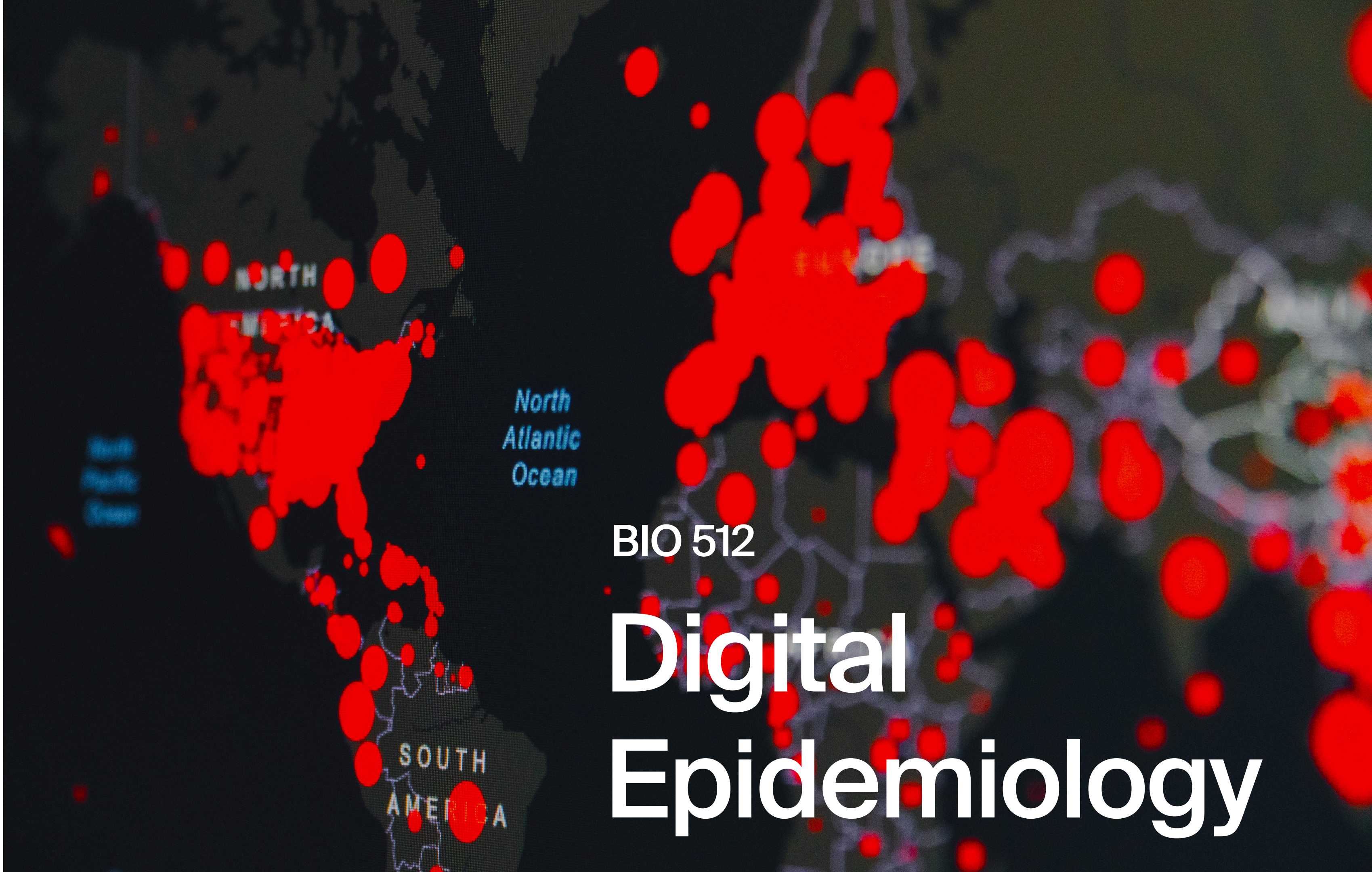
EPFL

Digital Epidemiology Lab BIO-521 Spring semester 202



BIO 512

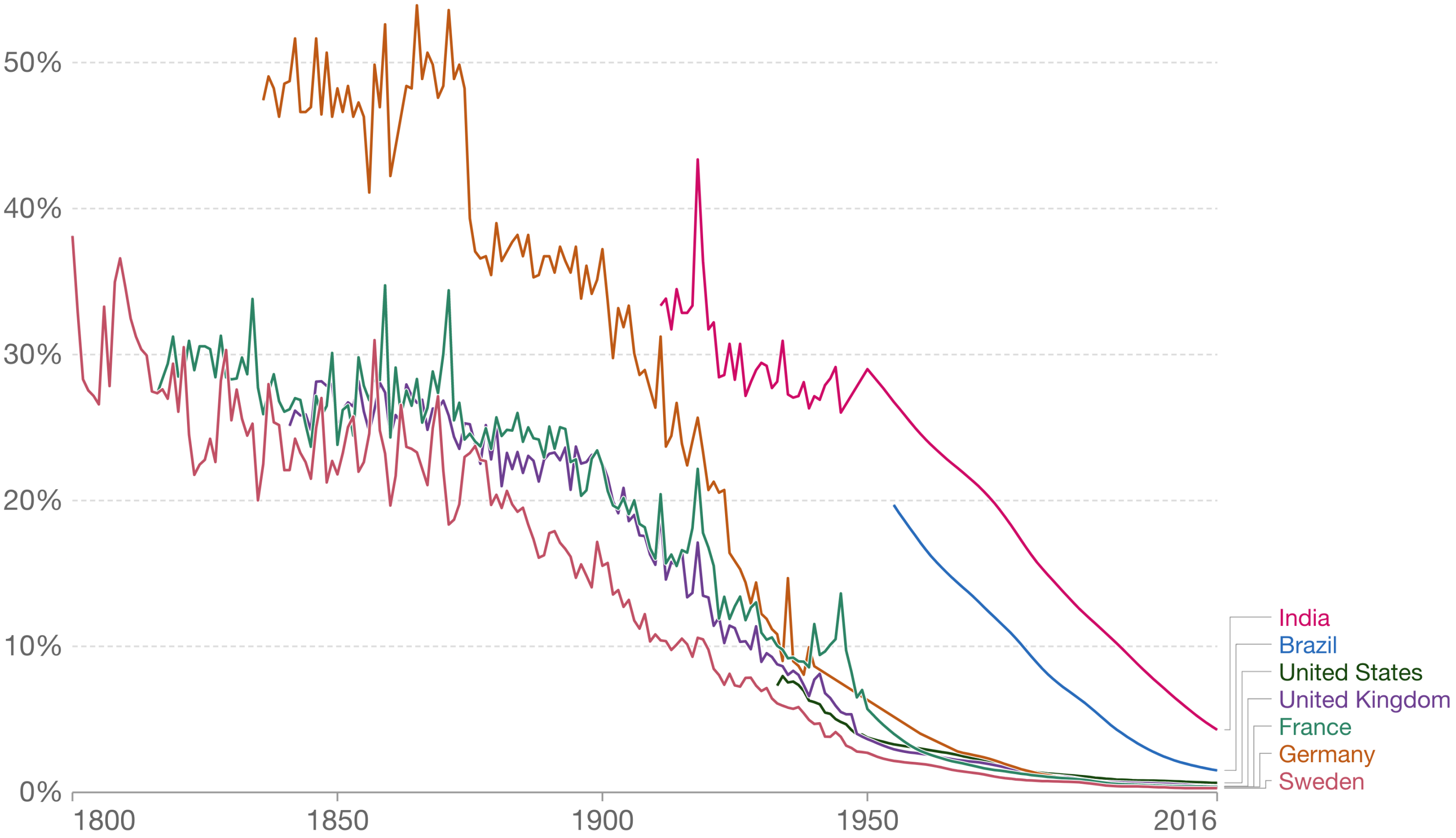
Digital Epidemiology

Infectious Disease Epidemiology
Learning Objectives

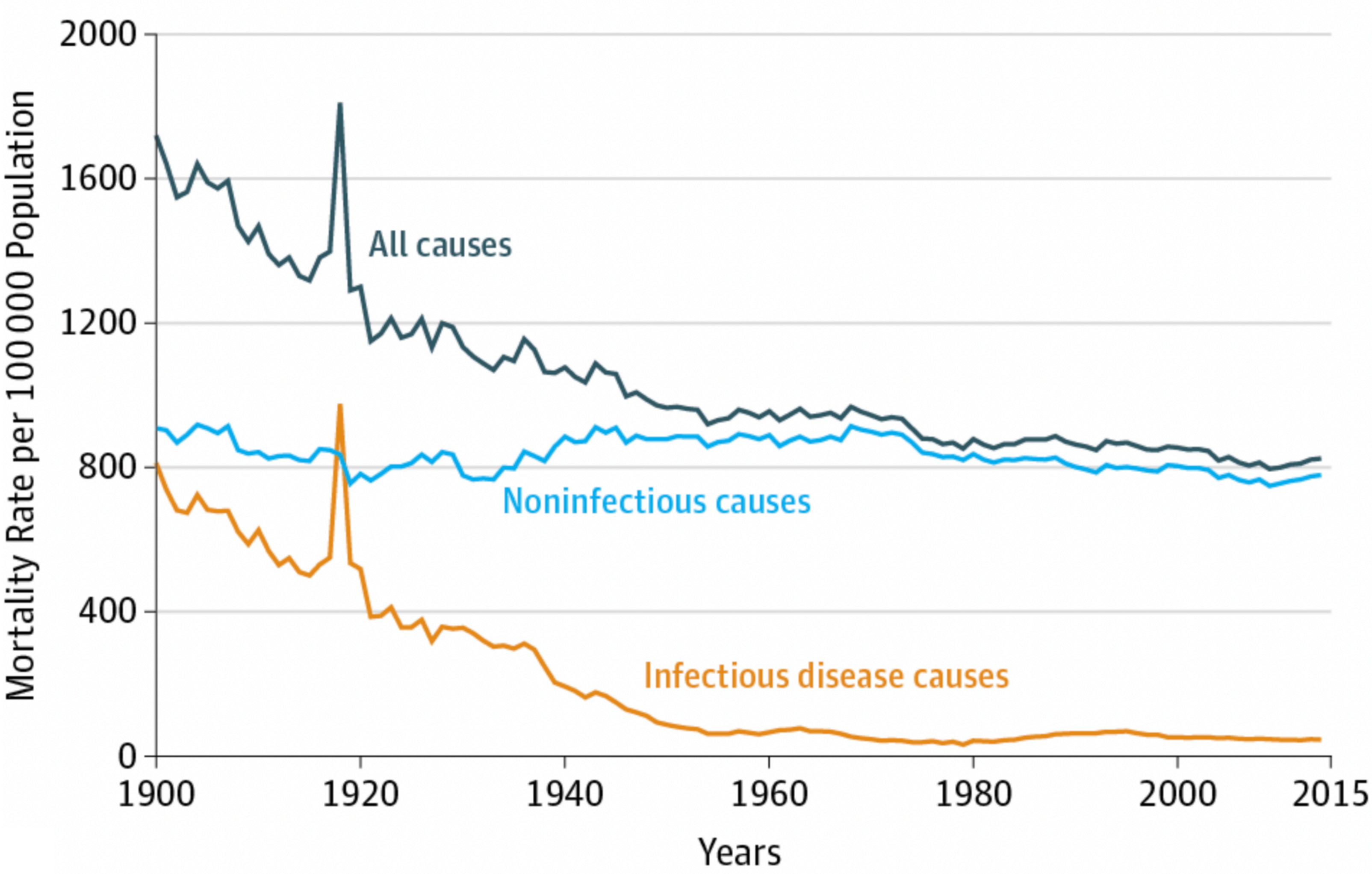
- Understand key concepts of infectious disease epidemiology:
  - Emergence
  - Transmission
  - Contagion
  - Course of infection
  - Heterogeneities
  - Vaccination
  - Control

