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Mathematical Modeling Dynamics of Infection

Joan L. Aron, PhD, MSc
Johns Hopkins University

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- Director, Science Communication Studies
- Associate Faculty, Department of Epidemiology
- Technical training in the application of mathematical models to population biology and epidemiology
  - Focus on infectious diseases

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Section A

Introduction (Aron)

Purpose of Introduction

- Scope of presentation
- Concepts in basic theory
- Themes in developing applications

Directly Transmitted Infections That Confer Lifelong Immunity

- **Theoretical**—simple structure
- **Practical**—broad application to childhood immunizable diseases
- **Historical**—classic epidemiology
- **Pedagogical**—generalization from one in-depth example

Mathematical Model

- A mathematical model is an explicit mathematical description of the **simplified** dynamics of a system. A model is therefore always “wrong,” but may be a useful approximation ($\cong$ rather than $=$), permitting conceptual experiments which would otherwise be difficult or impossible to do.

Mathematical Model Results

- Help determine the plausibility of epidemiological explanations
- Predict unexpected interrelationships among empirical observations (improve understanding)
- Help predict the impact of changes in the system

Important Concepts

- **Endemicity**—persistence of infection in a population
- **Age at infection**—age-dependent patterns of infection in a population
- **Mass immunization**—herd immunity

Themes in Developing Applications

- Simplicity vs. complexity
- Sharing concepts across disciplines

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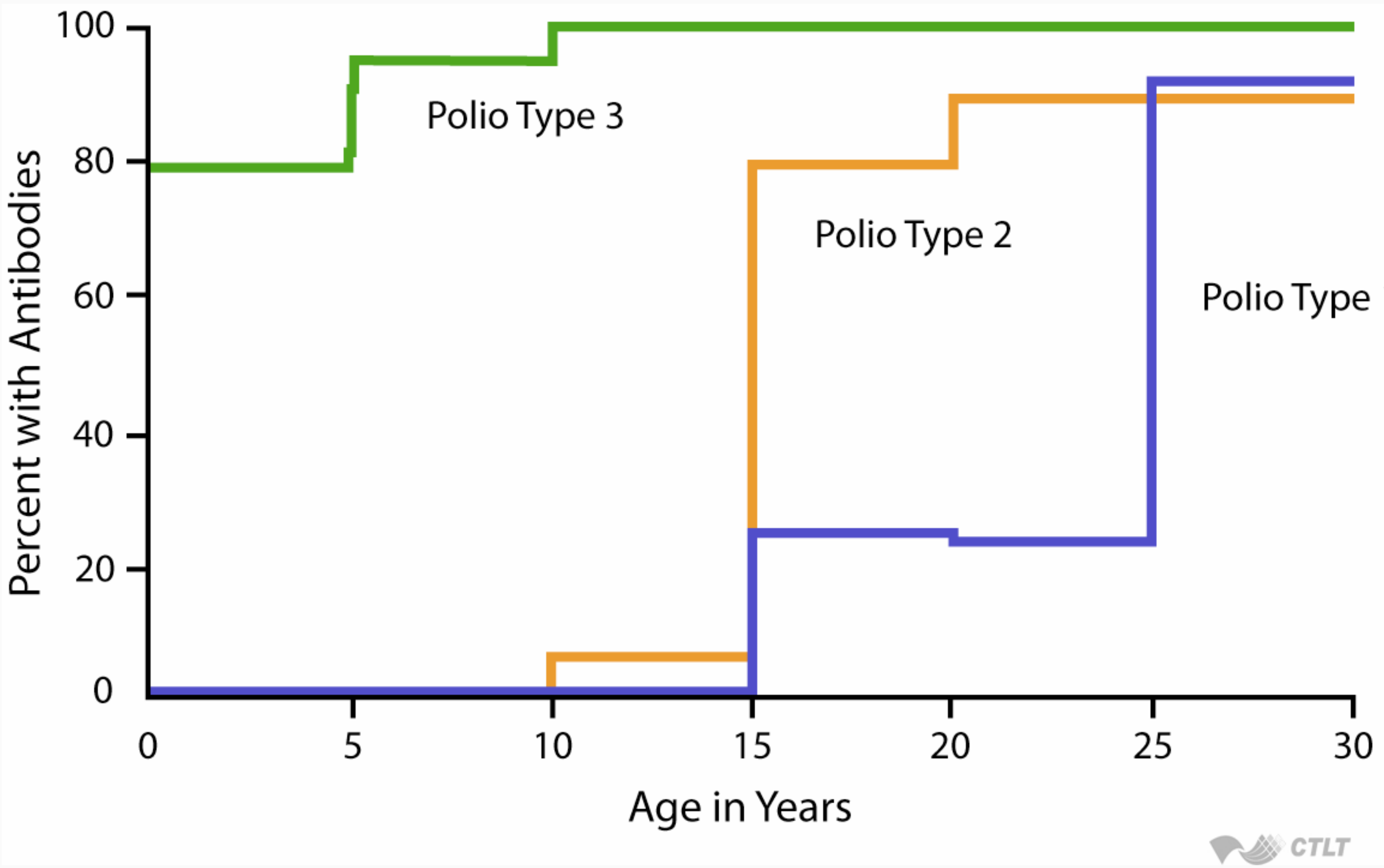
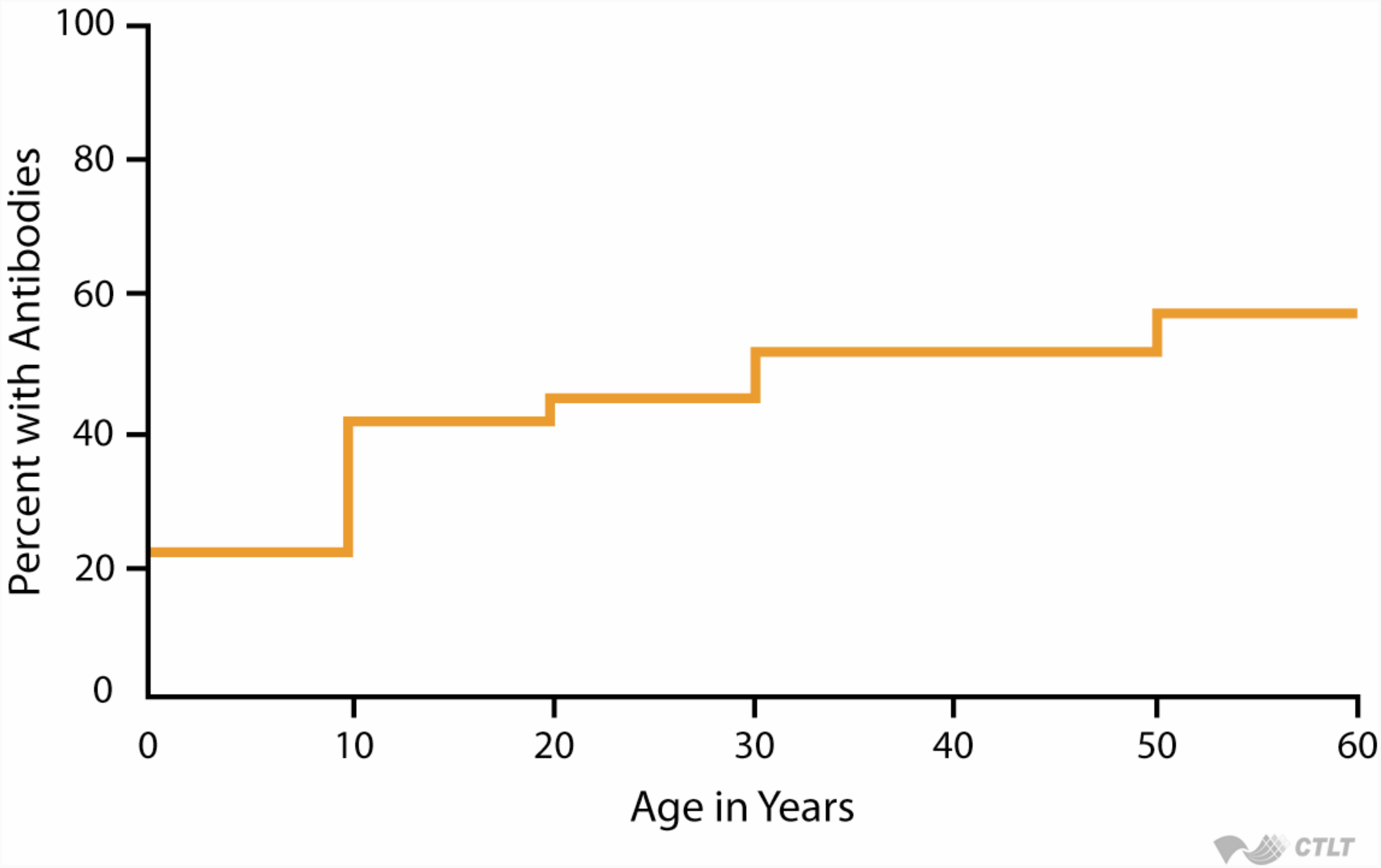
Section B

