



Silent, Immunizing Ebola Infections

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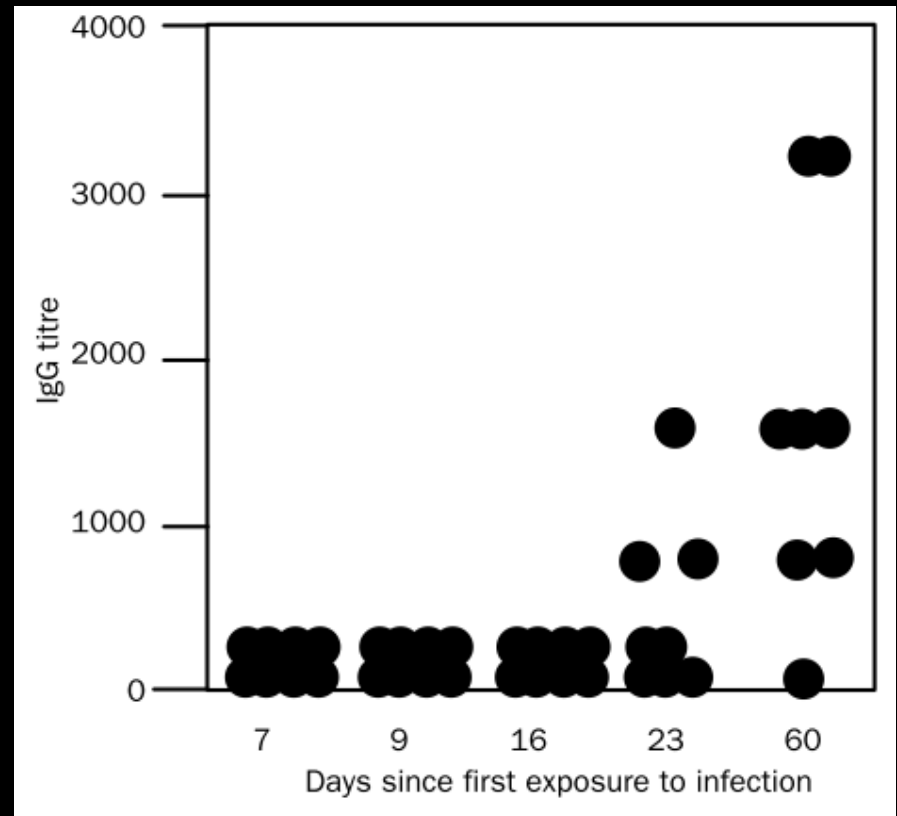


- Impressive makeshift PPE.
- Potentially aided by asymptomatic immunity?

Evidence for Asymptomatic Infections

Gabon Ebola Outbreak, 1996

- Followed direct contacts of infectious cases
- 24 identified who did not experience any symptoms
- 11/24 developed immune responses
- Not infectious

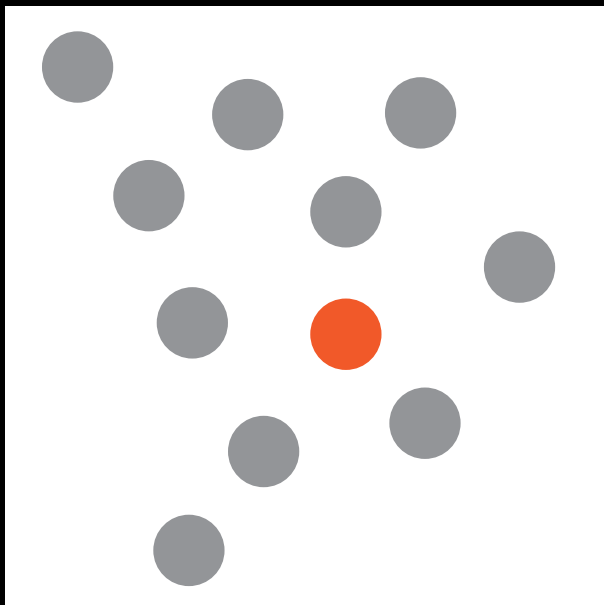


Leroy et al. 2000. *The Lancet*.

Estimating the Symptomatic Proportion

- 11 of 24 (46%) of asymptomatic contacts were infected
- Does not directly give symptomatic proportion.

Example

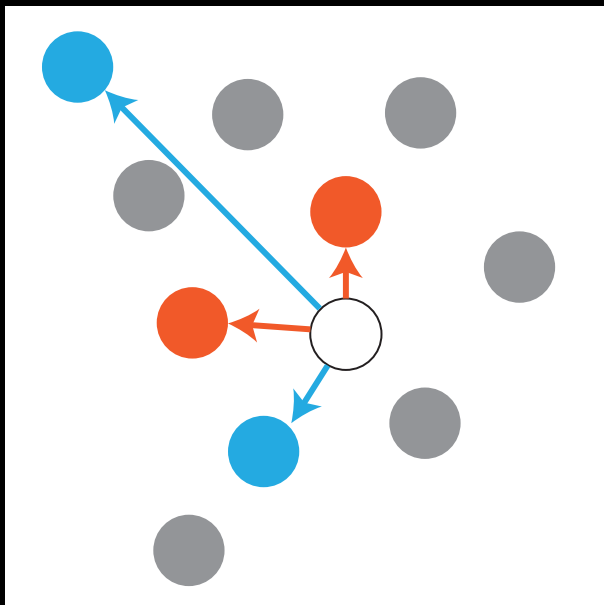


- 1 case infects 4 people, 2 symptomatic

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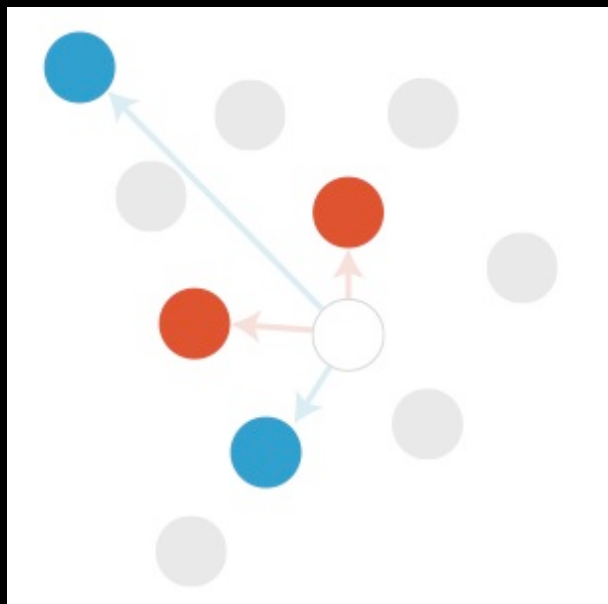


- 1 cases infects 4 people, 2 symptomatic
- What's the symptomatic proportion?

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Example

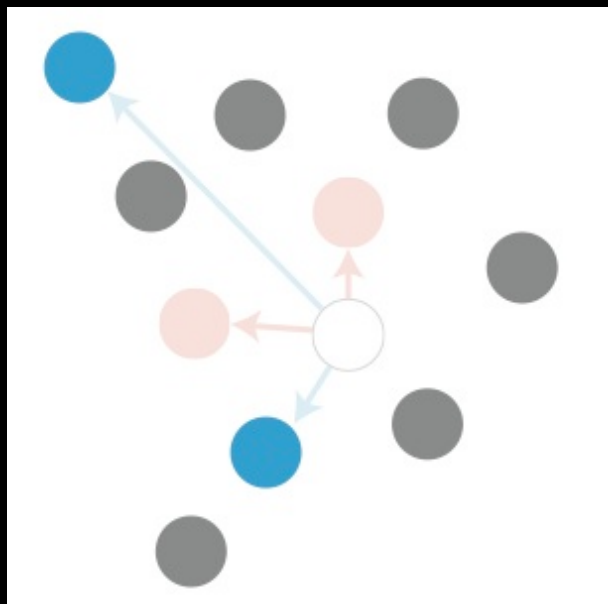


- 1 cases infects 4 people, 2 symptomatic
- What's the symptomatic proportion?
 $2/4 = 50\%$
- What's the proportion of asymptomatic contacts that were infected?

Estimating the Symptomatic Proportion

- 11 of 24 (46%) of asymptomatic contacts were infected
- Does not directly give symptomatic proportion.

Example



- 1 cases infects 4 people, 2 symptomatic
- What's the symptomatic proportion?
want this $2/4 = 50\%$
we estimate 20-60% based on available data
- What's the proportion of asymptomatic contacts that were infected?
have this $2/8 = 25\%$
estimated at 46% in Leroy et al. 2000

Asymptomatic Infection: The Rule, Not the Exception




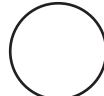
- Cholera
- Influenza
- Polio
- Pertussis
- Etc..

