# COVID-19

## Proactive testing to mitigate spread

IPAM Workshop on Mathematical Models in Understanding COVID-19

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University of Washington

Photo: Carl Bergstrom

## Analytic approximations

Ted Bergstrom, UCSB
Haoran Li, UCSB

## Stochastic network model

Ryan McGee, UW

with Ben Kerr, Omar Cornejo,
Mark Tanaka, Julian Homberger,
Hannah Williams, Alicia Zhou,

Photo: Carl Bergstrom

Photo: Carl Bergstrom

# Disclosures

I have a paid consulting relationship with Color Genomics, and I will be talking about some of that work today. I have no financial interest in the production or sales COVID of tests or treatments.

I do have vested interests in going places, seeing people, working at the office, eating at restaurants, drinking at the bar, playing sports, hearing live music, sending my son to school, sending my daughter to college, visiting Europe, visiting anywhere else, and photographing birds that can't be bothered to visit Seattle.

# A vaccine is coming

But it won't be a panacea—if it comes at all.

Photo: Carl Bergstrom

# We need something else

Something nimble.

Photo: Carl Bergstrom

# This is a talk about testing.

Photo: Carl Bergstrom

# Four roles for Covid-19 testing

Individual diagnosis, clearance, surveillance, and mitigation.

## 1. Individual diagnosis

Symptomatic patients, for treatment and peace of mind.

High sensitivity and specificity desired.

# Four roles for Covid-19 testing

Individual diagnosis, clearance, surveillance, and mitigation.

## 2. Clearance

Verify that patients and practitioners are uninfected prior to performing a procedure.

Travel? Other activities?

High sensitivity needed.
Specificity less essential.

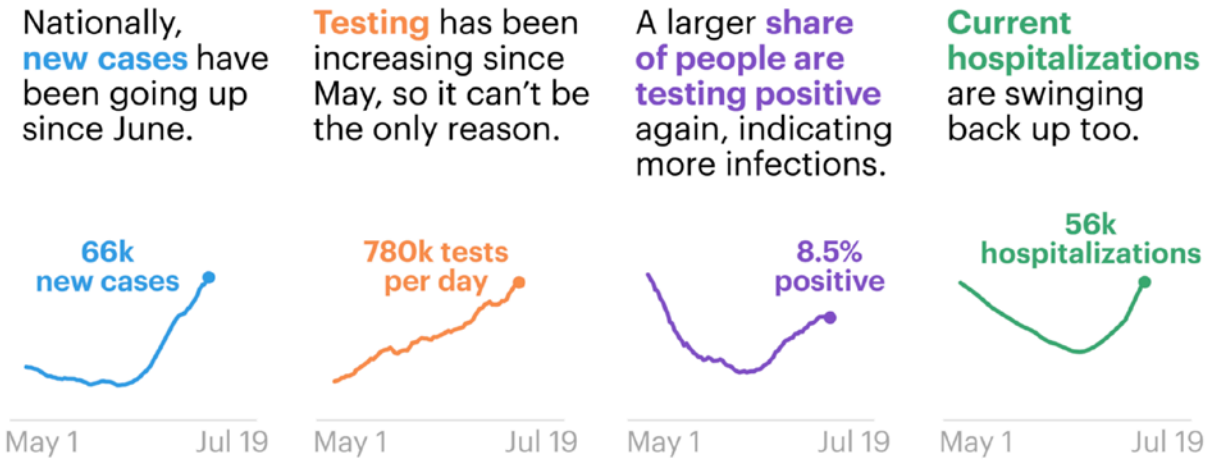
# Four roles for Covid-19 testing

Individual diagnosis, clearance, surveillance, and mitigation.

## 3. Surveillance

Public health officials want to track prevalence and trajectory of pandemic.

Can correct for lower sensitivity and (if common) lower specificity.




Chen and Ngu 2020 *ProPublica*

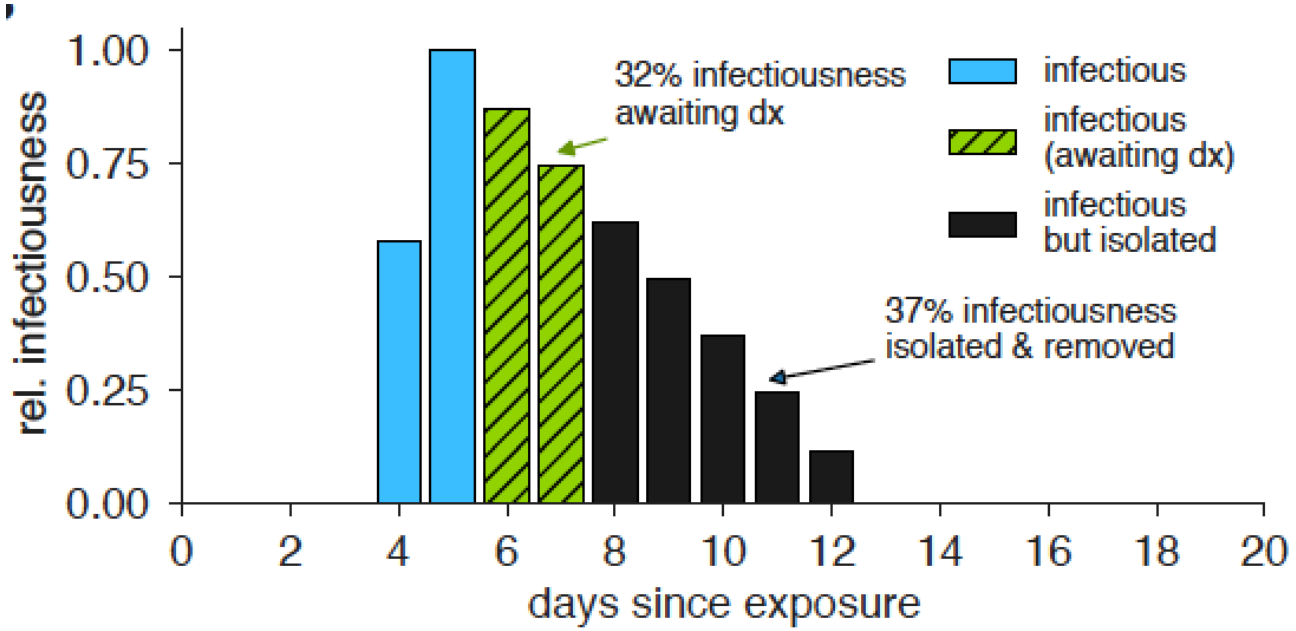
# Four roles for Covid-19 testing

Individual diagnosis, clearance, surveillance, and mitigation.

## 4. Mitigation

Find non-symptomatic cases and isolate / trace as a means of disease control.

Volume is more important than sensitivity or specificity.




Larremore et al. 2020 Test sensitivity is secondary to frequency and turnaround time for COVID-19 surveillance

# Speed is critical in all cases.

## 1. Individual health.

Patients don't want to wait.

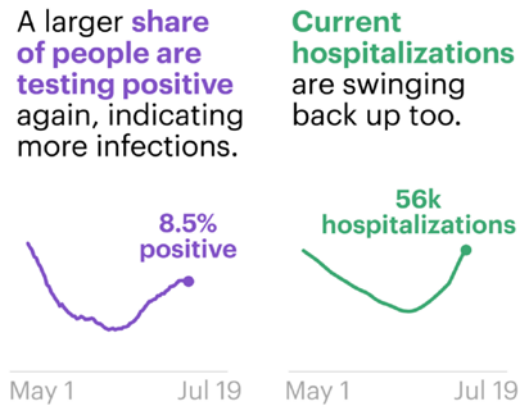
Treatments may depend on diagnosis.

## 2. Clearance

Tests should be point-of-care to minimize chance of becoming infectious after sampling.

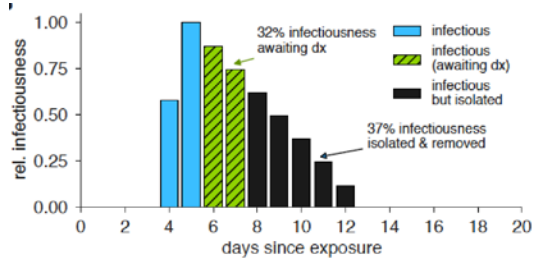
## 3. Surveillance

Heath officials need the latest information to make good decisions.




## 4. Mitigation

Every day's delay is an extra day an infected person is walking around spreading disease.




Helfert; 59th Med Wing; ProPublica; Larremore

# The CDC Is Wrong

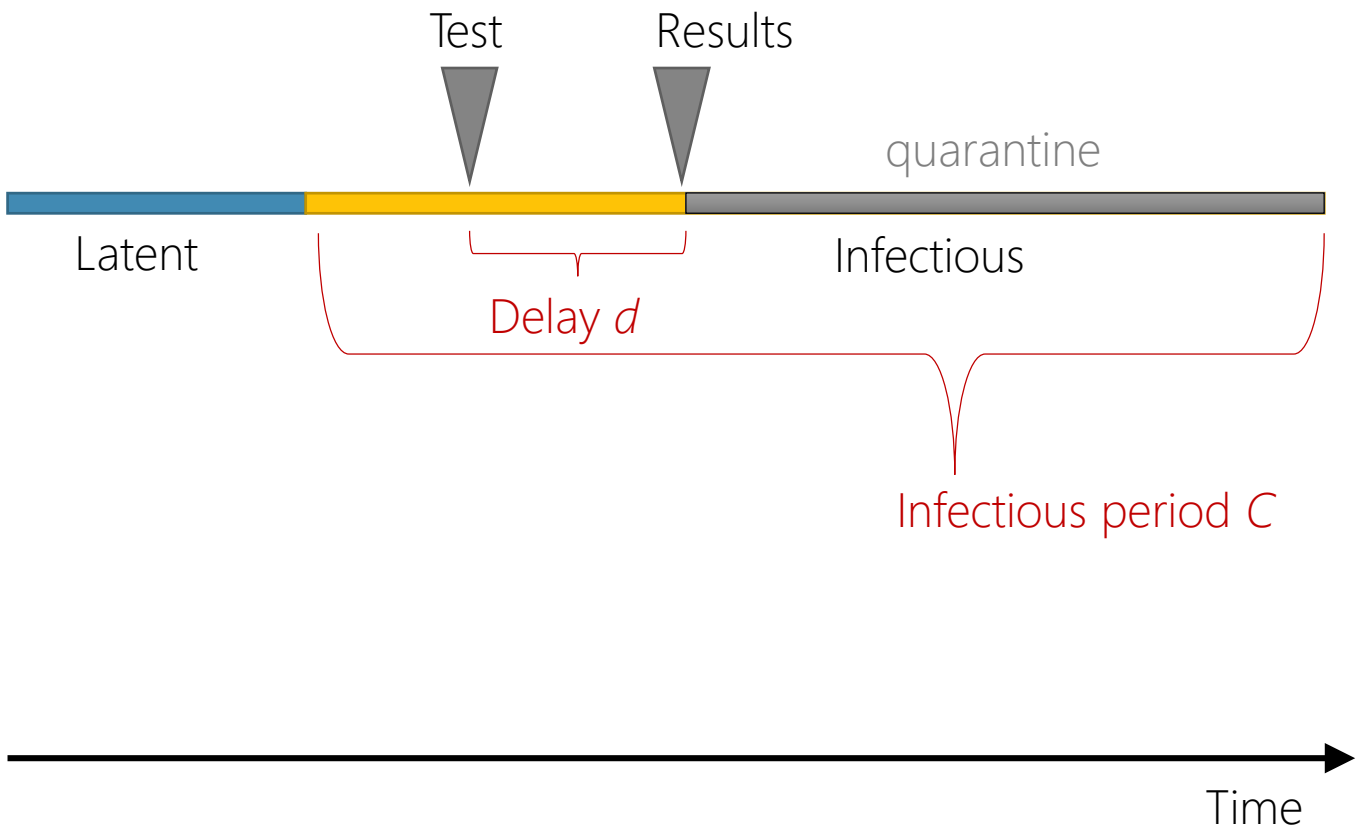
**Testing is essential for colleges to reopen safely**

*By Carl T. Bergstrom* | July 14, 2020

The CDC guidelines state that:

Testing of all students, faculty and staff for Covid-19 before allowing campus entry (entry testing) has not been systematically studied. It is unknown if entry testing in IHEs provides any additional reduction in person-to-person transmission of the virus beyond what would be expected with implementation of other infection preventive measures (e.g., social distancing, cloth face covering, hand washing, enhanced cleaning and disinfection). **Therefore, CDC does not recommend entry testing of all returning students, faculty, and staff.**

# The aim of proactive (mitigation) testing: Reducing exposure-days



| | |
|---|---|
| $C$ | # infectious days |
| $n$ | Testing periodicity |
| $q$ | False negative rate |
| $d$ | Delay for results |

By what fraction does testing and isolation reduce exposure days relative to no testing at all?

| | |
|---|---|
| $C$ | # infectious days |
| $n$ | Testing periodicity |
| $q$ | False negative rate |
| $d$ | Delay for results |

When testing periodicity is longer than infectious period, individuals will only be tested once while infectious.

