Digital health and computational epidemiology

Lesson 5

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Infectious diseases

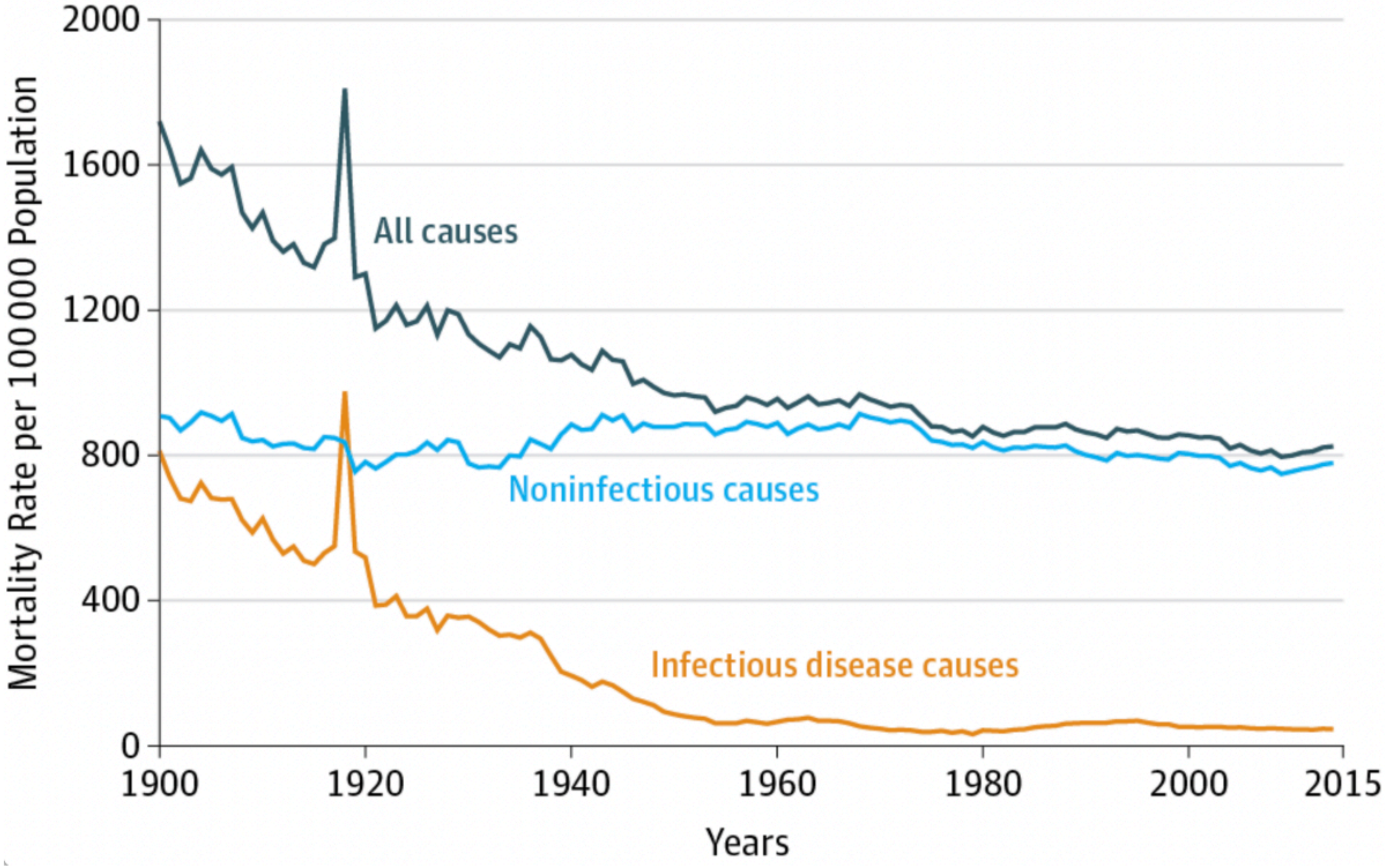
Infectious diseases

- So far, we haven't made any distinction regarding the type of health condition, either chronic, communicable or non-communicable.

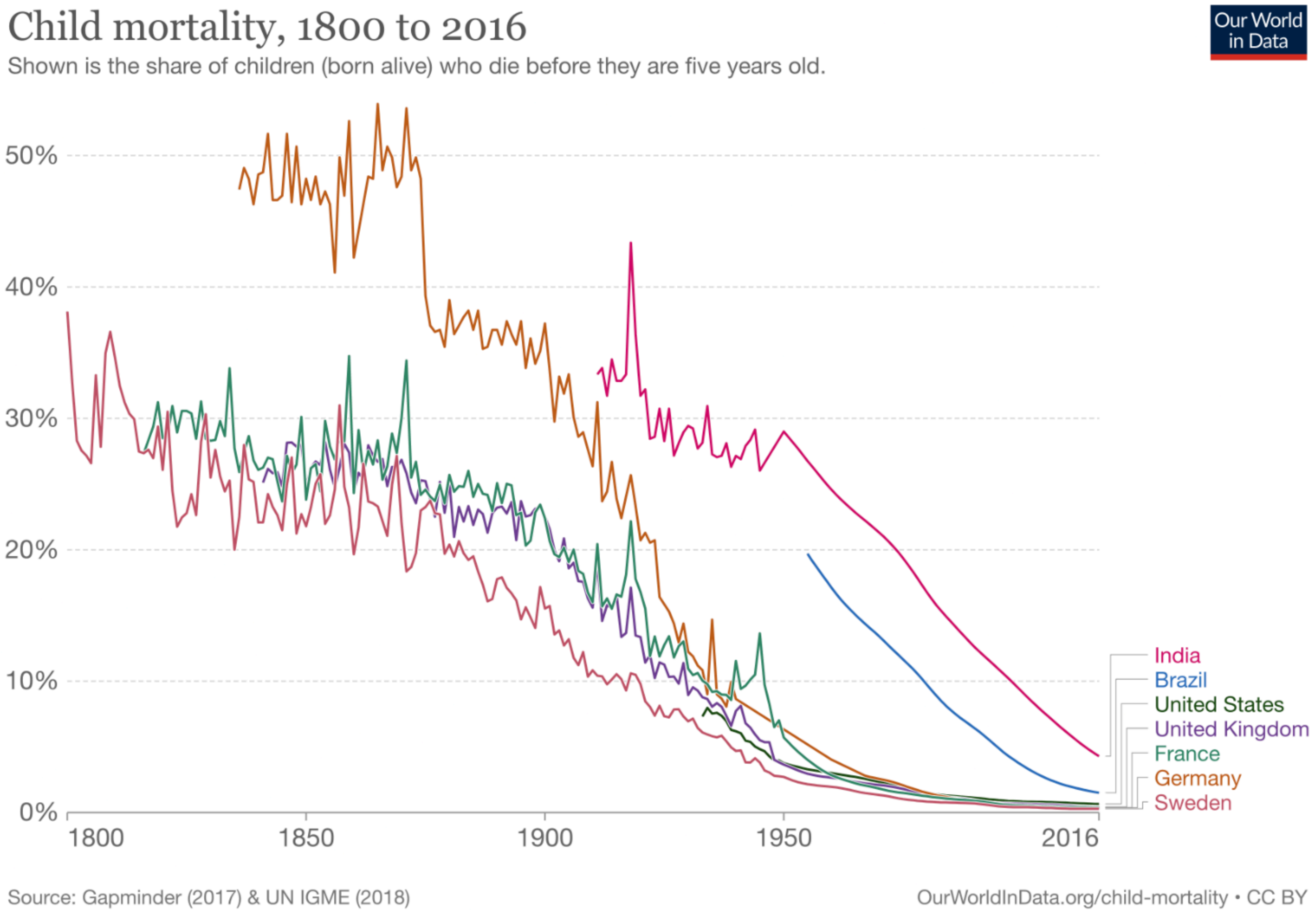
- In the next part of the course, we will focus on **infectious diseases** which represent a cornerstone example of mathematical and computational epidemiology.

- In this lecture, we will examine key concepts of infectious disease epidemiology that will be next translated into mathematical definitions.

Infectious diseases



Infectious diseases



Emergence

- Virtually all infectious diseases in humans are caused by viruses, bacteria, fungi, protozoa, and worms.

- These organisms are **parasites**, which means that they live in or on their **hosts**, from which they extract resources. In the infectious disease context, parasitic microorganisms causing diseases are typically called **pathogens**.

- Like any life form, pathogens evolve. In doing so, pathogens may all of a sudden be capable of infecting species that they haven't been capable of infecting before.

- For human infectious diseases, the original species from where the pathogen jumped - the reservoir species - is typically an animal species, and the disease is subsequently called **zoonosis, or zoonotic disease**.

Emergence

- Zoonoses account for about 6 out of 10 emerging infectious diseases

- Other sources are typically environmental, such as the soil or water.

- It should be noted that **not all infectious diseases are novel**, or *emerging*. Some, like chickenpox or Hepatitis C, have coevolved with humans for thousands or tens of thousands of years, and possibly even longer.

- For a jump from a reservoir to humans, humans need to be in contact with the reservoir species. Such condition happens more frequently in **specific parts of the world,** especially where species richness is high.

