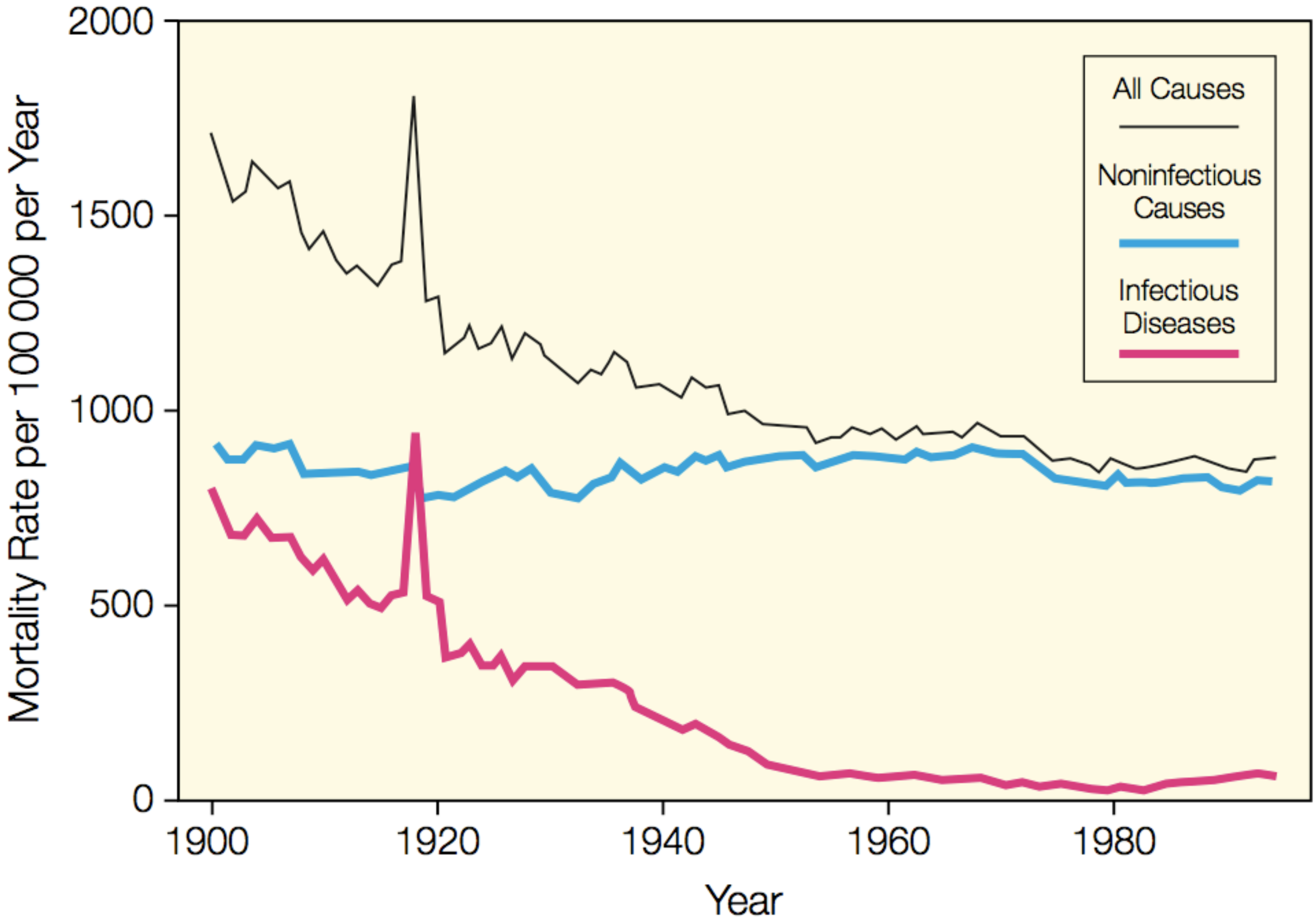
BMA 815: Mathematical Modeling of Infectious Diseases

