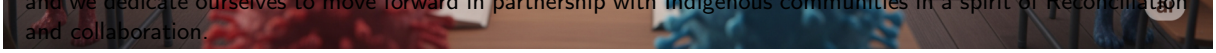

Epidemiology and mathematical epidemiology

MATH 8xyz – Lecture 02

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Among the first events recorded

- Epidemic events are among the first events recorded in History

- Indeed their effect was devastating at a time when medicine virtually did not exist and thus easily observed

First known epidemics (magentafrom Wikipedia) I

Event	Date	Location	Disease	Death toll
Plague of Megiddo	1350 BCE	Megiddo, land of Canaan	Unknown	Unknown
magentaPlague of Athens	429-426 BCE	Greece, Libya, Egypt, Ethiopia	Possibly typhus, typhoid fever or VHF	75–100K
magenta412 BCE epidemic	412 BCE	Greece, Roman Republic	Possibly influenza	Unknown
magentaAntonine Plague	165-180 CE (possibly up to 190 CE)	Roman Empire	Possibly smallpox	5–10M
Jian'an Plague	217 CE	Han dynasty	Possibly typhoid fever or VHF	Unknown

First known epidemics (magentafrom Wikipedia) II

magentaPlague of Cyprian	250-266 CE	Europe	Possibly smallpox	Unknown
magentaPlague of Justinian (1st plague pandemic)	541-549 CE	Europe and West Asia	Bubonic plague	15-100M (25-60% of population of Europe)
magentaRoman Plague of 590 (1st plague pandemic)	590 CE	Rome, Byzantine Empire	Bubonic plague	Unknown
magentaPlague of Sheroe (1st plague pandemic)	627-628 CE	Bilad al-Sham	Bubonic plague	25K+
magentaPlague of Amwas (1st plague pandemic)	638-639 CE	Byzantine Empire, West Asia, Africa	Bubonic plague	25,000+

First known epidemics (magentafrom Wikipedia) III

magentaPlague of 664 (1st plague pandemic)	664-689 CE	British Isles	Bubonic plague	Unknown
Plague of 698-701 (1st plague pandemic)	698-701 CE	Byzantine Empire, West Asia, Syria, Mesopotamia	Bubonic plague	Unknown
magenta735-737 Japanese smallpox epidemic	735-737 CE	Japan	Smallpox	2M (approx. 1/3 of Japanese population)
Plague of 746-747 (1st plague pandemic)	746-747 CE	Byzantine Empire, West Asia, Africa	Bubonic plague	Unknown

Epidemics with major human cost I

Rank	Epidemic/Pandemic	Disease	Human cost	Global mortality	Regional mortality	Date	Location
1	Black Death	Bubonic plague	75-200 M	17-54%	30-60% of European population	1346-1353	Europe, and Africa
2	Spanish flu	Influenza A/H1N1	17-100 M	1-5.4%		1918-1920	World
3	Plague of Justinian	Bubonic plague	15-100 M	7-56%	25-60% of European population	541-549	North A Europe East Asia
4	HIV/AIDS	HIV/AIDS	36.3 M (in 2020)	Total population change too large to calculate		1981-present	World

Epidemics with major human cost II

5	COVID-19	SARS-CoV-2	6.3-25 M (as of May 21, 2022)	0.1-0.3%		2019-present	World
6	Third plague pandemic	Bubonic plague	12-15 M			1855-1960	World
7	1545-1548 Cocoliztli epidemic	Cocoliztli	5-15 M	1-3%	27-80% of Mexican population	1545-1548	Mexico
8	Antonine Plague	Smallpox or measles	5-10 M	3-6	25-33% of Roman population	165-180 (possibly 190)	Roman Em
9	1520 Mexican smallpox epidemic	Smallpox	5-8 M	1-2%	23-37% of Mexican population	1519-1520	Mexico
10	1918-1922 Russian typhus epidemic	Typhus	2-3 M	0.1-0.16%	1-1.6% of Russian population	1918-1922	USSR
11	1957-1958 influenza pandemic	Influenza A/H2N2	1-4 M	0.03–0.1%		1957-1958	World

