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School of Biological Sciences
College of Sciences
Georgia Institute of Technology

Science and Projections for a Return to Campus

Greg Gibson
School of Biological Sciences
Center for Integrative Genomics
Bioinformatics Program

Joshua S. Weitz
School of Biological Sciences
School of Physics
Center for Microbial Dynamics & Infection
Quantitative Biosciences Program
jsweitz@gatech.edu

Email: jsweitz@gatech.edu
Web: http://ecotheory.biology.gatech.edu

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Prof. Joshua Weitz
Email: jsweitz@gatech.edu
Twitter: @joshuasweitz
Web: ecotheory.biosci.gatech.edu

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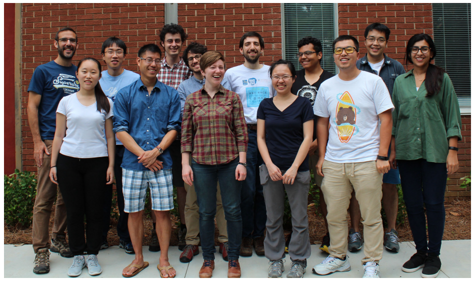
This work is the result of ongoing interdisciplinary collaborations:

Georgia Tech Team
Ashley Coenen
Dr. Stephen Beckett
Dr. David Demory
Marian Dominguez-Mirazo
Dr. Jeremy Harris
Dr. Joey Leung
Guanlin Li
Andreea Magalie
Daniel Muratore
Rogelio Rodriguez-Gonzalez
Dr. Adriana Sanz
Shashwat Shivam
Conan Zhao

Collaborators
Clio Andris, GT
Daniel Cornforth, GT
Aroon Chande, GT
Jonathan Dushoff, McMaster
Ceyhun Eksin, Texas A&M
Greg Gibson, GT
Mallory Harris, Stanford
Michael Hochberg, Montpellier
Seolha Lee, GT
Benjamin Lopman, Emory
Alicia Kraal, Emory
Kristin Nelson, Emory
Sang Woo Park, Princeton
Yorai Wardi, GT



Pre-Covid picture

Funding, disclosures, and thank you-s

Prof. Greg Gibson
Email: greg.gibson@biology.gatech.edu
Blog: http://genomestake.blogspot.com/
Web: https://cig.gatech.edu/

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This work is the result of ongoing interdisciplinary collaborations:

Mike Shannon

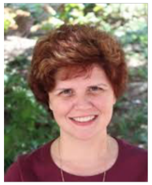
GTRI Leaders

Mike Farrell

Anton Bryksin

IBB Core Directors

Dalia Gulick



JulieAnne Williamson

Logistics

Alex Ortiz

Emily Ryan

CLIA Director

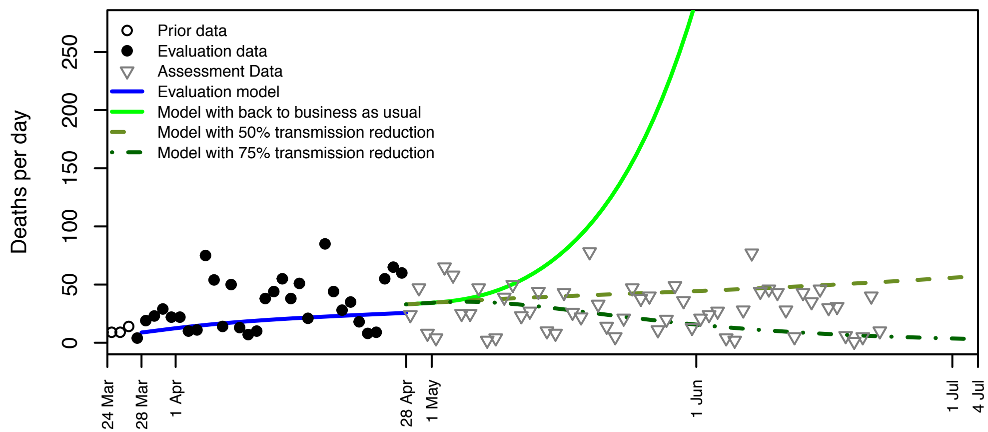
IT Leads

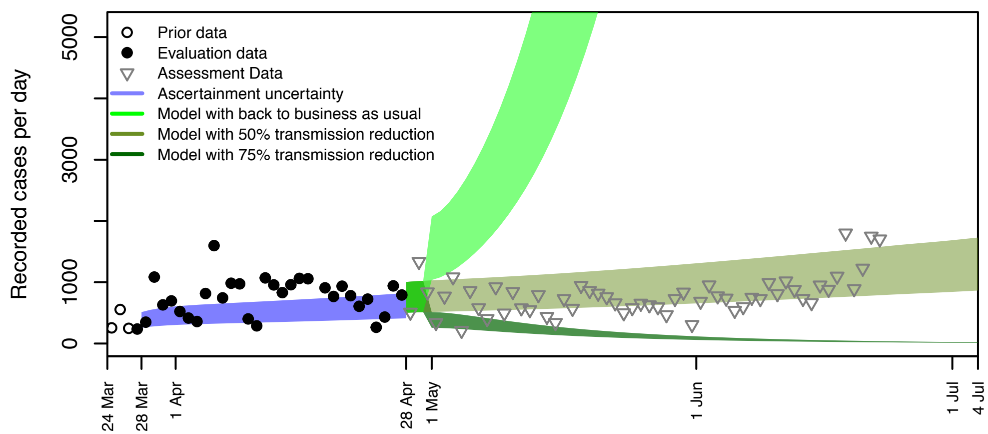
Aroon Chande
Brian Liu

LAB: Jessica Lin, German Khunteev, Naima Djeddar, Katie Ferguson, Chase Morey, several TBN

OTHER: Communications, Legal, Housing, Administration (Andrés Garcia, Chaouki Abdallah, Frank Neville)

Georgia Projections from late April 2020
Beckett et al. (medrxiv; Weitz group)



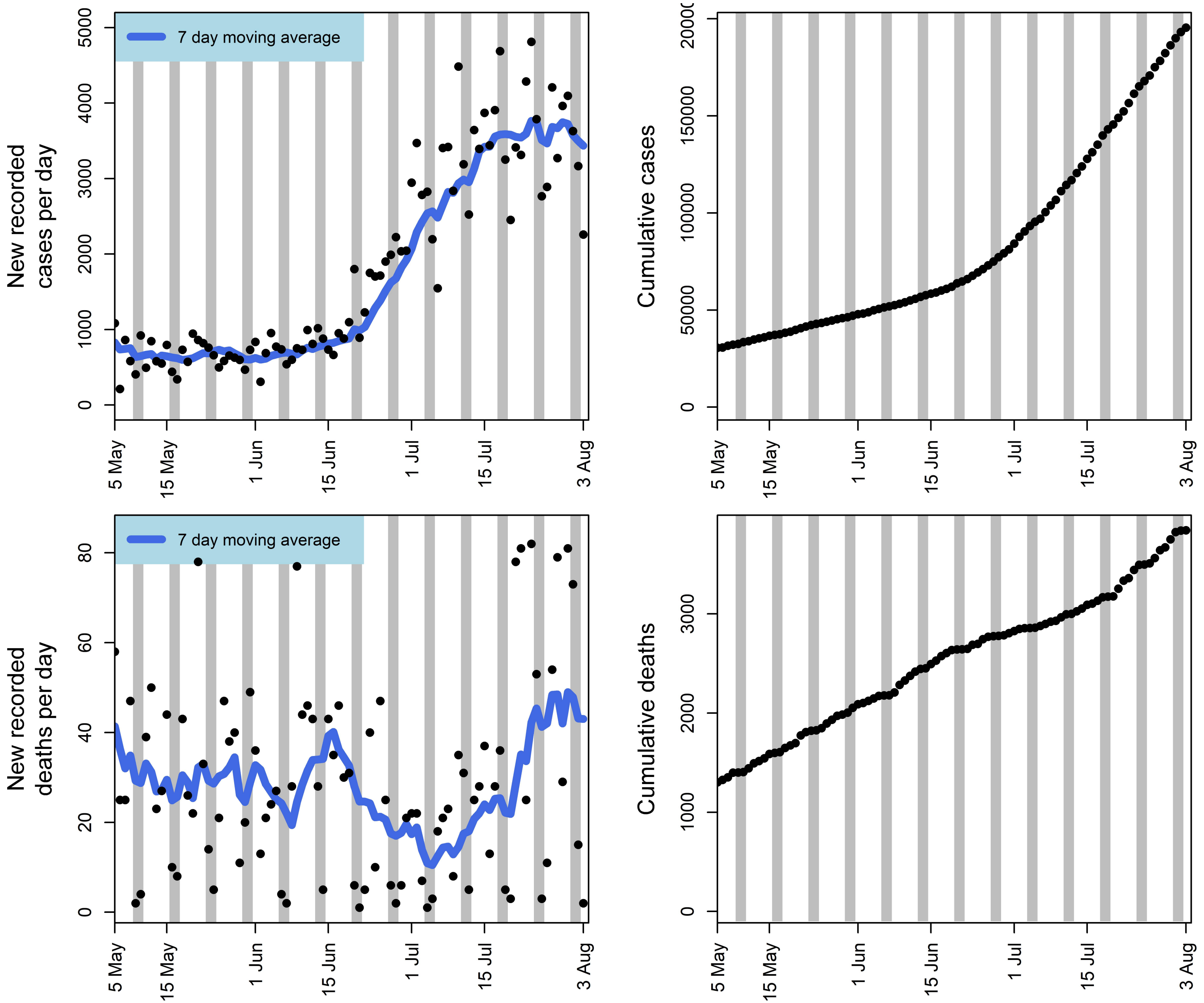


Summary:
Model trained w/age-structured model based on deaths/hospitalizations in April.

Predictions of continued ~50% social distancing suggested multi-month 'plateau' in cases.

Yet there were always far worse alternatives, given that we remain almost entirely immunologically naieve.

