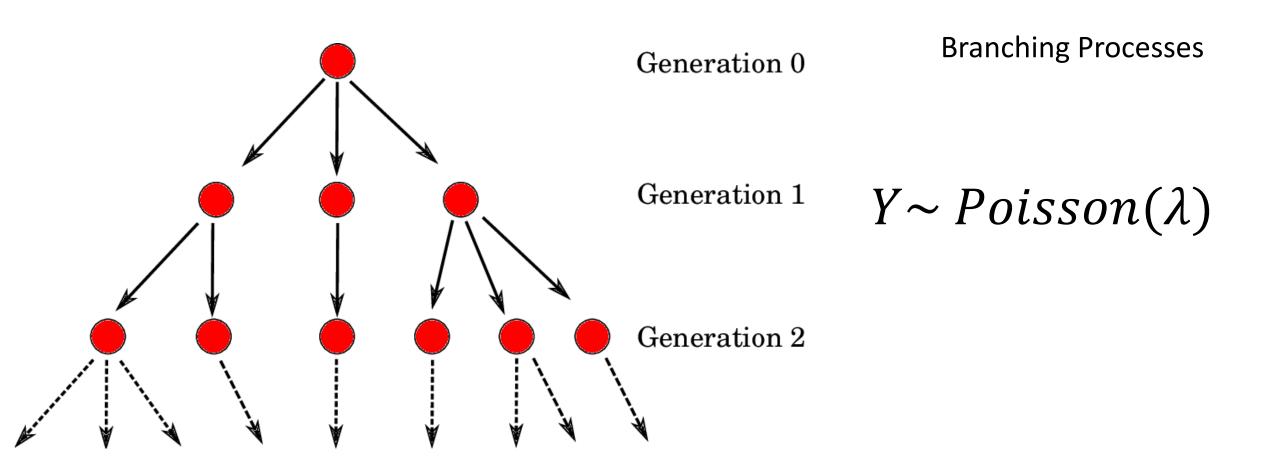
$Y \sim Poisson(\lambda)$

Y: Expected value of a specific event occurring (i.e., Infected Cases)

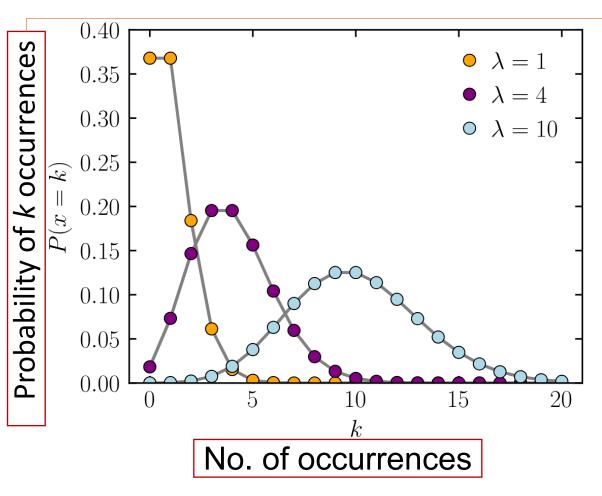
 λ : Mean no. of times a specific event occurs within a time unit $(i.e., R_0)$



No. secondary infected cases from a primary case~ $Poisson(R_0)$



$$f(k;\lambda) \sim Pois(\lambda)$$



Probability density function (PDF):

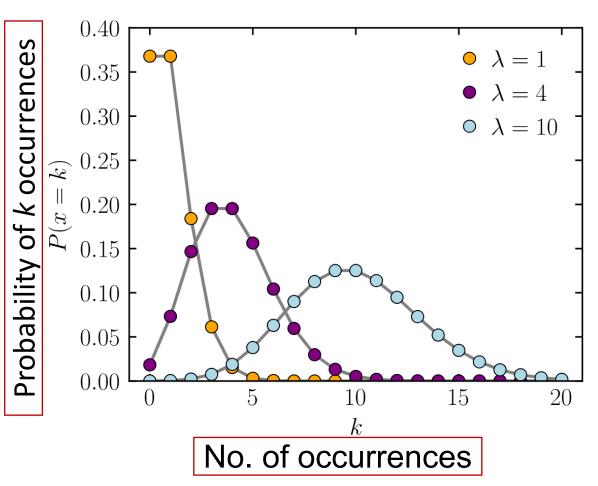
$$f(k;\lambda) = \Pr(X=k) = rac{\lambda^{\underline{k}}e^{-\lambda}}{\underline{k!}},$$