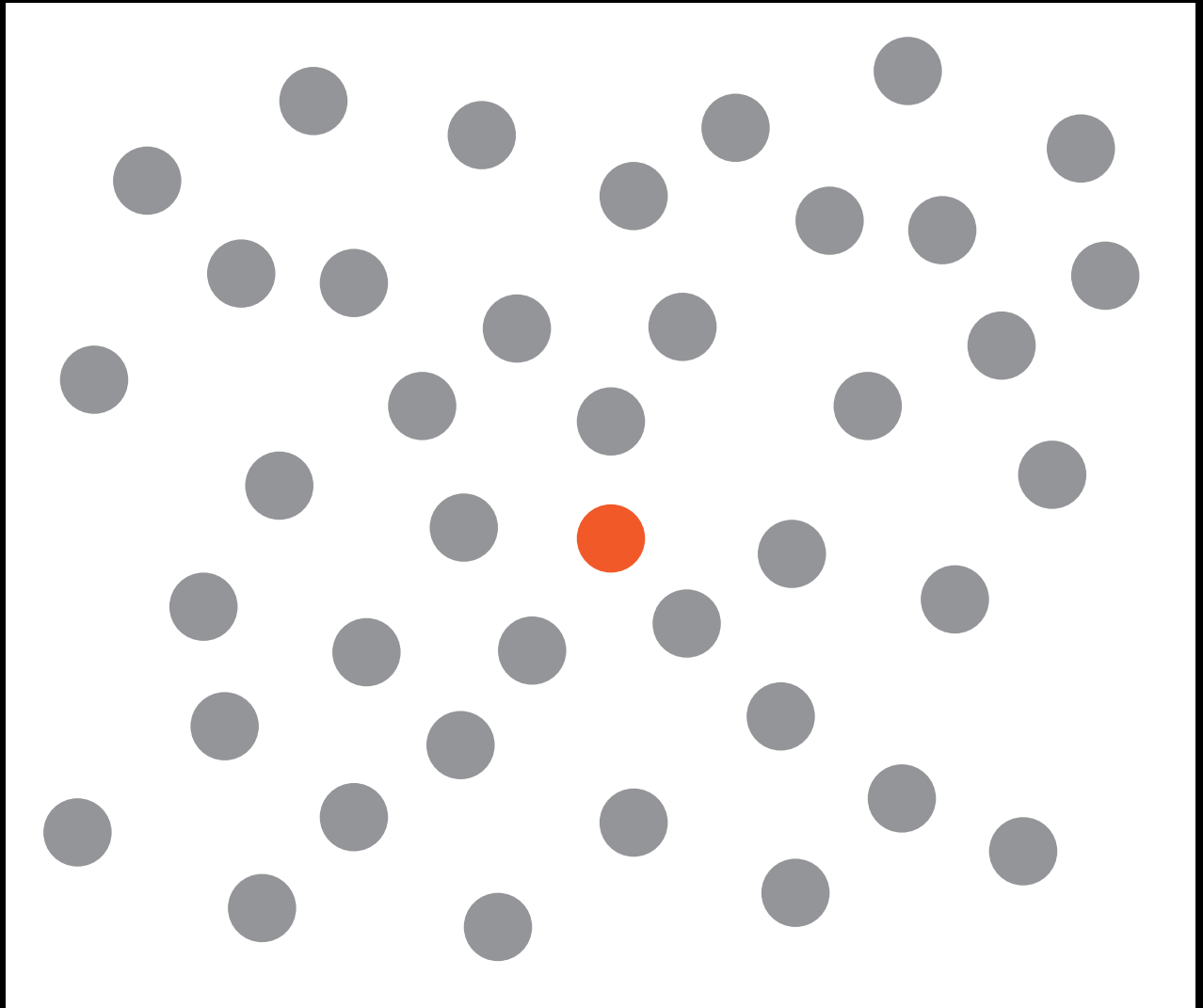
Potentially more important
for Ebola because of high
HCW risk.

Motivations for Understanding Silent Immunizing infections

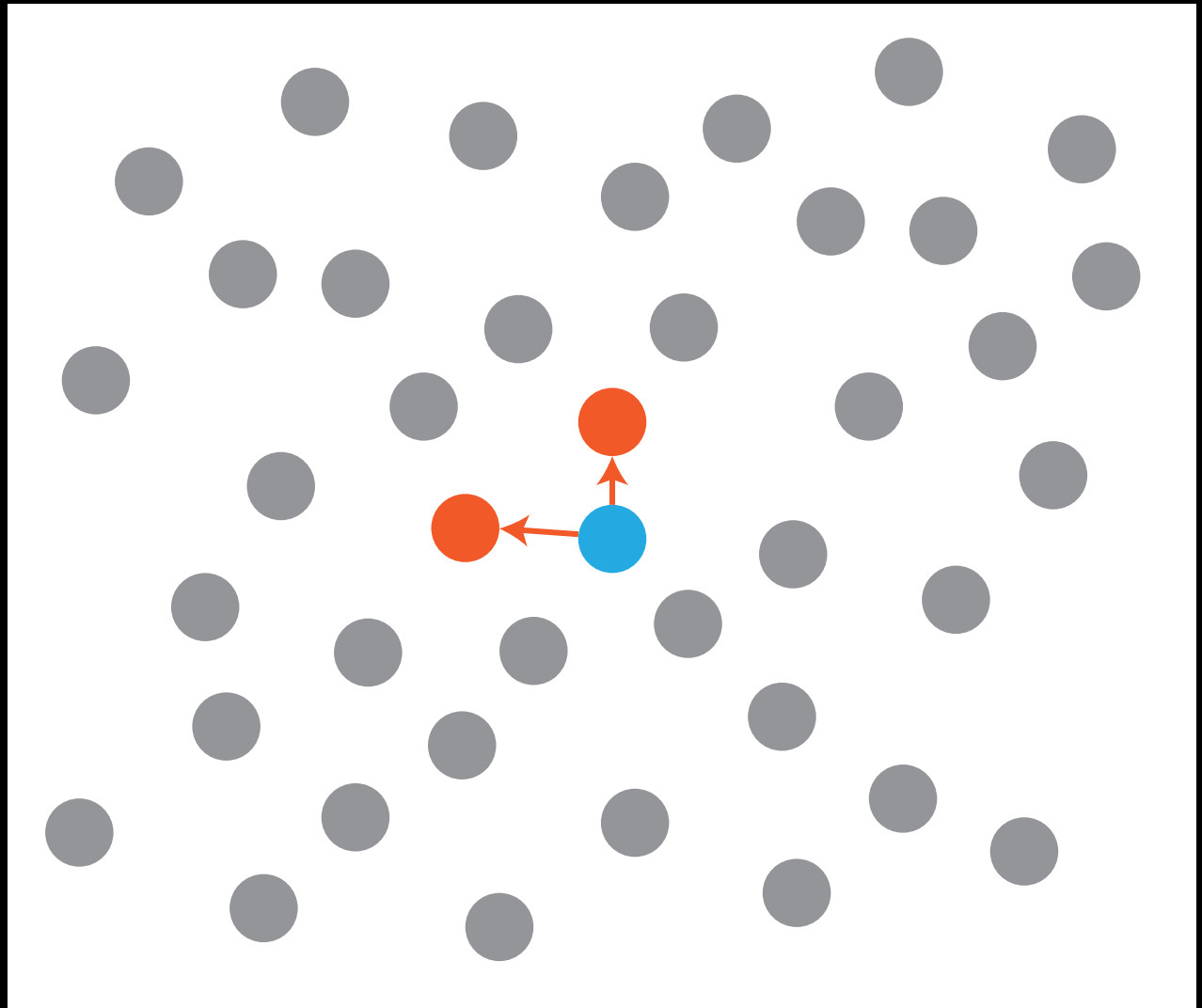
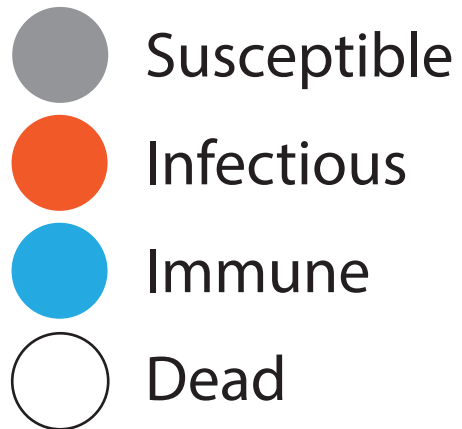
- Projections