Basic Theory—Endemicity (Aron)

Polio in Greenland (Pre-Vaccine)



Hepatitis B in Greenland (Pre-Vaccine)



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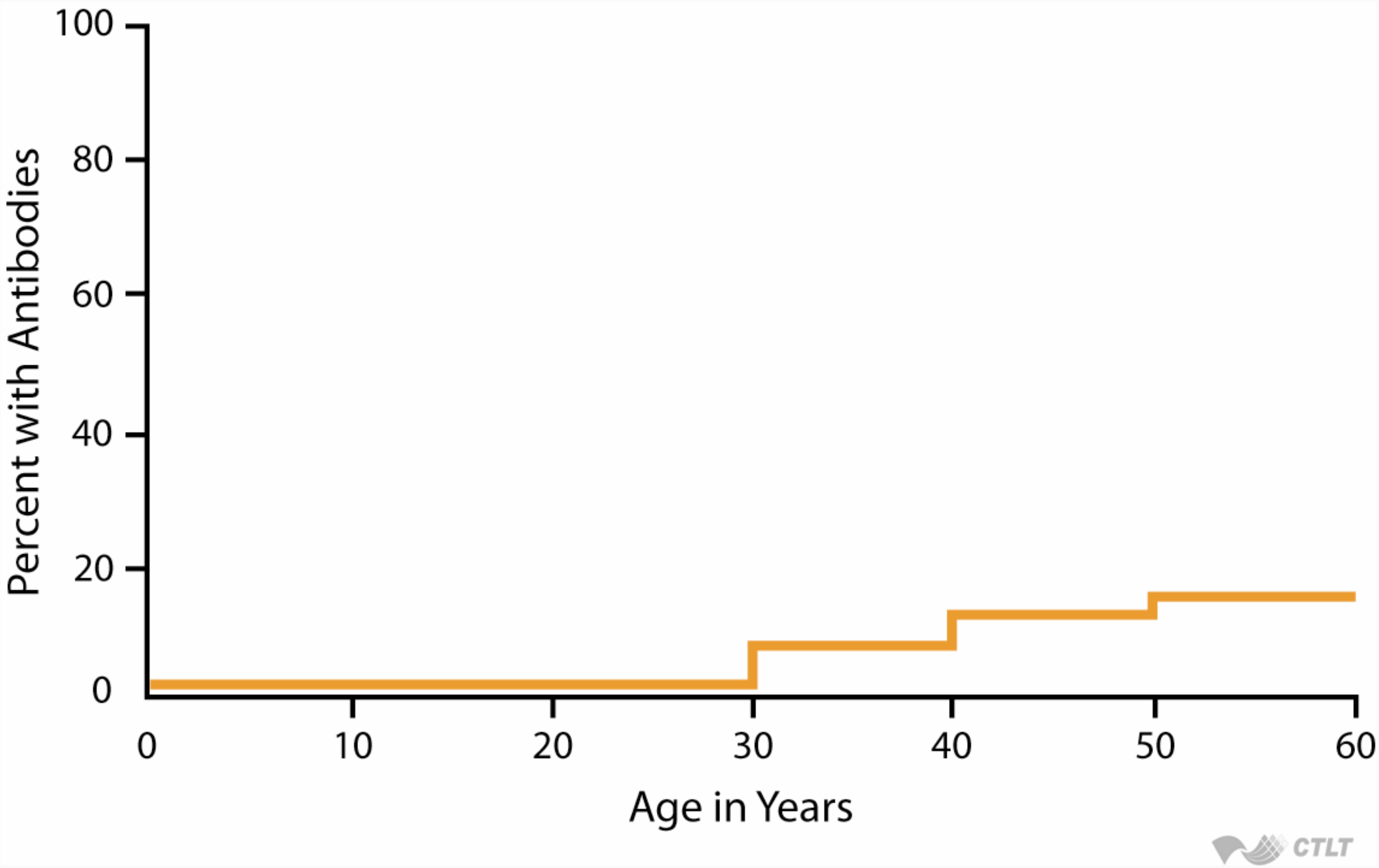