where

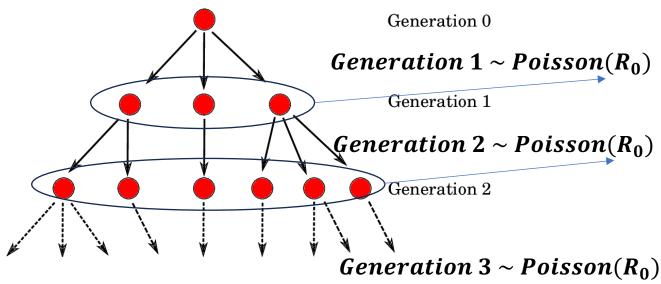
- ullet k is the number of occurrences ($k=0,1,2,\ldots$)
- e is Euler's number (e=2.71828...)
- •! is the factorial function.

- $E(X) = \lambda$
- $Var(X) = \lambda$

 $f(k;\lambda) \sim Pois(\lambda)$



 $Y \sim Poisson(\lambda)$

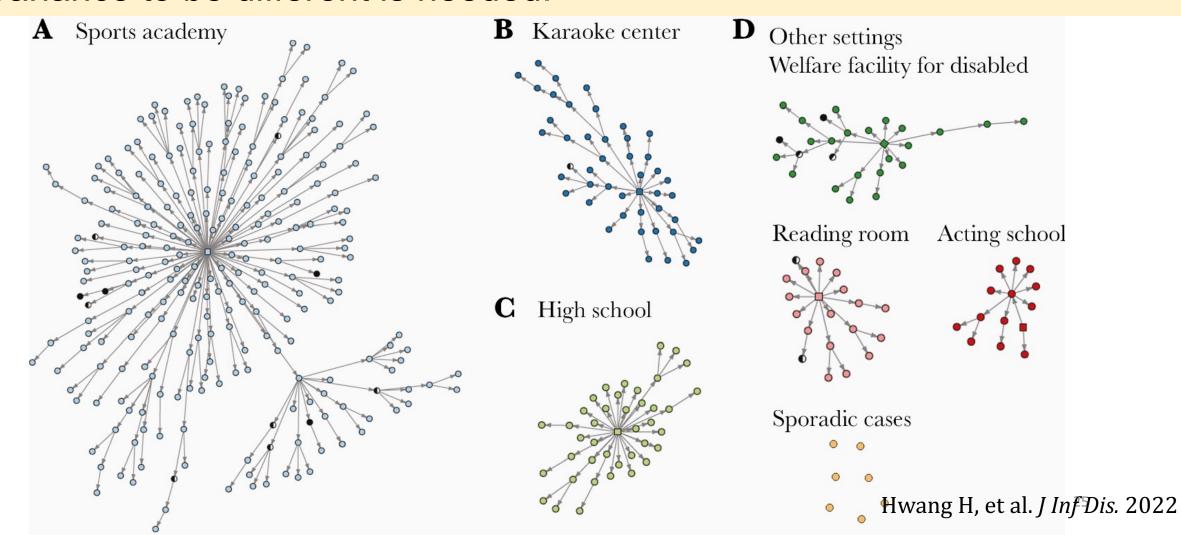


- $E(X) = \lambda$ $Var(X) = \lambda$



https://en.wikipedia.org/wiki/Probability_distributio?

More accurate model than the <u>Poisson distribution</u> by allowing the mean and variance to be different is needed.



