Heterogeneities in correlated infection traits explain surprising discrepancies in time intervals underlying R_0 estimates

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Estimating generation intervals in heterogeneous populations

Background

- Generation intervals link epidemic growth rates and R_0 (number of secondary cases per case)
- Generation interval: Infection to infection
- Serial interval: Symptom to symptom (see Fig 1)
- Infections are hard to observe, people use serial intervals as proxy

Objective

- Estimate differences between generation and serial intervals
- Develop a theoretical framework to understand and to compare these differences

Method

- We used rabies contact tracing data where time of infection and clinical signs are observed
- Simulate multivariate gamma distributions for infection traits (See Fig 3) and construct generation and serial intervals
- Estimation procedure using cluster bootstrap
  - Resample biters
  - Resample bites within biters

Findings

(I) No correlation: GIs have higher variance than SI

(II) Positive correlation: GIs have higher mean and variance

- Generation interval is 50% longer than serial interval for rabies

Implications

- Correlations in infection trait heterogeneities are important in estimating generation intervals
- Two possible sources of bias
  - (I) SI as a proxy for GI
  - (II) Correlation vs no correlation
- Ignoring correlation structures causes bias and overconfident R_0 estimates based on epidemic growth curves

Figure 1: Single transmission

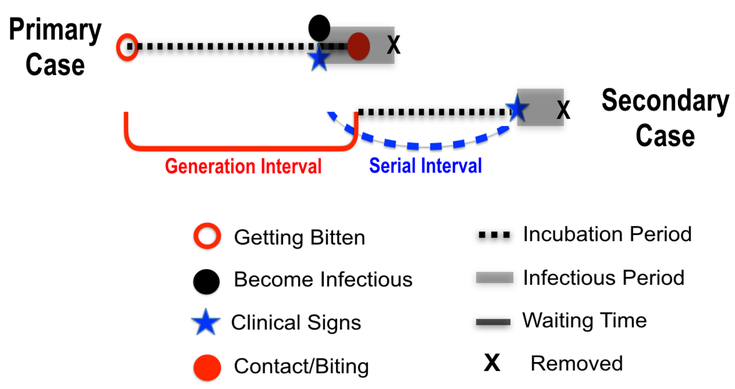
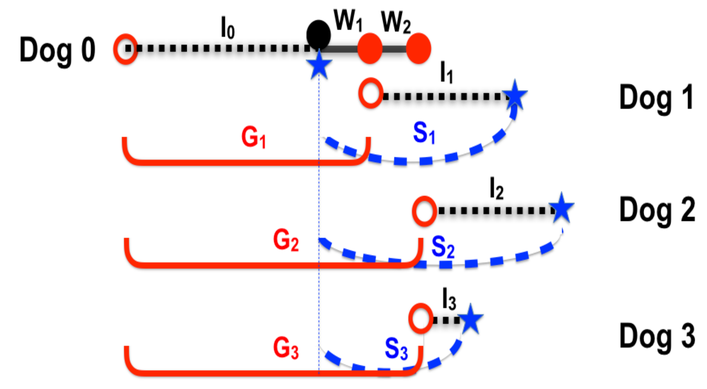
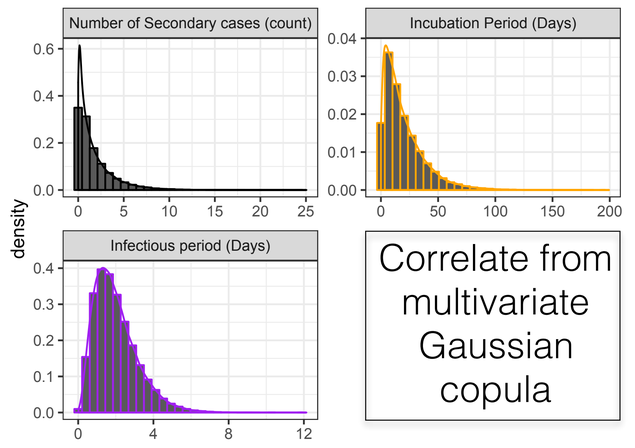


