

Digital Epidemiology

BIO 512

Introduction

Welcome!

- Marcel Salathé



- I'm a professor in SV with a joint appointment in IC.
- I run a group called digital epidemiology lab, based at Campus Biotech.
- I'm trained as a biologist, with a PhD in evolutionary biology.

Introduction

About This Class

- This is a class about digital epidemiology.
- You are the third cohort to go through this class.
- For the second time, the class will be lectures + project.
- Future generations of EPFL students will be grateful for your feedback. #PayItForward
- Today, we will first go through some organizational details of the class.

Introduction

Class Structure

- Lecture Phase + Project Phase
- Lecture phase ~ in the middle of the semester
- Project phased begins right after
- **Mid-term (and only) exam: 1. April 2024 (no joke)**

Introduction

Lecture Phase

- 9 lectures - these correspond to 10 chapters in the book.
- Book: www.digitalepibook.com
- Slides will be made available on Moodle before the lecture.
- ~2 chapters / week

- 18.02.25** Course Introduction
Chapter 1: Epidemiology
- 20.02.25** Chapter 2: Testing & Diagnostics
- 25.02.25** Chapter 3: Epidemiological Studies
- 27.02.25** Chapter 4: Infectious Disease Epidemiology
- 04.03.25** Chapter 5: Modeling Infectious Diseases
- 06.03.25** Chapter 6: Spatial Models & Network Models
- 11.03.25** Chapter 7: Digital Contact Tracing
- 13.03.25** no class
- 18.03.25** no class
- 20.03.25** Chapter 8: Digital Public Health Surveillance
- 25.03.25** Chapter 9: Digital Cohorts & Trials
- 27.03.25** Chapter 10: Ethics of Digital Epidemiology
- 01.04.25** **Midterm Exam**

Introduction

Exercises

- **No exercise sessions** - if you need help, ask us
- In this class, you are strongly encourage to use LLMs.
- Exercise due date: Sunday night of week after exercise has been handed out.
- Exercises will not be graded for correctness, but for **reasonable submission**. 1% of grade per exercise, except 2% for first exercise.

Introduction

Project Phase

- Goal: hands-on experience with building a digital epidemiology prototype
- Find your project in an ideation session (10. April)
- Pitch it to class on 15. April
- Work in groups of 3
- 2 graded assessments (6. May, 15. May)
- 1 progress report to class
- Demo Day - Presentation (27. May) 

- 03.04.25** Project Prototyping Workshop 1
- 08.04.25** Project Prototyping Workshop 2
- 10.04.25** Project ideation
- 15.04.25** Opening pitch to class
- 17.04.24** no class

PHASE 2: Project

- 29.04.25** No class - work on project
- 01.05.25** No class - work on project
- 06.05.25** **1st project assessment (graded, 5%)**
- 08.05.25** No class - work on project
- 13.05.25** 1st progress report to class
- 15.05.25** **2nd project assessment (graded, 10%)**
- 20.05.25** No class - submit report, not graded
- 22.05.25** No class - get feedback on written report
- 27.05.25** **Demo (graded 10%)**
Due date final written project report (graded, 20%)

Introduction

Midterm Exam

- Mid-term exam 45% of grade.
- Exam material is **everything discussed in class, and everything in the book.**
- You can take one sheet of A4 paper (hand written notes only) with you to the exam.

Introduction

Final grade

- Exercises: 10%
- Mid-term exam: 45%
- Project: $5\% + 10\% + 10\% \text{ (demo)} + 20\% \text{ (report)} = 45\%$
- You will always know where you stand, no surprises / gotchas

Introduction

Help & Communication

- TAs: Rohan Singh



- Marouane Toumi



- There is no office hour - if you have questions, we are always available to meet with you (contact us via Moodle).
- All communication **MUST GO** through Moodle (unless agreed otherwise)

Introduction

Lecture Structure

- 1/3 Basic concepts in epidemiology
- 1/3 Infectious disease dynamics, computational approaches
- 1/3 Digital approaches to epidemiology
- Discussion about ethical issues

Introduction

General Remarks

- This class mixes a lot fields and approaches. Life sciences, CS, math, reading, programming, quantitative and qualitative reasoning - we'll be all over the map. Welcome to novel approaches in a multidisciplinary world.
- This is a breadth-first class. You will learn many things from many different fields, and you'll likely find it useful in unexpected ways.
- This is not a class about COVID-19, but you'll hear it often.

RESPECT



Introduction

RESPECT

- Limit use of laptops and phones in class (ideally zero).
- We will do our best to help you succeed. If you find anything suboptimal to your learning process, please let us know.



Epidemiology

Learning Goals

- Understand what epidemiology is about
- Understand surveillance, and different types of it
- Understand the concepts of incidence and prevalence
- Understand how a case is defined
- Understand measures of morbidity
- Understand measures of mortality

What is epidemiology?

- Epidemiology (epi + demos + logos)
- The study of the distribution and determinants of health and disease in the population.
- *Who* is sick (*what*) or healthy, *when*, *where*, and *why*

- Epidemiology is about groups, not individuals
- Always ask: what group are we talking about?



Original article

From measures to models: an evaluation of air pollution exposure assessment for epidemiological studies of pregnant women

E Nethery,¹ S E Leckie,¹ K Teschke,^{1,2} M Brauer¹

► Additional appendices are published online only at <http://oem.bmjjournals.org/content/vol65/issue9>

¹ School of Environmental Health, The University of British Columbia, Vancouver, BC

ABSTRACT

Objectives: To evaluate exposure estimation methods such as spatially resolved land-use regression models and ambient monitoring data in the context of epidemiological studies of the impact of air pollution on pregnancy outcomes.

importance of capturing within-city spatial variability in air pollution exposure.^{13 14} Specifically, studies of traffic-related air pollution have used proximity (ie, living near a busy road),¹⁵ traffic volume or density measures^{5 16} or land-use regression (LUR)¹⁷ models as exposure indicators. LUR

Who?

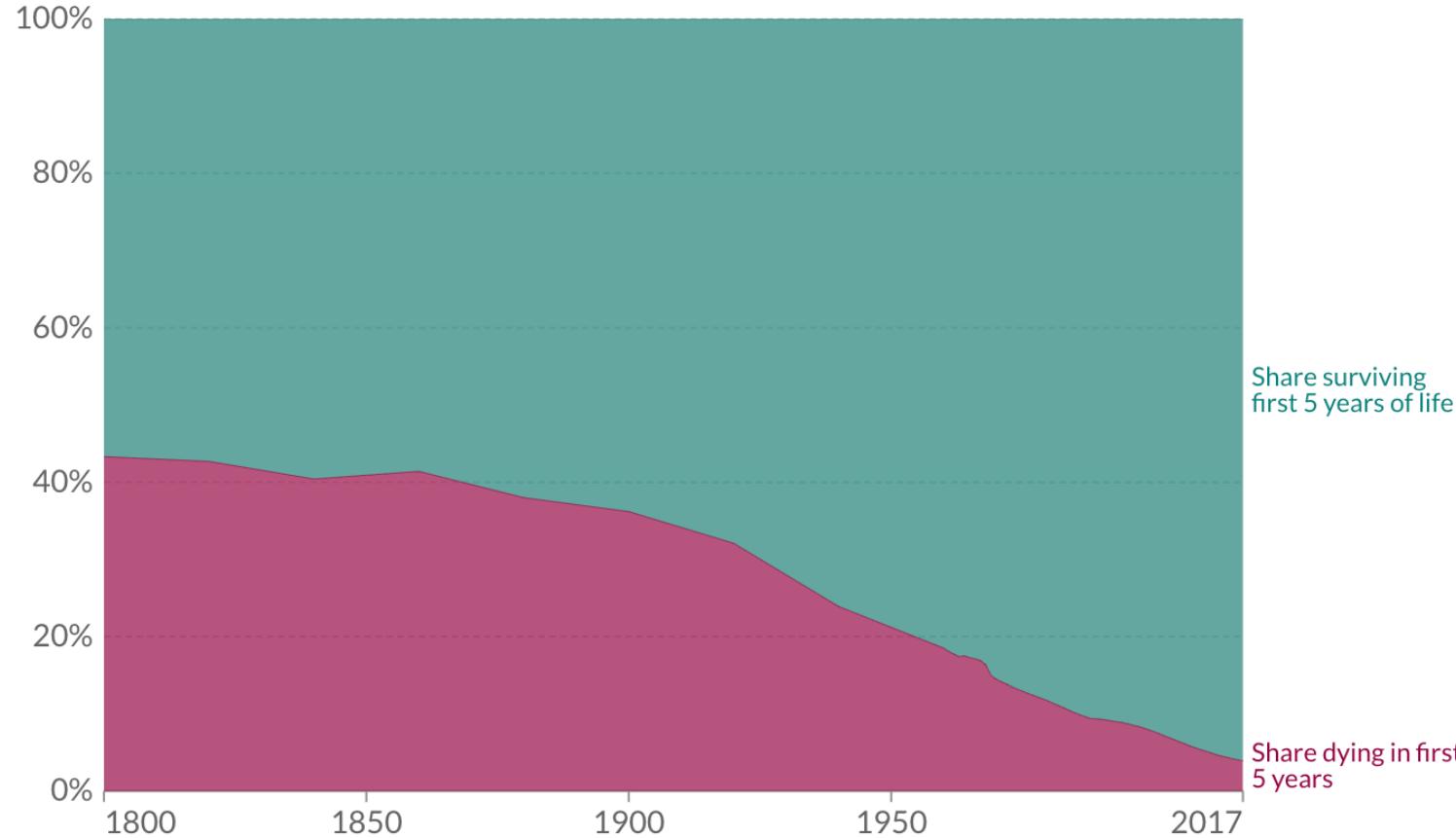
- How to study large groups: take a representative sample
- Descriptive statistics: helps us to *describe* the sample.
- Inferential statistics: helps us to *make inferences* about the larger group from the sample.
- Careful about biases

What?

- Morbidity
- Mortality
- Why this distinction?
 1. Death was ubiquitous already early in life

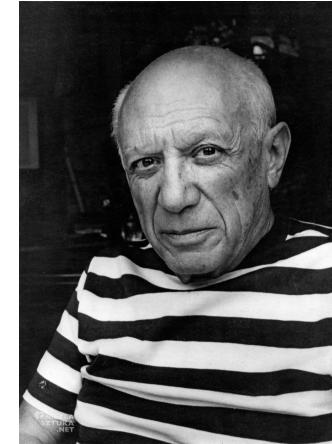
Global child mortality

Share of the world population dying and surviving the first 5 years of life.