 $f(k;\lambda) \sim Pois(\lambda)$



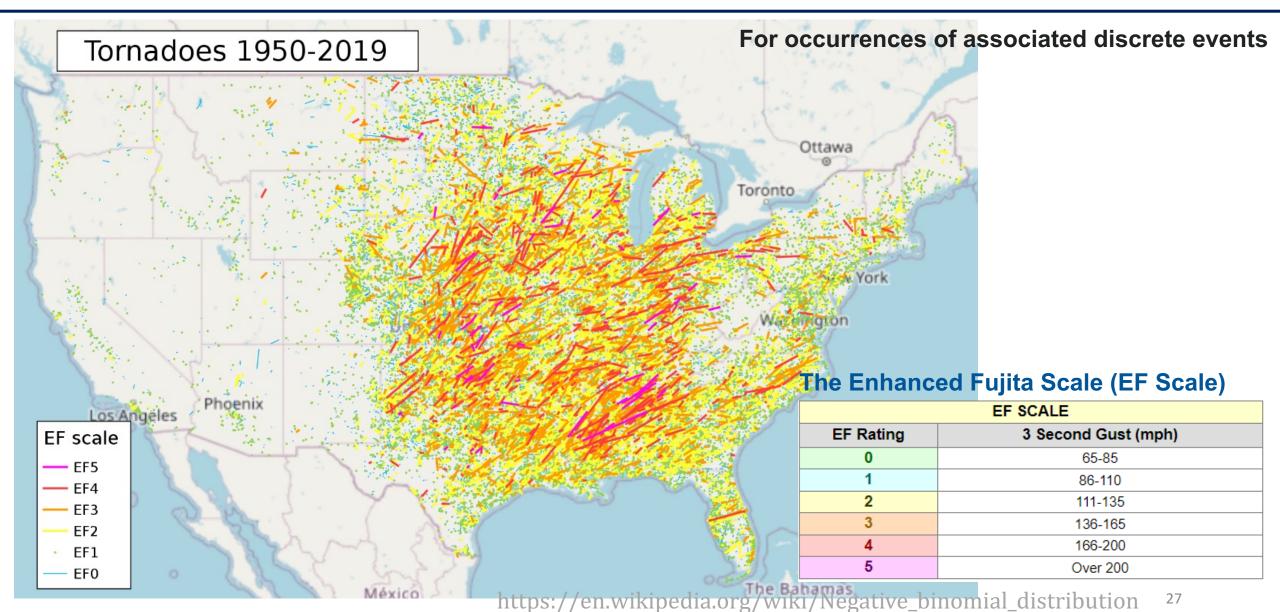
Siméon Denis Poisson (1781-1840) https://en.wikipedia.org/wiki/Probability_distribution

 $Y \sim NB(r, p)$



Blaise Pascal (1623-1662)

https://en.wikipedia.org/wiki/Blaise6_Pascal



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≡ Superspreading event

Article Talk

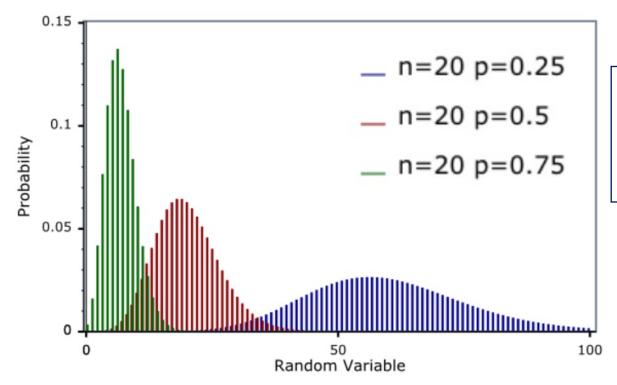
From Wikipedia, the free encyclopedia

A superspreading event (SSEV) is an event in which an infectious disease is spread much more than usual, while an unusually contagious organism infected with a disease is known as a superspreader. In the context of a human-borne illness, a superspreader is an individual who is more likely to infect others, compared with a typical infected person. Such superspreaders are of particular concern in epidemiology.