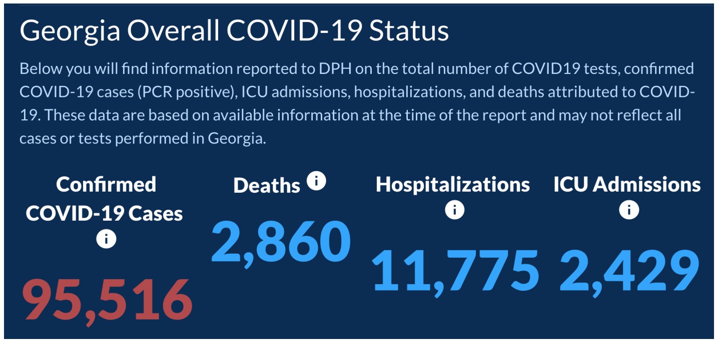
Report, Code, and Preprint:
https://weitzgroup.github.io/MAGEmodel_covid19_GA/

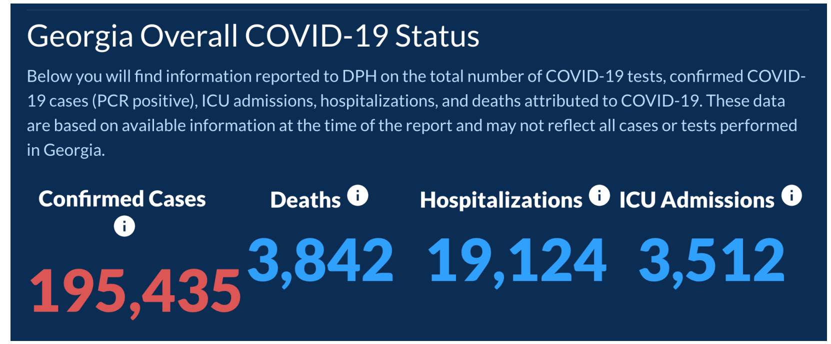


Courtesy: Dr. Stephen Beckett (Weitz group)

Covid-19:
A global pandemic with acute effects in GA

July 6





August 4

In the past month, Georgia has experienced:

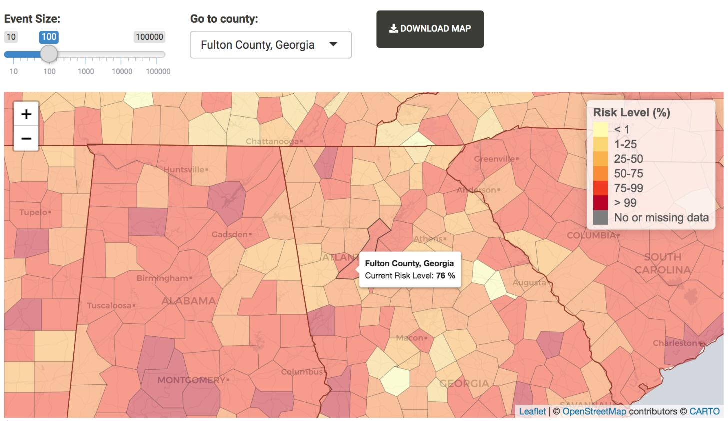
- ~50% of total reported cases since inception of epidemic.
- ~40% of total hospitalizations
- ~30% of ICU admissions
- ~25% of fatalities

Note: severe cases/fatalities lag multiple weeks behind case reports

Takeaway: This is a critical phase of the epidemic; a default mode of 'face-to-face learning' is not feasible, today's talk will focus on the science that can help guide decision-making processes @ GT.

Science and Projections for the Fall Term

Part 1 – Model Projections (JSW): What are the risks of a dynamic outbreak and how can individual actions (e.g., mask-wearing) and institutional efforts (e.g., testing/online learning) help reduce risk for al?

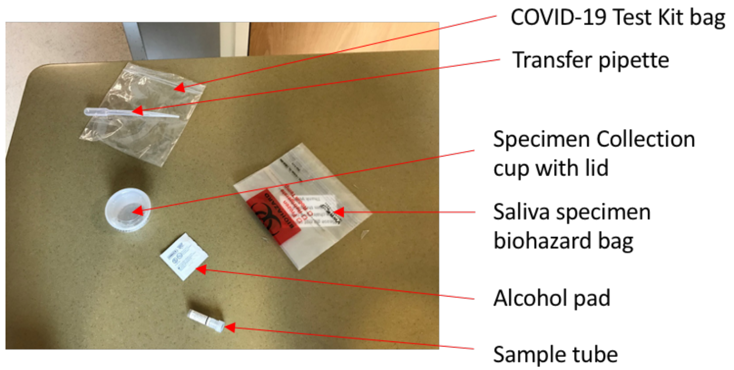


(Note: this map currently uses a web Mercator projection that inflates the size of states in northern latitudes and exaggerates the east-west distance between states in the northern latitudes.)

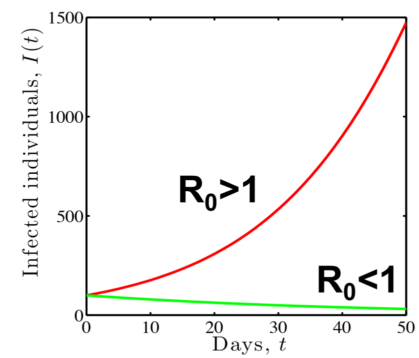
Risk dashboard (1.7M+ visitors in past month): https://covid19risk.biosci.gatech.edu/

Technical Refs: Park et al. Epidemics (2020); Park et al. JRSI (2020); Weitz et al. Nature Medicine (2020).

Part 2: Testing Initiatives (GG) How can large-scale testing be used to mitigate and reduce risk for all?

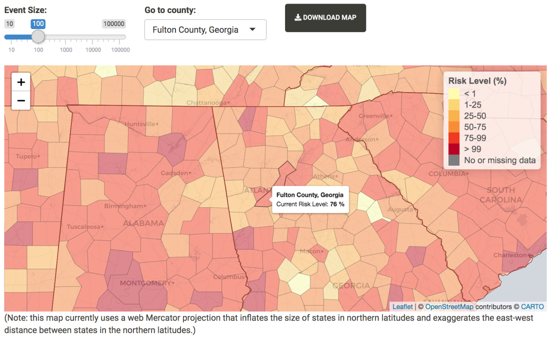


Part(ing) Thoughts: Action-Taking Amidst Uncertainty

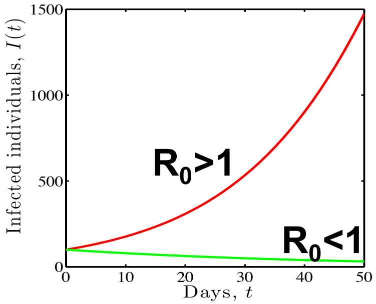


Part 1 – Model Projections

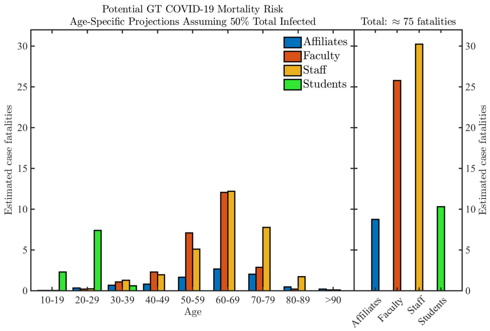
Risk of Exposure: What are the chances that one (or more) individuals in a group (e.g., classroom, dining hall, dorm, party) will have Covid-19?



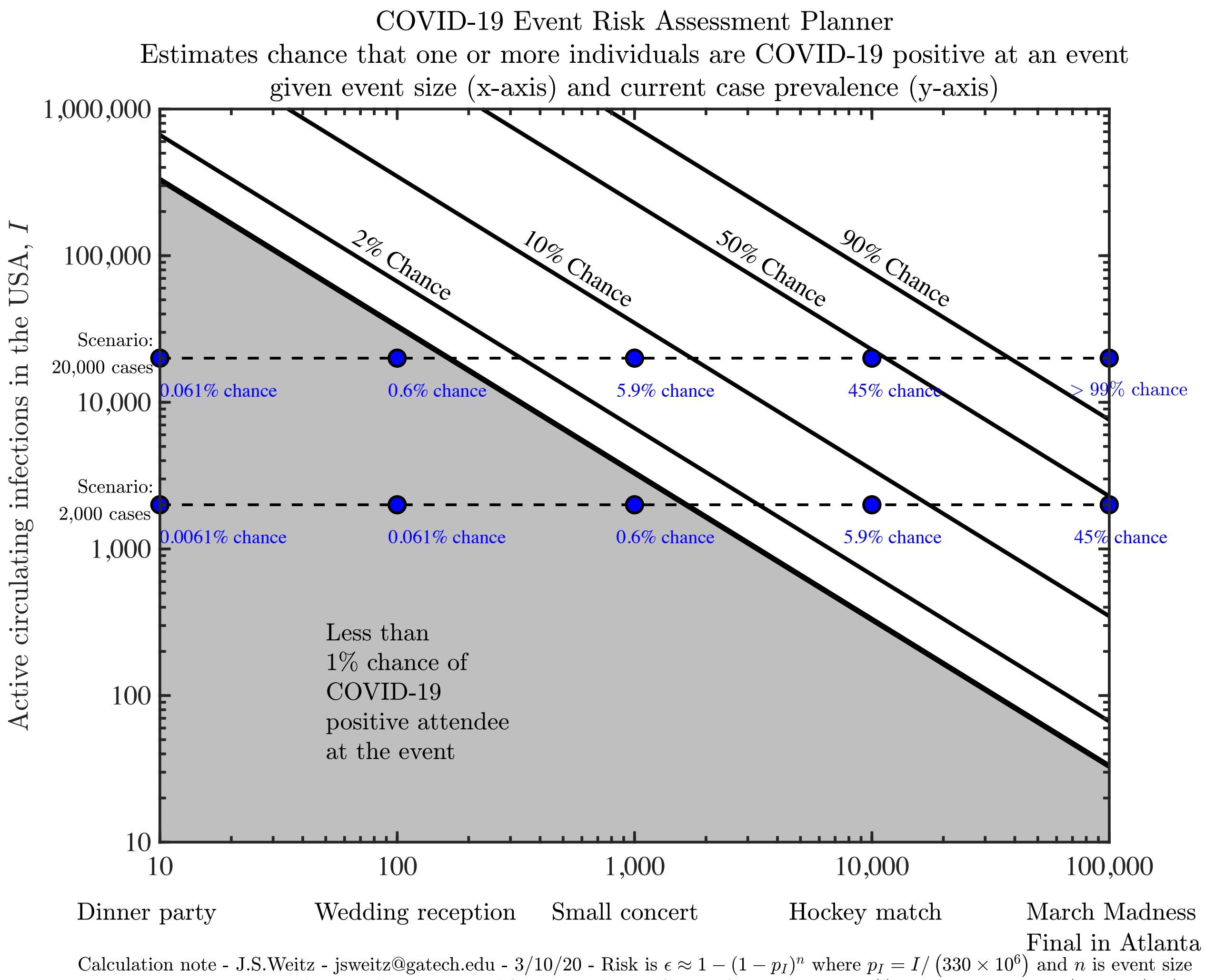
Risk of a Large Outbreak: What is the risk that imported cases will lead to a large epidemic outbreak in the GT student, staff, and faculty community?