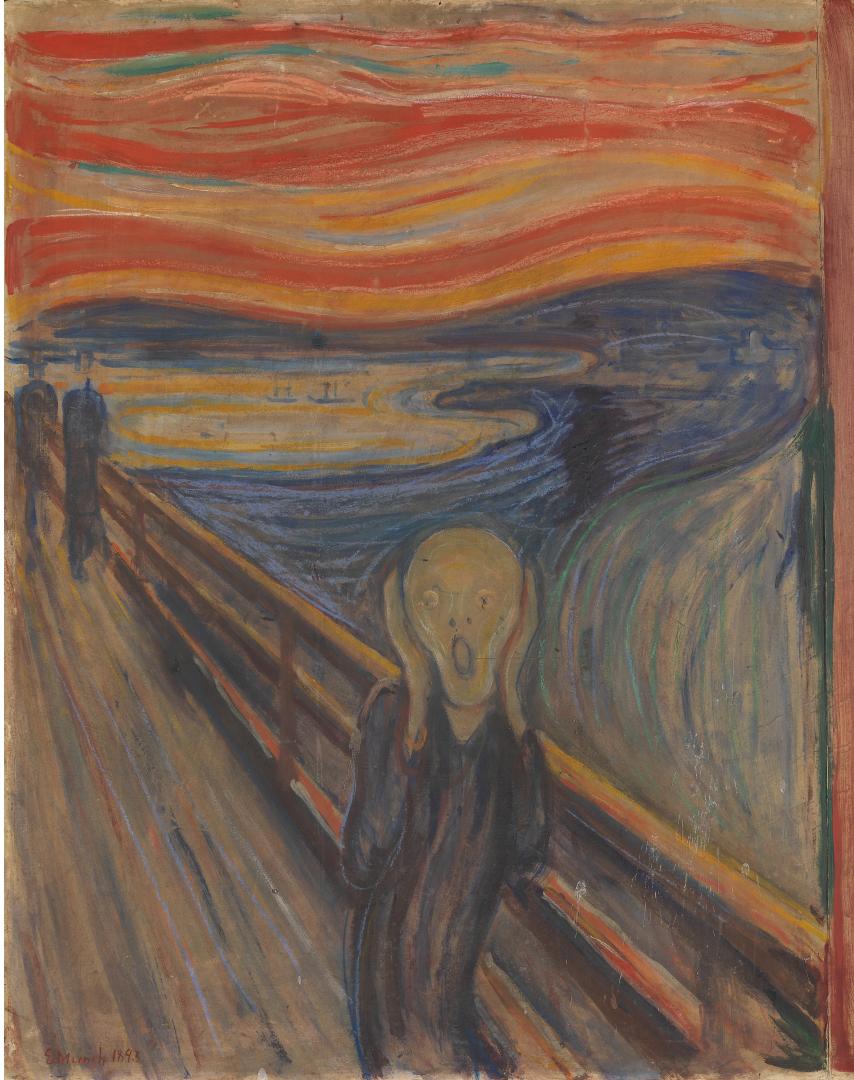




- Salvador Dalí: older brother (also Salvador), died of gastroenteritis before his second birthday. Dalí, who was born nine months later and given the same first name, believed for the rest of his life to be his dead brother's reincarnation.



- Pablo Picasso: lost sister to diphtheria when she was barely seven years old. Pleaded with God to save her in exchange for his sacrifice to give up painting, and he was convinced that her death was a sign that God wanted him to be a painter.



- Edvard Munch's older sister died at age fifteen of tuberculosis, the same disease that killed his mother when he was just a five year old boy. Munch processed this tragic event in several paintings throughout his career.

What?

- Morbidity
- Mortality
- Why this distinction?
 1. Death was ubiquitous already early in life
 2. Death is universally understood (as opposed to disease and disease severity, which can have different definitions)
 3. Death is final

When?

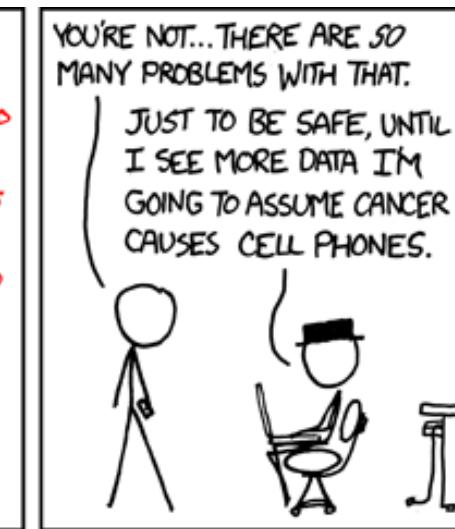
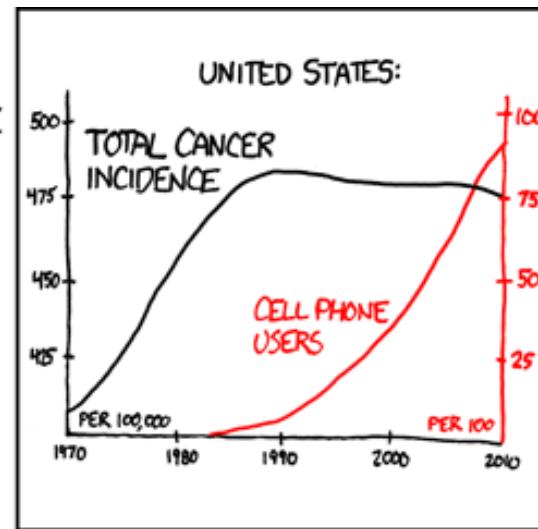
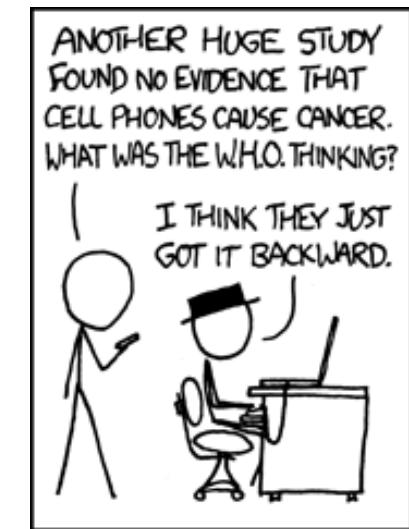
- When **during life** - childhood diseases and late-life diseases have different impacts
- When **in the calendar** - understanding timing of disease is critical to understand disease dynamics. E.g. many people getting sick at once, or a rapid growth of cases, has important implications.

Why?

- Epidemiology often finds associations (correlations) - but this are not the same as causation.
- Association can already be enough for action, or a call for more studies - but understanding causes is ideal, as it maximizes our ability to control an outcome.

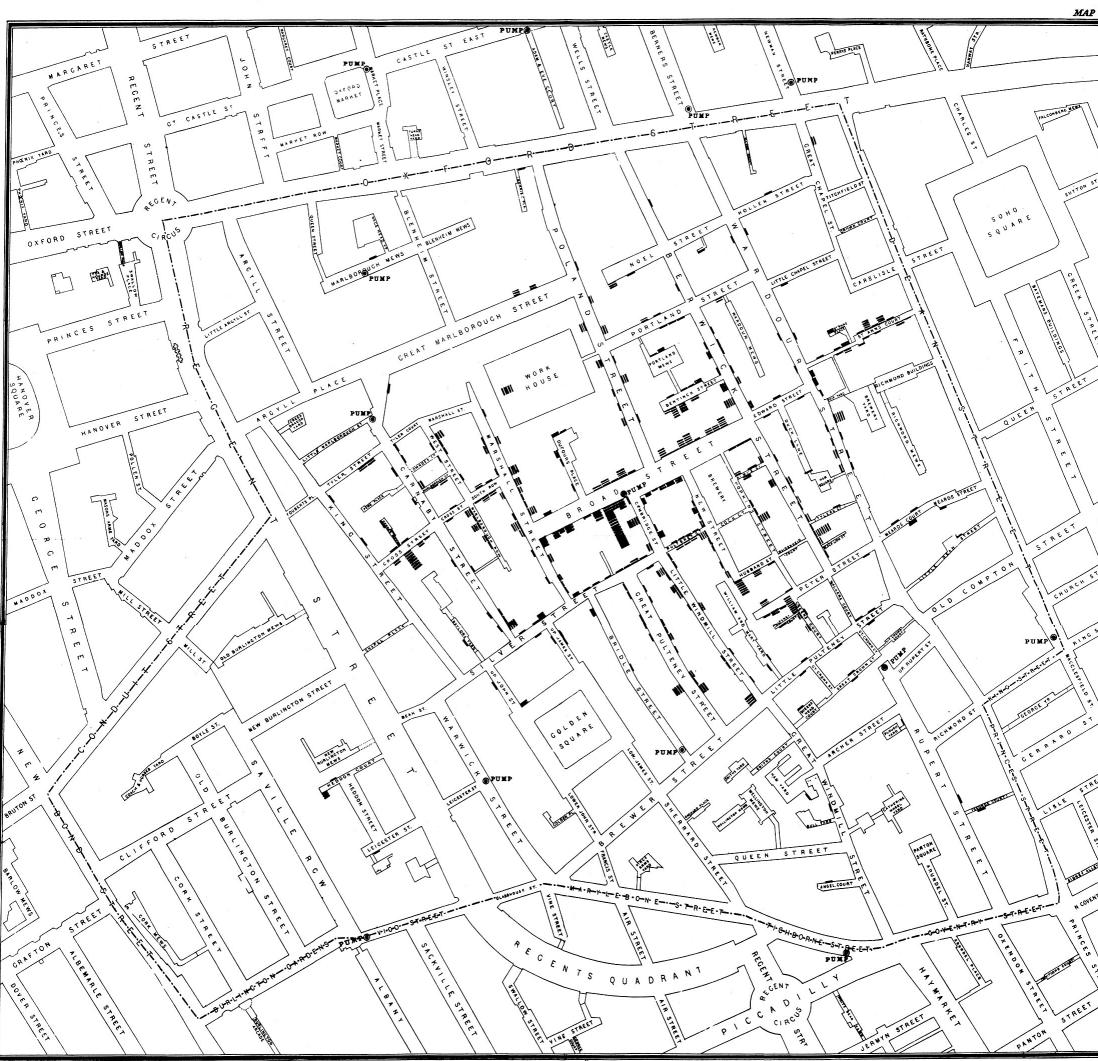
Epidemiology

Why?



Where?

- Cholera outbreak in Soho district London, 1854
- John Snow: Hypothesized that cholera was caused by agents in polluted water (not miasma)
- Cholera was a massive problem at the time - a 1849 outbreak killed 14,137 residents in London.



Epidemiology Surveillance

- Public health surveillance - many different definitions of what counts as surveillance.
- WHO: “the continuous, systematic collection, analysis and interpretation of health-related data”



Epidemiology Surveillance

- Passive vs active surveillance

NATIONAL NOTIFIABLE DISEASES SURVEILLANCE SYSTEM

To protect Americans from serious disease, the National Notifiable Diseases Surveillance System (NNDSS) helps public health monitor, control, and prevent about 120 diseases. These national notifiable diseases are important to monitor nationwide and include infectious diseases such as Zika, foodborne outbreaks such as *E. coli*, and noninfectious conditions such as lead poisoning. About 3,000 public health departments gather and use data on these diseases to protect their local communities. Through NNDSS, CDC receives and uses these data to keep people healthy and defend America from health threats.

