# Introduction Plan

## Principal Points

- Epidemiological triad:
  - Host
  - Agent
  - Environment
- When we think about infectious diseases and their control, we must think about each section of the triad and the interaction between them
- Many things exist on a continuum
  - Heterogeneity is about differences with respect that continuum
- Heterogeneity important for disease transmission, and how we think about disease and outbreaks, across range of scale
  - Each branch of the triad exhibits heterogeneity and the combination will result in an infection risk for an individual and the population
    - Multiple combinations of each can result in similar infection risks
  - Can broadly group the scales in which heterogeneity acts into 2 levels:
    - Individual level
      - Susceptibility to infection
        - Pharmaceutical interventions aim to address this
      - Contact patterns & exposure
      - Behavior
    - Population level
      - What tests are used - sensitivity and specificity are defined on population levels relative to deviations from true negative mean values (IgG/IgM/OD etc.)
      - Public health actions and interventions, e.g., outbreak responses, come at various levels of funding etc
      - Statistical heterogeneity indicates that different studies of the same effect will have different outcomes and need to be summarized in meta-analyses
      - Groups of individuals may respond more similarly to each other than to those in another group e.g., spatial proximity, or contact patterns by age
        - Overdispersion of $R_0$
          - $R_0$ defined at a population level to begin with, and can vary based on any 3 of the epidemiological triad components
- Heterogeneity is impossible to comprehensively model, and typically artificial groups are defined to simplify the modeling process
  - Much like heterogeneity, discretization occurs at both the individual and population scale:
    - Individual level
      - Susceptibility/serostatus of an individual based on a binary diagnostic test
      - Compartmental models are an example as an individual's immunological status exists on a continuum but is split into S I and R compartments, for example.
  - Population level
    - How to define an outbreak
      - Outbreak definitions are incredibly important as governments and public health agencies may only have resources to deploy to a handful of locations per budgetary cycle, so incorrectly describing an outbreak can disastrous outcomes through missed infections (and

        - it may be too late to meaningfully respond to) or opportunity costs from an inappropriately sensitive alert and response
    - Models are often made in continuous time, but observational data is often discrete - counts aggregated by each day at the minimum, and commonly weekly, biweekly, or monthly.
  - This process is called categorization, or discretization, and the process may result in groups that don't truly align with the underlying heterogeneity.
    - Important to carefully evaluate assumptions being made and think about uncertainty should be accounted for in the analysis
      - Observation

- Early models by Anderson & May assumed mean-field (homogeneous) mixing and no heterogeneity within each compartment

- As computational resources have expanded and become more common-place, it has become possible to increase model granularity: Agent-Based Models are routinely implemented in fields where heterogeneity is known to be incredibly important (STI models are often ABMs or network models)
  - Not necessarily improved predictive accuracy for respiratory infections as need far more data to parameterize the model, and many assumptions about the state of interactions still required

## Intro Summary

- Chapter 2: D4A
  - Defining heterogeneity in disease exposure rates between well-defined geographically coincident populations
  - Despite clear expectations that spatial proximity and moderate-high R0 disease in immunologically naive population would result in similar exposure rates, outcome heterogeneity is observed
    - Indicates underlying differences (heterogeneity) in behavior, given the absence of pharmaceutical interventions
- Chapter 3: LCA
  - Defining heterogeneity within a demographically homogeneous population to explain how behavior can drive disease transmission, and place limits on the effectiveness of expected interventions
  - Multidisciplinary research provides opportunities to model latent heterogeneous groups in a manner that should be more proportional to transmission dynamics that typical methods reliant on demographic information
- Chapter 4: Outbreak detection
  - Examine the interplay between the heterogeneity that exists in a population (infections) and how the uncertainty in the methods we use to define both infectious individuals and outbreaks compound to affect outbreak detection
  - Partially observed Markov process means we have to make decisions with incomplete information - can never truly optimize our outcomes
- Chapter 5: Early Warning Systems
  - Examine how compounding uncertainty introduced in Chapter 4 impacts the performance of early warning systems with imperfect observational processes
  - Indicates the limits of predictability
- Overarching summary:
  - There is a growing body of literature focused on uncertainty in disease transmission measurements and incorporation into models

- Thesis demonstrates how heterogeneity can drive infection dynamics & introduce uncertainty at each level the outbreak and observation process, and the importance of acknowledging the interaction between the levels.