The History and Future of the COVID-19 Pandemic in North Carolina

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Brief Disclaimer

 The following presentation represents my own personal scientific views and does not represent those of any other individual or institution.

• It is based on the information currently available to me and my current understanding of the scientific evidence.

• I have no direct conflicts of interest, but have served as an expert witness on cases where issues of the length of the pandemic are at issue.

The what and why of epidemiology?

 Epidemiologists study the distribution and causes of diseases in populations.

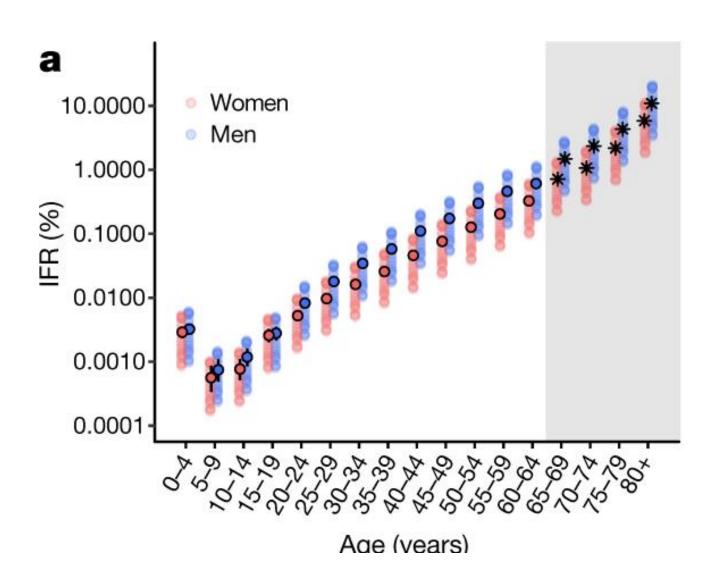
• I study *infectious disease dynamics*, or specifically how epidemics of infectious diseases evolve and change over time.

• Clinical researchers try to understand what factors make one patient recover why another dies, or what treatments work best to cure disease. Epidemiologists try to understand what makes epidemics worse in some places than others, and how to best control spread.

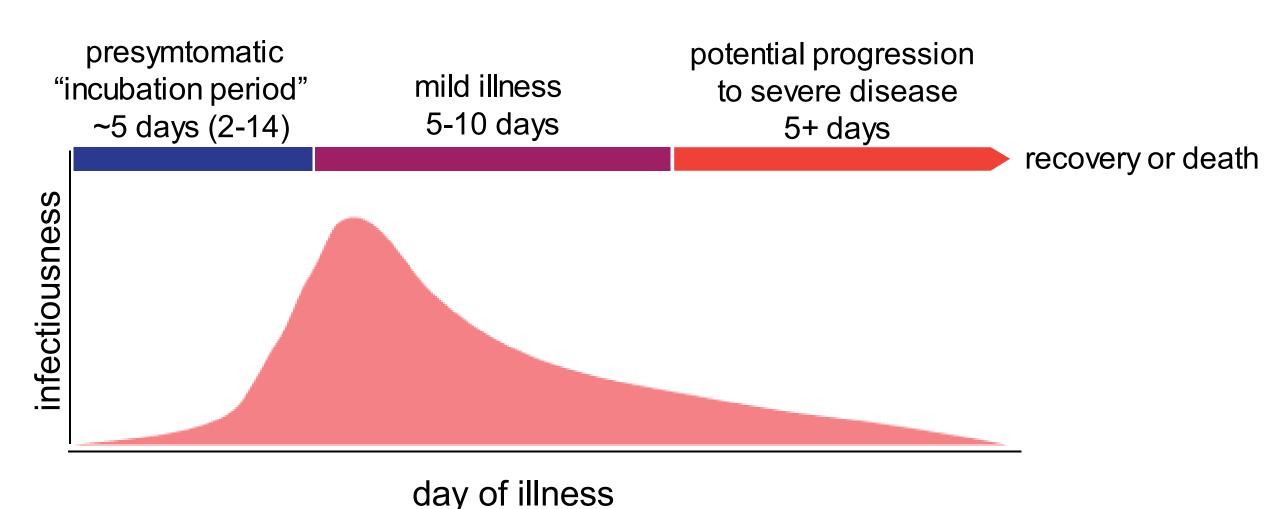
A Quick Primer on COVID-19 Epidemiology and Control

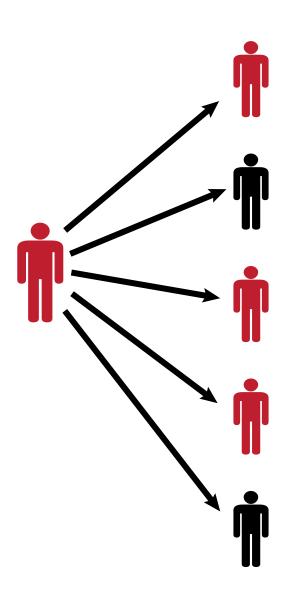
How deadly is COVID-19?