Epidemics with major human cost III

12	Hong Kong flu	Influenza A/H3N2	1-4 M	0.03-0.1%		1968-1969	World
13	1576 Cocoliztli epidemic	Cocoliztli	2-2.5 M	0.4-0.5%	50% of Mexican population	1576-1580	Mexico
14	735-737 Japanese smallpox epidemic	Smallpox	2 M	1%	33% of Japanese population	735-737	Japan
15	1772-1773 Persian plague	Bubonic plague	2 M	0.2–0.3%		1772-1773	Persia
16	Plague of Naples (1656)	Bubonic plague	1.25 M	0.2%		1656-1658	Southern I
17	1846-1860 cholera pandemic	Cholera	1+ M	0.08%		1846-1860	World
18	1629-1631 Italian plague	Bubonic plague	1 M	0.2%		1629-1631	Italy
19	1889-1890 flu pandemic	Influenza (disputed)	1 M	0.07%		1889-1890	World

“Forgotten” killers

- Tuberculosis (TB). In 2020, estimated 10 M cases of active TB, leading to 1.5 M deaths

- Malaria: 229 M cases and 409 000 deaths in 2019

Neglected tropical diseases (NTD)

Often endemic diseases, sometimes major causes of death, but out of sight of rich countries. From magentaWikipedia, noting that the precise list varies according to authors:

magentaBuruli ulcer	magentaChagas disease	Dengue & Chikungunya
magentaDracunculiasis	Echinococcosis	Yaws
Fascioliasis	magentaAfrican trypanosomiasis	magentaLeishmaniasis
magentaLeprosy	magentaLymphatic filariasis	Onchocerciasis
Rabies	Schistosomiasis	Soil-transmitted helminthiasis
Cysticercosis	Trachoma	Scabies and other ectoparasites
Snakebite envenoming	Mycetoma and deep mycoses	

The Black Death

The British Plague of 1547

The Plague of Marseille of 1720

Definition

gentaWiki **Epidemiology** is the study and analysis of the distribution (who, when, and where), patterns and determinants of health and disease conditions in defined populations

gentaBMJ **Epidemiology** is the study of how often diseases occur in different groups of people and why. Epidemiological information is used to plan and evaluate strategies to prevent illness and as a guide to the management of patients in whom disease has already developed

Etymology: *the study of what is upon the people*, derived from the Greek *epi* (*upon*, *among*), *demos* (*people*, *district*) and *logos* (*study*, *word*, *discourse*)

Who, when and where

Recall part of the definition on Wikipedia

> ***Epidemiology*** *is the study and analysis of the distribution (who, when, and where)*

A terminologically heavy domain

A few pointers:

- Moghadas and Laskowski. magentaReview of terms used in modelling influenza infection. NCCID 2014

- Milwid et al. magentaToward standardizing a lexicon of infectious disease modeling terms. Frontiers in Public Health 2016

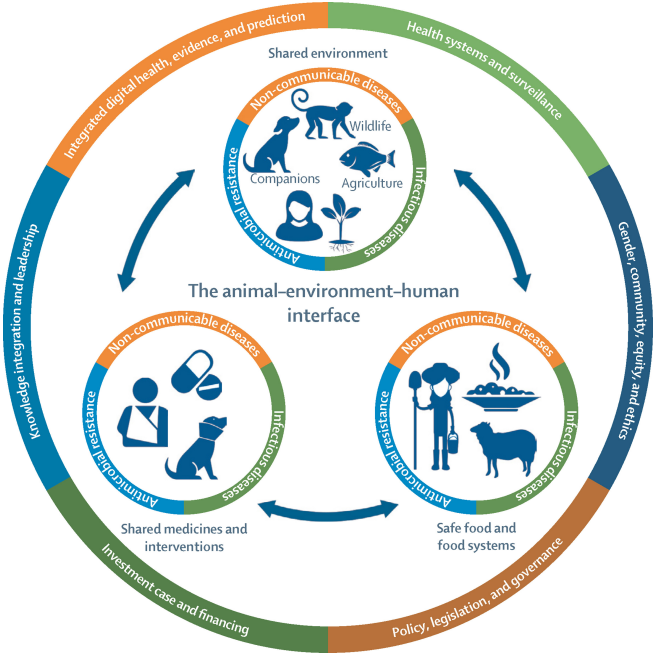
Who

- **Epidemiology** typically used when dealing with humans, but sometimes also generically when an easy description is sought; e.g., plant disease epidemiology

- **Epizootic**: denoting or relating to a disease that is temporarily prevalent and widespread in an animal population

- **Panzootic** is like a pandemic for animals

- **One Health**: considers health of humans, animals and their environment (including plants)


Integrated digital health, evidence, and prediction
Health systems and surveillance
Gender, community equity, and ethics
Policy, legislation, and governance
Investment case and financing
Knowledge integration and leadership
Shared environment
Non-communicable diseases
Infectious diseases
Antimicrobial resistance
Wildlife
Companions
Agriculture
The animal–environment–human interface
Shared medicines and interventions
Safe food and food systems

Incidence & Prevalence (when?)