Given $R_0 = 2$

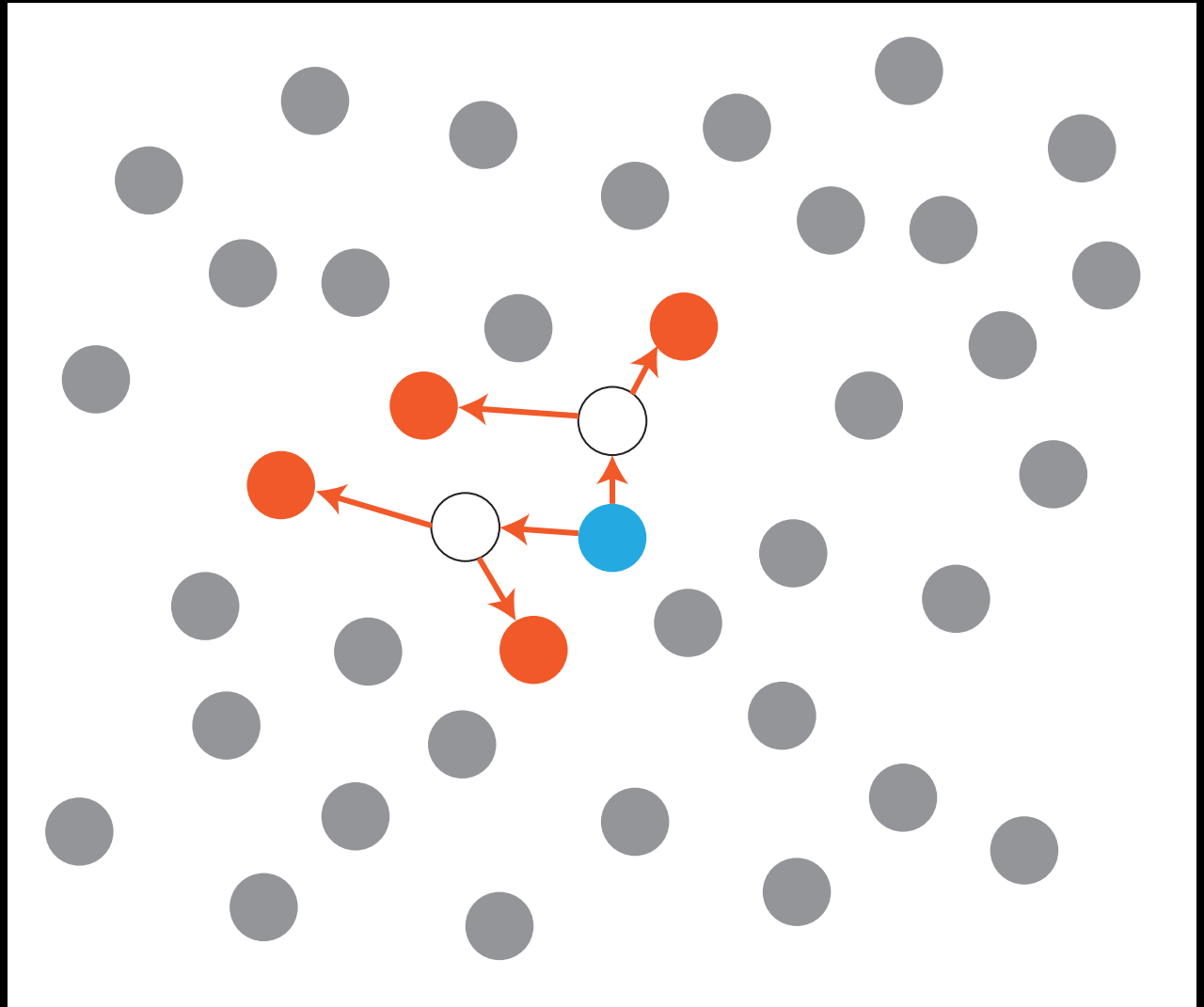
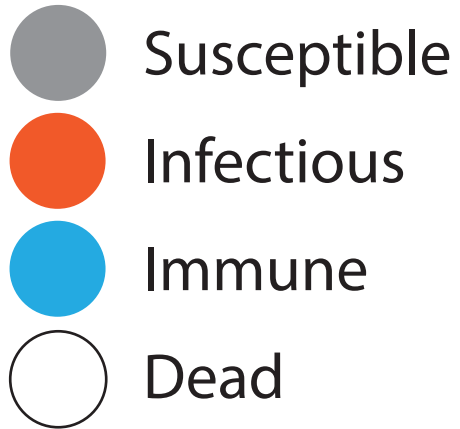
-  Susceptible
-  Infectious
-  Immune
-  Dead



After 1 generation interval (15 days)



After 2 generation intervals (30 days)

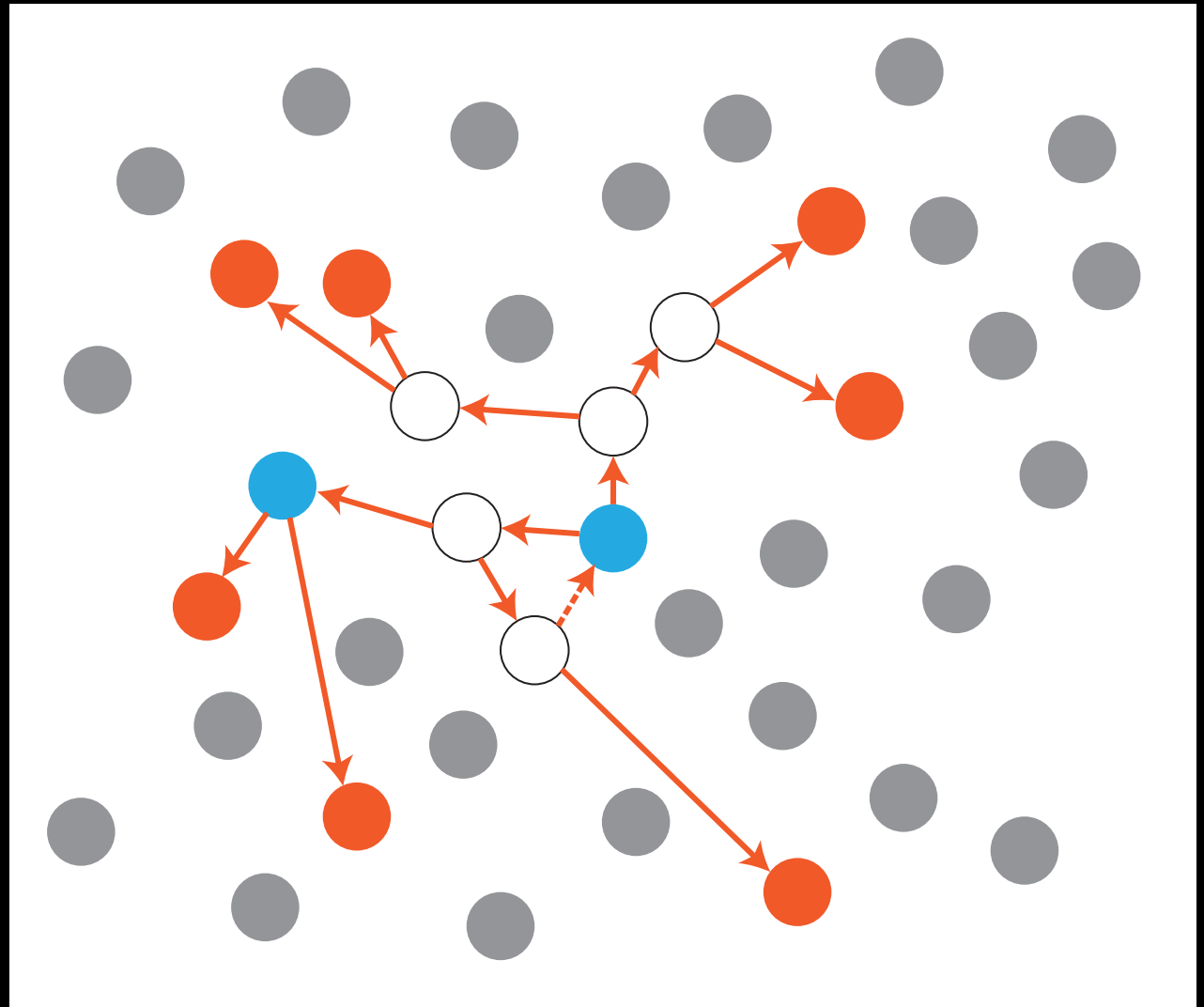


After 3 generation intervals (45 days)

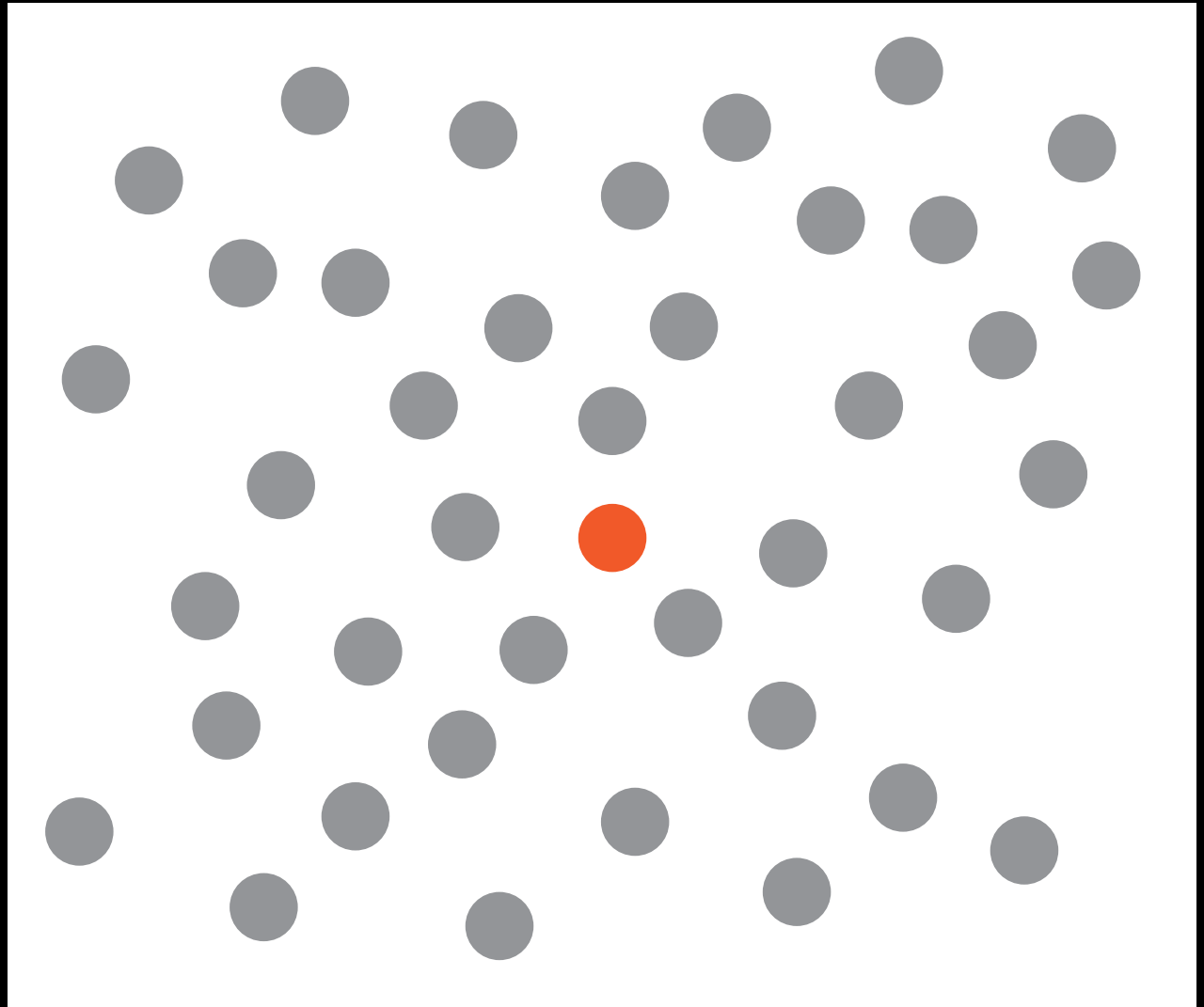
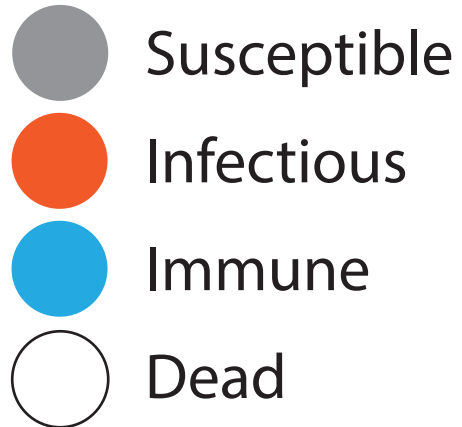
Contacts on survivors are "wasted"