- Negative binomial distribution
 - Distribution reflecting variation in individual infectiousness in the Poisson distribution
- Parameters
 - Mean (R_0)
 - Variance (kappa): Variation in individual infectiousness

Smaller K, \rightarrow Greater the variation (i.e., Highly likelihood SSE)

$$Y \sim NB(r, p)$$



Probability density function

$$NB(r,p) = {k+r-1 \choose k} \cdot (1-p)^k pr$$

- r No. successes by the trial is stopped
- Probability of success in each trial
- *k* No. of failures

•
$$E(X) = \frac{r(1-p)}{p}$$
•
$$Var(X) = \frac{r(1-p)}{p^2}$$

•
$$Var(X) = \frac{r(1-p)}{p^2}$$

Negative binomial distribution

$Y \sim Poisson(\lambda)$



No. secondary infected cases from a primary case \sim Poisson(R_0)

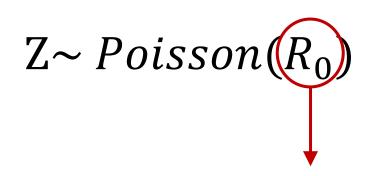
$Z \sim Poisson(R_0)$

Offspring distribution with mean R_0 : Not applicable when the variance is greater or less than the mean

(Failed to show heterogeneity)



Alternative: Negative binomial distribution (Poisson—Gamma mixture)



Negative binomial distribution (Poisson-Gamma mixture)

n 📮

Assuming $Gamma(\Gamma)$ distribution

$$R_0 \sim \Gamma\left(\alpha, \frac{p}{1-p}\right)$$

 α : shape parameter

p/1-p : scale parameter

p: probability

$$P(Z=z) = \frac{\Gamma(k+z)}{z! \Gamma(k)} \left(\frac{k}{k+R_0}\right)^k \left(\frac{R_0}{k+R_0}\right)^z$$

$$Z \sim NB(R_0, k)$$

Gamma-Poisson mixture

$$\int_{0}^{\infty} f_{Poisson(\lambda)}(z) \times f_{Gamma(\alpha, \frac{p}{1-p})}(\lambda) d\lambda$$

$$= \int_{0}^{\infty} \frac{\lambda^{z}}{z!} e^{\lambda} \times \frac{1}{\Gamma(\alpha)} \left(\frac{p}{1-p}\lambda\right)^{\alpha-1} e^{-\frac{p}{1-p}\lambda} \left(\frac{p}{1-p}d\lambda\right)$$

$$= \left(\frac{p}{1-p}\lambda\right)^{\alpha} \frac{1}{z!\Gamma(\alpha)} \int_{0}^{\infty} \lambda^{\alpha+z-1} e^{-\lambda\frac{p+1-p}{1-p}} d\lambda$$

$$= \left(\frac{p}{1-p}\lambda\right)^{\alpha} \frac{1}{z!\Gamma(\alpha)} \Gamma(\alpha+z) (1-p)^{z+\alpha} \int_{0}^{\infty} f_{Gamma(\alpha, \frac{p}{1-p})}(\lambda) d\lambda$$

$$= \frac{\Gamma(\alpha+z)}{z!\Gamma(\alpha)} (1-p)^{z} p^{\alpha}$$

$$\binom{z+r-1}{z}$$

Gamma-Poisson Mixture

$$f(z;\alpha,p) = \frac{\Gamma(\alpha+z)}{z!\Gamma(\alpha)} (1-p)^z p^{\alpha}$$

*
$$\alpha = k$$
, $p = \frac{k}{k+\mu}$ 대입 $(\mu = R_0)$

$$P(Z = z) = \frac{\Gamma(k+z)}{z! \Gamma(k)} \left(\frac{k}{k+R_0}\right)^k \left(\frac{R_0}{k+R_0}\right)^z$$
$$Z \sim NB(R_0, k)$$