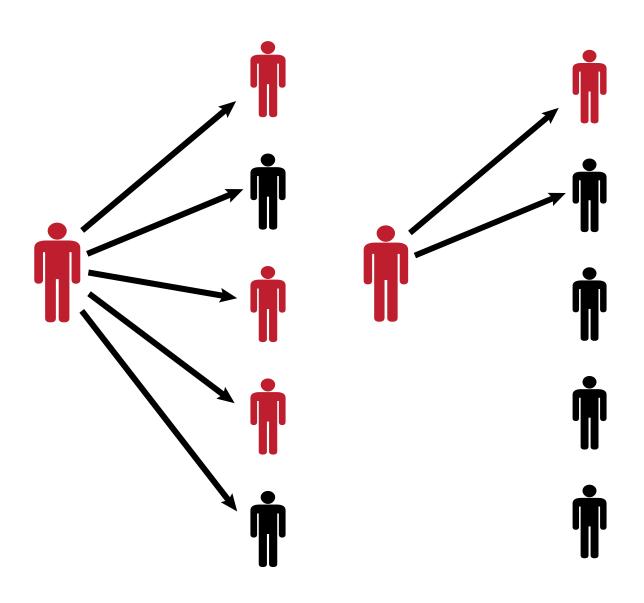
- In the US COVID-19 kills about 1 in every 200 people unvaccinated people who are infected.
 - some evidence this may be higher for Delta
- The probability of death is highly age dependent, doubling with about every 10 years of age.



The course of COVID-19 infection

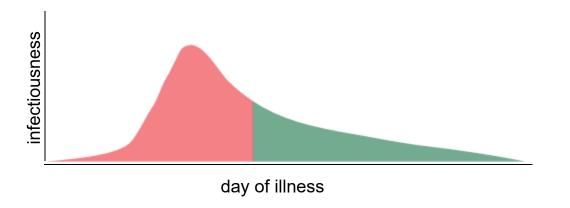


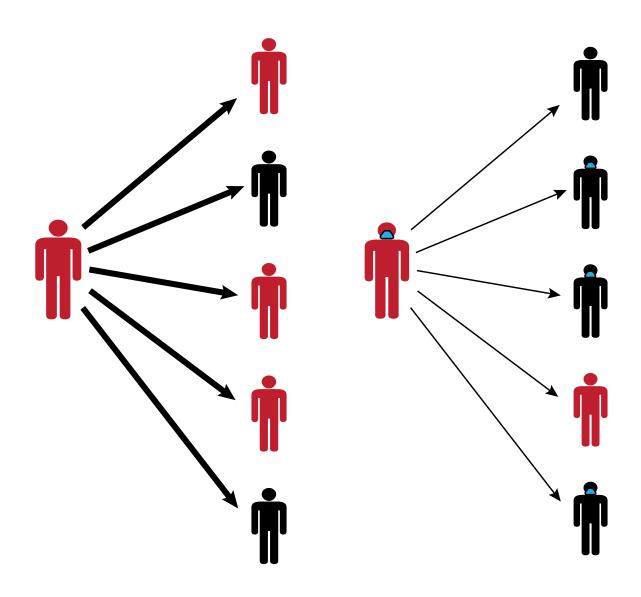




Reducing contacts

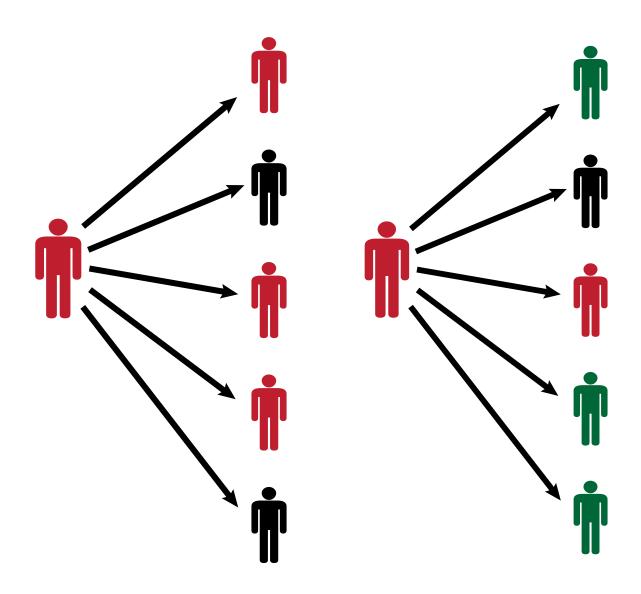
- mandated social distancing
- voluntary behavior change
- symptom screening
- test-trace-isolate programs
- regular prophylactic testing





Reducing per contact risk

- masks
- moving interactions outside
- ventilation
- hand washing

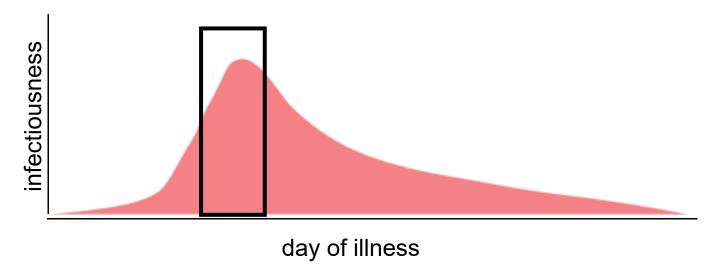


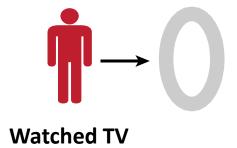
Reducing susceptibility

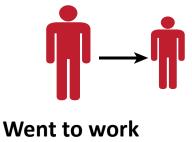
- vaccination
- prophylactic treatment
- natural infection*

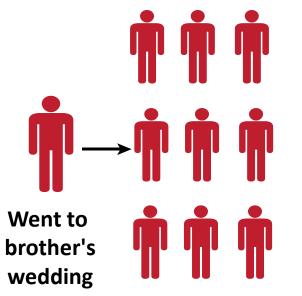
Why are 8% of people responsible for 80% of transmission?