Eventually causes epidemic decline.




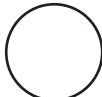
Not many survivors for highly fatal diseases.

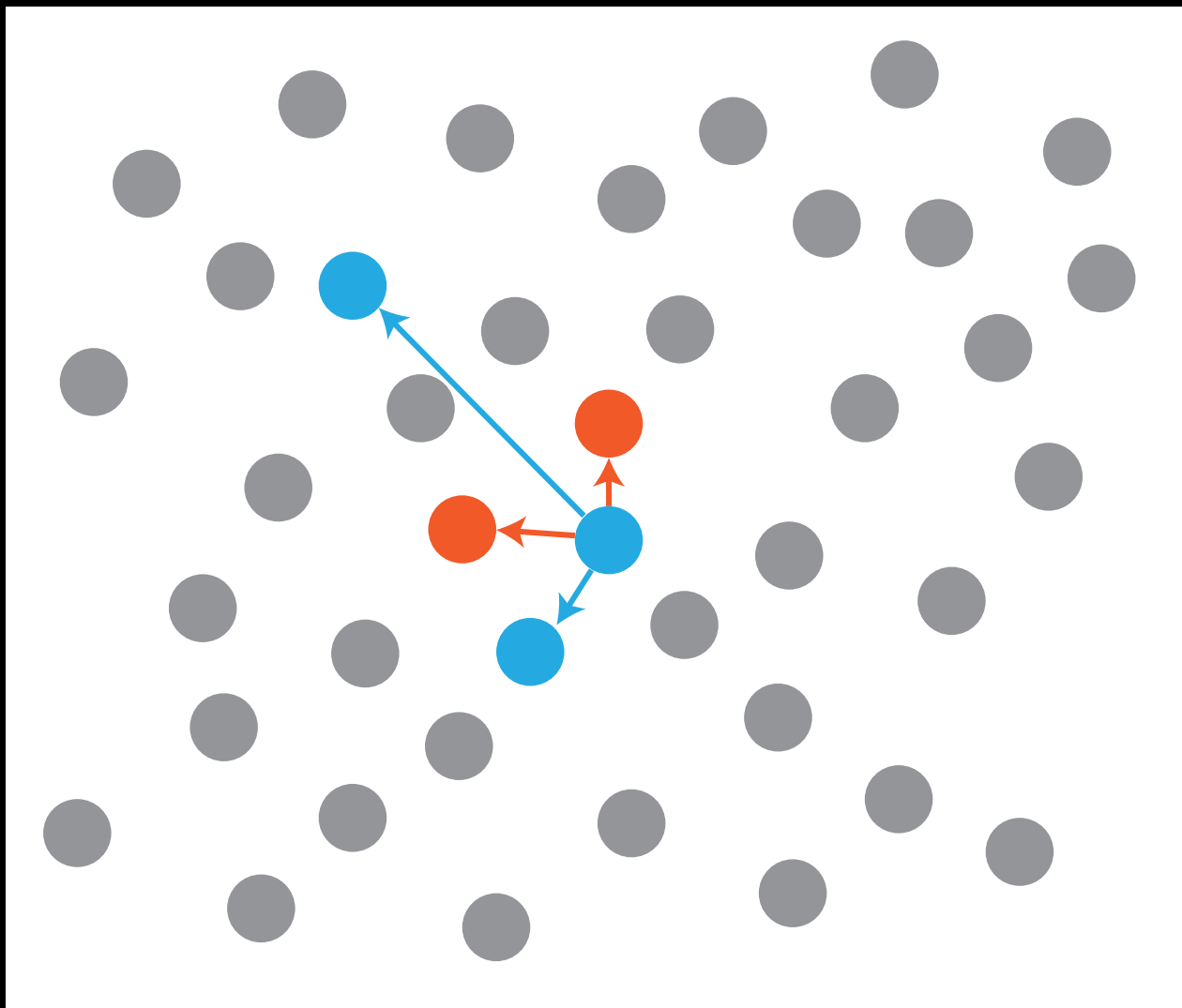


Given $R_0 = 2$ and 50% asymptomatic



15 days

-  Susceptible
-  Infectious
-  Immune
-  Dead

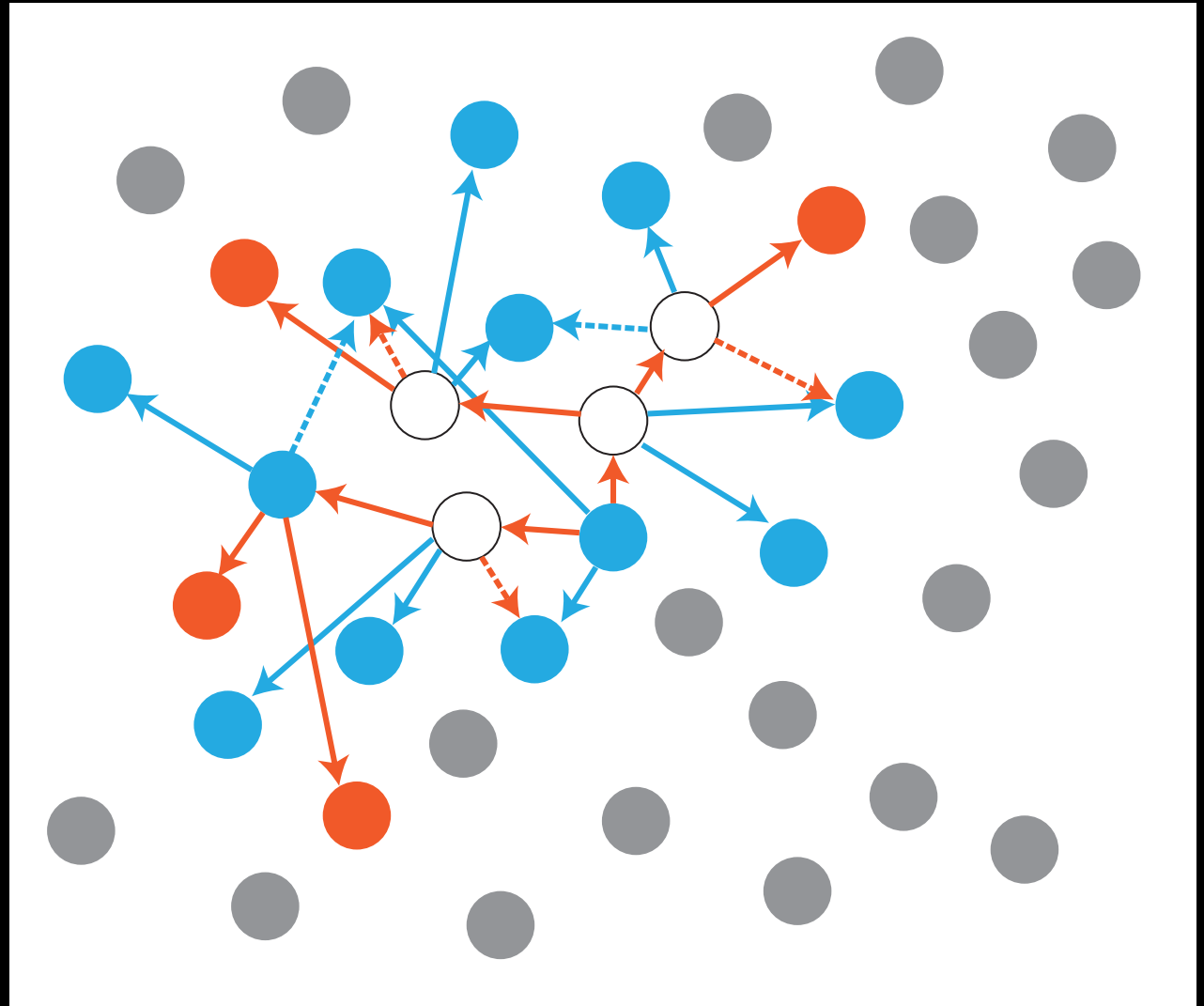


45 days