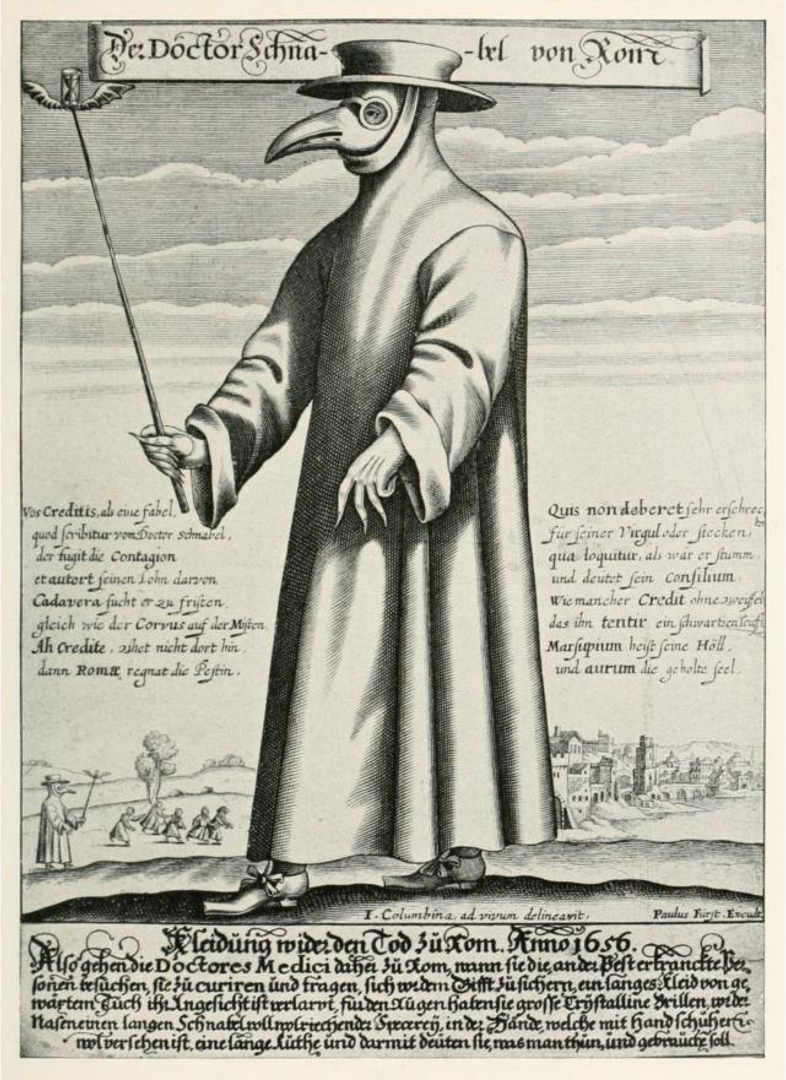
Child mortality, 1800 to 2016

Shown is the share of children (born alive) who die before they are five years old.



Source: Gapminder (2017) & UN IGME (2018)


Mortality Rate per 100 000 Population
2000
1600
1200
800
400
0
1900
1920
1940
1960
1980
2000
2015
Years
All causes
Noninfectious causes
Infectious disease causes



- Until mid 19th century, doctors had wrong conception of infectious disease spread (miasma, foul air).

Infectious Disease Epidemiology

Emergence

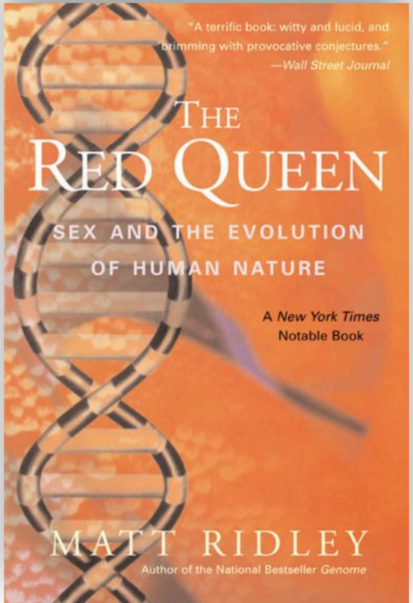
- Parasites: extract resources from another organism
- Host: an organism which provides resources to parasites

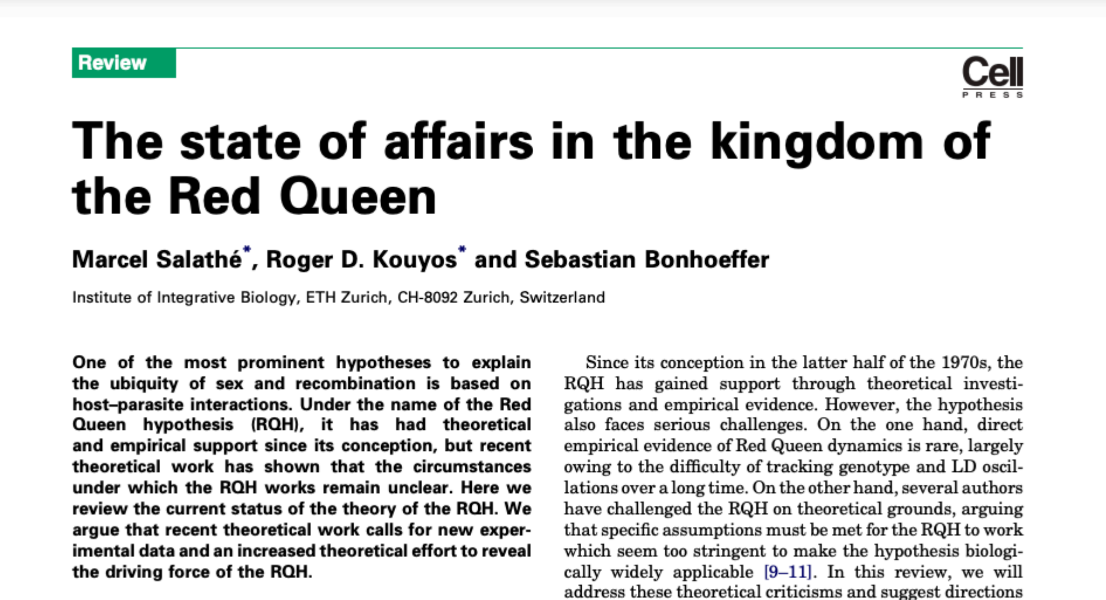
- Pathogen: disease-causing parasite

Infectious Disease Epidemiology

Emergence

- Parasitism as old as life - responsible for major adaptations, including sexual reproduction.





Review

Cell PRESS

The state of affairs in the kingdom of the Red Queen

Marcel Salathé*, Roger D. Kouyos* and Sebastian Bonhoeffer

Institute of Integrative Biology, ETH Zurich, CH-8092 Zurich, Switzerland

One of the most prominent hypotheses to explain the ubiquity of sex and recombination is based on host–parasite interactions. Under the name of the Red Queen hypothesis (RQH), it has had theoretical and empirical support since its conception, but recent theoretical work has shown that the circumstances under which the RQH works remain unclear. Here we review the current status of the theory of the RQH. We argue that recent theoretical work calls for new experimental data and an increased theoretical effort to reveal the driving force of the RQH.

Since its conception in the latter half of the 1970s, the RQH has gained support through theoretical investigations and empirical evidence. However, the hypothesis also faces serious challenges. On the one hand, direct empirical evidence of Red Queen dynamics is rare, largely owing to the difficulty of tracking genotype and LD oscillations over a long time. On the other hand, several authors have challenged the RQH on theoretical grounds, arguing that specific assumptions must be met for the RQH to work which seem too stringent to make the hypothesis biologically widely applicable [9–11]. In this review, we will address these theoretical criticisms and suggest directions