How did you spend your most infectious day?

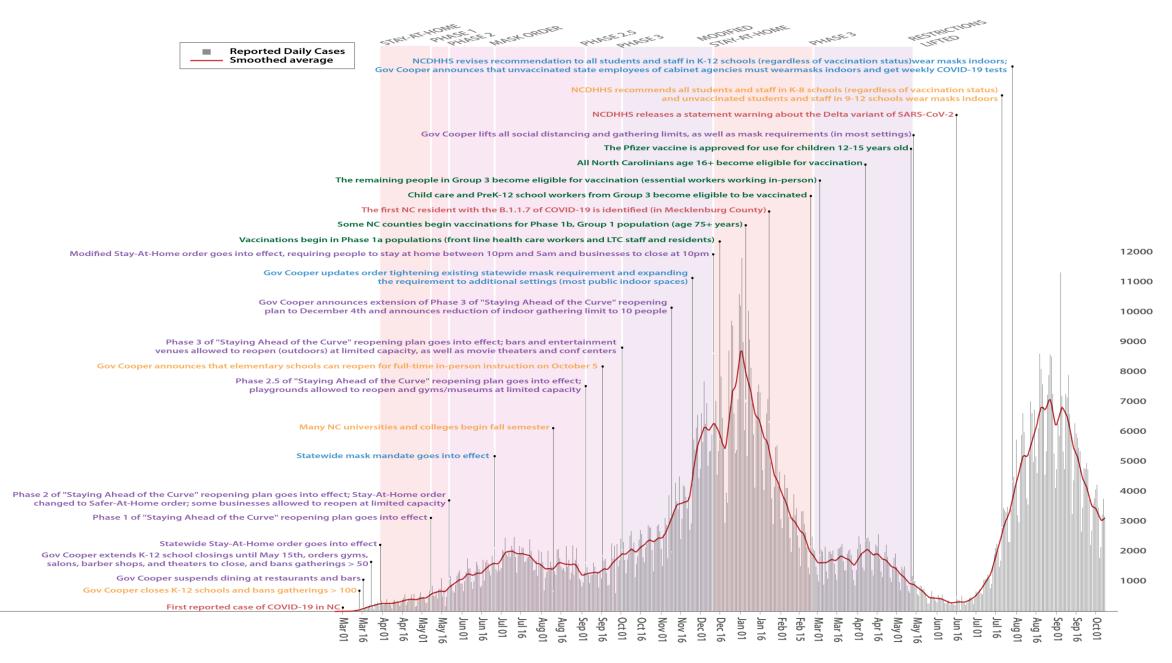






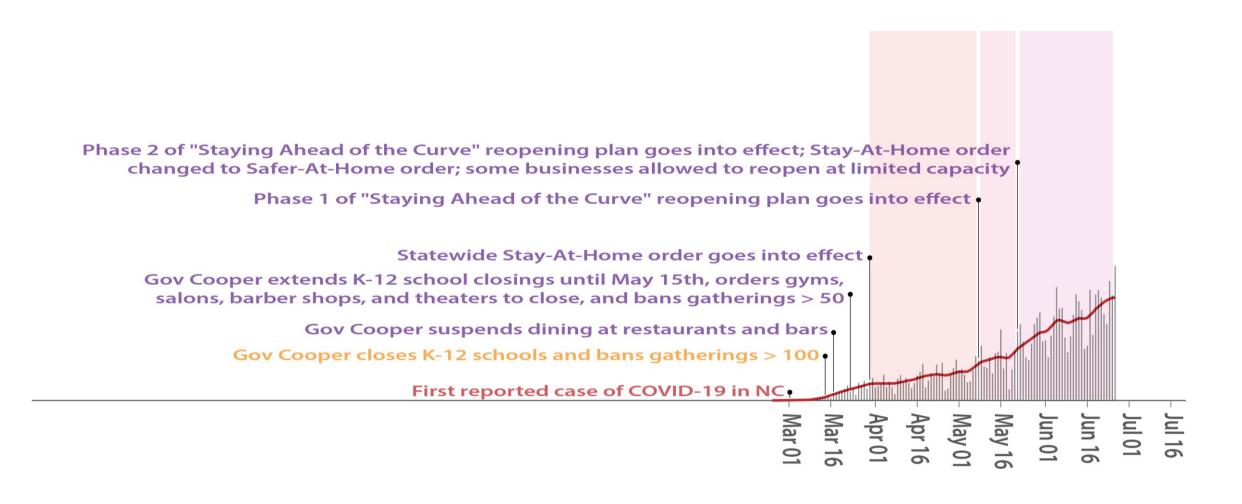


An annotated review of the COVID-19 pandemic in North Carolina



adapted from nc-covid.org with thanks to Paul Delamater

Spring 2020: Uncertainty and Lockdowns



Uncertainty in early 2020

- Infection fatality rate:
 - 1 in 1,000 to 1 in 60

- Transmission efficiency
 - R₀ in range 2-4
 - relative roles of different modes of transmission