Introduction

20th Century US Crude Mortality Rates

Armstrong et al. 1999, JAMA



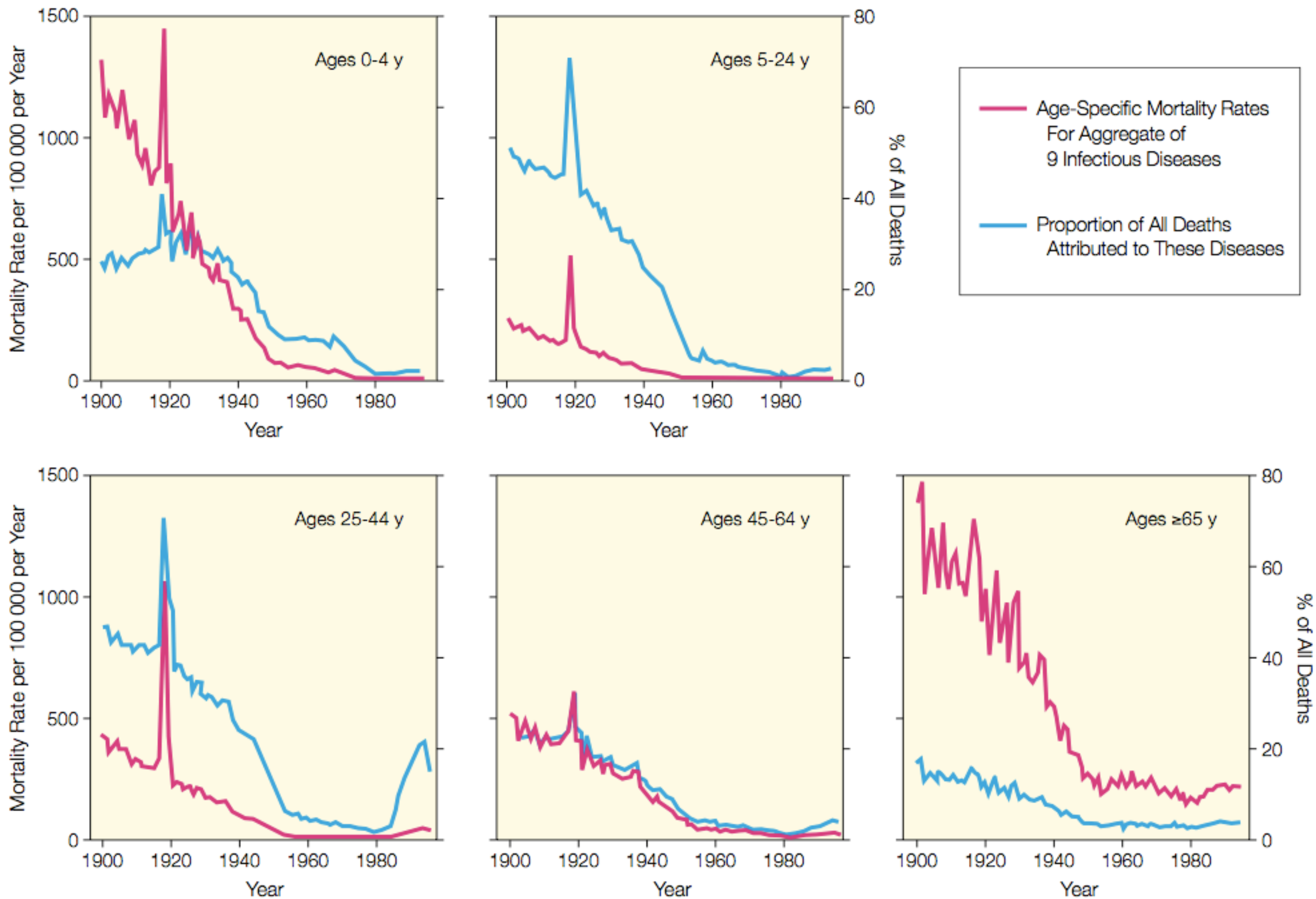
Spanish Flu

Large peak in 1918-19: Spanish influenza pandemic

Killed more people than 1st World War (20 to 40 million)