Incidence: number of new cases in a population generated within a certain time period

Prevalence: number of cases of a disease at a single time point in a population

$\Longrightarrow$ $I(t)$ in an epidemiological model is **prevalence**, not **incidence**

Exposition versus Exposed

- Some bright bulb (not sure who) in days of yore: let's call **exposed** someone who has contracted the disease but is not yet showing symptoms ($\Longrightarrow$ SEIR model)

- "Real" epidemiologist: let's trace people who were exposed to the virus, i.e., people having come into contact with the virus (whether they have contracted the disease or not)

- Interestingly, I have embarked on a quixotic quest to make people use L instead of E, only to be told by real epidemiologists that they don't care :)

Les différentes phases de la propagation

- Spreading infectious disease: sporadic isolated cases

- **Outbreak**: the number of cases rises rapidly locally

- **Epidemic**: rapid rise and spread of an infectious disease in a given region

- **Endemic**: persistence habituelle d'une maladie infectieuse et contagieuse dans une région donnée

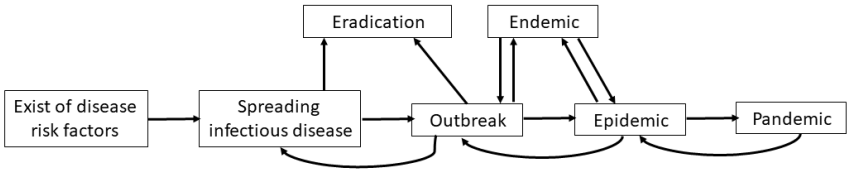
- **Pandemic**: épidémie qui s'étend au-delà des frontières des pays et qui peut se répandre sur un continent, un hémisphère ou dans le monde entier

Outbreak
sudden increase in occurrences of a disease in a particular time and place.

Endemic
constant maintained increase in occurrences of a disease in a geographic area.

Epidemic
rapid spread of disease to a large number of people in a given population within a short period of time.

Pandemic
spread across a large region, for instance multiple continents, or worldwide.

