Infectious Disease Epidemiology: a primer

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Lecture objective

- To discuss epidemiological concepts and measures typically used in infectious disease epidemiology and the challenges of estimating valid causal measures.

Lecture topics

- Historical perspective
- Effects of vaccines
- Basic reproduction number and control measures
- Herd immunity
- The effect of heterogeneities
- Wrapping it up

Historical perspective

Four peculiar features of infectious diseases

- Biological dimension: the presence of a microorganism provides a solid biological basis for understanding and intervene
  - The disease is the result of host-pathogen interaction - immunity
  - The possibility of identifying specific interventions: drugs and vaccines
- Ecological dimension: microorganisms have their own population dynamics and are subject to evolutionary pressures
  - Environmental transformations are crucial for the emergence of new epidemics: spillover
  - Emergence of new variants
- Social-historical dimension: epidemics shape history of societies and have deep social roots
  - Epidemics shape life experiences throughout history, with a particularly high burden on vulnerable populations, contributing to the perpetuation of cycles of poverty and social inequality
- Psychological dimension: microorganisms are external agents perceived as threatening
  - An external power that generates fear and apprehension, leading to unscientific interpretations (divine justice)

Epidemics as divine punishment

"And I looked, and behold, a pale horse! And its rider's name was Death, and Hades followed him. And they were given authority over a fourth of the earth, to kill with sword and with famine and with pestilence and by wild beasts of the earth."

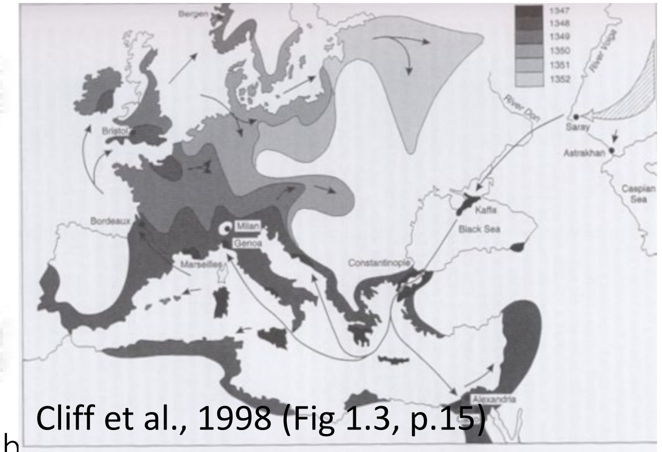
(The Book of Revelation, 6, viii)

Gustave Doré - Death on the Pale Horse (1865)
(Wikimedia Commons/Public Domain)

Plague & Flu Epidemics

http://alchemipedia.blogspot.com.b

Domenico Gargiulo. *Largo del Mercatello during the plague of 1656, Naples*



Cliff et al., 1998 (Fig 1.3, p.15)

Figure 1.3. Spread of the Black Death, 1347–1352. The main routeways of the spread of bubonic plague from Central Asia through the Mediterranean to Southern and Northern Europe. Source: Brock (1990), fig. 1.1, p. 5.

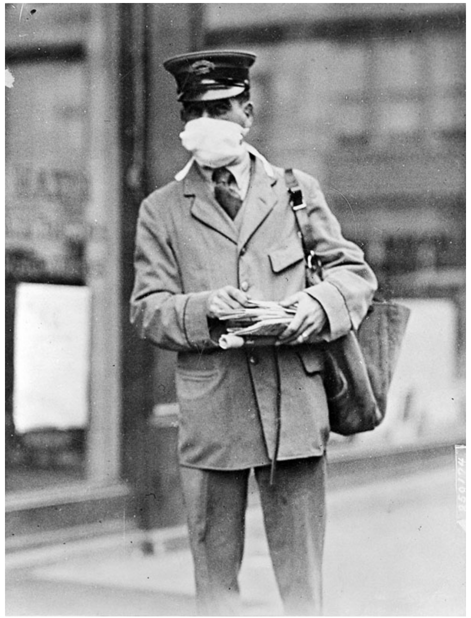
1347-1352 – Europe
~20 million deaths
~25-30% population

1334-1353 – World
~70-200 million deaths

1665 – London (~70.000 deaths)

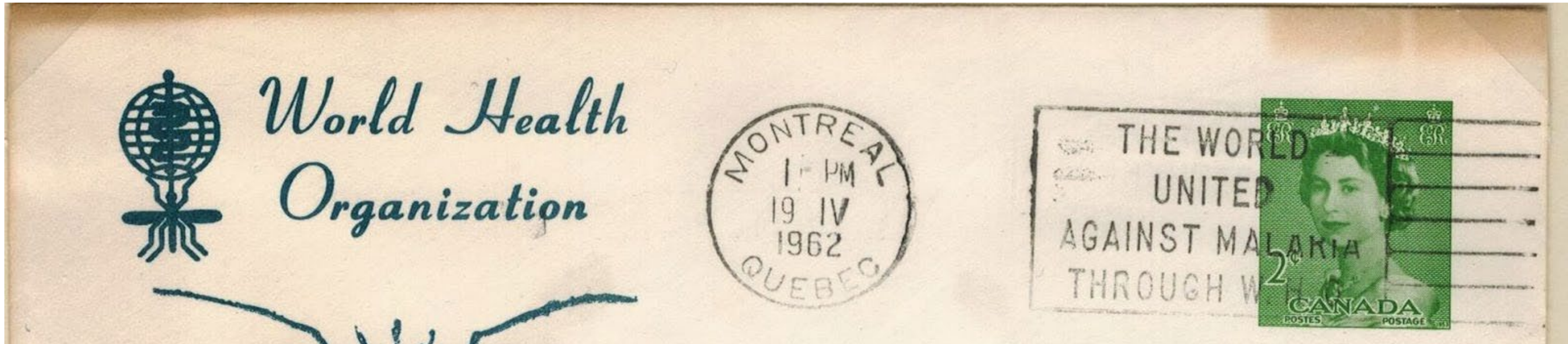
Collecting the dead for burial during the Great Plague (Wikimedia Commons/Public Domain)

Militares de Fort Riley, Kansas, 1918 (Wikimedia Commons/Public Domain)

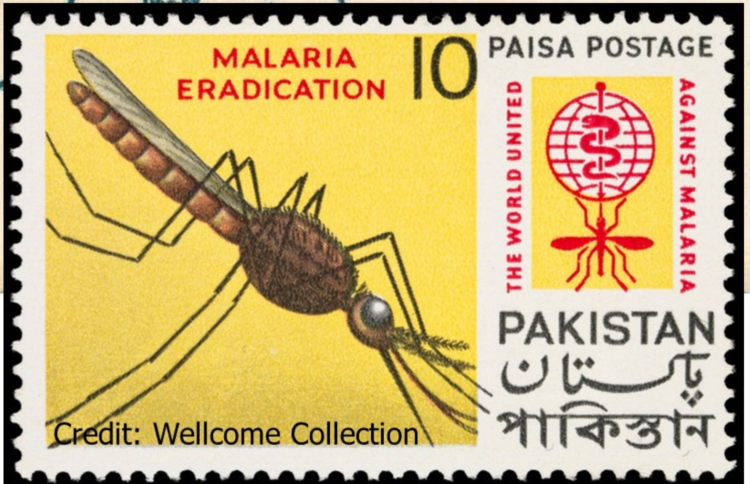


Postman wearing a mask during the 1918 flu epidemic. (NSHS RG2071.PHO-1)