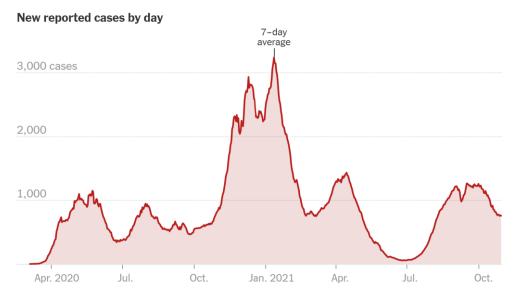
Relative susceptibility of children

When would we have a vaccine and how good would it be?

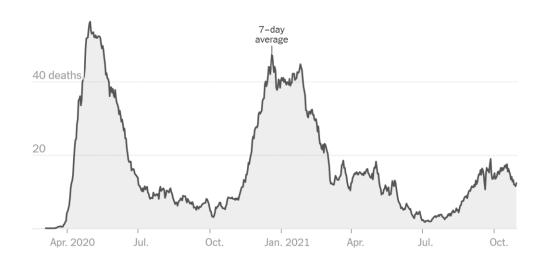
The Silent Epidemic

- Most cases have mild symptoms.
- Deaths and hospitalizations are delayed weeks or longer after infection.
- Testing in the United States was severely limited in the early stages of the pandemic.
- Hence early spread went largely undetected, and many states likely had large spring epidemics not reflected in their case numbers.