Risk of Severe Outcomes: In the event of a large epidemic outbreak, how might a Covid-19 outbreak impact the campus community?



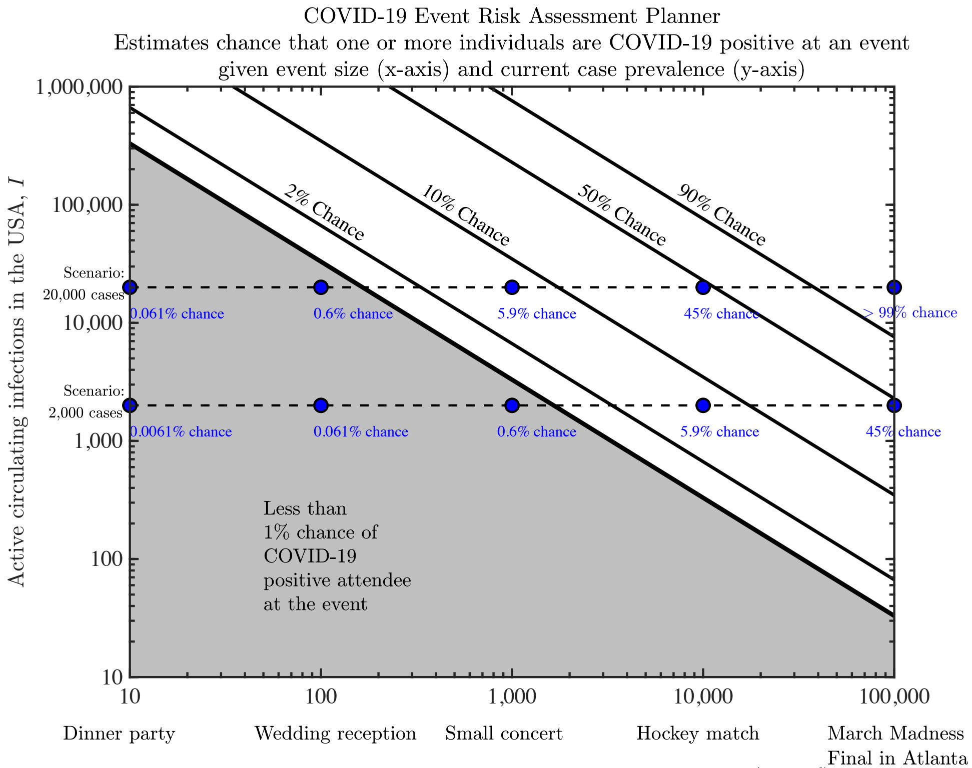
How can we translate data on case reports to something personal?



Calculation note - J.S.Weitz - jsweitz@gatech.edu - 3/10/20 - Risk is $\epsilon \approx 1-(1-p_I)^n$ where $p_I = I/\left(330\times10^6\right)$ and n is event size

Assumes incidence homogeneity, code https://github.com/jsweitz/covid-19-event-risk-planner

Q: What is the chance that one (or more) individuals are infected in a group?



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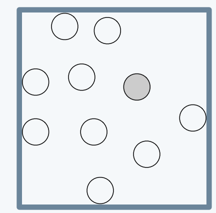
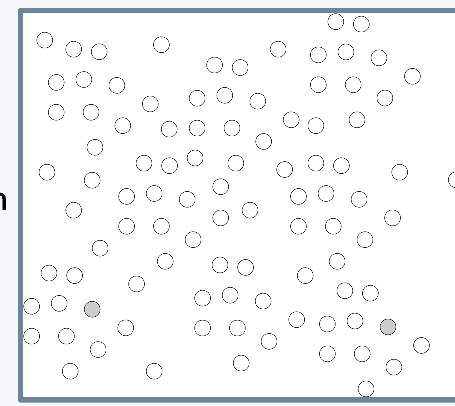
Assumes incidence homogeneity, code https://github.com/jsweitz/covid-19-event-risk-planner

$$\text{Risk} = 1 - (1-p)^n$$

Higher per-capita risk, even small events may include one (or more) Covid-19 infecteds.



Lower per-capita risk, large events may include one (or more) Covid-19 infected even when it seems hardly anyone is sick.



Risk of Exposure: Classrooms and Gatherings

COVID-19 Event Risk Assessment Planning Tool

RISK ESTIMATES BY COUNTY | REAL-TIME US AND STATE-LEVEL ESTIMATES | EXPLORE US AND STATE-LEVEL ESTIMATES | CONTINUOUS RISK ESTIMATES | PREVIOUSLY RELEASED CHARTS | TUTORIAL

This map shows the risk level of attending an event, given the event size and location (assuming 10:1 ascertainment bias).

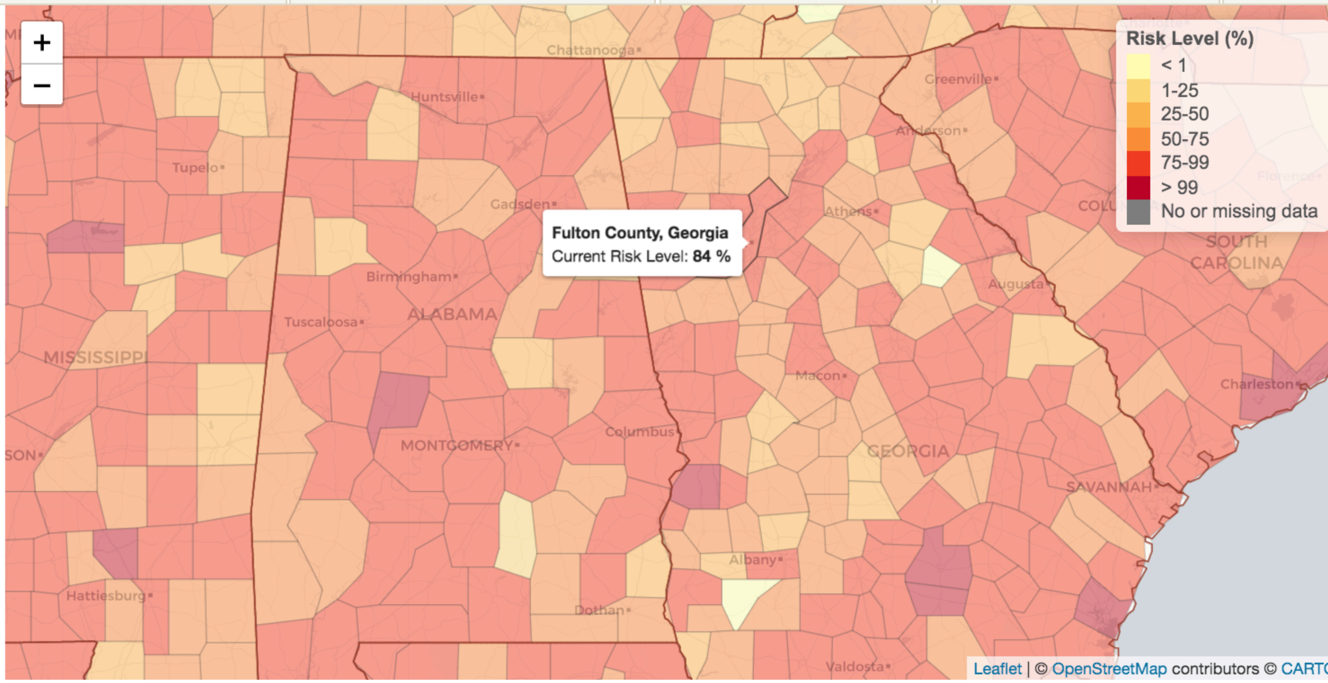
The risk level is the estimated chance (0-100%) that at least 1 COVID-19 positive individual will be present at an event in a county, given the size of the event

Choose an event size. Use the drop-down menu to choose a county you would like to zoom in on.

Event Size:

10 50 10000

10 25 50 100 500 5000



(Note: This map uses a Web Mercator projection that inflates the area of states in northern latitudes. County boundaries are generalized for faster drawing.)

Covid-19 Risk Assessment Calculator (joint w/Prof. Clio Andris and ABiL)
Website: https://covid19risk.biosci.gatech.edu/

Risk of Exposure Associated with Gatherings

Large gatherings are problematic for multiple reasons:

- Increased likelihood that someone in a group has Covid-19 (perhaps asymptomatically).
- More potential interactions to spread, i.e., the number of 'contacts' scales with n^2 (where n is the group size) – super-spreading.
- Harder to contact trace; close contacts in a gathering are not easy to reconstruct.

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Site	Estimated infections/reported cases, No. (range)[d]
Western Washington	11.2 (6.9-19.2)
New York City metro area (New York)	11.9 (8.6-15.4)
Louisiana	15.7 (10.6-22.4)
South Florida	11.2 (6.0-19.5)
Philadelphia metro area (Pennsylvania)	6.8 (3.6-11.1)
Missouri	23.8 (14.8-34.7)
Utah	10.5 (5.5-15.5)
San Francisco Bay area (California)	9.0 (3.2-22.7)
Connecticut	6.0 (4.3-7.8)
Minneapolis-St Paul-St Cloud metro area (Minnesota)	10.2 (4.3-19.5)

Havers et al., JAMA 2020

Risk assessment:

Risk that one (or more) individuals has Covid-19 is $1-(1-p)^n$ where p is the circulating infection rate (we estimate from cases x ascertainment bias)

Risk of Exposure: Associated with Gatherings

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Risk assessment:
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Mitigation steps:

1. Reduce group sizes whenever possible (in and out of class).

Example: Classroom of 25 has ~50% chance one or more have Covid-19.

2. Mask wearing enforced in all buildings that have common spaces, even when alone (all teaching policies should be clear that individuals w/out masks cannot be in a lab/class/bldg).