Post WWII: an era of optimism

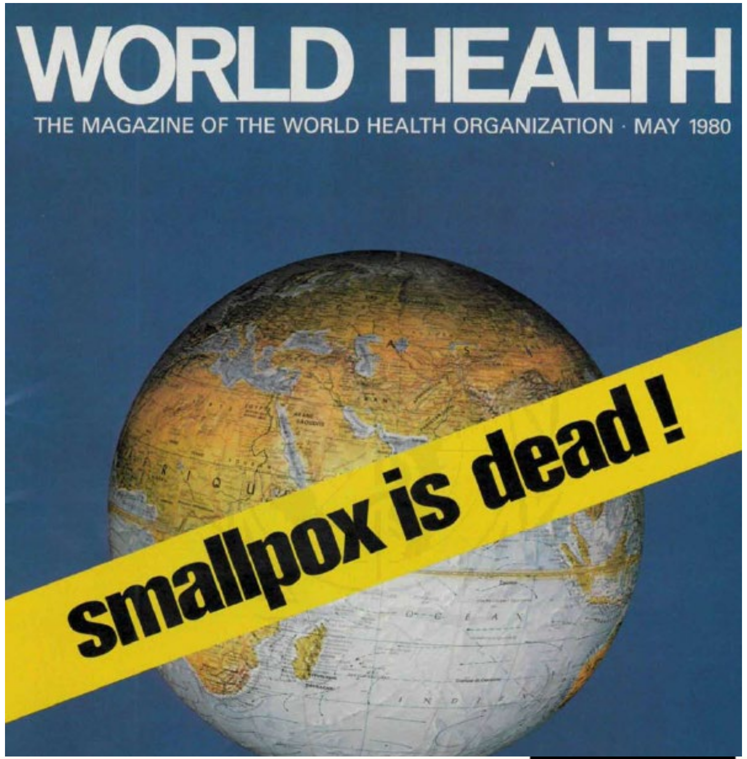


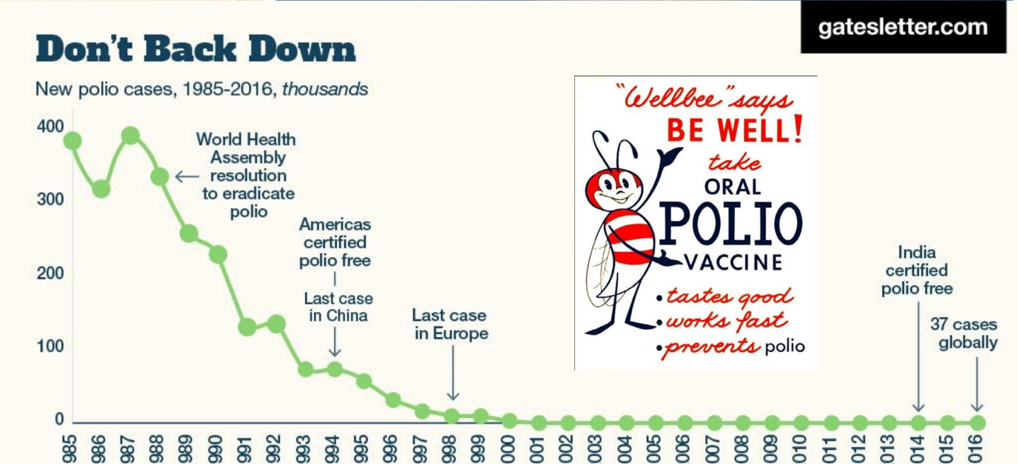
http://postalhistorycorner.blogspot.com.br/2013/10/world-health-organization-1962-anti.html



Credit: Wellcome Collection

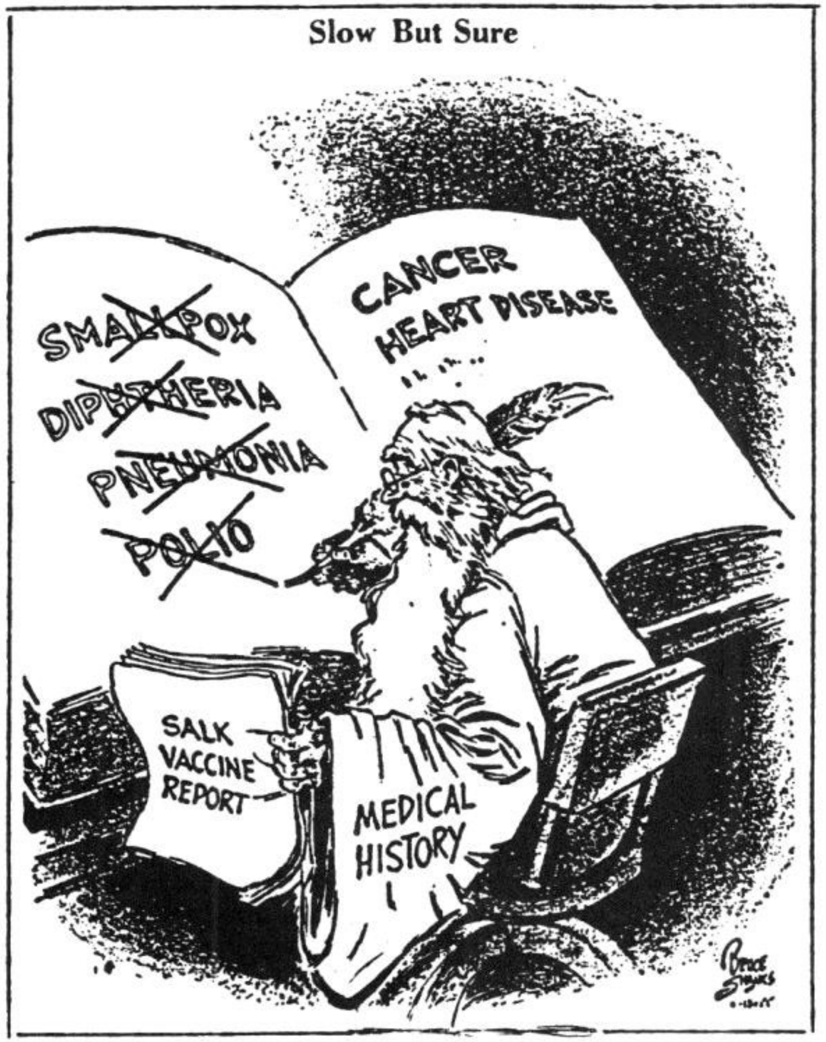
https://www.nlm.nih.gov/exhibition/visualculture/images/a025617t.jpg




Don't Back Down

New polio cases, 1985-2016, *thousands*

The end of infectious diseases?

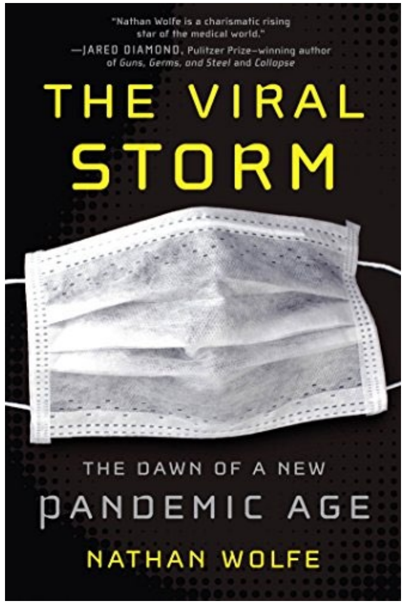

Slow But Sure

Buffalo Evening News, 1955.

Fonte: Reingold, Epidemiologic Reviews, 2000

A new scenario: EID

Author: Abijith k.a - https://commons.wikimedia.org/wiki/



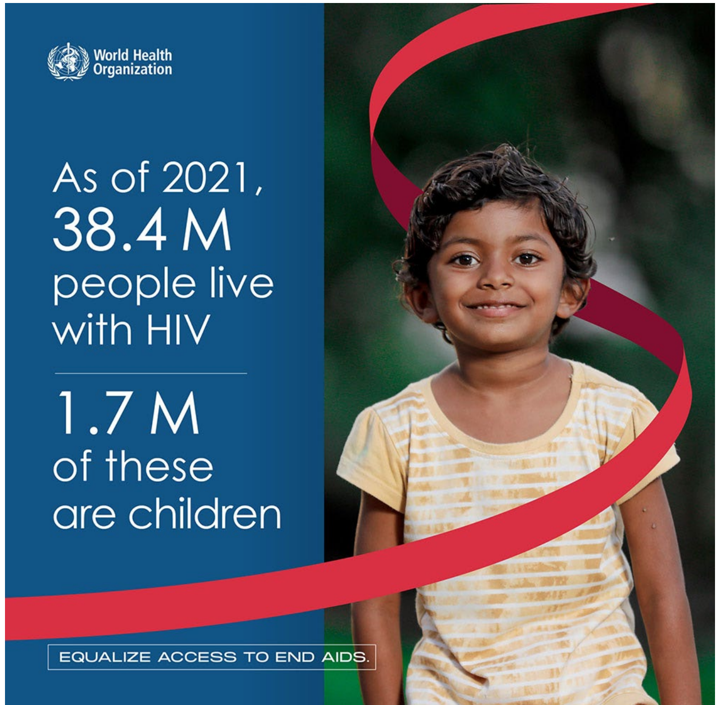
"Nathan Wolfe is a charismatic rising star of the medical world."
—JARED DIAMOND, Pulitzer Prize–winning author of *Guns, Germs, and Steel* and *Collapse*

THE VIRAL STORM

THE DAWN OF A NEW PANDEMIC AGE

NATHAN WOLFE

Reuters/Edgar Su/2020



As of 2021, 38.4 M people live with HIV

1.7 M of these are children

EQUALIZE ACCESS TO END AIDS.