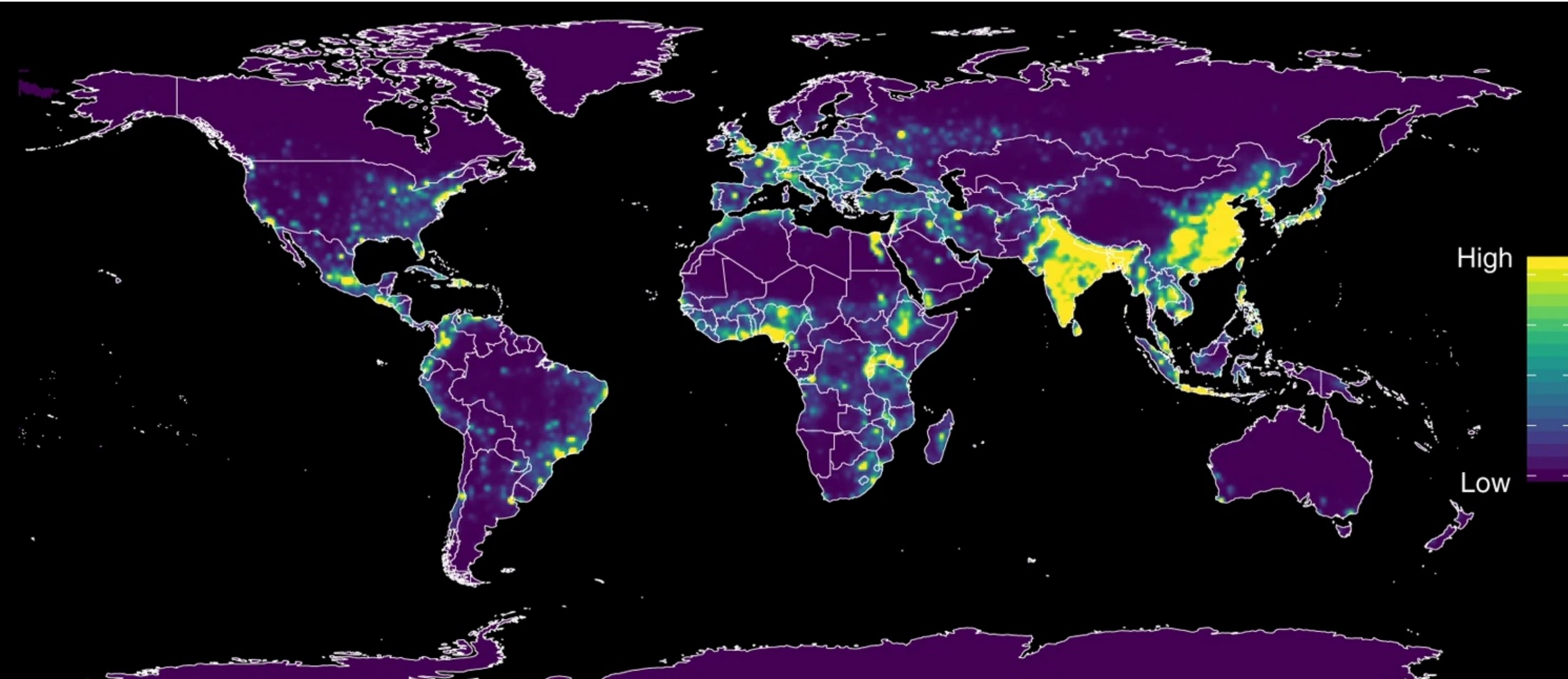
Infectious Disease Epidemiology

Emergence

- Zoonosis - jump from an animal reservoir species

Infectious Disease Epidemiology

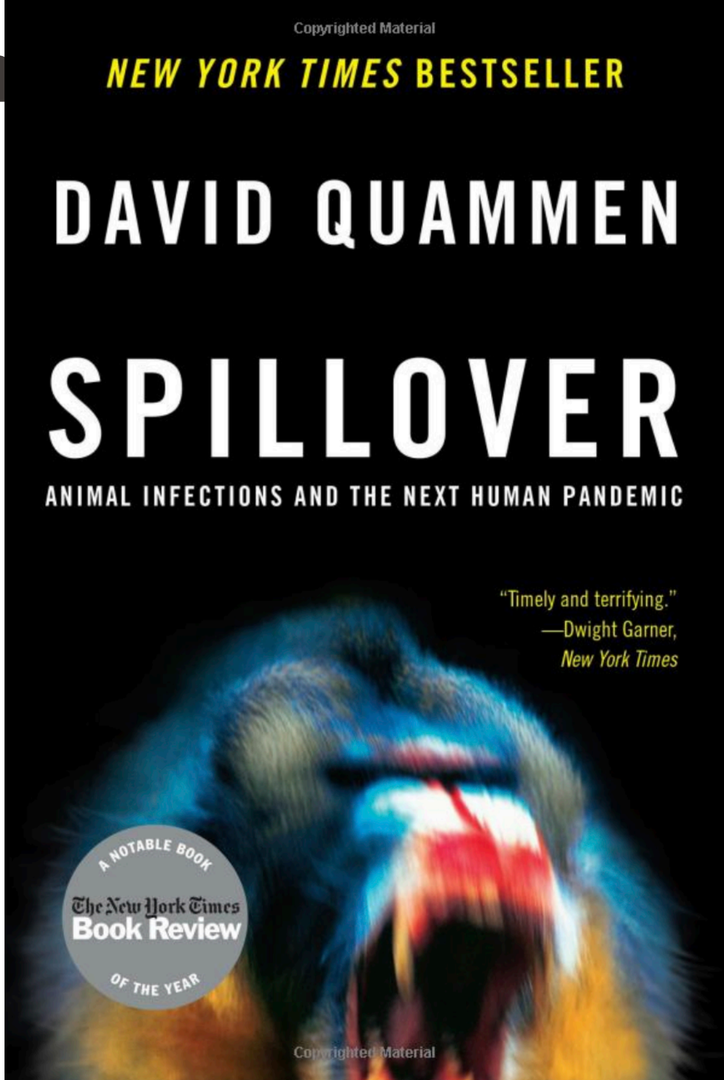
Emergence



Infectious Disease Epiden

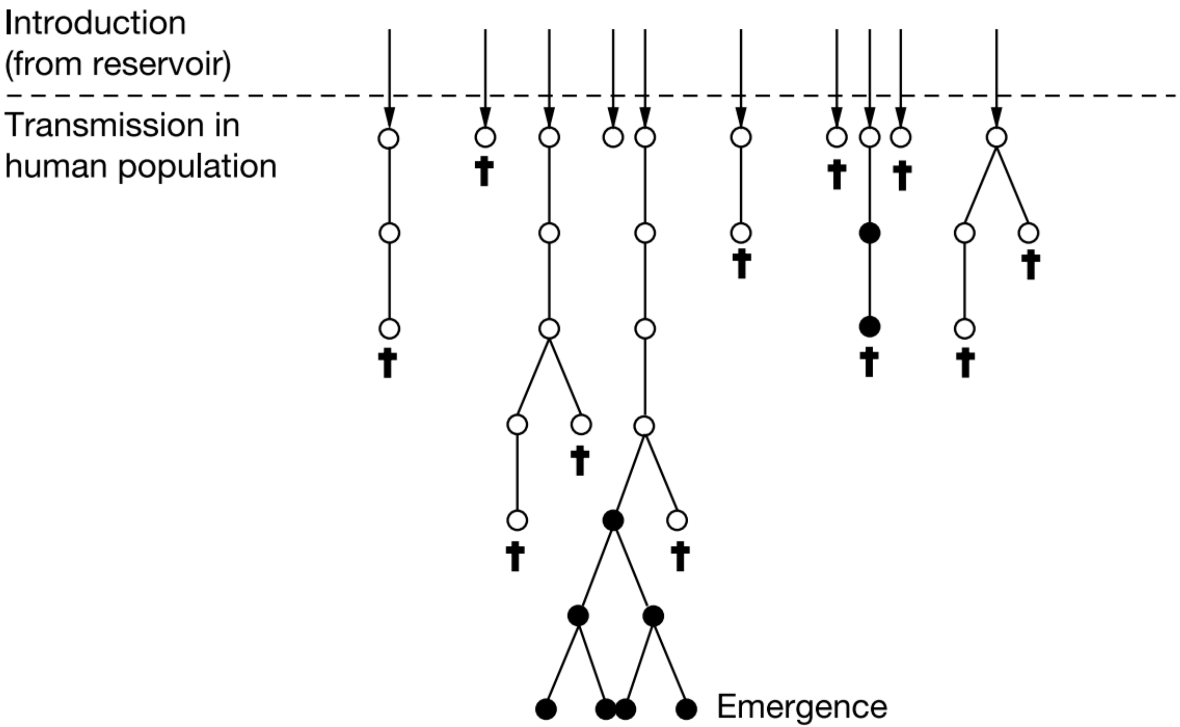
Emergence

- Spill-over events



Infectious Disease Epidemiology

Emergence



Modified from Antia et al. 2003

Cumulative number of confirmed human cases for avian influenza A(H5N1) reported to WHO, 2003-2023

Country	2003-2009*		2010-2014*		2015-2019*		2020		2021		2022		2023		Total	
	cases	deaths	cases	deaths	cases	deaths	cases	deaths	cases	deaths	cases	deaths	cases	deaths	cases	deaths
Azerbaijan	8	5	0	0	0	0	0	0	0	0	0	0	0	0	8	5
Bangladesh	1	0	6	1	1	0	0	0	0	0	0	0	0	0	8	1
Cambodia	9	7	47	30	0	0	0	0	0	0	0	0	0	0	56	37
Canada	0	0	1	1	0	0	0	0	0	0	0	0	0	0	1	1
China	38	25	9	5	6	1	0	0	0	0	1	1	0	0	54	32
Djibouti	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0
Egypt	90	27	120	50	149	43	0	0	0	0	0	0	0	0	359	120
India	0	0	0	0	0	0	0	0	1	1	0	0	0	0	1	1
Indonesia	162	134	35	31	3	3	0	0	0	0	0	0	0	0	200	168
Iraq	3	2	0	0	0	0	0	0	0	0	0	0	0	0	3	2
Lao People's Democratic Republic	2	2	0	0	0	0	1	0	0	0	0	0	0	0	3	2
Myanmar	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0
Nepal	0	0	0	0	1	1	0	0	0	0	0	0	0	0	1	1
Nigeria	1	1	0	0	0	0	0	0	0	0	0	0	0	0	1	1
Pakistan	3	1	0	0	0	0	0	0	0	0	0	0	0	0	3	1
Spain	0	0	0	0	0	0	0	0	0	0	2	0	0	0	2	0
Thailand	25	17	0	0	0	0	0	0	0	0	0	0	0	0	25	17
Turkey	12	4	0	0	0	0	0	0	0	0	0	0	0	0	12	4
United Kingdom of Great Britain and Northern Ireland	0	0	0	0	0	0	0	0	1	0	0	0	0	0	1	0
United States of America	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1	0
Viet Nam	112	57	15	7	0	0	0	0	0	0	0	0	0	0	127	64
Total	**468**	**282**	**233**	**125**	**160**	**48**	**1**	**0**	**2**	**1**	**4**	**1**	**0**	**0**	**868**	**457**

* 2003-2009, 2010-2014 and 2015-2019 total figures. Breakdowns by year available on subsequent tables.
Total number of cases includes number of deaths.
WHO reports only laboratory-confirmed cases.
All dates refer to onset of illness
Source: WHO/GIP, data in HQ as of 26 January 2023

World Health Organization

Infectious Disease Epidemiology

Transmission

- Contagion: In a new host, a pathogen needs to be able to transmit itself from one individual to the next.
- Transmission mode vs Transmission route

Infectious Disease Epidemiology
Transmission

- Contact: the link between (potential) infecting individual and infected individual. Depends on transmission.

Infectious Disease Epidemiology

Transmission

- Cholera: caused by *Vibrio cholerae*. Ingested through water, can cause severe dehydration which can lead to death (CFR ~2%)

Source: https://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0000898

Infectious Disease Epidemiology
Waterborne transmission

- Cholera
- Salmonella* (Typhoid fever)
- Hepatitis A and E
- Polio**

* mostly foodborne
** ~95% asymptomatic

Infectious Disease Epidemiology
Airborne transmission

- Airborne: aerosols and droplet. Respiratory diseases, measles, chickenpox, TB, pneumonic plague, etc.

- Before COVID:
  < 5 µm: aerosol
  > 5 µm: droplets

- Aerosol transmission
- Droplet transmission

Infectious Disease Epidemiology
Airborne transmission

- Airborne: aerosols and droplet. Respiratory diseases, measles, chickenpox, TB, pneumonic plague, etc.

- Before COVID:
  ~~< 5 µm: aerosol~~
  ~~> 5 µm: droplets~~

- Aerosol transmission
- Droplet transmission

Infectious Disease Epidemiology
Airborne transmission

- Aerosols up to 100 µm can remain suspended for long time.
- Viral load in aerosols higher than in droplets
- Aerosol likely the dominant transmission mode
- Both play a role, but droplet only over short distances. Aerosol over short AND long distances.

Infectious Disease Epidemiology

Airborne transmission

- Influenza: still thought to be mostly droplet, but evidence is shaky after COVID-19.

Transmission of influenza A in human beings

Gabrielle Brankston, Leah Gitterman, Zahir Hirji, Camille Lemieux, Michael Gardam

Planning for the next influenza pandemic is occurring at many levels throughout the world, spurred on by the recent spread of H5N1 avian influenza in Asia, Europe, and Africa. Central to these planning efforts in the health-care sector are strategies to minimise the transmission of influenza to health-care workers and patients. The infection control precautions necessary to prevent airborne, droplet, and contact transmission are quite different and will need to be decided on and planned before a pandemic occurs. Despite vast clinical experience in human beings, there continues to be much debate about how influenza is transmitted. We have done a systematic review of the English language experimental and epidemiological literature on this subject to better inform infection control planning efforts. We have found that the existing data are limited with respect to the identification of specific modes of transmission in the natural setting. However, we are able to conclude that transmission occurs at close range rather than over long distances, suggesting that airborne transmission, as traditionally defined, is unlikely to be of significance in most clinical settings. Further research is required to better define conditions under which the influenza virus may transmit via the airborne route.

Source: Brankston et al 2007

Infectious Disease Epidemiology
Airborne transmission

Bulletin of Mathematical Biology (2008) 70: 820–867
DOI 10.1007/s11538-007-9281-2

ORIGINAL ARTICLE

Quantifying the Routes of Transmission for Pandemic Influenza

Michael P. Atkinson[a], Lawrence M. Wein[b,*]

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Received: 2 January 2007 / Accepted: 3 October 2007 / Published online: 16 February 2008

- A mathematical model
- “An analysis of this model in conjunction with influenza and rhinovirus data suggests that aerosol transmission is far more dominant than contact transmission for influenza.”
- close contacts unlikely to generate enough transmission

Source: Atkinson & Wein, 2008

Infectious Disease Epidemiology
Airborne transmission

Transmission of Influenza Virus via Aerosols and Fomites in the Guinea Pig Model

Samira Mubareka,[1] Anice C. Lowen,[1] John Steel,[1] Allan L. Coates,[4] Adolfo García-Sastre,[1,2,3] and Peter Palese[1,3]

[1]Department of Microbiology, [2]Emerging Pathogens Institute, and [3]Department of Medicine, Mount Sinai School of Medicine, New York, New York; [4]Division of Respiratory Medicine, Hospital for Sick Children, and Research Institute for Physiology and Experimental Medicine, University of Toronto, Toronto, Ontario, Canada

Limited data on the relative contributions of different routes of transmission for influenza virus are available. Person-to-person transmission is central to seasonal and pandemic spread; nevertheless, the modes of spread are a matter of ongoing debate. Resolution of this discussion is paramount to the development of effective control measures in health care and community settings. Using the guinea pig model, we demonstrated that transmission of influenza A/Panama/2007/1999 (H3N2) virus through the air is efficient, compared with spread through contaminated environmental surfaces (fomites). We also examined the aerosol transmission efficiencies of 2 human influenza virus A strains and found that A/Panama/2007/1999 influenza virus transmitted more efficiently than A/Texas/36/1991 (H1N1) virus in our model. The data provide new and much-needed insights into the modes of influenza virus spread and strain-specific differences in the efficiency of transmission.

Source: Mubareke, 2009

Infectious Disease Epidemiology

Airborne transmission

Possible Role of Aerosol Transmission in a Hospital Outbreak of Influenza

Bonnie C. K. Wong,[1] Nelson Lee,[1] Yuguo Li,[4] Paul K. S. Chan,[2] Hong Qiu,[3] Zhiwen Luo,[4] Raymond W. M. Lai,[2] Karry L. K. Ngai,[2] David S. C. Hui,[1] K. W. Choi,[1] and Ignatius T. S. Yu[3]

Departments of [1]Medicine and Therapeutics, [2]Microbiology, and [3]Community and Family Medicine, The Chinese University of Hong Kong, and [4]Department of Mechanical Engineering, University of Hong Kong, Hong Kong, China

Background. We examined the role of aerosol transmission of influenza in an acute ward setting.

Methods. We investigated a seasonal influenza A outbreak that occurred in our general medical ward (with open bay ward layout) in 2008. Clinical and epidemiological information was collected in real time during the outbreak. Spatiotemporal analysis was performed to estimate the infection risk among patients. Airflow measurements were conducted, and concentrations of hypothetical virus-laden aerosols at different ward locations were estimated using computational fluid dynamics modeling.

Results. Nine inpatients were infected with an identical strain of influenza A/H3N2 virus. With reference to the index patient's location, the attack rate was 20.0% and 22.2% in the "same" and "adjacent" bays, respectively, but 0% in the "distant" bay ($P = .04$). Temporally, the risk of being infected was highest on the day when noninvasive ventilation was used in the index patient; multivariate logistic regression revealed an odds ratio of 14.9 (95% confidence interval, 1.7–131.3; $P = .015$). A simultaneous, directional indoor airflow blown from the "same" bay toward the "adjacent" bay was found; it was inadvertently created by an unopposed air jet from a separate air purifier placed next to the index patient's bed. Computational fluid dynamics modeling revealed that the dispersal pattern of aerosols originated from the index patient coincided with the bed locations of affected patients.