Zoonosis

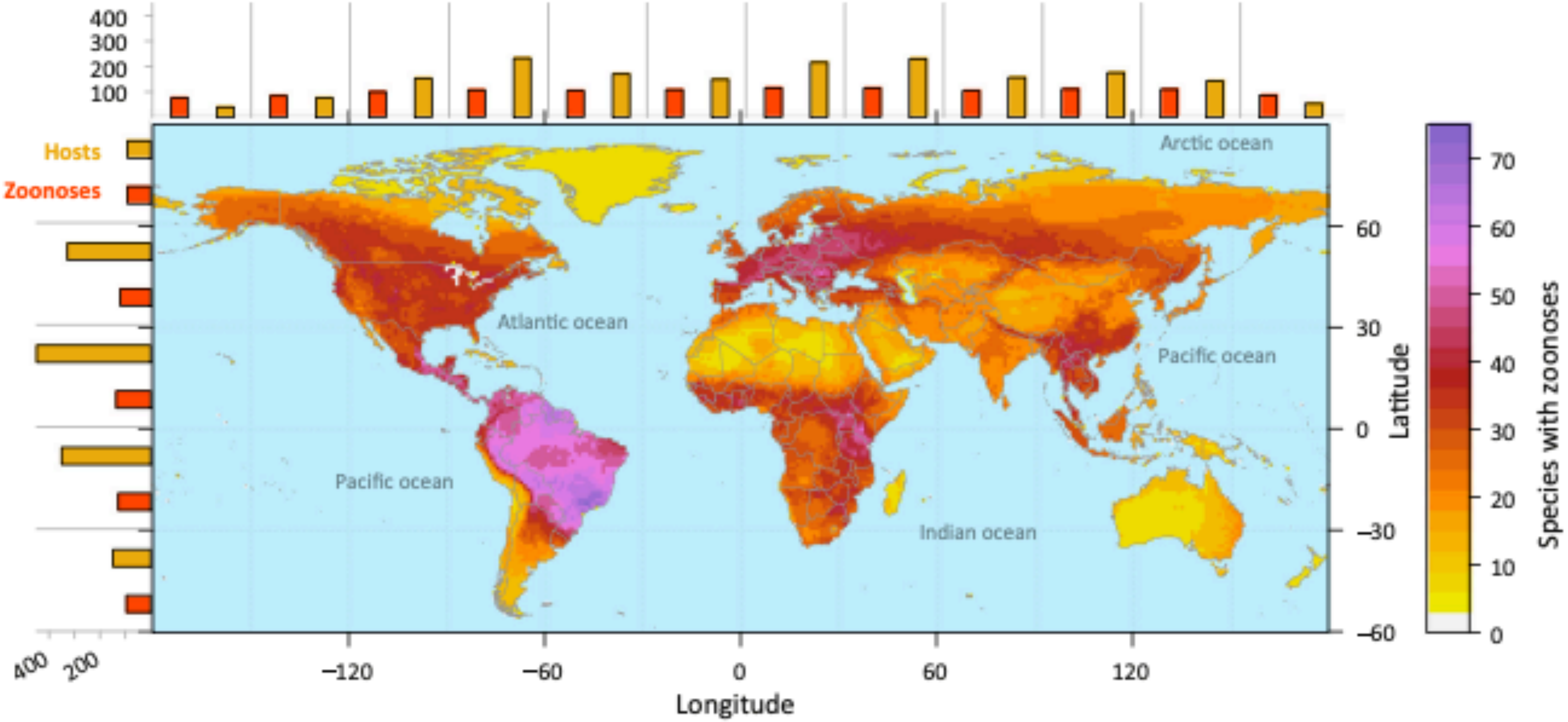
Trends in Parasitology

CellPress

Review

Global Patterns of Zoonotic Disease in Mammals

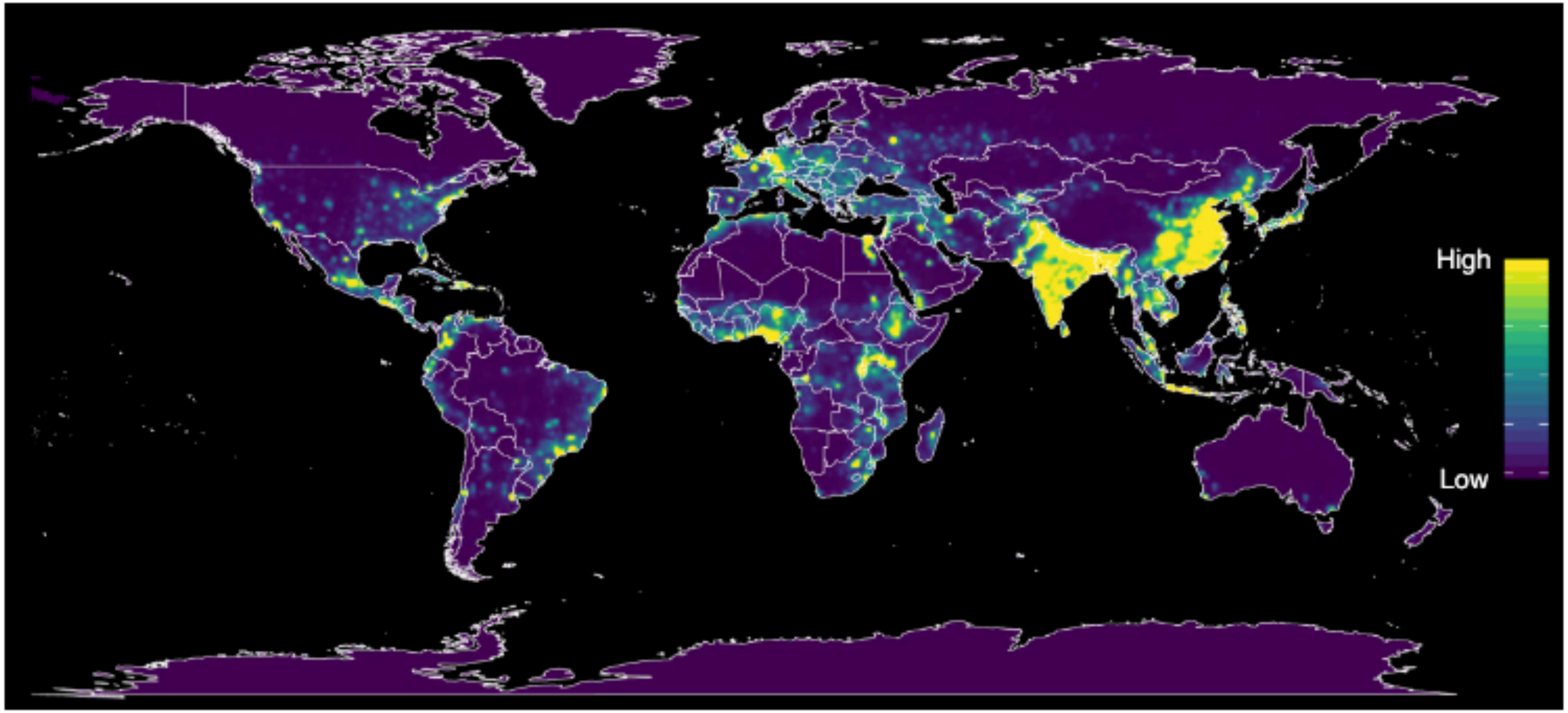
Barbara A. Han,[1,*] Andrew M. Kramer,[2] and John M. Drake[2,3]



Trends in Parasitology

Figure 1. Geographic Ranges of Zoonotic Mammal Hosts. Mammal reservoirs of zoonotic diseases are globally distributed, with noteworthy hotspots in Amazonia and Eurasia. Overlapping geographic ranges of mammal species recognized to carry one or more zoonotic diseases, with counts of unique host species (gold bars) and unique zoonotic pathogens (red bars) found within 30° latitudinal and longitudinal bands. This map depicts 5007 total wild mammal species from 27 orders.

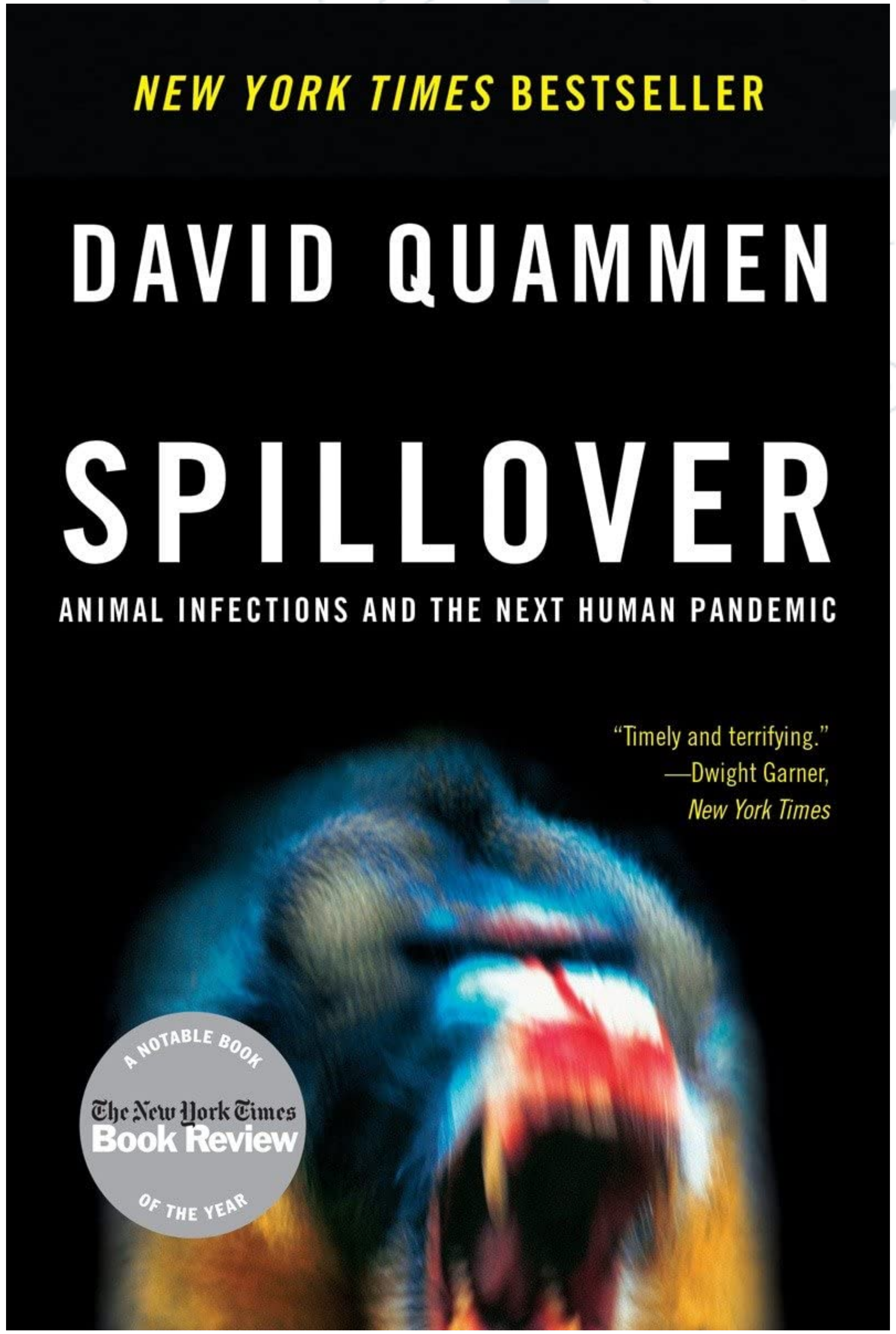
Zoonosis



A global map of predicted relative risk distribution of zoonotic events for the emergence of infectious disease from Allen et al. Nat Comm 2017.

Spill-over

- The event of a non-human pathogen jumping to a human host is called a **spill-over** event.
- The initial jump, however, is but the first step. The pathogen needs to be capable of establishing an infection in the new host.
- Even when an infection can be established, the pathogen now needs to succeed at the final step, which is to transmit to another individual of the new host species (**human-to-human transmission**).
- This newly started infection chain may still stutter and come to an end before it can take off and trigger an outbreak.
- If the chain does not break, the spillo-over will cause an outbreak or even a pandemic



Transmission

- The process of **contagion** is the key aspect of infectious diseases.
- **Transmission modes:** describe the physical method by which pathogens are transported from one host individual to another.
- **Transmission routes:** describe the physical exit and entrance location of the hosts.
- The transmission mode of cholera is **waterborne**; the transmission route is generally the **faecal-oral route**.
- Other modes: foodborne, vector-borne, airborne, body fluids.