Effects of vaccines

Events in populations

Independent

↓

Incidence in an individual does not depend on prevalence in the population

↓

Non infectious diseases

Accidents

Dependent

↓

Incidence in an individual depends on prevalence in the population

↓

Some infectious diseases

Implications

- Transmission is a non-linear process
- Assessment of risk factors and interventions need to take into account baseline differences in the risk of infection
- Interventions have at least two different types of effects: direct and indirect
- It is necessary to examine the possible future impact of different intervention scenarios

↓

Specific methods and concepts are needed to describe and understand the complexity involved in the transmission process

Effects of vaccines

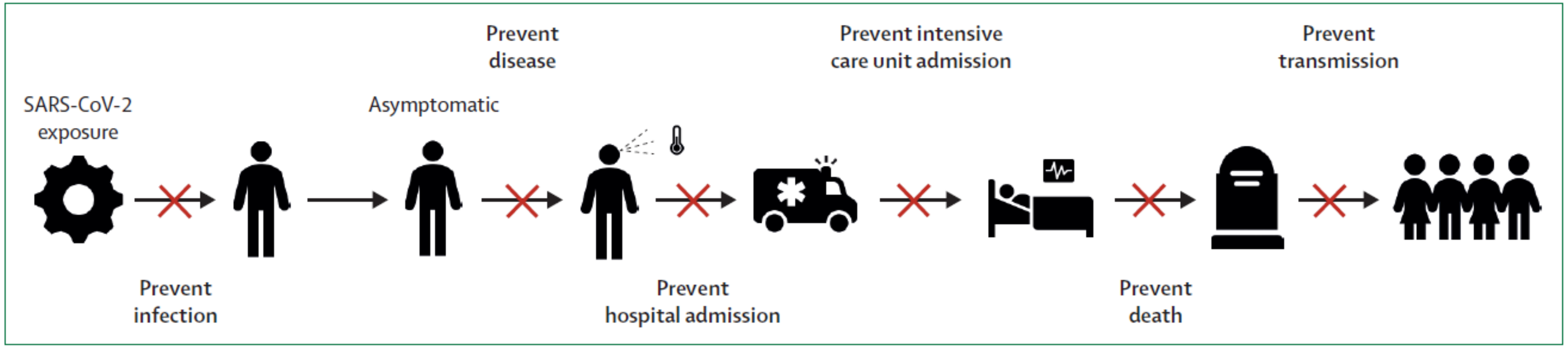
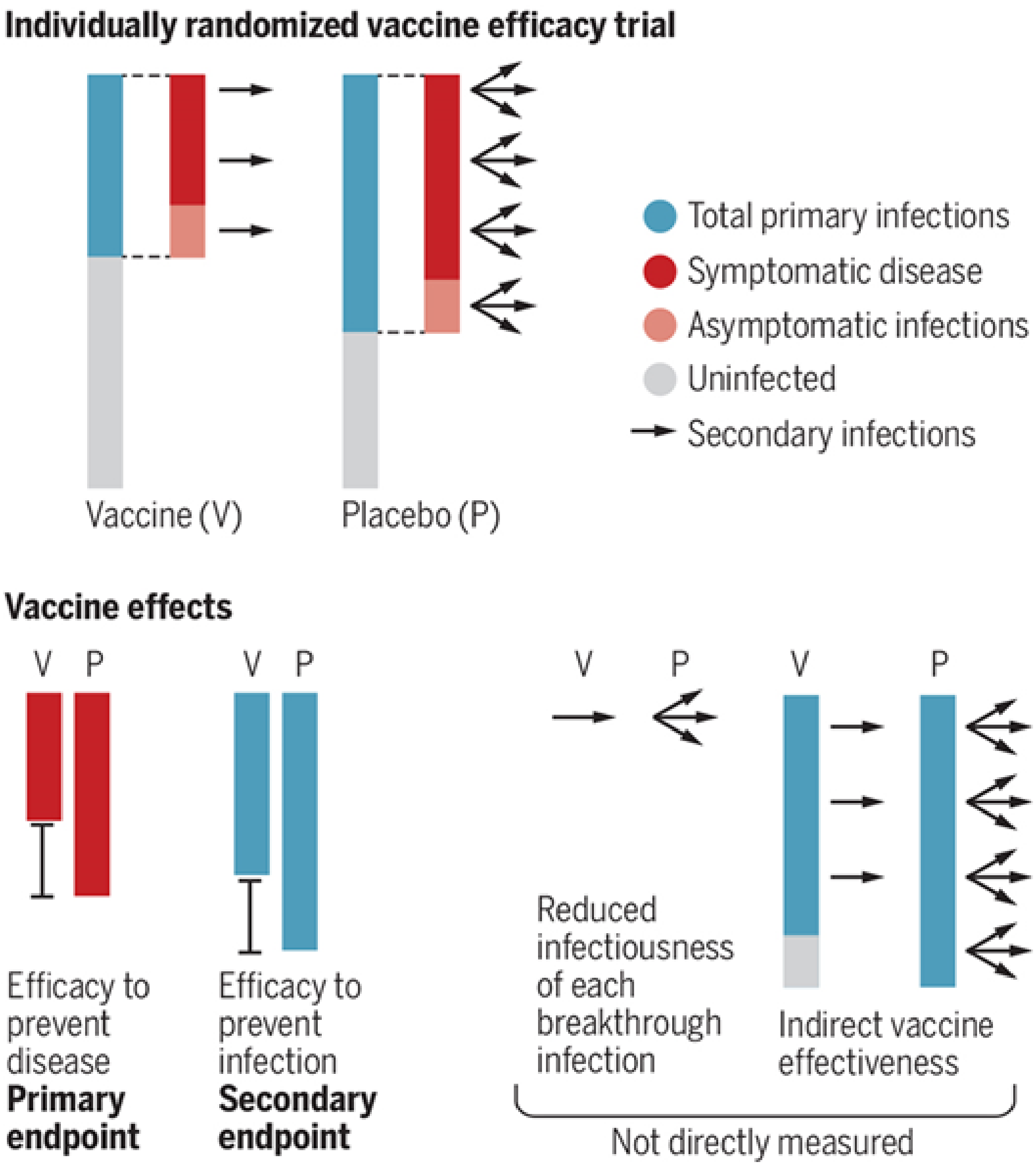


Figure 1: Potential endpoints of an efficacious COVID-19 vaccine
An efficacious COVID-19 vaccine could reduce the likelihood of infection of an individual, severity of disease in an individual, or degree of transmission within a population.

- Direct effects: protective effects on the individual receiving the intervention
  - Estimated efficacies for covid-19 vaccines refer to individual protection (direct effect - clinical protection)
- Indirect effects: arising from changes in the level of transmission of the infectious agent in the population as a result of a vaccination program
  - group immunity
  - Reduced transmissibility

Hodgson SH et al. What defines an efficacious COVID-19 vaccine? A review of the challenges assessing the clinical efficacy of vaccines against SARS-CoV-2. Lancet Infect Dis. 2021 Feb;21(2):e26-e35. doi: 10.1016/S1473-3099(20)30773-8.

Effects of vaccines



Vaccine effects

Vaccines provide direct protection by reducing susceptibility to disease or infection. Vaccines provide indirect protection by reducing the number of people infected in a population or their infectiousness. These vaccine effects can be assessed in clinical trials by measuring the efficacy to prevent disease, to prevent infection, and to reduce infectiousness, as well as in studies to assess indirect effects of the vaccine (*15*).