Mortality highest among 20-40 yr olds (seasonal flu typically most deadly to young and old)

Figure 3. Age-Specific Mortality Rates for an Aggregate of 9 Infectious Diseases and Proportion of All Deaths Attributable to These Diseases



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28% of all Americans infected, 675 000 deaths
Half of all deaths of Americans in WWI were due to influenza

Very unfortunate timing, with health care infrastructure already stretched, ? malnutrition, ? mass migration of troops and civilians

Disease Trends

Slight increase in disease deaths at the end of 20th century

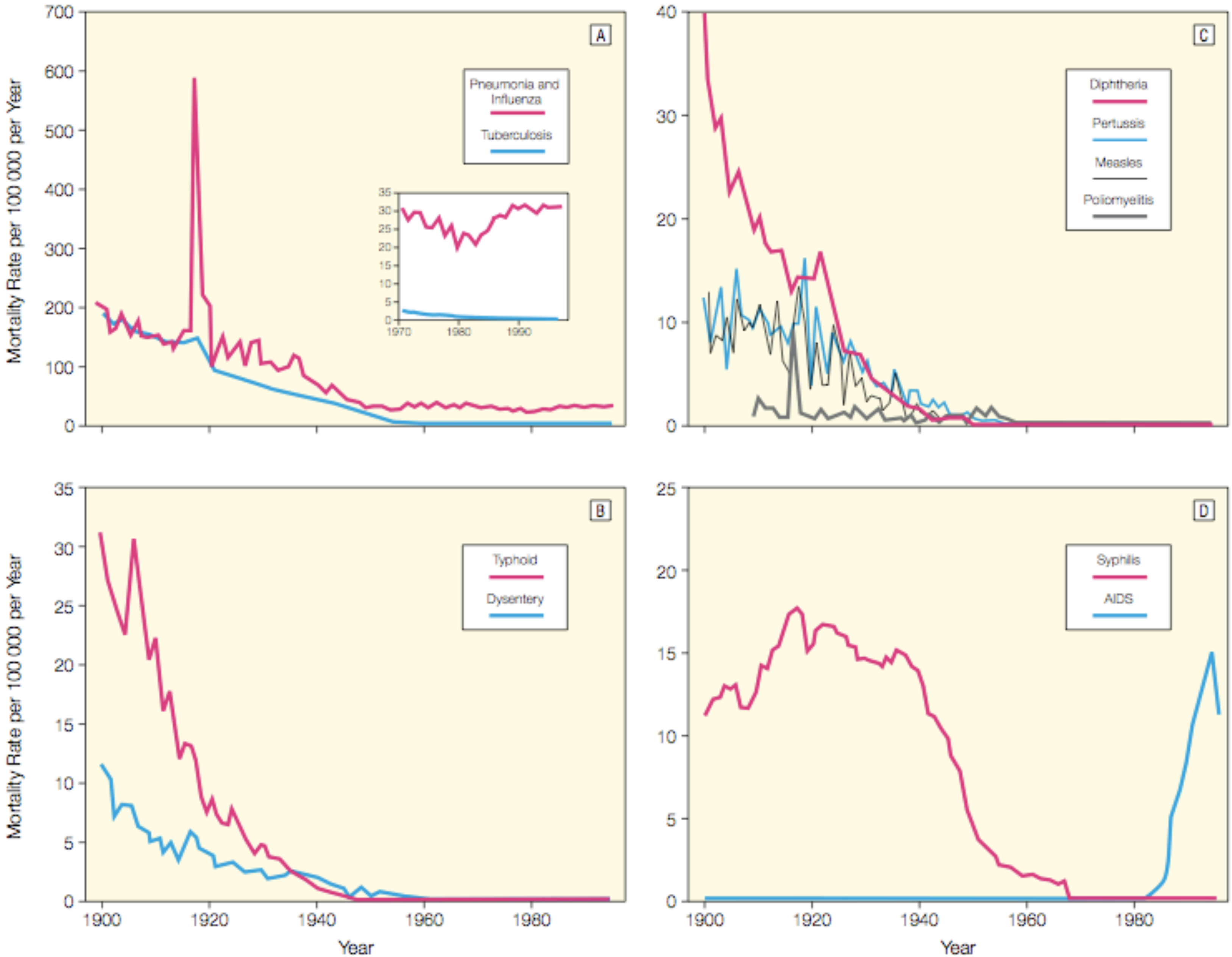
Largely HIV-related

But also age-related

