Improving Public Health Measures: Advances in Risk Analysis

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Where are we?

- The Age of Ignorance (no understanding of science, no control, all R no B)
  - Cotton Mather on colonial times: "A dead child was a sight no more surprising than a broken pitcher"
- The Age of Discovery (revolution in science, ability to understand and control disease, take R to get B)
- The Age of Miracles (idea of the magic pill or magic bullet, science can cure any problem, pursue B with abandon)
- The Age of Risk Management (science is critical, but we have to make good choices to avoid overkill, balancing R and B)

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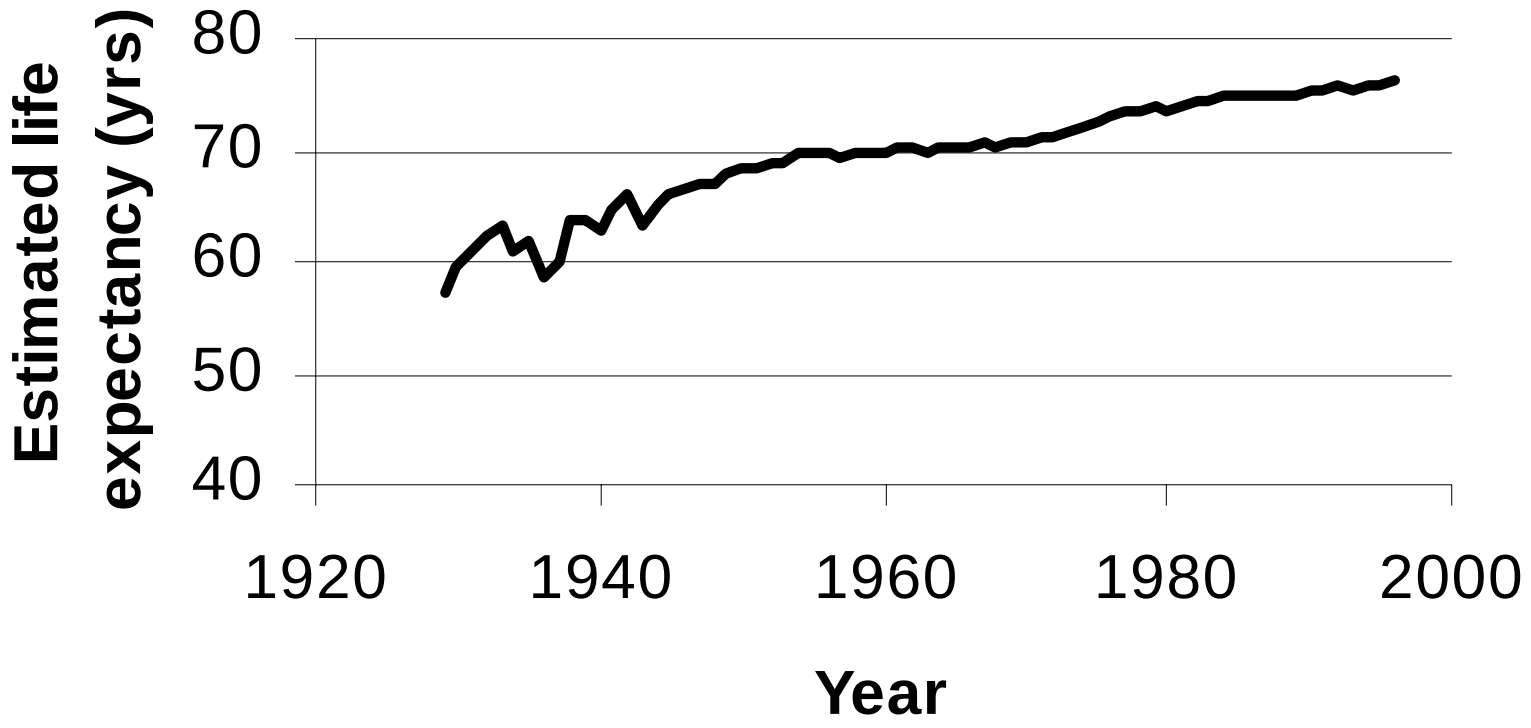
What does this mean for public health? Longer lives…



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Great progress – a few examples