Marc Lipsitch, and Natalie E. Dean Science 2020;370:763-765

Study designs for assessing vaccine effects

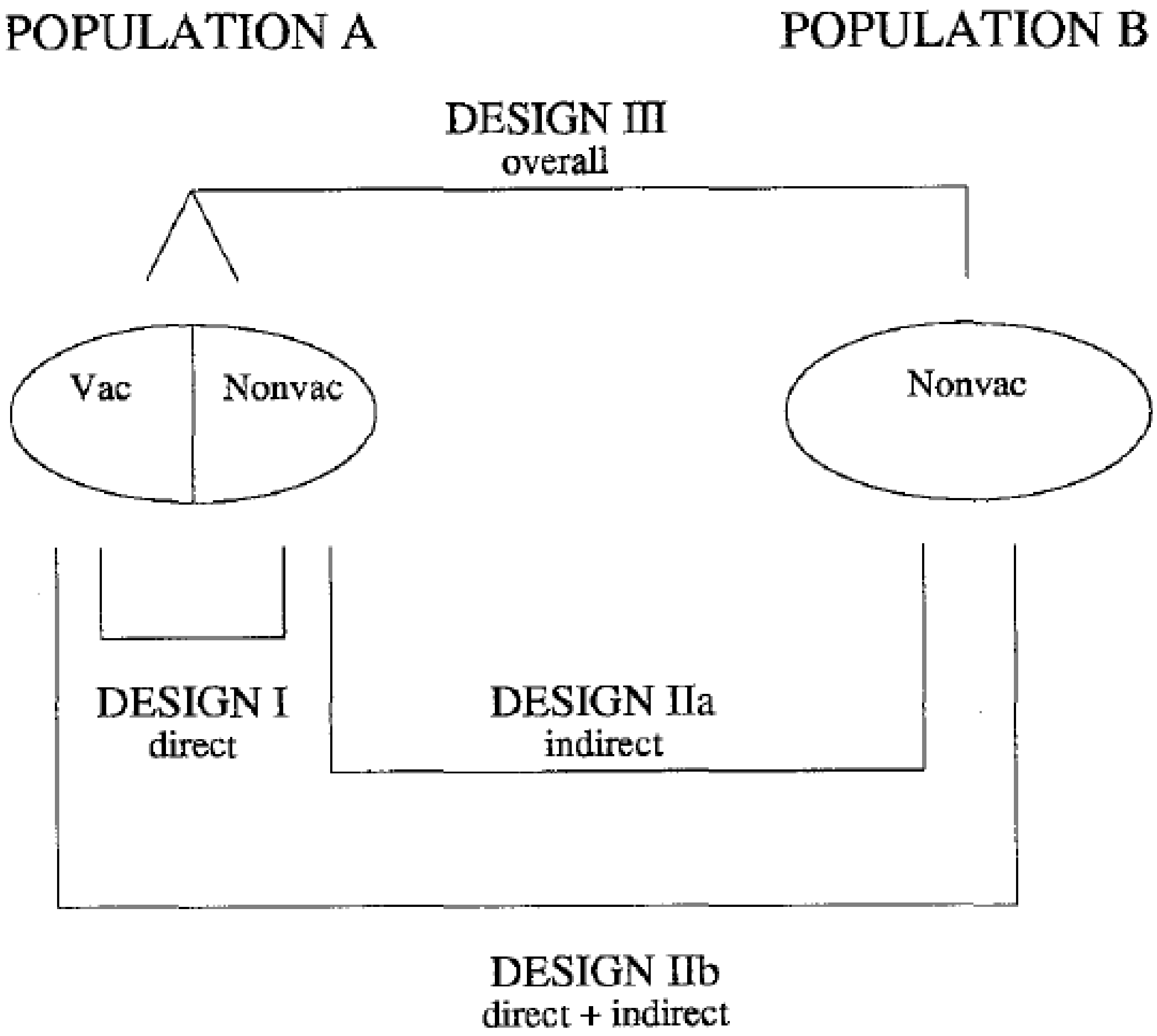


FIGURE 1.

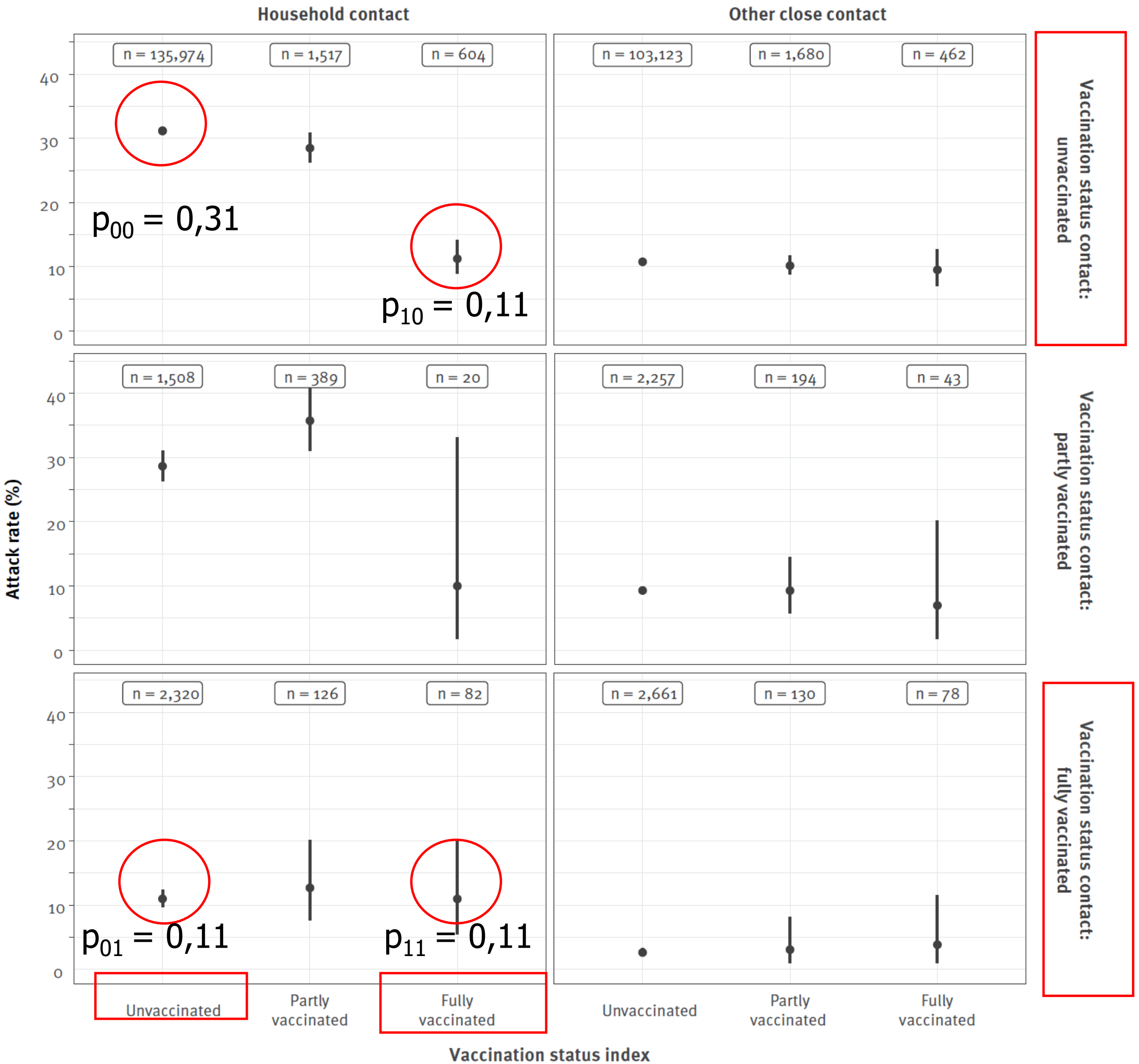
Types of effects of interventions against infectious disease, and different study designs based on comparison populations for their evaluation.

M. Elizabeth Halloran[1] *and Claudio J. Struchiner*[2]

Epidemiology September 1991, Volume 2 Number 5

Vaccine effects – conditional measures (attack rate)

Crude attack rate of SARS-CoV-2 among contacts, by vaccination status of the index (left to right) and vaccination status of the contact (top to bottom), the Netherlands, 1 February–27 May 2021 (n = 113,582 index cases, n = 253,168 contacts)



$p_{00} = 0,31$

$p_{10} = 0,11$

$p_{01} = 0,11$

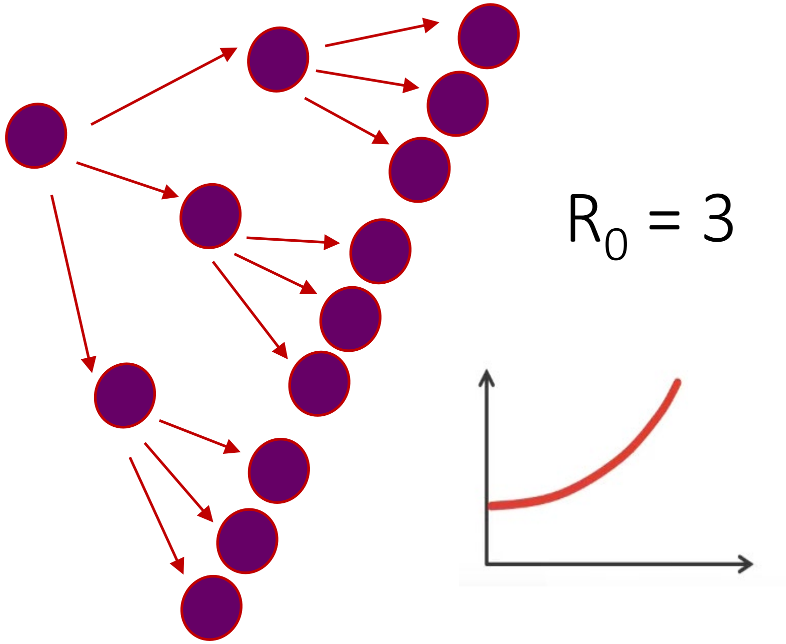
$p_{11} = 0,11$

de Gier B et al. Vaccine effectiveness against SARS-CoV-2 transmission and infections among household and other close contacts of confirmed cases, the Netherlands, February to May 2021. Euro Surveill 2021;26:2100640.