Conclusions. Our findings suggest a possible role of aerosol transmission of influenza in an acute ward setting. Source and engineering controls, such as avoiding aerosol generation and improving ventilation design, may warrant consideration to prevent nosocomial outbreaks.

- A outbreak in hospital ward setting
- "A directional indoor airflow was found; it was inadvertently created by an unopposed air jet from a separate air purifier placed next to the index patient's bed."

Source: Mubareke, 2009

Infectious Disease Epidemiology

Airborne transmission

Detection of Infectious Influenza Virus in Cough Aerosols Generated in a Simulated Patient Examination Room

John D. Noti,[1] William G. Lindsley,[1] Francoise M. Blachere,[1] Gang Cao,[4] Michael L. Kashon,[1] Robert E. Thewlis,[1] Cynthia M. McMillen,[1,2] William P. King,[3] Jonathan V. Szalajda,[3] and Donald H. Beezhold[1]

[1]Health Effects Laboratory Division (HELD), National Institute for Occupational Safety and Health (NIOSH), Centers for Disease Control and Prevention (CDC), and [2]Department of Microbiology, Immunology and Cell Biology, School of Medicine, West Virginia University, Morgantown; [3]Policy and Standards Development Branch, National Personal Protective Technology Laboratory, NIOSH/CDC, Pittsburgh, Pennsylvania; and [4]Harbin Institute of Technology, Shen Zhen Graduate School, HIT Campus, Shen Zhen University Xi Li, China

(See the Editorial Commentary by Cowling, on pages 1578–80.)

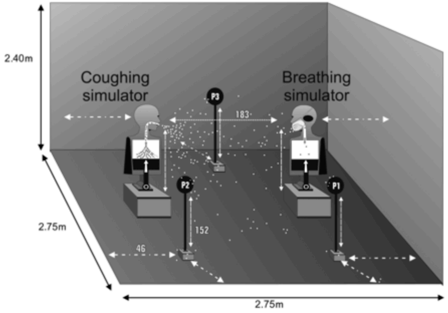
Background. The potential for aerosol transmission of infectious influenza virus (ie, in healthcare facilities) is controversial. We constructed a simulated patient examination room that contained coughing and breathing manikins to determine whether coughed influenza was infectious and assessed the effectiveness of an N95 respirator and surgical mask in blocking transmission.

Methods. National Institute for Occupational Safety and Health aerosol samplers collected size-fractionated aerosols for 60 minutes at the mouth of the breathing manikin, beside the mouth, and at 3 other locations in the room. Total recovered virus was quantitated by quantitative polymerase chain reaction and infectivity was determined by the viral plaque assay and an enhanced infectivity assay.

Results. Infectious influenza was recovered in all aerosol fractions (5.0% in >4 µm aerodynamic diameter, 75.5% in 1–4 µm, and 19.5% in <1 µm; n = 5). Tightly sealing a mask to the face blocked entry of 94.5% of total virus and 94.8% of infectious virus (n = 3). A tightly sealed respirator blocked 99.8% of total virus and 99.6% of infectious virus (n = 3). A poorly fitted respirator blocked 64.5% of total virus and 66.5% of infectious virus (n = 3). A mask documented to be loosely fitting by a PortaCount fit tester, to simulate how masks are worn by healthcare workers, blocked entry of 68.5% of total virus and 56.6% of infectious virus (n = 2).

Conclusions. These results support a role for aerosol transmission and represent the first reported laboratory study of the efficacy of masks and respirators in blocking inhalation of influenza in aerosols. The results indicate that a poorly fitted respirator performs no better than a loosely fitting mask.

- A simulated patient examination room
- “Infectious influenza was recovered in all aerosol fractions.”



Source: Noti et al, 2012

Infectious Disease Epidemiology
Airborne transmission

ARTICLE

Received 4 Oct 2012 | Accepted 24 Apr 2013 | Published 4 Jun 2013

DOI: 10.1038/ncomms2922

Aerosol transmission is an important mode of influenza A virus spread

Benjamin J. Cowling[1], Dennis K. M. Ip[1], Vicky J. Fang[1], Piyarat Suntarattiwong[2], Sonja J. Olsen[3,4], Jens Levy[3], Timothy M. Uyeki[4], Gabriel M. Leung[1], J. S. Malik Peiris[1,5], Tawee Chotpitayasunondh[2], Hiroshi Nishiura[1,6] & James Mark Simmerman[7]

Influenza A viruses are believed to spread between humans through contact, large respiratory droplets and small particle droplet nuclei (aerosols), but the relative importance of each of these modes of transmission is unclear. Volunteer studies suggest that infections via aerosol transmission may have a higher risk of febrile illness. Here we apply a mathematical model to data from randomized controlled trials of hand hygiene and surgical face masks in Hong Kong and Bangkok households. In these particular environments, inferences on the relative importance of modes of transmission are facilitated by information on the timing of secondary infections and apparent differences in clinical presentation of secondary infections resulting from aerosol transmission. We find that aerosol transmission accounts for approximately half of all transmission events. This implies that measures to reduce transmission by contact or large droplets may not be sufficient to control influenza A virus transmission in households.

- Application of a mathematical model to data from randomized controlled trials in Hong Kong and Bangkok households
- “Measures to reduce transmission by contact may not be sufficient to control influenza transmission”

Source: Cowling et al, 2013

Infectious Disease Epidemiology
Airborne transmission

Viable influenza A virus in airborne particles expelled during coughs versus exhalations

William G. Lindsley,[a] Francoise M. Blachere,[a] Donald H. Beezhold,[a] Robert E. Thewlis,[a] Bahar Noorbakhsh,[a] Sreekumar Othumpangat,[a] William T. Goldsmith,[a] Cynthia M. McMillen,[a] Michael E. Andrew,[a] Carmen N. Burrell,[b] John D. Noti[a]

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Correspondence: William G. Lindsley, National Institute for Occupational Safety and Health, 1095 Willowdale Road, M/S 4020, Morgantown, WV 26505-2845, USA. E-mail: wlindsley@cdc.gov

Accepted 25 February 2016.

Background To prepare for a possible influenza pandemic, a better understanding of the potential for the airborne transmission of influenza from person to person is needed.

Objectives The objective of this study was to directly compare the generation of aerosol particles containing viable influenza virus during coughs and exhalations.

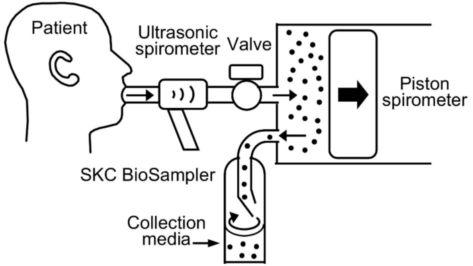
Methods Sixty-one adult volunteer outpatients with influenza-like symptoms were asked to cough and exhale three times into a spirometer. Aerosol particles produced during coughing and exhalation were collected into liquid media using aerosol samplers. The samples were tested for the presence of viable influenza virus using a viral replication assay (VRA).

Results Fifty-three test subjects tested positive for influenza A virus. Of these, 28 (53%) produced aerosol particles containing viable influenza A virus during coughing, and 22 (42%) produced aerosols with viable virus during exhalation. Thirteen subjects had both cough aerosol and exhalation aerosol samples that contained viable virus, 15 had positive cough aerosol samples but negative exhalation samples, and 9 had positive exhalation samples but negative cough samples.

Conclusions Viable influenza A virus was detected more often in cough aerosol particles than in exhalation aerosol particles, but the difference was not large. Because individuals breathe much more often than they cough, these results suggest that breathing may generate more airborne infectious material than coughing over time. However, both respiratory activities could be important in airborne influenza transmission. Our results are also consistent with the theory that much of the aerosol containing viable influenza originates deep in the lungs.

Keywords Aerosols, air microbiology, airborne transmission, cough, infectious disease transmission, influenza.

- Influenza patients were asked to cough and exhale into a spirometer



Source: Lindsley et al, 2016

Infectious Disease Epidemiology
Airborne transmission

Epidemiology and Infection

cambridge.org/hyg

Probable transmission routes of the influenza virus in a nosocomial outbreak

S. Xiao[1], J. W. Tang[2,3], D. S. Hui[4], H. Lei[1,5], H. Yu[1] and Y. Li[1]

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Original Paper

Cite this article: Xiao S, Tang JW, Hui DS, Lei H, Yu H, Li Y (2018). Probable transmission routes of the influenza virus in a nosocomial outbreak. *Epidemiology and Infection* **146**, 1114–1122. https://doi.org/10.1017/S0950268818001012

Received: 8 January 2018
Revised: 11 March 2018
Accepted: 3 April 2018
First published online: 6 May 2018

Key words:
Fomite; influenza; long-range airborne; multi-route transmission; nosocomial outbreaks

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Abstract

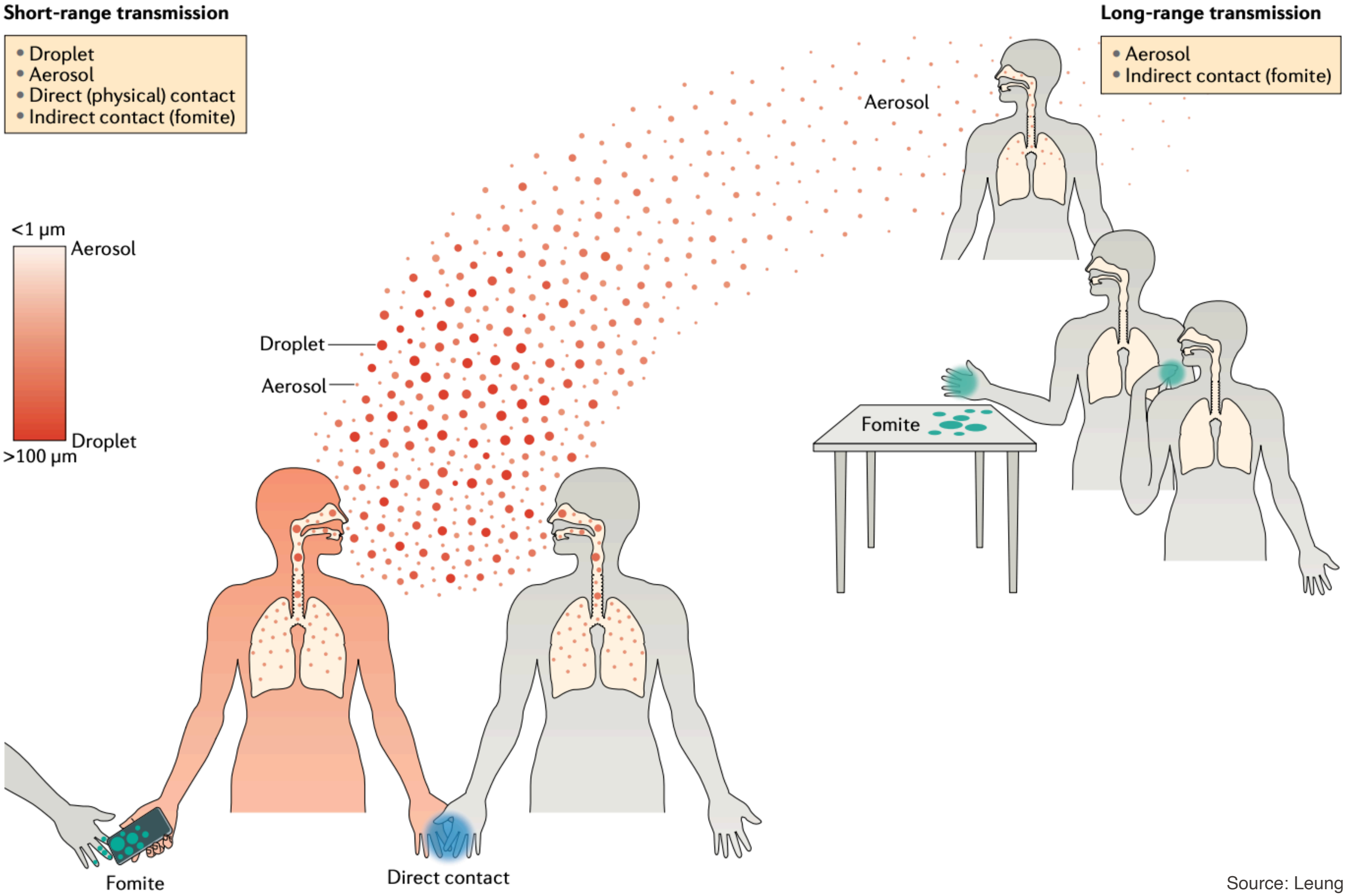
Influenza is a long-standing public health concern, but its transmission remains poorly understood. To have a better knowledge of influenza transmission, we carried out a detailed modelling investigation in a nosocomial influenza outbreak in Hong Kong. We identified three hypothesised transmission modes between index patient and other inpatients based on the long-range airborne and fomite routes. We considered three kinds of healthcare workers' routine round pathways in 1140 scenarios with various values of important parameters. In each scenario, we used a multi-agent modelling framework to estimate the infection risk for each hypothesis and conducted least-squares fitting to evaluate the hypotheses by comparing the distribution of the infection risk with that of the attack rates. Amongst the hypotheses tested in the 1140 scenarios, the prediction of modes involving the long-range airborne route fit better with the attack rates, and that of the two-route transmission mode had the best fit, with the long-range airborne route contributing about 94% and the fomite route contributing 6% to the infections. Under the assumed conditions, the influenza virus was likely to have spread via a combined long-range airborne and fomite routes, with the former predominant and the latter negligible.