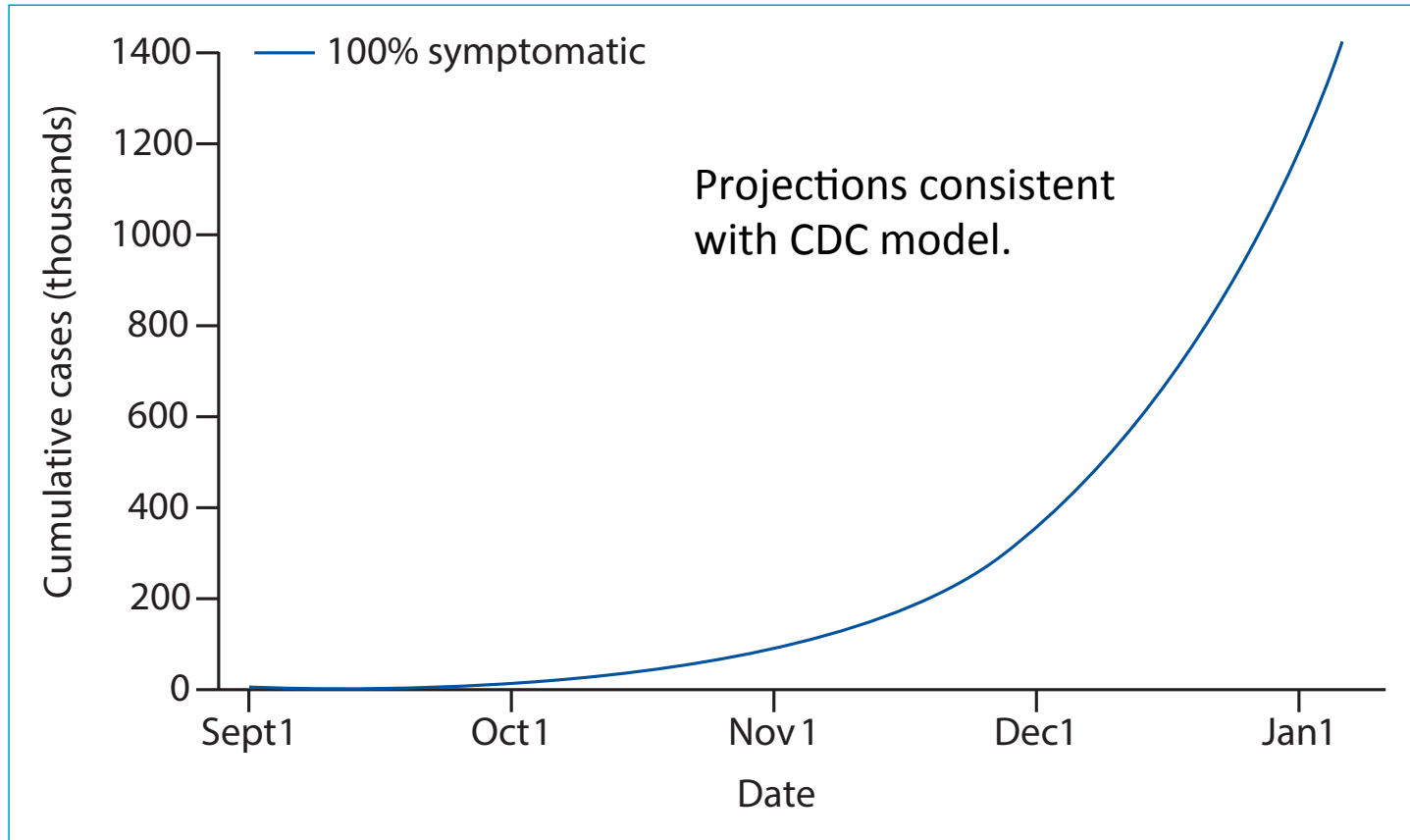
Contacts are
“wasted” on immune
individuals early in
epidemic.

Immunity
accumulates in small
clusters with lots of
risk (HCW & families).

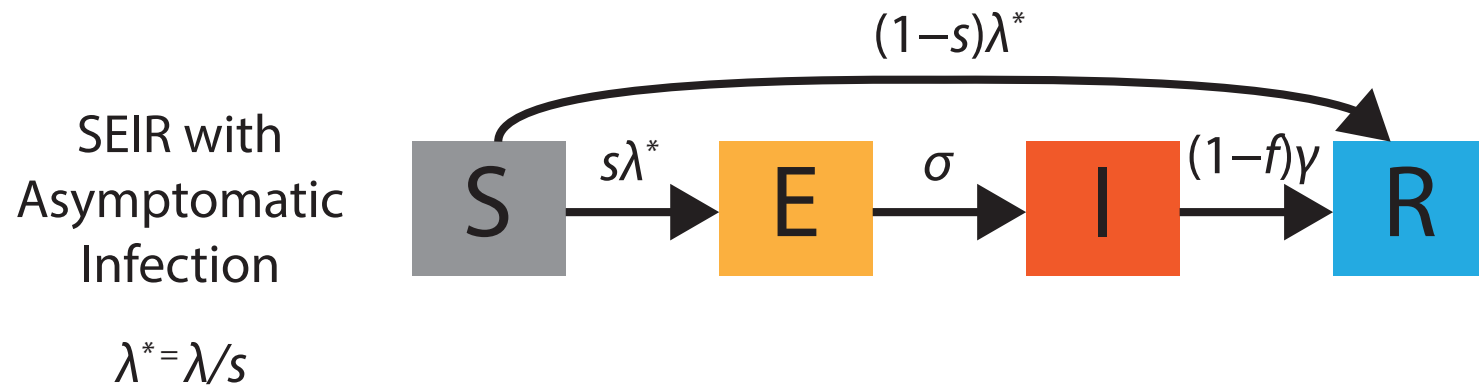
Most immune
individuals not
survivors.



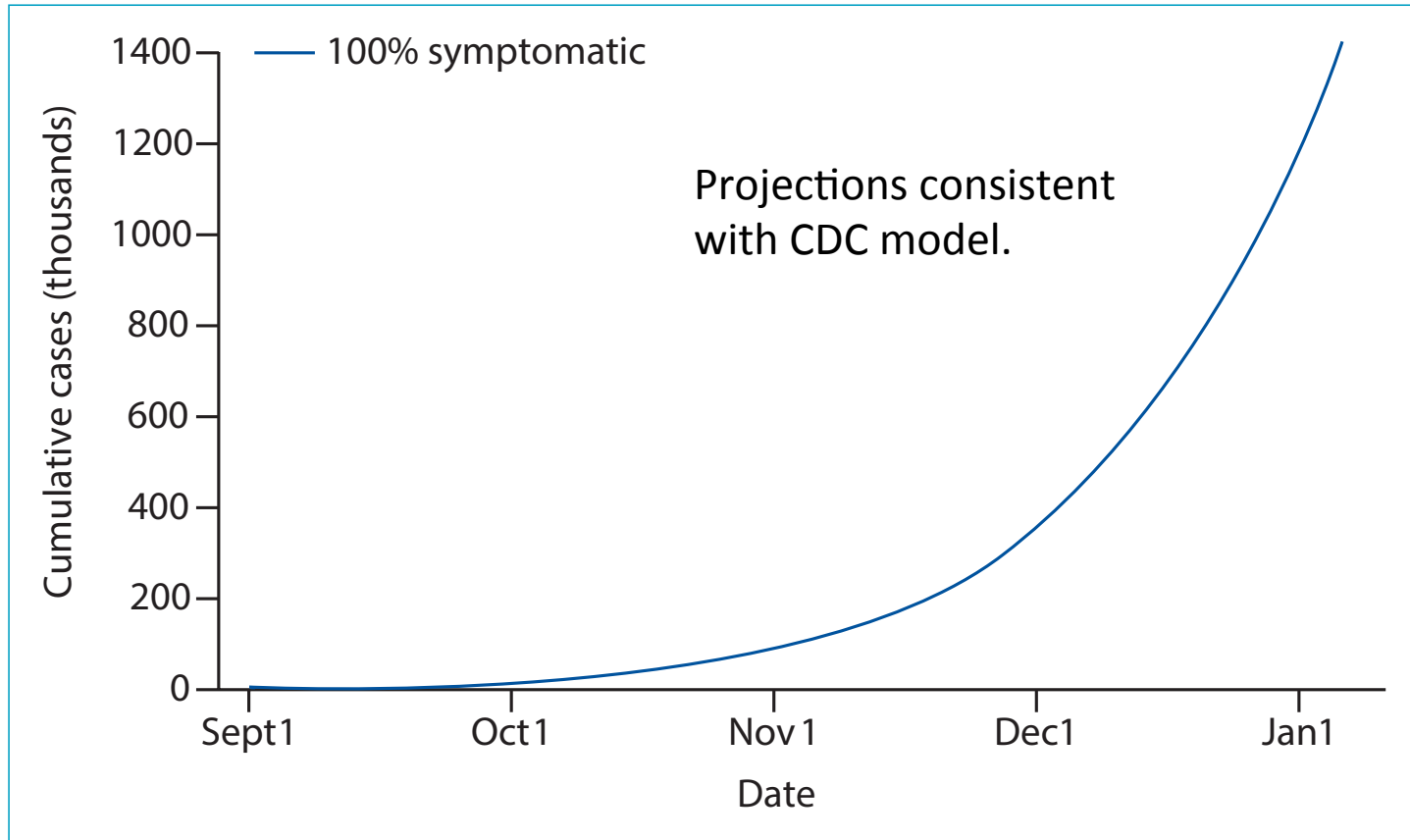
Effect of Silent Immunity on Outbreak Projections