Contacts

- The concept of **contact** in infectious disease strongly depends on the mode of transmission.
- When talking about infectious diseases, terms like “household contacts”, “contact tracing”, “contact networks”, and others are quite common.
- The nature of a “contact” will depend on the transmission mode, and specific pathogen we are considering.

Vector-borne transmission

- Vector-borne transmission denotes the mode by which pathogens are transmitted through a **vector**.
- Vectors can be any living organism.
- Typically, they are **mosquitoes** and ticks.
- Examples: malaria, Zika, yellow fever, dengue fever, chikungunya fever, West Nile fever, and Japanese encephalitis

Vector-borne transmission

Guzzetta *et al. BMC Medicine* (2020) 18:226
https://doi.org/10.1186/s12916-020-01674-y

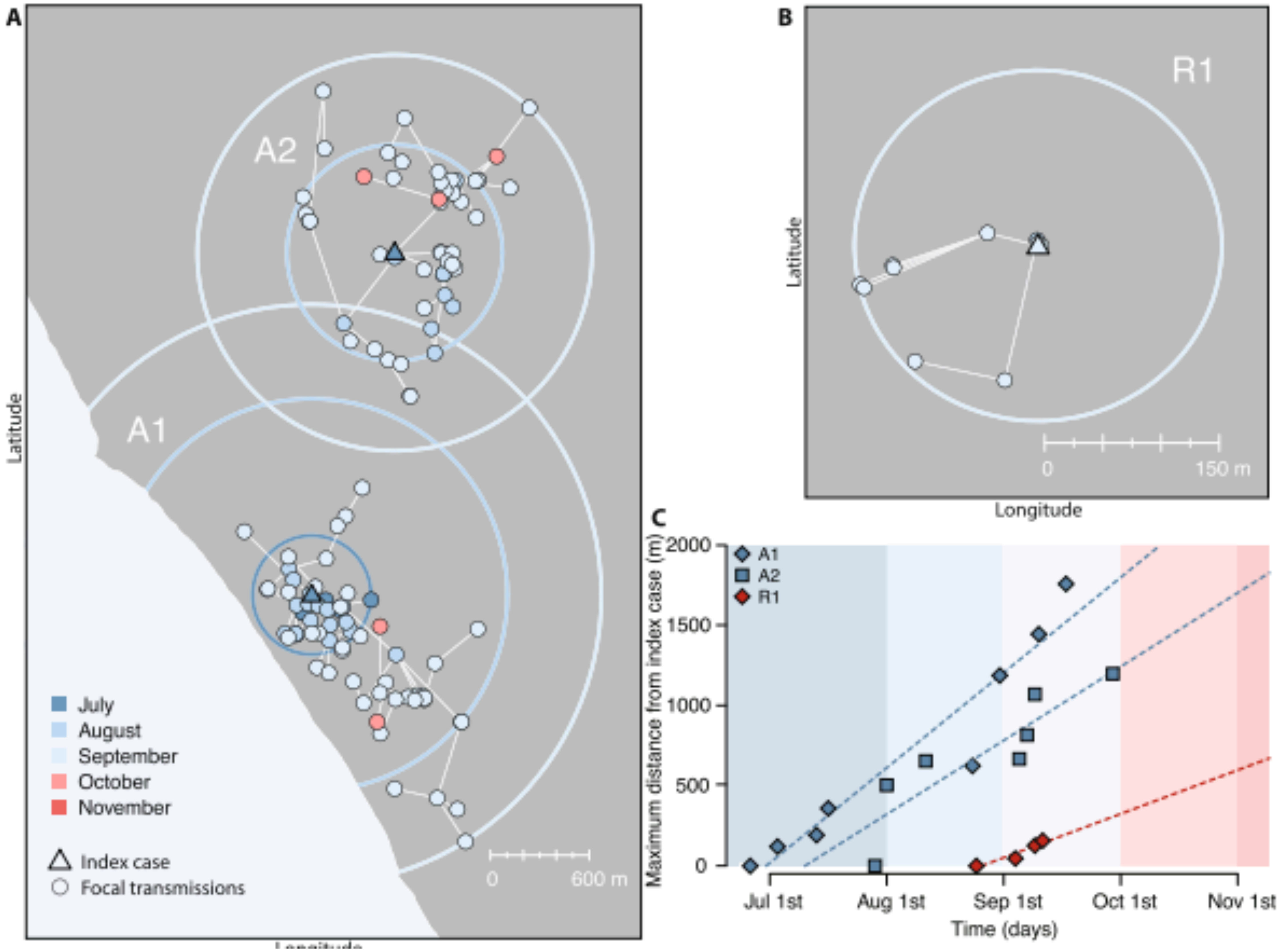
BMC Medicine

RESEARCH ARTICLE Open Access

Check for updates

Spatial modes for transmission of chikungunya virus during a large chikungunya outbreak in Italy: a modeling analysis

Giorgio Guzzetta[1†], Francesco Vairo[2*†], Alessia Mammone[2], Simone Lanini[2], Piero Poletti[1], Mattia Manica[3], Roberto Rosa[3,4], Beniamino Caputo[5], Angelo Solimini[5], Alessandra Della Torre[5], Paola Scognamiglio[2], Alimuddin Zumla[6,7†], Giuseppe Ippolito[2†] and Stefano Merler[1†]



Airborne transmission

- Airborne transmission denotes the transmission mode by which **pathogens are transmitted through the air**.
- This is the mode of transmission of most **respiratory diseases**.
- Usually, a distinction is made based on the size of the particles that contain the pathogens:
- **Aerosol transmission:** particles that can remain suspended in the air
- **Droplet transmission:** larger particles that fall to the ground within 1-2 m

Aerosol vs droplets

- **Droplet transmission was assumed** to be the **dominant transmission** mode for many respiratory pathogens, while aerosol transmission was generally assumed to be of minor importance.

- Now, mainly due to COVID-19, it is understood that aerosols up to 100 μm in size can remain suspended in the air for hours, and travel far beyond 1-2 meters.

- The number of pathogens in aerosol is substantially higher than that of droplets.

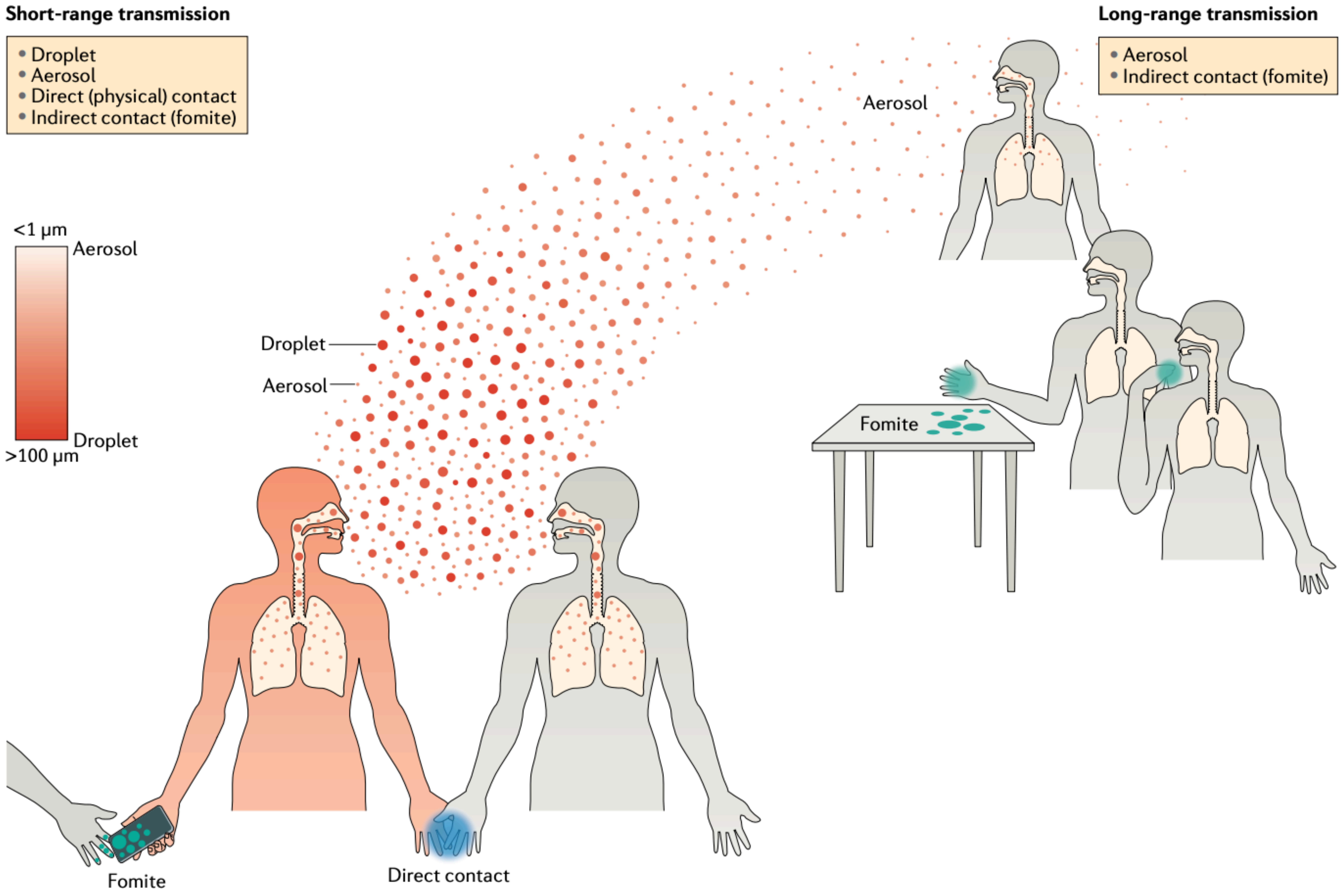
- **Aerosol transmission** is **now assumed to be an important**, if not the dominant transmission mode of COVID-19, and many other respiratory diseases such as influenza.

- Differences between aerosol and droplets lead to different containment strategies: social distancing makes sense if transmission mode is droplet driven.

Contact transmission

- **Contact transmission** refers to physical contact.
- This can occur directly or indirectly, via surfaces.
- The latter mode is called **fomite transmission**.
- Again, this mode of transmission leads to different strategies in the adoption of preventive measures.
- However, fomite transmission has been often hard to establish in an experimental setting.