Expected exposure days

tested — true positive — false negative — not tested

$$E(C,\tau) = \int_0^{C-d} \frac{1}{n}\Big((1-q)(t+d) + q\,C\Big)dt + \int_{C-d}^{n} \frac{1}{n} C\,dt$$

Simplifies to $$E(C,\tau) = C - \frac{(1-q)(C-d)^2}{2n}$$

| | |
|---|---|
| $C$ | # infectious days |
| $n$ | Testing periodicity |
| $q$ | False negative rate |
| $d$ | Delay for results |

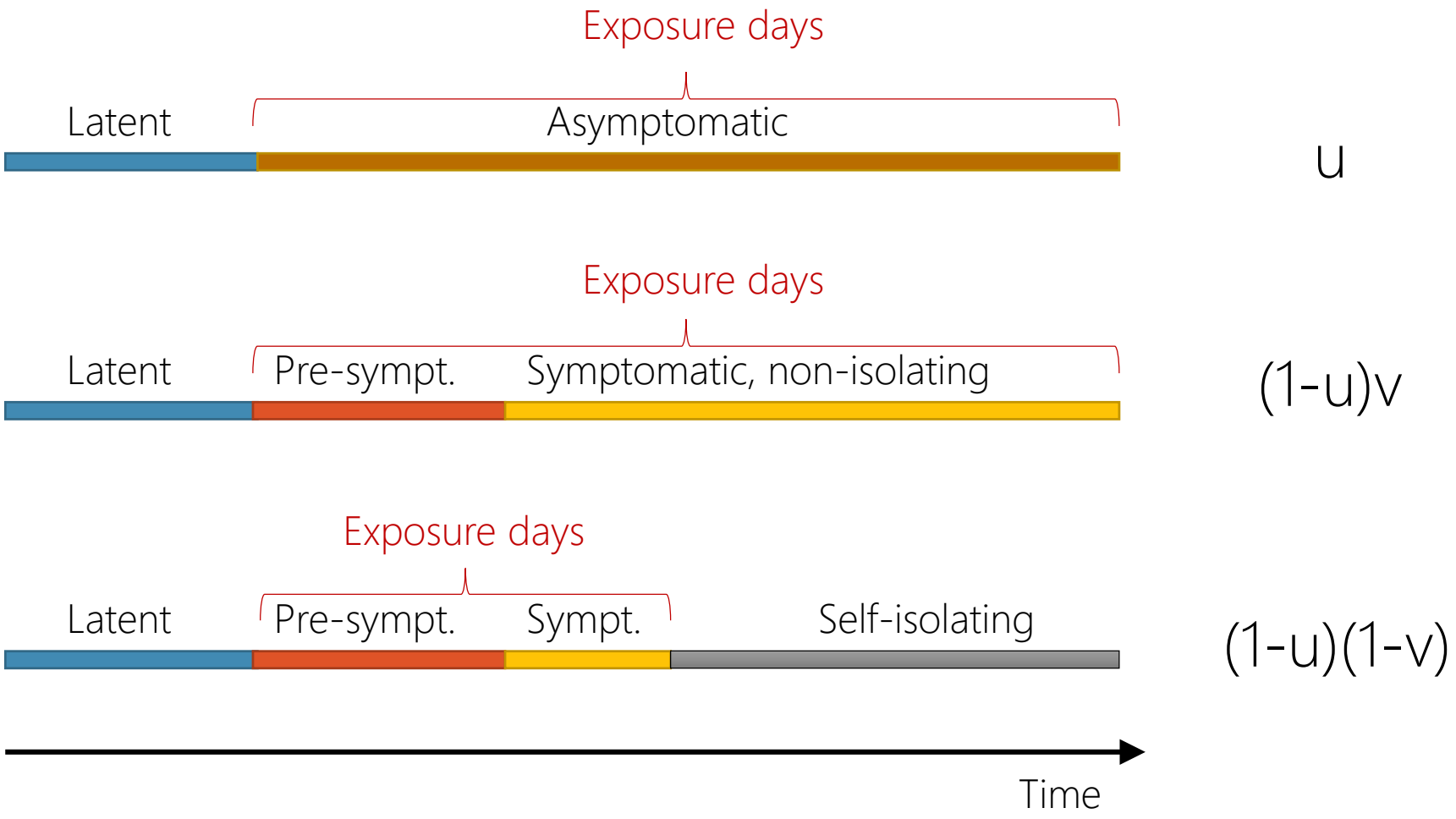
When testing periodicity is shorter than the infectious period, you get multiple chances to catch an infection.

After a bit of algebra, you can still get a nice expression for the expected exposure days.

$$E(C,\tau) = \left(\frac{n}{2} + d + \frac{nq}{1-q}\right) + q^{\bar{x}}\left(\frac{1}{2n}\left(qr^2 - (n-r)^2\right) - \frac{nq}{1-q}\right)$$

Where $\bar{x} = \left\lfloor \frac{C-d}{n} \right\rfloor$ and $r = C - d - n\,\bar{x}$

# But some symptomatic individuals can self-isolate. We need to account for this.



# Compare infectious days with testing to infectious days without.

$$\phi = \frac{E \text{ with testing}}{E \text{ without testing}}$$

# Compare infectious days with testing to infectious days without.

$$\phi = \frac{E \text{ with testing}}{(1-(1-u)v)C + (1-u)v\,y}$$

Asymptomatic or don't isolate

Self-isolate

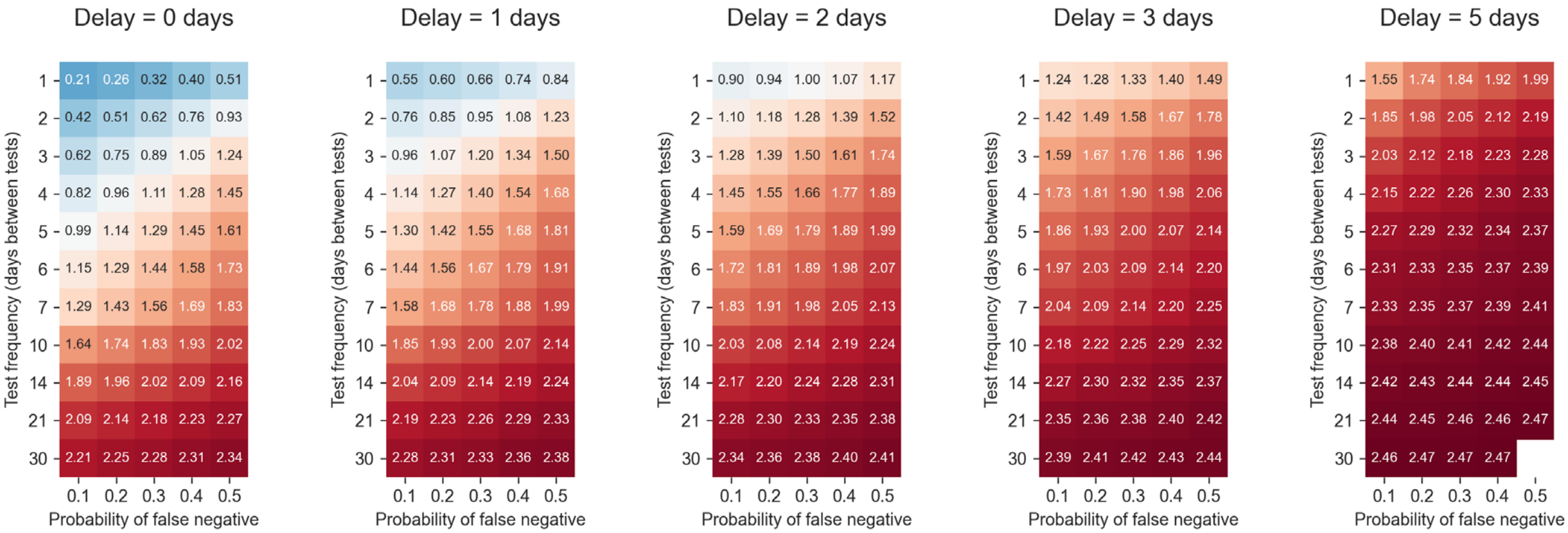
# Compare infectious days with testing to infectious days without.

$$\phi = \frac{\big(1-(1-u)v\big)E(C,\tau) + (1-u)vE(y,\tau)}{\big(1-(1-u)v\big)C + (1-u)v\,y}$$

Asymptomatic or don't isolate

Self-isolate

# Results


Delay = 0 days
Test frequency (days between tests)
1 0.21 0.26 0.32 0.40 0.51
2 0.42 0.51 0.62 0.76 0.93
3 0.62 0.75 0.89 1.05 1.24
4 0.82 0.96 1.11 1.28 1.45
5 0.99 1.14 1.29 1.45 1.61
6 1.15 1.29 1.44 1.58 1.73
7 1.29 1.43 1.56 1.69 1.83
10 1.64 1.74 1.83 1.93 2.02
14 1.89 1.96 2.02 2.09 2.16
21 2.09 2.14 2.18 2.23 2.27
30 2.21 2.25 2.28 2.31 2.34
0.1 0.2 0.3 0.4 0.5
Probability of false negative
Delay = 1 days
Test frequency (days between tests)
1 0.55 0.60 0.66 0.74 0.84
2 0.76 0.85 0.95 1.08 1.23
3 0.96 1.07 1.20 1.34 1.50
4 1.14 1.27 1.40 1.54 1.68
5 1.30 1.42 1.55 1.68 1.81
6 1.44 1.56 1.67 1.79 1.91
7 1.58 1.68 1.78 1.88 1.99
10 1.85 1.93 2.00 2.07 2.14
14 2.04 2.09 2.14 2.19 2.24
21 2.19 2.23 2.26 2.29 2.33
30 2.28 2.31 2.33 2.36 2.38
0.1 0.2 0.3 0.4 0.5
Probability of false negative
Delay = 2 days
Test frequency (days between tests)
1 0.90 0.94 1.00 1.07 1.17
2 1.10 1.18 1.28 1.39 1.52
3 1.28 1.39 1.50 1.61 1.74
4 1.45 1.55 1.66 1.77 1.89
5 1.59 1.69 1.79 1.89 1.99
6 1.72 1.81 1.89 1.98 2.07
7 1.83 1.91 1.98 2.05 2.13
10 2.03 2.08 2.14 2.19 2.24
14 2.17 2.20 2.24 2.28 2.31
21 2.28 2.30 2.33 2.35 2.38
30 2.34 2.36 2.38 2.40 2.41
0.1 0.2 0.3 0.4 0.5
Probability of false negative
Delay = 3 days
Test frequency (days between tests)
1 1.24 1.28 1.33 1.40 1.49
2 1.42 1.49 1.58 1.67 1.78
3 1.59 1.67 1.76 1.86 1.96
4 1.73 1.81 1.90 1.98 2.06
5 1.86 1.93 2.00 2.07 2.14
6 1.97 2.03 2.09 2.14 2.20
7 2.04 2.09 2.14 2.20 2.25
10 2.18 2.22 2.25 2.29 2.32
14 2.27 2.30 2.32 2.35 2.37
21 2.35 2.36 2.38 2.40 2.42
30 2.39 2.41 2.42 2.43 2.44
0.1 0.2 0.3 0.4 0.5
Probability of false negative
Delay = 5 days
Test frequency (days between tests)
1 1.55 1.74 1.84 1.92 1.99
2 1.85 1.98 2.05 2.12 2.19
3 2.03 2.12 2.18 2.23 2.28
4 2.15 2.22 2.26 2.30 2.33
5 2.27 2.29 2.32 2.34 2.37
6 2.31 2.33 2.35 2.37 2.39
7 2.33 2.35 2.37 2.39 2.41
10 2.38 2.40 2.41 2.42 2.44
14 2.42 2.43 2.44 2.44 2.45
21 2.44 2.45 2.46 2.46 2.47
30 2.46 2.47 2.47 2.47
0.1 0.2 0.3 0.4 0.5
Probability of false negative

# The real world is not so simple

- Disease dynamics
- Social network structure
- Heterogeneity of disease trajectory, infectivity, etc.
- Varying test sensitivity over time
- Non-compliance with testing and isolation