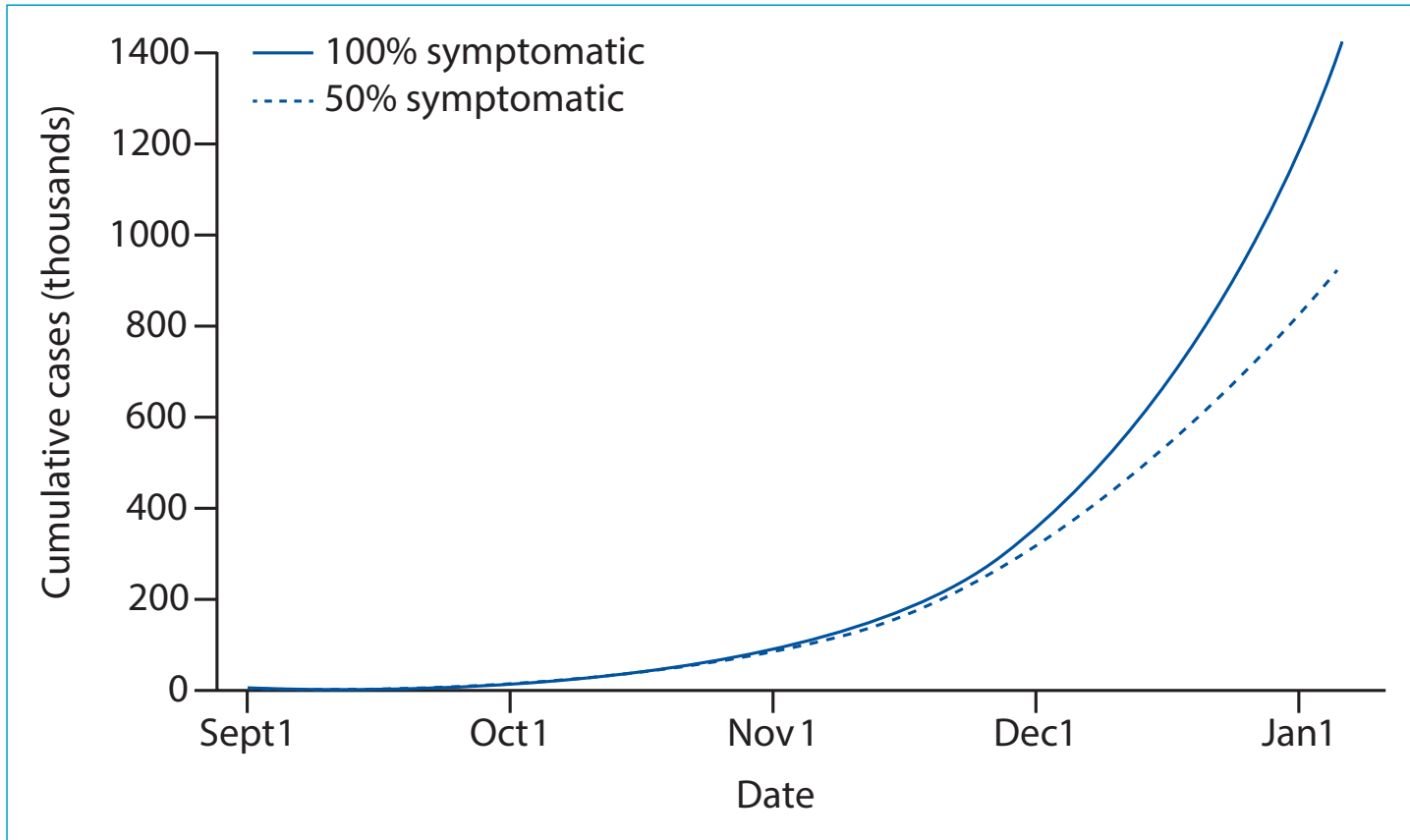
Model Diagrams



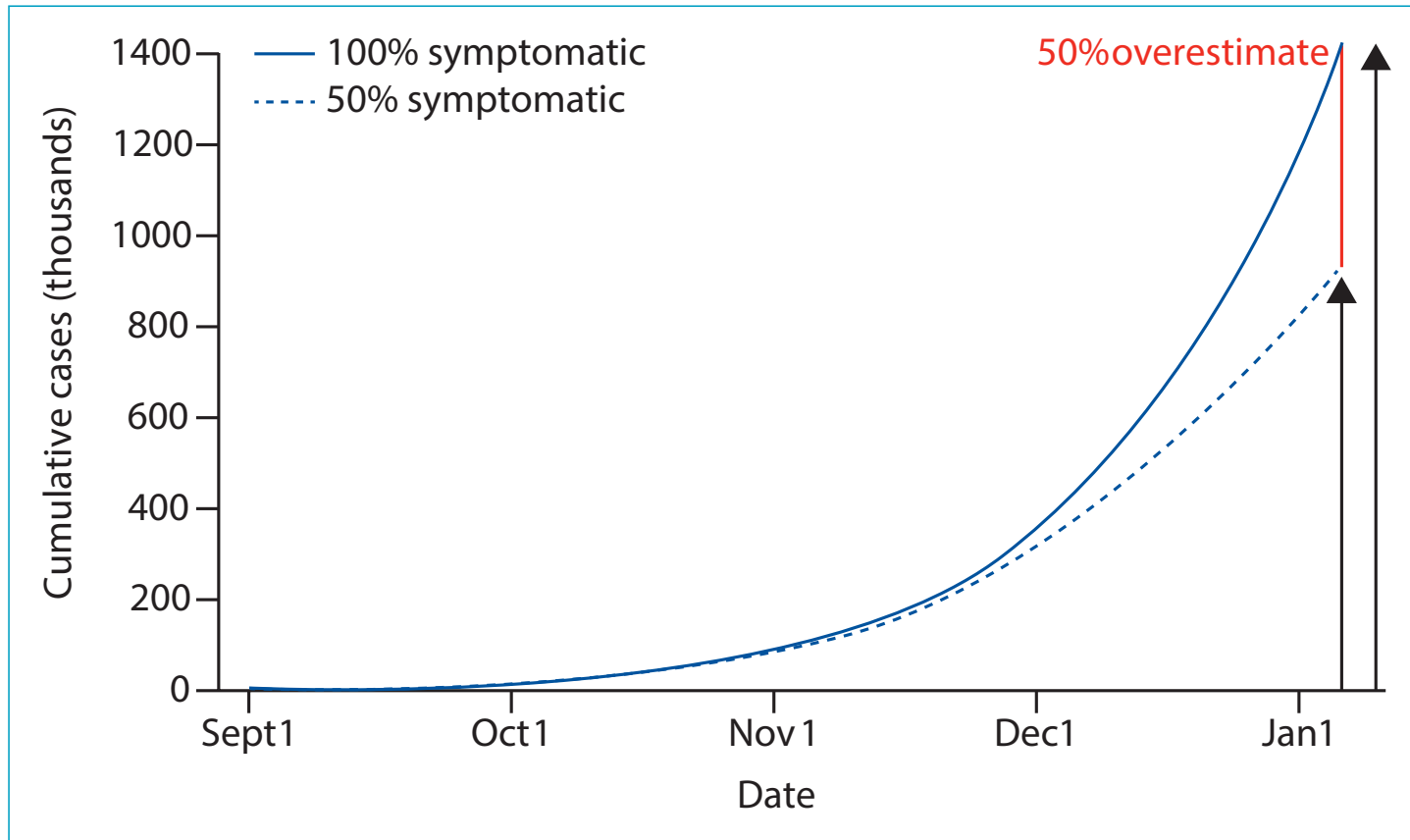
Effect of Silent Immunity on Outbreak Projections