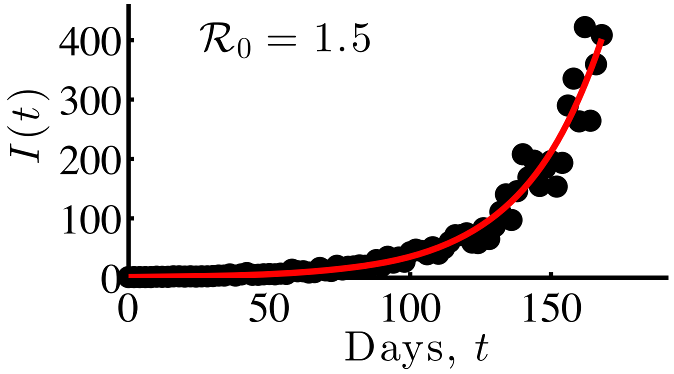
3. The safe modality for teaching right now is: **online**; until risks diminish, testing is initiated.

What Happens Next: Conditions for epidemic growth

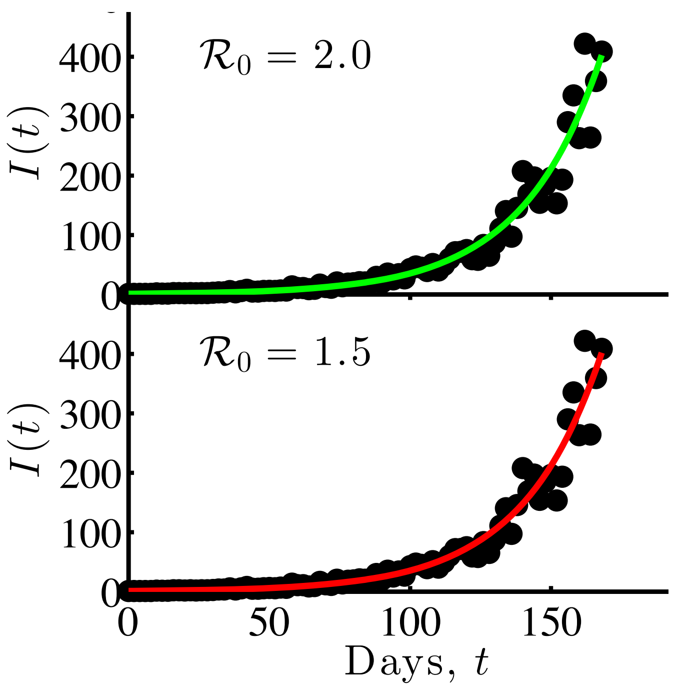
$$\mathcal{R}_0 \equiv \overbrace{\beta}^{\text{infections per time}} \times \overbrace{T_I}^{\text{infectious period}}$$

Where infections per time, β, is a product of:

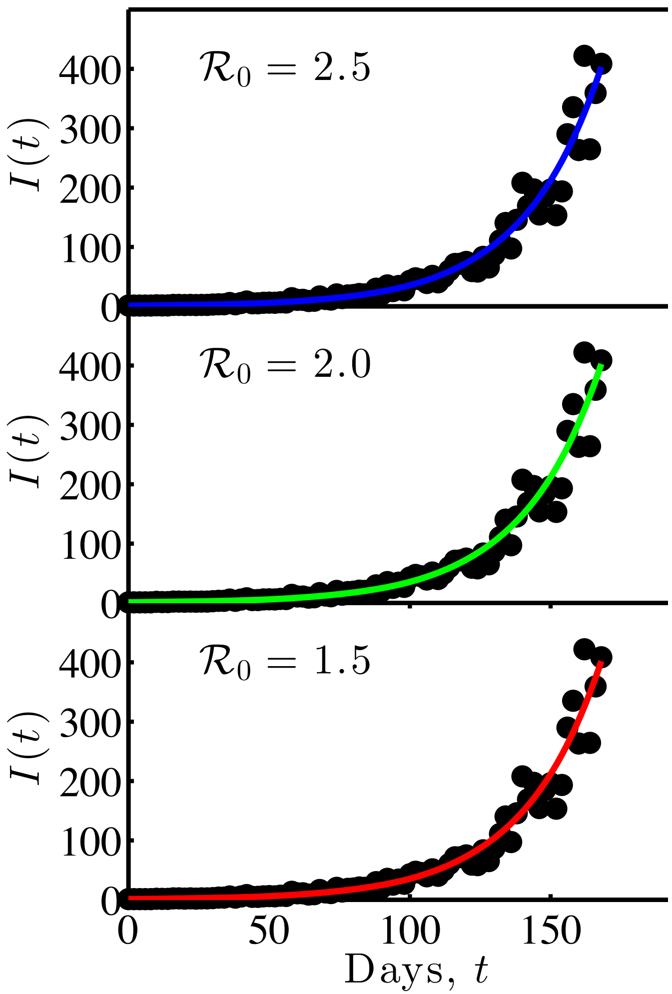
- Contacts by infectious individuals per unit time
- Probability of contact with a susceptible (S_0/N)
- Probability that the contact transmits the disease



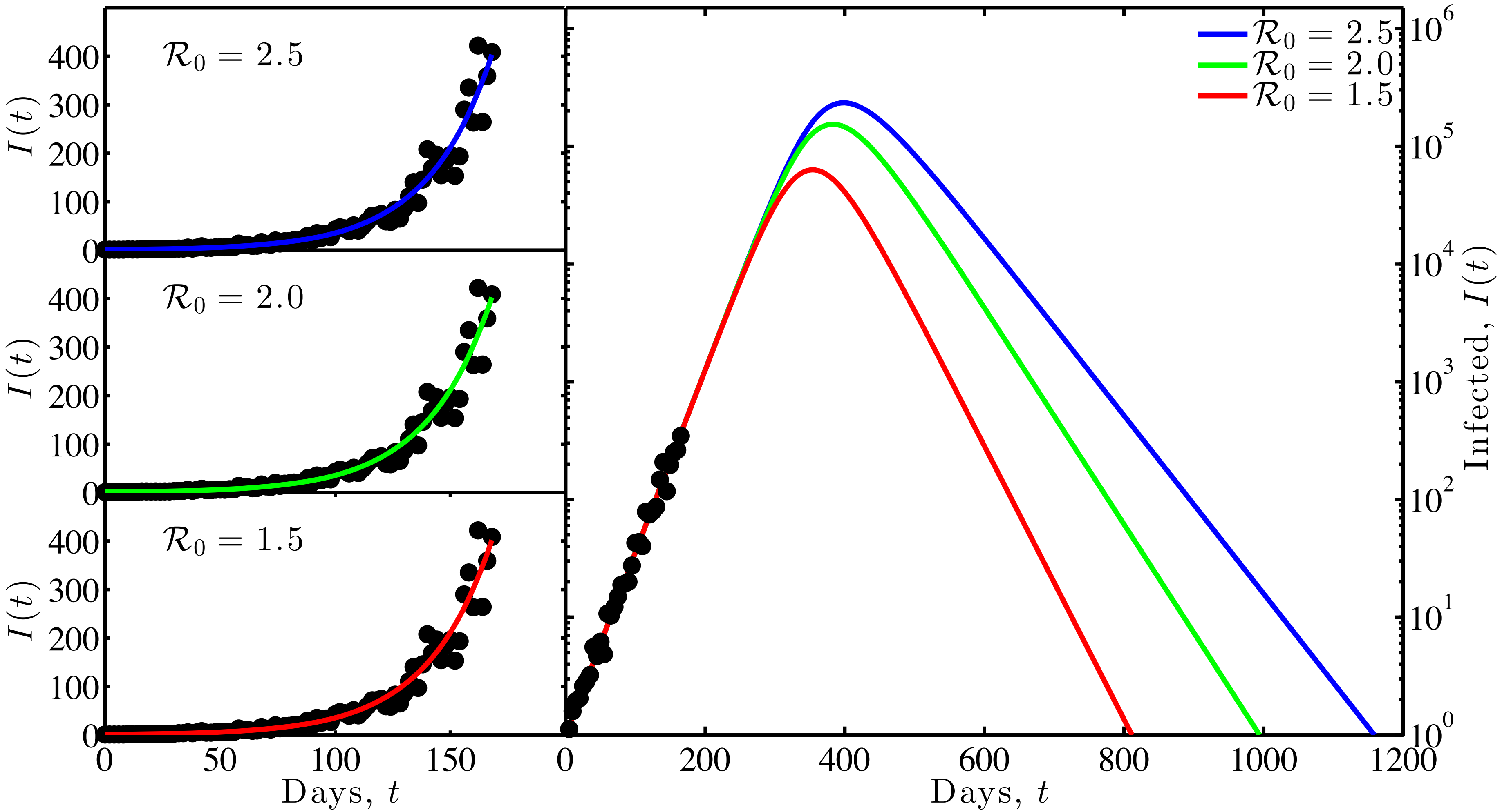
$\mathcal{R}_0 = 1.5$
400
300
200
100
0
$I(t)$
0
50
100
150
Days, t