Kermack-McKendrick Threshold Theorem Assumptions

- Population densities
  - **S**usceptibles (X)
  - **I**nfectives (Y)
  - **R**emovals (Z) - immune or dead
- SIR model
- Closed population (X + Y + Z = N)

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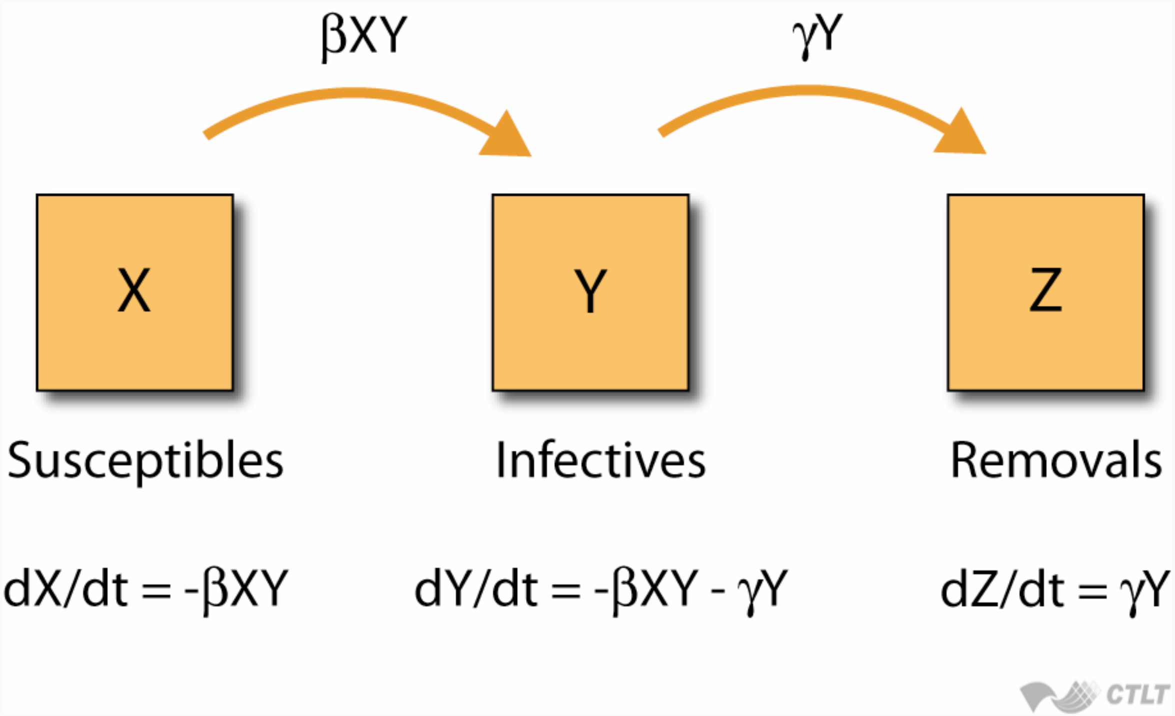
- SIR model
- Closed population (X + Y + Z = N)
- Direct transmission and mass-action mixing (βXY) transfers X to Y
- Removal of infectives (γY) transfers Y to Z

Kermack-McKendrick Threshold Theorem Assumptions



Kermack-McKendrick Threshold Theorem Results

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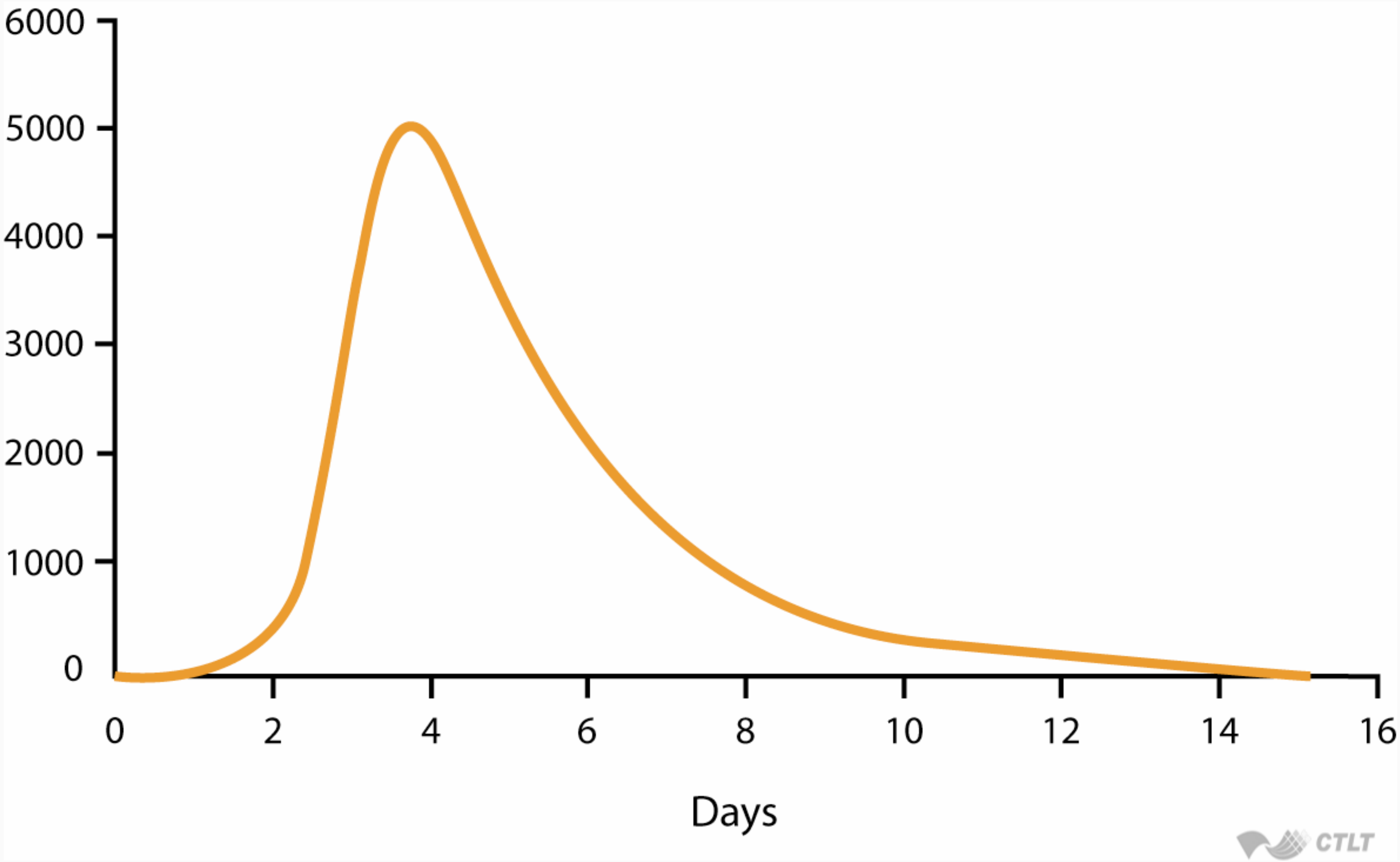
   At $t = 0$, $dY/dt = (\beta X - \gamma) Y > 0$ if $X > \gamma / \beta$ (Note: $X \cong N$)