- Modelling investigation
- Best fit of 1'140 scenario: model with 94% long-range airborne route

Source: Xiao et al, 2018

Infectious Disease Epidemiology
Contact Transmission

- Physical Transmission, e.g. Mpox via skin leasons
- Fomite transmission (via object) - e.g. hospital acquired bacterial infections



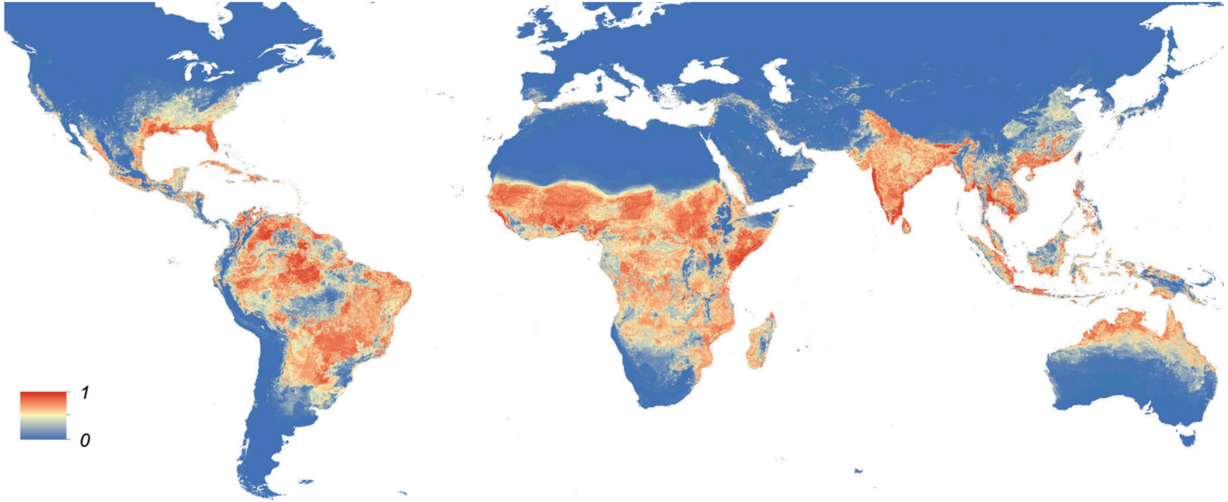
Source: Leung et al, 2021

Infectious Disease Epidemiology
Vector-borne Transmission

- Mostly through mosquitoes, ticks, and fleas.
- Malaria, Dengue, Zika, Chikungunya, West nile; Lyme disease; bubonic plague

Infectious Disease Epidemiology

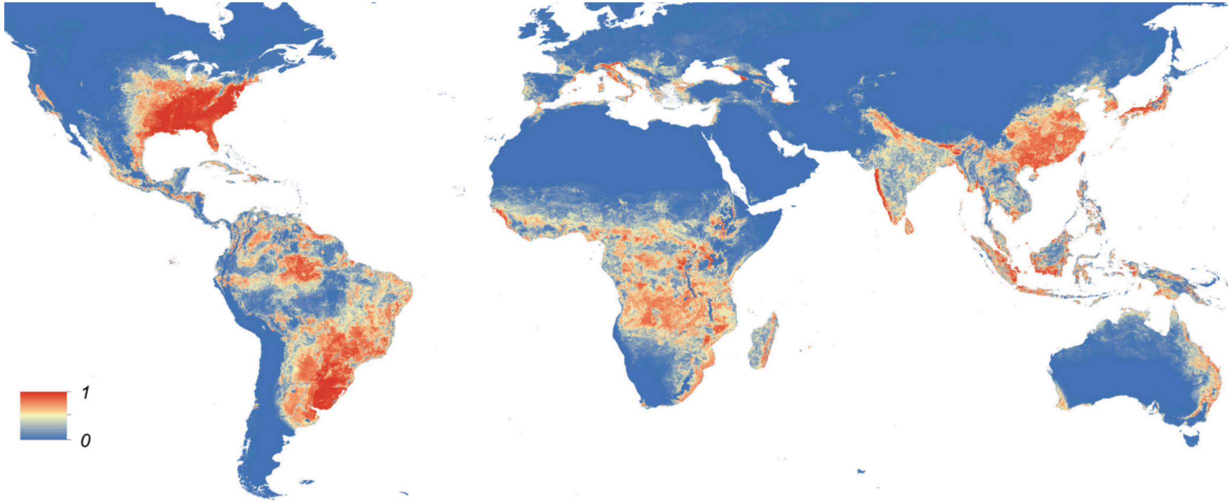
Vector-borne Transmission



Aedes aegypti (Yellow fever mosquito)

Source: Kraemer et al, 2015

Infectious Disease Epidemiology
Vector-borne Transmission



Aedes albopictus (Asian tiger mosquito)

Source: Kraemer et al, 2015

Infectious Disease Epidemiology

Vector-borne Transmission

- Malaria: caused by different species of the genus *Plasmodium* (unicellular eukaryotes) - transmitted through mosquitoes
- Caused an estimated 627,000 deaths out of 241 million cases in 2020

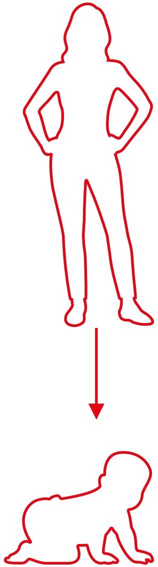
Infectious Disease Epidemiology
Body fluid transmission

- Sexually transmitted diseases, e.g. HIV/AIDS, Hepatitis B
- Epstein-Barr virus (mononucleosis) transmissible through saliva, but HIV is not

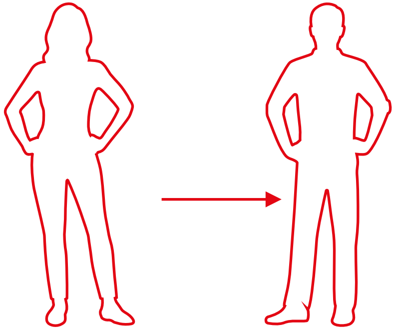
Infectious Disease Epidemiology
Food borne transmission

- Salmonella, Norovirus, E.Coli - but rather part of complex transmission chains

Infectious Disease Epidemiology
Vertical vs horizontal transmission

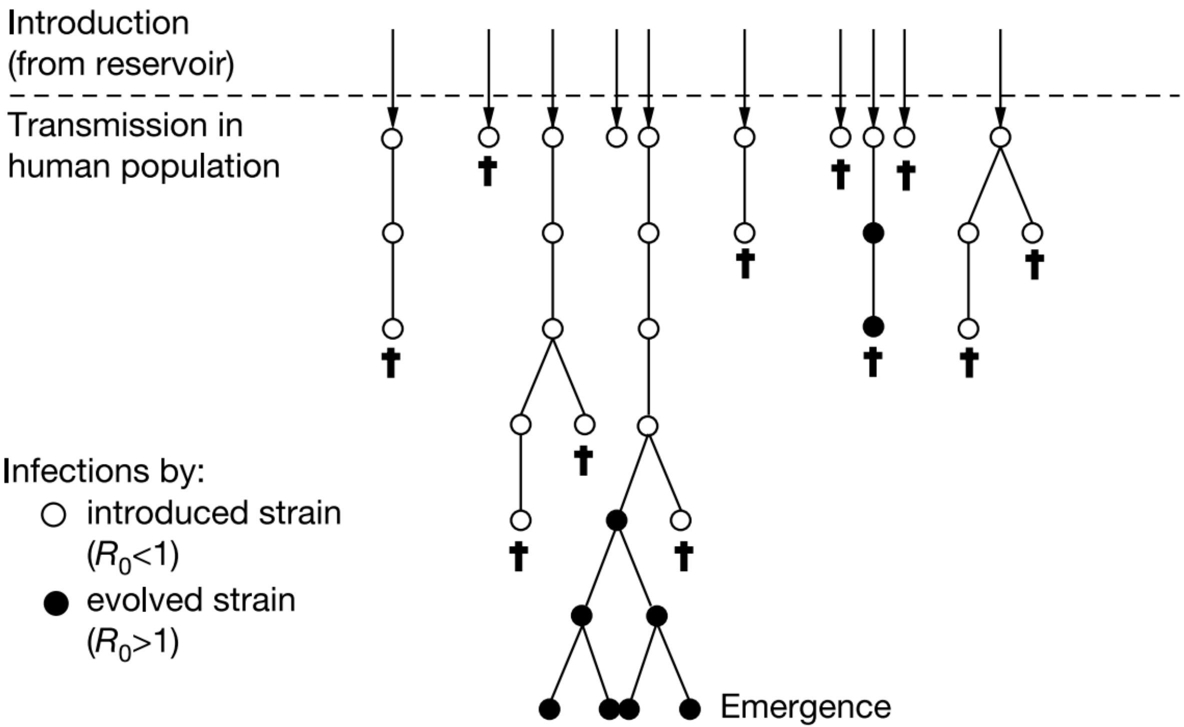


congenital
infection



Infectious Disease Epidemiology

Contagion



Source: Antia et al. 2003

Infectious Disease Epidemiology

Contagion

- Reproductive number R: number of “offspring infections” per infection (on average)

- R_0 at t = 0
- R_e at t > 0

- $R_e = R_0$ * fraction of susceptible

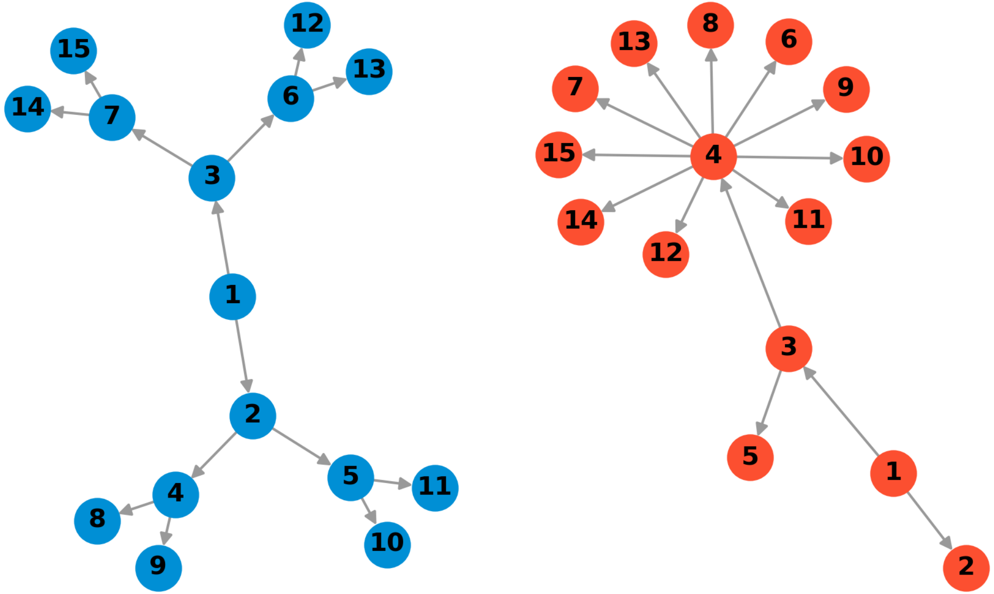
Source: Antia et al. 2003

Disease	Transmission	R_0	HIT[a]
Measles	Aerosol	12–18[40][7]	92–94%
Chickenpox (varicella)	Aerosol	10–12[41]	90–92%
Mumps	Respiratory droplets	10–12[42]	90–92%
Rubella	Respiratory droplets	6–7[b]	83–86%
Polio	Fecal–oral route	5–7[b]	80–86%
Pertussis	Respiratory droplets	5.5[47]	82%
Smallpox	Respiratory droplets	3.5–6.0[48]	71–83%
HIV/AIDS	Body fluids	2–5[49]	50–80%
COVID-19 (ancestral strain)	Respiratory droplets and aerosol[50]	2.9 (2.4–3.4)[51]	65% (58–71%)
SARS	Respiratory droplets	2–4[52]	50–75%
Diphtheria	Saliva	2.6 (1.7–4.3)[53]	62% (41–77%)
Common cold (e.g., rhinovirus)	Respiratory droplets	2–3[54][*medical citation needed*]	50–67%
Monkeypox	Physical contact, body fluids, respiratory droplets	2.1 (1.5–2.7)[55]	53% (31–63%)
Ebola (2014 outbreak)	Body fluids	1.8 (1.4–1.8)[56]	44% (31–44%)
Influenza (seasonal strains)	Respiratory droplets	1.3 (1.2–1.4)[57]	23% (17–29%)
Andes hantavirus	Respiratory droplets and body fluids	1.2 (0.8–1.6)[58]	16% (0–36%)[c]
Nipah virus	Body fluids	0.5[59]	0%[c]
MERS	Respiratory droplets	0.5 (0.3–0.8)[60]	0%[c]