(death rates shown are "crude" rates: don't control for changing age distribution of the population)

Influenza in the elderly

Figure 4. Crude Mortality Rates for 10 Infectious Diseases



The inset in Figure 4A shows the pneumonia and influenza mortality rate from 1970 to 1996. Statistics for poliomyelitis were not listed separately on mortality charts until 1909 (Figure 4C). AIDS indicates acquired immunodeficiency syndrome.

Why the Advances?

1.Public Health Measures

Increased understanding of mechanisms of infection and transmission

Improved infrastructure: water supply and sanitation

Social and community factors can be important

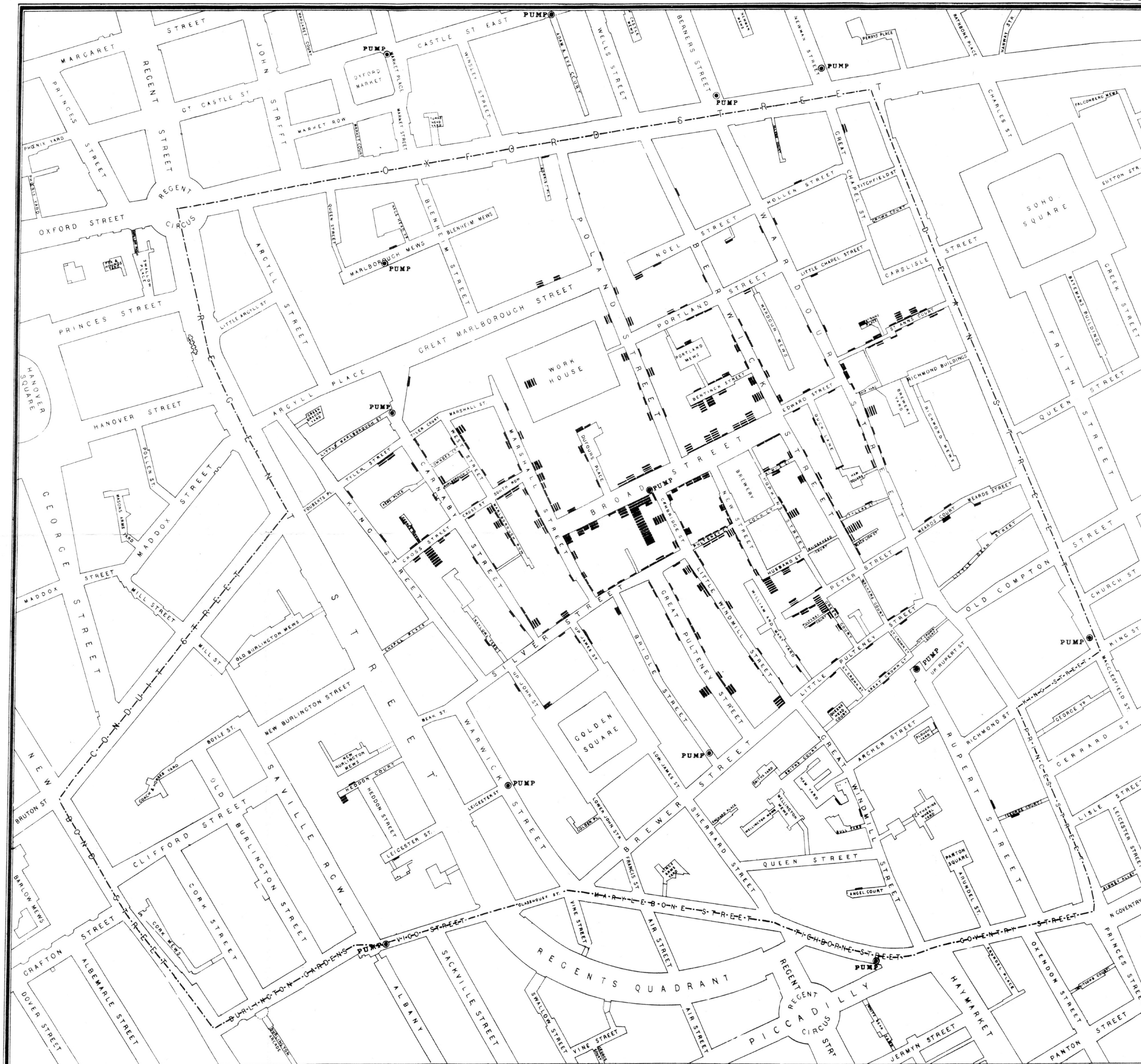
Historical example: John Snow and Cholera