- Diagnosis of disease based on gross physical characteristics --> laboratory analyses of body fluids and genetic testing and interventions that save lives
- Sulfanilamide --> numerous antibiotics
- Focus on feeding and milk composition for infants

  --> pasteurization, refrigeration, infant formulas, dehydration treatments, and improvements in medical care

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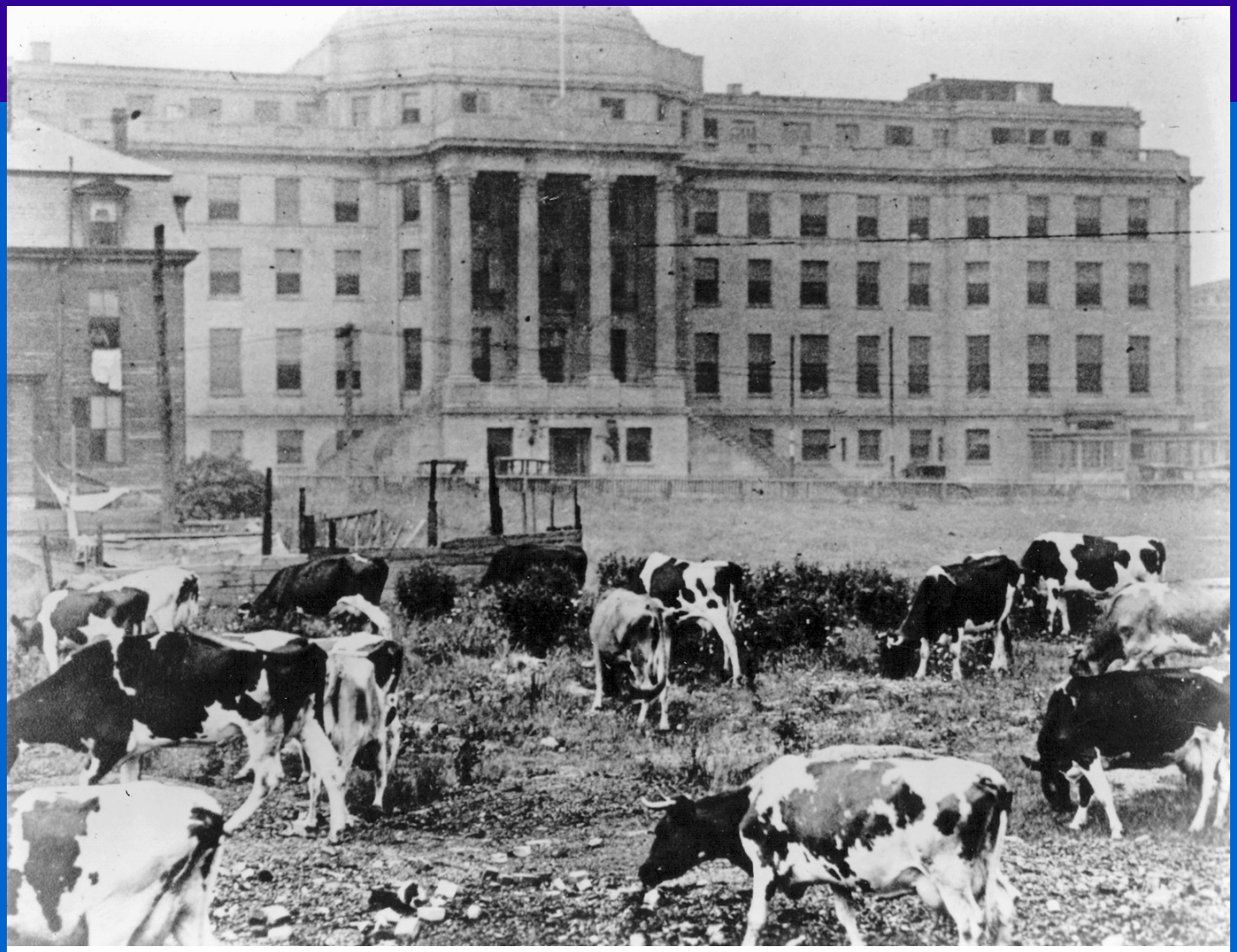
Hunnewell Building, Circa 1914



Photograph courtesy of Children's Hospital Archives, Boston, MA.