EPFL

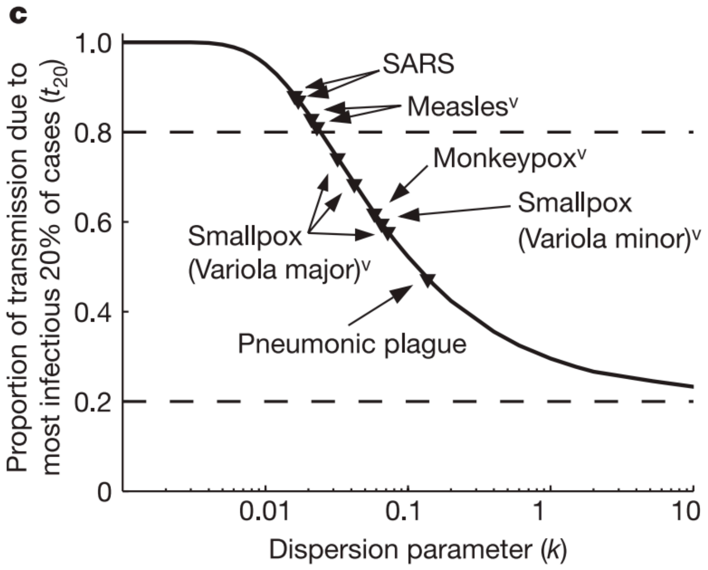
Infectious Disease Epidemiology

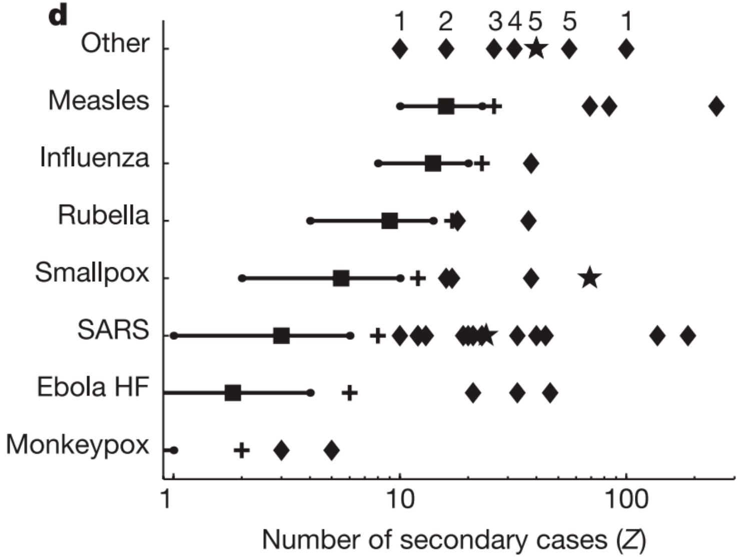
Superspreading



Infectious Disease Epidemiology

Superspreading

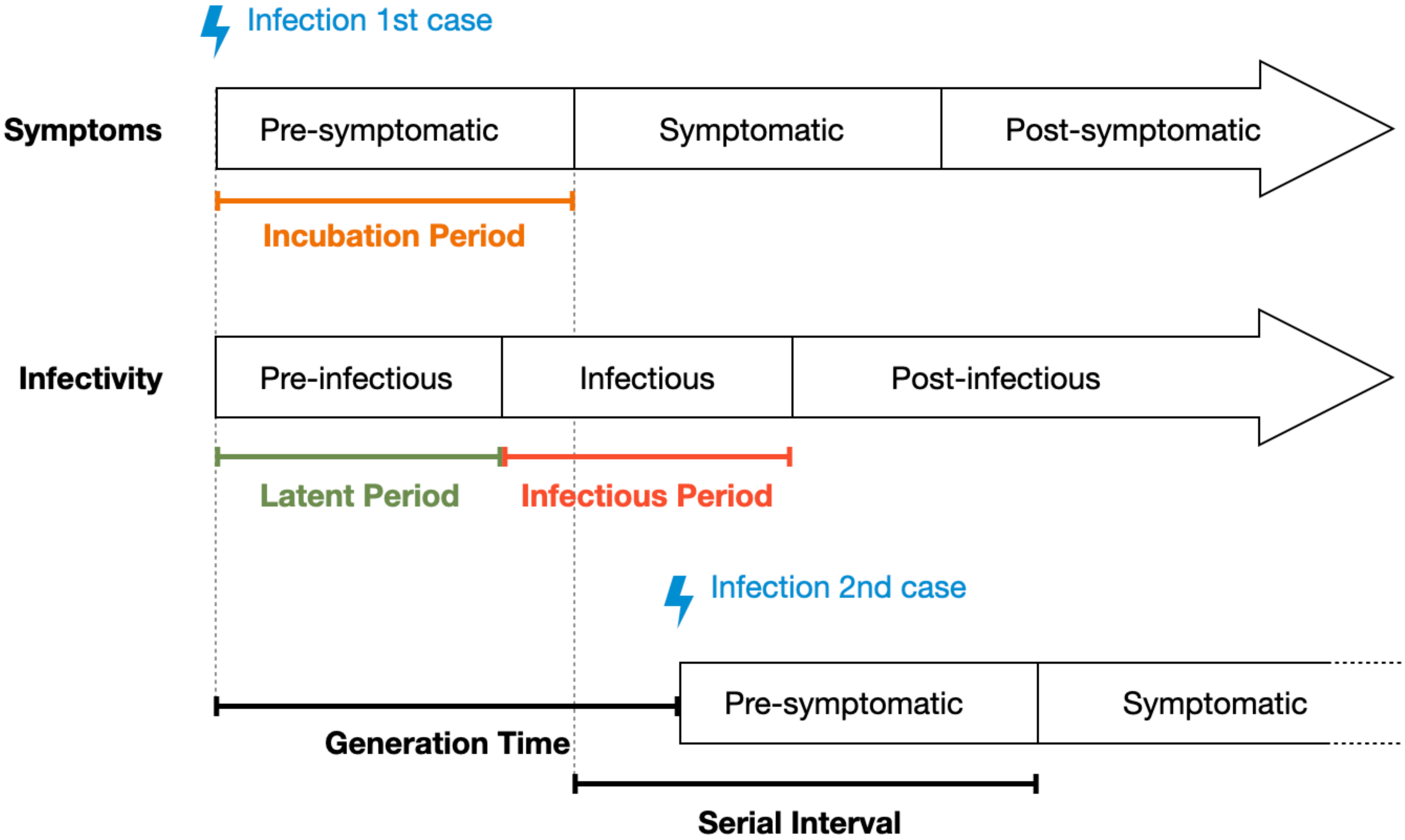




Source: Lloyd-Smith et al. 2005

Infectious Disease Epidemiology
Course of Infection

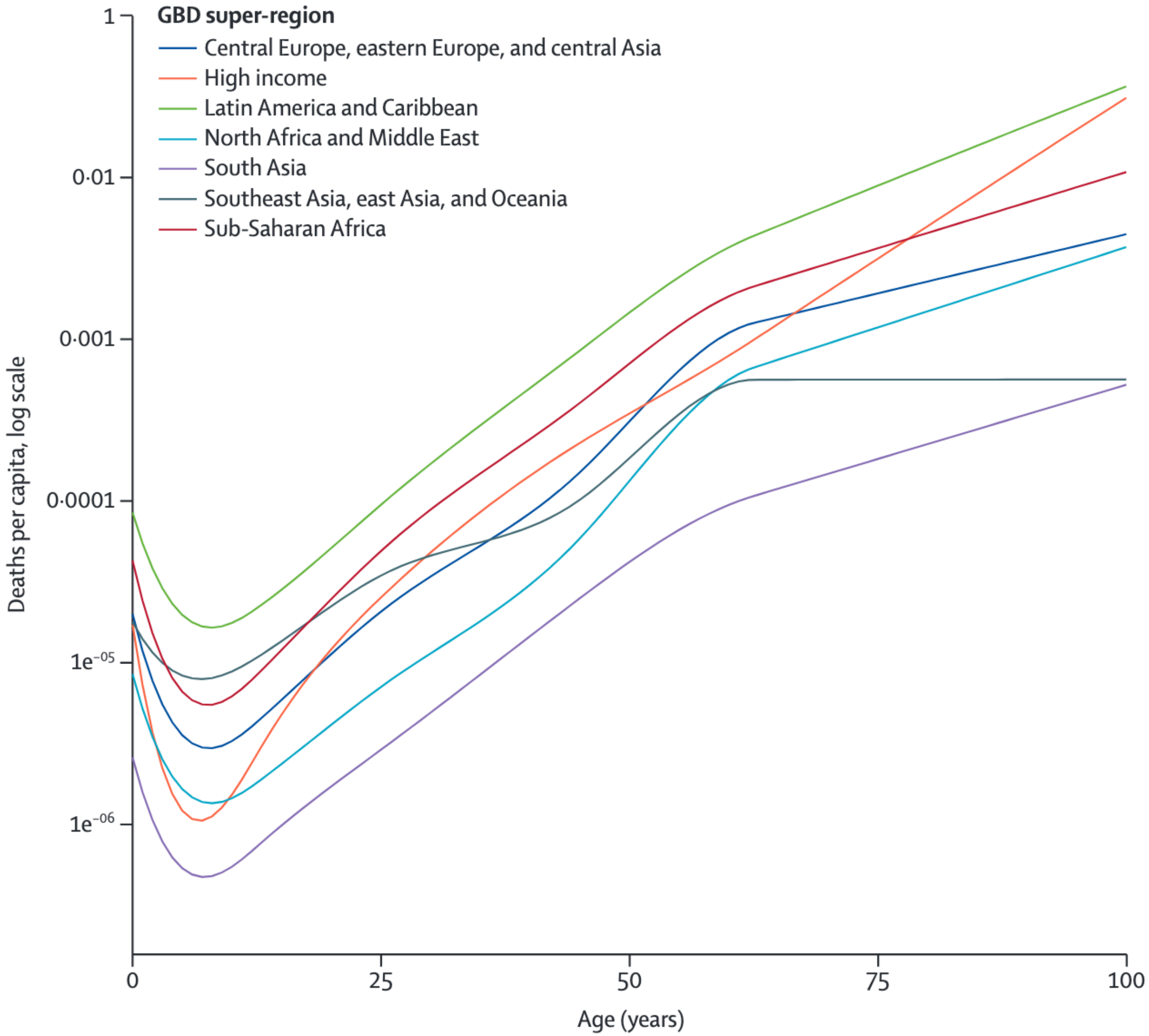
- Immune system: innate & adaptive
- Pathogen enters body - is there any response? The earlier and the more specific, the better (that is why first encounters are the most dangerous)