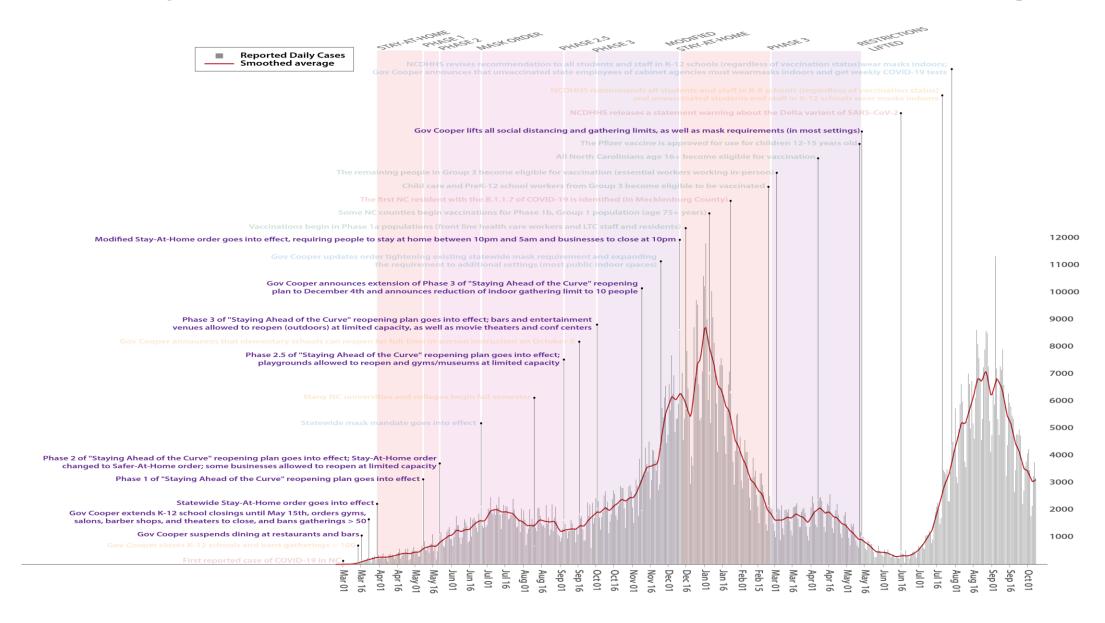
Maryland



New reported deaths by day

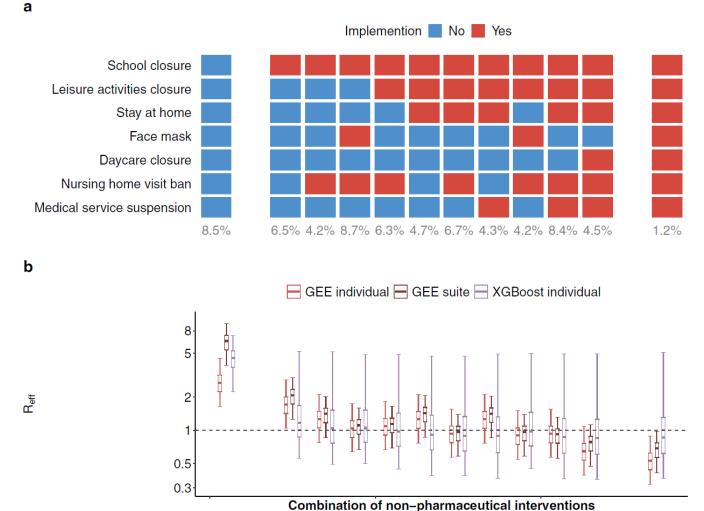


The impact of lockdowns and social distancing



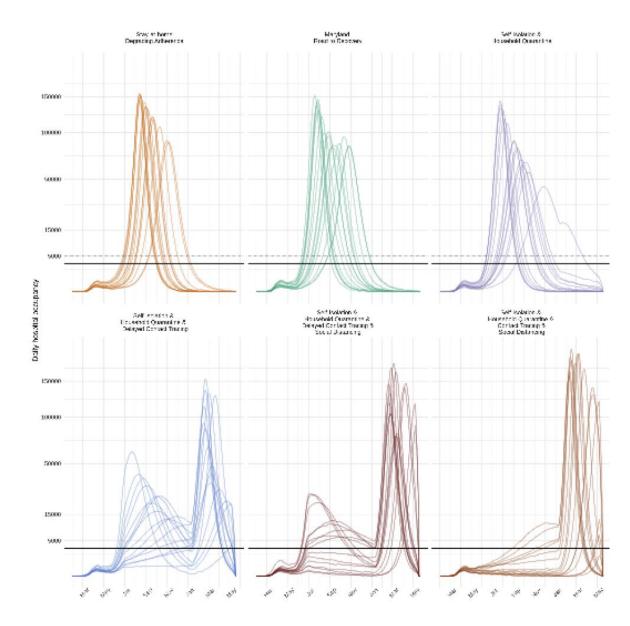
How well do "lockdowns" work?

- The vast majority of studies show that layered social distancing measures such as business closures, limits on gatherings and stay at home orders, reduce COVID-19 spread.
- Multiple measures are needed to contain COVID-19 spread.
- Impacts are delayed.
- Globally, sustained lockdowns have universally resulted in "turning the curve" of the local epidemic.

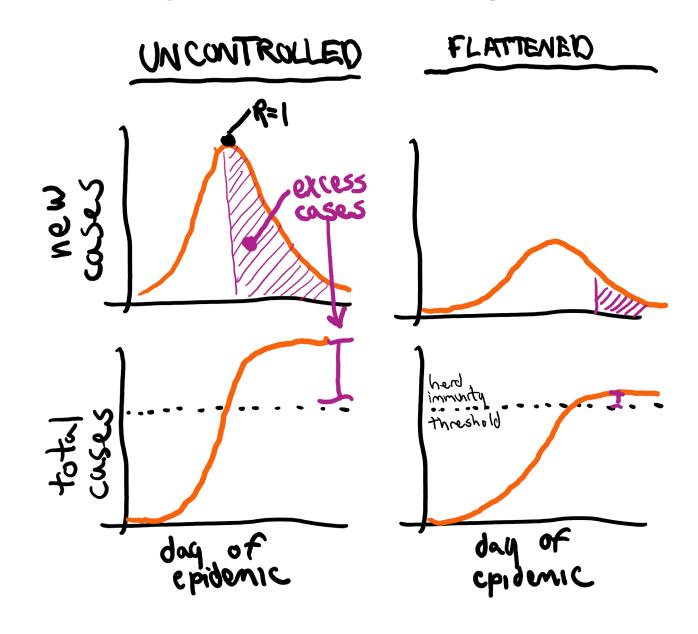


Kicking the can down the road?

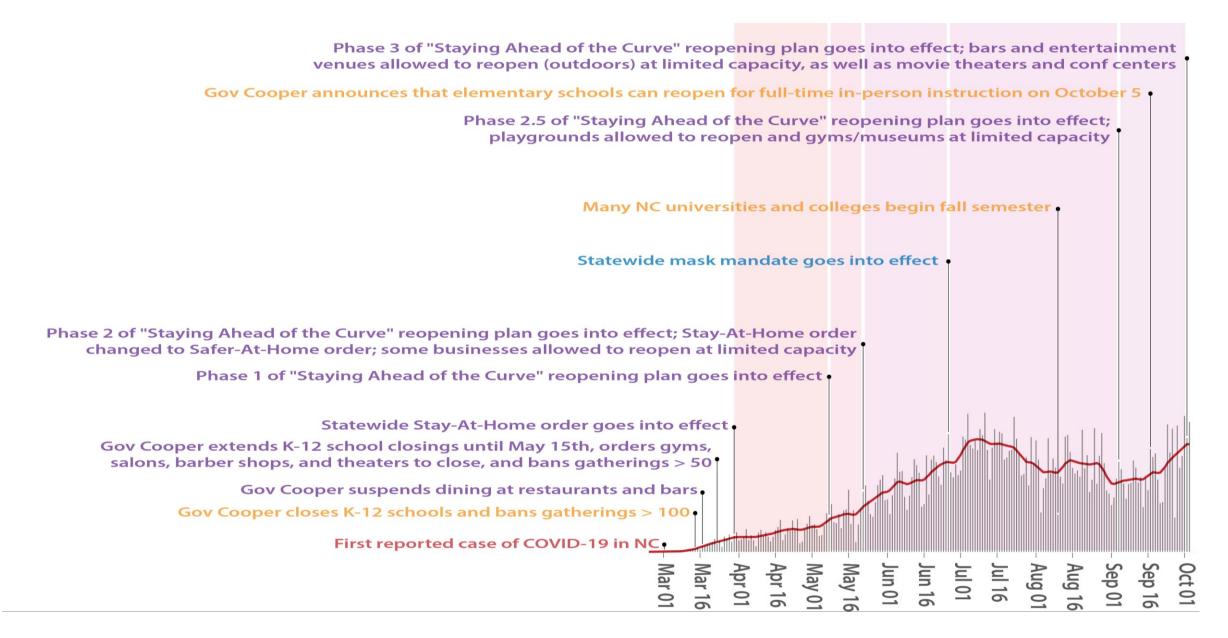
- Highly effective control measures stop the accumulation of immunity in the population.
- Hence they the population remains susceptible to outbreaks once they are lifted.
- They buy critical time for building hospital capacity, improving treatment, and development of a vaccine.