Overview


Short-range transmission
Droplet
Aerosol
Direct (physical) contact
Indirect contact (fomite)
Long-range transmission
Aerosol
Indirect contact (fomite)
<1 μm
Aerosol
Droplet
>100 μm
Droplet
Aerosol
Aerosol
Fomite
Fomite
Direct contact

Other modes

- **Body fluid transmission** can occur during sex, childbirth, blood transfusion, etc.
- Infectious diseases that can be transmitted through body fluids can be sexually transmitted diseases, such as HIV/AIDS and Hepatitis B, but also other diseases such as the Epstein-Barr virus.
- **Vertical transmission** means a disease is transmitted across generations, from parent to offspring. **Horizontal transmission** means that a disease can be transmitted among people that are not in a parent-offspring relationship.
- When a pathogen enters the human body through **contaminated food**, we speak of **foodborne transmission** (often involving more complex chains).

Contagion

- When one person infects another person who infects the next person, and so on, we speak of an *infection chain*.

- Early in an outbreak, infection chains can still stutter, and come to a halt. But they can also rapidly expand and lead to a large epidemic.

- We need a way to quantify the dynamics of contagion. This brings us to a core concept of infectious disease epidemiology: the **basic reproductive number R_0.**

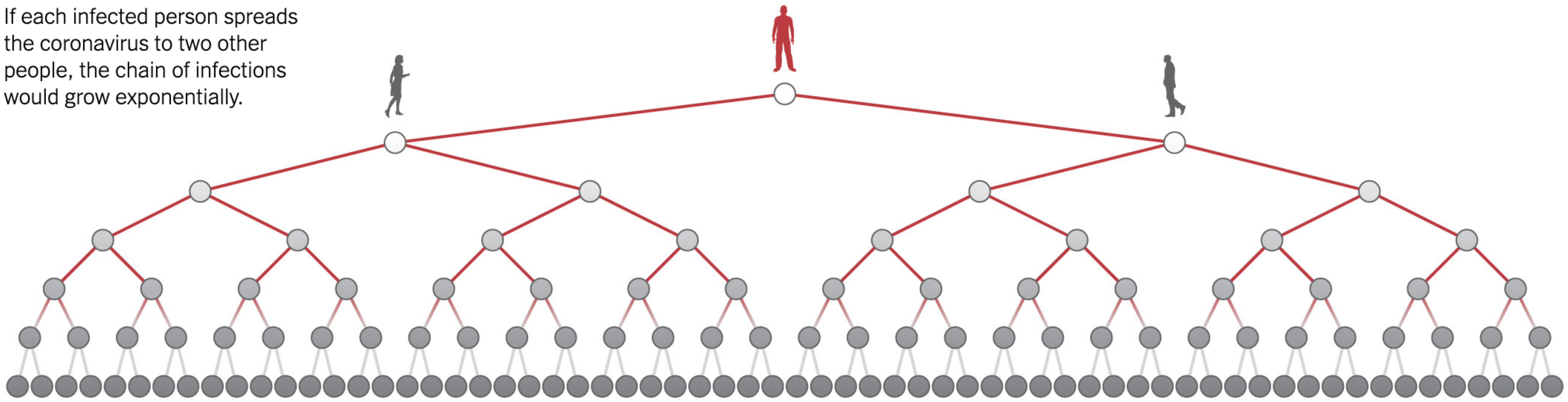
The basic reproductive number

The **basic reproductive number R_0** represents the average number of individuals that are infected by an infectious one during his infectious period, in a fully susceptible population (at the beginning of the outbreak).

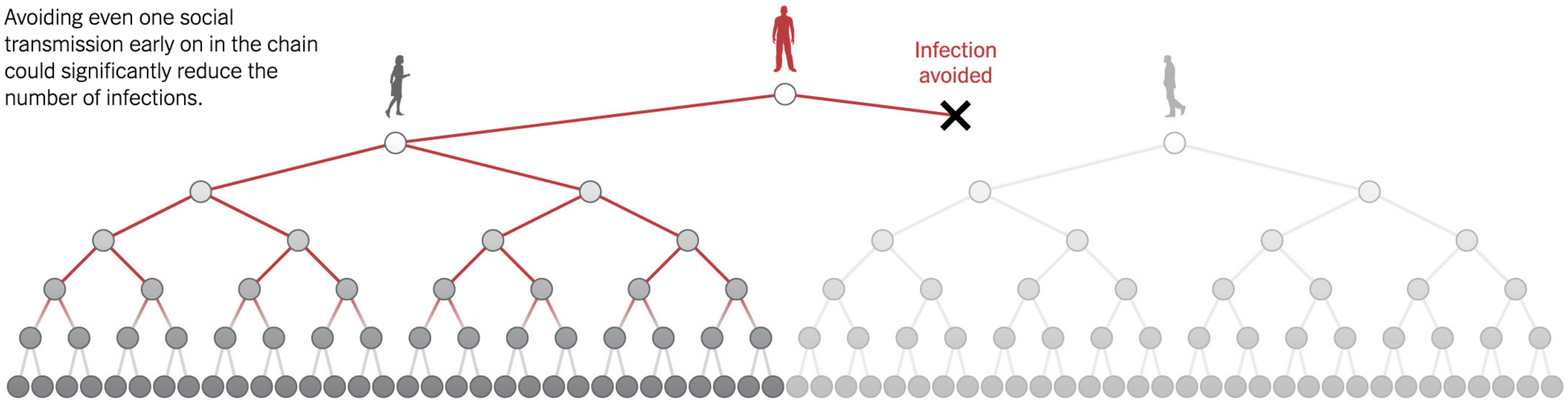
$$\boxed{R_0 > 1} \longrightarrow$$ The epidemic will grow

The basic reproductive number

If each infected person spreads the coronavirus to two other people, the chain of infections would grow exponentially.



Avoiding even one social transmission early on in the chain could significantly reduce the number of infections.



By Jonathan Corum

The reproductive number

- As the epidemic progresses, the effective reproductive number or **time-varying reproductive number R(t)** measures the same quantity in a not fully susceptible population.

- R depends on a number of factors. On the one hand, **it depends on the biological properties of the pathogen** itself.

- On the other hand, **R depends on the host behaviour**. Changes in behaviour, the adoption of preventive measures, the reduction of contacts, can bring **R below the threshold 1**.