Repeated cholera epidemics in Victorian London

August/September 1854, John Snow found a concentration of cases: within 250 yards of a particular intersection, he found more than 500 deaths in 10 days

He suspected contaminated water, so removed the handle of the local water pump

The number of cases dropped off



C.F. Cheffins, Lith, Southampton Bldgs. London.

SCALE 30 INCHES TO A MILE.

Figure 1.15 (D) Central section of John Snow's map of deaths from cholera in Soho, London, 1854

John Snow Celebrated in the Traditional English Manner

… but see "Map Making and Myth Making", Brody et al. 2000, Lancet

Why the Advances?

2. Drugs that treat and cure infection

e.g. antibiotics (penicillin discovered 1928), and more recently antivirals

Direct benefit to treated individual, but also an indirect benefit *to population* due to reduced transmission

3. Vaccination

Stimulate immune system, e.g. using a killed virus, or a live attenuated virus, or …

e.g. measles: 100-fold drop in number of cases in the US

Smallpox: eradicated in mid 1970s
Rinderpest: late confirmed case in 2001, declared eradicated in 2011
Polio: coming close to eradication

Advances in the Fight Against Infectious Disease

Infectious diseases no longer such a major issue in the West

William Stewart (US Surgeon General), 1967:

"The time has come to close the book on infectious diseases, and declare the war against pestilence won."

Advances in the Fight Against Infectious Disease

Unclear whether Stewart actually made that statement:

Spellberg & Taylor-Blake (2013, Infect Dis Poverty)

On the exoneration of Dr. William H. Stewart: debunking an urban legend

No source of the quote was identified. However, a trail of source documents was identified that clearly serves as the basis for subsequent, incorrect attribution of the quote to Dr. Stewart. In multiple source documents, Dr. Stewart made statements to the opposite effect, clearly recognizing that infectious diseases had not been conquered. The urban legend was created by a combination of lack of primary witnesses to the originating speech, misunderstanding of points made by Dr. Stewart in the speech, and increasing societal concern about emerging and re-emerging infectious diseases.

Advances in the Fight Against Infectious Disease

Infectious diseases no longer such a major issue in the West, but still significant killers in developing world

e.g. malaria: ~250 million cases/yr, 900 000 deaths/yr

In 2005, 10 million children under five died, a large fraction of which was due to infectious diseases

400,000 rotavirus deaths,
250,000 measles deaths

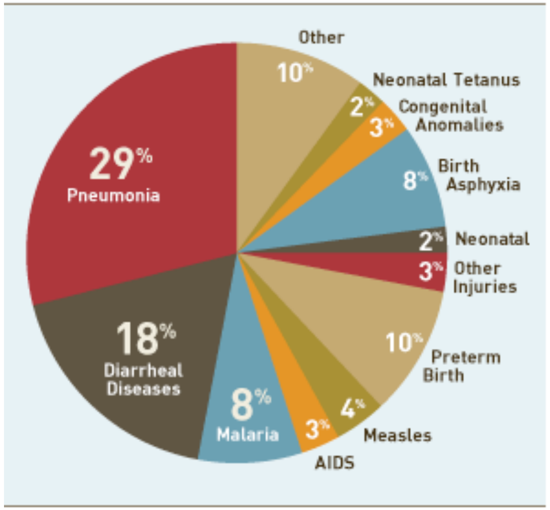


CHART 2: A few diseases cause over half of children's deaths.