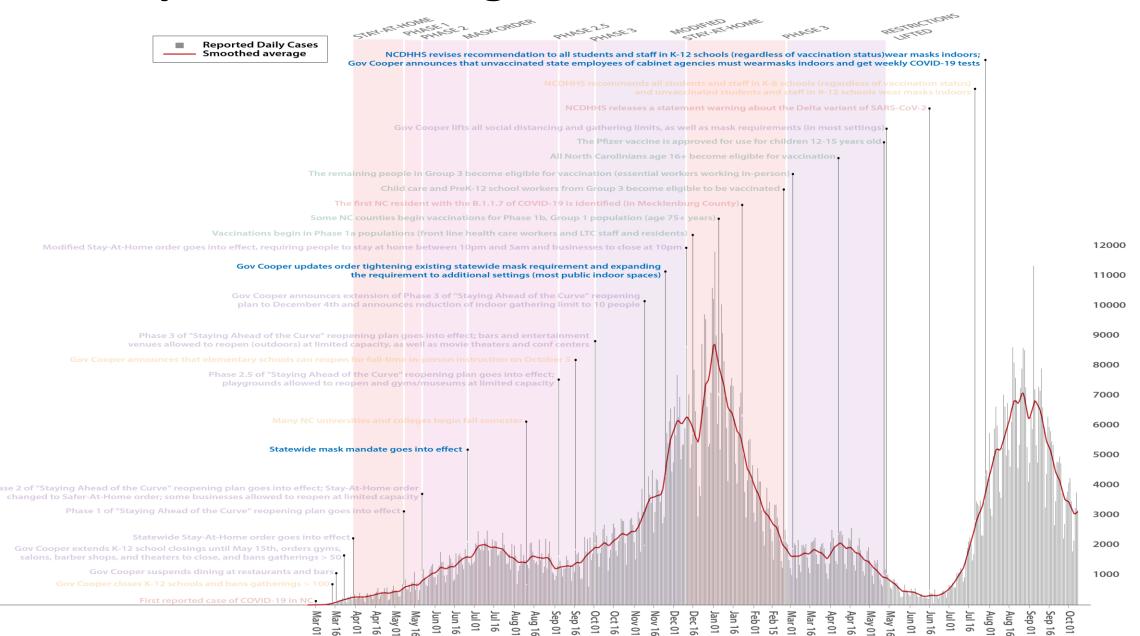
Herd immunity and flattening the curve.



Summer 2020: A brief respite

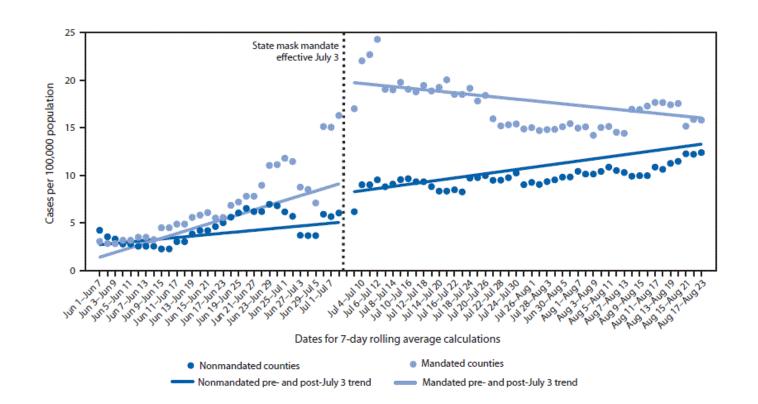


The impact of masking?