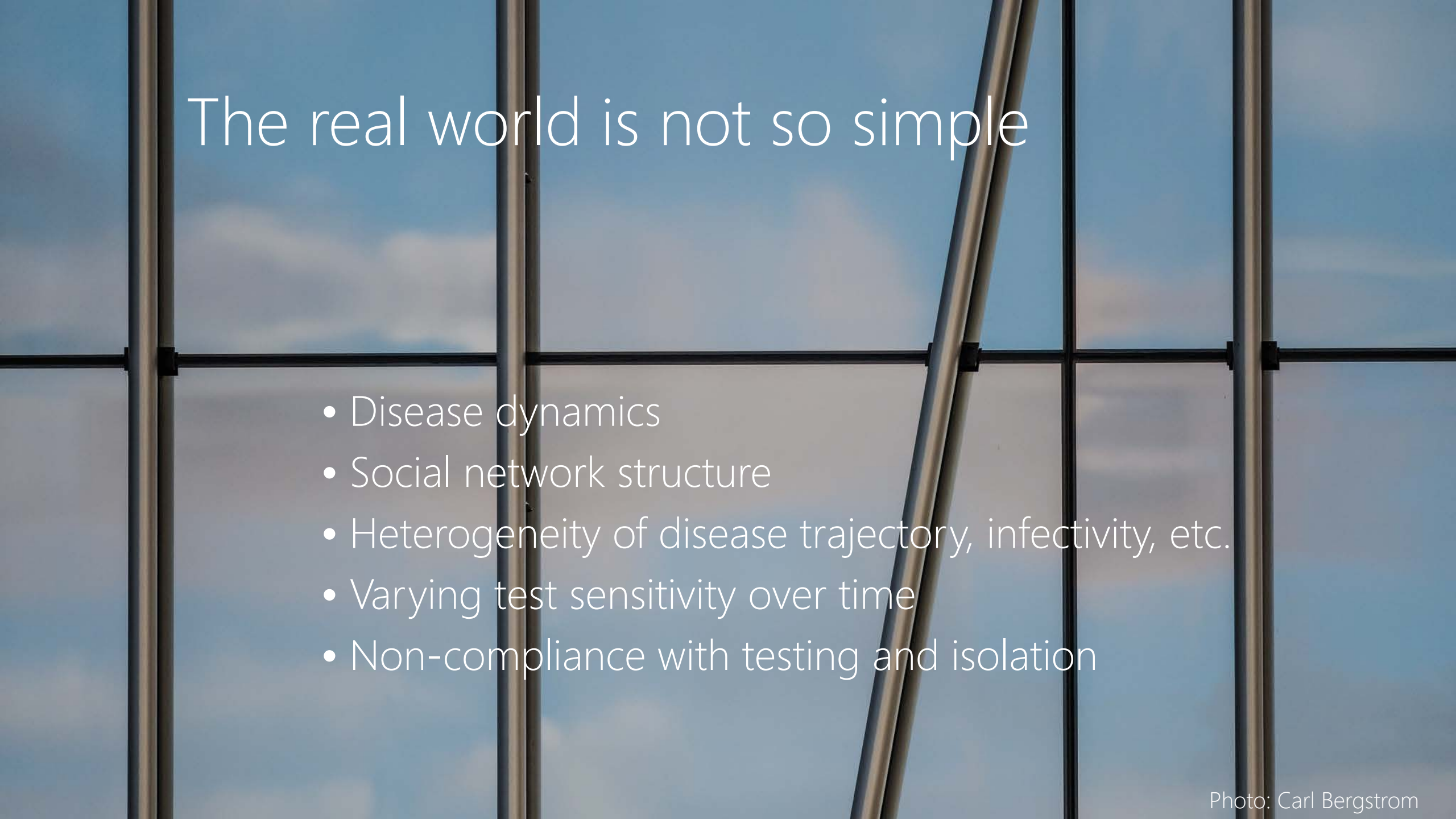
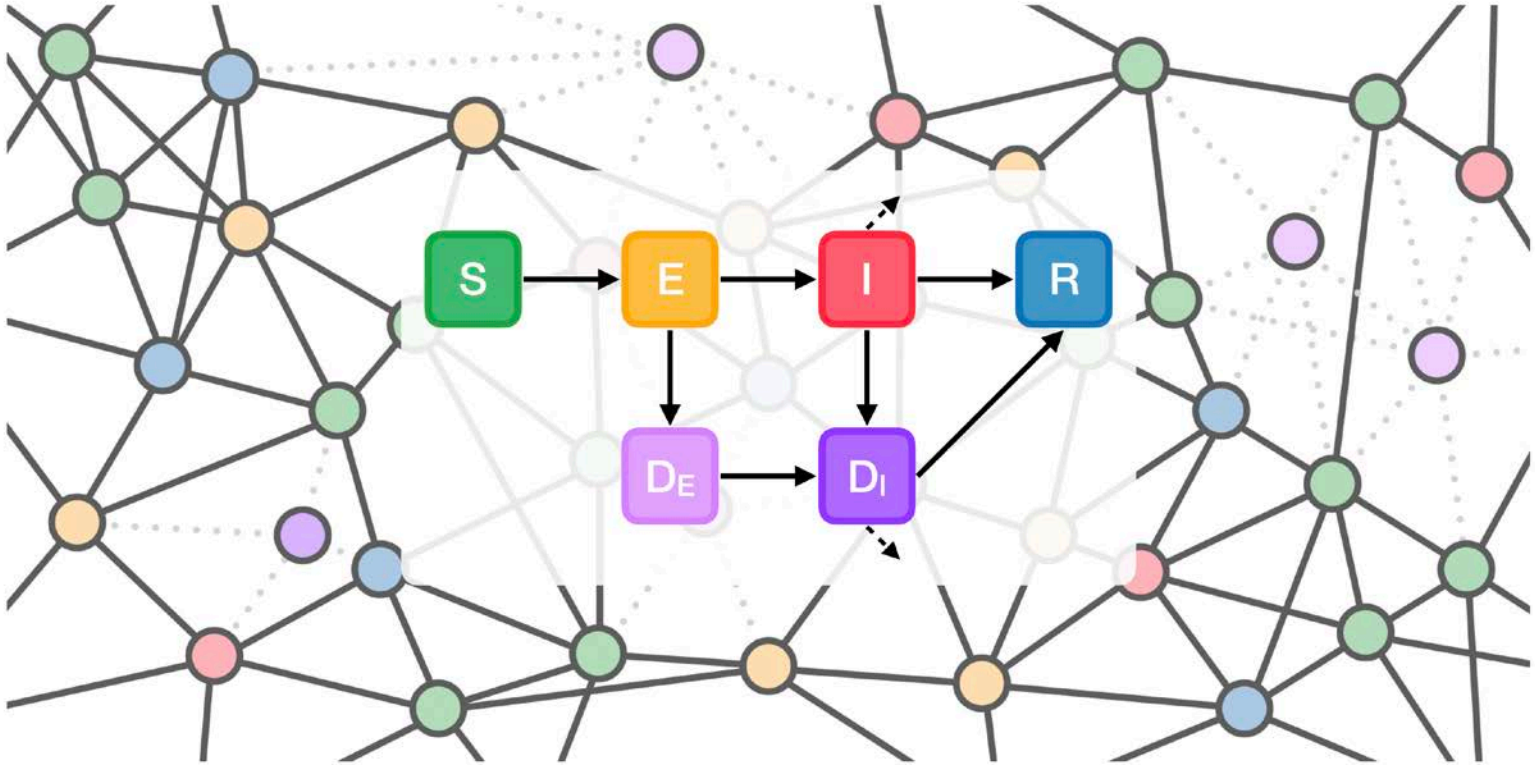


Photo: Carl Bergstrom

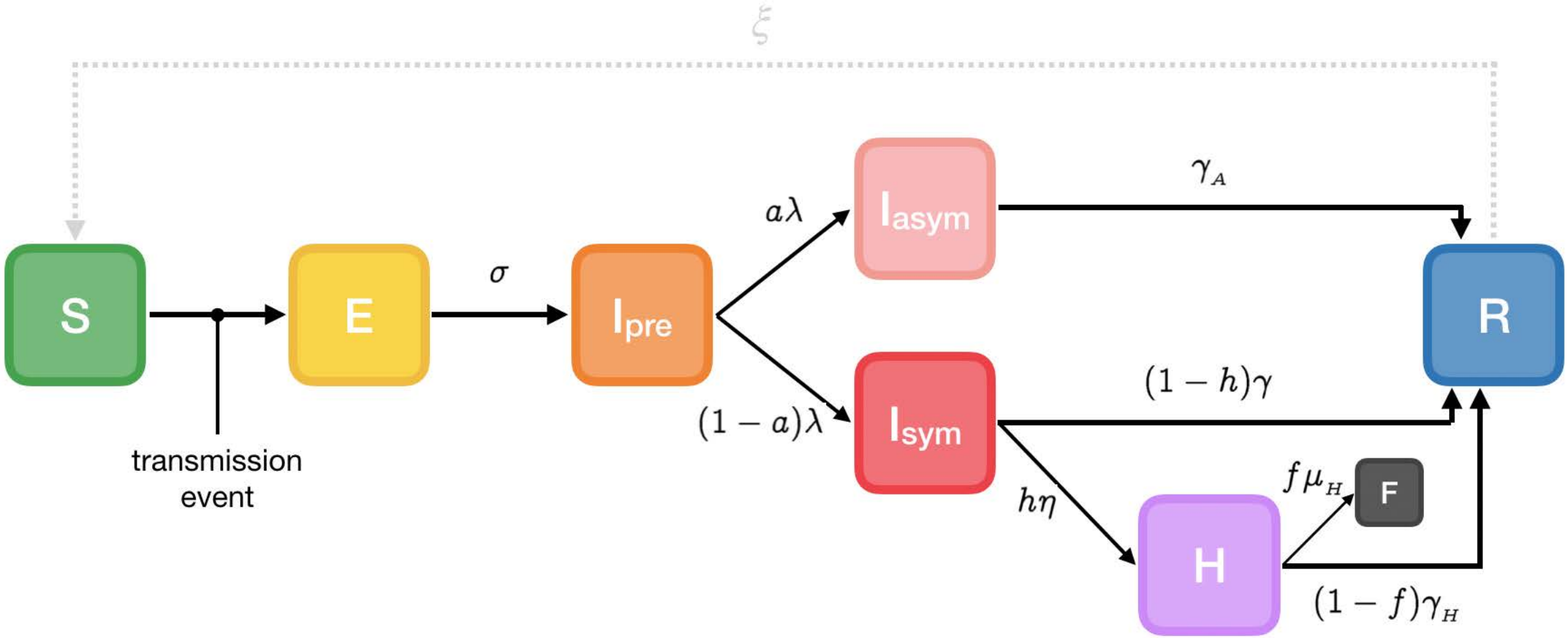
# Ryan McGee's SEIRS+ framework

Open source python-based stochastic SEIRS model with multi-level network structure, network interventions (targeted testing, social distance, contact tracing, isolation, etc.)