Accessible version: <https://www.cdc.gov/nndss/about/index.html>

NNDSS BY THE NUMBERS



120 diseases under surveillance

- infectious diseases
- bioterrorism agents
- sexually transmitted diseases
- noninfectious conditions



About 3,000 public health departments send disease data to 60 state, territorial, and other public health departments, who then send the data to CDC



Nearly 2.7 million disease events reported through NNDSS each year



100% of the American population protected

Epidemiology Surveillance

- Passive vs active surveillance

Article

Suppression of a SARS-CoV-2 outbreak in the Italian municipality of Vo'

<https://doi.org/10.1038/s41586-020-2488-1>

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 Check for updates

Enrico Lavezzo^{1,13}, Elisa Franchini^{1,13}, Constanze Ciavarella², Gina Cuomo-Dannenburg², Luisa Barzon¹, Claudia Del Vecchio¹, Lucia Rossi³, Riccardo Manganelli¹, Arianna Loreanian¹, Nicolò Navarin^{4,5}, Davide Abate¹, Manuela Sciro³, Stefano Merigliano⁶, Ettore De Canale³, Maria Cristina Vanuzzo³, Valeria Besutti³, Francesca Saluzzo¹, Francesco Onelia¹, Monia Pacenti³, Saverio G. Parisi¹, Giovanni Carretta³, Daniele Donato³, Luciano Flor³, Silvia Cocchio⁷, Giulia Masi¹, Alessandro Sperduti^{4,5}, Lorenzo Cattarino², Renato Salvador⁶, Michele Nicoletti⁸, Federico Caldart⁹, Gioele Castelli⁹, Eleonora Nieddu⁹, Beatrice Labella⁹, Ludovico Fava⁸, Matteo Drigo⁸, Katy A. M. Gaythorpe², Imperial College COVID-19 Response Team^{*}, Alessandra R. Brazzale⁹, Stefano Toppo^{1,5}, Marta Trevisan¹, Vincenzo Baldo⁷, Christl A. Donnelly^{2,10}, Neil M. Ferguson², Ilaria Dorigatti^{2,14} & Andrea Crisanti^{1,11,14} 

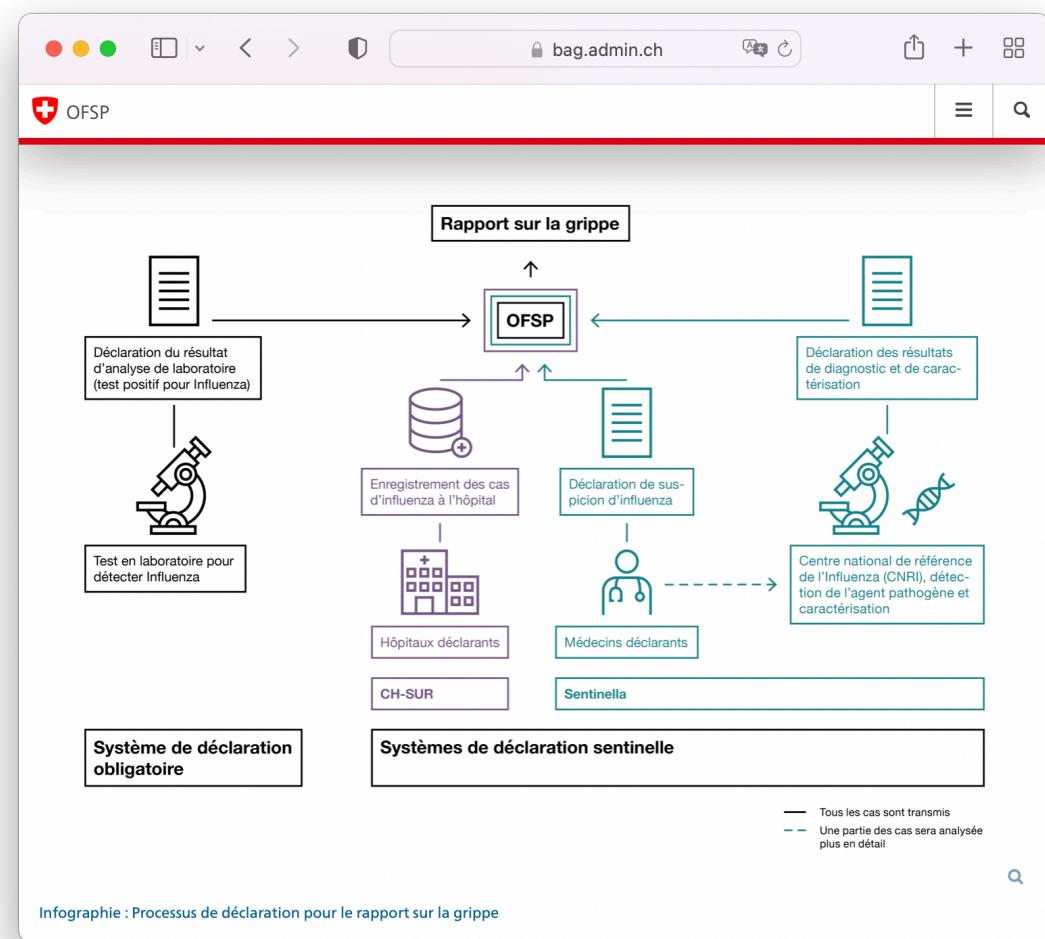
On 21 February 2020, a resident of the municipality of Vo', a small town near Padua (Italy), died of pneumonia due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection¹. This was the first coronavirus disease 19 (COVID-19)-related death detected in Italy since the detection of SARS-CoV-2 in the Chinese city of Wuhan, Hubei province². In response, the regional authorities imposed the lockdown of the whole municipality for 14 days³. Here we collected information on the demography, clinical presentation, hospitalization, contact network and the presence of SARS-CoV-2 infection in nasopharyngeal swabs for 85.9% and 71.5% of the population of Vo' at two consecutive time points. From the first survey, which was conducted around the time the town lockdown started, we found a prevalence of infection of 2.6% (95% confidence interval (CI): 2.1–3.3%). From the second survey, which was conducted at the end of the lockdown, we found a prevalence of 1.2% (95% CI: 0.8–1.8%). Notably, 42.5% (95% CI: 31.5–54.6%) of the confirmed SARS-CoV-2 infections detected across the two surveys were asymptomatic (that is, did not have symptoms

Epidemiology Surveillance

- Population-based vs sentinel surveillance

Epidemiology Surveillance

- Influenza:
1-5% of physicians
voluntarily reporting



Epidemiology Surveillance

- Case-based vs aggregate surveillance

often a question of resources

Epidemiology Surveillance

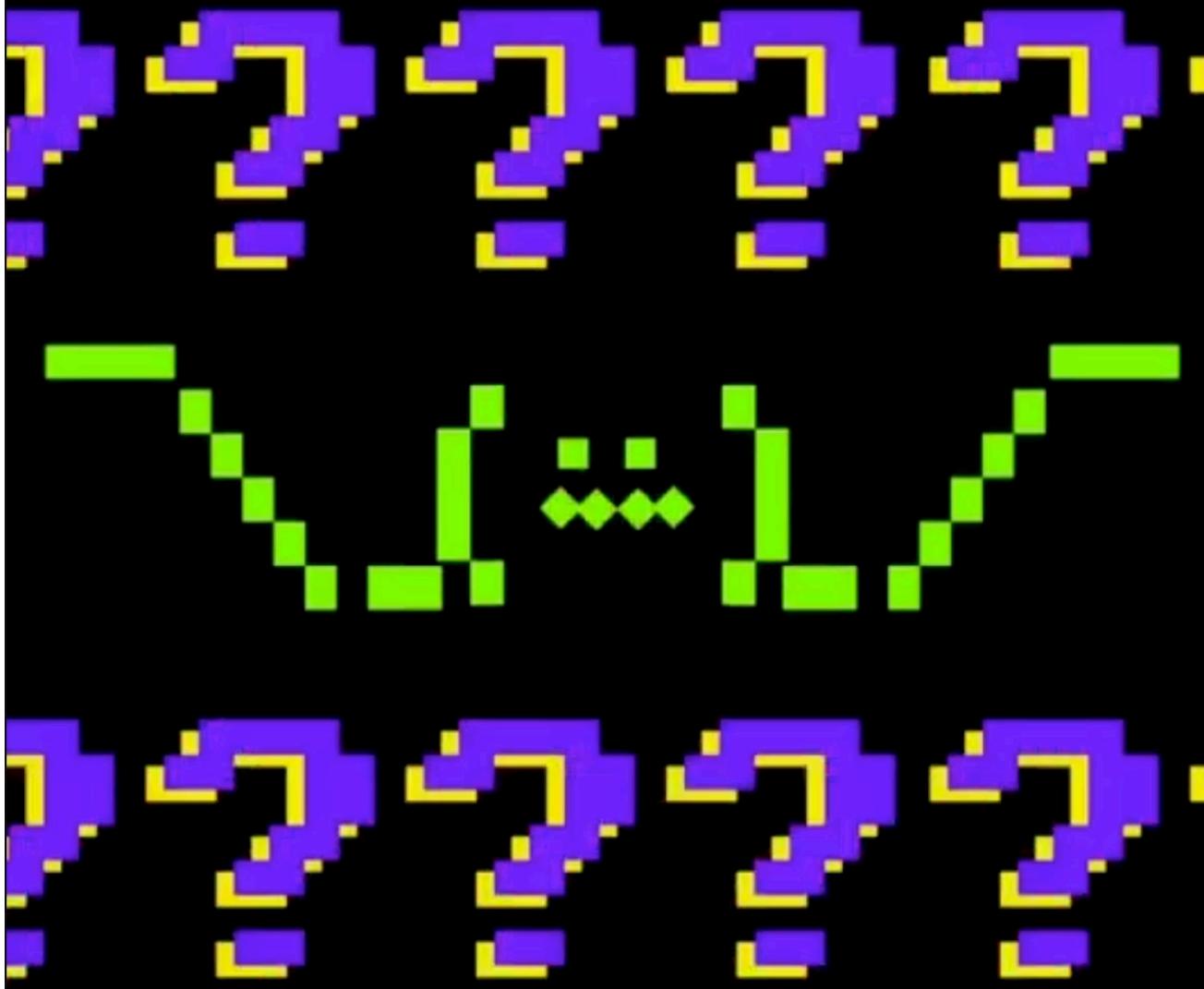
- Syndromic vs laboratory surveillance

Digital public health surveillance always syndromic, but may change soon.

Epidemiology Surveillance

- Event-based vs indicator-based surveillance

Most of digital public health surveillance is event-based



Epidemiology

Incidence and Prevalence

- Incidence: number of new cases during a specified period of time.
- Prevalence: number of cases present during a specified period of time.