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Great progress

- The iron lung and deformities associated with polio --> immunizations for polio and many other diseases and eradication of small pox

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Public health improvements

- Are we winning the war with germs?
  - Certainly doing better with respect to health outcomes (e.g., saving lives once lost to some infections, and reducing the severity and spread of infections)
  - Public perception now that infectious disease is not as much of a problem (immunization)
- Wait
  - BIG issues remain with antibiotic resistance/“Superbugs”/ new diseases
  - Prevailing assumption that releases of organisms would be unintentional (i.e., we’re fighting nature)
  - Infectious disease still a leading cause of death

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Context

- Given the background of ID, what does BT preparedness look like and how does it fit in with basic public health?
- What tools can help us understand the risks and measure the impacts of interventions?
- How will we know that a BT preparedness program works?
- What decisions get made about characterizing the different agents?

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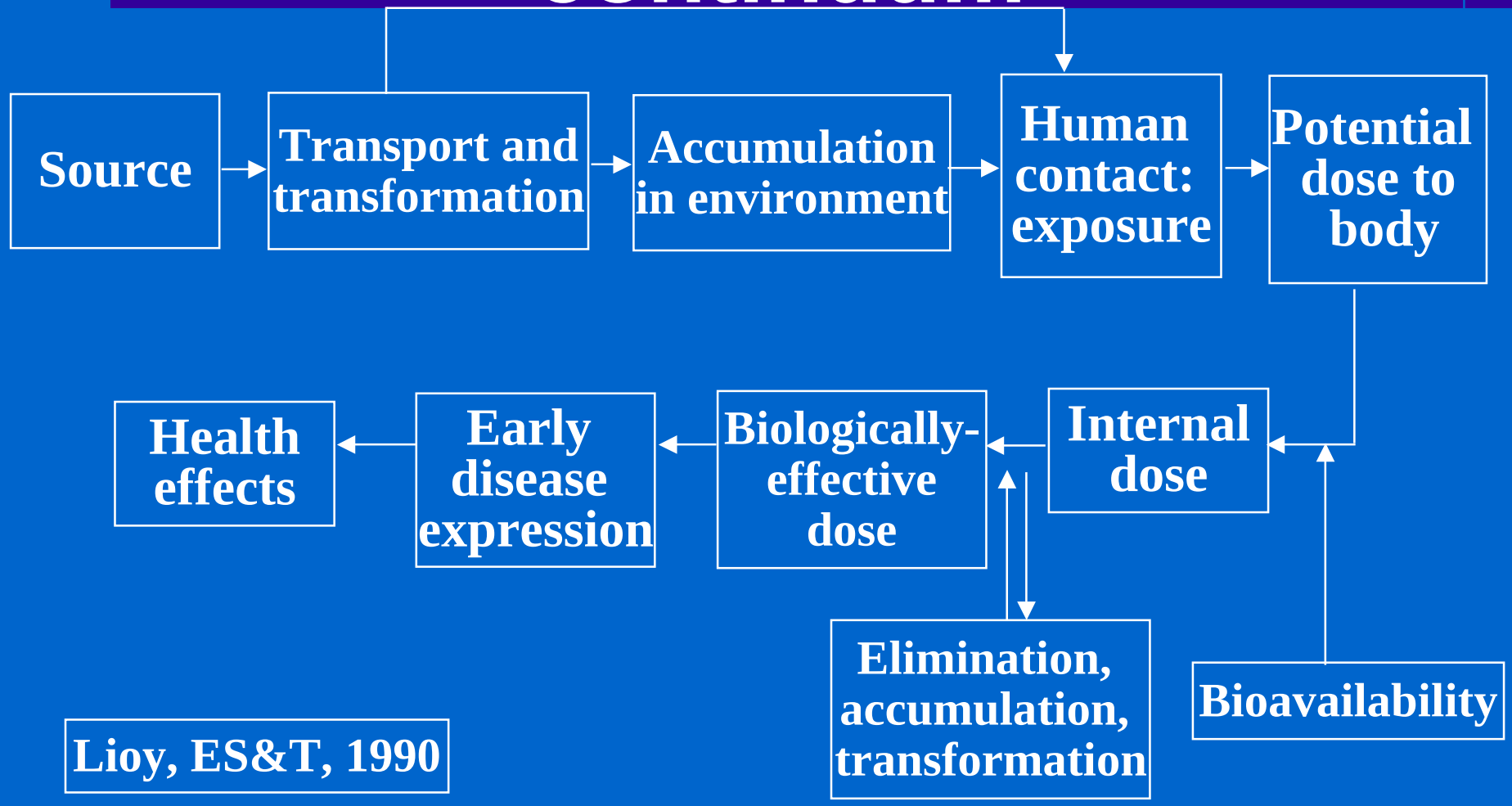
Human health risk continuum