$$E(Z) = \mu$$

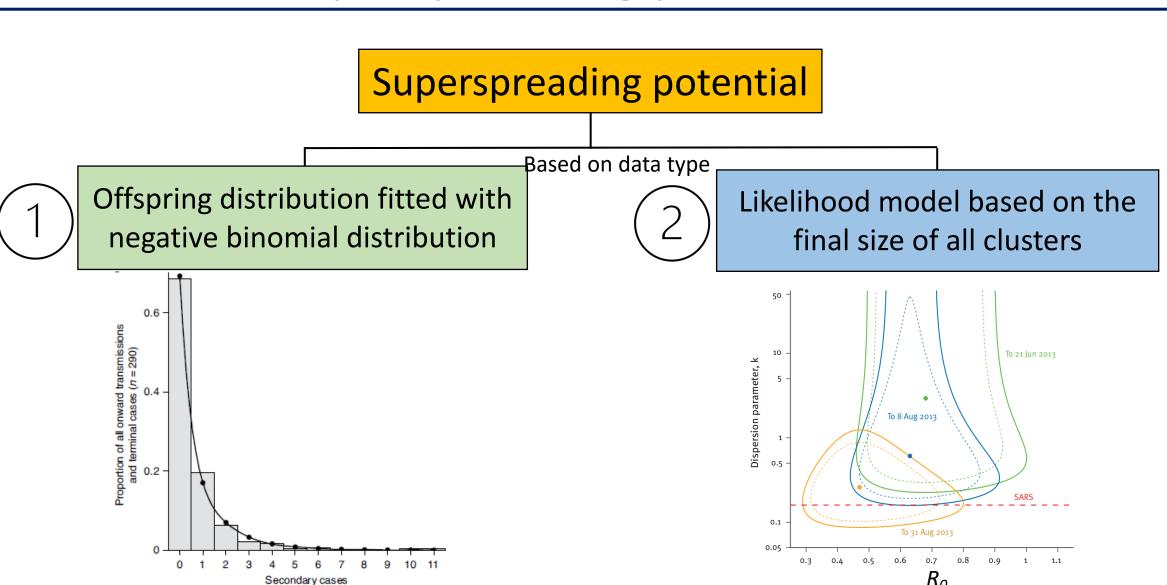
$$Var(Z) = \mu + \frac{\mu^2}{k} = R_0 + \frac{{R_0}^2}{k}$$