   The rate at which susceptibles become infectives (βXY) must exceed the rate at which infectives are removed (γY)

Kermack-McKendrick Threshold Theorem Results

2. At the end of the epidemic (if there is one), the population consists of…
   i. Susceptibles below **threshold** density
   ii. No infectives
   iii. Removals

SIR Epidemic Population Density of Infectives



Defining the Threshold

- N = 8,700 people per square mile
- β = (.001 sq mi per day) (.4 probability of transmission per contact)
- γ = .5 per day ($1/\gamma$ = 2 days mean duration of infectiousness)
- γ / β = 1,250 people per square mile
  - $N > \gamma / \beta$
  - 8,700 > 1,250
- 1 secondary case
  - $\beta N / \gamma > 1$
  - 6.96 > 1

Kermack-McKendrick Threshold Theorem Epidemiology

- Epidemics cannot begin in a very low-density population. If begun, they cannot be sustained (i.e., become **endemic**) without an influx of susceptibles.
- Epidemics can wax and wane as a function of the **supply of susceptibles.** An old epidemic theory postulated the need for increases and decreases in the transmissibility of the agent.

Kermack-McKendrick Threshold Theorem Epidemiology

- The eradication of an infection by mass immunization can be understood in terms of reducing the density of susceptibles below a threshold. This effect is called **“herd immunity”** since the population may be protected from outbreaks even if there are some susceptibles in the population. Thus, eradication is theoretically possible with less than 100% immunization.

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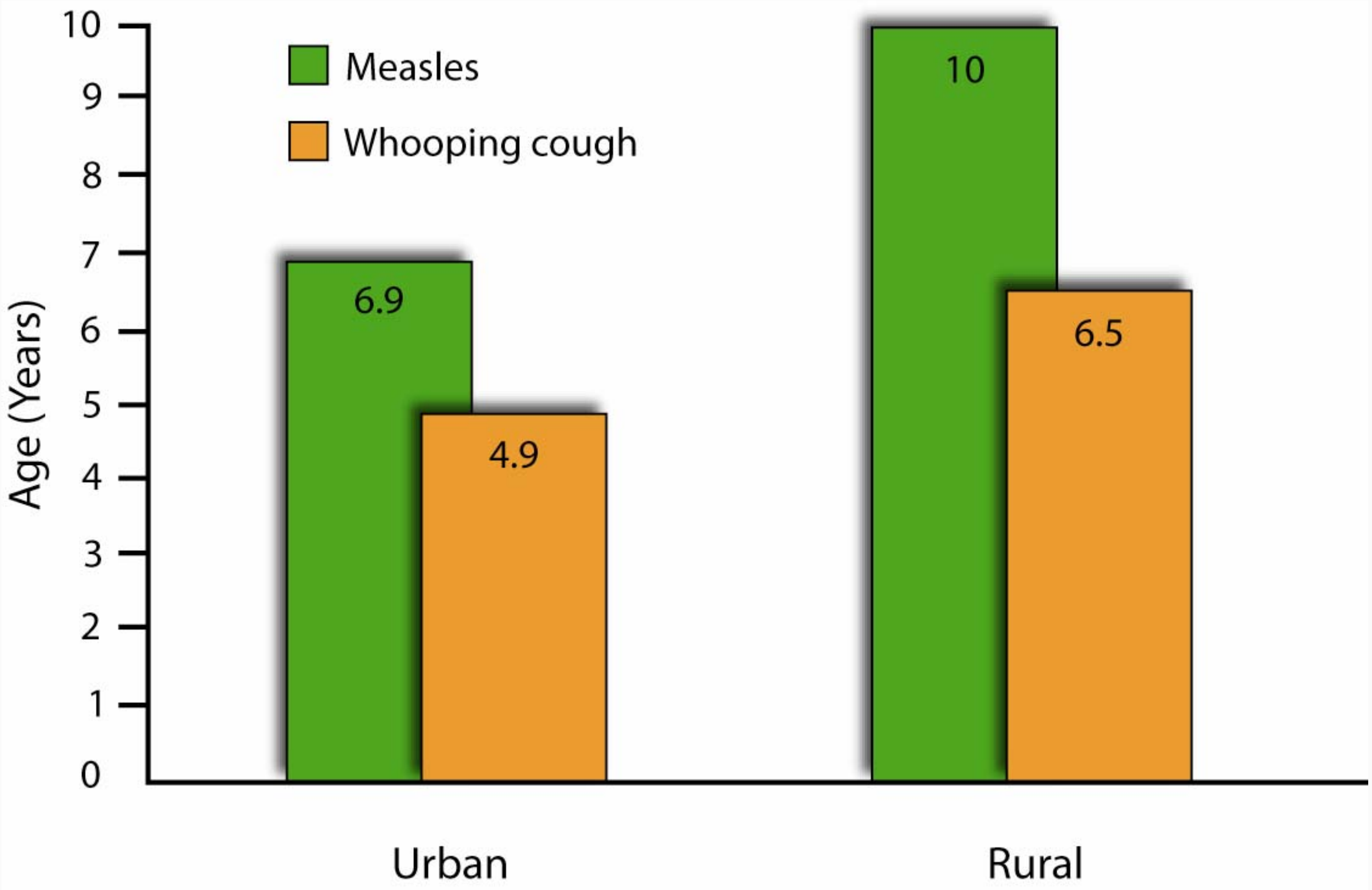
Section C