Epidemiology

Incidence and Prevalence

- Incidence: number of new cases during a specified period of time.
- Prevalence: number of cases present during a specified period of time.
- Attack rate: incidence / population at risk (also called incidence rate)

Epidemiology

Incidence and Prevalence

- Incidence: a measure of risk
- Prevalence: a measure of “diseases pressure / burden” in the system

Epidemiology

Incidence and Prevalence

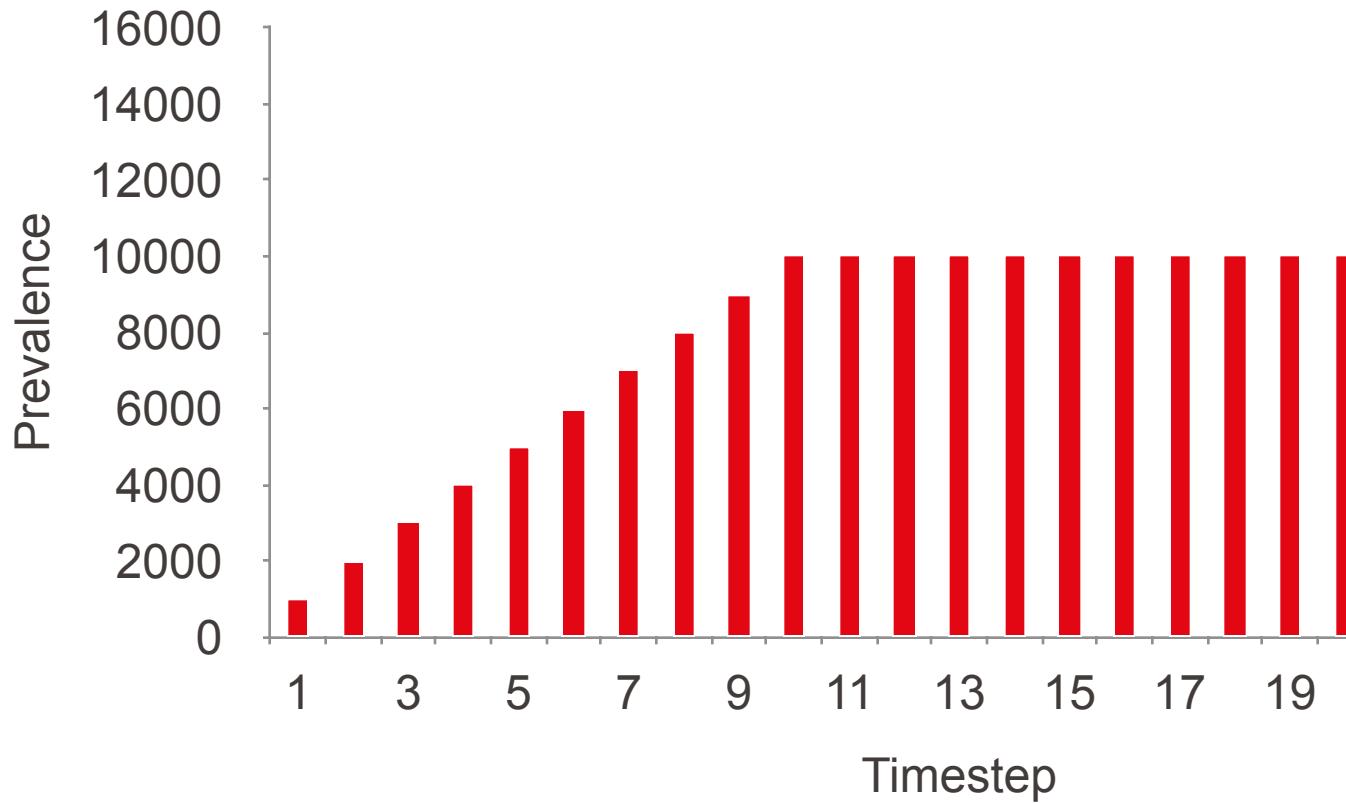
- Case study: A public health *improvement* leads to an increase in prevalence. How is this possible?

Assume:

1. Incidence of 1000 new cases per time step
2. Disease incurable
3. Disease 100% lethal after 10 time steps

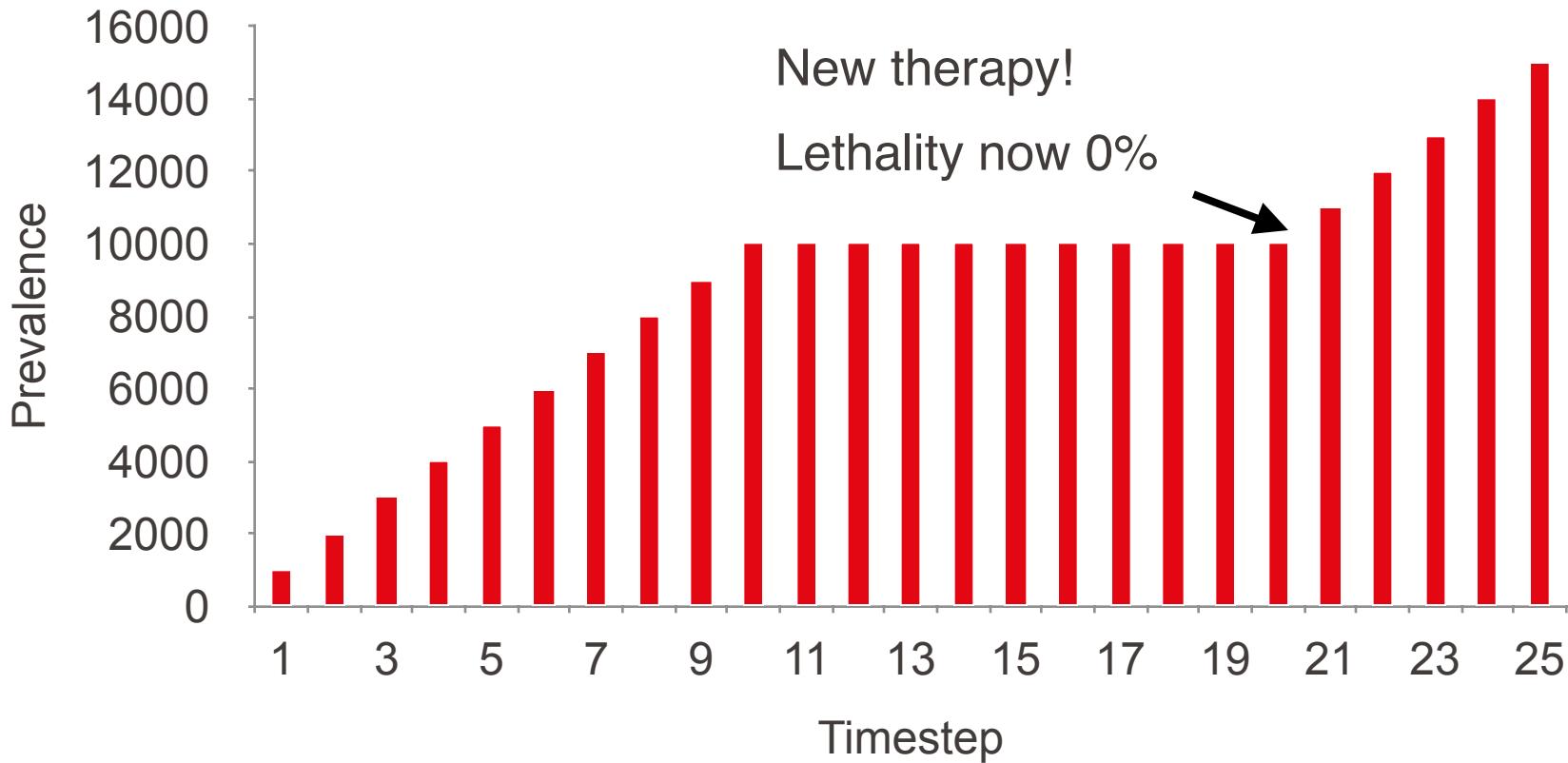
Epidemiology

Incidence and Prevalence



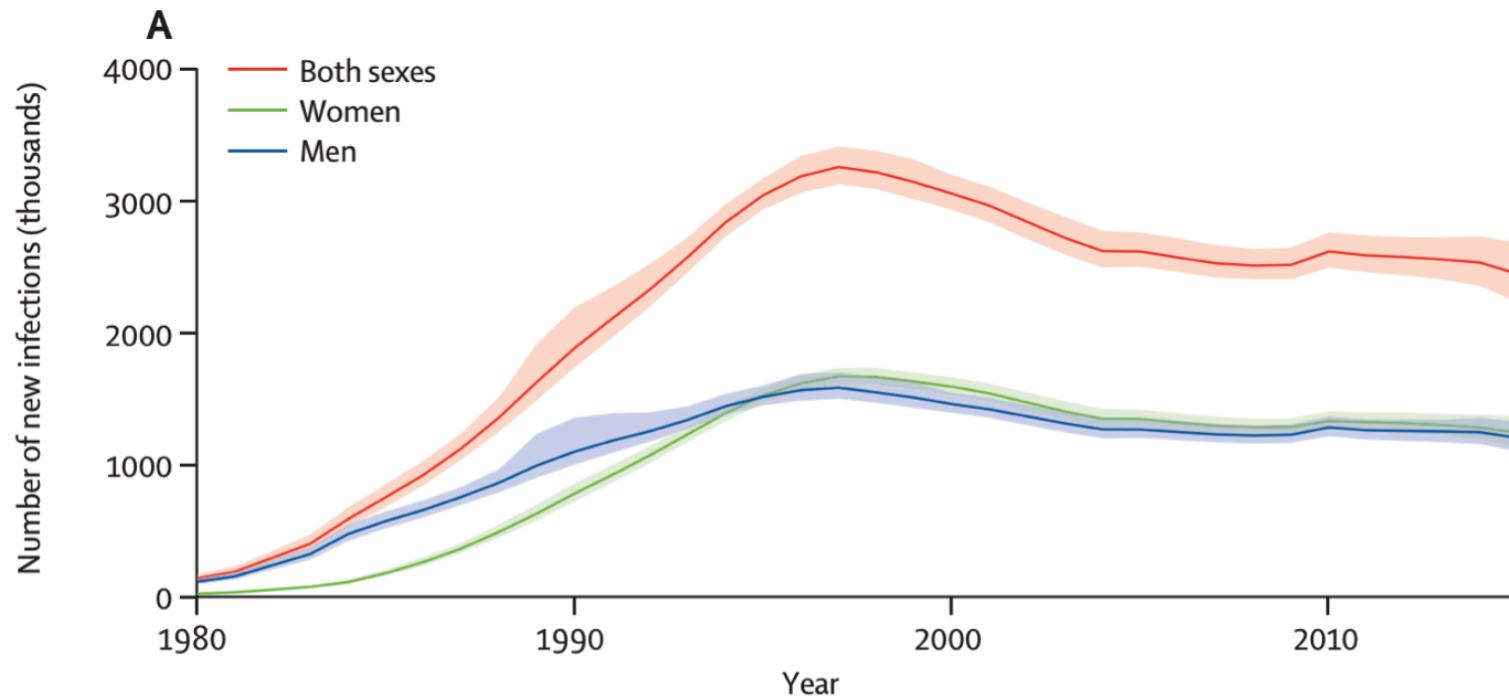
Epidemiology

Incidence and Prevalence



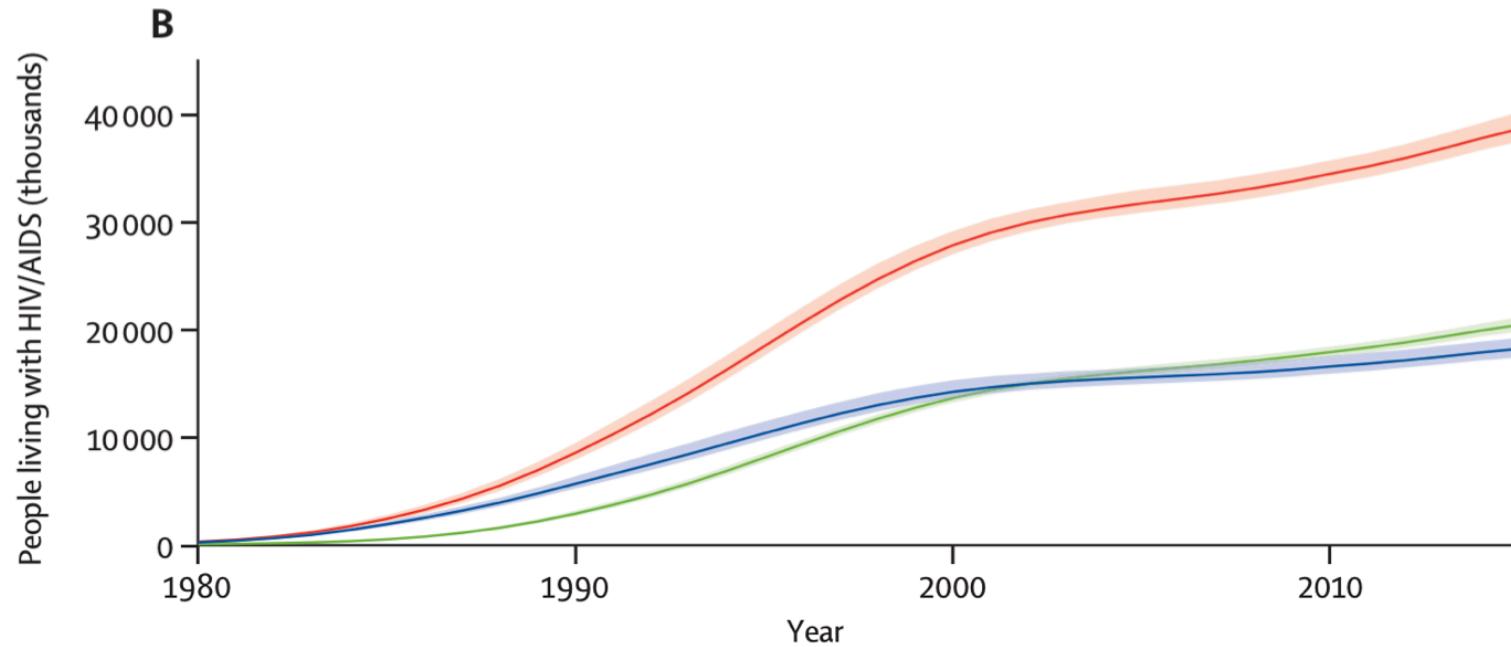
Epidemiology

HIV Incidence



Epidemiology

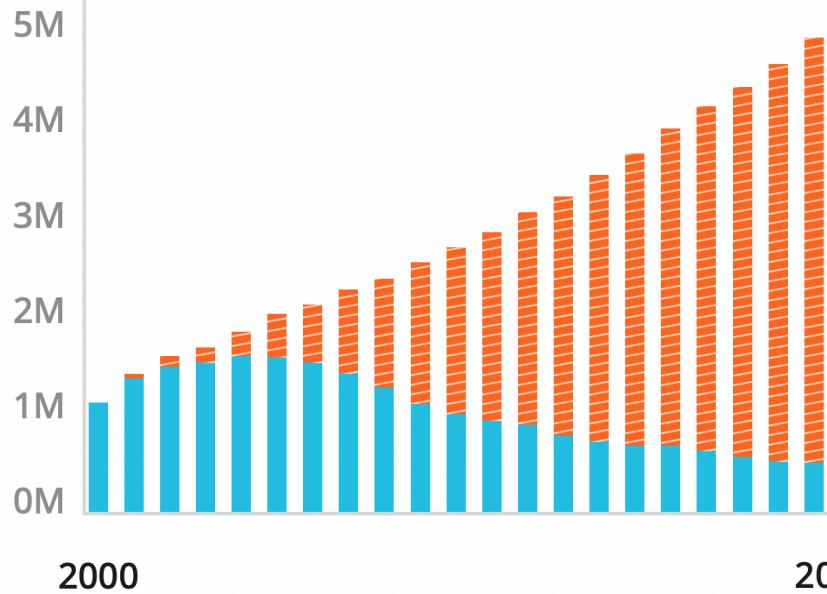
HIV Prevalence



A dramatic shift toward progress in the HIV/AIDS epidemic

AIDS-related deaths

Deaths per year



Legend

- Estimated AIDS-related deaths without prevention or antiretroviral treatments (ARVs)
- AIDS-related deaths

+290%

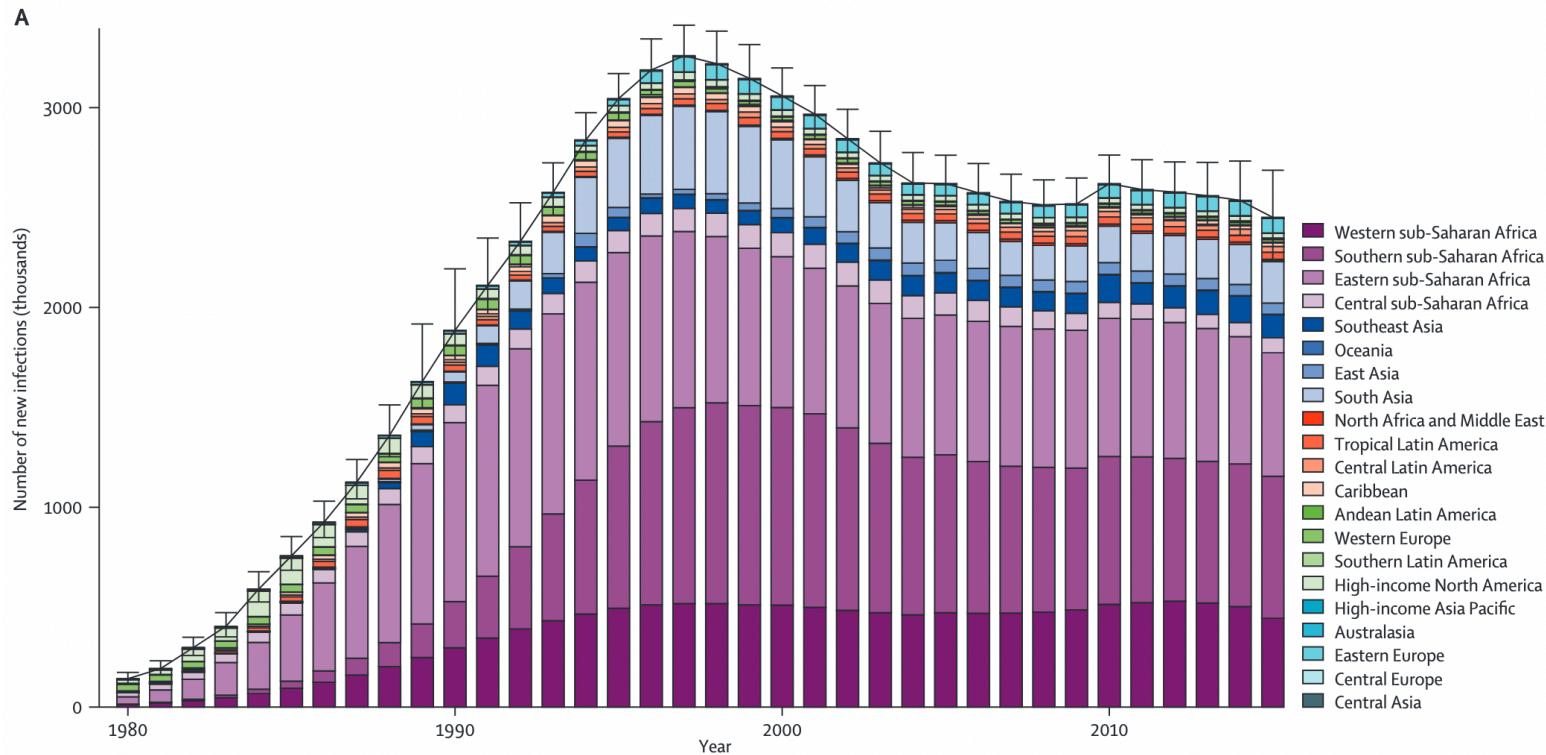
Increase in AIDS-related deaths if no prevention or ARVs

-60%

Actual decline in AIDS-related deaths

Epidemiology

HIV Incidence

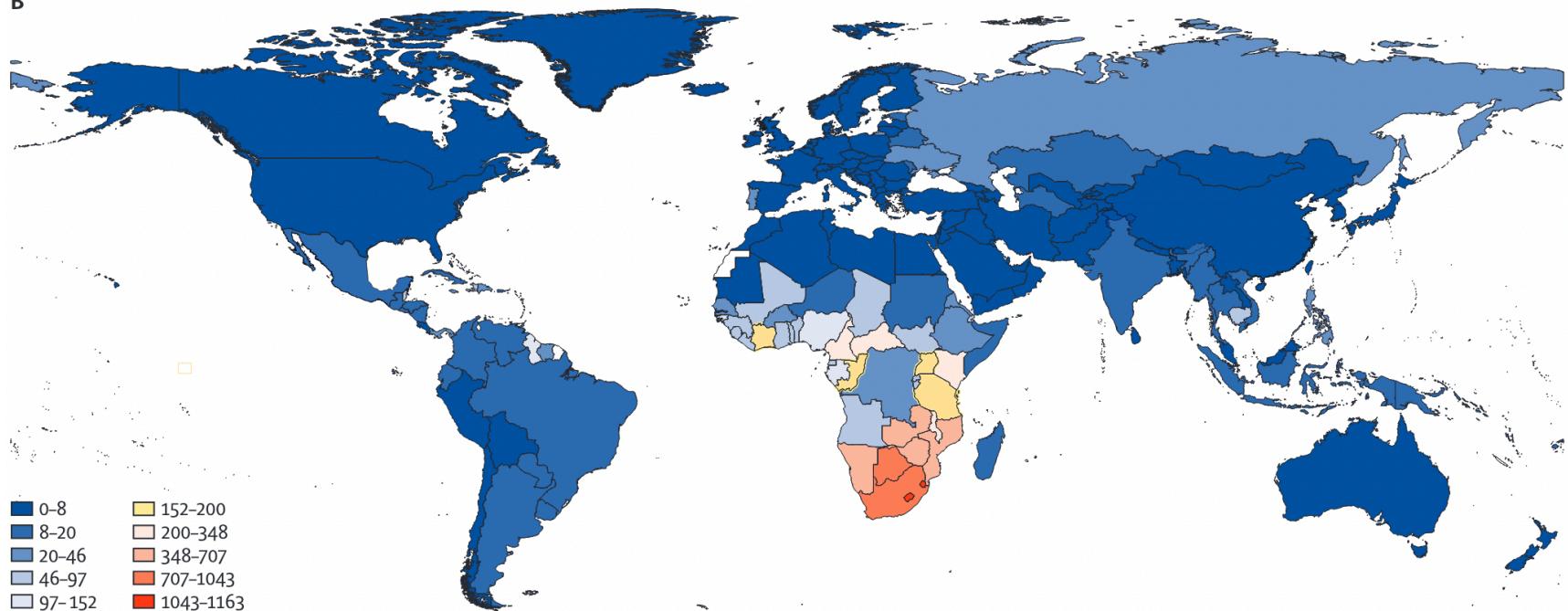


Bars show the mean number of estimated new infections within a given year.

Epidemiology

HIV Incidence

B



Rates are per 100 000 people.