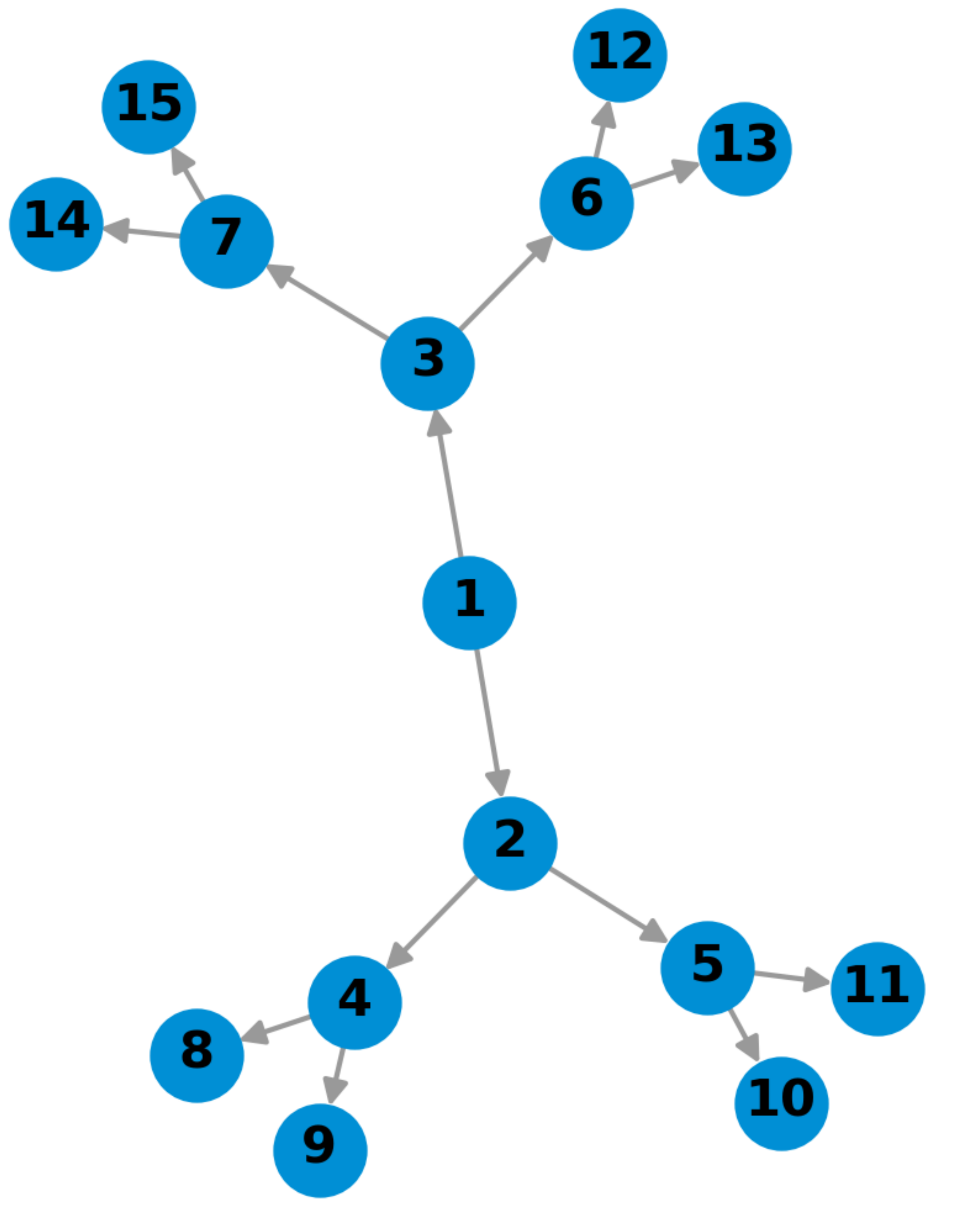
Reproductive number

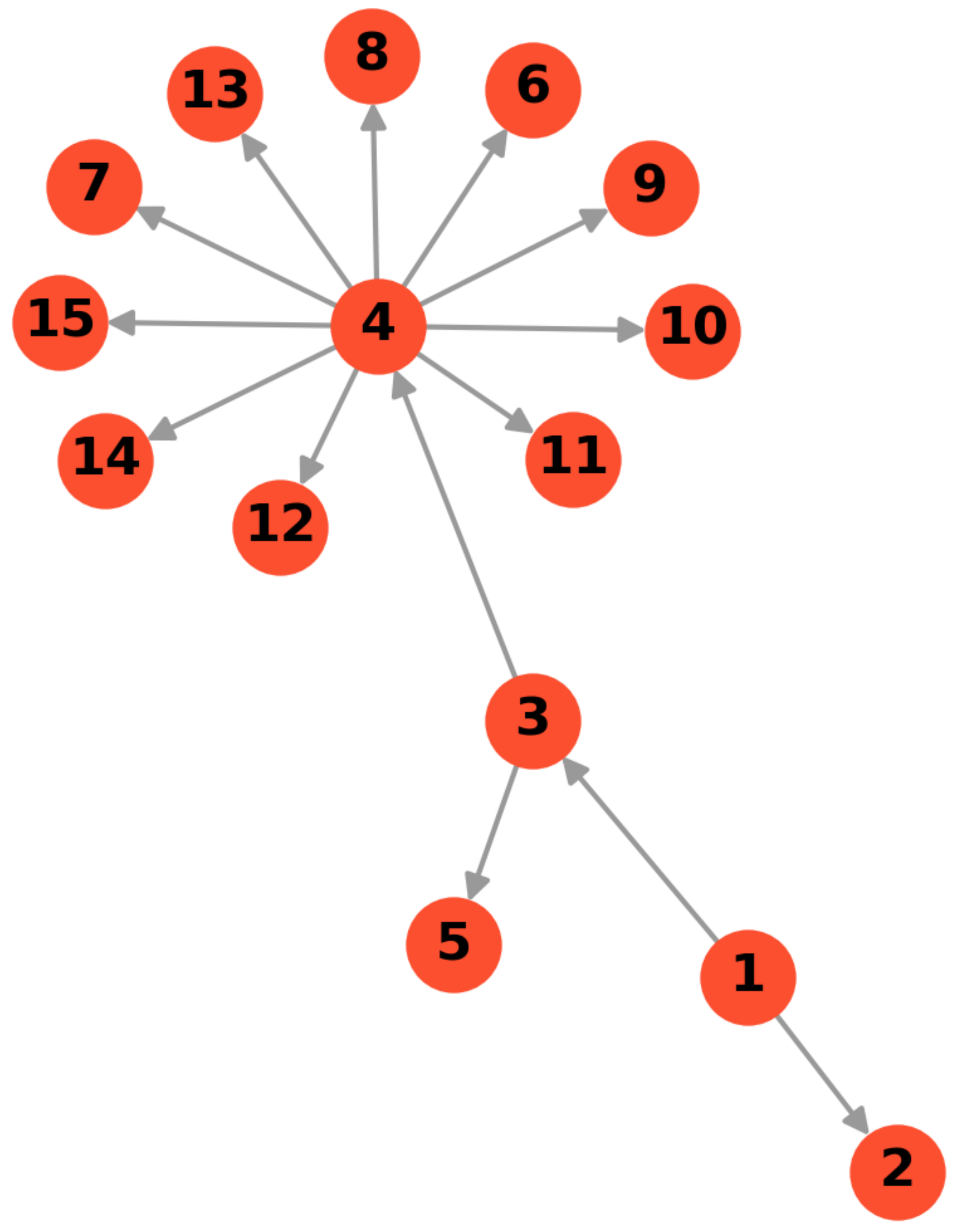
TABLE 2.1.
Some Estimated Basic Reproductive Ratios.

Infectious Disease	*Host*	*Estimated R_0*	*Reference*
FIV	Domestic Cats	1.1–1.5	Smith (2001)
Rabies	Dogs (Kenya)	2.44	Kitala et al. (2002)
Phocine Distemper	Seals	2–3	Swinton et al. (1998)
Tuberculosis	Cattle	2.6	Goodchild and Clifton-Hadley (2001)
Influenza	Humans	3–4	Murray (1989)
Foot-and-Mouth Disease	Livestock farms (UK)	3.5–4.5	Ferguson et al. (2001b)
Smallpox	Humans	3.5–6	Gani and Leach (2001)
Rubella	Humans (UK)	6–7	Anderson and May (1991)
Chickenpox	Humans (UK)	10–12	Anderson and May (1991)
Measles	Humans (UK)	16–18	Anderson and May (1982)
Whooping Cough	Humans (UK)	16–18	Anderson and May (1982)

Super-spreading

- The (basic) reproductive number represents only an **average value**!
- Understanding the distribution around this mean is important because of so-called **superspreader** events.
- A superspreader event is an event in which an index case infects many more people than R.





In both cases above, R=2 but the chains are very different…

Super-spreading

RESEARCH ARTICLE

Transmission heterogeneities, kinetics, and controllability of SARS-CoV-2

KAIYUAN SUN, WEI WANG, LIDONG GAO, YAN WANG, KAIWEI LUO, LINGSHUANG REN, ZHIFEI ZHAN, XINGHUI CHEN, SHANLU ZHAO, YIWEI HUANG, QIANLAI SUN, ZIYAN LIU, MARIA LITVINOVA, ALESSANDRO VESPIGNANI, MARCO AJELLI, CÉCILE VIBOUD, AND HONGJIE YU fewer Authors

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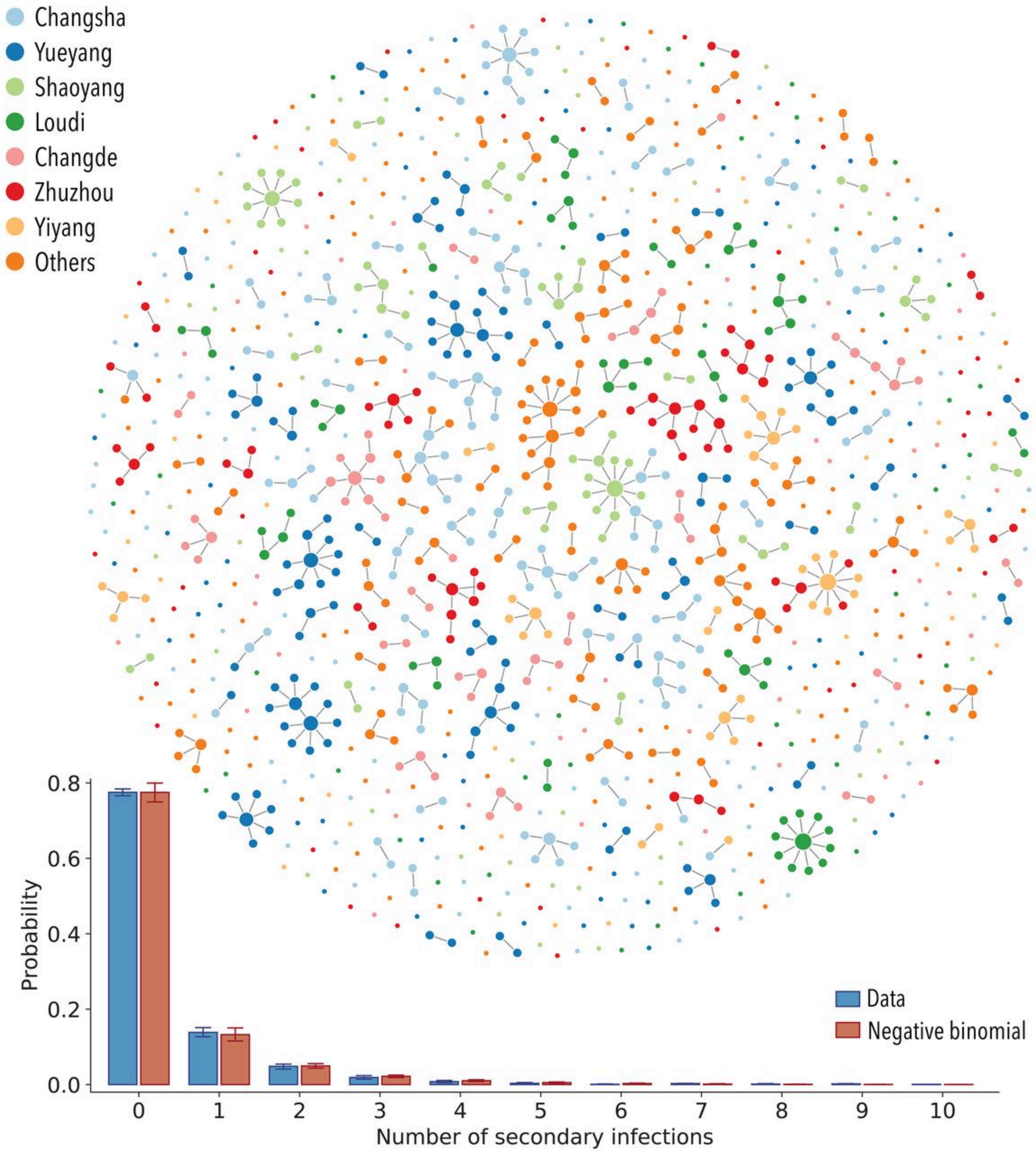
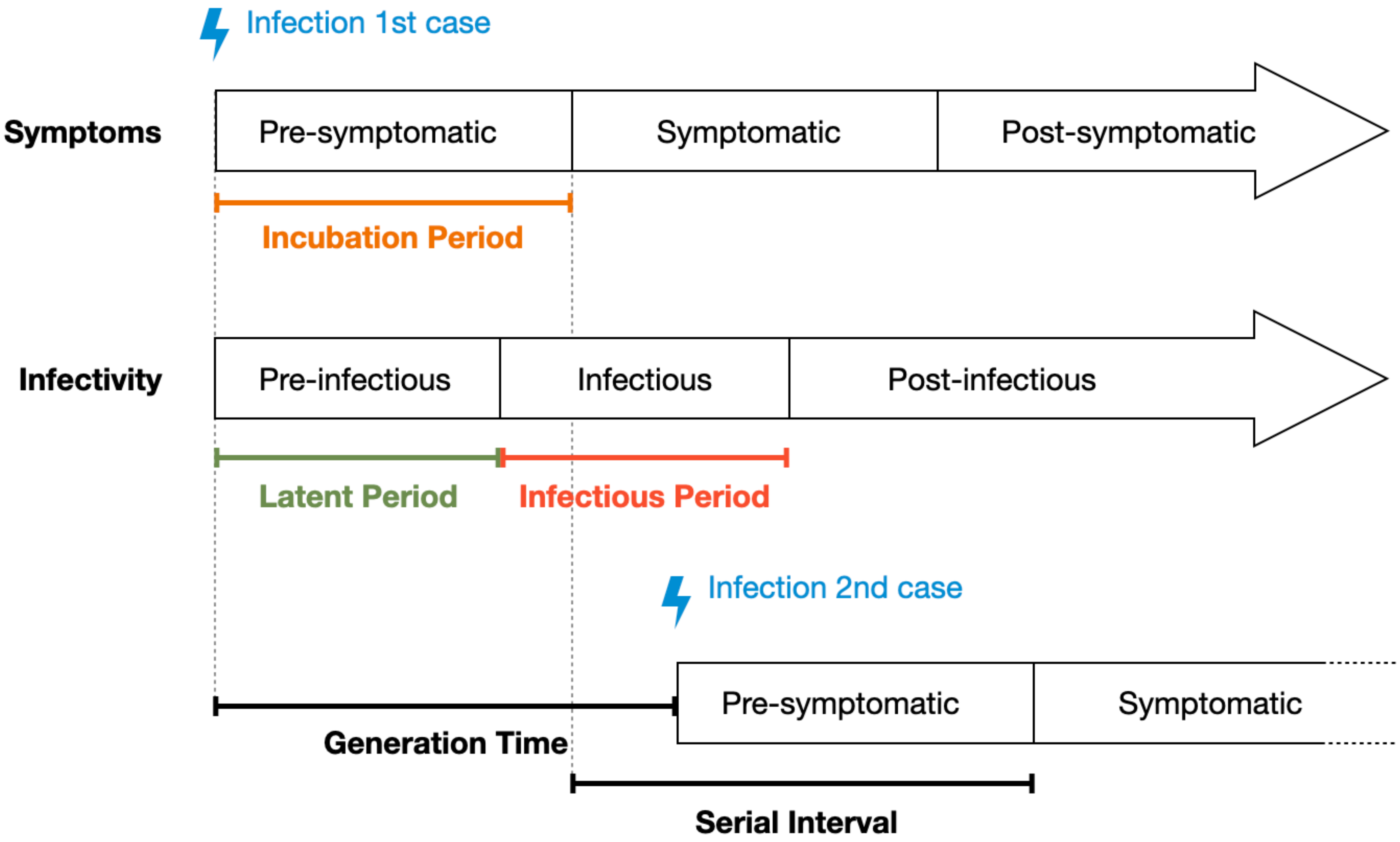
SCIENCE • 24 Nov 2020 • Vol 371, Issue 6526 • DOI: 10.1126/science.abe2424