Basic Theory—Age at Infection (Aron)

Average Age of Infection: Measles and Whooping Cough

- Average age of infection (years), Maryland, U.S.A., 1908–1917



Basic Reproduction Ratio R

- R is the number of secondary cases generated from a single infective case introduced into a susceptible population. Infection persists (endemicity) if $R > 1$ and there is steady influx (births) of susceptibles, i.e., an open population.

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R $\cong$ (β N) (1 / γ)

(Effective Contact Rate) (Mean Duration of Infectiousness)

2 days

c (Contact Rate) q (Probability of Transmission per Contact)

8.7 people per day .4

Basic Reproduction Ratio R

- Larger R is associated with greater contact rate (greater population density), greater duration of infectiousness or probability of transmission per contact (greater infectiousness)

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- Larger R is associated with greater contact rate (greater population density), greater duration of infectiousness or probability of transmission per contact (greater infectiousness)
- At endemic equilibrium, $(X / N) = (1 / R)$. That is, susceptible fraction decreases with larger R. If L = mean life expectancy and A = mean age at infection, $(X / N) \cong (A / L)$. That is, earlier infections imply fewer are susceptible (never infected). So $R \cong L / A$.
- Larger R is associated with lower average age at infection

Average Age of Infection: Measles and Whooping Cough

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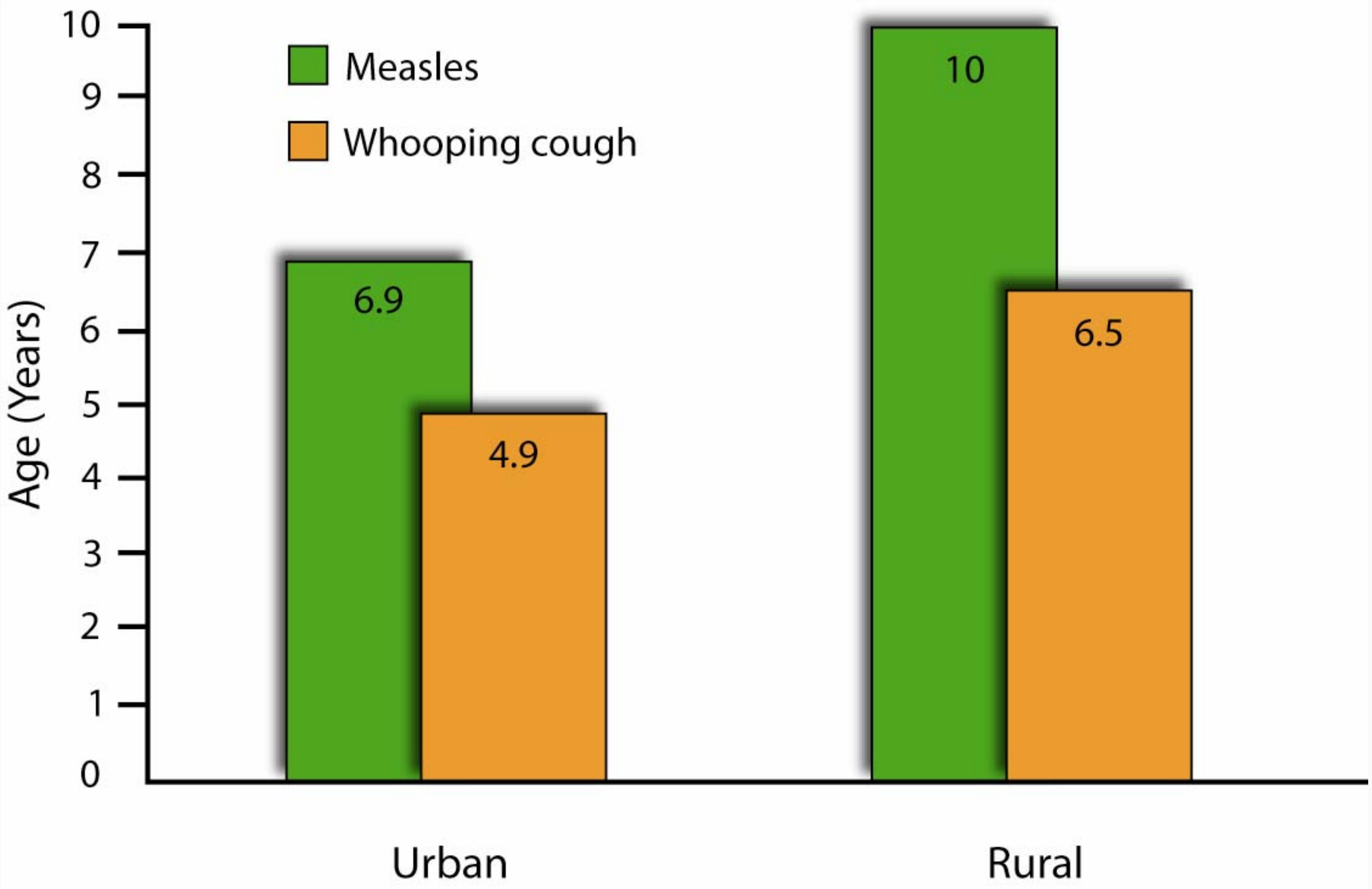
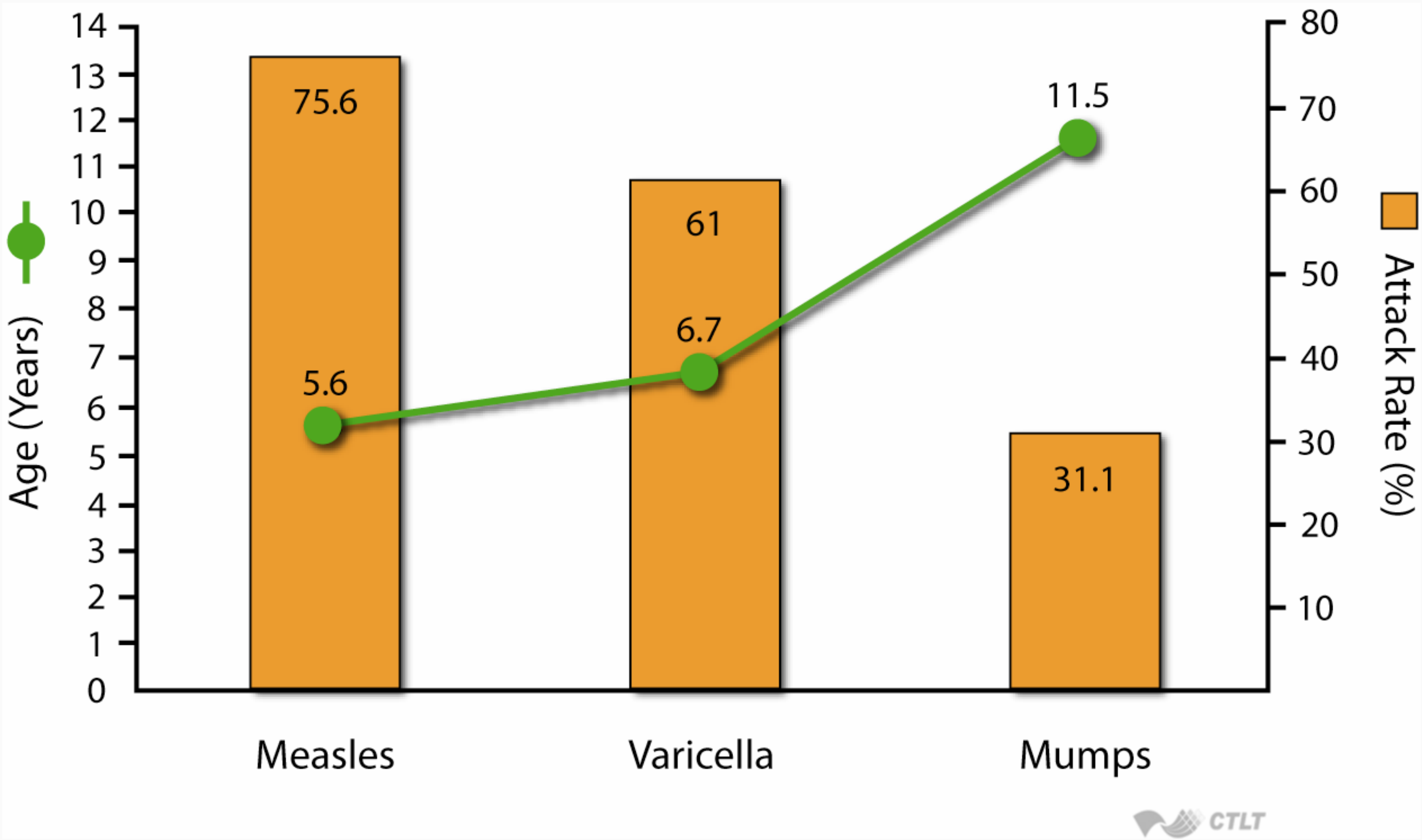