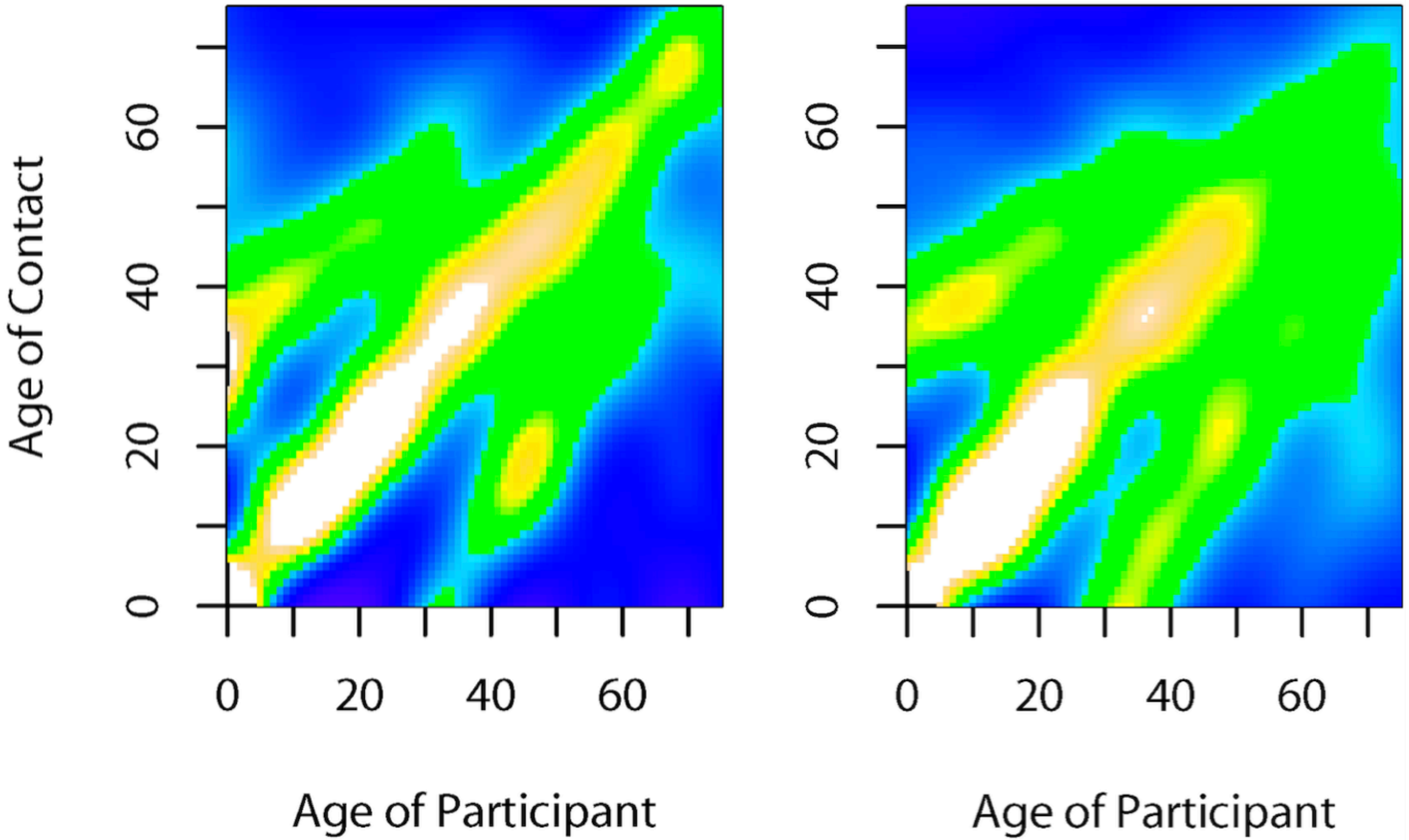

Infection 1st case
Symptoms
Pre-symptomatic
Symptomatic
Post-symptomatic
Incubation Period
Infectivity
Pre-infectious
Infectious
Post-infectious
Latent Period
Infectious Period
Infection 2nd case
Pre-symptomatic
Symptomatic
Generation Time
Serial Interval

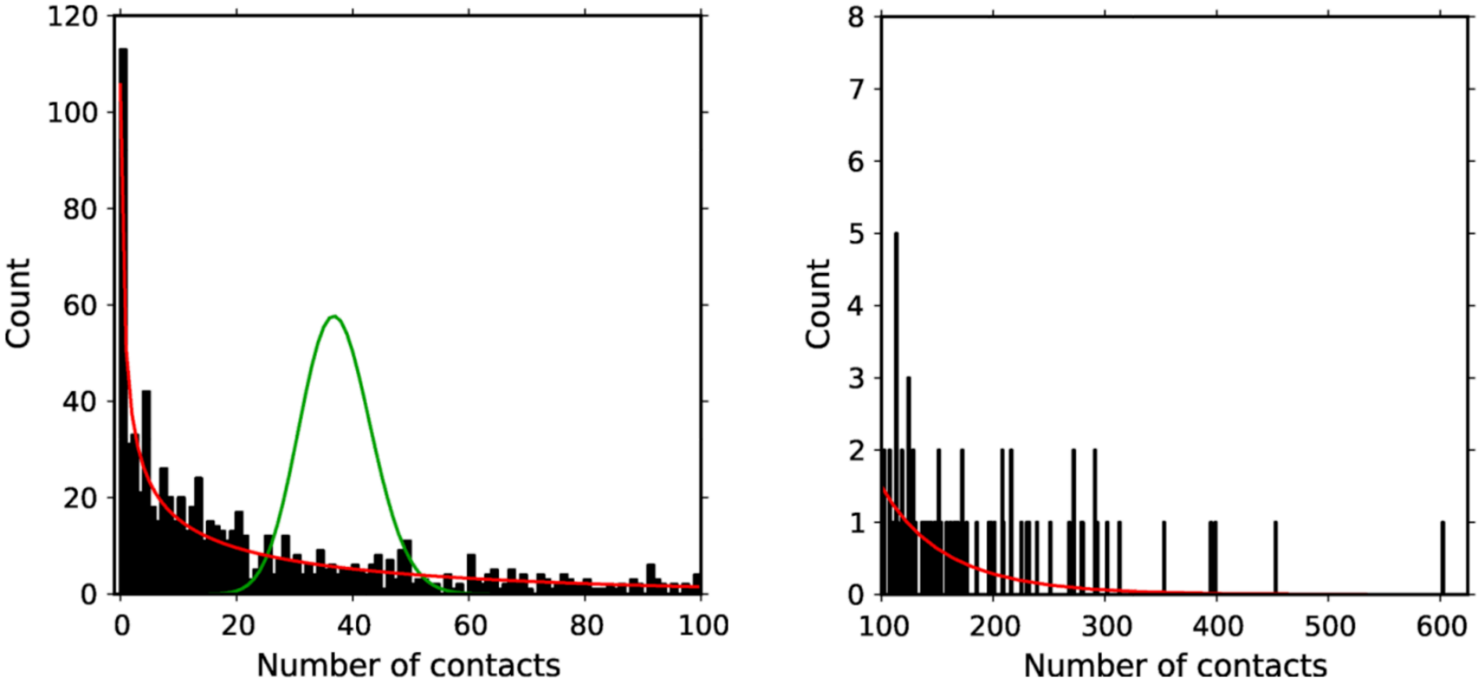
Infectious Disease Epidemiology

Heterogeneties

- Heterogeneities in contact, age, and space are three major contributors to outcomes - but there are many other important heterogeneities


GBD super-region
Central Europe, eastern Europe, and central Asia
High income
Latin America and Caribbean
North Africa and Middle East
South Asia
Southeast Asia, east Asia, and Oceania
Sub-Saharan Africa
Deaths per capita, log scale
1
0·01
0·001
0·0001
1e−05
1e−06
0
25
50
75
100
Age (years)


Age of Contact
0
20
40
60
0
20
40
60
Age of Participant
0
20
40
60
0
20
40
60
Age of Participant

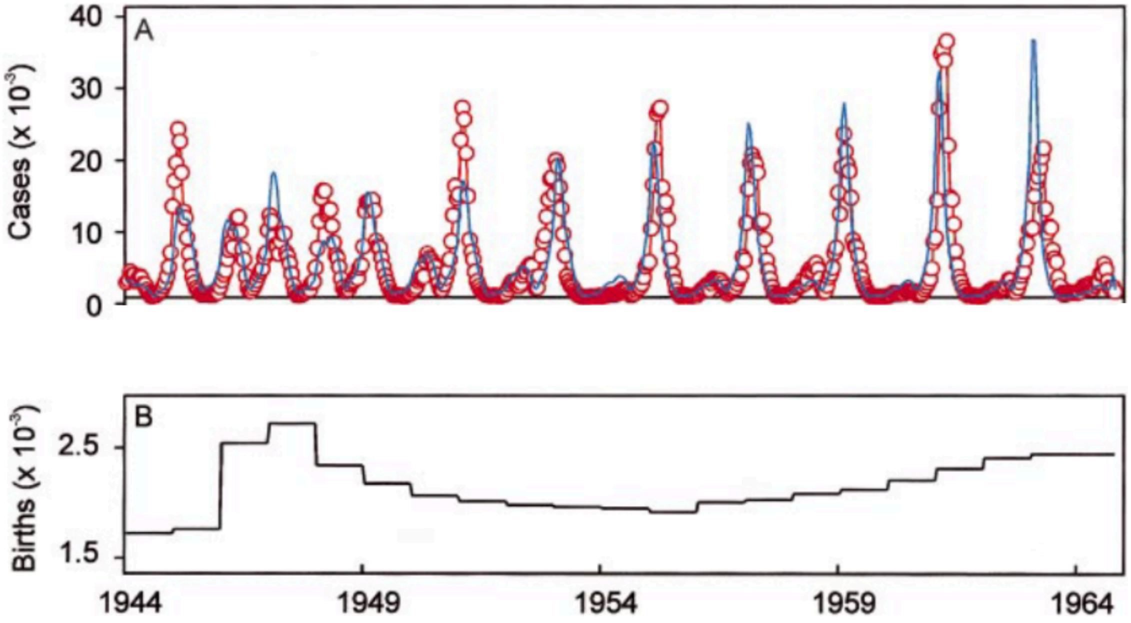


Count
Number of contacts
0
20
40
60
80
100
120
0
20
40
60
80
100
Count
Number of contacts
0
1
2
3
4
5
6
7
8
100
200
300
400
500
600

$$R_0 = r * k * (1 + CV^2)$$

Infectious Disease Epidemiology
Heterogeneties

- Spatial population distribution highly non-random / non-even



Infectious Disease Epidemiology

Vaccination

- Variolation: inoculation with smallpox from another patient in hope of a milder disease course (mortality ~ 2%), compared to natural infection (mortality ~30%).
- Vaccination (from vacca, cow): Edward Jenner (18th century) observed that people infected with milder cowpox rarely got smallpox.
- Effect of vaccines depends on immune response they can induce

Infectious Disease Epidemiology

Vaccination

- Whole pathogen vaccines (with attenuated or killed pathogen), e.g. MMR vaccine
- Subunit / acellular vaccines (parts of pathogen), e.g. acellular Pertussis vaccine
- Nucleic acid vaccines (e.g. mRNA vaccines)

Infectious Disease Epidemiology
Vaccination

- Vaccines are rarely perfect, must be continuously evaluated.
- Vaccine efficacy: how well does a vaccine perform in a trial?
- Vaccine effectiveness: how well does a vaccine perform in the real world?

- Vaccines can: block infection AND/OR reduce transmission AND/OR reduce severity

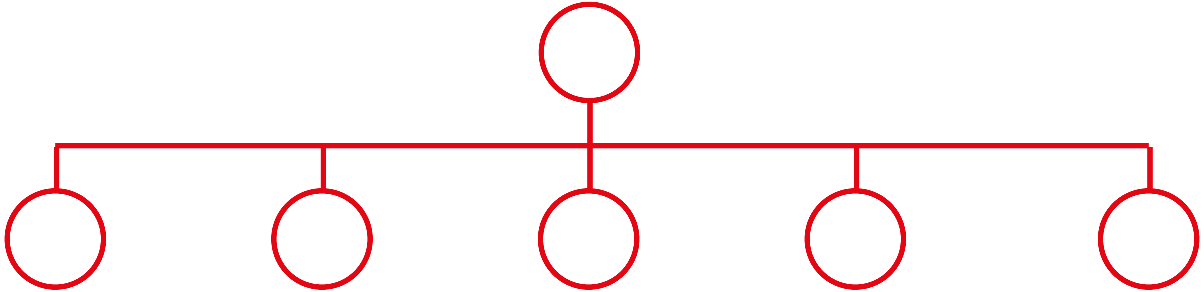
Infectious Disease Epidemiology

Herd Immunity

- Infection protection conferred by others who are vaccinated - assumes vaccine is infection blocking (or at least transmission reducing).

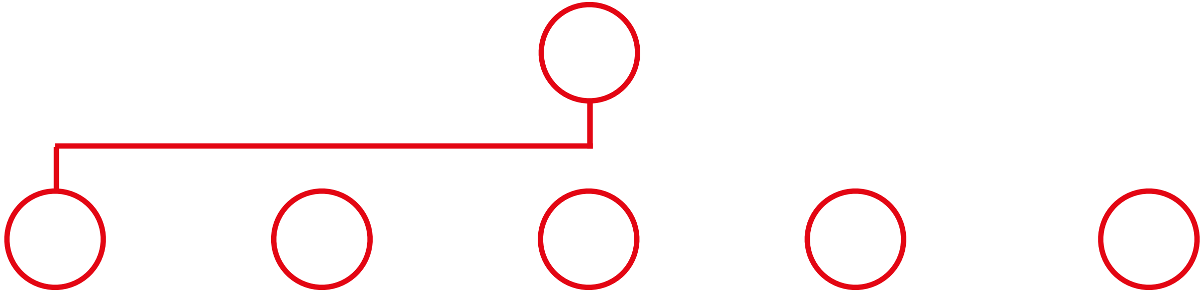
Infectious Disease Epidemiology
Herd Immunity

- Herd immunity *threshold* - fraction of population that needs to be vaccinated in order to bring R < 1.