Figure 2: Multiple transmission in rabies



- Generation Interval: Same Incubation period (from biter) + different wait time
- Serial Interval: Different wait time + different incubation (from offspring)

Figure 3: Simulation framework



1. Simulate incubation, infectious period and number of secondary cases using multivariate gamma distribution for each biter
2. Duplicate transmission events via number of secondary cases
3. Uniformly sample waiting times within biter's infectious period for each transmission
4. Simulate new incubation period for each transmission.
5. Construct GI and SI (See Fig 1)

Figure 4: Empirical rabies GI and SI

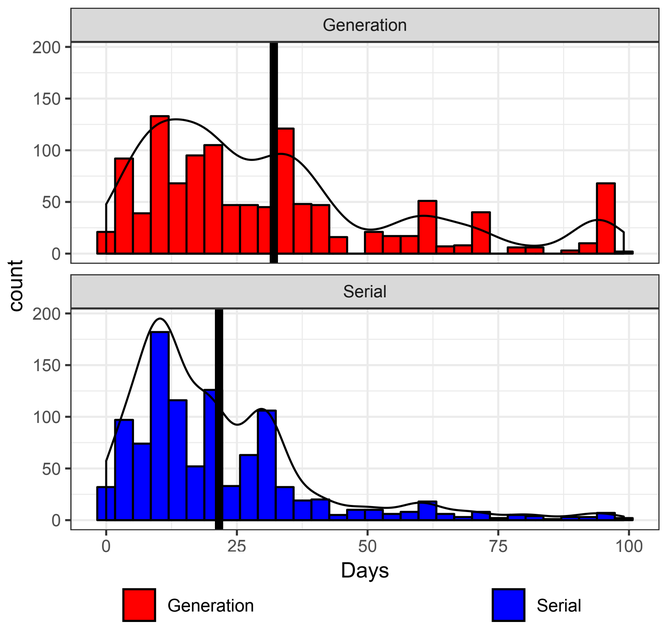
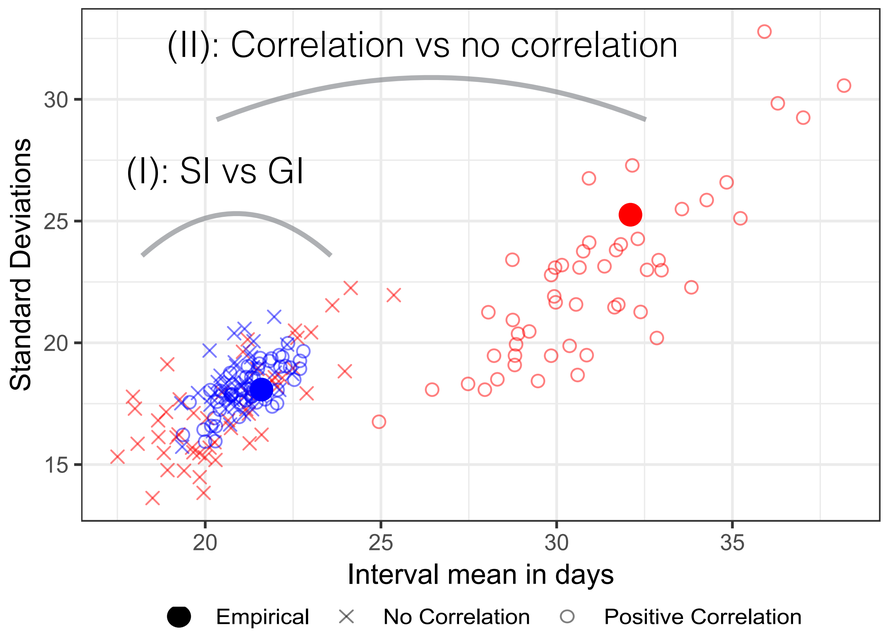


Figure 5: Simulated GI and SI distributions



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