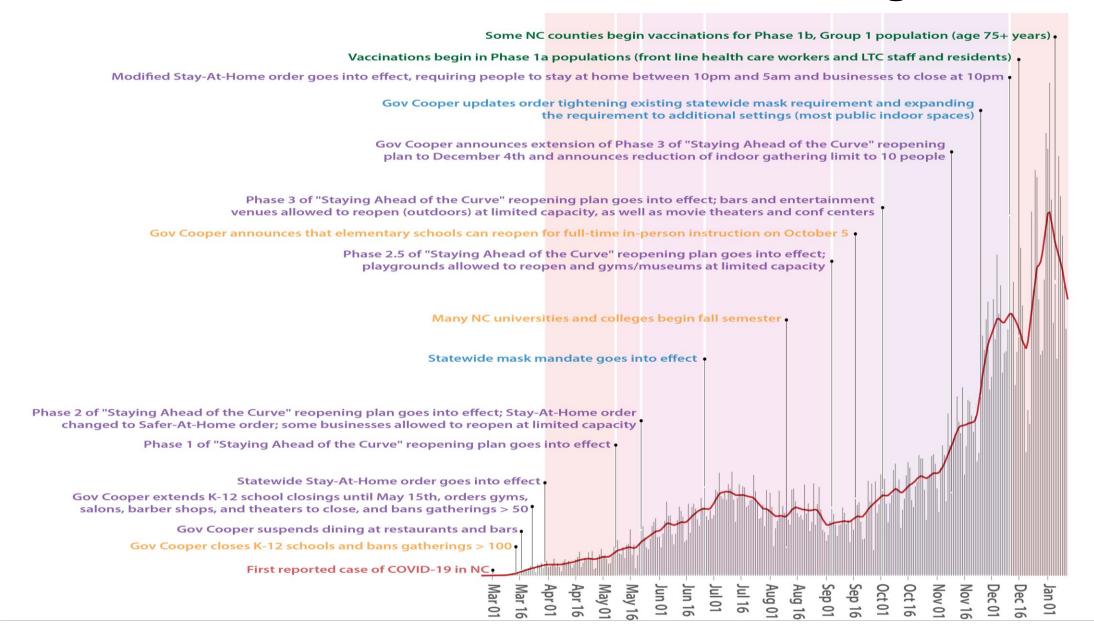
The impact of masks

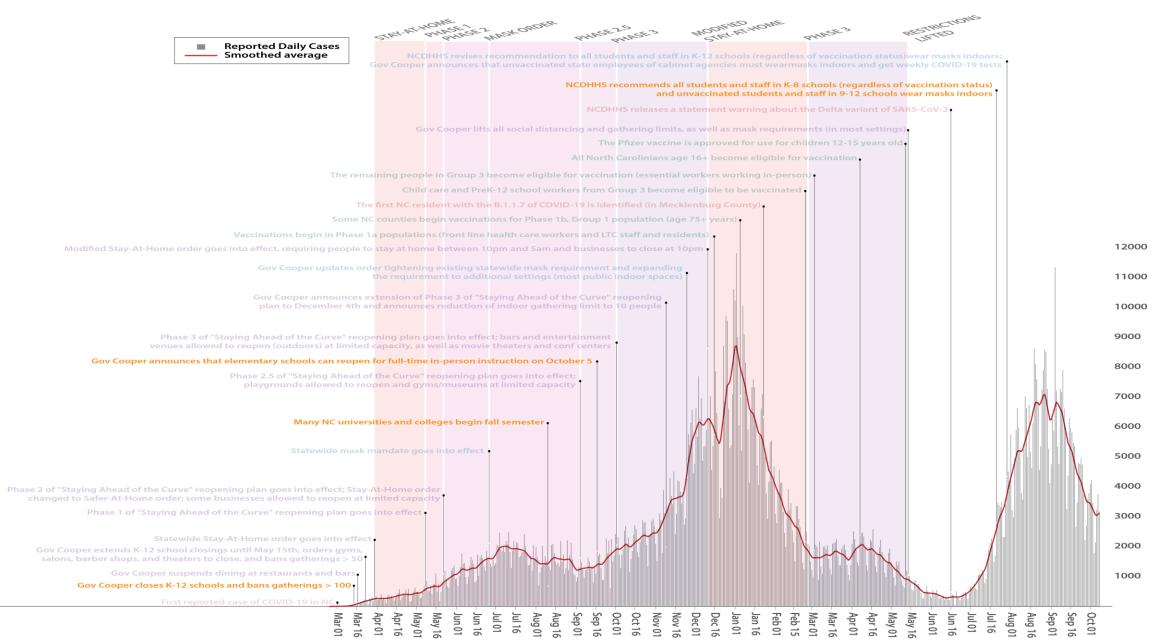
- Masks decrease an individuals chance of being infected by 60-70% with strong adherence.
- Masking mandates decrease the efficiency of community COVID-19 transmission by 10-20% (US Spring/Summer 2020 data)