Lower the k, larger the variance

 \Rightarrow Increase of heterogeneity

k: shape parameter and dispersion parameter

 R_0 : basic reproduction number



Adam DC, et al. Nat Med. 2021

Kucharski AJ, et al. Eurosurveillance. 2015

Superspreading potential

Superspreading potential

Info. of infector-infectee pair

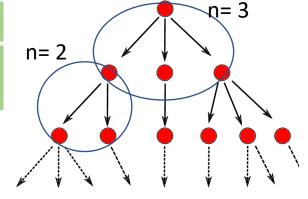
Info. of final size of cluster

Offspring distribution fitted with negative binomial distribution

Likelihood model based on the final size of all clusters

No. of secondary cases (i.e., infectee) from each infectors

Infector	Α	В	С	D	E	F	G	Н
No. offspring	11	10	6	6	5	4	4	



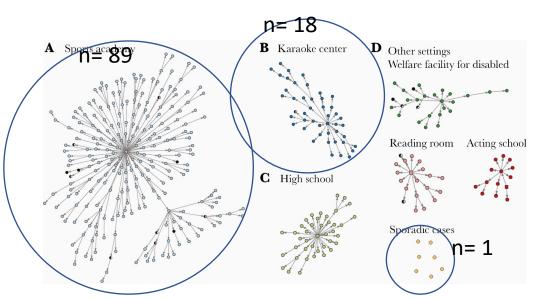
Superspreading potential

Superspreading potential

Offspring distribution fitted with negative binomial distribution

Likelihood model based on the final size of all clusters

1		_		•
Final	No.	Of (cluster	size

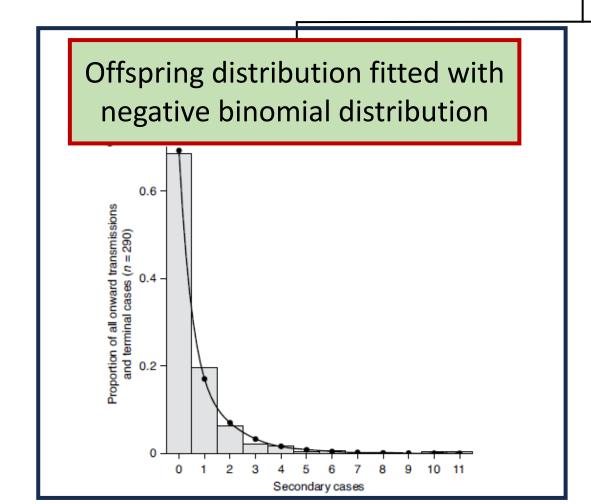


	Number of MERS clusters of a given size						
Cluster size	Breban et al. [6] ^c	Cauchemez et al. [7]	Poletto et al. [5] ^c				
1	11	27	42				
2	2	2	7				
3	3	4	2				
4	1	3	-				
5	2	2	2				
7	_	1	_				
10	-	-	1				
13	-	1	-				
22	_	-	1				
24	1	-	_				
26 K11	charski AI	et al <i>Furo</i> s	urveillance				

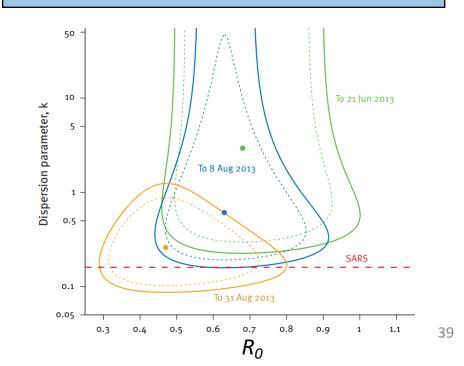
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Superspreading events

Superspreading potential



Likelihood model based on the final size of all clusters



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R package for Fitting Distributions

fitdistr

Maximum-likelihood Fitting of Univariate Distributions

Description

Maximum-likelihood fitting of univariate distributions, allowing parameters to be held fixed if desired.

Usage

```
fitdistr(x, densfun, start, ...)
```

Arguments

A numeric vector of length at least one containing only finite values.

Either a character string or a function returning a density evaluated at its first argument.

Distributions "beta", "cauchy", "chi-squared", "exponential", "gamma", "geometric", "log-normal", "lognormal", "logistic", "negative binomial", "normal", "Poisson", "t" and "weibull" are recognised, case being ignored.

A named list giving the parameters to be optimized with initial values. This can be omitted for some of the named distributions and must be for others (see Details).

Additional parameters, either for densfun or for optim. In particular, it can be used to specify bounds via lower or upper or both. If arguments of densfun (or the density function corresponding to a character-string specification) are

included they will be held fixed.

library(MASS)

"fitdistr" function estimates the parameters '\(\mu'\) and 'size' of the log normal distribution

- 1 Add data
- 2 Plot histogram
 - for distribution assumption
- 3 Negative binomial distribution fitting by MLE fitting
- Estimates the R_0 and k
- (4) Plot PDF
- \bigcirc 95% confidence interval for R_0 and k

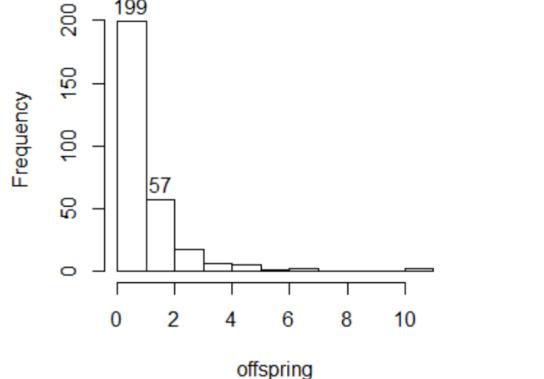
1 Add data

```
1  # offspring distribution
2  offspring <- c(rep(0,199),rep(1,57),rep(2,18),rep(3,6),rep(4,5),5,rep(6,2),10,11)
3  offspring
4  # frequency table
5  table(offspring)</pre>
8 7 199
```