Empirical Inverse Relationship

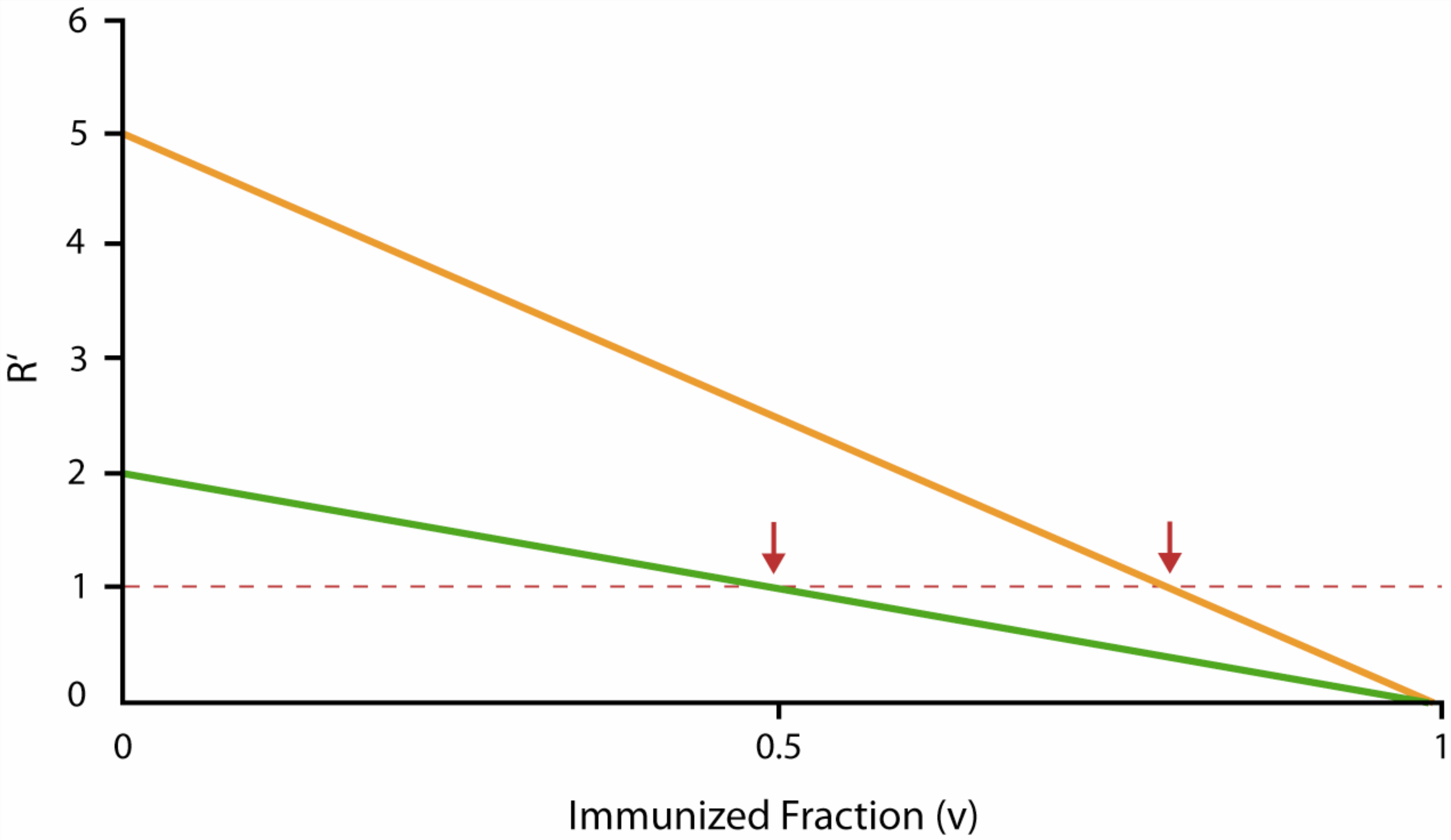
- Infectiousness and average age



Section D

Basic Theory—Mass Immunization (Aron)

Basic Reproduction Ratio after Immunization



Effect of Mass Immunization

$R' \cong R(1 - v)$ to define threshold for eradication

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Eradication if $R' < 1$; immunization level $v > 1 - (1/R)$

$R = 2$; $v > 50\%$

$R = 5$; $v > 80\%$

$R = 10$; $v > 90\%$

$R = 20$; $v > 95\%$

Herd immunity

Effect of Mass Immunization

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$R = 2;\ v > 50\%$

$R = 5;\ v > 80\%$

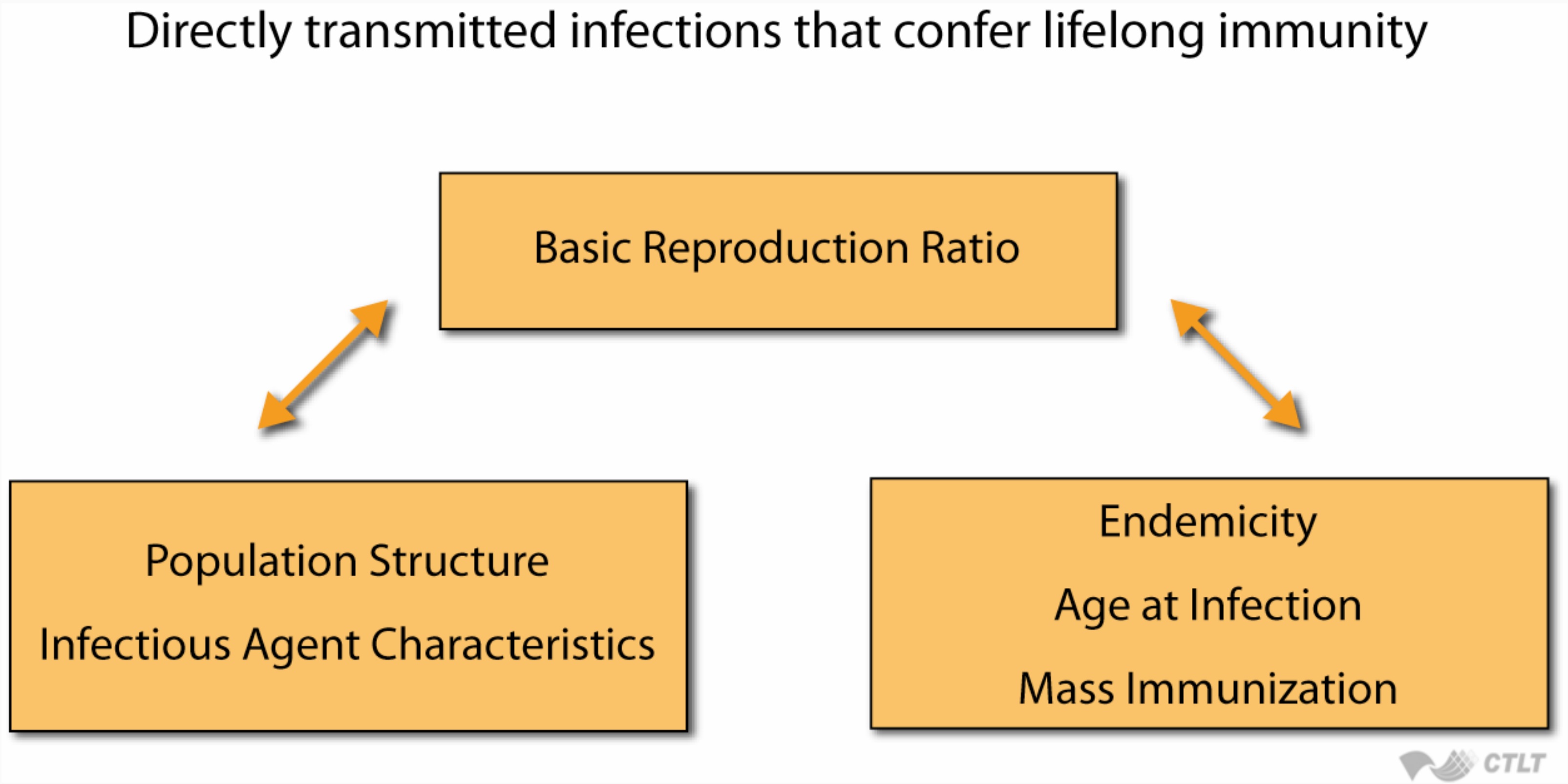
$R = 10;\ v > 90\%$

$R = 20;\ v > 95\%$

Herd immunity

If $1 < R' < R$, infection persists in the population with reduced incidence and higher mean age

Summary of Basic Theory



Section E

Developing Applications—Simplicity vs. Complexity (Aron)

Maps and Mathematical Models

- Maps are like models because they selectively include information in order to achieve a specific purpose
- What is the best road map?
  - Scenic highways for tourism?
  - High clearance for large trucks?
  - Sized to fit on one computer screen?