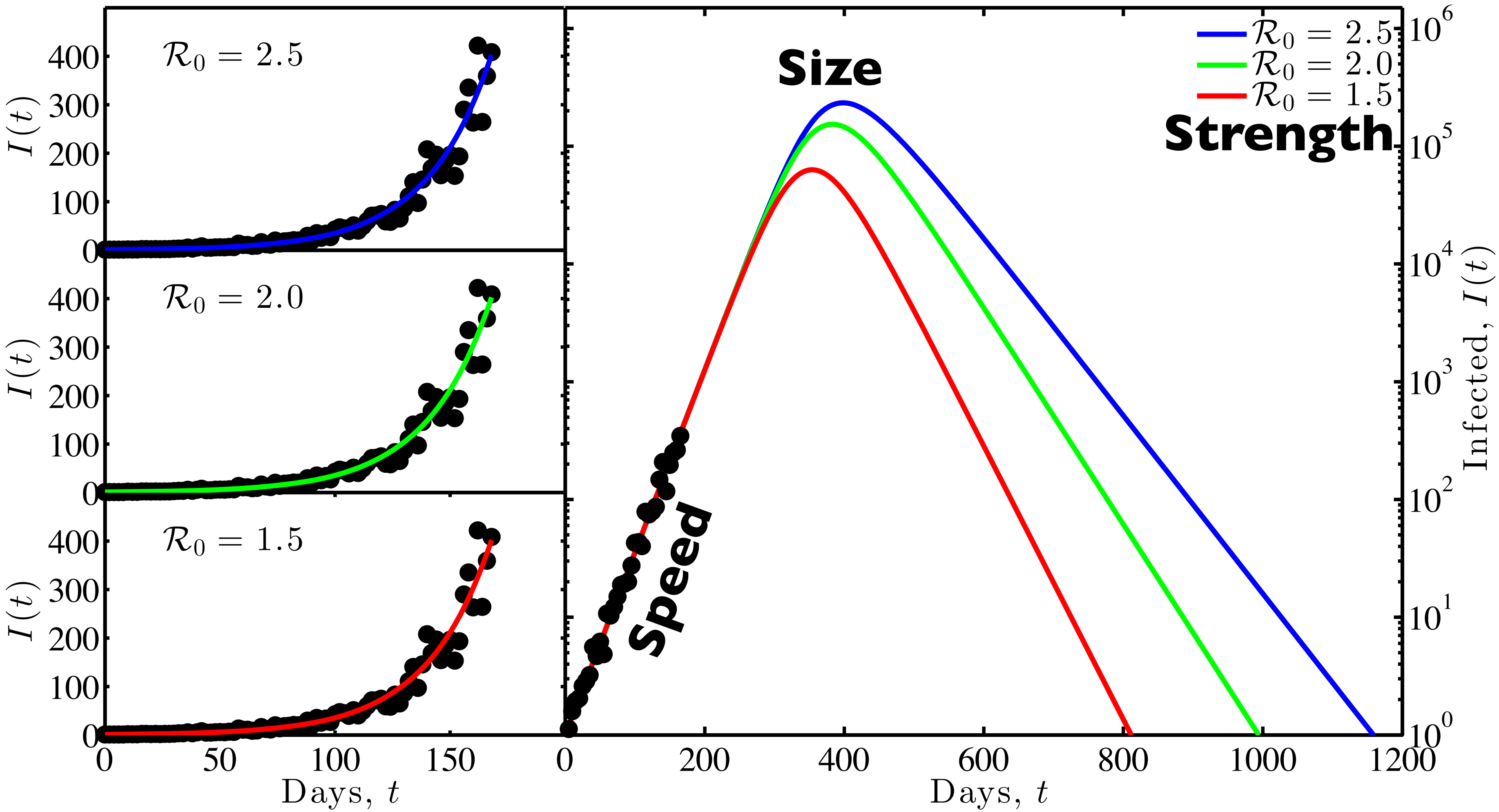
$\mathcal{R}_0 = 2.0$
$\mathcal{R}_0 = 1.5$
$I(t)$
0
100
200
300
400
0
50
100
150
Days, t



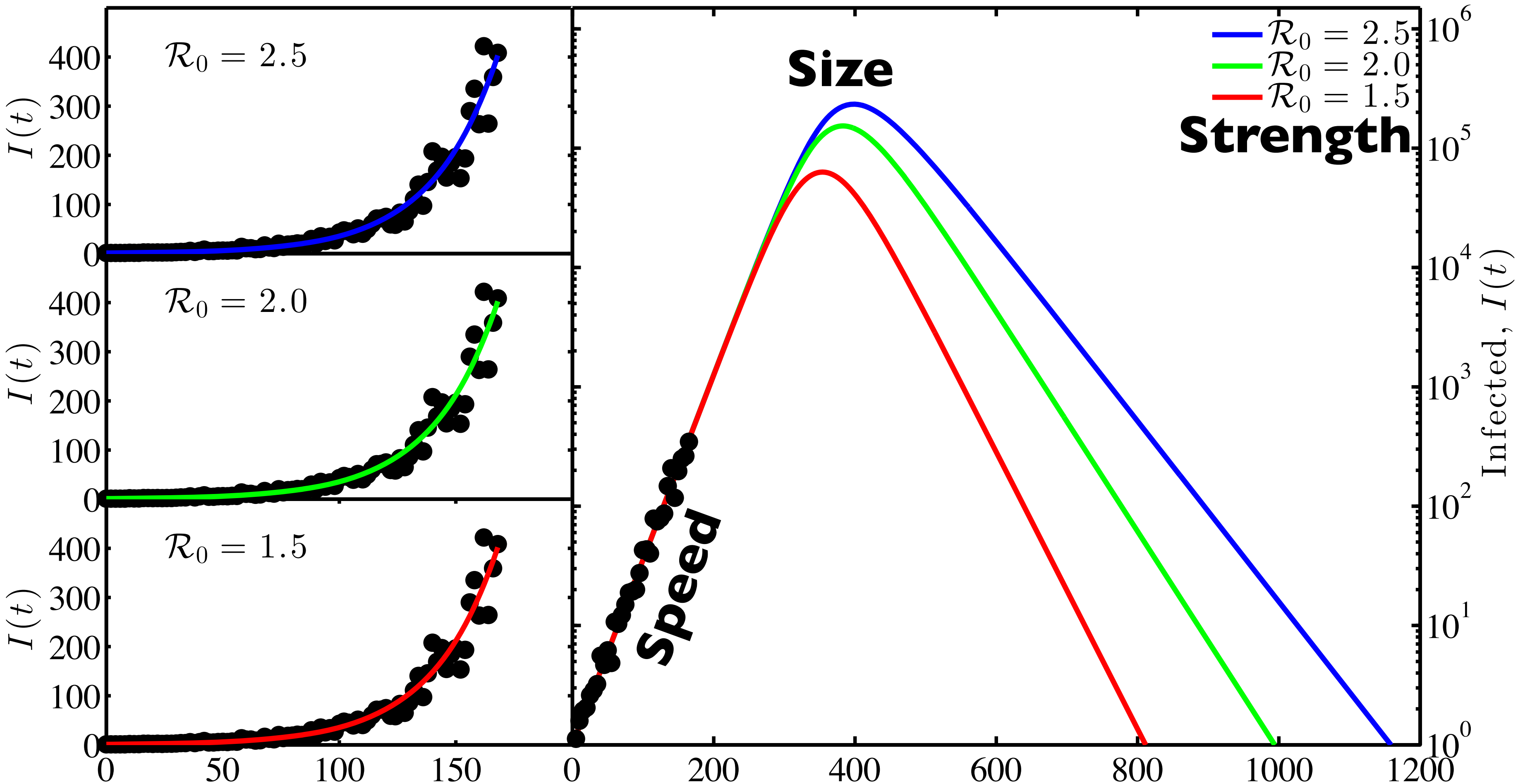
$\mathcal{R}_0 = 2.5$
$\mathcal{R}_0 = 2.0$
$\mathcal{R}_0 = 1.5$
$I(t)$
400
300
200
100
0
0
50
100
150
Days, t



$\mathcal{R}_0 = 2.5$
$\mathcal{R}_0 = 2.0$
$\mathcal{R}_0 = 1.5$
$I(t)$
0
100
200
300
400
0
50
100
150
Days, t
$\mathcal{R}_0 = 2.5$
$\mathcal{R}_0 = 2.0$
$\mathcal{R}_0 = 1.5$
0
200
400
600
800
1000
1200
Days, t
10^0
10^1
10^2
10^3
10^4
10^5
10^6
Infected, $I(t)$



$\mathcal{R}_0 = 2.5$
$\mathcal{R}_0 = 2.0$
$\mathcal{R}_0 = 1.5$
$I(t)$
Days, t
Size
Strength
Speed
Infected, $I(t)$



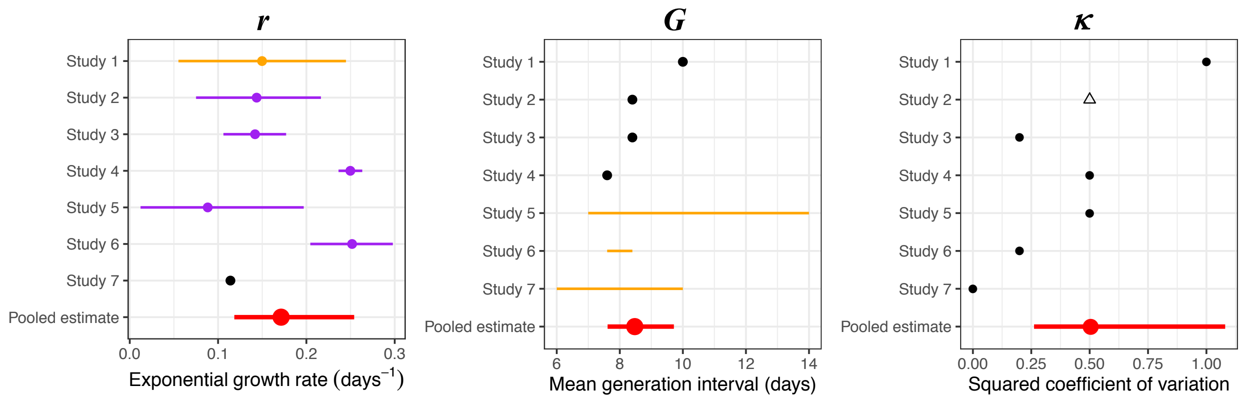
Tentative conclusion: We can measure the 'speed', but inferring the 'strength' (and by extension, predicting the 'size') of an epidemic is harder.

Pooled estimates via a speed-strength relationship (technically using generation intervals)
Park et al., J. Roy. Soc. Interface (2020)

Sang Woo Park

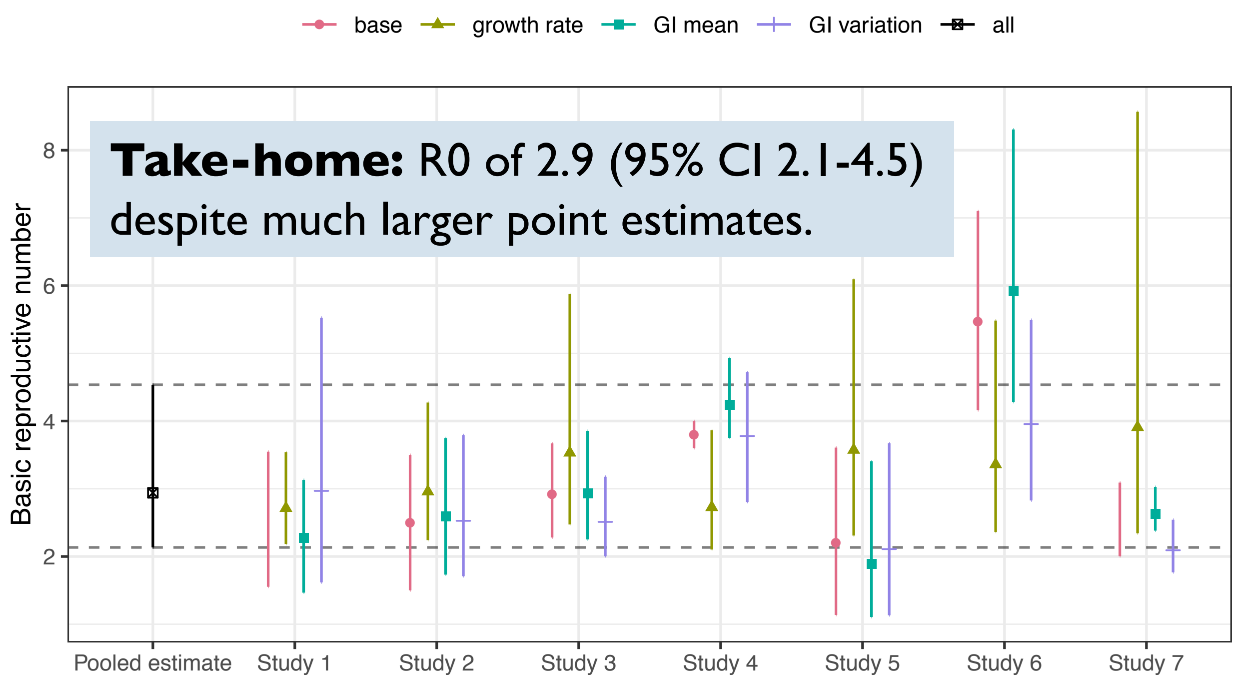
Jonathan Dushoff

Step 1: estimate latent uncertainty in 'parameters'.



