Reproduction numbers and superspreading – how to measure disease transmission

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INI talk
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cmmid.github.io/ncov
Village with 1,000 people and one person infected with malaria

Ross R, *Prevention of Malaria*, 1911

Acarologiste via WikiCommons
Village with 1,000 people and one person infected with malaria

48,000 mosquitoes

Ross R, *Prevention of Malaria*, 1911
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Village with 1,000 people and one person infected with malaria

- 48,000 mosquitoes
- 12,000 bite humans

Ross R, *Prevention of Malaria*, 1911

Acarologiste via WikiCommons
Village with 1,000 people and one person infected with malaria

- 48,000 mosquitoes
- 12,000 bites to humans
- 12 bites by infected humans

Ross R, *Prevention of Malaria*, 1911

Acarologiste via WikiCommons
Village with 1,000 people and one person infected with malaria

- 48,000 mosquitoes
- 12,000 bite humans
- 12 bite infected humans
- 4 survive to be infectious

Ross R, *Prevention of Malaria*, 1911

Acarologiste via WikiCommons
Village with 1,000 people and one person infected with malaria

48,000 mosquitoes
12,000 bite humans
12 bite infected humans
4 survive to be infectious
1 bites another human

Ross R, Prevention of Malaria, 1911
Acarologiste via WikiCommons
“Basic Reproduction Rate of malaria, definition. The number of infections distributed in a community as the direct result of the presence in it of a single primary non-immune case.”

– George MacDonald, 1952
“Basic Reproduction Rate of malaria, definition. The number of infections distributed in a community as the direct result of the presence in it of a single primary non-immune case.”

– George MacDonald, 1952
Reproduction number
‘R’
New cases

- **R above 1**
- **R less than 1**
- **R = 1**

Initial cases

Time
If we could observe all transmission events, in theory could measure R directly...

... but generally not possible
Delay from case showing symptoms to person they infect showing symptoms given by the ‘serial interval’

Average growth in cases during this period given by R
If serial interval is 1 day and R=2...
If serial interval is 1 day and $R=2$...
If serial interval is 1 day and $R=2$...
If serial interval is 1 day and $R=2$...

... after 3 days would expect 8 times more new cases
Can estimate R if we know when the outbreak started... and with how many cases.
Can estimate R if we know when the outbreak started... and with how many cases... and how long the serial interval is...
Can estimate R if we know when the outbreak started... and with how many cases... and how long the serial interval is... and how many cases there have been over time.
Can estimate $R$ if we know when the outbreak started... and with how many cases... and how long the serial interval is... and how many cases there have been over time.
• By 16th January, 41 confirmed COVID-19 cases in Wuhan, China.
• Three cases detected abroad (2 in Thailand, 1 in Japan).
• By 16th January, 41 confirmed COVID-19 cases in Wuhan, China.

• Three cases detected abroad (2 in Thailand, 1 in Japan).

Based on flight patterns, likely to already been thousands of cases in Wuhan


Imai et al, *Imperial College Report 1*, 2020
Woman returning from Iran is B.C.'s sixth case of new coronavirus

Most Of Canada’s New Cases Of COVID-19 Are Linked To The U.S.

CASE 154

Case 154 is an imported case involving a 52-year-old British man.

He arrived in Singapore on Mar 6 and was confirmed to have COVID-19 infection on Mar 9 morning and is currently warded in an isolation room at NCID.
Early estimates suggested $R = 2.2$ (90% CI: 1.4–3.8)
R can change over time

Note: illustrative figure only!
R can change over time

Control measures introduced

New infections

Time

R > 1

R < 1

Note: illustrative figure only!
New infections

Time

R > 1

R < 1

Fully lift measures (i.e. same R as before)

Control measures introduced

Change in control measures

Allow higher risk activities

Allow lower risk activities

Keep measures

R can change over time

Note: illustrative figure only!
Serial interval vs generation time

Du et al, *EID*, 2020
Serial interval vs generation time

Du et al, *EID*, 2020
Serial interval vs generation time

Du et al, EID, 2020
Serial interval vs generation time

1st person infected

Infected 2nd person

1st case becomes symptomatic

Du et al, EID, 2020
Serial interval vs generation time

- **Generation time**
  - Infects 2nd person
- **Incubation period**
  - 1st person infected
  - 1st case becomes symptomatic

Du et al, *EID*, 2020
Serial interval vs generation time

![Diagram showing the relationship between serial interval, generation time, and incubation period.]