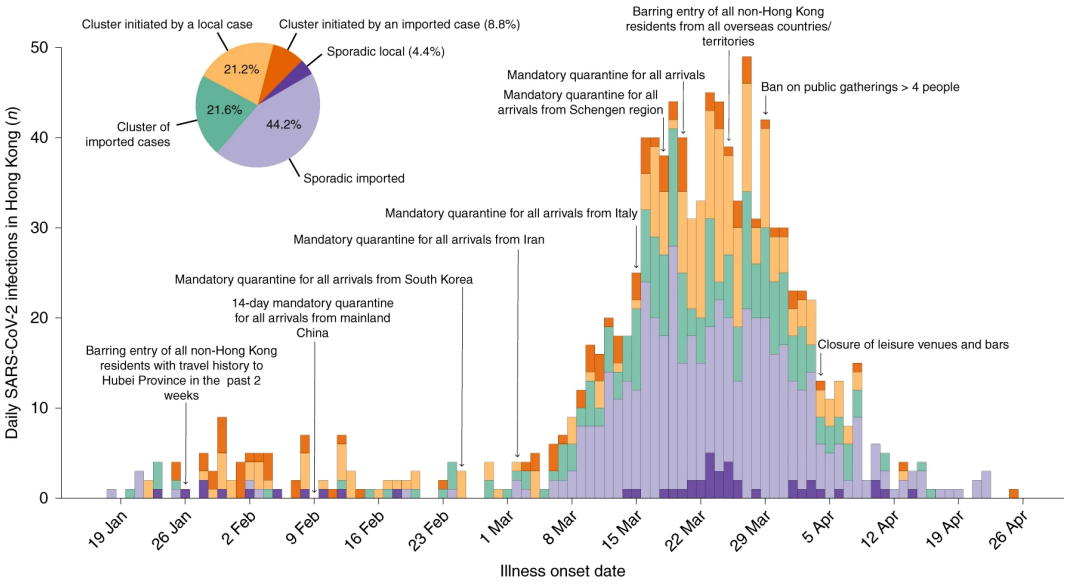


Epidemic curves

- Used to record the occurrence of new cases as a function of time

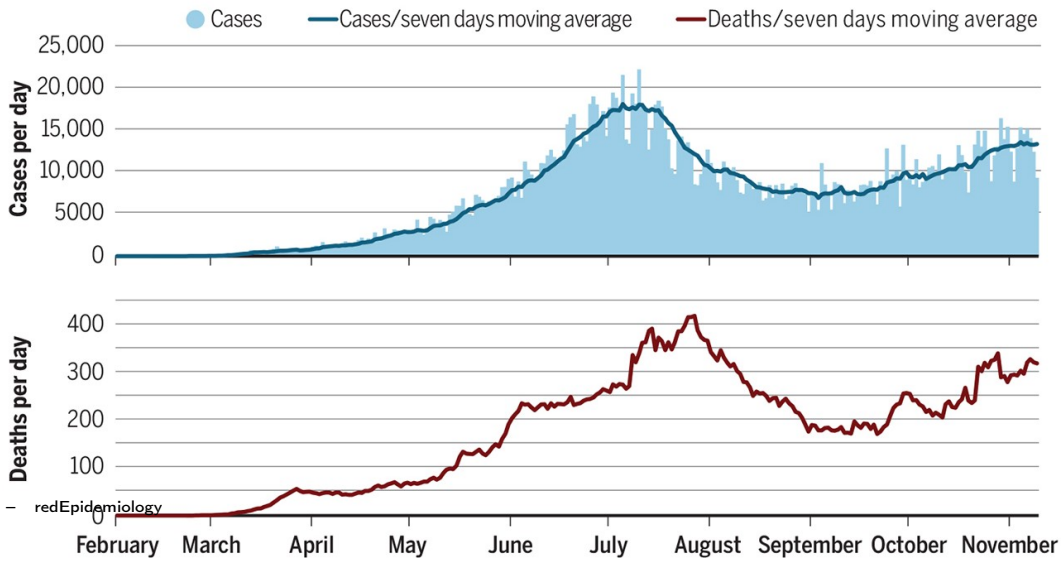
- When not too many cases, usually "individualised" (bar plots)

- When number of cases is large, continuous curve


Cluster initiated by a local case
Cluster initiated by an imported case (8.8%)
Sporadic local (4.4%)
21.2%
21.6%
44.2%
Cluster of imported cases
Sporadic imported
Barring entry of all non-Hong Kong residents from all overseas countries/ territories
Mandatory quarantine for all arrivals
Mandatory quarantine for all arrivals from Schengen region
Ban on public gatherings > 4 people
Mandatory quarantine for all arrivals from Italy
Mandatory quarantine for all arrivals from Iran
Mandatory quarantine for all arrivals from South Korea
14-day mandatory quarantine for all arrivals from mainland China
Barring entry of all non-Hong Kong residents with travel history to Hubei Province in the past 2 weeks
Closure of leisure venues and bars
Daily SARS-CoV-2 infections in Hong Kong (n)
0
10
20
30
40
50
19 Jan
26 Jan
2 Feb
9 Feb
16 Feb
23 Feb
1 Mar
8 Mar
15 Mar
22 Mar
29 Mar
5 Apr
12 Apr
19 Apr
26 Apr
Illness onset date

COVID-19 cases and deaths in Africa

The trend of daily reported cases of COVID-19 for the African continent, February to November 2020, shows the first peak of cases occurred July to August (mostly attributed to the Southern African Region) followed by a second peak, which started in October (mostly attributed to the Northern Region).



Some terminology for "where"

- **Epidemic**: diseases that are *visited upon* a population

- **Pandemic**: (will revisit this later in the course) epidemic that has spread across a large region, e.g., multiple continents or worldwide

- **Endemic**: diseases that *reside within* a population

- We don't say "panendemic"

Where? magenta1854 cholera outbreak

Cholera outbreak near Broad Street, London (UK)