Lioy, ES&T, 1990

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The need for risk and decision analyses

- **Risk analysis and decision analysis are used to integrate information and sift it down into a usable form**
- **Used support many actions:**
  - **Initiating regulatory activity or treatments**
  - **Setting protective standards**
  - **Selecting products, technologies, or substances**
  - **Siting hazardous facilities, isolation choices**
  - **Cleaning up or control of contaminated areas**
  - **Initiating research and establishing priorities**
  - **Others....**
- **Key component of decision (but not only)**

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Decision tools

- Risk analysis
- Benefit-cost analysis
- Cost-effectiveness analysis
- Decision analysis
- Comparative risk analysis

All share common elements to some degree, but differences do matter

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Variability vs. uncertainty

- Variability - heterogeneity or diversity in a well-characterized population which is usually not reducible through further measurement or study
- Uncertainty - ignorance about a poorly characterized phenomenon that is sometimes reducible through further measurement or study
- Variability and Uncertainty = f(decision context)
  - NRC (1994): "Uncertainty forces decision makers to judge how probable it is that risks will be overestimated or underestimated for every member of the exposed population, whereas variability forces them to cope with the certainty that different individuals will be subjected to Techniques exist to maintain these separately
  - risks both above and below any reference point one chooses."

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Risk estimates do matter

- Example 1 – uncertainty about the effectiveness of airbags in motor vehicles
- Example 2 – variability in the mortality risk to people on the ground from crashing airplanes

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Cost-effectiveness analysis

- One of many tools
- Growing role in medical decision making
- Panel on Cost-effectiveness in Health and Medicine
  - Total costs/Total effectiveness (Incremental ratio)
  - Recommended methods (QALYs, 3% discount rate, societal perspective)
- Typical CEA ignores uncertainty, variability, time, preferences and other attributes, troubles with zeros, criteria for “acceptability”

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Why care about dynamic nature?

- Optimal strategies change with time
- Dynamics may be very important to model to characterize the benefits of herd immunity
- Times of major shifts (e.g., perceptions of risk and benefits change going from wild type cases to vaccine-associated cases, with eradication risk shifts to polio in bio warfare)
- When we assess the CE ratio may matter in terms of policy

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Changing CE model components

- Most vaccine CEA's assume constant probabilities of getting infection (for both vaccinated and unvaccinated children) – may not capture big herd immunity effects (e.g. mass vaccination reduces risks for unvaccinated as well as vaccinated people)
- Other time-dependent factors:
  - Costs (For single vaccine and program, do these go up, down, or stay the same over time?)
  - Preferences and values
  - Societal dynamics (urbanization, more women working so staying home has greater opportunity costs)
  - Technology

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Do these matter?

- Consider a case study on polio
  - Long history
  - … but not too long
  - Numerous interventions
  - Near eradication
  - Good time to remind people
  - Story of many successes
  - Could make the transition from ID to possible BW agent if public health community successful

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Project: Background

- Herd immunity effects following polio vaccination.
- E.g. mass vaccination of 95% of infants will reduce the probability for unvaccinated persons as well.
- Other time-dependent factors:
  - price of vaccine
  - with discounting of health and dollars: ->point of time of disease is important
  - demography, technology, etc.