Expanded SIR Model: Age Differences in Contact Rates

Simple

- No age structure
- Semi-quantitative results
- Direction of change
- “Average age will increase”

Complex

- Age differences in contact rates
- Quantitative results
- Magnitude of change
- “Average age will rise by 2.5 years”

Expanded SIR Model: Measles in England and Wales

Simple

- No age structure
- Ai (1 - p) = A
- If p = .50, Ai = 2 A
- 50% immunization doubles average age of infection

Complex

- 50% vaccine uptake from 1970 to 1980
- Average age rose from 4.5 to 5.5 years
- Higher contact at school entry

Expanded SIR Model: Measles in England and Wales

Threshold for Eradication % Effective Immunization	Explanation of Differences Adult Contact Rates
96%	High Contact
89%	Intermediate Contact
76%	Low Contact

Expanded SIR Model: Latent Period

Simple

- No latent period
- Equilibrium reservoir of infection
- Effective immunization thresholds

Complex

- Latent period
- SEIR where E is exposed but latent
- Speed of epidemiological response to immunization level
- Speed of epidemic

Expanded SIR Model: Latent Period

No latent period

- Generation time from case to case is duration of infectiousness

Latent period

- Generation time from case to case is duration of latency plus infectiousness
- Measles generation time approximately 14 days

Expanded SIR Model: Stochastic Effects

Simple

- Deterministic
- Fixed rules for change
- Circulation of many infectives
- Pre-immunization
- Moderate levels of immunization

Complex

- Stochastic
- Chance events
- Circulation of few infectives
- High levels of immunization
- Clusters of cases

Expanded SIR Model Stochastic and Heterogeneous

- The initial location of the “seed” in a network of susceptible hosts may strongly affect the total number of cases
- A given historical experience of an epidemic is only one possible realization of a contagion process. The outcome could have been different.

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Section F

Developing Applications—Sharing Concepts Across Disciplines (Aron)

Analogy Between Lasers and Epidemics

- SIR model

Lasers	Epidemics
Intensity of light	Infective population

Analogy Between Lasers and Epidemics

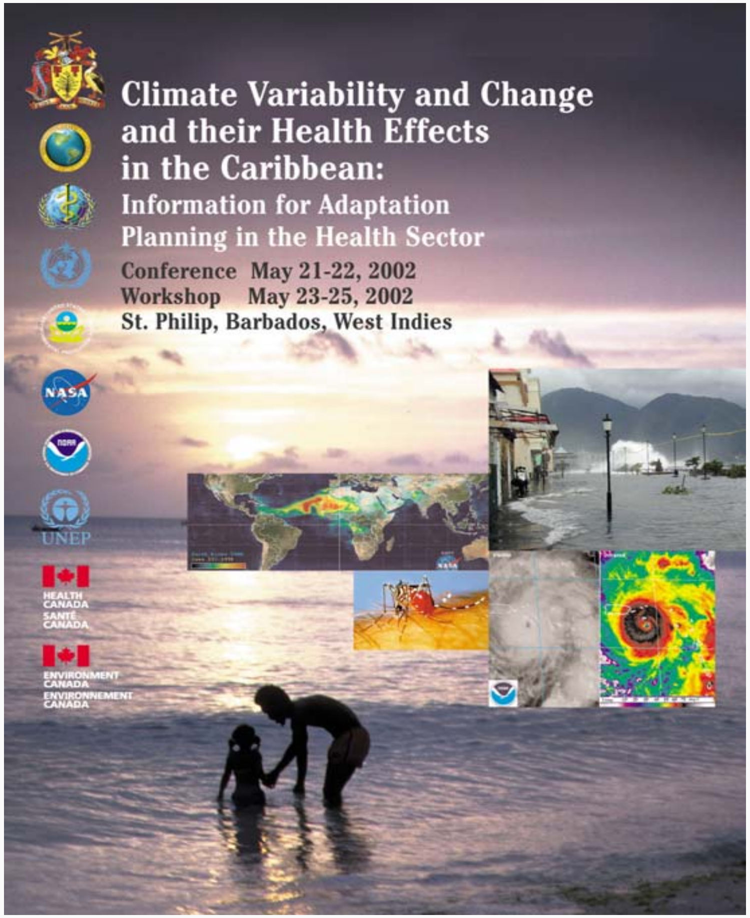
- The idea for the laser came during discussions of population models in the 1950s. (Townes received the Nobel Prize for Physics in 1964.)
- This analogy is the basis for using laser experiments to analyze the behavior of epidemics
  - Kim, Roy, Aron, Carr, and Schwartz (2005)

Health and Environment: Linking Global Change to Health

- Linking models of earth science dynamics with models of the spread of disease
- Sustainable development as a theme in public health (World Health Organization/Pan American Health Organization)

Climate and Health in the Caribbean: WHO Book

- http://chiex.net/publications_2003.htm



Perception of Risk: Linking Science to Decisions

- "Very few surprises are surprises to everyone"
- Prior to explosion of U.S. space shuttle Challenger, NASA had two assessments of failure of solid rocket boosters

Administrators — 1 in 100,000

Engineers — 1 in 35

Perception of Risk: Linking Science to Decisions

- Was there undue pressure to nail the [International Space Station] Node 2 launch date to the February 19, 2004, signpost? The management and workforce of the shuttle and space station programs each answered the question differently.
- NASA MANAGEMENT: There was definitely no undue pressure
- NASA WORKFORCE: There was considerable management focus on Node 2 and resulting pressure to hold firm to that launch date, and individuals were becoming concerned that safety might be compromised

— Report of the Columbia Accident Investigation Board, August 2003

Comments on Models

"Although the model suppresses a great deal of detail, it is complicated enough to make understanding difficult. When you discover some new aspect of its behavior, it can be difficult to track down the mechanism responsible. Thus, **adding more structure in the cause of realism would not necessarily teach us much.** We might well reach a point where we could not understand the model any better than we understand the real world."

Comments on Models

“Realistic modeling of spatial and temporal phenomena generally demands **disaggregation** (i.e., large detailed models and/or databases)—but in terms of decision making, such levels of disaggregation are usually counterproductive. Decision making demands **aggregation,** and therein lays the dilemma. From a scientific viewpoint, we must disaggregate ‘to be real’—from a decision-making viewpoint, we must aggregate ‘to be real’.”