- **1st person infected**
- **2nd case becomes symptomatic**
- **1st case becomes symptomatic**

**Incubation period**

**Generation time**

**Serial interval**

*Du et al, EID, 2020*
Two methods for calculation

Gostic et al, MedRxiv, 2020
Two methods for calculation

A

B

C

$t_i$ infection
$t_s$ symptom onset

time

Gostic et al, MedRxiv, 2020
Estimating R over time

Singapore

Iran

Estimate of when infections occurred

Reported cases
Data generally reflects the past

Observed data reflect past transmission events.

- infection
- symptom onset
- hospital admission
- outpatient testing
- ICU admission
- death or recovery

Gostic et al, MedRxiv, 2020
Adjusting to look back in time can ‘smooth’ estimates

Gostic et al, MedRxiv, 2020
What influences R?
DOTS

Duration

Transmission probability

Opportunities

Susceptibility
Duration $\times$ Opportunities $\times$ Transmission probability $\times$ Susceptibility $= R$
Duration \times Opportunities (D \times O) \times Transmission probability (T) \times Susceptibility (S) = R
Can use real-time social mixing data to estimate $R$.

Post-lockdown in UK: “We found a 74% reduction in the average daily number of contacts observed per participant (from 10.8 to 2.8).”
Can use real-time social mixing data to estimate $R$.

Post-lockdown in UK:
“We found a 74% reduction in the average daily number of contacts observed per participant (from 10.8 to 2.8).”

Jarvis et al, *BMC Medicine*, 2020
Other digital data sources

Citymapper Mobility Index

https://citymapper.com/cmi/compare

Google Community Mobility Reports

https://www.google.com/covid19/mobility/
$$D \times O \times T \times S = R$$

- **Duration**
- **Transmission probability**
- **Opportunities**
- **Susceptibility**
Example: controlling HIV

\[ D \times O \times T \times S = R \]

Treatment

Safe sex

Fewer partners

PrEP
Example: controlling COVID-19

Isolation

Masks/PPE

Social distancing

Vaccine?

D x O x T x S = R
Basic reproduction number

\[D \times O \times T \times S = R\]

\[= R_0 \quad \text{...hence} \quad R_0 \times S = R\]
If $R_0 \times R = S$

...then $R < 1$ when $S < 1/R_0$
If $R_0 \times R = S$

...then $R < 1$ when $S < 1/R_0$

...so wouldn’t expect epidemics if proportion immune is above “herd immunity threshold” of $1 - 1/R_0$

i.e. if $R_0 = 2$, threshold would be 50%
Individual-level variation in transmission
COVID-19 transmission chains in Hong Kong
Estimating variation in transmission (method 1)
Estimating variation in transmission (method 1)

Index case → Secondary cases

Fit statistical distribution to data

80% of transmission generated by around 20% of infections

Adam et al, Research Square, 2020
Estimating variation in transmission (method 2)

80% of transmission generated by around 10 – 20% of infections

Grantz et al, hopkinsidd.github.io, 2020
Where are transmission clusters reported?
\[ D \times O \times T \times S = R \]

- **Duration**
- **Transmission probability**
- **Opportunities**
- **Susceptibility**
COVID-19 transmission chains in Hong Kong
Superspreading makes it less likely a single case will lead to sustained transmission.
Superspreading makes it less likely a single case will lead to sustained transmission.
‘Superspreading’ makes outbreaks more explosive once they take off...

...but less likely to spark initially
Isolation & contact tracing
Isolation, contact tracing & quarantine more successful if infection less transmissible and clear symptoms while infectious

Fraser et al, *PNAS*, 2014
Isolation, contact tracing & quarantine more successful if infection less transmissible and clear symptoms while infectious. 

Fraser et al, *PNAS*, 2014

Isolation, contact tracing & quarantine more successful if infection less transmissible and clear symptoms while infectious

Fraser et al, PNAS, 2014
He et al, Nature Med, 2020
“The probability of control decreases with long delays from symptom onset to isolation, fewer cases ascertained by contact tracing, and increasing transmission before symptoms.”
Need to consider level of infection as well as $R$.
As infections decline, can focus more on transmission links

Percentage of infected persons who were diagnosed while in quarantine

- In quarantine at the time of diagnosis
- Not in quarantine at the time of diagnosis
- No infections

57% of those who were diagnosed were in quarantine

[chart showing percentage]

covid.is/data
Finally

Thank you to all the public health teams, scientists and front-line medical staff working globally on COVID-19.

And all those whose rapid sharing of data and insights has provided an essential early evidence base.

For more on our group’s work: cmmid.github.io/ncov