Epidemiology

HIV Incidence and Prevalence

	Country/Region	Adult prevalence of HIV/AIDS ^[1]	Number of people with HIV/AIDS	Annual deaths from HIV/AIDS ^[3]	Year of estimate
1	 Eswatini	27.90%	200,000	2,300	2019
2	 Lesotho	23.10%	340,000	4,800	2019
3	 Botswana	22.20%	380,000	5,000	2019
4	 Zimbabwe	21.40%	1,400,000	20,000	2019
5	 South Africa	13.30%	7,500,000	72,000	2019
6	 Namibia	12.70%	210,000	3,000	2019
7	 Mozambique	12.10%	2,200,000	51,000	2019
8	 Zambia	12.10%	1,200,000	17,000	2019
9	 Malawi	9.50%	1,100,000	13,000	2016
10	 Equatorial Guinea	7.00%	65,000	1,800	2019
79	 United States	0.36%	1,189,700	-	2019 ^[13]
102	 Switzerland	0.20%	17,000	-	2019

- Point prevalence vs period prevalence
- Seroprevalence

Seroprevalence of anti-SARS-CoV-2 IgG antibodies in Geneva, Switzerland (SEROCoV-POP): a population-based study



Silvia Stringhini, Ania Wisniak*, Giovanni Piumatti*, Andrew S Azman*, Stephen A Lauer, Hélène Baysson, David De Ridder, Dusan Petrovic, Stephanie Schrempt, Kailing Marcus, Sabine Yerly, Isabelle Arm Vernez, Olivia Keiser, Samia Hurst, Klara M Posfay-Barbe, Didier Trono, Didier Pittet, Laurent Gétaz, François Chappuis, Isabella Eckerle, Nicolas Vuilleumier, Benjamin Meyer, Antoine Flahault, Laurent Kaiser, Idris Guessous

Summary

Background Assessing the burden of COVID-19 on the basis of medically attended case numbers is suboptimal given its reliance on testing strategy, changing case definitions, and disease presentation. Population-based serosurveys measuring anti-severe acute respiratory syndrome coronavirus 2 (anti-SARS-CoV-2) antibodies provide one method for estimating infection rates and monitoring the progression of the epidemic. Here, we estimate weekly seroprevalence of anti-SARS-CoV-2 antibodies in the population of Geneva, Switzerland, during the epidemic.

Lancet 2020; 396: 313-19

Published Online

June 11, 2020

[https://doi.org/10.1016/S0140-6736\(20\)31304-0](https://doi.org/10.1016/S0140-6736(20)31304-0)

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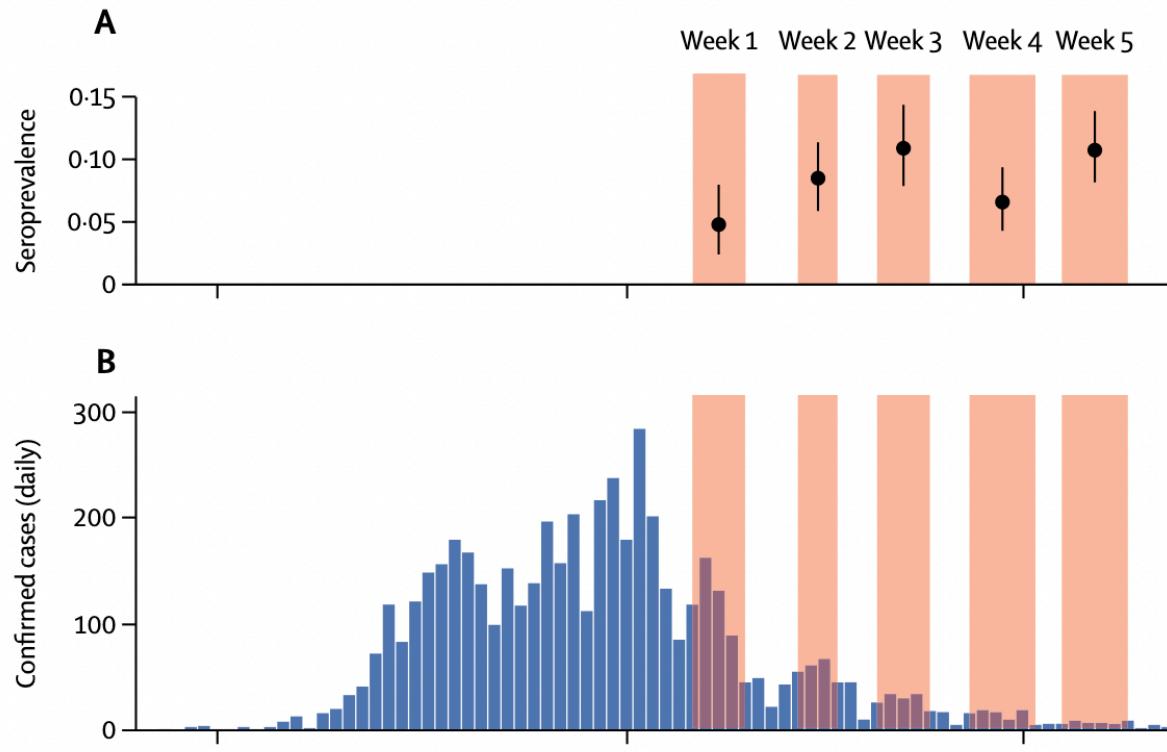
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Methods The SEROCOV-POP study is a population-based study of former participants of the Bus Santé study and their household members. We planned a series of 12 consecutive weekly serosurveys among randomly selected participants from a previous population-representative survey, and their household members aged 5 years and older. We tested each participant for anti-SARS-CoV-2-IgG antibodies using a commercially available ELISA. We estimated seroprevalence using a Bayesian logistic regression model taking into account test performance and adjusting for the age and sex of Geneva's population. Here we present results from the first 5 weeks of the study.

Findings Between April 6 and May 9, 2020, we enrolled 2766 participants from 1339 households, with a demographic distribution similar to that of the canton of Geneva. In the first week, we estimated a seroprevalence of 4.8% (95% CI 2.4–8.0, n=341). The estimate increased to 8.5% (5.9–11.4, n=469) in the second week, to 10.9% (7.9–14.4, n=577) in the third week, 6.6% (4.3–9.4, n=604) in the fourth week, and 10.8% (8.2–13.9, n=775) in the fifth week. Individuals aged 5–9 years (relative risk [RR] 0.32 [95% CI 0.11–0.63]) and those older than 65 years (RR 0.50 [0.28–0.78]) had a significantly lower risk of being seropositive than those aged 20–49 years. After accounting for the time to seroconversion, we estimated that for every reported confirmed case, there were 11.6 infections in the community.

Epidemiology

Seroprevalence



Epidemiology

Seroprevalence

The preliminary results of this study provide an important benchmark to assess the state of the COVID-19 epidemic. At what appears to be the tail end of the first wave of the pandemic in Switzerland, about one in ten people have developed detectable antibodies against SARS-CoV-2, despite the fact that it was one of the more heavily affected areas in Europe.¹⁵ Thus, assuming that the presence of the IgG antibodies measured in this study is, at least in the short term, associated with protection, these results highlight that the vast majority of the population is still immunologically naive to this new virus.

Over the course of the 5 study weeks, we observed an increase in seroprevalence from about 5% to about 11%, which is to be expected considering time to seroconversion after symptoms (median 10·4 days [IQR 8·1–13·4]) and that the peak of the epidemic was reached the week before the start of our survey (appendix p 8). As expected, our study also confirms that cases identified during the acute phase of disease provide little information on the state of the outbreak. Indeed, we observed that in the community, there were 11 infections for every COVID-19 confirmed case in Geneva, reflecting the variability in disease severity, testing access or practices, and care-seeking behaviours.

Epidemiology

Case Definition

- A set of criteria that defines a case for a given health condition.
- Can vary over time, and over different places
- Often divided in *suspected*, *probable*, and *confirmed* cases

Suspected case of SARS-CoV-2 infection (3 options)

A A person who meets the clinical **OR** epidemiological criteria:

Clinical criteria:

- acute onset of fever **AND** cough (ILI)

OR

- acute onset of **ANY THREE OR MORE** of the following signs or symptoms: fever, cough, general weakness/fatigue¹, headache, myalgia, sore throat, coryza, dyspnoea, nausea/diarrhoea/anorexia

OR

Epidemiological criteria²:

- contact of a probable or confirmed case, or linked to a **COVID-19 cluster**.³

B A patient with **severe acute respiratory illness**

(SARI: acute respiratory infection with history of fever or measured fever of $\geq 38^{\circ}\text{C}$; and cough; with onset within the last 10 days; and requires hospitalization)

C A person

with no clinical signs or symptoms **OR** meeting epidemiologic criteria with a **positive professional-use or self-test SARS-CoV-2 Antigen-RDT**.⁴

¹ Signs separated with slash (/) are to be counted as one sign.

² In light of the heightened transmissibility of emerging variants and the high likelihood that any close contact could be infected, epidemiological criteria alone are included in order to qualify asymptomatic contacts for testing, when possible, for the countries with the capacity to adapt more sensitive testing strategies; this is particularly relevant in high-risk populations and settings.

³ A group of symptomatic individuals linked by time, geographic location and common exposures, containing at least **one NAAT-confirmed** case or at least **two** epidemiologically linked, symptomatic (meeting clinical criteria of Suspect case definition A or B) persons with **positive professional use OR self-test Ag-RDT** (based on 297% specificity of test and desired $>99.9\%$ probability of at least one positive result being a true positive)

Note: Clinical and public health judgment should be used to determine the need for further investigation in patients who do not strictly meet the clinical or epidemiological criteria. Surveillance case definitions should not be used as the sole basis for guiding clinical management.

Probable case of SARS-CoV-2 infection (2 options)

A A patient who meets **clinical criteria AND** is a **contact of a probable or confirmed case**, or linked to a **COVID-19 cluster**³

B **Death**, not otherwise explained, in an adult with **respiratory distress** preceding death **AND** who **was a contact of a probable or confirmed case or linked to a COVID-19 cluster**

Confirmed case of SARS-CoV-2 infection (2 options)

A A person with a **positive Nucleic Acid Amplification Test (NAAT)**, **regardless of** clinical criteria **OR** epidemiological criteria

B A person **meeting clinical criteria AND/OR** epidemiological criteria (suspect case A) **with a positive professional-use or self-test SARS-CoV-2 Antigen-RDT**.⁴

⁴ **Ag-RDT antigen-detection rapid diagnostic tests (Ag-RDT)** are available for use by trained professionals or for self-testing by individuals:

- **Professional-use SARS-CoV-2 antigen-RDT** : WHO EUL-approved Ag-RDT, in which sample collection, test performance and result interpretation are done by a trained operator

- **Self-test SARS-CoV-2 antigen-RDT** : WHO EUL-approved Ag-RDT in which sample collection, test performance and result interpretation are done by individuals by themselves.