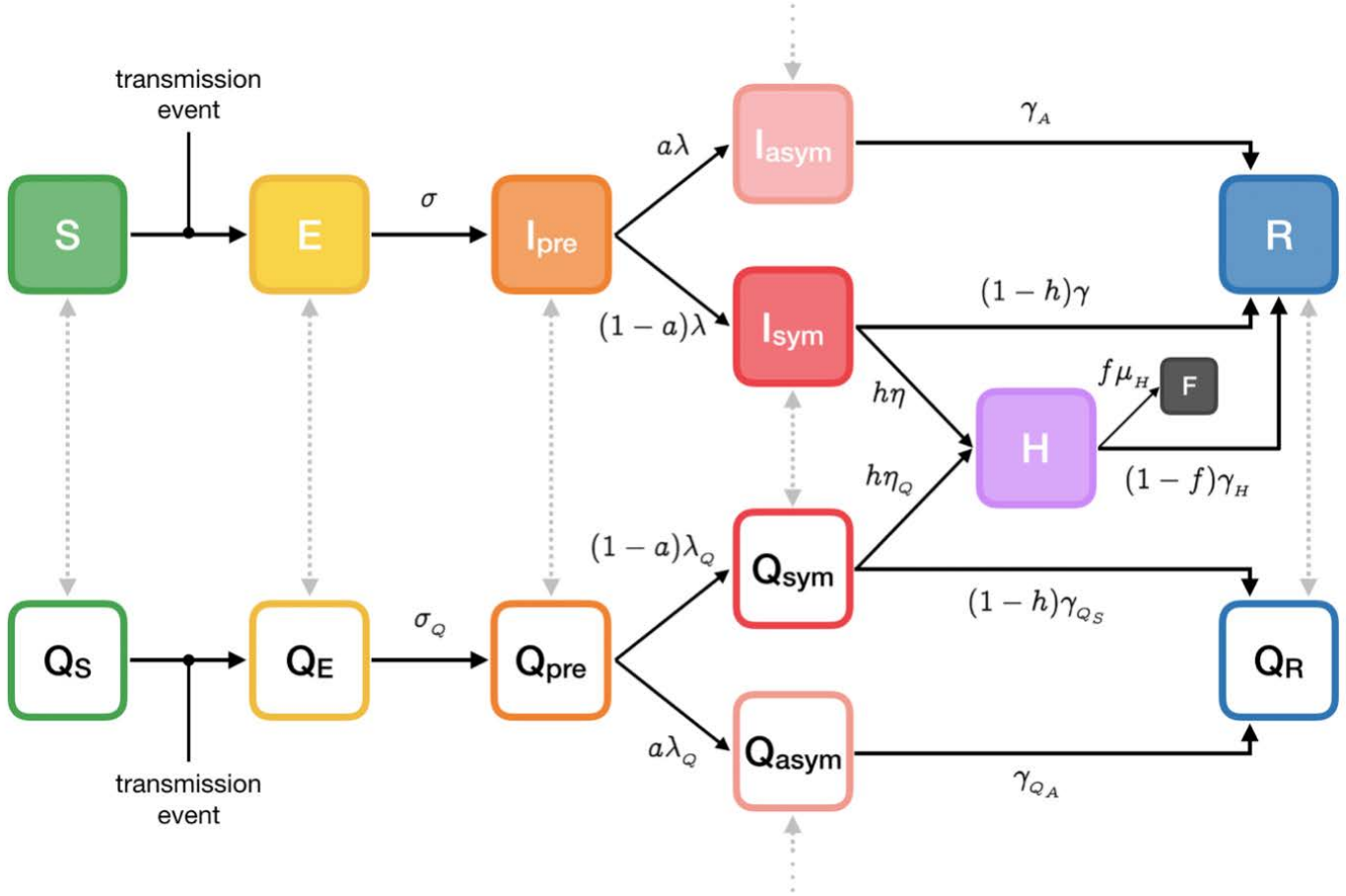

**https://github.com/ryansmcgee/seirsplus**

# Stochastic disease dynamics



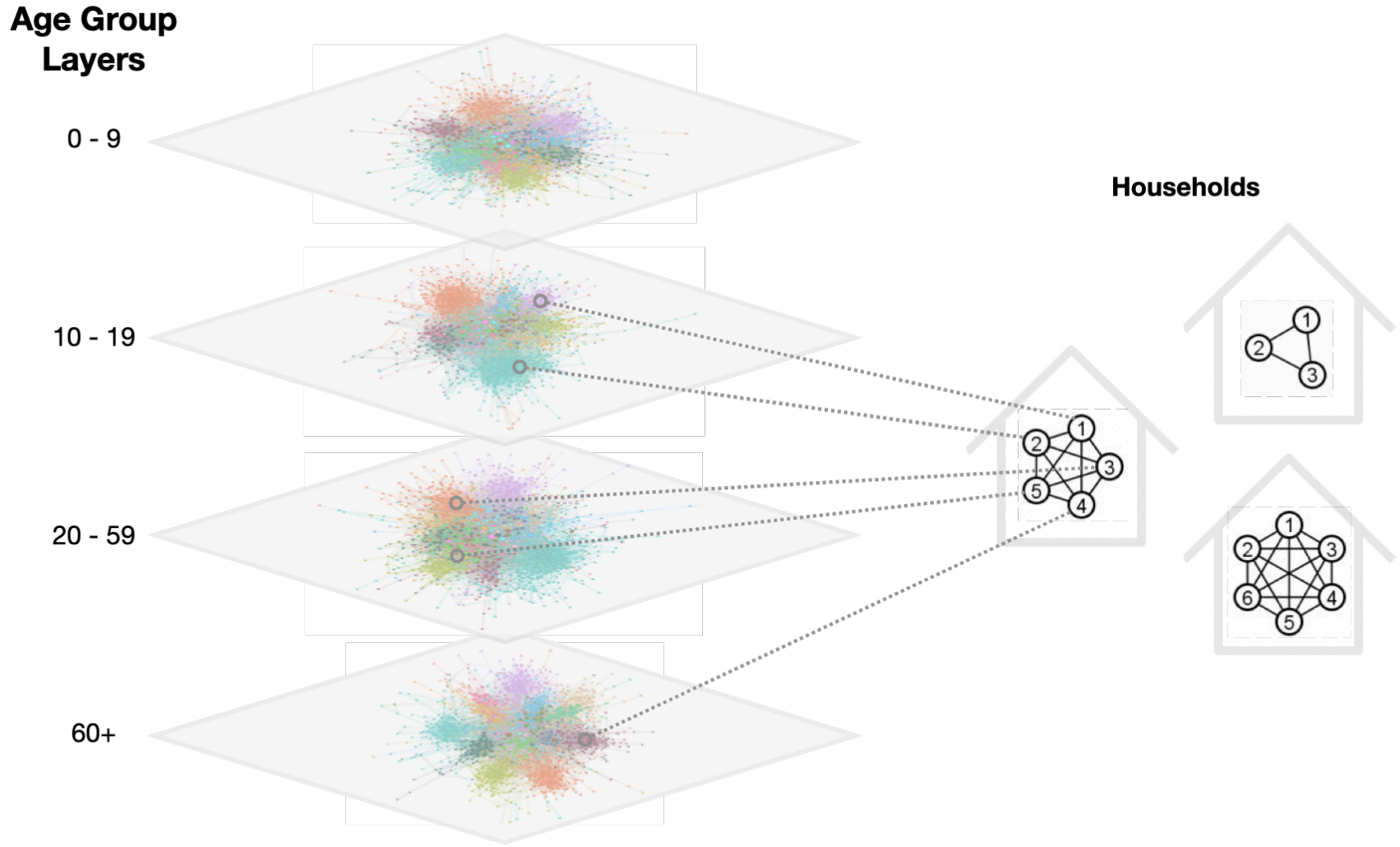

**https://github.com/ryansmcgee/seirsplus**

# Testing, tracing, and isolation




**https://github.com/ryansmcgee/seirsplus**

# Multi-level network structure

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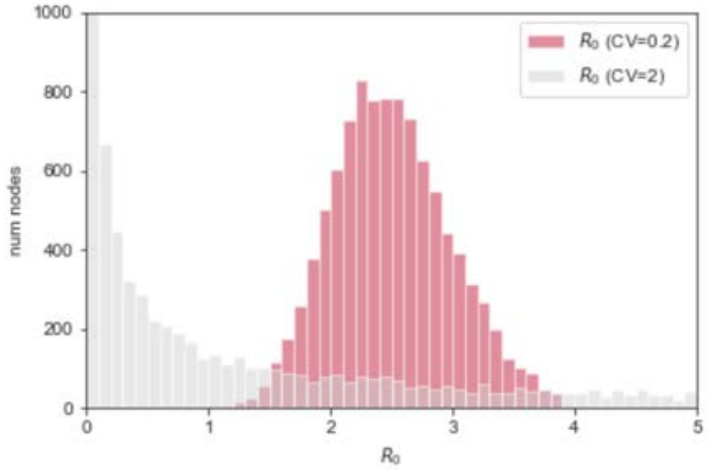
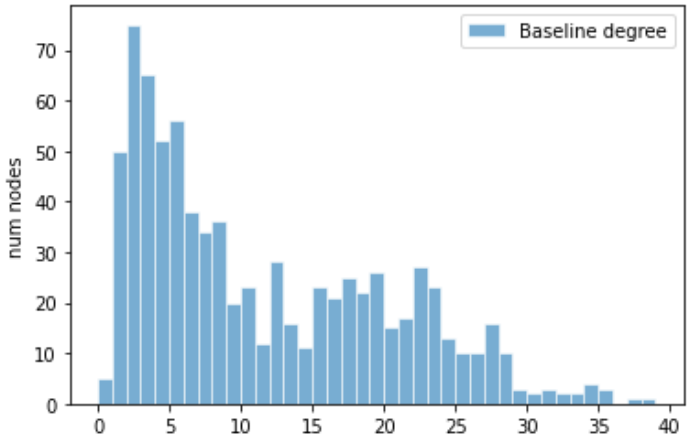
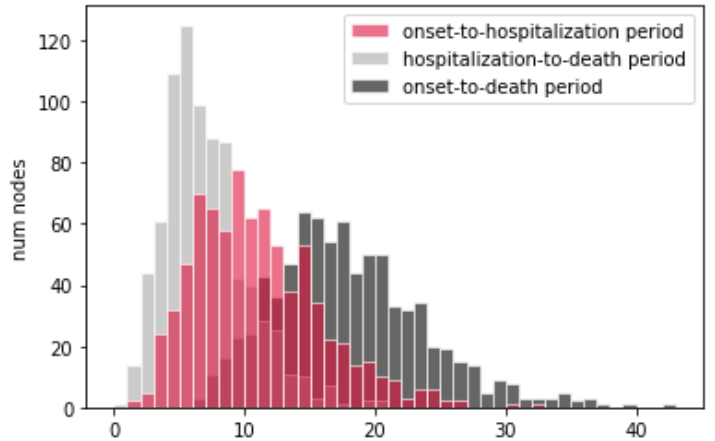
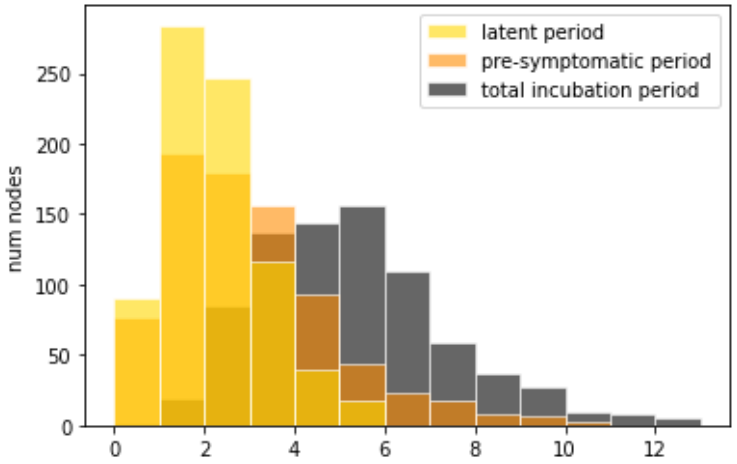
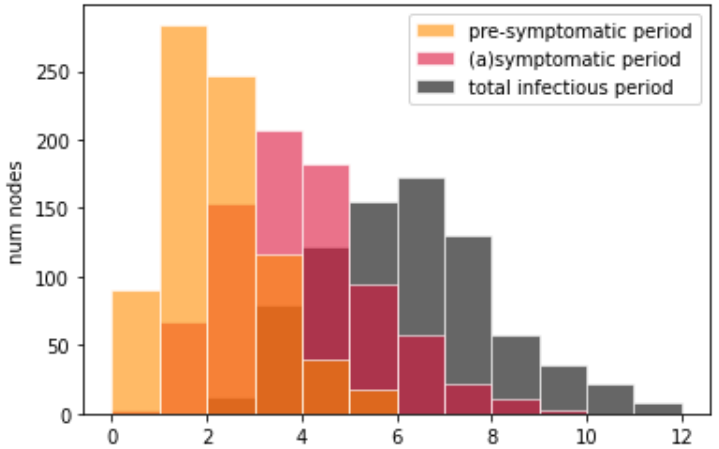
# Individual heterogeneity