Infectious Disease Epidemiology
Herd Immunity

- Herd immunity *threshold* - fraction of population that needs to be vaccinated in order to bring $R < 1$.

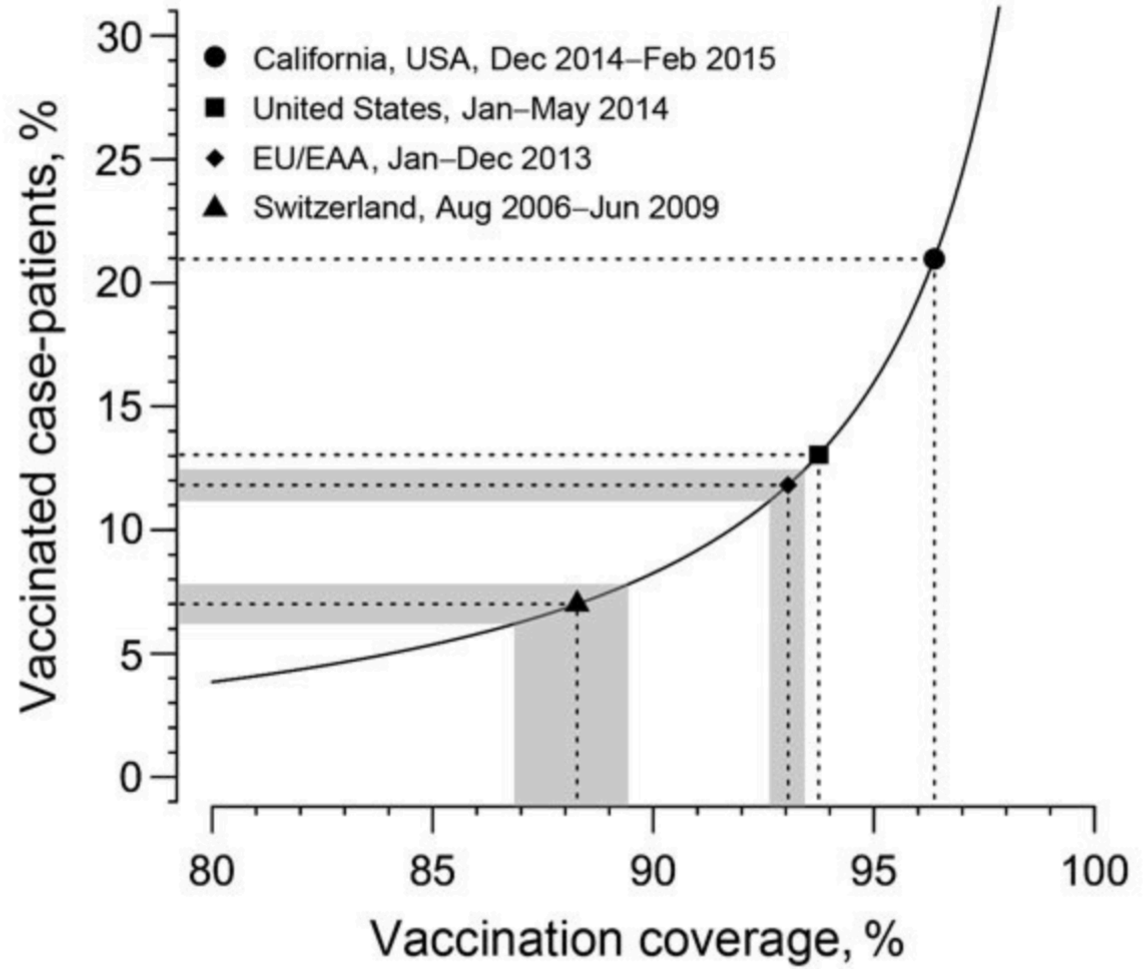


$$c > 1 - \left(\frac{1}{R_0}\right)$$

Infectious Disease Epidemiology
Herd Immunity

- Even with substantial herd immunity, you can have some outbreaks. Somewhat counter intuition, many in those outbreaks may be vaccinated.

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



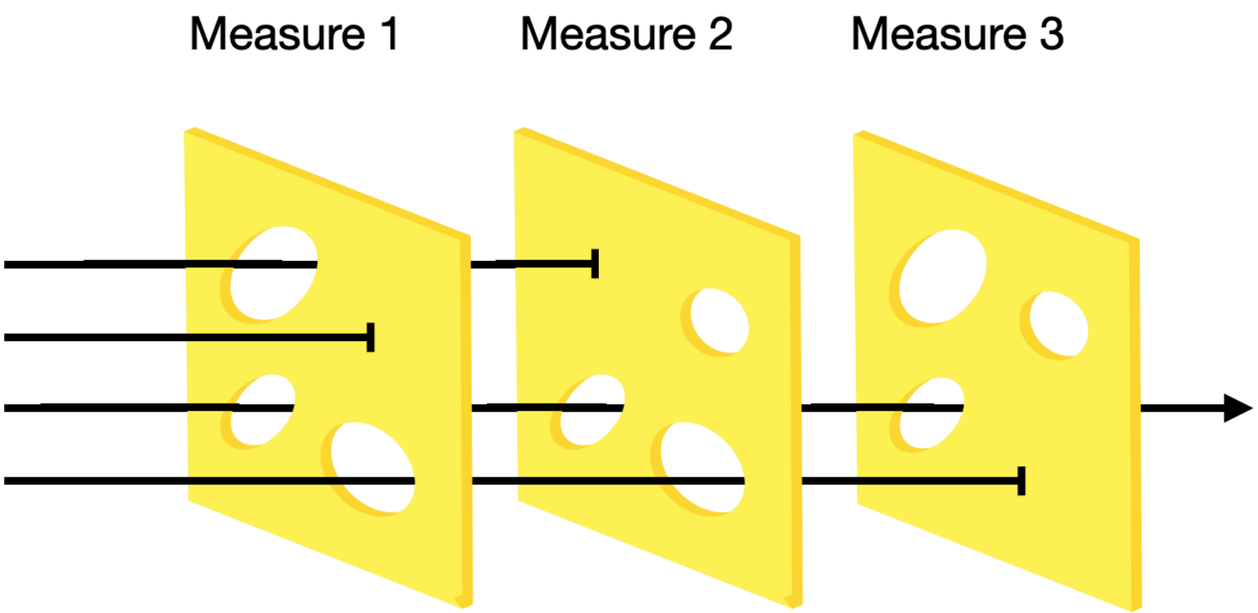
30
25
20
15
10
5
0
Vaccinated case-patients, %
California, USA, Dec 2014–Feb 2015
United States, Jan–May 2014
EU/EAA, Jan–Dec 2013
Switzerland, Aug 2006–Jun 2009
80
85
90
95
100
Vaccination coverage, %

Infectious Disease Epidemiology
Control

- pharmaceutical and non-pharmaceutical interventions (NPIs)
- pre-exposure and post-exposure

Infectious Disease Epidemiology

Control



Infectious Disease Epidemiology

Control

- Border closure and control

Infectious Disease Epidemiology

Control

- Border closure and control
- Social and physical distancing

Infectious Disease Epidemiology
Control

- Border closure and control
- Social and physical distancing
- Closures (events, schools, restaurants, etc.)

EPFL

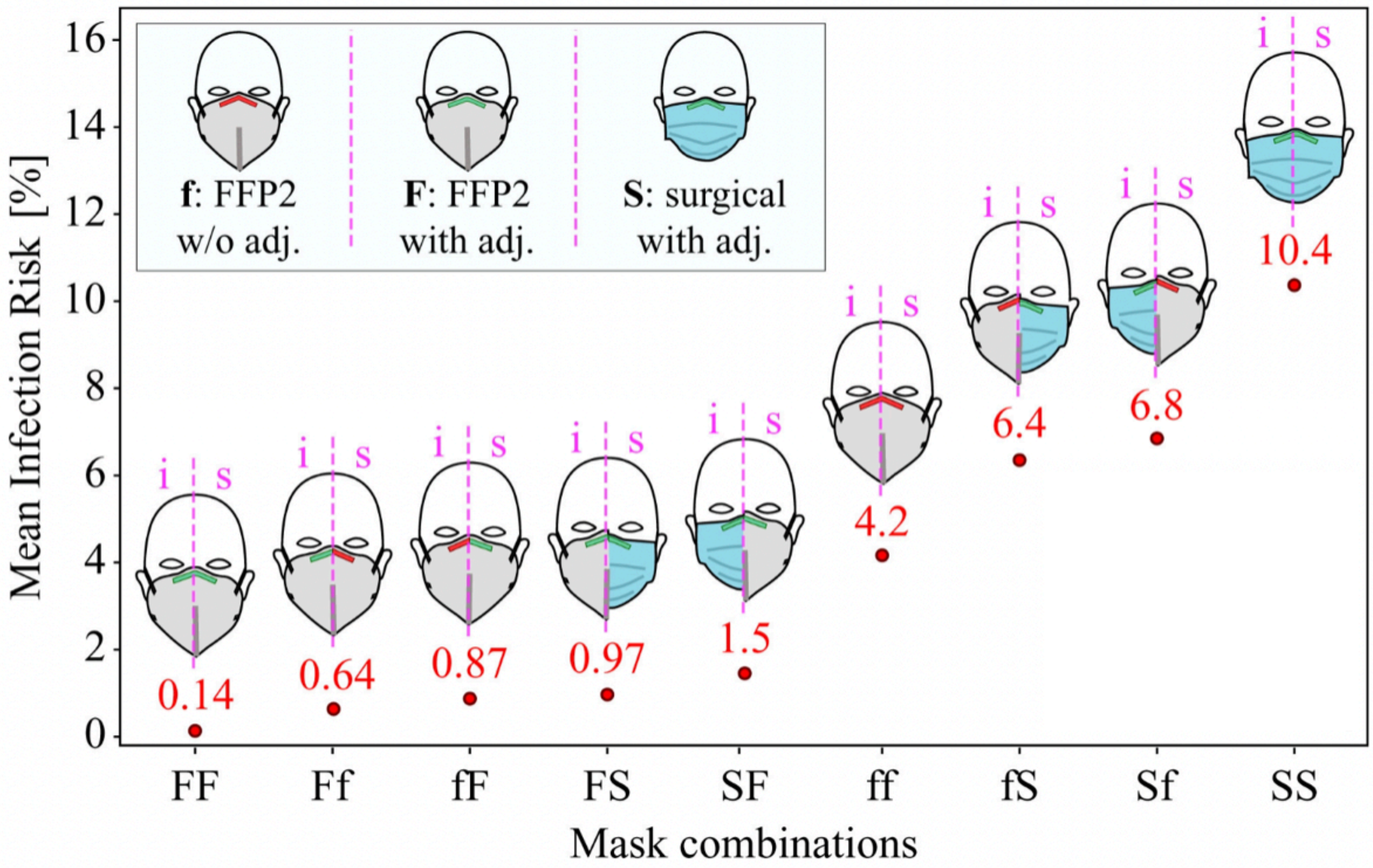
Infectious Disease Epidemiology
Control

- Border closure and control
- Social and physical distancing
- Closures (events, schools, restaurants, etc.)
- TTIQ: Test, contact trace, isolate or quarantine

Infectious Disease Epidemiology

Control

- Border closure and control
- Social and physical distancing
- Closures (events, schools, restaurants, etc.)
- TTIQ: Test, contact trace, isolate or quarantine
- Masks


f: FFP2 w/o adj.
F: FFP2 with adj.
S: surgical with adj.
Mean Infection Risk [%]
Mask combinations
FF
Ff
fF
FS
SF
ff
fS
Sf
SS
0.14
0.64
0.87
0.97
1.5
4.2
6.4
6.8
10.4
i
s
0
2
4
6
8
10
12
14
16

Infectious Disease Epidemiology
Control

- Border closure and control
- Social and physical distancing
- Closures (events, schools, restaurants, etc.)
- TTIQ: Test, contact trace, isolate or quarantine
- Masks
- Clean indoor air

Infectious Disease Epidemiology
Control

- Border closure and control
- Social and physical distancing
- Closures (events, schools, restaurants, etc.)
- TTIQ: Test, contact trace, isolate or quarantine
- Masks
- Clean indoor air
- Disinfection