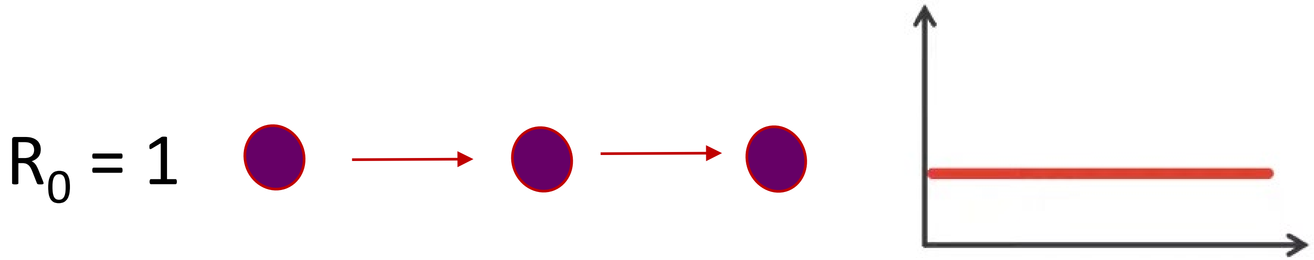
Basic reproduction number and control measures

Basic reproduction number (*R_0*)

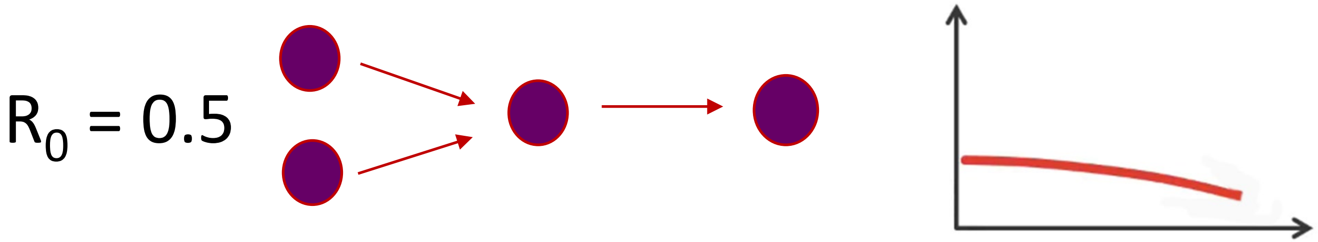
- Microparasites (viruses, bacteria): number of secondary cases produced by a single case, during its entire period of infectivity, when introduced into a fully susceptible population
- Macroparasites (worms): expected number of mature female offspring produced by a single female over her lifetime



$R_0 = 3$



$R_0 = 1$



$R_0 = 0.5$

The basic reproduction number and epidemics

Necessary condition for an epidemic to occur

$R_0 > 1$

Preventing the spread of a disease is...

$R_0 < 1$

R_0 – basic structure

$$R_0 \propto \text{Number of potential infectious contacts that an average person has per unit of time} \times \text{Risk of transmission per contact} \times \text{Duration of infectivity}$$

Control measures that reduce any of these components may have an effect on reducing disease spread

Intuitions from the R_0 - Covid-19

- Quarantine, isolation and physical distancing: ↓ contact rate
- Use of masks: ↓ probability of transmission per contact
- Vaccination: ↓ the proportion of susceptible and risk of transmission
- Treatment: ↓ duration of infectivity and the risk of transmission

R_0 – vector-borne diseases

$$\boldsymbol{R_0} \propto \underbrace{\text{Number of potential infectious contacts that an average person has per unit of time}}_{\text{Function of the vectorial capacity and the number of susceptibles}} \times \text{Risk of transmission per contact} \times \text{Duration of infectivity}$$

R_0 – vector-borne diseases (malária example)

$$R_0 \propto \underbrace{\text{Number of potential infectious contacts that an average person has per unit of time}} \times \text{Risk of transmission per contact} \times \text{Duration of infectivity}$$

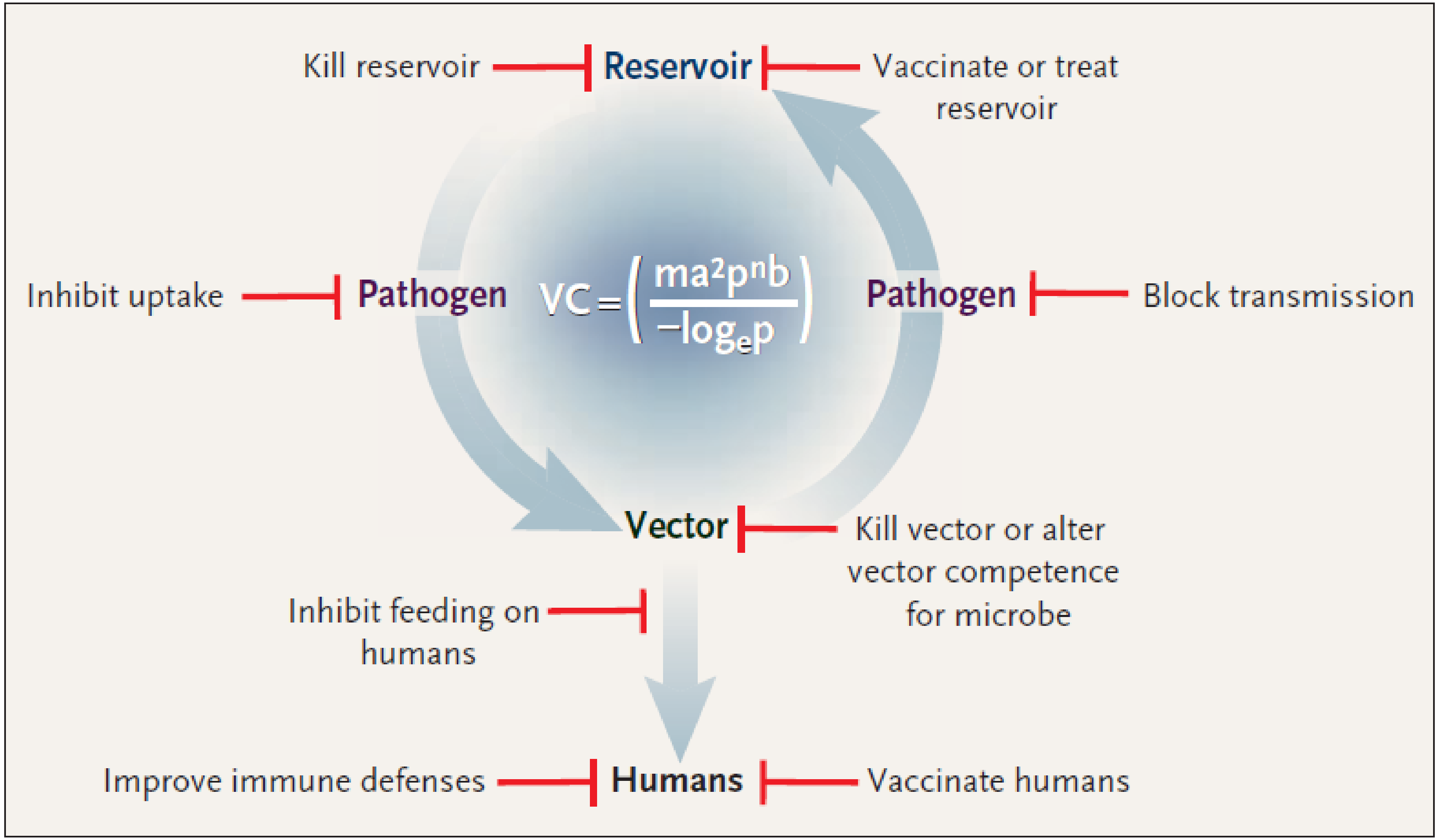
- m = mosquitoes per person
- a = human biting rate (0 to 1)
- b = vectorial competence (0 a 1)
- p^n = probability that the mosquito survives the extrinsic incubation period (0 a 1)
- 1/-ln(p) = survival time after extrinsic incubation period

- c = probability of infection at each bite (0 to 1)

R = recovery rate

$$\boxed{R_0 \propto \frac{m \times a^2 \times b \times p^n \times c}{-\ln(p) \times R}}$$

Strategies to interrupt vector-borne diseases



Kill reservoir
Reservoir
Vaccinate or treat reservoir

Inhibit uptake
Pathogen

$$VC = \left(\frac{ma^2p^nb}{-\log_e p} \right)$$

Pathogen
Block transmission

Vector
Kill vector or alter vector competence for microbe

Inhibit feeding on humans

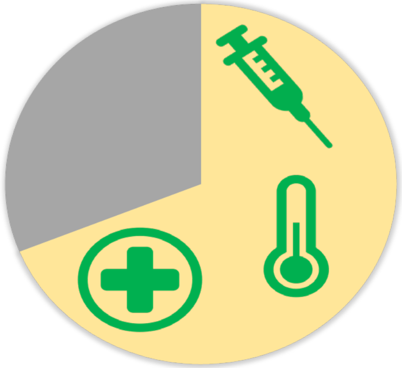
Improve immune defenses
Humans
Vaccinate humans

The Ross–Macdonald Model of Vectorial Capacity and Strategies to Interrupt Vector-Transmitted Infectious Diseases.