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Retrospective Polio CEA Model(1)

- Ideally, we have for all vaccine programs:
  - $Cost(t)=(V(t)tg(t)vc(t) + (D(t)-D^0(t)) H(t))e^{rt}$
  - $Effectiveness(t)=(D^0(t)-D(t)) Q(t)$

vc(t) = vaccine coverage (as function of time)

V(t) = vaccine costs per completed vaccine schedule

tg(t) = target group r = interest to year 2000 dollars

D(t) = disease burden (incidence) under mass vaccination

$D^0(t)$ = incidence in absence of immunization program

H(t),Q(t) = health costs resp. QALYs lost per disease case

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Retrospective Polio CEA Model(2)

- Cumulative cost-effectiveness ratio:

$$CCE(t) = \frac{\text{integrated discounted costs until } t}{\text{integrated discounted health gains until } t}$$

- Cost-effectiveness ratio:

$CE = CCE(T_{end})$ Suggested T_{end} : 2015

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Retrospective Polio CEA Model(3)

- The disease incidence with or without immunization program can be calculated with a transmission model -> requiring assumptions about transmission, and data

- For every variable except incidence, real historic data will be used.

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Concept of Transmission Models: SIR Models

- S(t) = number of *susceptibles:*those individuals that could get infection
- I(t) = number of *infecteds:*those that are infectious: they can contaminate susceptibles
- R(t) = number of *removeds:*those that are immune to infection (*recovereds*, *resistants*)
- Transition rates between S, I, R->differential eqns.
- λ (t) = β*I(t) = force of infection= per susceptible rate of infection, β is the *transmission coefficient*

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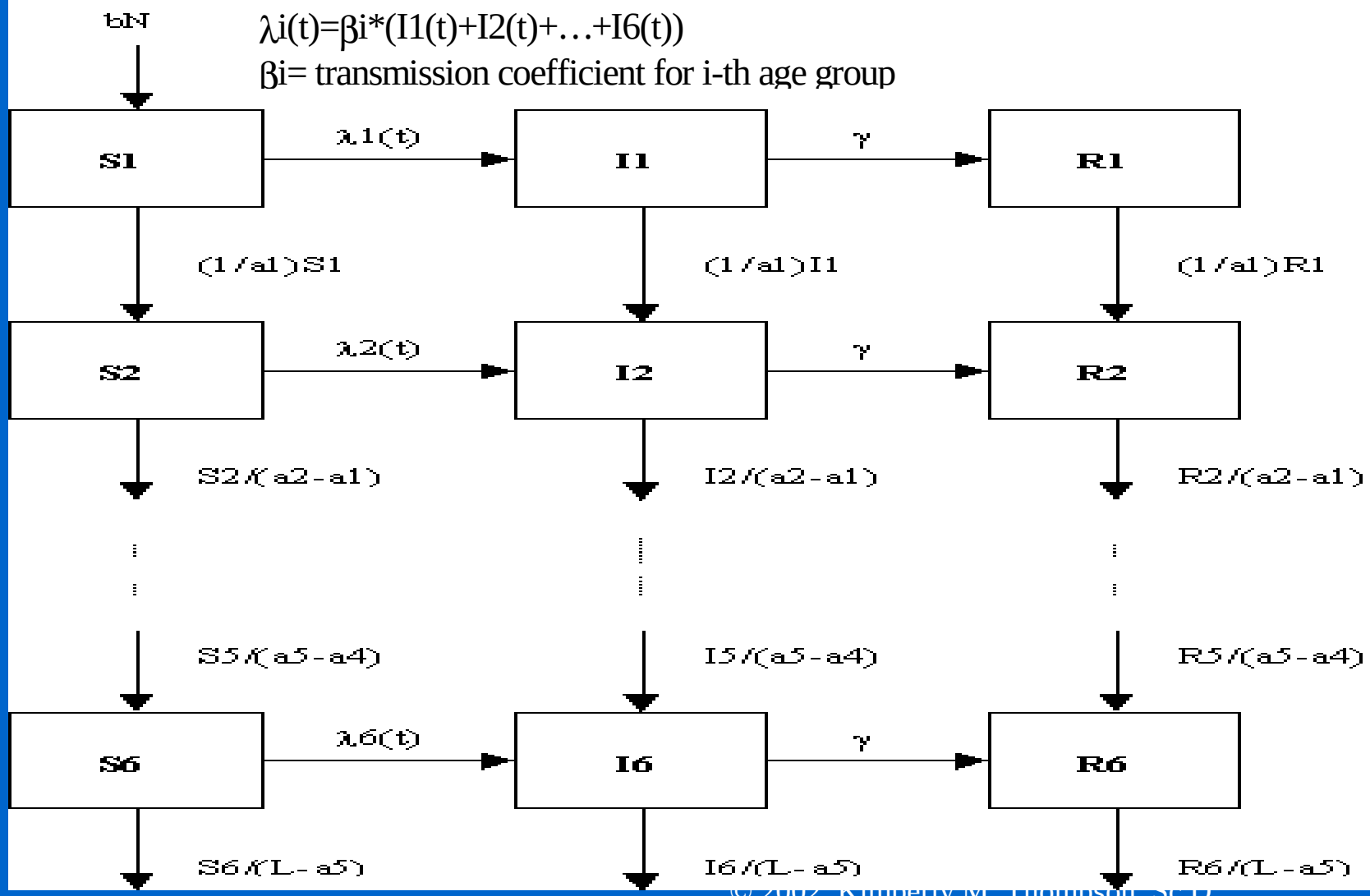
Transmission model (1)