Increasing Threat of Infectious Diseases

1. Emerging Infectious Diseases

e.g. SARS (a coronavirus): flu-like disease appeared mid Nov. 2002 in China
    approx. 8500 cases, 950 deaths
  Avian influenza (H5N1 influenza A)
  Swine flu (H1N1 influenza A)
  Ebola (filovirus): roughly 2/3 of all cases are fatal
  HIV
  BSE (mad cow disease)/variant CJD

Many of these have long resided in animal populations, but crossed to humans

Is this becoming more of a problem?
- Not clear. Many infections have jumped before
- Why might jumps to humans become more frequent?
  - Ecological reasons (humans increasing pressure on species)
  - Behavioral changes (perhaps increased movement of people is an issue?)
  - BSE : changes in animal feed practices
  - HIV : bushmeat?
- Or is it that we are looking more closely?

Increasing Threat of Infectious Diseases

2. Drug Resistance (Evolutionary problem)

Malaria, TB, HIV, many antibiotic resistant bacteria

MRSA (Methicillin-resistant *Staphylococcus aureus*) particularly an issue in hospitals

Role of HIV in spread of drug resistant TB

Major problem if we only have a single drug

Many diseases that we thought had been conquered could make reappearances

3. Vaccine Refusals/Scares

Perception of pros and cons of vaccination change, particularly if infections are seen as being less of a major issue

MMR/autism scares … linked to later outbreaks of measles?

Increasing Threat of Infectious Diseases

4. Deliberate Reintroduction: Bioterrorism

Anthrax: bacterium that produces spores

Incidents, soon after Sept. 11th, led to 5 fatalities and had a major impact on postal services and caused much public panic

Smallpox: lab samples remain even after eradication

Debate over vaccination, given that vaccine has health risk

Mass vaccination or targeted vaccination?

Do we wait until there's an outbreak? Could we act quickly enough?

5. Concern over genetic engineering and other experimentation

e.g. experiments on virulence of influenza viruses ("gain of function" experiments)

resurrecting eradicated viruses?

Where Do Mathematical Approaches Come Into All This?

1. Models to make predictions
   "weather forecasts" (use a statistical or a mechanistic model?)

2. Models and statistical techniques to make sense of data
   e.g. try to find mechanisms that explain certain features of a data set
   Are data consistent with some hypothesis or model?

   Quantitative framework within which to ask questions…
   … can help us to formulate questions in a precise way
   … and help determine what data we need to collect

3. Predict implications of a given set of mechanisms on large-scale behavior
   e.g. scale up from rules specified at the level of individuals to behavior that is seen at the population
   nonlinearity makes it difficult to predict outcome without modeling

4. Can use models to ask "what-if" questions
   e.g. compare alternative control strategies

5. Can we generalize across diseases?

The Usual Modeling Caveats…

Need to have faith in our models, or at least understand their limitations

Need to spell out their assumptions (doesn't always happen in research papers…)

Not all assumptions are crucial… some details are more or less important
It's not always obvious beforehand… but we can use models to explore this

All of this depends on what questions you ask of a model
A model may work well for one use, but not for another

Simplicity vs complexity: how detailed should our model be?

Simpler models: easier to analyze, simulate and understand, have fewer parameters,
unlikely to be "realistic"

Detailed models: opposite of above
can be more realistic, provided that we have enough information
on the processes governing a system (rare!)

Non-specialists often prefer complex model, reassured to see detail