Klempner et al., 2007. Taking a bite out of vector-transmitted infectious diseases. N Engl J Med. 356(25):2567-9.

Herd immunity

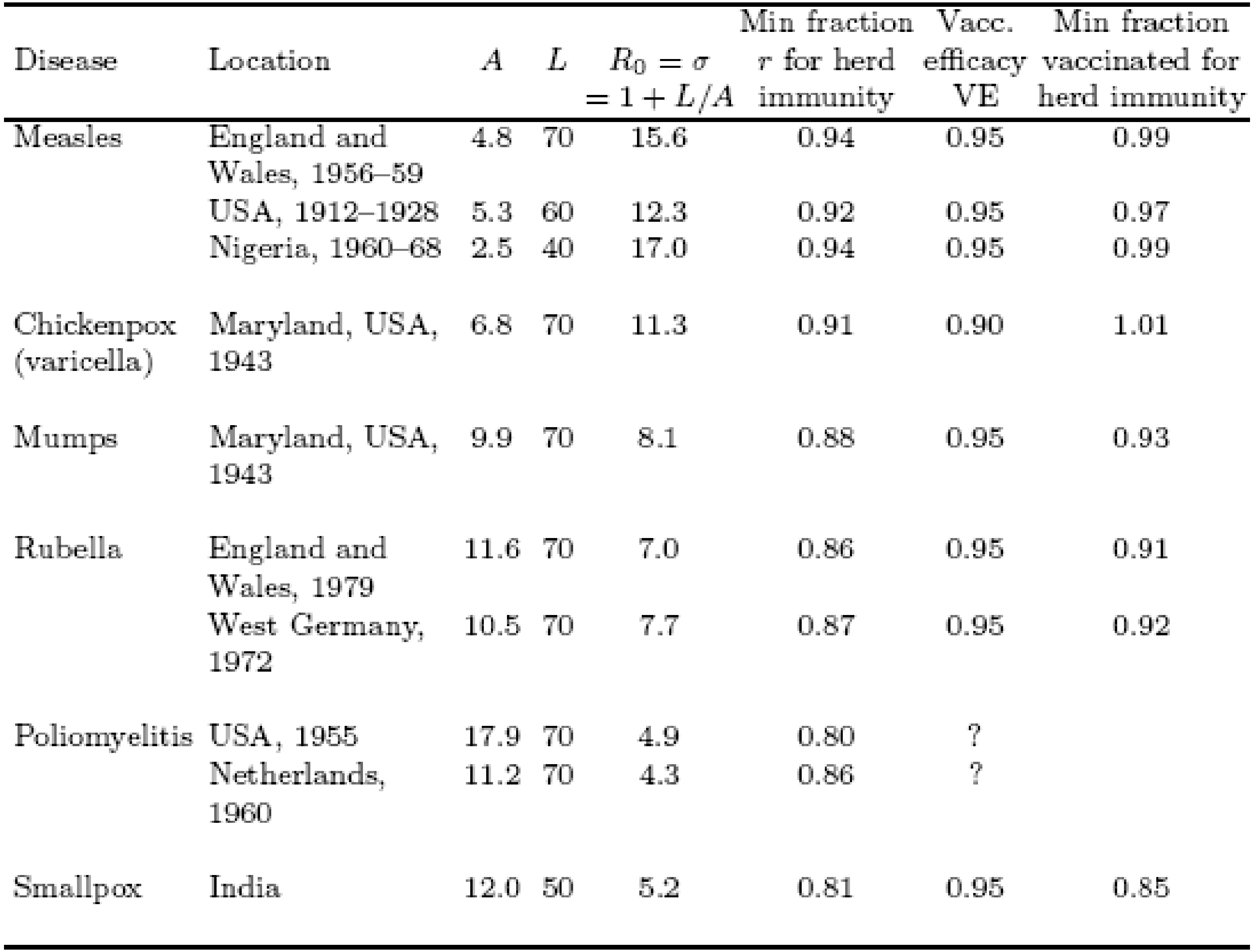
Herd immunity



- **Basic definition**: the proportion of individuals with immunity in a given population.
- **Consequences (group effect)**: If a significant proportion of the population has immunity to an infectious agent then the remainder of the population (non-immune and susceptible) becomes indirectly protected from infection.
- Proportion of the population that needs to be immune to prevent an epidemic from occurring ≈ $1 – 1 / R_0$
- **Hence, if R_0≈3, then herd immunity threshold to stop transmission ≈ 60-70%**

John & Samuel (2000) doi: 10.1023/a:1007626510002

R_0 and herd immunity



Disease	Location	A	L	$R_0 = \sigma$ $= 1 + L/A$	Min fraction r for herd immunity	Vacc. efficacy VE	Min fraction vaccinated for herd immunity
Measles	England and Wales, 1956–59	4.8	70	15.6	0.94	0.95	0.99
	USA, 1912–1928	5.3	60	12.3	0.92	0.95	0.97
	Nigeria, 1960–68	2.5	40	17.0	0.94	0.95	0.99
Chickenpox (varicella)	Maryland, USA, 1943	6.8	70	11.3	0.91	0.90	1.01
Mumps	Maryland, USA, 1943	9.9	70	8.1	0.88	0.95	0.93
Rubella	England and Wales, 1979	11.6	70	7.0	0.86	0.95	0.91
	West Germany, 1972	10.5	70	7.7	0.87	0.95	0.92
Poliomyelitis	USA, 1955	17.9	70	4.9	0.80	?	
	Netherlands, 1960	11.2	70	4.3	0.86	?	
Smallpox	India	12.0	50	5.2	0.81	0.95	0.85

Hethcote, The Basic Epidemiology Models, 2005, p. 43

Is herd immunity for Covid-19 possible?

Feature

KOBI WOLF/BLOOMBERG/GETTY

About 50% of Israel's population has so far been fully vaccinated against COVID-19, yet herd immunity remains elusive.

WHY HERD IMMUNITY FOR COVID IS PROBABLY IMPOSSIBLE

Even with vaccination efforts in full force, the theoretical threshold for vanquishing COVID-19 looks to be out of reach. **By Christie Aschwanden**

As COVID-19 vaccination rates pick up around the world, people have reasonably begun to ask: how much longer will this pandemic last? It's an issue surrounded with uncertainties. But the once-popular idea that enough people will eventually gain immunity to SARS-CoV-2 to block most transmission – a 'herd-immunity threshold' – is starting to look unlikely.

That threshold is generally achievable only with high vaccination rates, and many scientists had thought that once people started being immunized en masse, herd immunity would permit society to return to normal. Most estimates had placed the threshold at 60–70% of the population gaining immunity, either through vaccinations or past exposure to the virus. But as the pandemic enters its second year, the thinking has begun to shift. In February, independent data scientist Youyang Gu changed the name of his popular COVID-19 forecasting model from 'Path to Herd Immunity' to 'Path to Normality'. He said that reaching a herd-immunity threshold was looking unlikely because of factors such as vaccine hesitancy, the emergence of new variants and the delayed arrival of vaccinations for children.

Gu is a data scientist, but his thinking aligns with that of many in the epidemiology community. "We're moving away from the idea that we'll hit the herd-immunity threshold and then the pandemic will go away for good," says epidemiologist Lauren Ancel Meyers, executive director of the University of Texas at Austin COVID-19 Modeling Consortium. This shift reflects the complexities and challenges of the pandemic, and shouldn't overshadow the fact that vaccination is helping. "The vaccine will mean that the virus will start to dissipate on its own," Meyers says. But as new variants arise and immunity from infections potentially wanes, "we may find ourselves months or a year down the road still battling the threat, and having to deal with future surges".