Epidemiology

Case Definition

Suspected case of SARS-CoV-2 infection (3 options)

A

A person who meets the clinical **OR** epidemiological criteria:

Clinical criteria:

- acute onset of fever AND cough (ILI)

OR

- acute onset of **ANY THREE OR MORE** of the following signs or symptoms: fever, cough, general weakness/fatigue¹, headache, myalgia, sore throat, coryza, dyspnoea, nausea/diarrhoea/anorexia

OR

Epidemiological criteria² :

- contact of a probable or confirmed case, or linked to a **COVID-19 cluster**.³

B

A patient with **severe acute respiratory illness**

(SARI: acute respiratory infection with history of fever or measured fever of ≥ 38 °C; and cough; with onset within the last 10 days; and requires hospitalization)

C

A person

with no clinical signs or symptoms **OR** meeting epidemiologic criteria with a **positive professional-use or self-test** SARS-CoV-2 Antigen-RDT.⁴

Epidemiology

Case Definition

Probable case of SARS-CoV-2 infection (2 options)

- A** A patient who meets **clinical criteria** AND is a **contact of a probable or confirmed case**, or linked to a **COVID-19 cluster³**
- B** **Death**, not otherwise explained, in an adult with **respiratory distress** preceding death AND who **was a contact of a probable or confirmed case** or linked to a **COVID-19 cluster³**

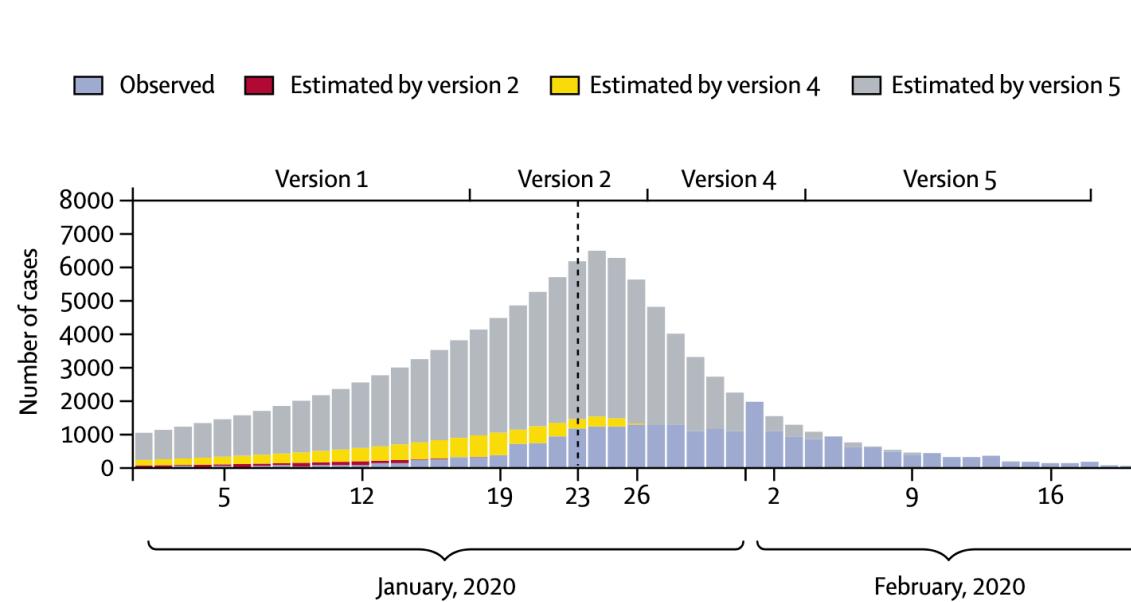
Confirmed case of SARS-CoV-2 infection (2 options)

- A** A person with a positive **Nucleic Acid Amplification Test (NAAT)**, **regardless of clinical criteria OR epidemiological criteria**
- B** A person meeting clinical criteria **AND/OR** epidemiological criteria (suspect case A) with a **positive professional-use or self- test SARS-CoV-2 Antigen-RDT.⁴**

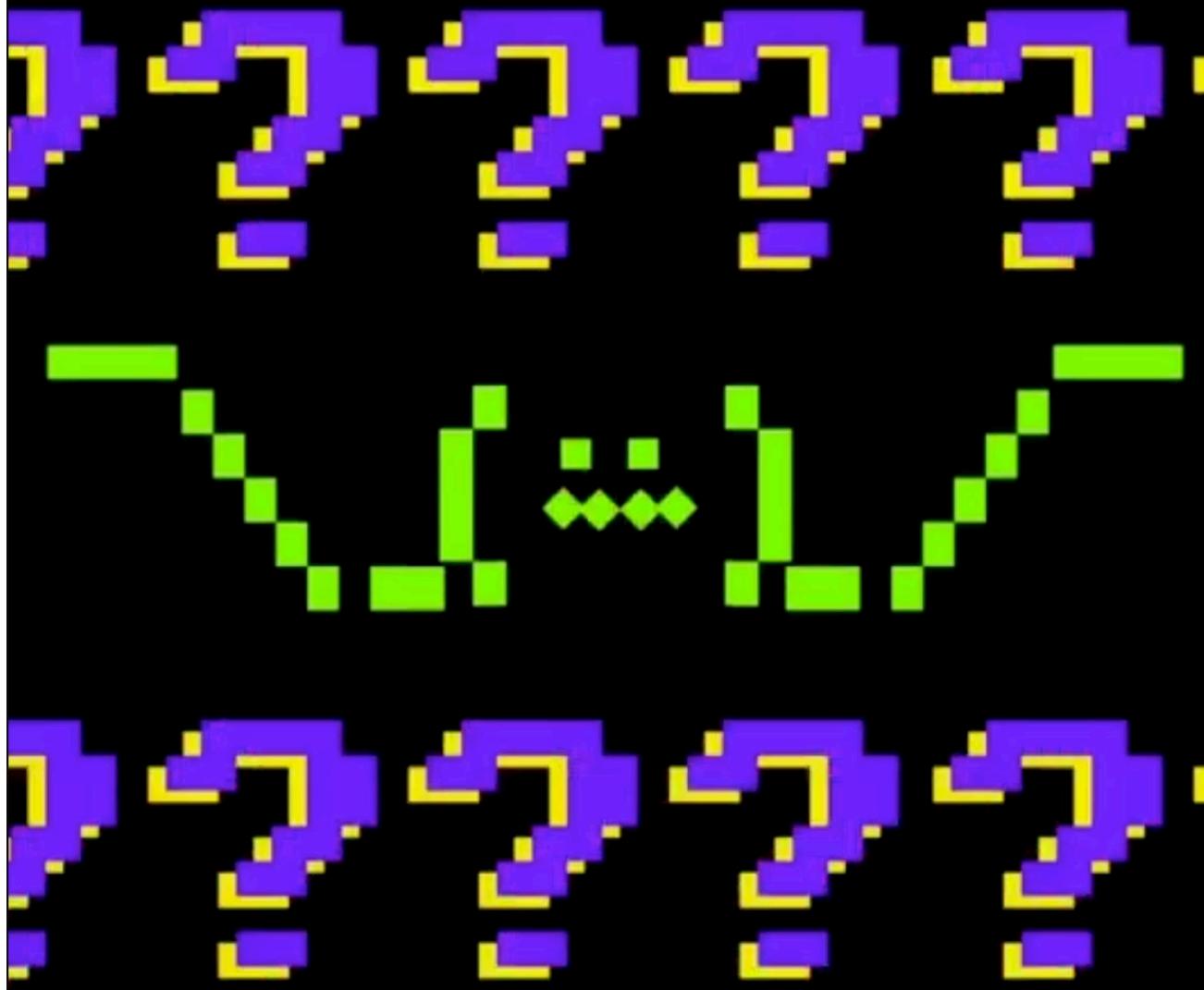
Epidemiology

Case Definition

- Case definitions can change over time, especially during the early phases of newly emerging diseases.



Criteria	Jan 15-17 Version 1	Jan 18-21 Version 2	Jan 22-26 Version 3	Jan 27-Feb 3 Version 4	Feb 4-17 Version 5 Hubei	Feb 4-17 Version 5 outside Hubei	Feb 18-March 2 Version 6	March 3-now Version 7
Epidemiological history								
Travel history or residence								
Areas surrounding Wuhan								
Other areas with reported cases				*				
Wuhan								
Wet markets in Wuhan								
Contact with individuals								
With PCR confirmation of SARS-CoV-2								
With symptoms, from areas surrounding Wuhan†								
With symptoms, from areas with reported cases†				*				
With symptoms, from Wuhan†								
Occurring in a cluster				‡				\$
Clinical manifestations								
Symptoms								
Respiratory symptoms								
Fever								
Blood cell counts								
Radiographic evidence of pneumonia								
Unsuccessful antibiotic treatment								
Clinical tests								
Serological evidence of infection								
RT-PCR positive								
Whole genome sequencing confirmed homology to SARS-CoV-2								



Epidemiology

Morbidity

- Disease = reduction in health due to a biological factor (contrast with accidents / non-intentional injury)
- Factor can be external, i.e. pathogen -> infectious disease
- Factor can be internal, i.e cancer -> non-communicable disease (NCD)
- (Note that 10-15% of humans cancers are currently known to be caused by viruses)

Epidemiology

Disease Severity

- Many diseases have a range, from fully asymptotic to deadly.

Epidemiology

Disease Severity

Patient State	Descriptor	Score
Uninfected	Uninfected; no viral RNA detected	0
Ambulatory mild disease	Asymptomatic; viral RNA detected	1
	Symptomatic; independent	2
	Symptomatic; assistance needed	3
Hospitalised: moderate disease	Hospitalised; no oxygen therapy*	4
	Hospitalised; oxygen by mask or nasal prongs	5
Hospitalised: severe diseases	Hospitalised; oxygen by NIV or high flow	6
	Intubation and mechanical ventilation, $pO_2/FiO_2 \geq 150$ or $SpO_2/FiO_2 \geq 200$	7
	Mechanical ventilation $pO_2/FiO_2 < 150$ ($SpO_2/FiO_2 < 200$) or vasopressors	8
	Mechanical ventilation $pO_2/FiO_2 < 150$ and vasopressors, dialysis, or ECMO	9
Dead	Dead	10

Epidemiology

Disease Severity

- Even when severe disease is relatively rare, in absolute numbers, they can overwhelm a healthcare system.

Epidemiology

Disease Severity

- Frequencies of different severities hard to measure - cases visible to healthcare system most likely more severe than average.

Summary of main findings

(1) For all 130 included studies, the IQR for the proportion of asymptomatic SARS-CoV-2 was 14% to 50%, prediction interval 2% to 90%) and for 84 studies based on screening of defined populations, IQR 20% to 65% (prediction interval 4% to 94%). In 46 studies that identified participants through contact tracing of index cases and outbreak investigations, the summary proportion from meta-analysis was 19% (95% CI 15% to 25%, prediction interval 2% to 70%). (2)

The risk ratio for the secondary attack rate from asymptomatic compared with symptomatic infections was 0.32 (95% CI 0.16 to 0.64, prediction interval 0.11 to 0.95) and for presymptomatic infections compared with symptomatic infection was 1.00 (95% CI 0.37 to 2.71, prediction interval 0.11 to 9.12). (3) In mathematical modelling studies, estimated proportions of all SARS-CoV-2 infections that result from transmission from asymptomatic individuals were mostly below 15%, and from presymptomatic individuals mostly higher than 40%. Evidence

LETTER

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The global distribution and burden of dengue

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Dengue is a systemic viral infection transmitted between humans by *Aedes* mosquitoes¹. For some patients, dengue is a life-threatening illness². There are currently no licensed vaccines or specific therapeutics, and substantial vector control efforts have not stopped its rapid emergence and global spread³. The contemporary worldwide distribution of the risk of dengue virus infection⁴ and its public health burden are poorly known^{2,5}. Here we undertake an exhaustive assembly of known records of dengue occurrence worldwide, and use a formal modelling framework to map the global distribution of dengue risk. We then pair the resulting risk map with detailed longitudinal information from dengue cohort studies and population surfaces to infer the public health burden of dengue in 2010. We predict dengue to be ubiquitous throughout the tropics, with local spatial variations in risk influenced strongly by rainfall, temperature and the degree of urbanization. Using cartographic approaches, we estimate there to be 390 million (95% credible interval 284–528) dengue infections per year, of which 96 million (67–136) manifest apparently (any level of disease severity). This infection total is more than three times the dengue burden estimate of the World Health Organization². Stratification of our estimates by country allows comparison with national dengue reporting, after taking into account the probability of an apparent

geographical range of endemic transmission⁹. Although the historical expansion of this disease is well documented, the potentially large burden of ill-health attributable to dengue across much of the tropical and subtropical world remains poorly enumerated.