$\lambda i(t)=\beta i*(I1(t)+I2(t)+\ldots+I6(t))$

βi= transmission coefficient for i-th age group



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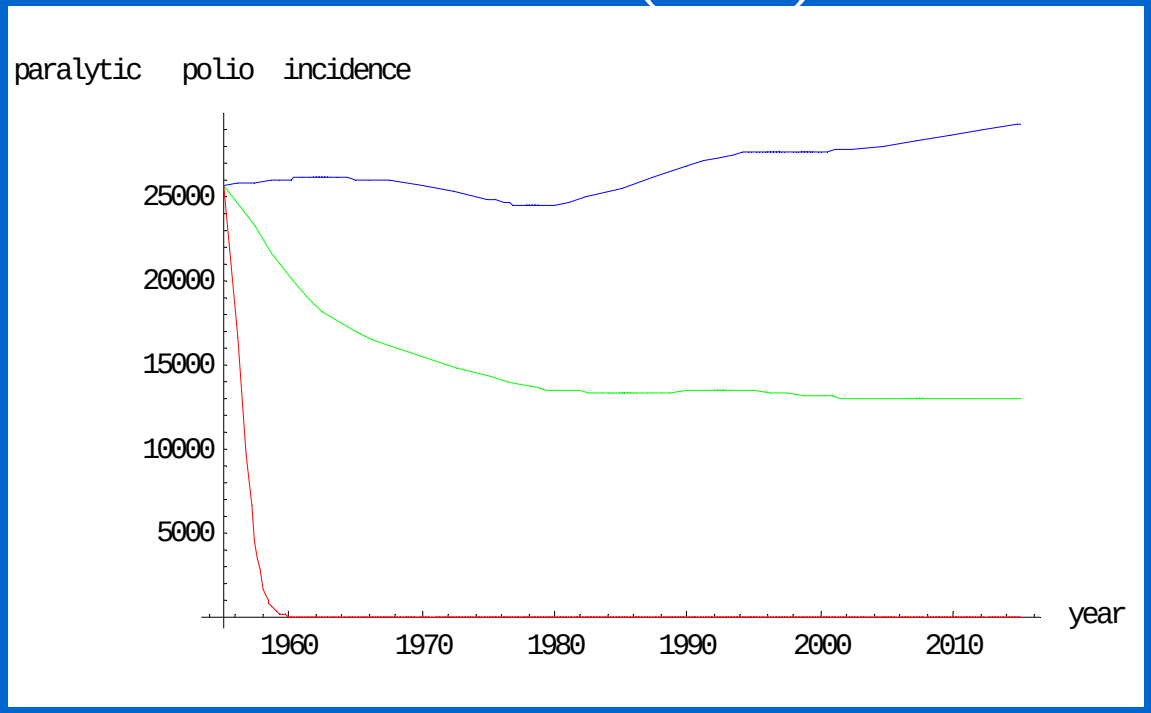
Example Results

Vaccine 1, paralytic polio incidence with static(green) and dynamic(red) transmission model and without vaccine(blue):



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Insights

- Risk analysis and decision analysis tools have evolved to the point where they are helpful in characterizing and understanding the trade-offs associated with tough choices
- Must consider the dynamics of the disease to accurately quantify the health benefits
- Complex problem – analysis is needed
  - No zero risk
  - Real trade-offs

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