Long-term prospects for the pandemic probably include COVID-19 becoming an endemic disease, much like influenza. But in

520 | Nature | Vol 591 | 25 March 2021

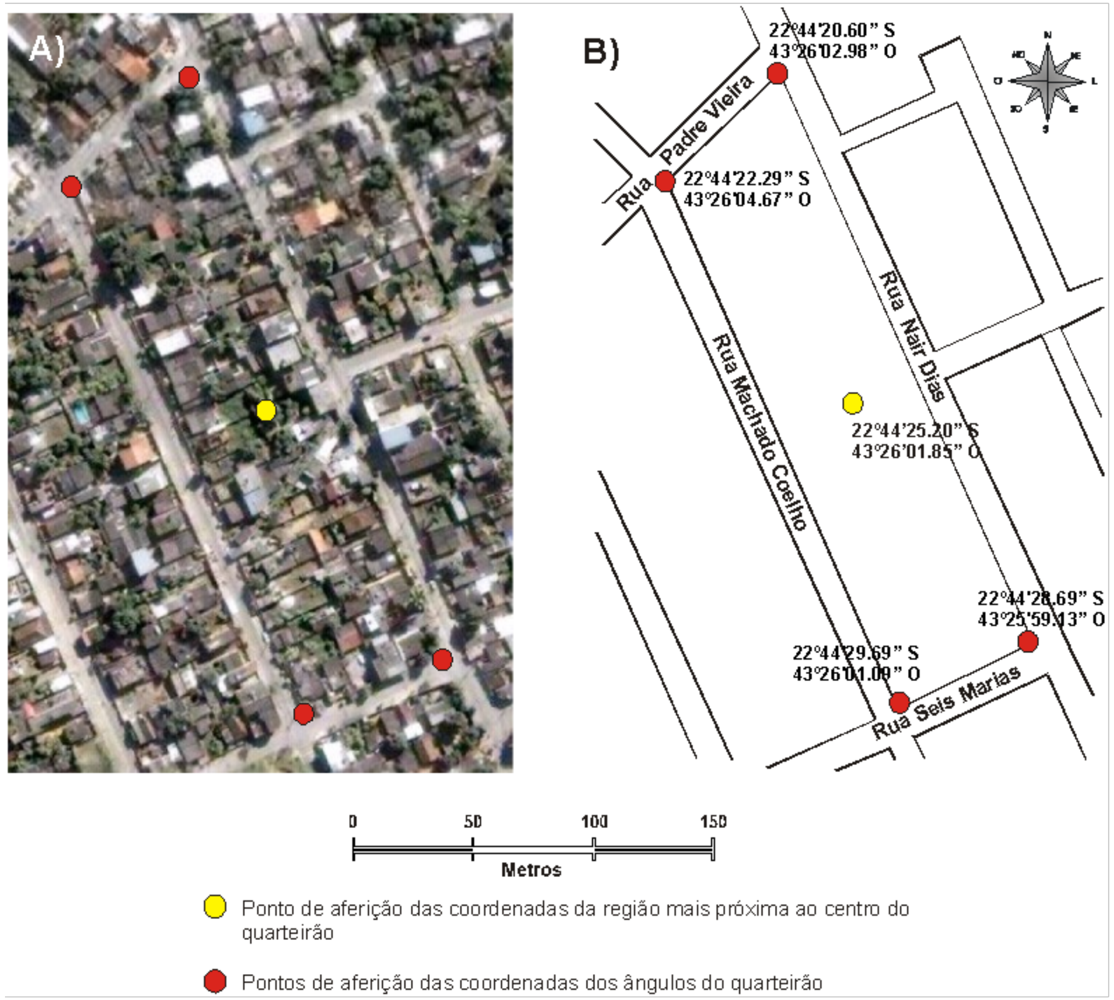
- High threshold for herd immunity (>70%)
- Immunity to infection modulated by age, intensity of infection and still little known
- Vaccines primarily provide clinical protection rather than immunity to infection.
- Moderate effectiveness of some vaccines
- Variants
- Vaccine hesitancy

The effect of heterogeneities

Heterogeneity – a practical problem for control

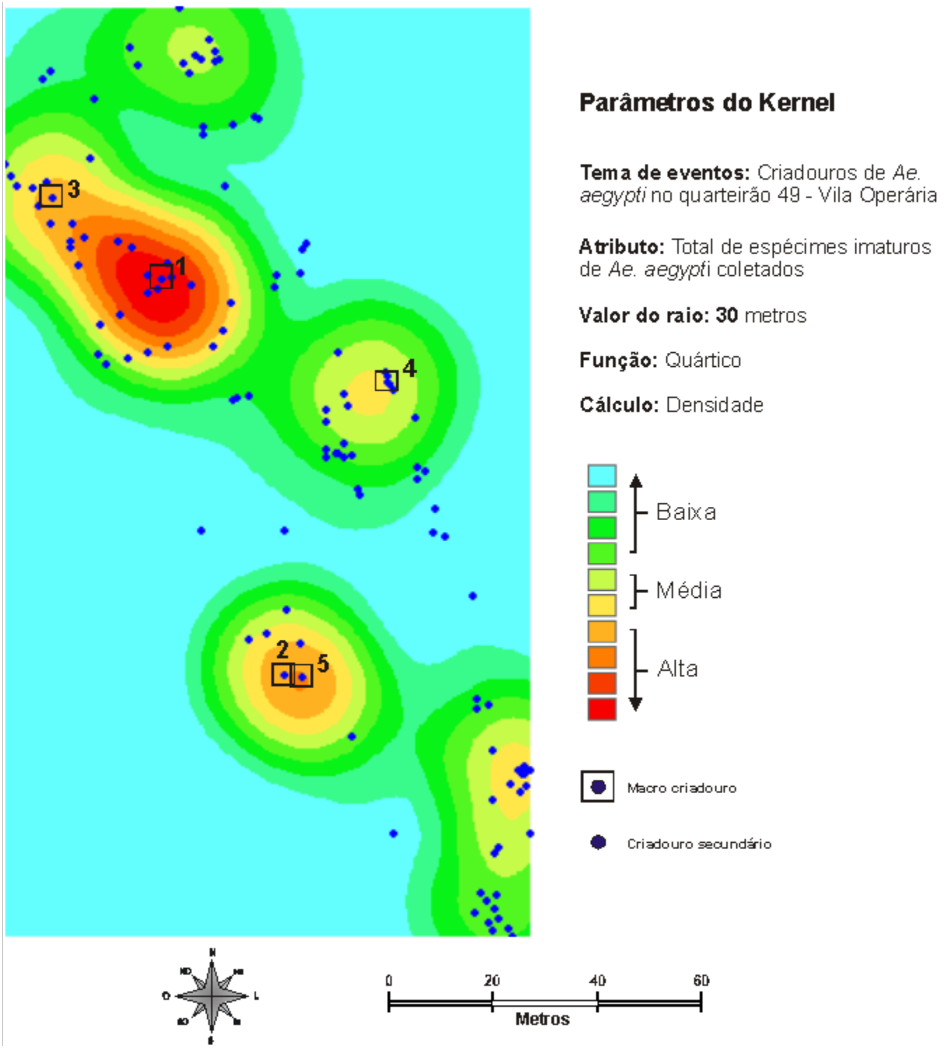
- If in a geographic area the force of transmission varies due to spatio-temporal heterogeneity in the:
  - contact patterns
  - use of preventive measures
  - distribution of risk factors
- Then the 20/80 rule may operate
- 20% of individuals/groups contribute with 80% of transmission

Spatial distribution of productivity of breeding sites, block 49, Vila Operária, Nova Iguaçu / RJ - Brazil



🟡 Ponto de aferição das coordenadas da região mais próxima ao centro do quarteirão

🔴 Pontos de aferição das coordenadas dos ângulos do quarteirão



Parâmetros do Kernel

Tema de eventos: Criadouros de *Ae. aegypti* no quarteirão 49 - Vila Operária

Atributo: Total de espécimes imaturos de *Ae. aegypti* coletados

Valor do raio: 30 metros

Função: Quártico

Cálculo: Densidade

Baixa

Média

Alta

▣ Macro criadouro

● Criadouro secundário

Lagrotta, 2006

Land use and cover, Acre state, 1990 and 1999

Figura 5. Mapas de uso e cobertura da terra na porção leste do Estado do Acre para os anos de 1990(a) e 1999(b), obtidos a partir de dados TM/Landsat-5. Projeção Universal Transverse de Mecartor, Datum Horizontal - SAD-69