Course of infection

- The time between initial infection and the possibility of transmission to the next host is called the **latent period**, or pre-infectious period
- Once the latent period is over, the host enters the **infectious period**, which lasts until the immune system has sufficiently cleared the infection so that transmission is not possible anymore.
- The time between the initial infection and the appearance of symptoms is called the **incubation period.**
- **The incubation period and the latent period need not overlap.**
- The average time it takes from the symptom onset of an index case to the symptom onset of secondary cases is called the **serial interval**.
- The average time it takes from the infection of the index case, to the infection of the secondary cases, called the **generation time**.

Course of infection



Course of infection

Thread

Adam Kucharski @adamjkucharski

In hindsight, it can be easy to forget that all the parameters we now have for COVID - from incubation period and clinical progression to severity and transmissibility - had to be estimated by someone. A thread on some of the crucial early work in this area... 1/

9:50 AM · Mar 10, 2023 · **44.1K** Views

40 Retweets **2** Quote Tweets **157** Likes

Tweet your reply

Reply

Adam Kucharski @adamjkucharski · 6h

Replying to @adamjkucharski

17 Jan 2020. Estimation of unreported cases in Wuhan based on exported international cases, by Imai et al: imperial.ac.uk/mrc-global-inf... 2/

> imperial.ac.uk
> Report 1 - Estimating the potential total number ...
> Report 1 - Estimating the potential total number of novel Coronavirus (2019-nCoV) cases in Wuhan ...

1 · 7 · 2,898

Adam Kucharski @adamjkucharski · 6h

4 Feb 2020. Estimation of incubation period based on known exposure windows, by @salauer_biostat et al: medrxiv.org/content/10.110... 3/

> medRχiv THE PREPRINT SERVER FOR HEALTH SCIENCES
> medrxiv.org
> The incubation period of 2019-nCoV from publicl...
> A novel human coronavirus (2019-nCoV) was identified in China in December, 2019. There is ...

Adam Kucharski @adamjkucharski · 6h

18 Feb 2020. Estimation of duration from symptom onset to hospitalisation and death, adjusting for as-yet-unknown outcomes, by @nlinton_epi et al: medrxiv.org/content/10.110... 4/

> medRχiv THE PREPRINT SERVER FOR HEALTH SCIENCES
> medrxiv.org
> Incubation Period and Other Epidemiological Cha...
> The geographic spread of 2019 novel coronavirus (COVID-19) infections from the epicenter of ...

1 · 1 · 7 · 1,674

Adam Kucharski @adamjkucharski · 6h

4 Mar 2020. Estimate of secondary attack rates (including among younger groups) from contact tracing data, by @QifangB et al: medrxiv.org/content/10.110... 5/

> medRχiv THE PREPRINT SERVER FOR HEALTH SCIENCES
> medrxiv.org
> Epidemiology and Transmission of COVID-19 in S...
> Background Rapid spread of SARS-CoV-2 in Wuhan prompted heightened surveillance in ...

1 · 1 · 7 · 1,719

Adam Kucharski @adamjkucharski · 6h

8 Mar 2020. Estimate of generation time (i.e. delay from one infection to the next) accounting for underlying transmission dynamics, by Ganyani et al: medrxiv.org/content/10.110... 6/

> medRχiv THE PREPRINT SERVER FOR HEALTH SCIENCES
> medrxiv.org
> Estimating the generation interval for COVID-19 b...
> Background Estimating key infectious disease parameters from the COVID-19 outbreak is ...

1 · 1 · 7 · 1,705

Course of infection

- For SARS-Cov-2, the mean incubation period of the Omicron variant is about 3.5 days, and the mean serial interval is 6.8 days.

- For influenza, the mean incubation period is about one day, with a serial interval of 3-4 days.

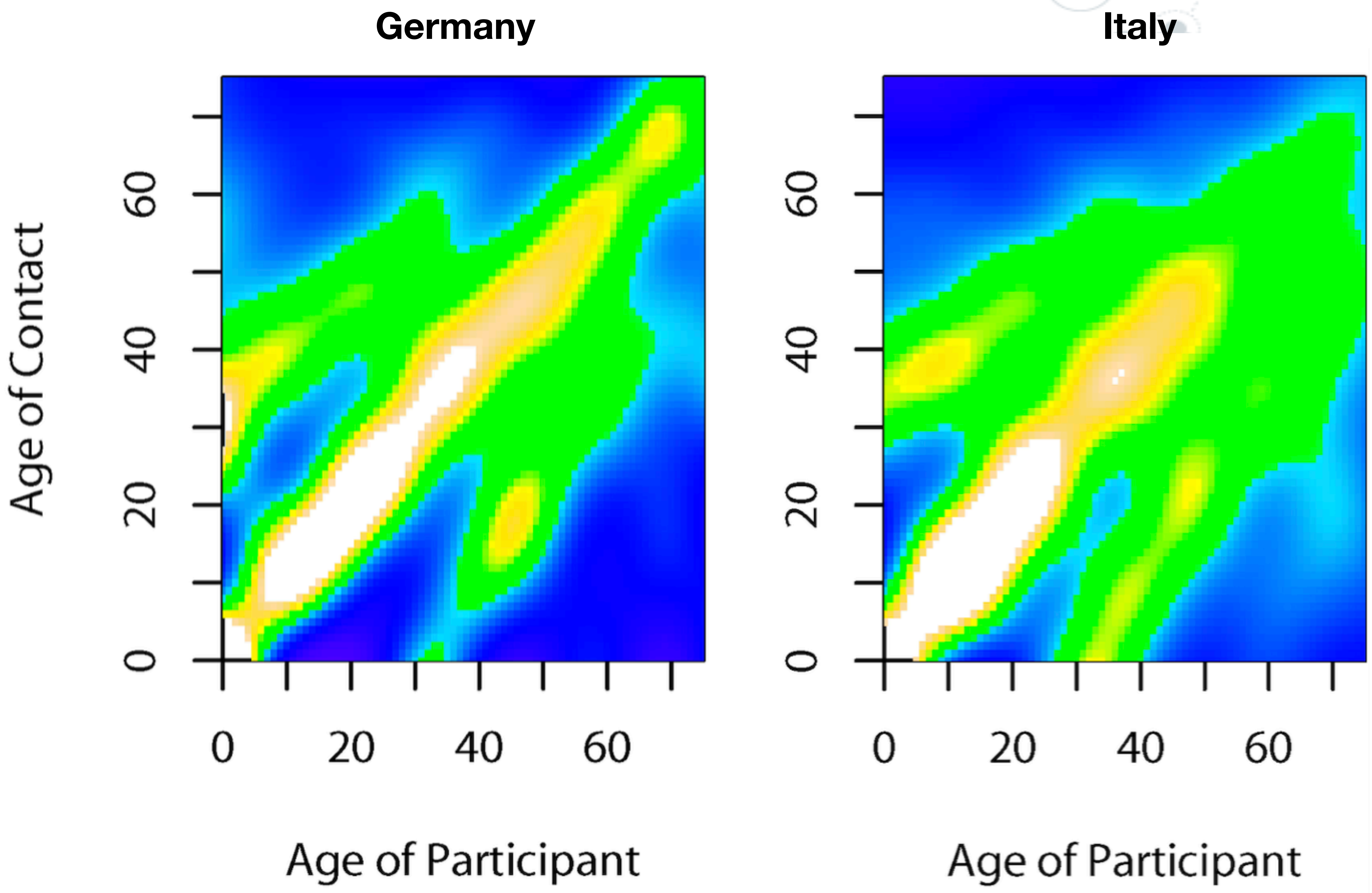
- For Tuberculosis, the **median incubation period** has been estimated to be a **few months to two years** - similarly for the median serial interval.