2 Plot histogram

- for distribution assumption

```
7 # plot histogram
8 hist(offspring)
9 hist(offspring, right = F)
생략또는 right =T: ~이상
Right =F: ~미만
```



- (3) Negative binomial distribution fitting by MLE
 - Estimates the R_0 and k

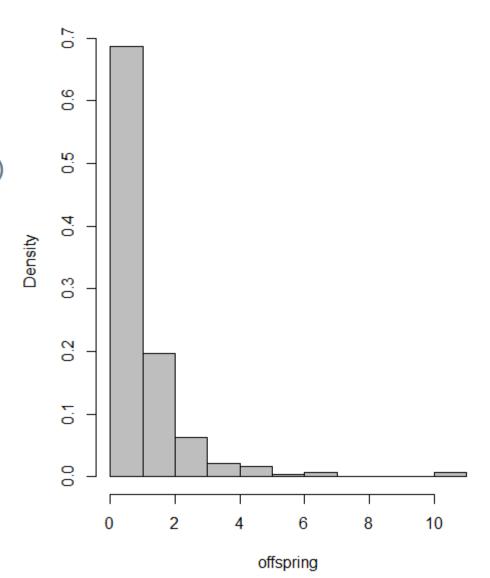
```
# fitting negative binomial distribution
library(MASS)
fit <- fitdistr(offspring, "negative binomial")
fit

Fitting NB distribution by MLE</pre>
```

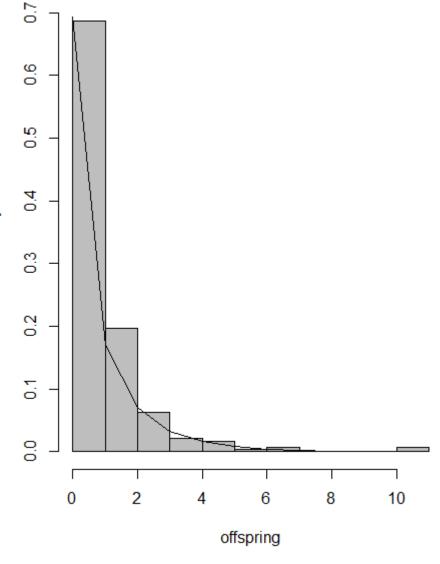
```
> fit \hat{k} size \hat{R}_0 mu 0.42580272 0.58275962 (0.08797182) (0.06899078)
```

4 Plot PDF

```
# plot PDF
hist(offspring, prob=T, col="gray",right = F)
```



4 Plot PDF



(5) 95% confidence interval of R_0 and k33 # Estimate 95th percentile of size and mu 34 conf interval <- confint(fit, level = 0.95) 35 print(conf interval) > # Estimate 95th percentile of size and mu > conf_interval <- confint(fit_nb, level = 0.95)</pre> > print(conf_interval) 2.5 % 97.5 % size 0.2533811 0.5982243 mu 0.4475402 0.7179791

Summary

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References

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- Kucharachi AJ, et al. The role of superspreading in Middle East respiratory syndrome coronavirus (MERS-CoV) transmission. Eurosurveillance 2015
- Ryu S, et al. Transmission dynamics and control of two epidemic waves of SARS-CoV-2 in South Korea. *BMC Infectious Diseases 2021*
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- Ryu S, et al. Serial interval and transmission dynamics during the SARS-CoV-2 Delta variant predominance, South Korea. *Emerging Infectious Diseases* 2022
- Ryu S, et al. Effect of Nonpharmaceutical interventions on Transmission of Severe Acute Respiratory Syndrome Coronavirus 2, South Korea, 2020. *Emerging Infectious Diseases* 2020