Lorena et al. (2004). Espaço & Geografia, Vol.7, No 1 (2004), 47:76

Empirical evidence

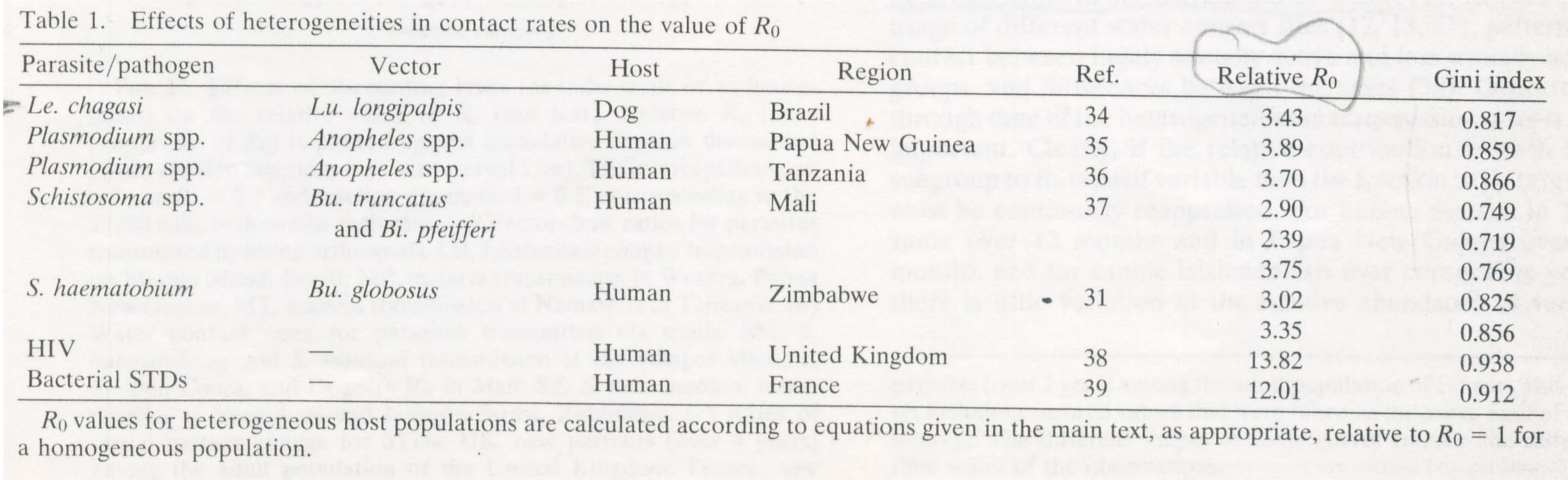


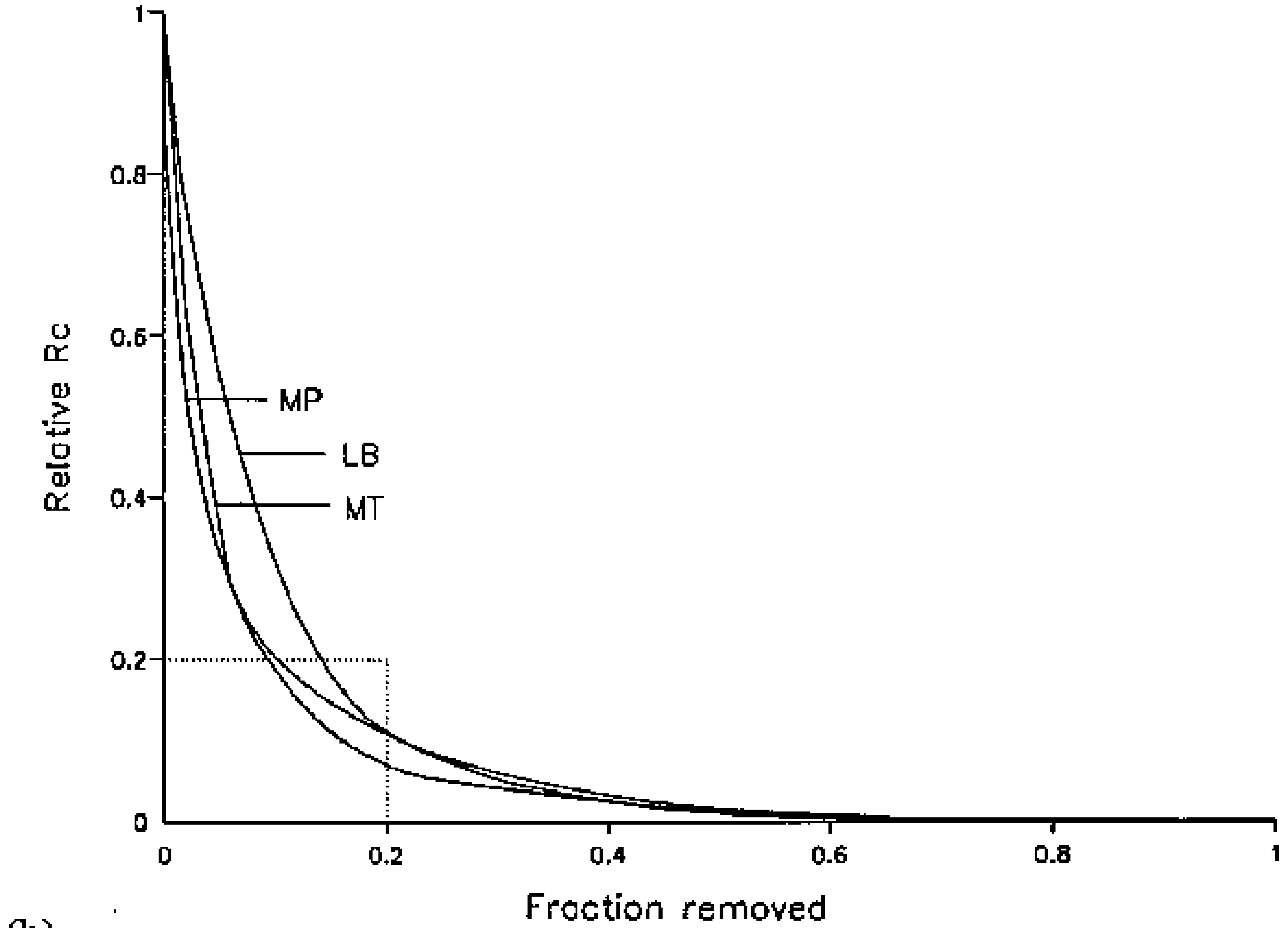
Table 1. Effects of heterogeneities in contact rates on the value of R_0

Parasite/pathogen	Vector	Host	Region	Ref.	Relative R_0	Gini index
Le. chagasi	*Lu. longipalpis*	Dog	Brazil	34	3.43	0.817
Plasmodium spp.	*Anopheles* spp.	Human	Papua New Guinea	35	3.89	0.859
Plasmodium spp.	*Anopheles* spp.	Human	Tanzania	36	3.70	0.866
Schistosoma spp.	*Bu. truncatus* and *Bi. pfeifferi*	Human	Mali	37	2.90	0.749
					2.39	0.719
					3.75	0.769
S. haematobium	*Bu. globosus*	Human	Zimbabwe	31	3.02	0.825
					3.35	0.856
HIV	—	Human	United Kingdom	38	13.82	0.938
Bacterial STDs	—	Human	France	39	12.01	0.912

R_0 values for heterogeneous host populations are calculated according to equations given in the main text, as appropriate, relative to $R_0 = 1$ for a homogeneous population.

Woolhouse *et al.* *Proc. Natl. Acad. Sci. USA 94 (1997)*

Empirical evidence



Woolhouse *et al.* *Proc. Natl. Acad. Sci. USA 94 (1997)*

High-risk or population intervention strategies?

- High-risk strategy: targeted to reducing the disease's impact and complications in a population subset considered at highest risk.
- Population strategy: proposes a preventive approach for the entire population.
- In chronic diseases with high prevalence, population-based strategies are preferable, since both the highest-risk groups and the whole population benefit from the preventive measures.
- Otherwise, for communicable diseases, targeting the groups at greatest risk (of transmitting or acquiring the infection) can be more efficient for limiting transmission to the entire population.
- A combination of the two approaches is commonly used, for instance, in HIV/AIDS, with population strategies using promotion of condom use, alongside campaigns targeted to groups at increased risk such as sex workers.

Rose G. The strategy of preventive medicine. Oxford/New York: Oxford University Press; 1992.
Koopman JS, Simon CP, Riolo CP. When to control endemic infections by focusing on high-risk groups. Epidemiology 2005; 16:621-7.
Chang LW et al. Combination implementation for HIV prevention: moving from clinical trial evidence to population-level effects. Lancet Infect Dis 2013; 13:65-76.

Wrapping it up

Main messages

- Infectious diseases are not going to disappear and will be challenging us even more profoundly
- Population interventions have many different potential effects and need a variety of approaches for assessing them
- The basic reproduction number is good for helping us have a grasp of the potential of disease spread, but its empirical use needs caution
- Herd immunity is not equal to vaccine coverage or the prevalence of markers of immunity; it depends on the level of population-specific protection against infection
- Heterogeneity is bad and good. Bad because it leads to an increase in the force of transmission. Good because it allows us to use control measures efficiently.

THANK YOU!