Heterogeneities

- The dynamics of contagion is affected by several factors and their heterogeneities can have a significant impact on the course of an outbreak.
- Heterogeneity in age and mixing
- Heterogeneity in contacts
- Heterogeneity in space

Age mixing

- Contact patterns are highly age-stratified.
- **assortative mixing** based on age can lead to markedly different age-related prevalence patterns than those that would be expected **if mixing was random**



Mossong et al. PLOS Medicine 2008

Heterogeneities in contacts

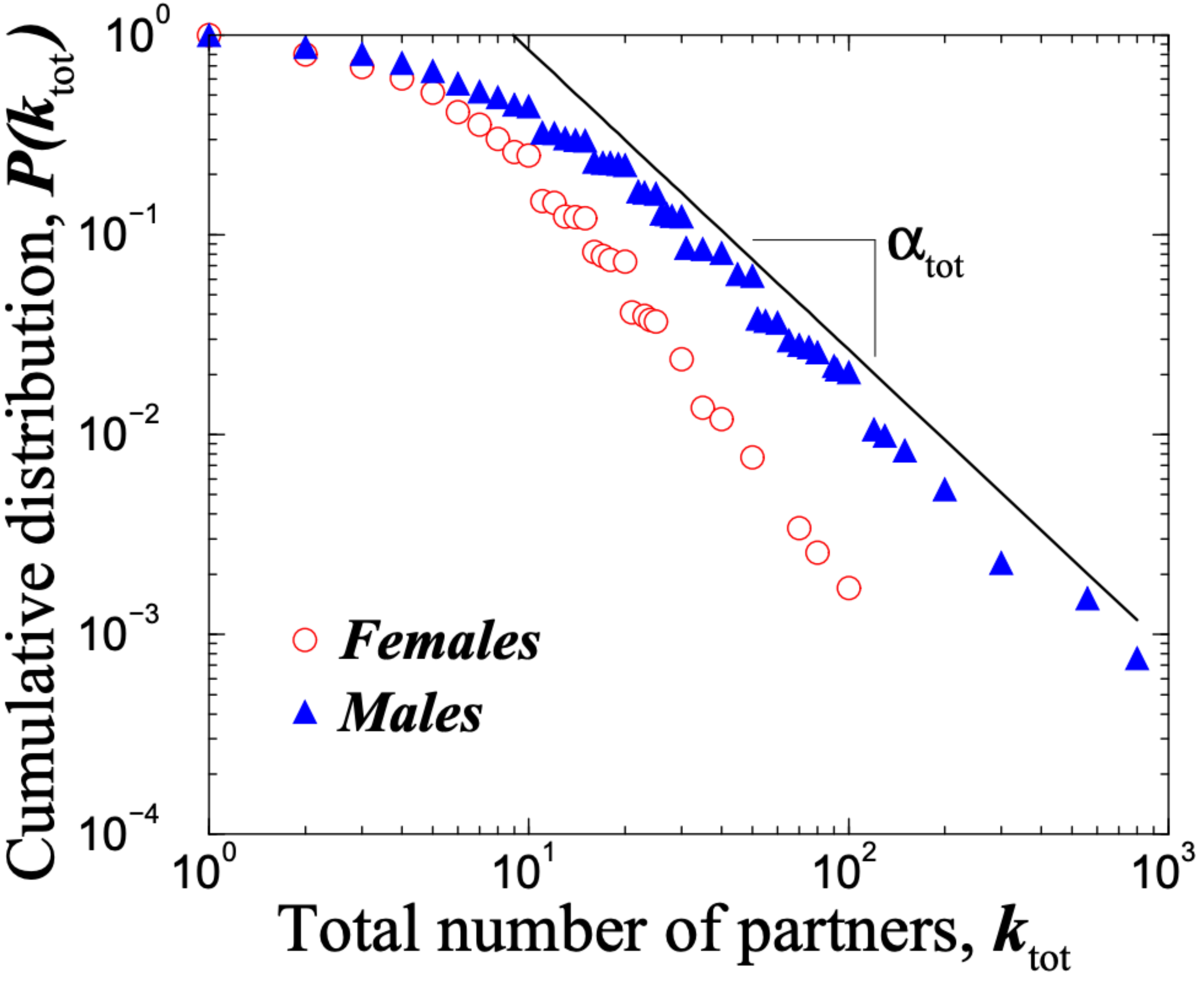
- **Distributions of contacts are often highly heterogeneous (power-law)**

Published: 21 June 2001

The web of human sexual contacts

Fredrik Liljeros, Christofer R. Edling, Luís A. Nunes Amaral, H. Eugene Stanley & Yvonne Åberg

Nature **411**, 907–908 (2001) | Cite this article



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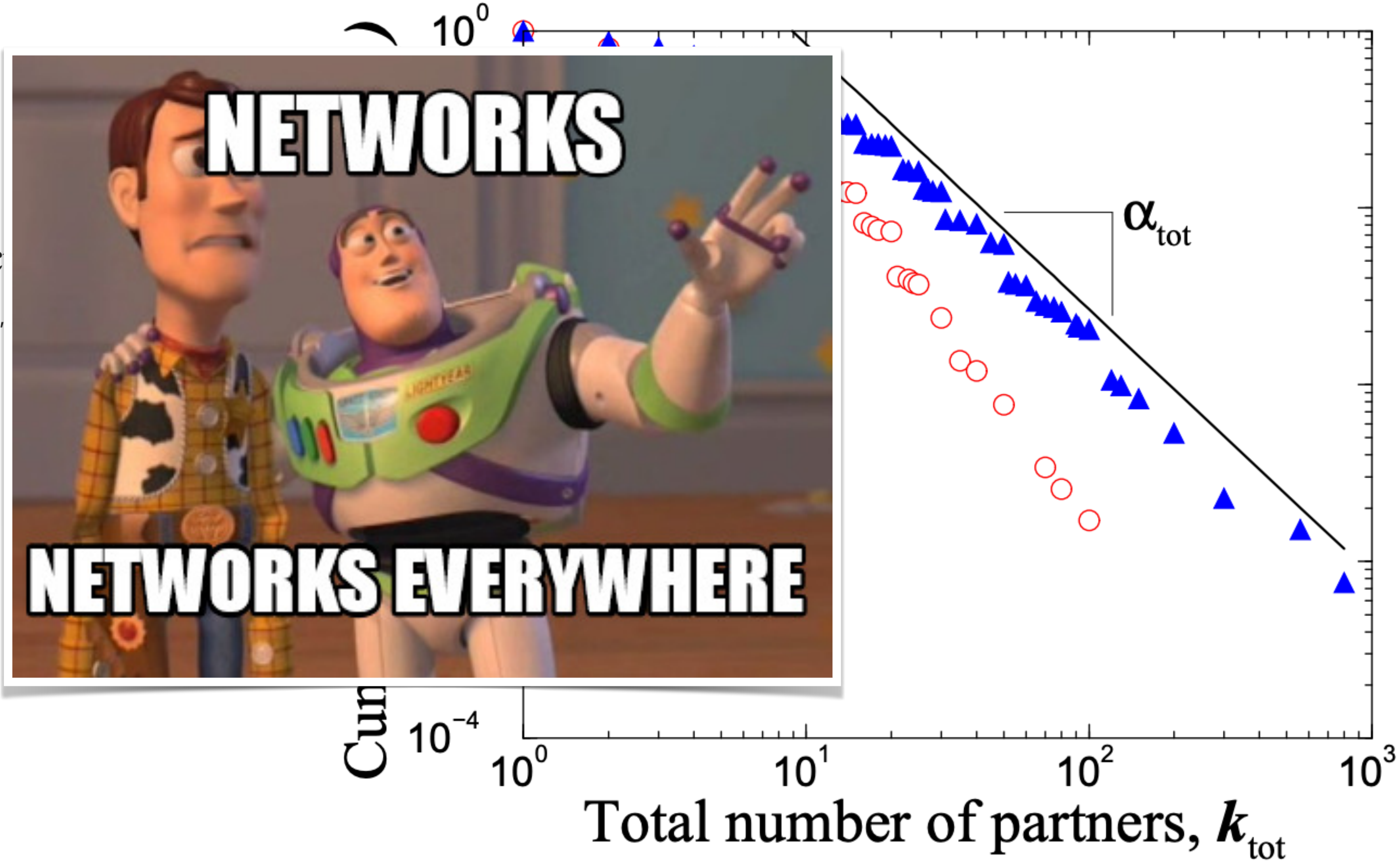
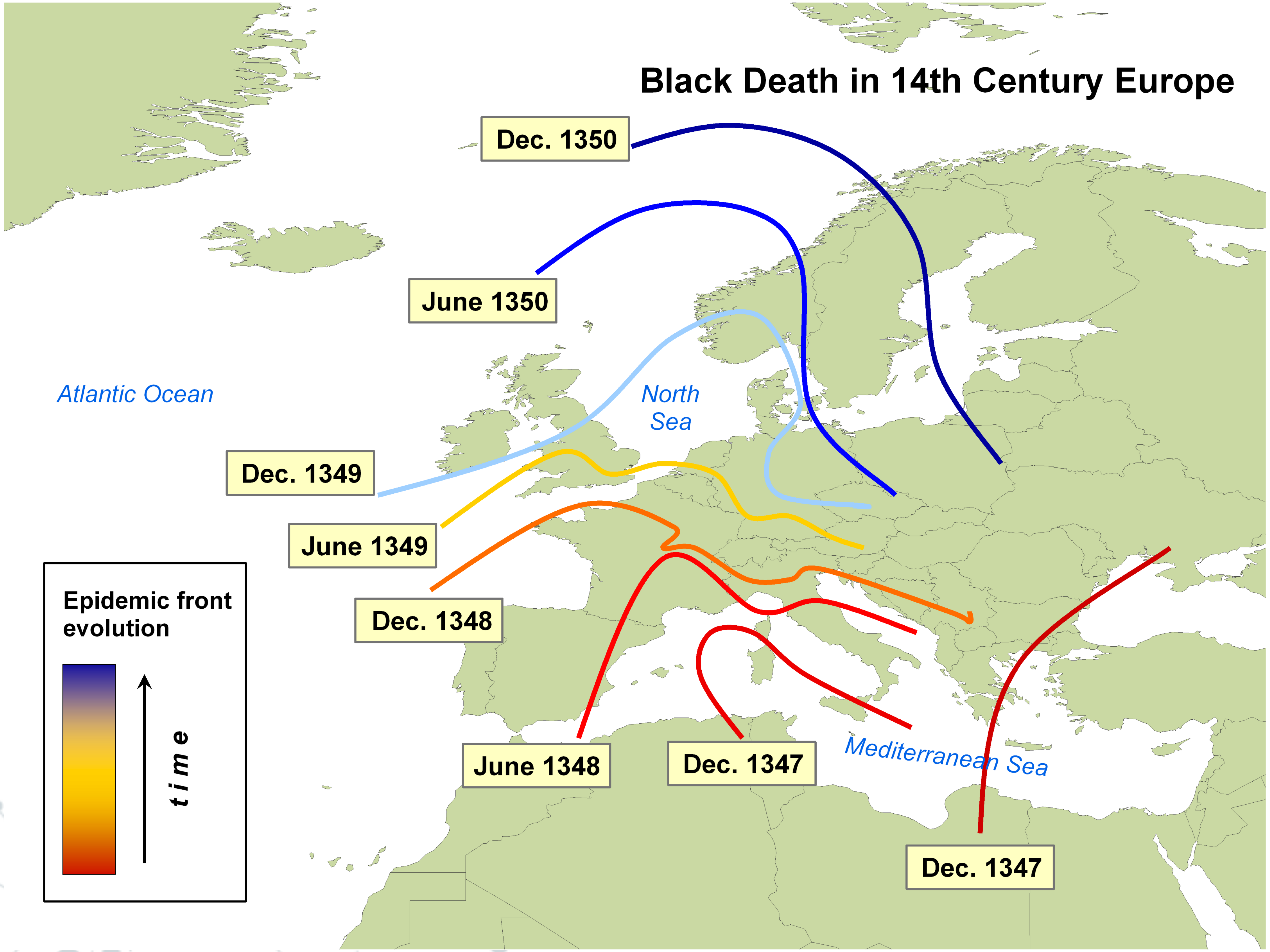
9337 Accesses | **1137** Citations | **14** Altmetric | Metrics