Knowledge of the geographical distribution and burden of dengue is essential for understanding its contribution to global morbidity and mortality burdens, in determining how to allocate optimally the limited resources available for dengue control, and in evaluating the impact of such activities internationally. Additionally, estimates of both apparent and inapparent infection distributions form a key requirement for assessing clinical surveillance and for scoping reliably future vaccine demand and delivery strategies. Previous maps of dengue risk have used various approaches combining historical occurrence records and expert opinion to demarcate areas at endemic risk^{10–12}. More sophisticated risk-mapping techniques have also been implemented^{13,14}, but the empirical evidence base has since been improved, alongside advances in disease modelling approaches. Furthermore, no studies have used a continuous global risk map as the foundation for dengue burden estimation.

The first global estimates of total dengue virus infections were based on an assumed constant annual infection rate among a crude approximation of the population at risk (10% in 1 billion (ref. 5) or 4% in 2

Epidemiology

Disease Severity

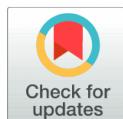


RESEARCH ARTICLE

Contributions from the silent majority dominate dengue virus transmission

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Epidemiology

Disease Severity

of people with asymptomatic infections is 80% (median) that of people with apparent or inapparent symptomatic infections (95% credible interval (CI): 0–146%). Due to their numerical prominence in the infectious reservoir, clinically inapparent infections in total could account for 84% (CI: 82–86%) of DENV transmission. Of infections that ultimately result in any level of symptoms, we estimate that 24% (95% CI: 0–79%) of onward trans-

Epidemiology

Disease Severity

- How to quantify impact? We want to compare disease, and make comparison over time and space.
- $DALY = YLD + YLL$

Epidemiology

Disease Severity

- How to quantify impact? We want to compare disease, and make comparison over time and space.

DALY

Disability Adjusted Life Year is a measure of overall disease burden, expressed as the cumulative number of years lost due to ill-health, disability or early death

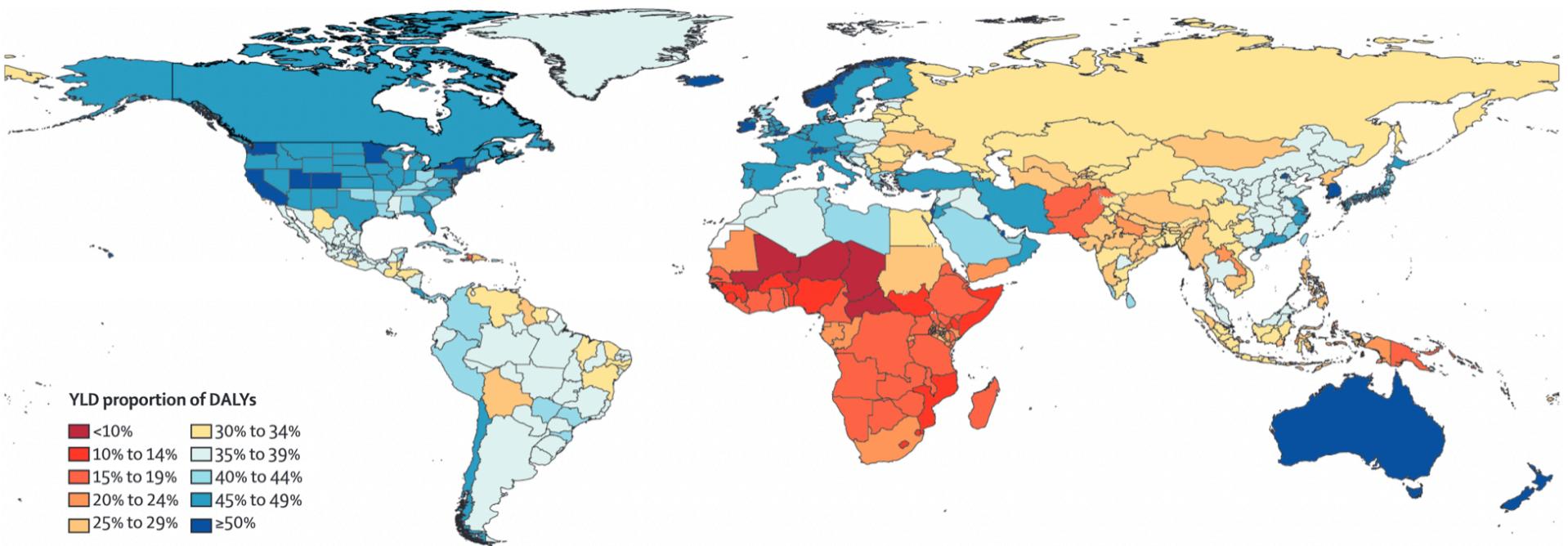
$$= \text{YLD} + \text{YLL}$$

Years Lived with Disability Years of Life Lost



Epidemiology

Disease Severity



Epidemiology

Morbidity

- Comorbidities = presence of more than one health condition
- US: >27% of US adults have chronic comorbidities

Epidemiology

Mortality

- How deadly is a disease?
- How deadly is it in a population -> mortality
- How deadly is it for an individual -> lethality

Epidemiology

Mortality

- Mortality rate: people dying of disease / population of interest, in a specified period of time

Number of deaths for leading causes of death:

- Heart disease: 695,547
- Cancer: 605,213
- COVID-19: 416,893
- Accidents (unintentional injuries): 224,935
- Stroke (cerebrovascular diseases): 162,890
- Chronic lower respiratory diseases: 142,342
- Alzheimer's disease: 119,399
- Diabetes: 103,294
- Chronic liver disease and cirrhosis: 56,585
- Nephritis, nephrotic syndrome, and nephrosis: 54,358

- US Data 2021
(population size
331.9 million)

Epidemiology

Mortality

- Swiss Data 2019 (population size 8.575 million)

<https://www.bfs.admin.ch/bfs/en/home/statistics/health/state-health/diseases/cancer.html>

Cancer		
2019	Men	Women
Cancer epidemiology		
Number of new cases ¹	25 302	21 107
Incidence rate ²	428.5	334.7
Cumulative risk before age 70, as a %	23.9	20.4
Number of deaths from cancer	9 322	7 870

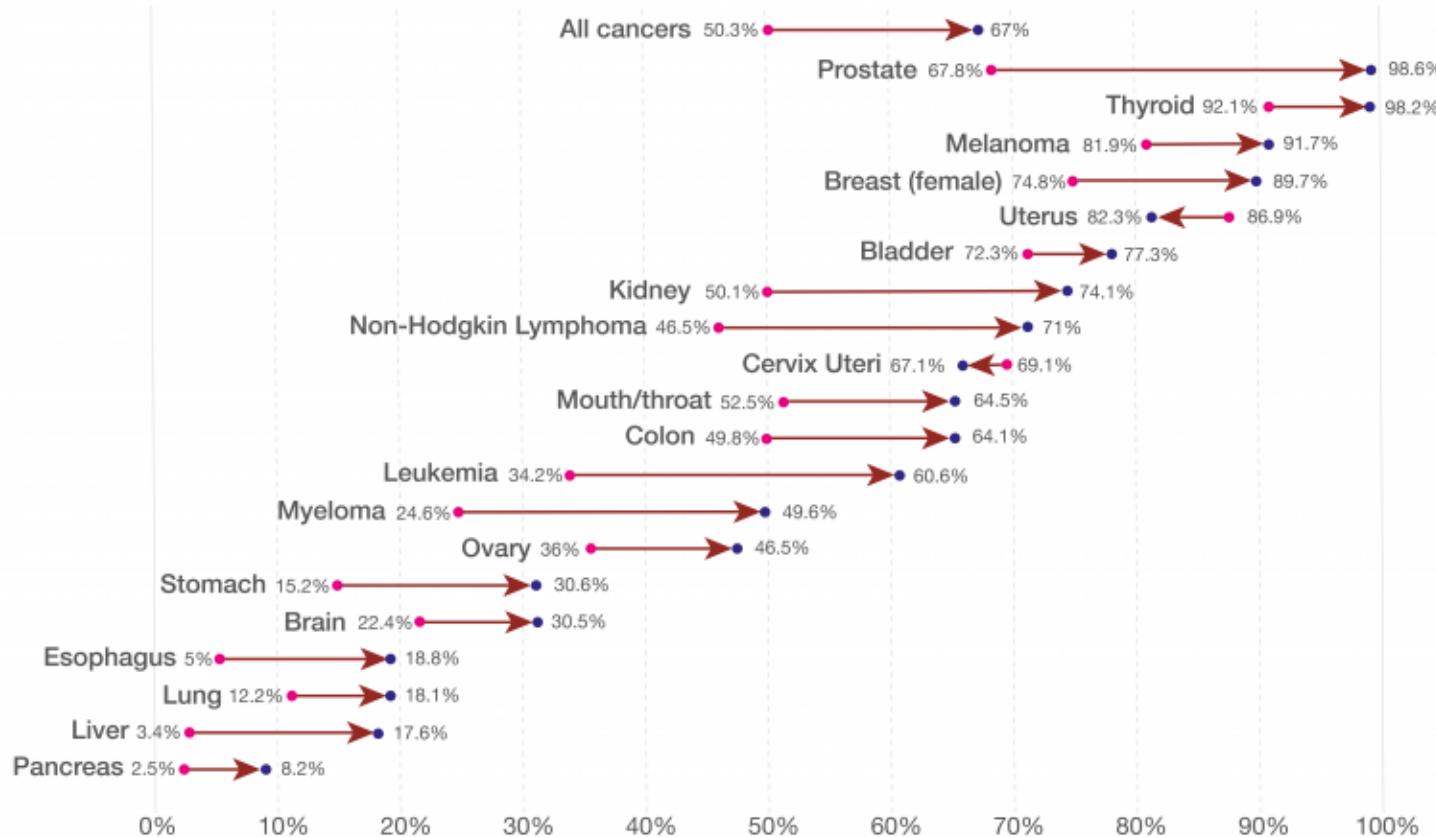
Epidemiology

Lethality

- How deadly is the disease once you have it? For *chronic* diseases, often expressed in survival rates per time period.

Five-year cancer survival rates in the USA

Average five-year survival rates from common cancer types in the United States, shown as the rate over the period 1970-77 [●] and over the period 2007-2013 [●]: 1970-77 → 2007-2013
This five-year interval indicates the percentage of people who live longer than five years following diagnosis.



Epidemiology

Lethality

- How deadly is the disease once you have it? For *acute* diseases, expressed in case fatality rate (CFR).
- $\text{CFR} = \text{number of deaths due to disease} / \text{cases}$

Epidemiology

Lethality

- IFR = number of deaths due to disease / infections
- Since infections often unknown, we need to estimate it from cases
- In early phase of outbreak, we haven't seen all deaths yet

Epidemiology

Lethality

- IFR of COVID: now known to be 0.5% and 1% (pre-vaccine)
- IFR of influenza: 0.03% - 0.1%

Epidemiology

Lethality

- Malaria: CFR: 0.3%
- Untreated HIV: CFR 99+%
- Huge range of lethaliities: from almost non-lethal (certain childhood diseases, CFR < 0.001%), to fully lethal (rabies after onset of symptoms, CFR 100%)