Studied by magentaJohn Snow

> *I found that nearly all the deaths had taken place within a short distance of the [Broad Street] pump*

magentaWHO pandemic (influenza) phases

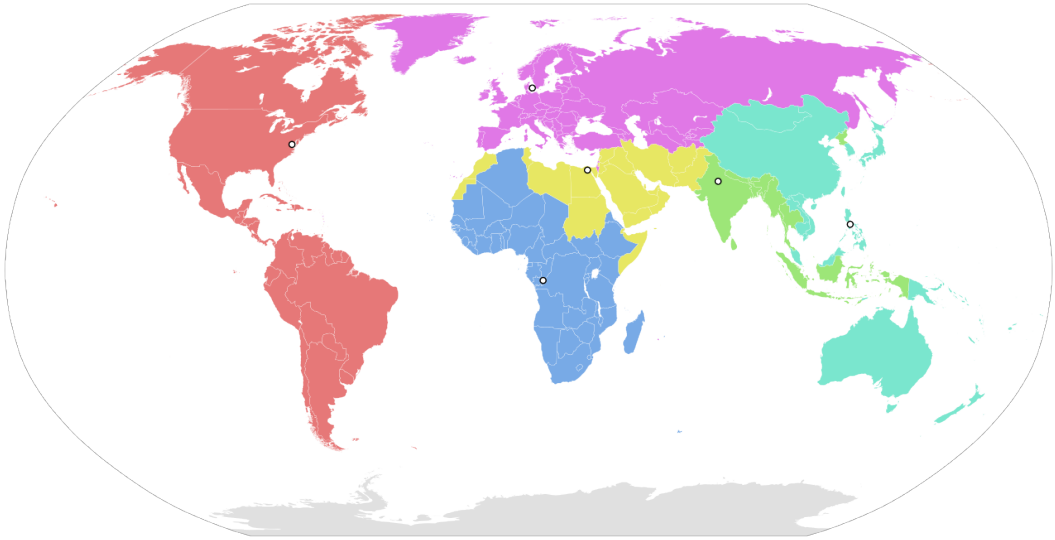
Period	Phase	Description
Interpandemic	1	No animal influenza virus circulating among animals has been reported to cause infection in humans
	2	Animal influenza virus circulating in domesticated or wild animals known to have caused infection in humans and therefore considered a specific potential pandemic threat

magentaWHO pandemic (influenza) phases

Period	Phase	Description
Pandemic alert	3	Animal or human-animal influenza reassortant virus has caused sporadic cases or small clusters of disease in people, but has not resulted in H2H transmission sufficient to sustain community-level outbreaks
	4	Human-to-human transmission of an animal or human-animal influenza reassortant virus able to sustain community-level outbreaks has been verified

magentaWHO pandemic (influenza) phases

Period	Phase	Description
Pandemic alert	5	Same identified virus has caused sustained community-level outbreaks in at least 2 countries in 1 WHO region
Pandemic	6	In addition to criteria in Phase 5, same virus has caused sustained community-level outbreaks in at least 1 other country in another WHO region



Fighting against infections

*Epidemiological information is used to plan and evaluate **strategies to prevent illness** and as a guide to the **management of patients** in whom disease has already developed*

- Preventing illness
  - Prophylactic measures
  - Vaccination

- Managing illness
  - Prevention of further spread (e.g., in hospital)
  - Treatment

Immunisation

- Smallpox first disease for which it was known

- Mentioned in a 1549 Chinese book

- China: powdered smallpox scabs blown up noses of the healthy; variolation-induced mortality not negligible (0.5-2%) but lower than normal (20%)

- 1798: Edward Jenner introduces safer inoculation with cowpox (vaccination)

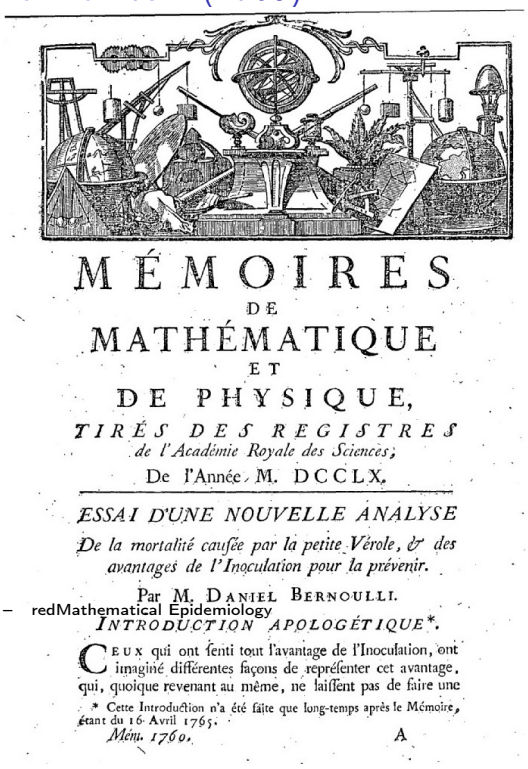
- 1880s: Pasteur extends vaccination to chicken cholera and anthrax in animals and human rabies

At the time, *herd immunity* was not understood so this was for personal protection

Domain is quite old ..