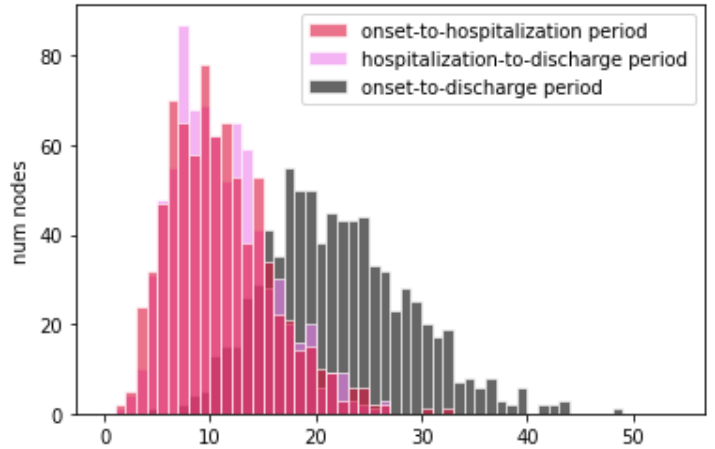


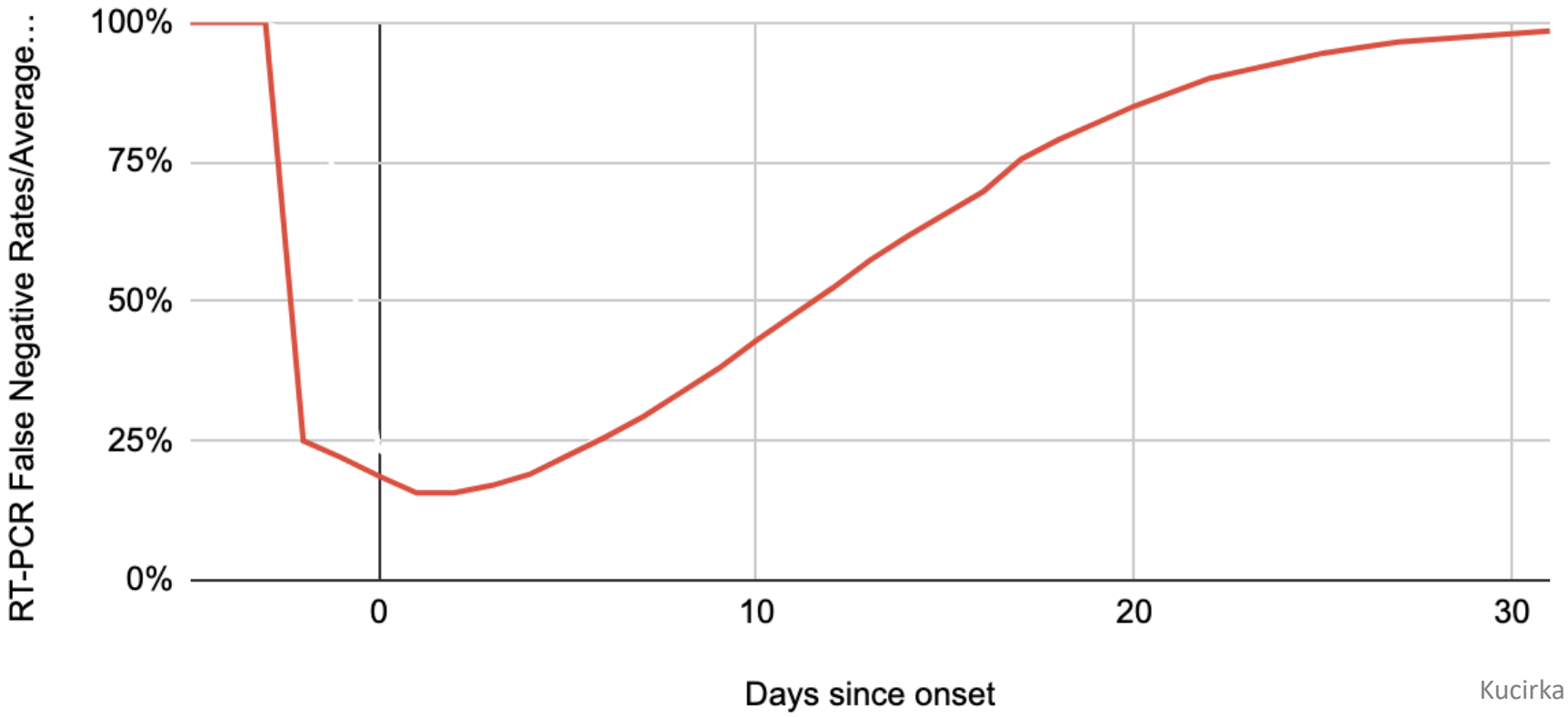



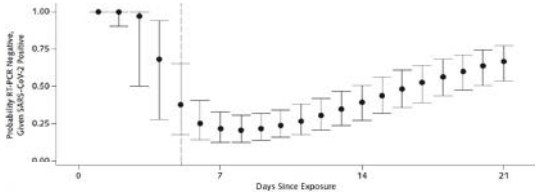




**https://github.com/ryansmcgee/seirsplus**

# Test sensitivity




Kucirka et al. 2020 *Ann. Int. Med.*



**https://github.com/ryansmcgee/seirsplus**

# Use case: workplace testing

color

**Setting**: workplaces of size 50-1000.

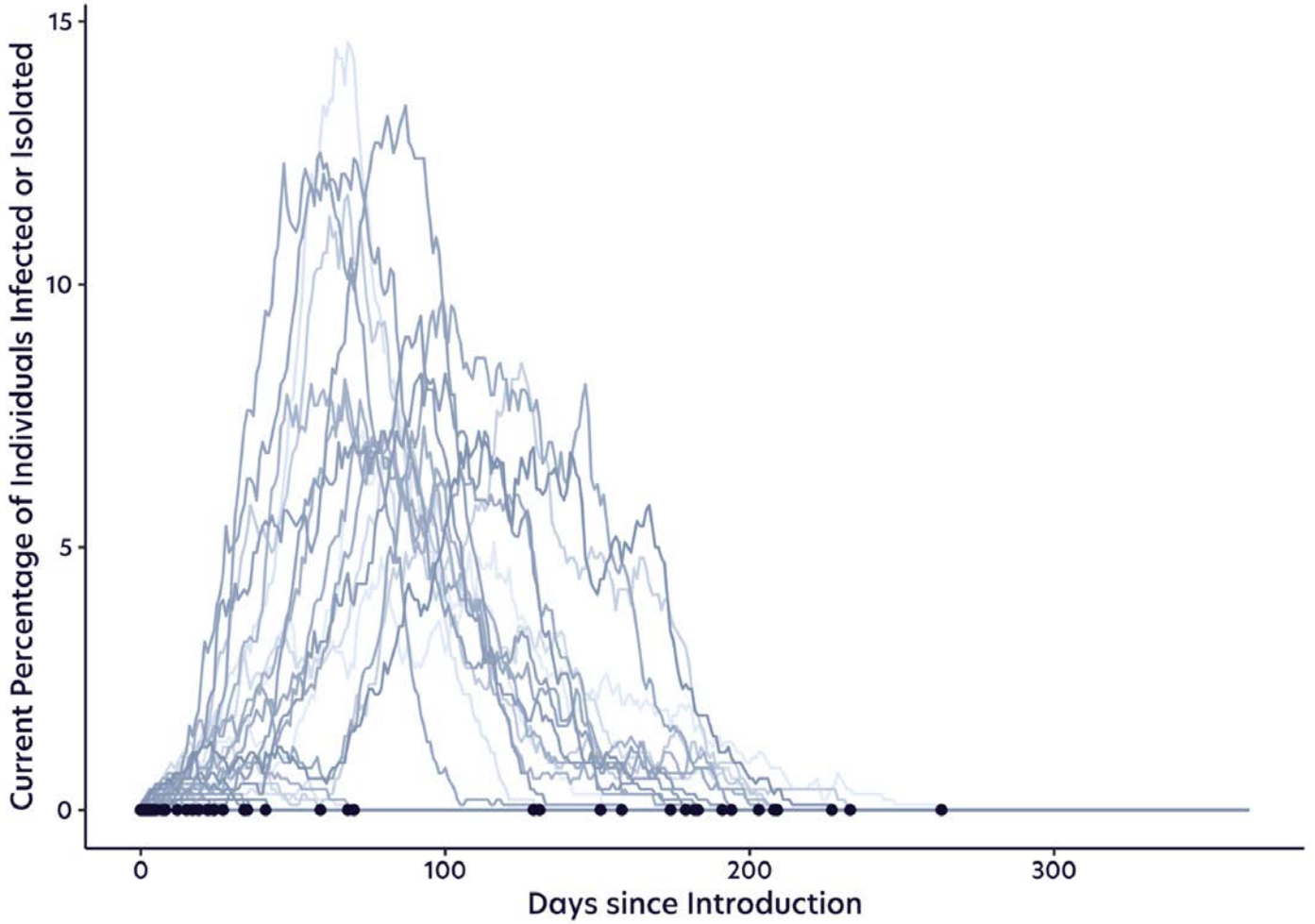
**Intervention:** self-administered workplace testing via nasal swab.

**Network:** single-layer FARZ network with 40% global transmission

**Outcome measure**: size of epidemic resulting from one introduction

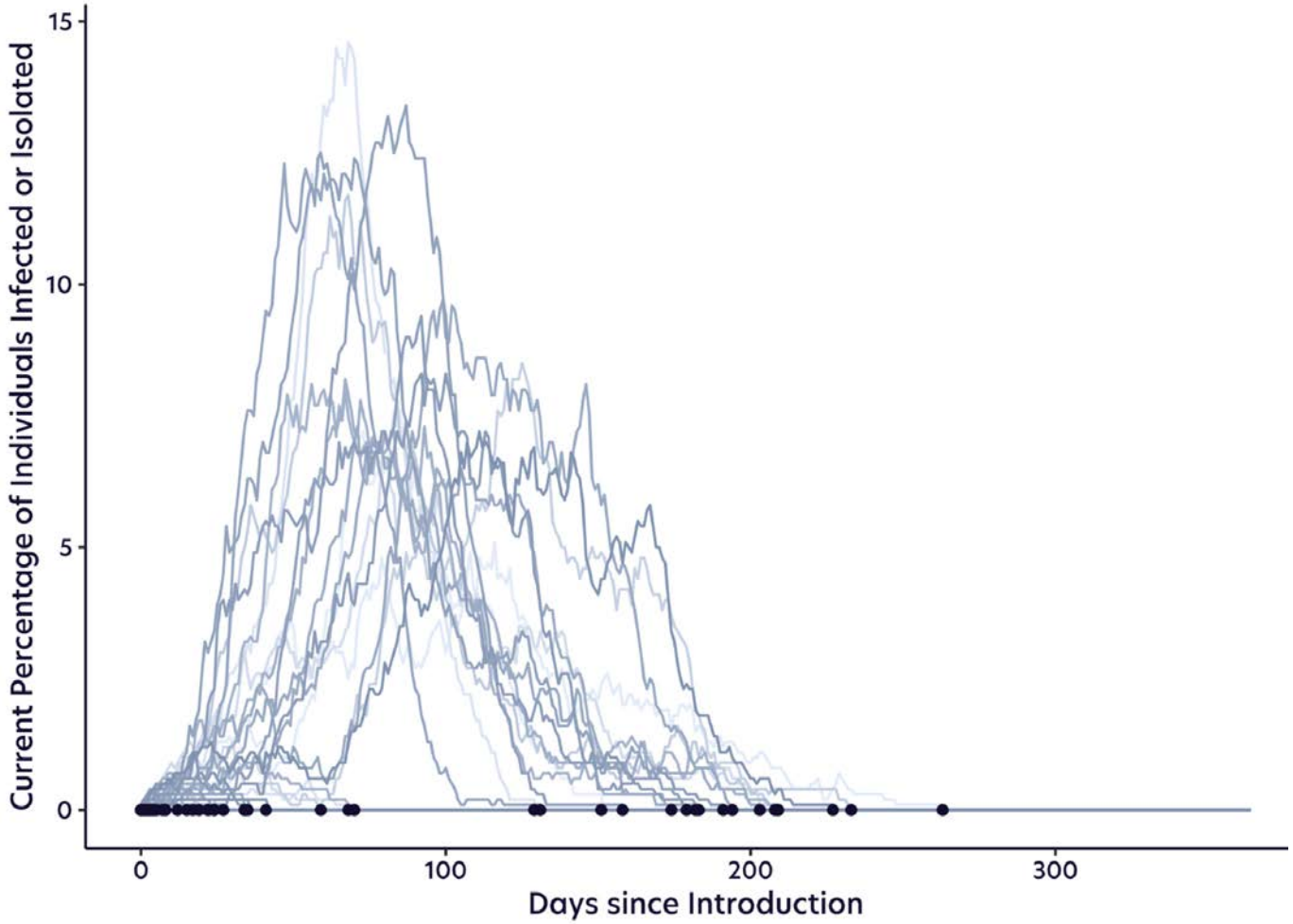
**https://www.color.com/covid-19-outbreak-model**

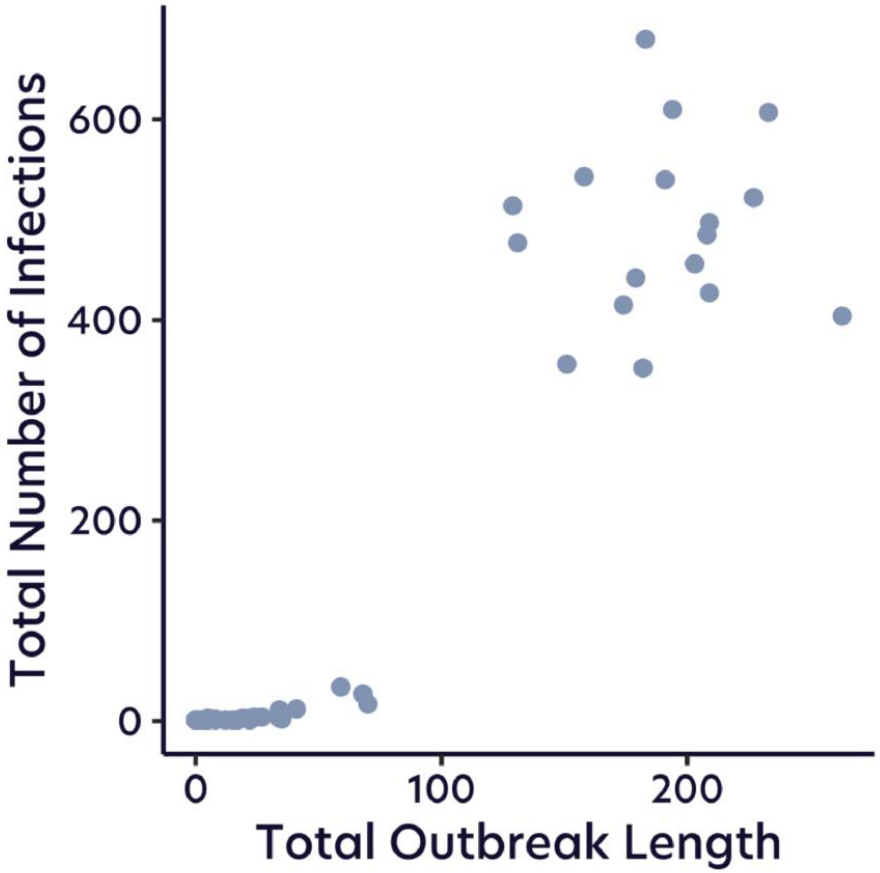
# Simulation trajectories




**https://www.color.com/covid-19-outbreak-model**

# Most outbreaks fizzle




https://www.color.com/covid-19-outbreak-model

# Testing helps

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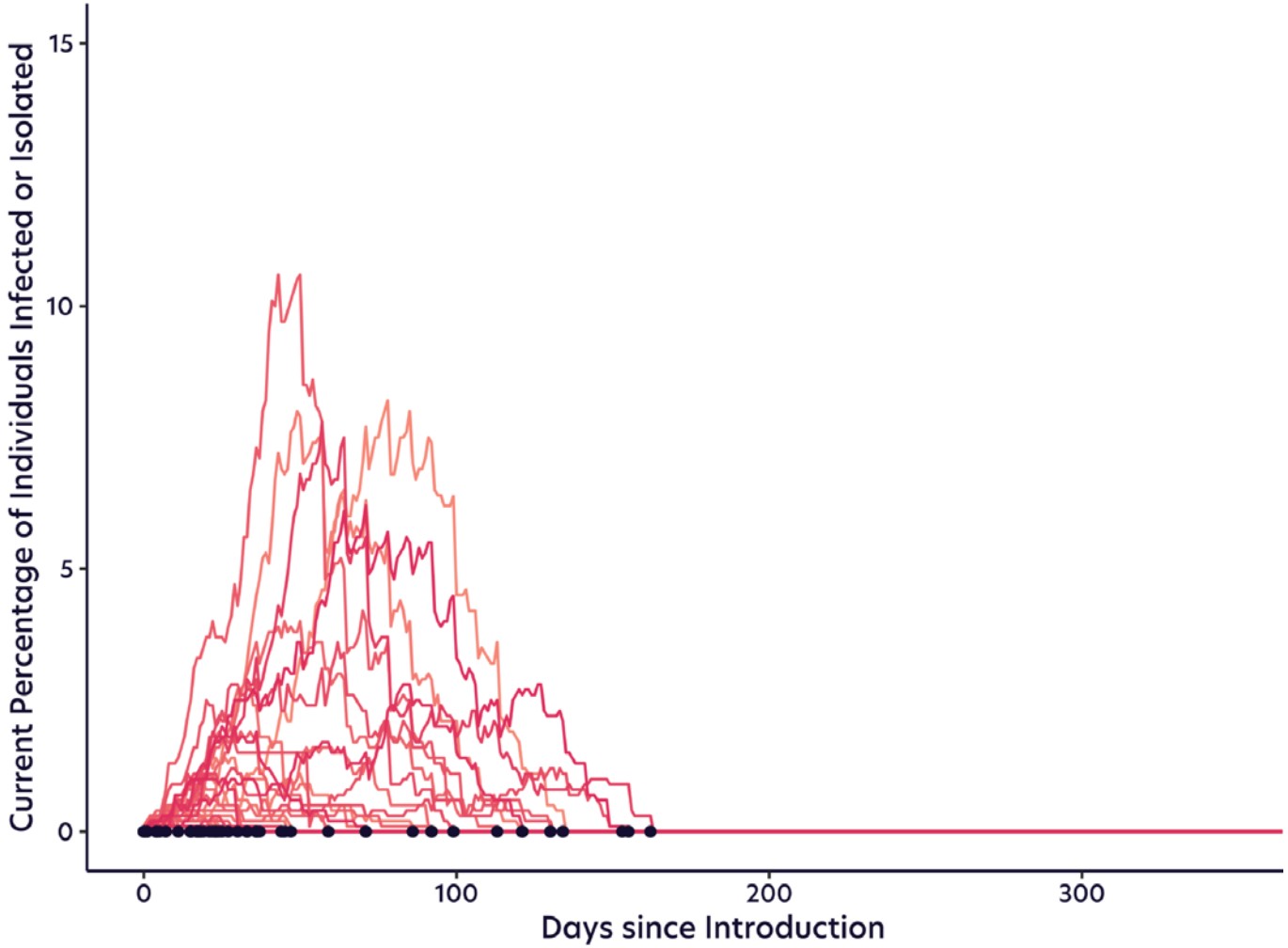