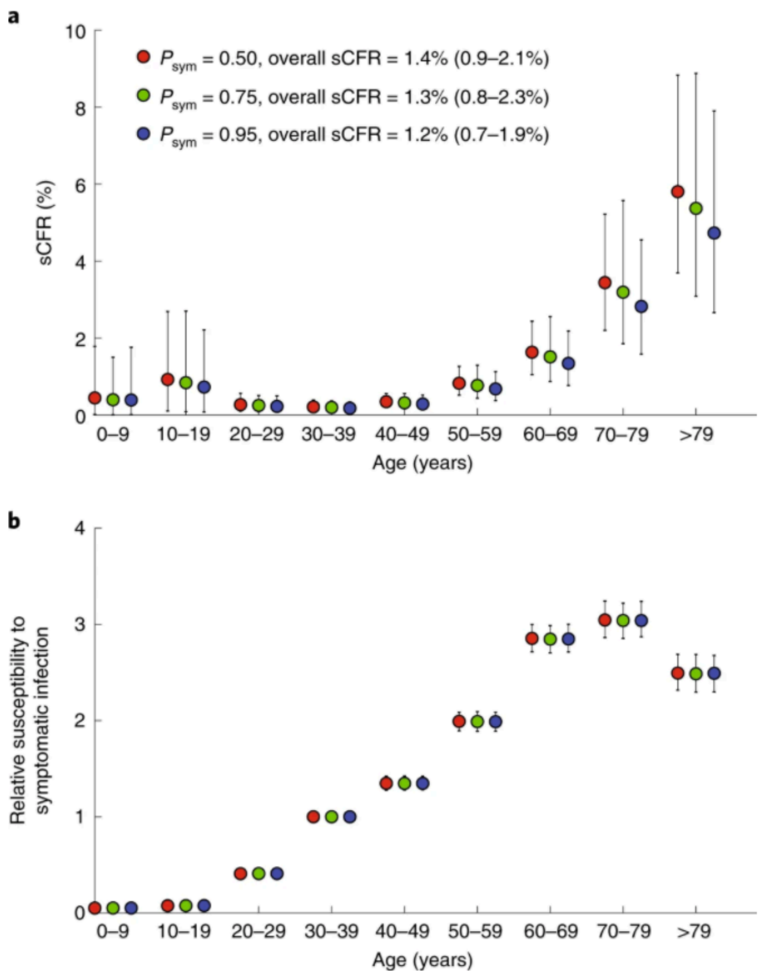
Step 2: incorporate different types of uncertainty into R0 estimates by study or as part of a 'pooled' estimate (using a Bayesian multi-level model)

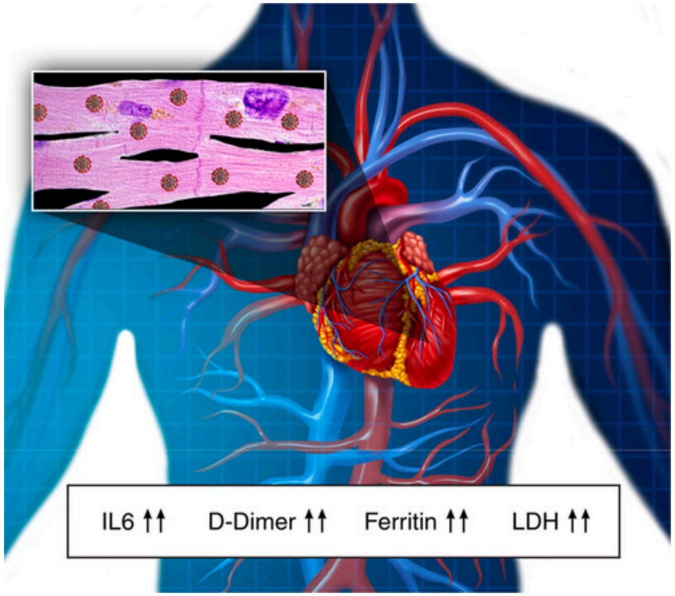
$$\mathcal{R}_0 = \left(1 + \kappa r \bar{G}\right)^{1/\kappa}$$



The Many Impacts of Covid-19: Severity and Age

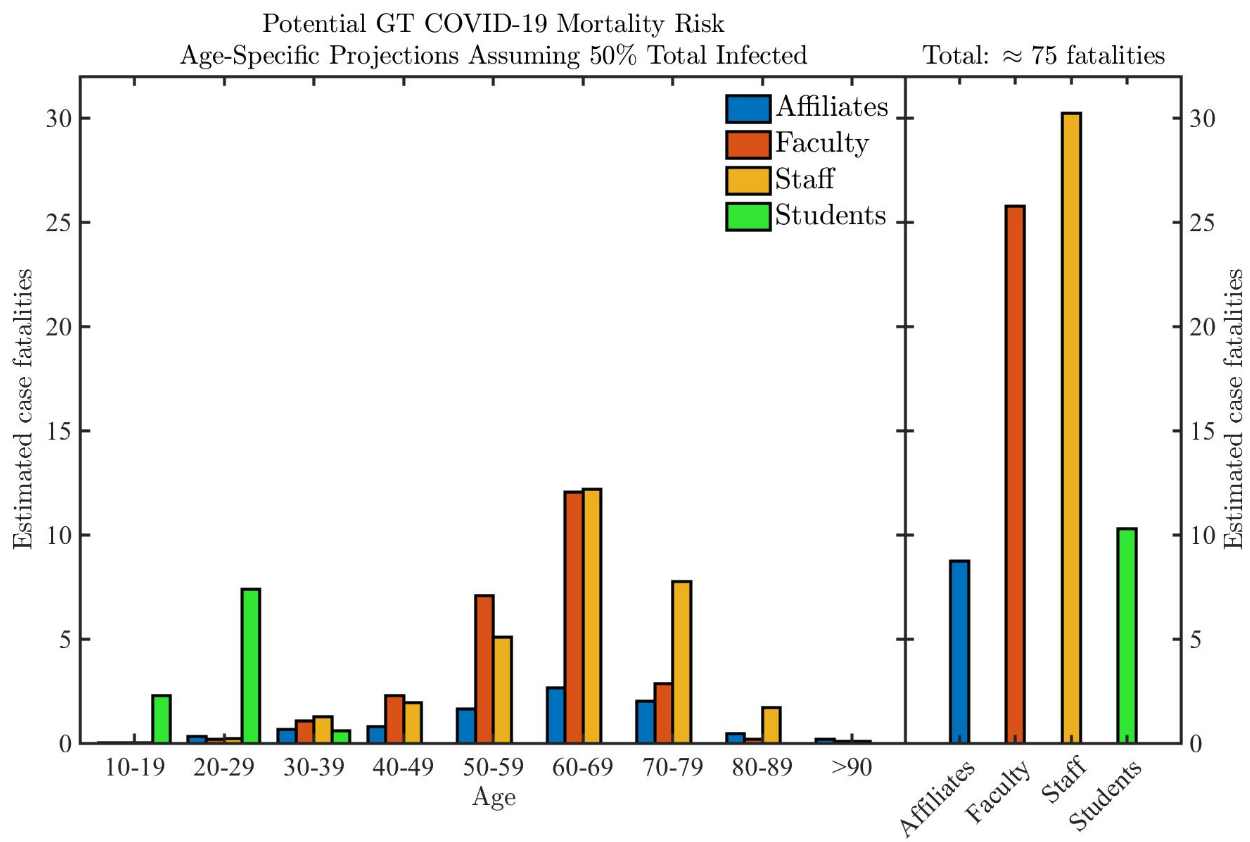
From: Estimating clinical severity of COVID-19 from the transmission dynamics in Wuhan, China





Increasing evidence of myocardial damage (Clerkin et al., Circulation, 2020)

Risk of Severe Outcomes: A Community of Students, Staff, and Faculty



Take-away: this scenario is based on an <u>unmitigated</u> epidemic at full campus capacity; and highlights the need for action-taking. Assumes 50% infection of the community, with age-stratified risk, but not including co-morbidity information; data on age distributions from GT IRP. Analysis based on ICL and HK analysis of age-stratified risk.

Risk of Severe Outcomes: A Community of Students, Staff, and Faculty

Covid-19 has many kinds of severe outcomes:

- Lung/cardiac damage (perhaps 'silently').
- Long-term health problems (breathing, and damage to other tissue function).
- Extended hospitalization.
- Increased fatality with age.

Take-away: Per-capita, staff and faculty are at greater risk, but students can also have severe outcomes; strategy should be to take steps to <u>reduce</u> transmission.