.. but has only become a thing in recent years!

Daniel Bernoulli (1760)



MÉMOIRES
DE
MATHÉMATIQUE
ET
DE PHYSIQUE,
TIRÉS DES REGISTRES de l'Académie Royale des Sciences;
De l'Année M. DCCLX.

ESSAI D'UNE NOUVELLE ANALYSE
De la mortalité causée par la petite Vérole, & des avantages de l'Inoculation pour la prévenir.

Par M. DANIEL BERNOULLI.

INTRODUCTION APOLOGÉTIQUE.*

CEUX qui ont senti tout l'avantage de l'Inoculation, ont imaginé différentes façons de représenter cet avantage, qui, quoique revenant au même, ne laissent pas de faire une

* Cette Introduction n'a été faite que long-temps après le Mémoire, étant du 16 Avril 1765.

Mém. 1760. A

- magentaBNF scan or magentapdf
- Probably the first epidemic model
- About petite vérole (smallpox) inoculation

Ross (early 1900)

- On 20 August 1897, observed malaria parasites in the gut of a mosquito fed several days earlier on a malaria positive human
- Nobel Prize for Medicine 1902
- Started considering malaria eradication using mathematical models; for some history, read magentathis 2012 paper

Kermack and McKendrick (1927+)

- We spend a lot more time on this in magentaLecture 05

- Groundbreaking set of papers starting in 1927

- We will see one particular case, the most well known, but I point out here and point out in Lecture 05 that this is just the tip of the iceberg of their work

Macdonald, Dietz and malaria

- Read for instance magentathis paper, which presents a history of the development of the so-called Ross-Macdonald model

- Klaus Dietz also worked a lot on malaria

Some activity later, but not much until 1990s

- In recent years, explosion

- Since the beginning of COVID-19: just nuts..

Some landmarks in mathematical epidemiology (IMBO)

- Macdonald. The epidemiology and control of malaria. 1957
- Baroyan, Rvachev et al. Deterministic epidemic models for a territory with a transport network. Kibernetika, 1967
- Hethcote & Yorke. Gonorrhea Transmission Dynamics and Control. LNBM 56, 1984
- Anderson & May. Infectious diseases of humans: dynamics and control. 1991
- Capasso. Mathematical Structures of Epidemic Systems. LNBM 97, 1993
- Hethcote. The mathematics of infectious diseases. SIAM Review, 2000
- van den Driessche & Watmough. Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission. MBS, 2002

A more recent trend

- Some rare numerical work $\leq$ 1980s, mostly simulation of math models

  - Baroyan, Rvachev et al. magentaComputer modelling of influenza epidemics for the whole country (USSR). *Advances in Applied Probability* (1971)
  - Rvachev & Longini. magentaA mathematical model for the global spread of influenza. *Mathematical Biosciences* (1986)
  - Flahault, Letrait et al. magentaModelling the 1985 influenza epidemic in France. *Statistics in Medicine* (1988)

- More and more frequent now, to the point that some modelling studies are purely simulation-based

Agent-based models (ABM)

- Early in the life of these models, they were called IBM (individual-based models)

- Over the years, a "philosophical" distinction has emerged:
  - IBM are mathematical models that consider individuals as the units; e.g., DTMC, CTMC, branching processes, etc.
  - ABM are computational models whose study is, for the most part, only possible numerically

Network models

- Network models endow vertices with simple systems and couple them through graphs

- Can be ABM, but some networks can also be studied analytically

Has happened all along, undergoing a transformation

- Epidemiology has long relied on data
- Many developments in statistics originate there
- Data has traditionally been better for chronic diseases than for infectious ones
- Near-real-time surveillance of infectious diseases ongoing since the 1980s (e.g., Réseau Sentinelles)
- SARS-CoV-1 saw the beginning of a move towards real-time emerging infectious disease data
- With SARS-CoV-2, the system has really progressed a lot, both in terms of "citizen science" and governmental initiatives