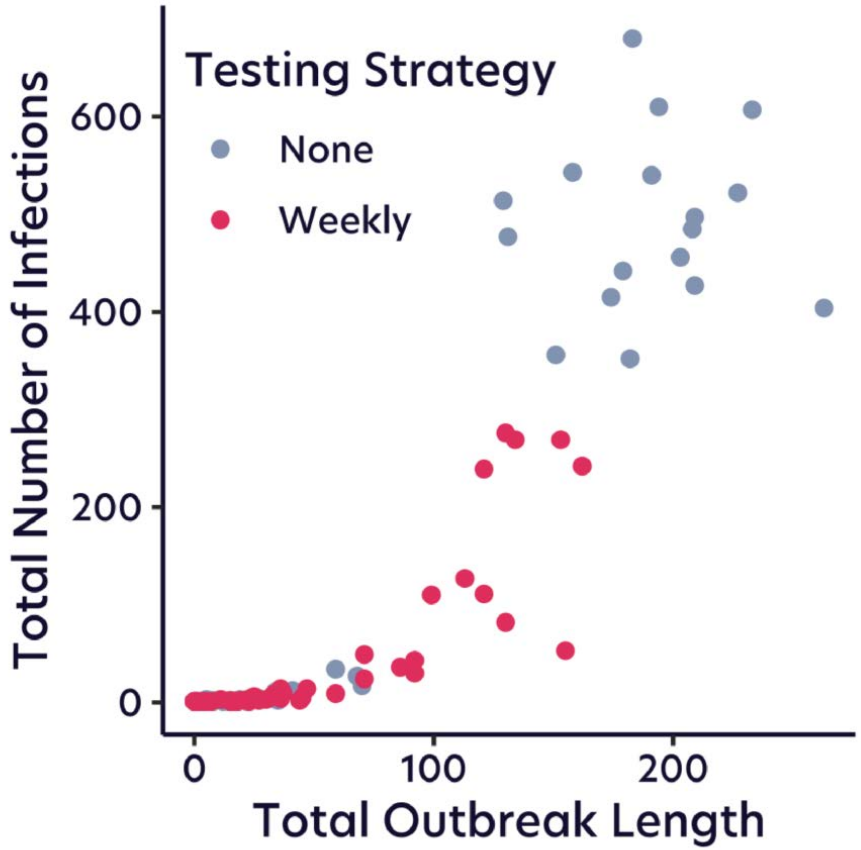


https://www.color.com/covid-19-outbreak-model

# Testing helps a lot

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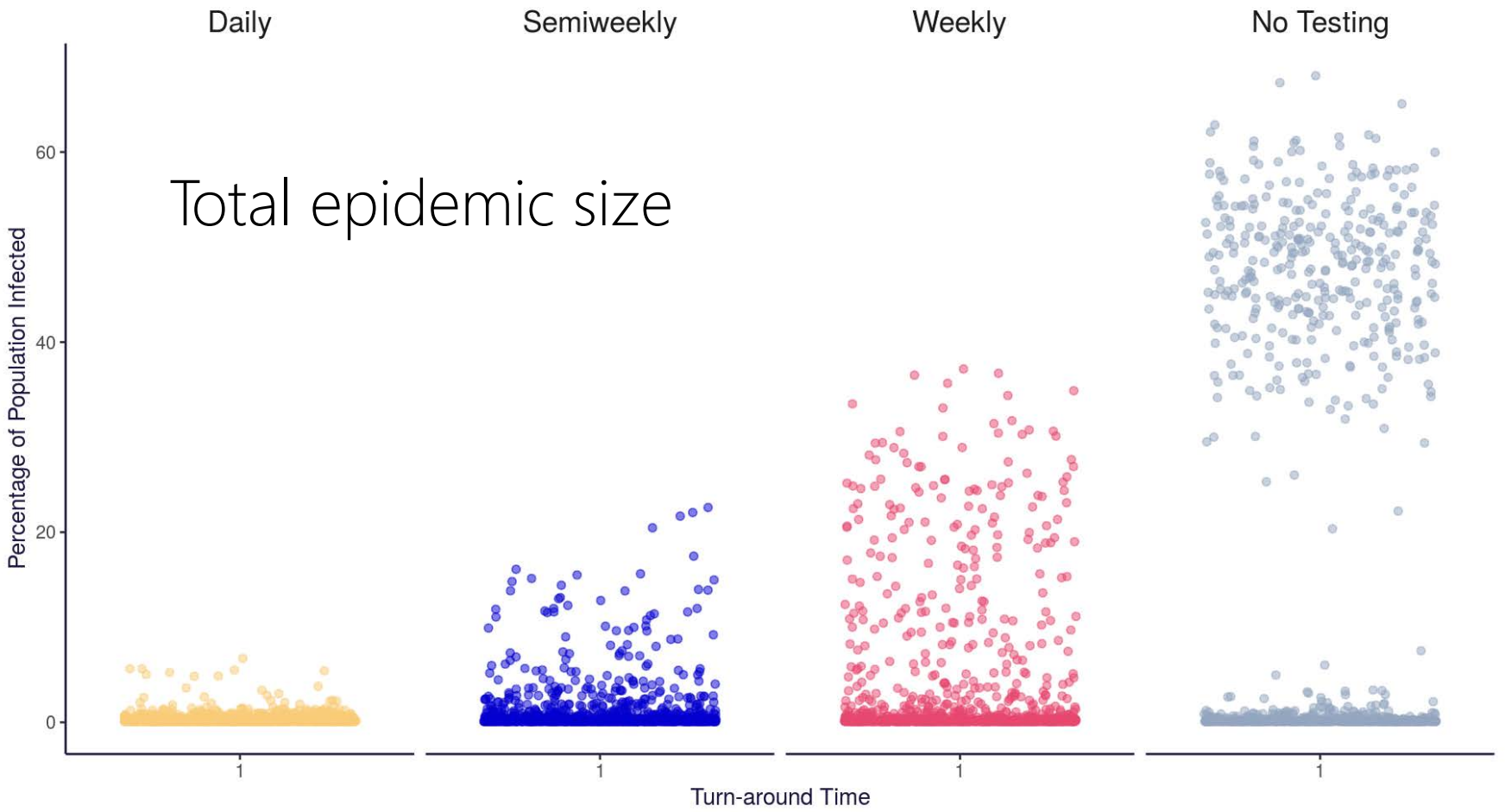
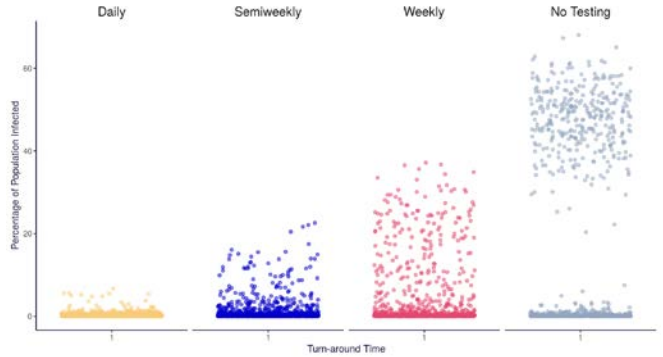



**https://www.color.com/covid-19-outbreak-model**

# Outbreak sizes

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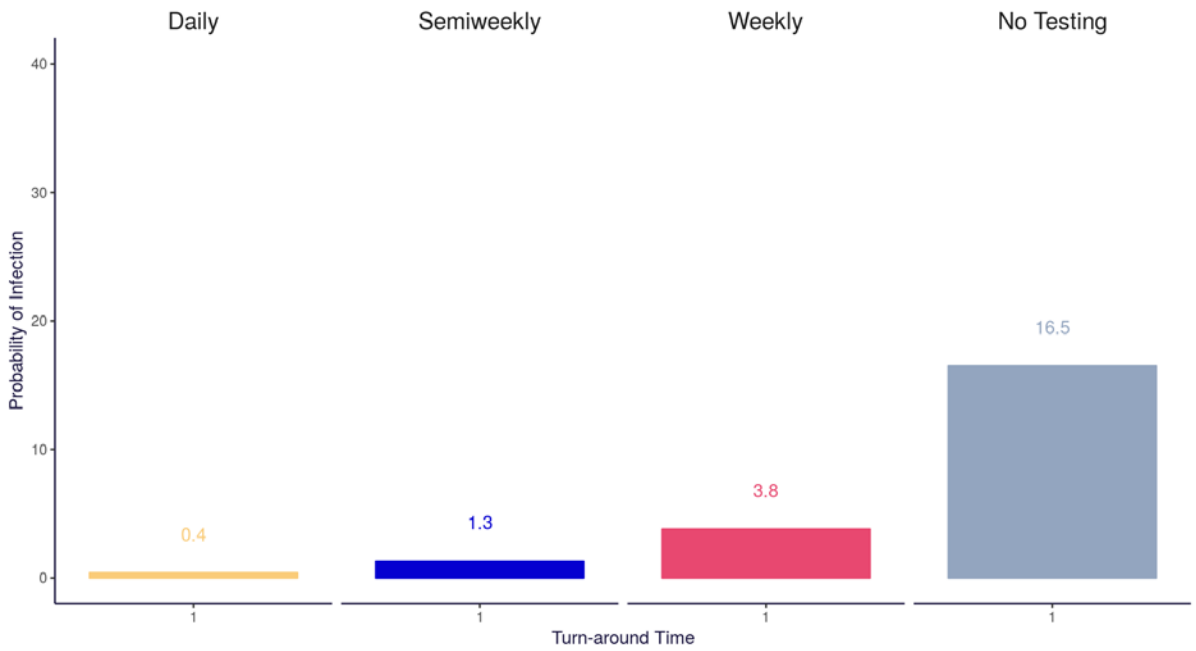
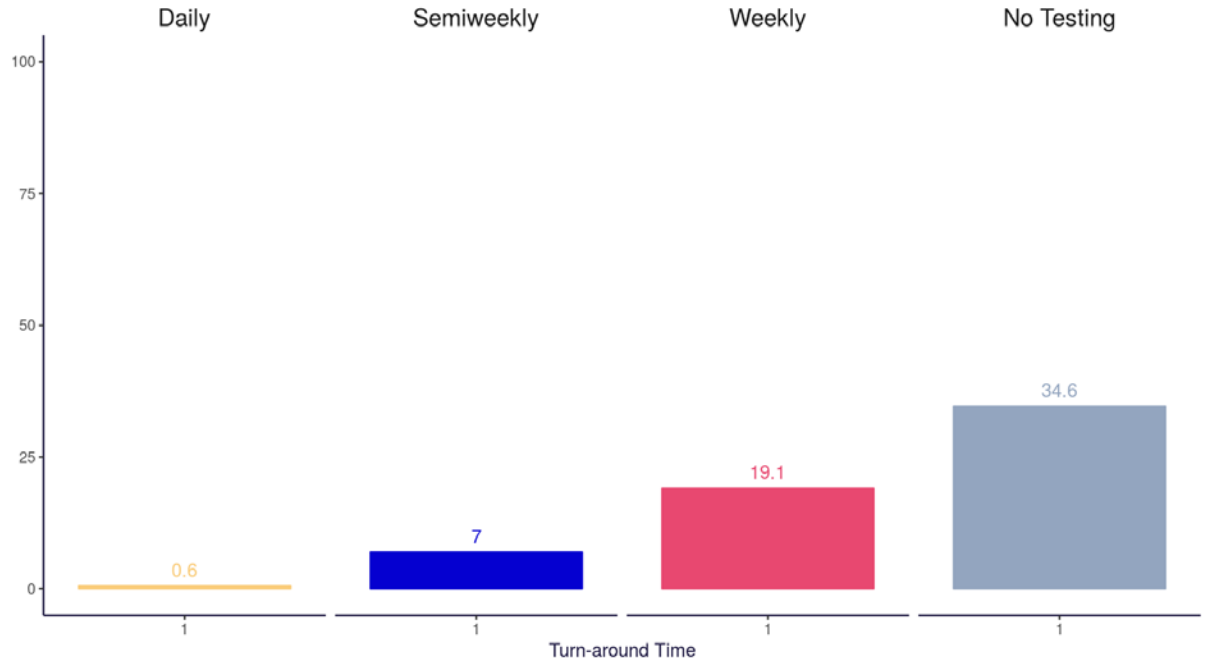
## Mean fraction infected