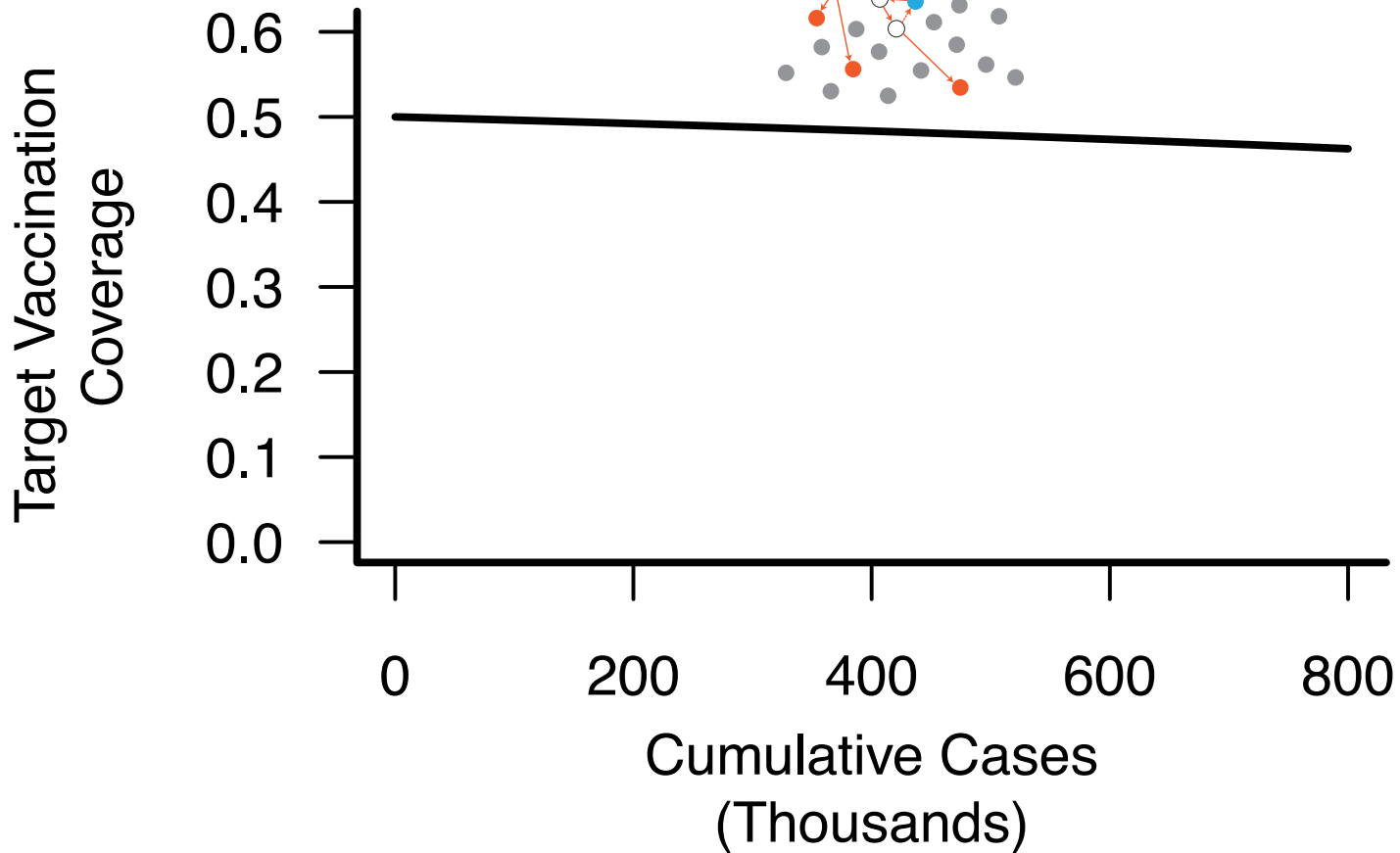
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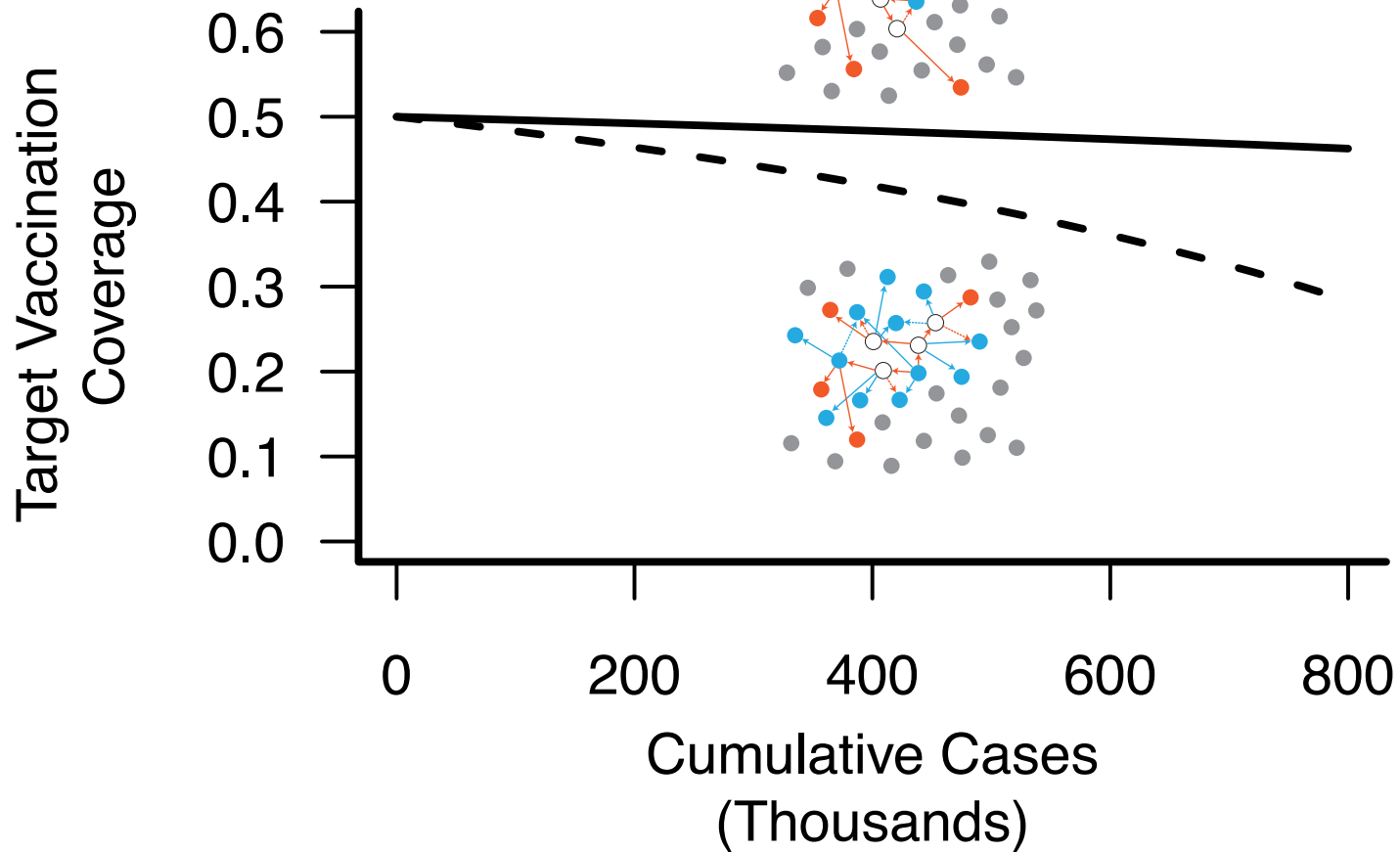
Effect of Silent Immunity on Outbreak Projections



Effect of Silent Immunity on Vaccination



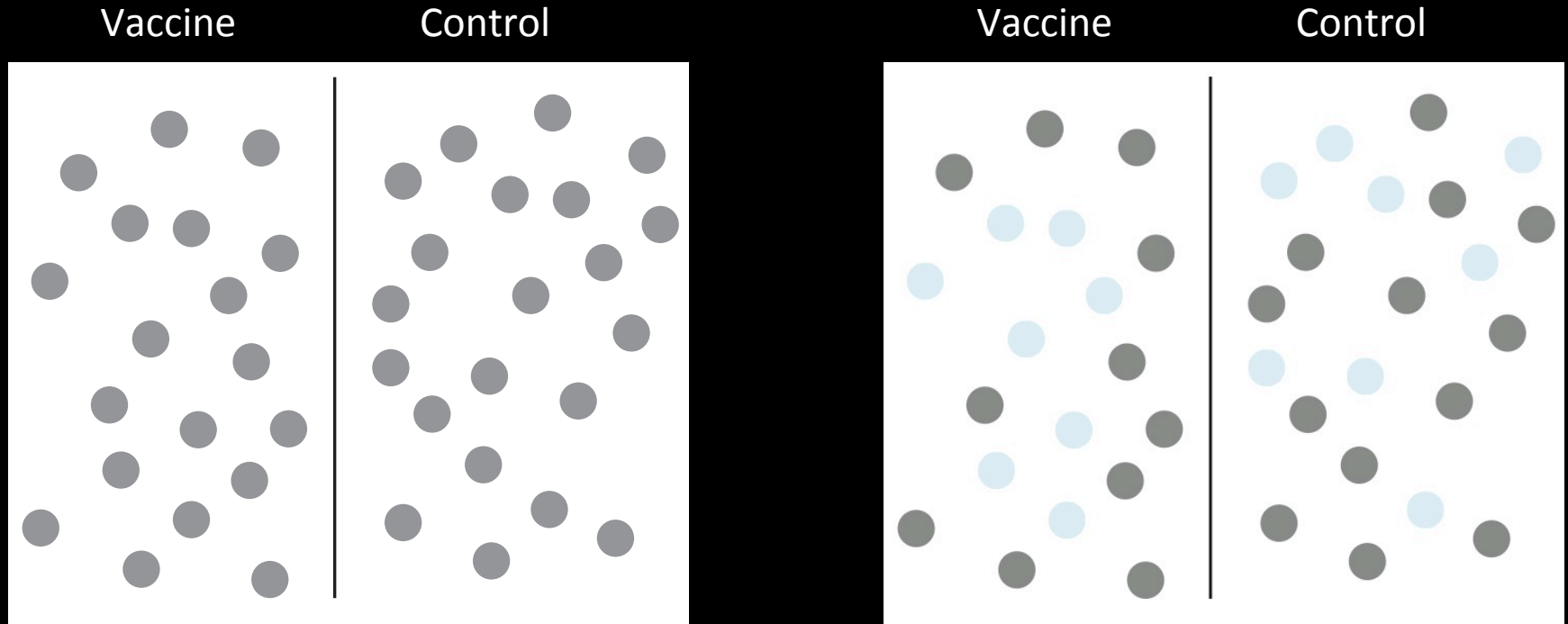
Effect of Silent Immunity on Vaccination