Mitigation steps:

<u>1. Operate as liberally as possible with respect to starting w/online teaching as default.</u>

<u>2. Consider reducing in-person interactions whenever possible, shift-work, reducing density</u>

<u>3. Baseline R0 ~ 3 implies need >67% aggregate reduction to halt an initial outbreak.</u>

<u>4. We are all in this together: protect each person to protect us all.</u>

Conditions for epidemic growth also suggest opportunities for **control**

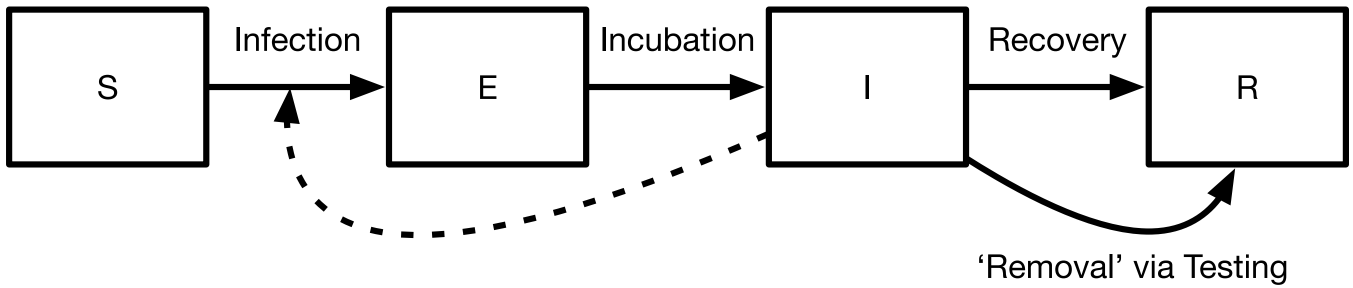
$$\mathcal{R}_0 \equiv \overbrace{\beta}^{\text{infections per time}} \times \overbrace{T_I}^{\text{infectious period}}$$

Hospitalization & treatment

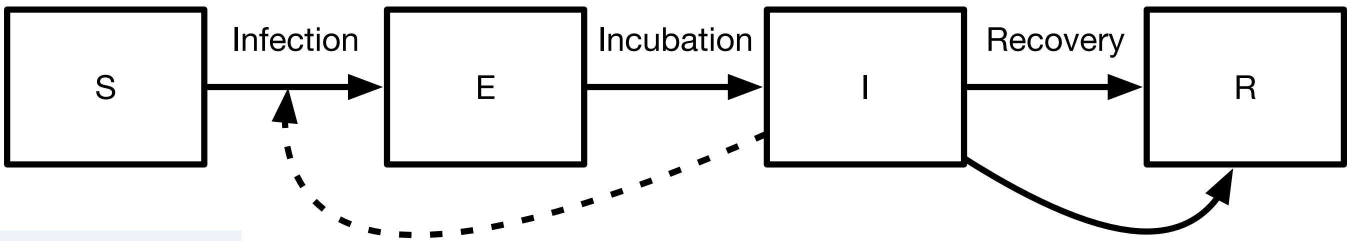
Where infections per time, β, is a product of:

- Contacts by infectious individuals per unit time — **Testing & targeted isolation**
- Probability of contact with a susceptible (S_0/N) — **Tracing/quarantine, travel reduction, shield immunity**
- Probability that the contact transmits the disease — **Process engineering & PPE (masks)**

Testing as Mitigation - Principles



Testing as Mitigation - Principles

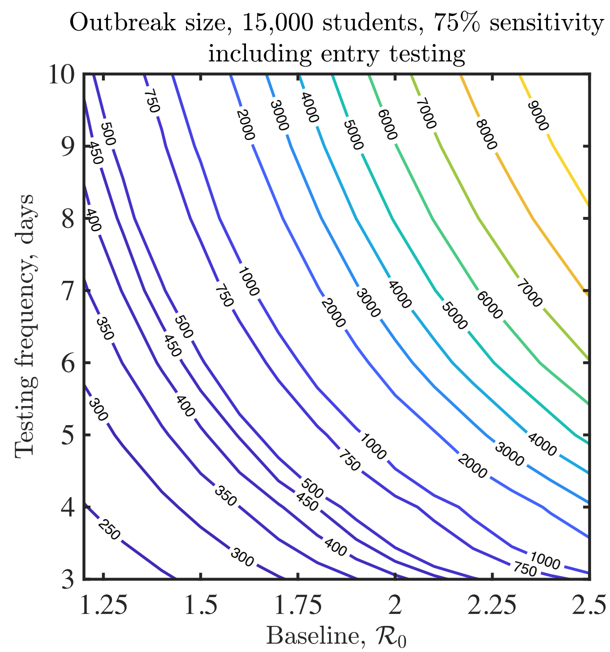


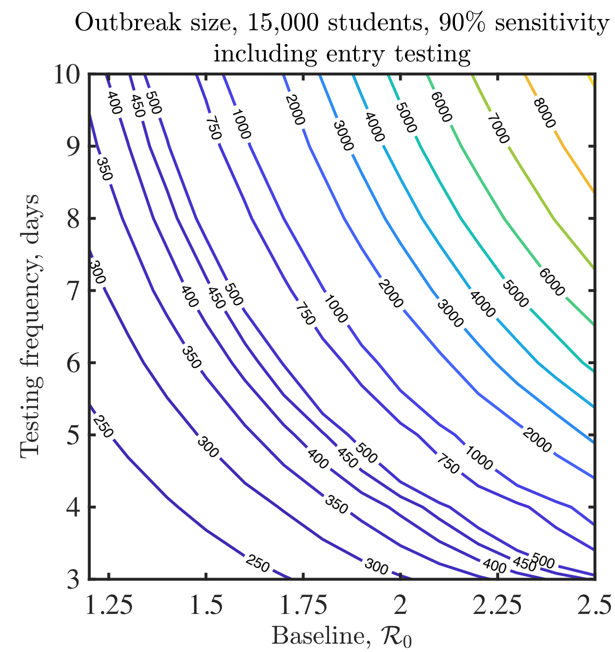
Test frequency is key. Being able to retest <7 days is essential.

General NPIs are key: Keeping R0<1.5 essential to avoid >1000s of cases (wear masks!).

Test sensitivity matters, but speed matters more.

Entry testing helps to reduce case load.





Part 2 – Testing to Mitigate Spread

1. Keep the initial infection rate as low as possible

- Start with 100 cases, then steady state for the term can be kept to <10% range
- Start with 400 cases, it will be increasingly hard to control.

2. Reduce transmission rate from 1.3 to 1.5 range, to steady state (1.0) or less

- Every fraction of R_0 above 1 must be offset by mitigation of an equivalent fraction (e.g., shared dorms rooms is 1 new infection; a party could be dozens or more).
- Without testing, 100 this week becomes 150 next week, so we need to find and isolate 50 cases; if incidence is 1% and there are 10,000 students, then we have to test 5,000 a week

→ **Comprehensive Testing, At Least 1x Per Week of Students (and Staff/Faculty on campus), starting at Re-entry is essential**

Testing – FDA Regulations

Pooled Testing for SARS-CoV-2

	Surveillance Testing	Screening Testing	Diagnostic Testing
CLIA-Certified Laboratory	Yes	Yes	Yes
Non-CLIA-Certified Laboratory	Yes	No	No
CLIA Requirements Apply to Pooled Testing Procedure	No	Yes	Yes
Test System Must Be FDA Authorized or Offered Under the Policies in FDA's Guidance	No	Yes	Yes

Testing – Types

1. Serological tests - Detects your own antibodies, tells whether you've previously had SARS-CoV-2
2. Antigen tests - Detects viral proteins, but still under development (Leavey, Finn, Lu …)
3. Isothermal tests - Rapid moderate complexity diagnostic test at STAMPS (25 / day)
4. **PCR tests - Detects viral RNA, amenable to pooling, so scales to thousands per day**

- Nasopharyngeal Swabs: Gold Standard, harder to process and handle safely
- Saliva: Not yet approved, but easily collected and processed and very safe

→ We're aiming for 1300 to 2500 saliva surveillance tests per day

Testing – Accuracy (and Predictive Value)

	Cases (Incidents)	Controls (Unaffected)	Predicted Values (PPV/NPV)
Called Positive	90	99	0.48
Called Negative	10	9801	1

Accuracy
0.99

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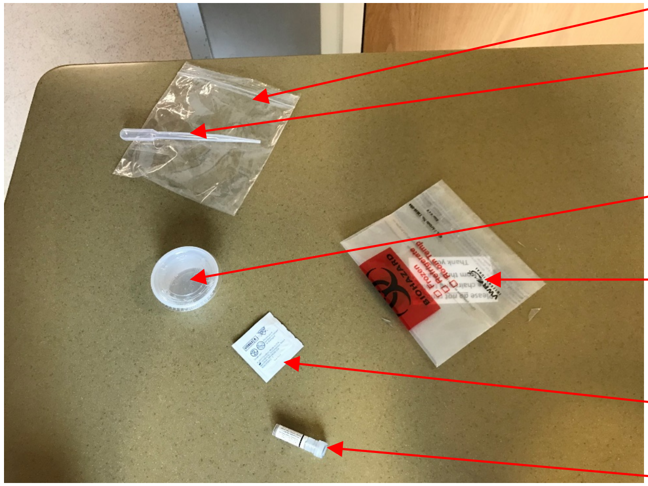
Called Positive	90	99	0.48
Called Negative	10	9801	1

Accuracy
0.99

Same Test, 2,000 instead of 10,000: Finding True Positives requires comprehensive testing

	Cases (Incidents)	Controls (Unaffected)	Predicted Values (PPV/NPV)
Called Positive	18	20	0.48
Called Negative	2	1960	1