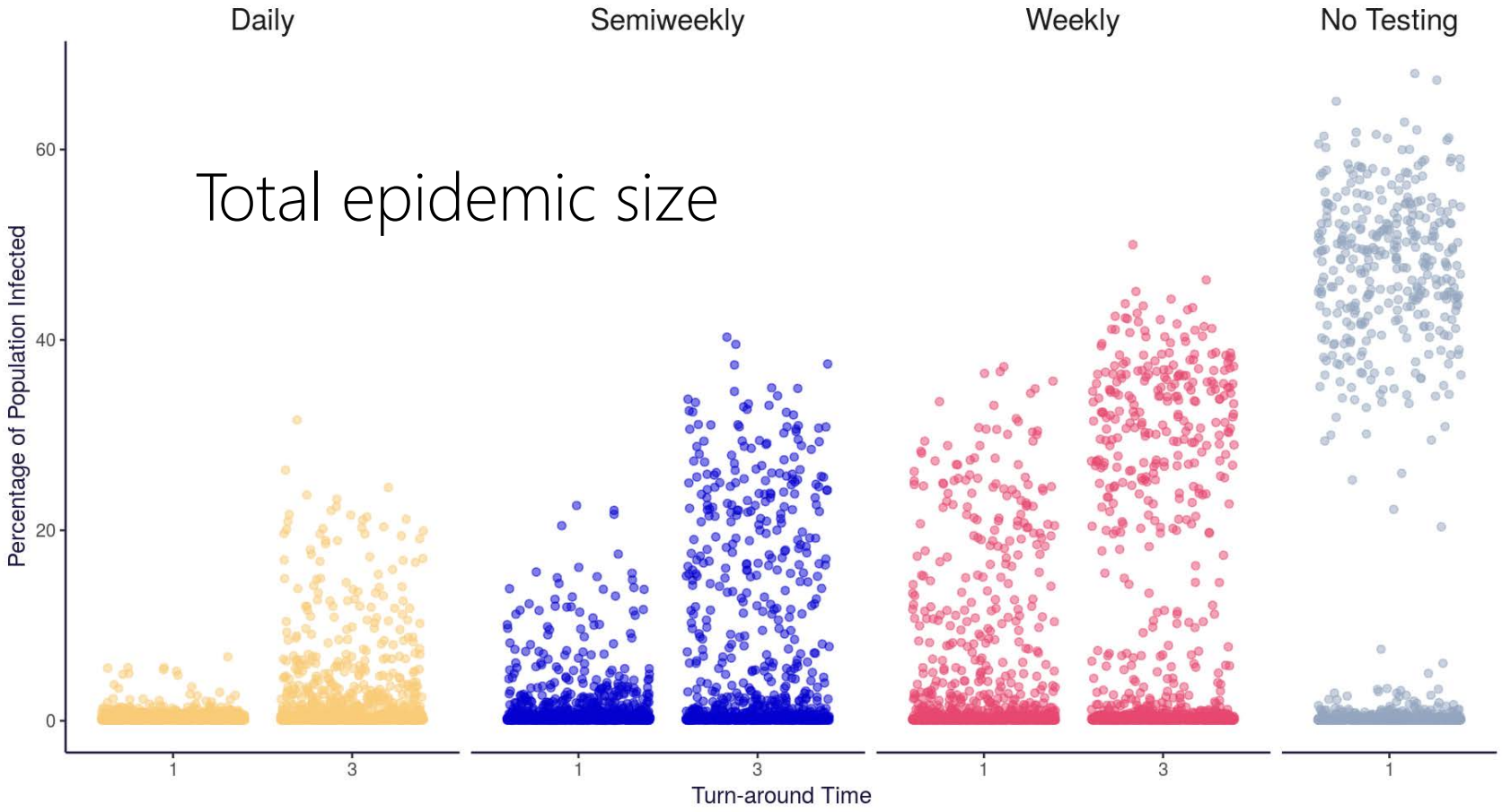


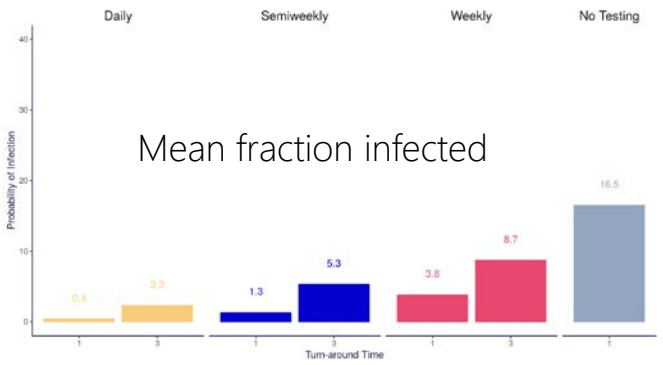

## Fraction of introductions infecting >5%

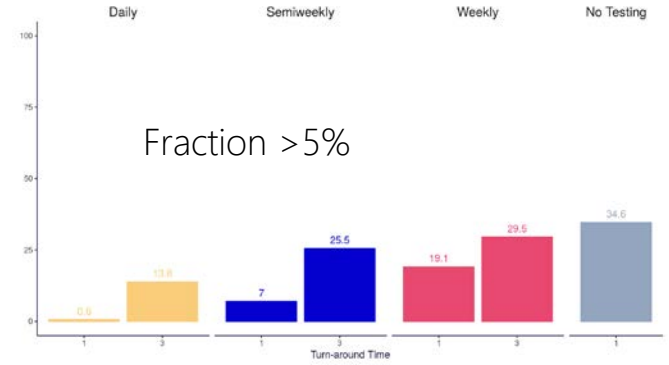



**https://www.color.com/covid-19-outbreak-model**

# Speed is of the essence




**https://www.color.com/covid-19-outbreak-model**

# Use case: community test-trace-isolate

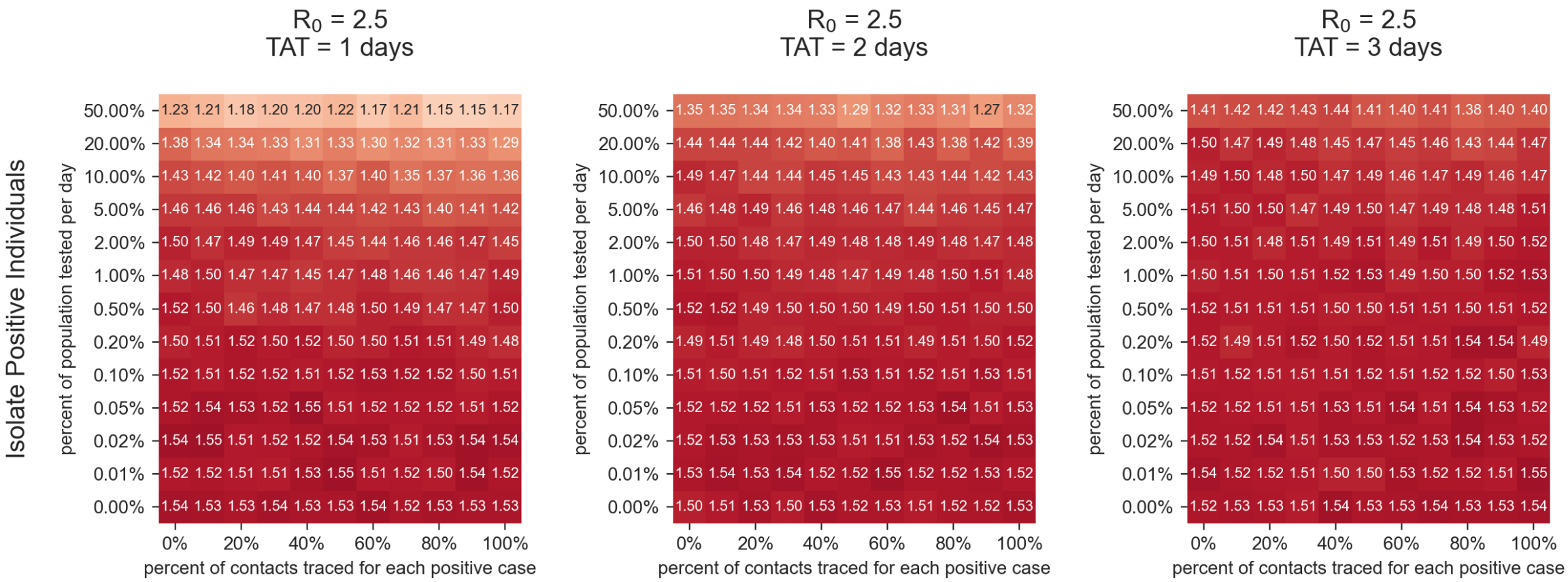
**Setting**: Community of 50,000

**Intervention:** test-trace-isolate

**Network:** multilayer FARZ with household, school, workplace structure.

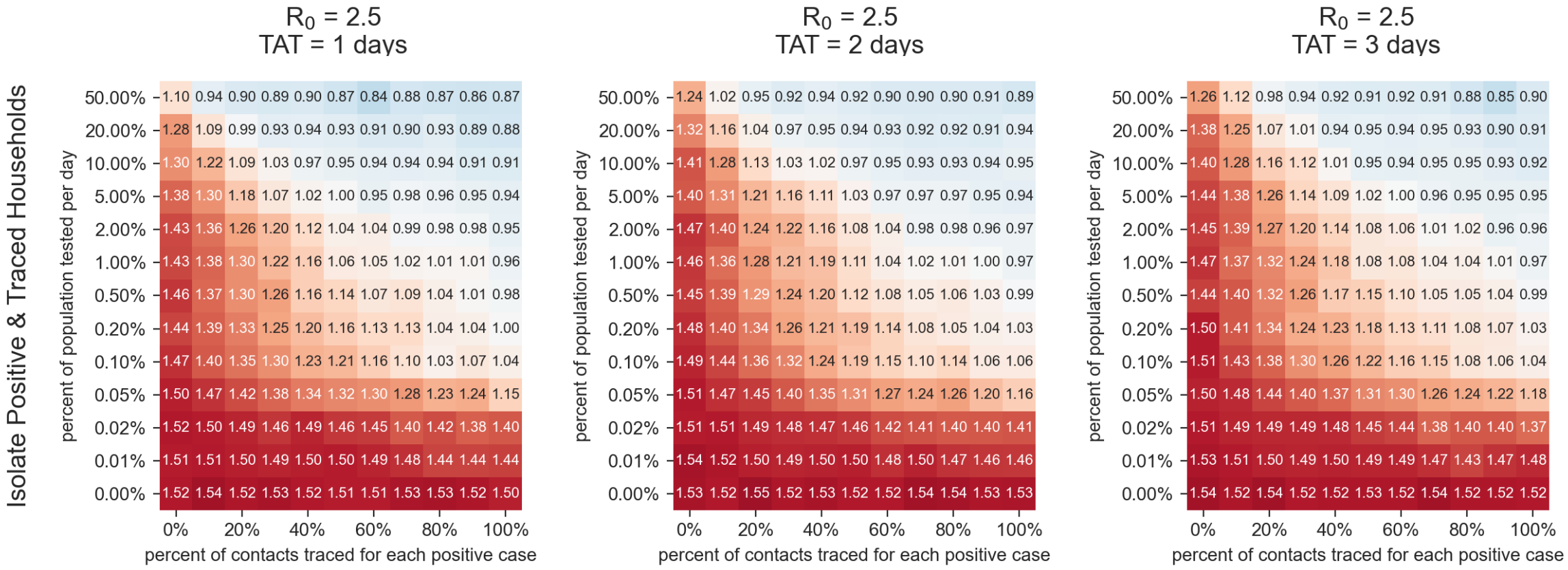
**Outcome measure**: change in effective R value

# Test and isolate only



# Test, trace, and isolate

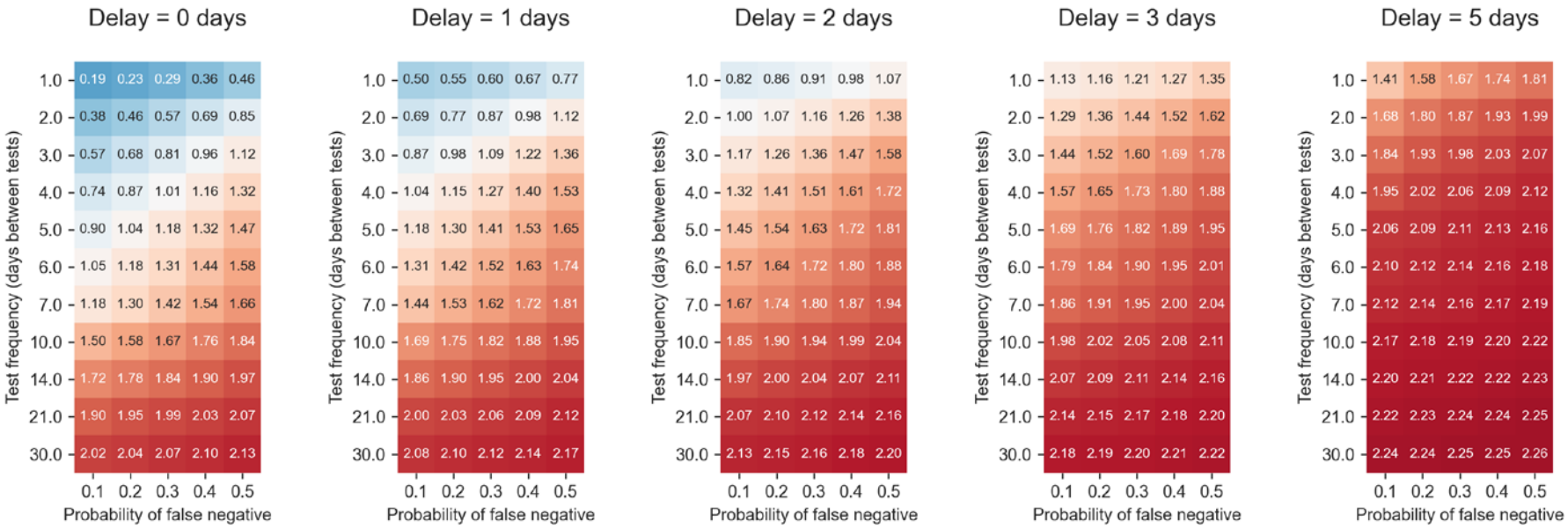
## Households of positive tests are isolated.
## Contacts traced in two days, and isolated along with household.