Motivations for Understanding Silent Immunizing infections

- Projections
- Sample size calculations for vaccine trials

Sample size calculations for vaccine trials

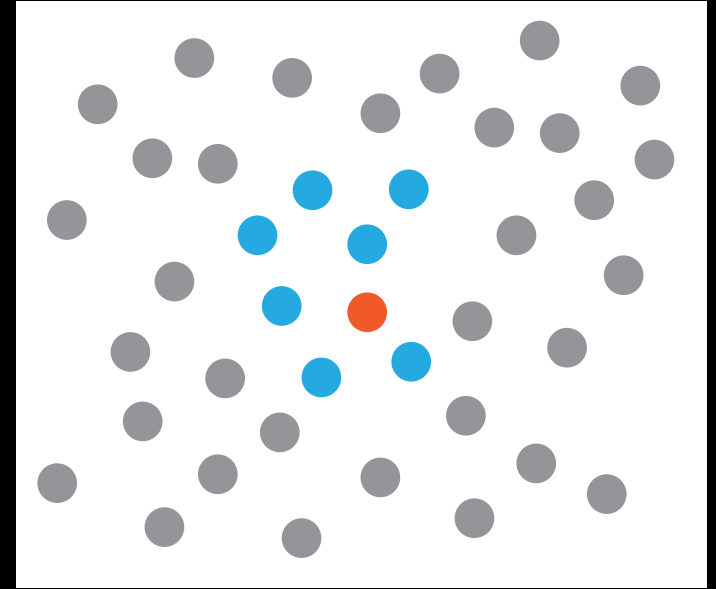
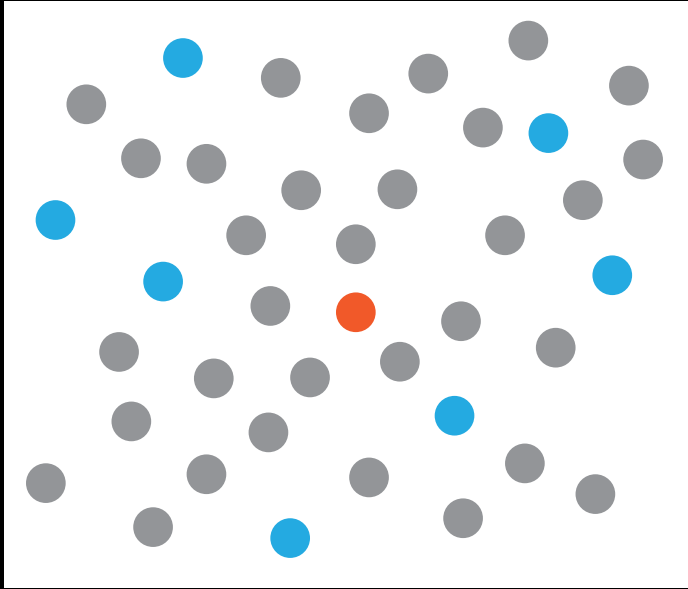


Pre-existing naturally acquired immunity reduces effective sample size of study.

Motivations for Understanding Silent Immunizing infections

- Projections
- Sample size calculations for vaccine trials
- Leverage immune individuals in outbreak control

Leverage Immune Individuals in Outbreak Control



Identify immune individuals (survivors and asymptomatics),
allocate them to front-line roles.

Similar to ring vaccination.

Two Critical Questions

- Are asymptotically infected individuals immune?
- Can we reliably identify them?

Must answer both of these before we can move forward on interventions.

Actionable Item 1: Domestic Studies

- Collect blood from contacts of Ebola cases in the US

Duncan's family, Dallas nurses, NYC case

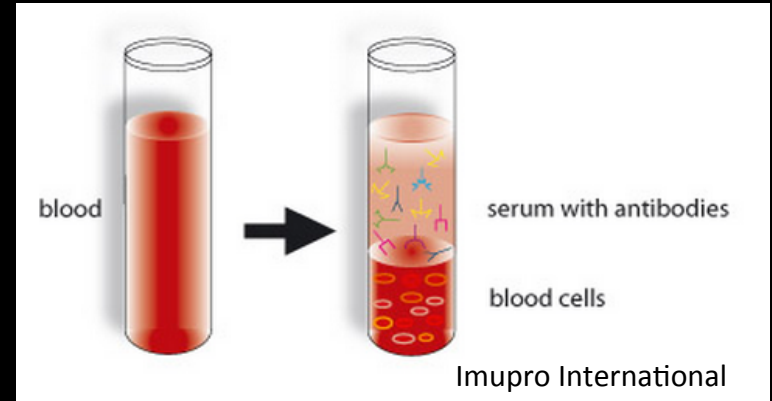
- Serology, PCR, other immunological assays
- Calculate the asymptomatic proportion

Duncan had > 70 contacts. If just two of them test positive, symptomatic proportion = 50%.

Can be done immediately,
BSL-4 lab (RMNL) ready to do assays given samples.

Actionable Item 2: Animal Model Studies

- No NHP model for *asymptomatic* infection
- Collect blood from
 - EVD survivors
 - asymptotically infected indiv.
- Give plasma or fractionated antibodies to NHPs, then challenge them

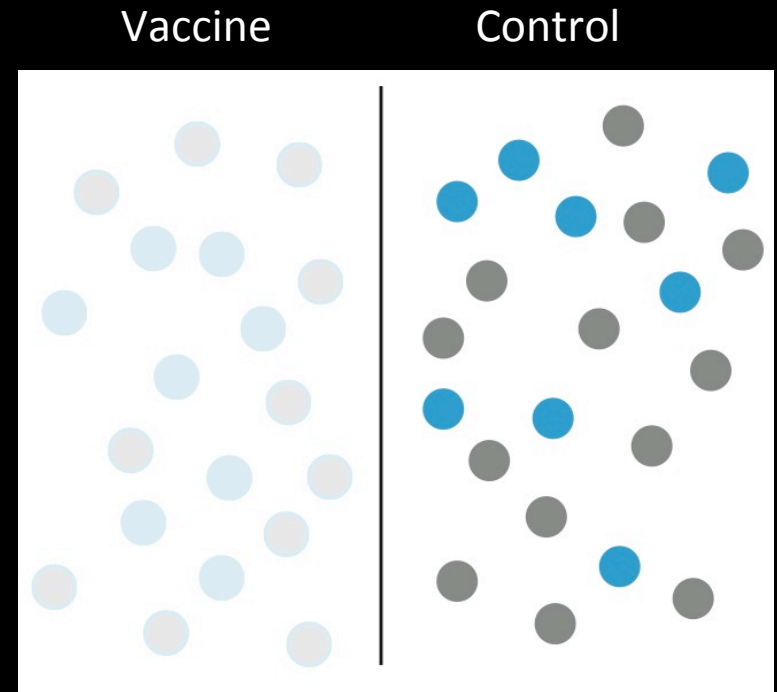


Actionable Item 3: Vaccine Efficacy Trials

- Baseline serum can help estimate asymptomatic proportion.
- Difference in Ebola risk in



in control arm indicates protective immunity.

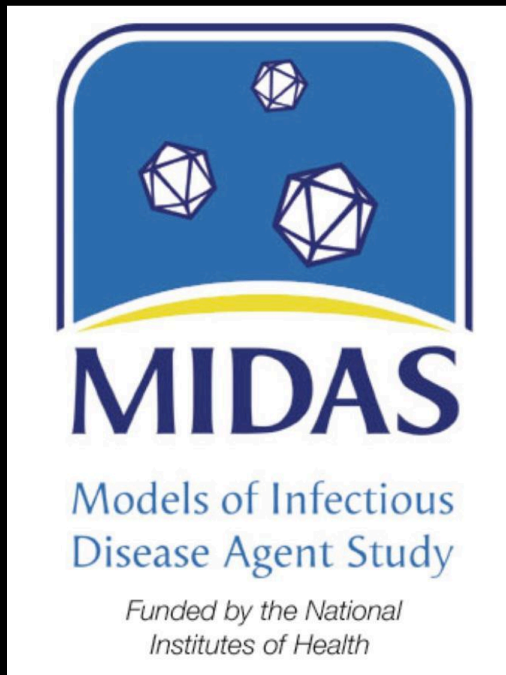


- Any study of front-line workers → use serology to learn more.

MUST balance with risk of blood draws, resource scarcity

Acknowledgements

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Attribution:

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Code: <http://ebola.ici3d.org/>

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