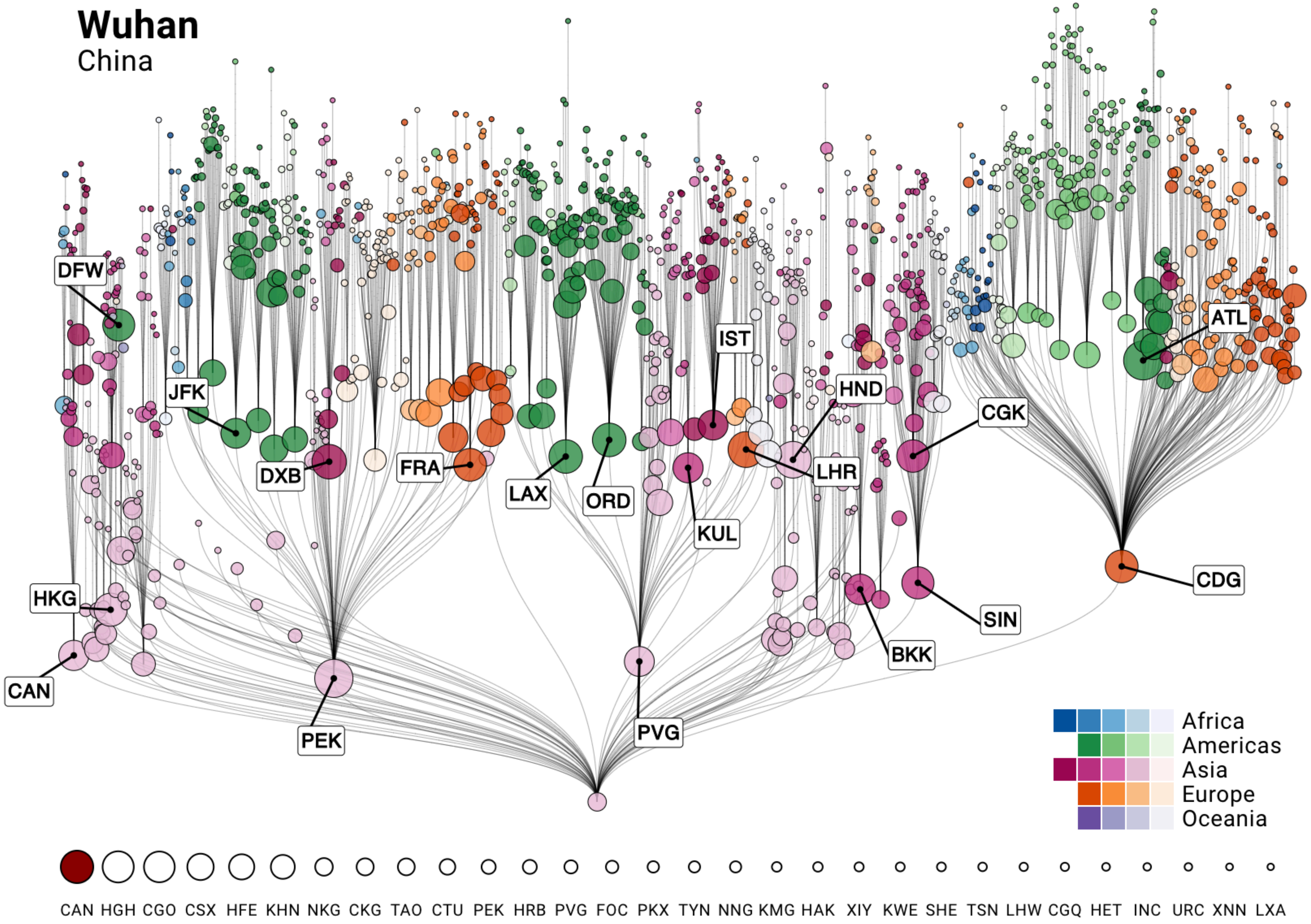
Heterogeneities in space



The black death in the XIV century

a continuous diffusion wave process

Heterogeneities in space



SARS-CoV-2 in the XXI century

a network driven diffusion process

Source: Robert Koch Institute

Vaccination

- Vaccines essentially trick the body into developing immune memory against a pathogen, without exposing the body to the risk of a natural infection by that pathogen.

- The effect of vaccination depends on the **type of immunity** that the vaccine induces. In the same way that immunity through natural infection can be **lifelong, or waning,** immunity through vaccination can have various consequences.

- Some vaccines can be **infection-blocking**.

- With infection-blocking vaccines, we can observe the phenomenon of **herd immunity,** that is the indirect protection of those who have no immunity, either because they cannot establish it biologically, or because they are not vaccinated.

Vaccination

- Vaccines, like any other pharmacological intervention, are not perfect. Their **effectiveness** must be continuously evaluated.
- **Efficacy** is the capacity of the vaccine to prevent a certain outcome (disease, symptoms, contagion, deaths) in the experimental trial.
- **Effectiveness** is the same capacity when evaluated in the whole population, in the field. The effectiveness of a vaccine is never 100%.
- Even if a vaccine has a very high effectiveness, we will observe cases of vaccinated infected individuals.

Vaccination

- What is the probability of being vaccinated, given that one has been infected? P(V|I)?

- Again, we can solve this with Bayes' theorem.

$$P(V|I) = \frac{P(I|V)P(V)}{P(I)}$$

$$P(V|I) = \frac{P(I|V)P(V)}{P(I|V)P(V) + P(I|\neg V)P(\neg V)}$$

Vaccination

$$P(V|I) = \frac{P(I|V)P(V)}{P(I|V)P(V) + P(I|\neg V)P(\neg V)}$$

$$P(I|V) = 1 - V_e \qquad P(V) = c \qquad \boxed{P(I|\neg V) \simeq 1}$$

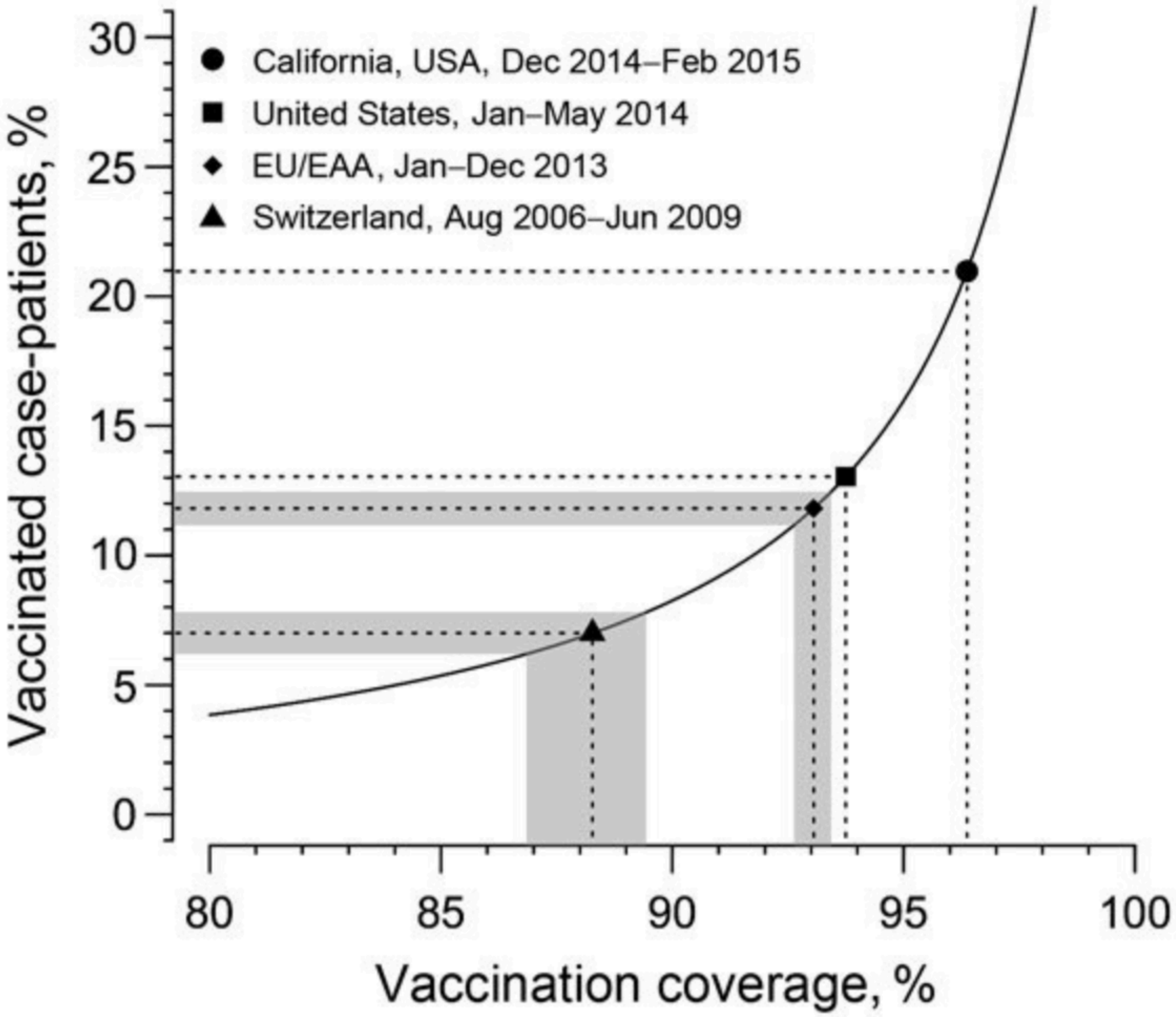
For a highly infectious pathogen such as measles

$$P(V|I) = \frac{c(1 - V_e)}{1 - cV_e}$$

Vaccination

- 2014/2015 measles outbreak in California
- V_e = 99%
- Coverage = 95%
- P(V|I) = 16%

$$P(V\,|\,I) = \frac{c(1 - V_e)}{1 - cV_e}$$



Source: Althaus and Salathé (2015)

Control and mitigation

- **Pharmaceutical interventions**:
  - **Pre-exposure**: prophylaxis (PrEp for HIV)
  - **Post-exposure**: vaccination, antivirals, antibiotics
- **Non-pharmaceutical interventions:**
  - **Mobility restrictions:** border control, quarantines
  - **Social distancing:** closures of workplaces, schools, etc.
  - **Test, tracing and isolation**
  - **Masking and indoor air purification**

Control and mitigation

- **Computational approaches** have been extensively used to assess the impact of all types of intervention strategies.
- Computational models have been used to
  - evaluate the effectiveness of vaccination and the impact on the spread of diseases
  - evaluate the effectiveness of border closures, mobility restrictions, social distancing, testing, etc.
- These will be the topic of the next lectures.

Next… mathematical modelling