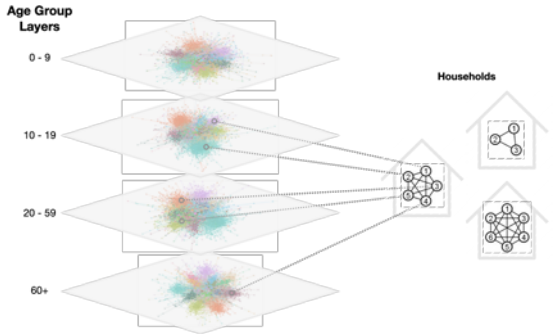


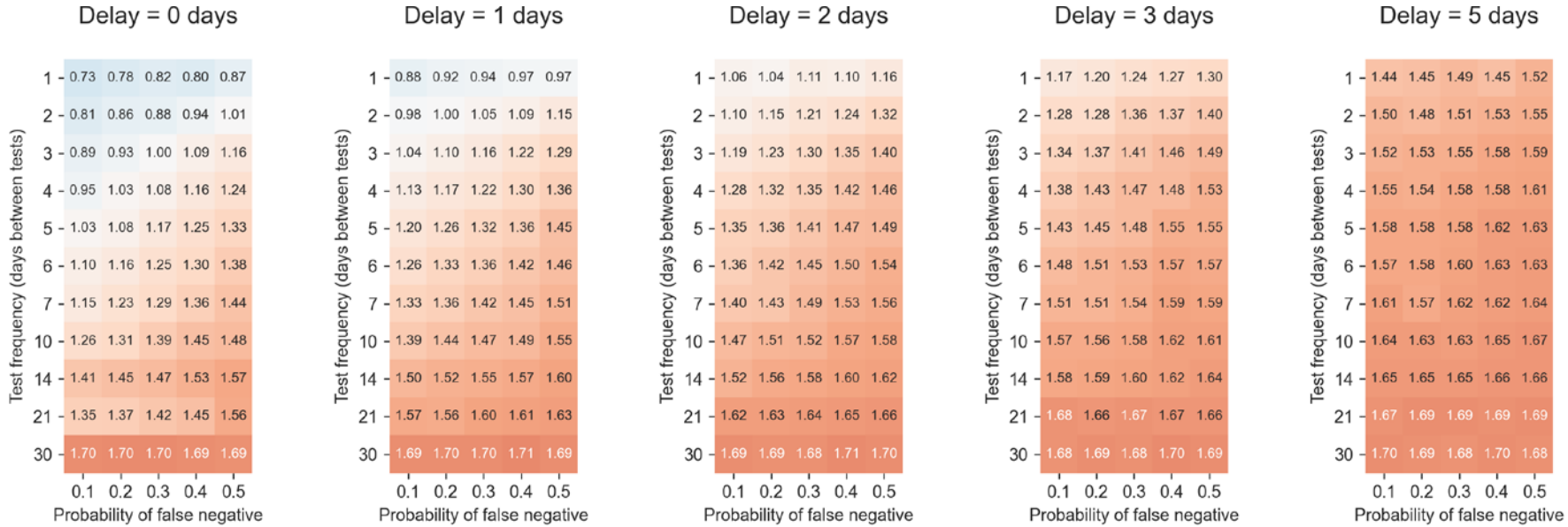
# Comparing with the analytic approximation

$$\phi = \frac{(1-(1-u)v)E(C,\tau) + (1-u)vE(y,\tau)}{(1-(1-u)v)C + (1-u)v\,y}$$

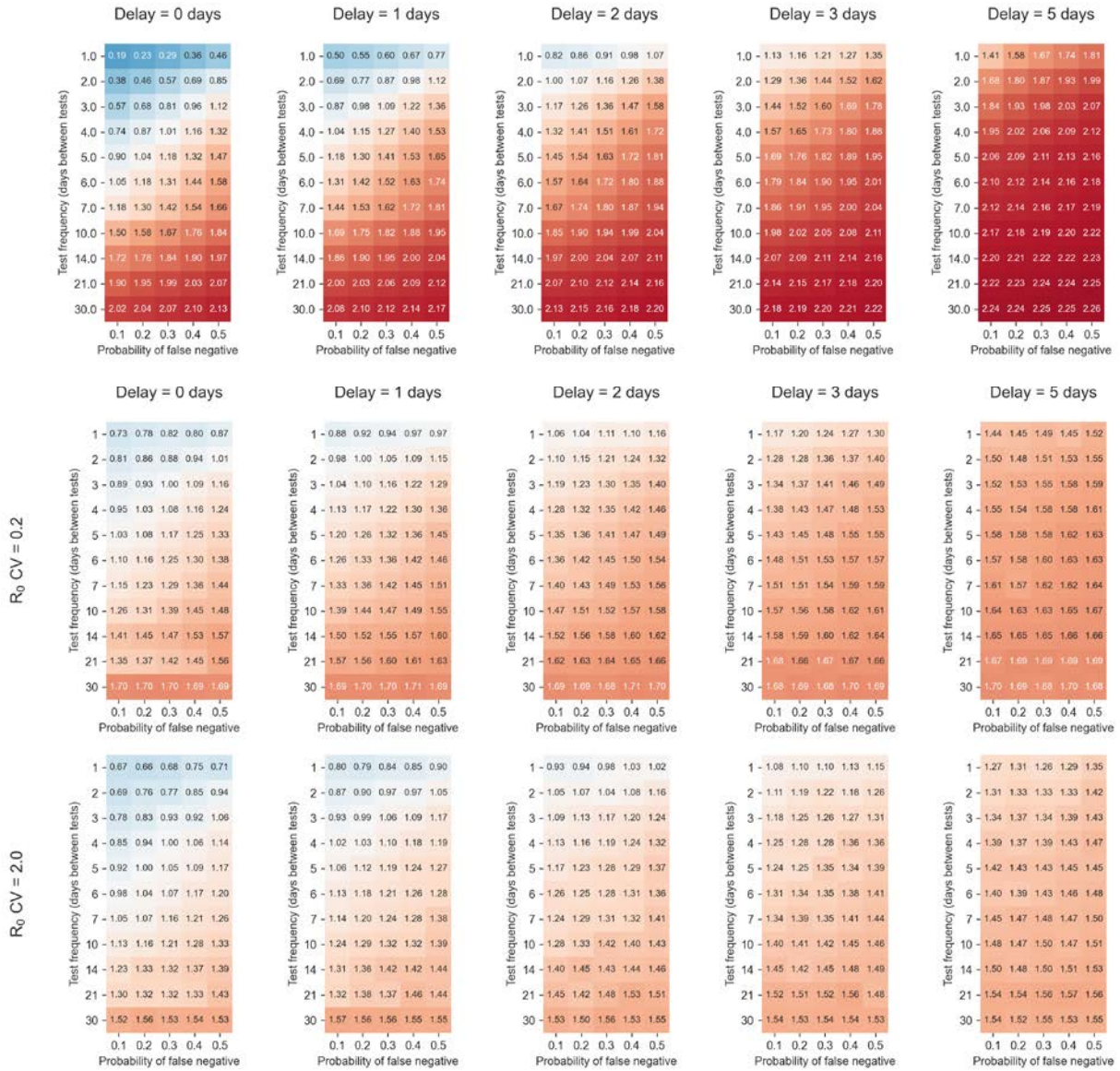
Asymptomatic or don't isolate — Self-isolate



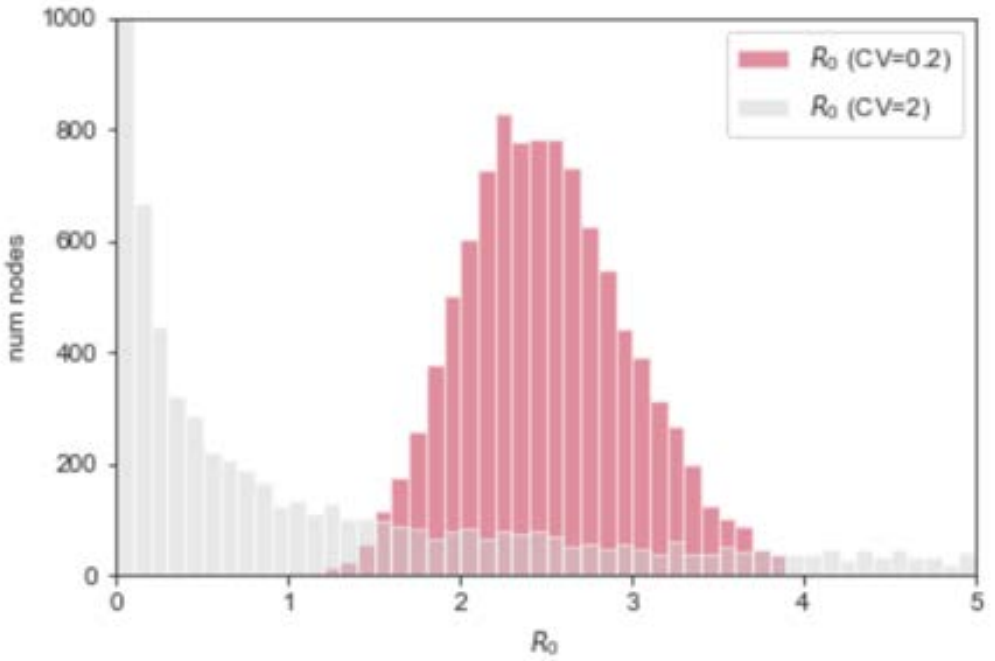



# Comparing with the analytic approximation




$$\phi = \frac{\big(1-(1-u)v\big)E(C,\tau) + (1-u)vE(y,\tau)}{\big(1-(1-u)v\big)C + (1-u)v\,y}$$

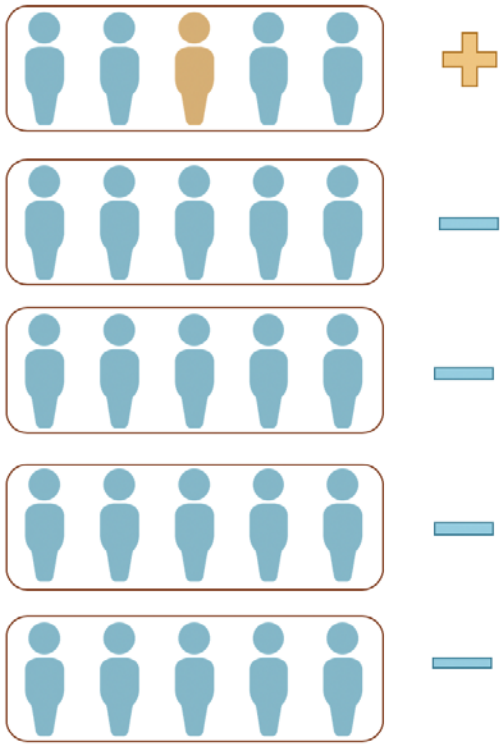
Asymptomatic or don't isolate — Self-isolate



# Pooled testing stretches capacity.

Using standard testing it would take 25 tests to determine which of these 25 people are infected with Covid.

# Pooled testing stretches capacity.

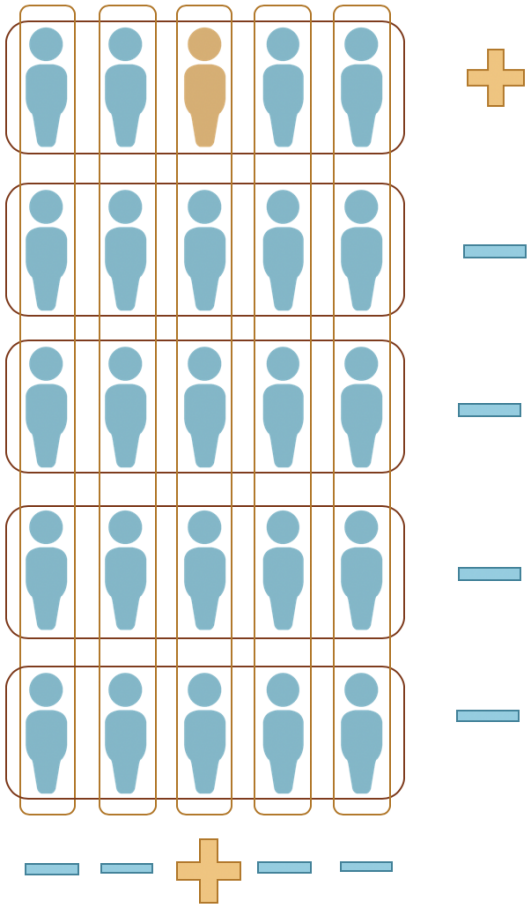


5 pooled tests

5 individual tests

Pooling stretches test capacity but requires re-testing stored samples from batches that test positive.

# Pooled testing stretches capacity.



Double-pooling stretches test capacity without having to go back and re-test

# Take-home messages

Proactive testing can help control the epidemic…

…but the speed of turnaround is essential.

Simple models give decent approximations and allow
quick exploration of speed / sensitivity / volume / cost tradeoffs.

Network structure and heterogeneity matter—especially for rapid spread.

Photo: Carl Bergstrom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