Sampling Approach



COVID-19 Test Kit bag

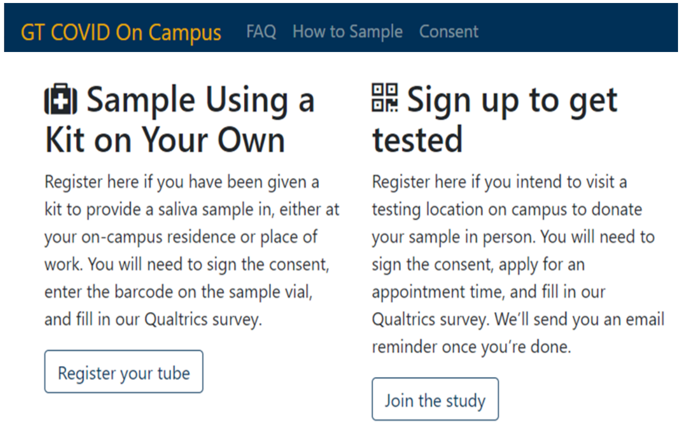
Transfer pipette

Specimen Collection cup with lid

Saliva specimen biohazard bag

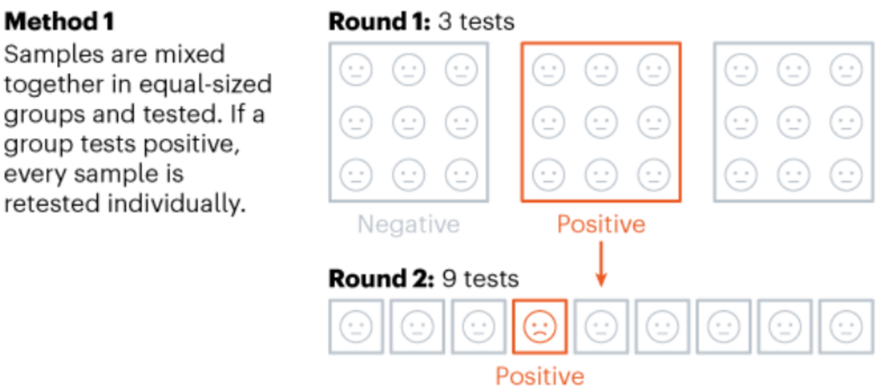
Alcohol pad

Sample tube

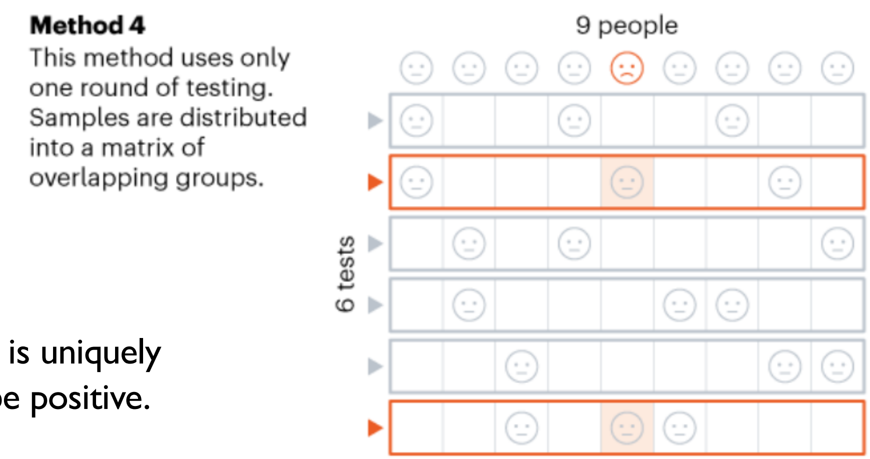


http://covid19.biosci.gatech.edu

Pooled Testing



← Single Pool “Dorfman” design



Double Pool design →

We will test 28 people in 8 pools of 7, where each person is uniquely in one pair of wells. If incidence is 1% then ¼ of sets will be positive.
If incidence is 2% we switch to 6 pools of 5
If incidence is 5% we switch to 4 pools of 3, but we're all in trouble!

Nature July 10, 2020 (Smriti Mallapati)

Notification

1. Since we are performing surveillance, we cannot return individual results

2. If you don't hear anything, you were probably not in a positive pool

   BUT it does not mean you are negative for SARS-CoV-2

   - Sometimes there is no virus in a particular sample
   - With pooling, sometimes the signal may dilute below the detection threshold
   - We might make mistakes occasionally
   - You may become positive after testing

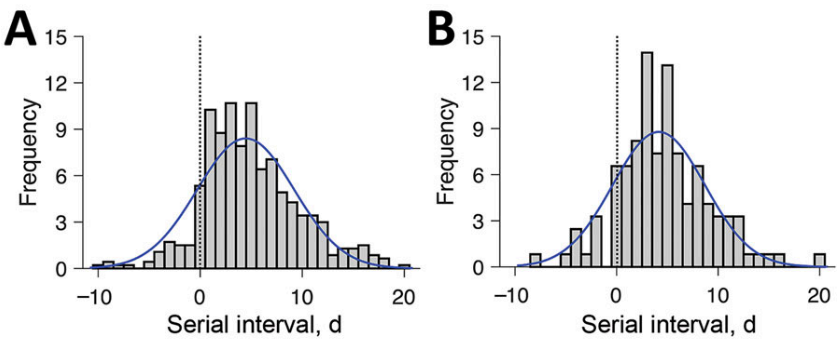
3. If we infer that you are positive, either:

Plan A: We retest your individual sample with a CLIA certified test then inform you
Plan B: We call back members of each positive pool for a CLIA nasal swab test
If you are called back, it does not mean you are positive

→ **The Goal is to Identify as many True Positives as we can**

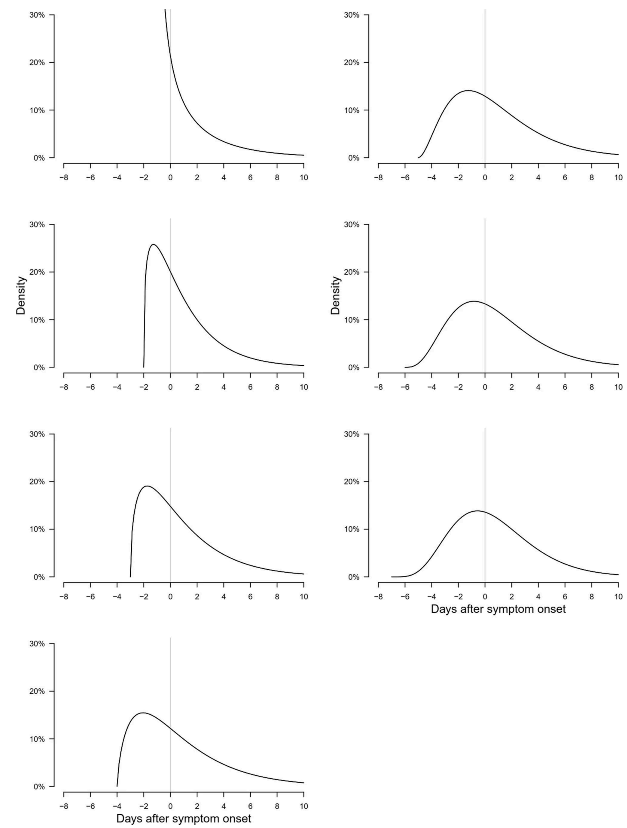
Parting Thoughts

A Critical Point in Approaching Covid-19 in Younger Adults: Asymptomatic/Presymptomatic/Mild Transmission is Real



Negative serial intervals (Du et al. CDC EEID, 2020)

Takeaway: Large-scale outbreaks in adolescents and young adults are possible (N. Georgia YMCA camp; Rutgers football team, etc.); many (but not all) without symptoms, and can then cascade to the greater community.



Estimated infectious profile includes significant presymptomatic transmission (He et al., Nature Medicine, 2020)

Institutional Efforts Will not Be Enough – Collective Efforts are Needed

Chron | Local | US & World | Sports | Business | Entertainment | Life | Coupons | Jobs

Will I get COVID-19 at this party? This interactive tool can help you decide the risk of going out

By Abigail Rosenthal Published 10:11 am CDT, Thursday, July 30, 2020

AUSTIN

No parties at UT Austin this fall – on or off campus – school official says

Covid-19 and Education Restart: Take-aways and Recommendations

Testing:
Arrival testing for all community members until complete; reducing the size of initial outbreak, and then use repeated, pool testing to continue to 'remove' cases from circulation and reduce outbreak size.

Mask-wearing:
Enforceable inside buildings, i.e., students asked to leave a room/building if necessary and return to dorm to get mask (aim for ~100% compliance). Increased distribution of disposable masks around campus.

Teaching Modality:
Online should be the default mode; hybrid can include occasional face-to-face interactions and increase as conditions warrant (but conditions currently do not warrant it).

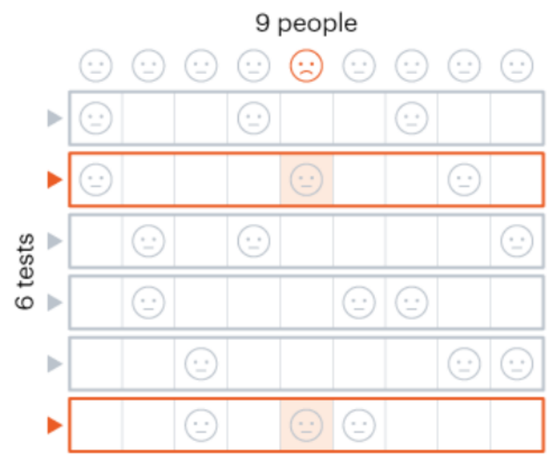
Essential Interactions and Risk:
Reduce indoor gatherings whenever possible, consider a ban on parties, find an equivalent substitute, protect and inform essential workers (often hardest hit); devise plans to protect and respect the entire campus community.

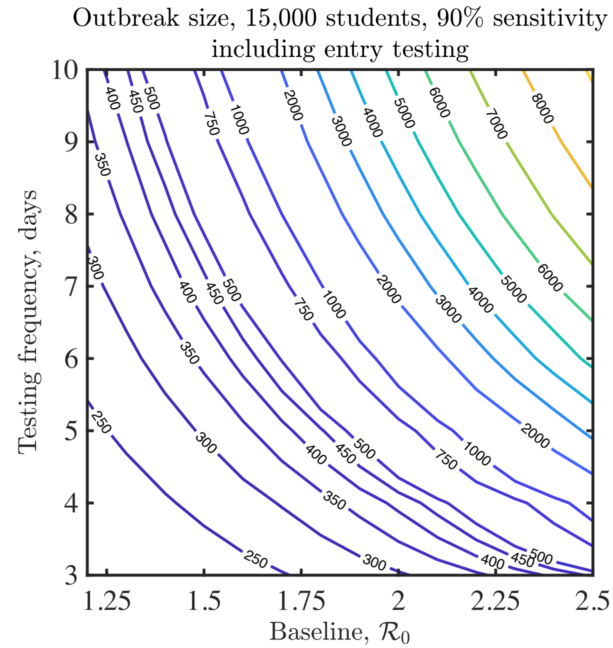
Georgia Tech

Georgia Tech School of Biological Sciences

Questions?

Method 4
This method uses only one round of testing. Samples are distributed into a matrix of overlapping groups.





Greg Gibson
School of Biological Sciences
Center for Integrative Genomics
Bioinformatics Program
greg.Gibson@biology.gatech.edu

Joshua S. Weitz
School of Biological Sciences
School of Physics
Center for Microbial Dynamics & Infection
Quantitative Biosciences Program
jsweitz@gatech.edu