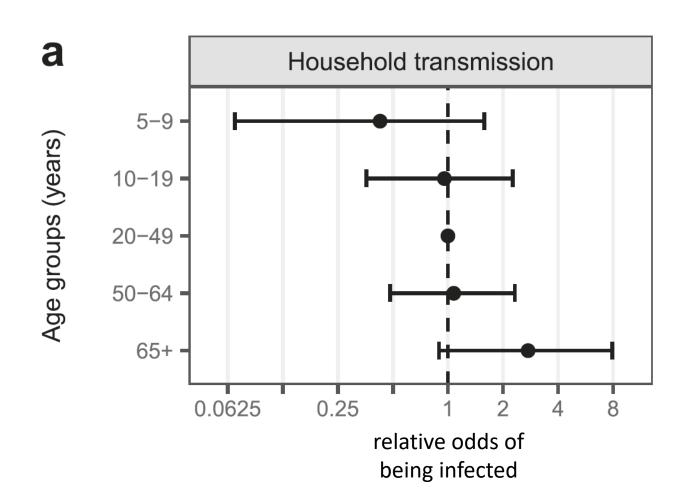
	Country	Respirator (0=no)	Infection	Events, face mask (n/N)	Events, no face mask (n/N)		RR (95% CI)	% weight (random)
Health-care setting								
Scales et al (2003)66	Canada	0	SARS	3/16	4/15	-	0.70 (0.19-2.63)	3.2
Liu et al (2009)51	China	0	SARS	8/123	43/354	-	0.54 (0.26-1.11)	6.7
Pei et al (2006)61	China	0	SARS	11/98	61/115	-	0.21 (0.12-0.38)	7.9
Yin et al (2004)75	China	0	SARS	46/202	31/55	-	0-40 (0-29-0-57)	10-3
Park et al (2016)59	South Korea	0	MERS	3/24	2/4	•	0.25 (0.06-1.06)	2-8
Kim et al (2016)48	South Korea	0	MERS	0/7	1/2		0.13 (0.01-2.30)	0.8
Heinzerling et al (2020)44	USA	0	COVID-19	0/31	3/6 ←	• <u>-</u> _	0.03 (0.002-0.54)	0-9
Nishiura et al (2005) ⁵⁵	Vietnam	0	SARS	8/43	17/72		0.79 (0.37-1.67)	6.5
Nishiyama et al (2008)56	Vietnam	0	SARS	17/61	14/18	→	0.36 (0.22-0.58)	9.0
Reynolds et al (2006)64	Vietnam	0	SARS	8/42	14/25	-	0.34 (0.17-0.69)	6-7
Loeb et al (2004)53	Canada	1	SARS	3/23	5/9	-	0.23 (0.07-0.78)	3-6
Wang et al (2020)41	China	1	COVID-19	0/278	10/215 -	-	0.04 (0.002-0.63)	0-9
Seto et al (2003) ⁶⁷	China	1	SARS	0/51	13/203		0.15 (0.01-2.40)	0.9
Wang et al (2020)70	China	1	COVID-19	1/1286	119/4036		0.03 (0.004-0.19)	1-7
Alraddadi et al (2016)34	Saudi Arabia	1	MERS	6/116	12/101	•	0.44 (0.17-1.12)	5.0
Ho et al (2004)45	Singapore	1	SARS	2/62	2/10	• :	0.16 (0.03-1.02)	1.9
Teleman et al (2004) ⁶⁸	Singapore	1	SARS	3/26	33/60	•	0.21 (0.07-0.62)	4.2
Wilder-Smith et al (2005) ⁷²	Singapore	1	SARS	6/27	39/71		0.40 (0.19-0.84)	6.5
Ki et al (2019)47	South Korea	1	MERS	0/218	6/230	-	0.08 (0.005-1.43)	0-8
Kim et al (2016)49	South Korea	1	MERS	1/444	16/308	•	0.04 (0.01-0.33)	1.6
Hall et al (2014)43	Saudi Arabia	1	MERS	0/42	0/6		(Not calculable)	0
Ryu et al (2019)65	South Korea	1	MERS	0/24	0/10		(Not calculable)	0
Park et al (2004) ⁵⁸	USA	1	SARS	0/60	0/45	!	(Not calculable)	0
Peck et al (2004)60	USA	1	SARS	0/13	0/19		(Not calculable)	0
Burke et al (2020)37	USA	1	COVID-19	0/64	0/13	1	(Not calculable)	0
Ha et al (2004)42	Vietnam	1	SARS	0/61	0/1	1	(Not calculable)	0
Random subtotal (P=50%)				126/3442	445/6003		0-30 (0-22-0-41)	81.9
Non-health-care setting								
Lau et al (2004)50	China	0	SARS	12/89	25/98	-	0.53 (0.28-0.99)	7.5
Wu et al (2004)74	China	0	SARS	25/146	69/229	-	0.57 (0.38-0.85)	9-7
Tuan et al (2007) ⁶⁹	Vietnam	0	SARS	0/9	7/154		1.03 (0.06-16-83)	0.9
Random subtotal (I ² =0%)				37/244	101/481	$ \diamond $	0.56 (0.40-0.79)	18-1
Unadjusted estimates, overall (P=48%)				163/3686	546/6484	\$	0.34 (0.26-0.45)	100-0
Adjusted estimates, overall (1 COVID-19, 1 MERS, 8 SARS)						\Diamond	aOR 0-15 (0-07-0-34)	
Interaction by setting, p=0-0	49; adjusted for	N95 and dista	nce, p=0-11		_		aRR 0-18 (0-08-0-38)	
						\leftarrow	10	
						Favours face mask Favours n	no face mask	

Fall 2020 to Winter 2021: The winter surge

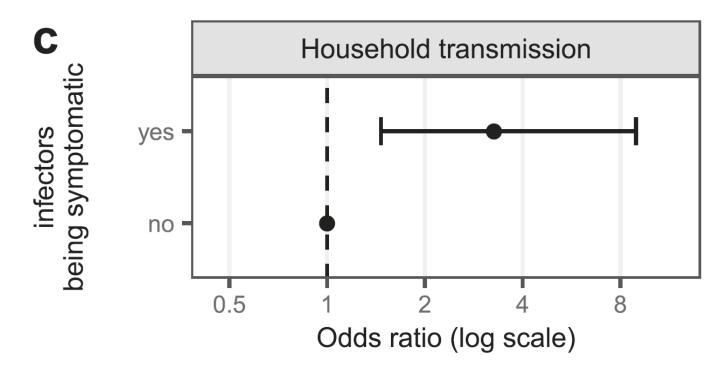




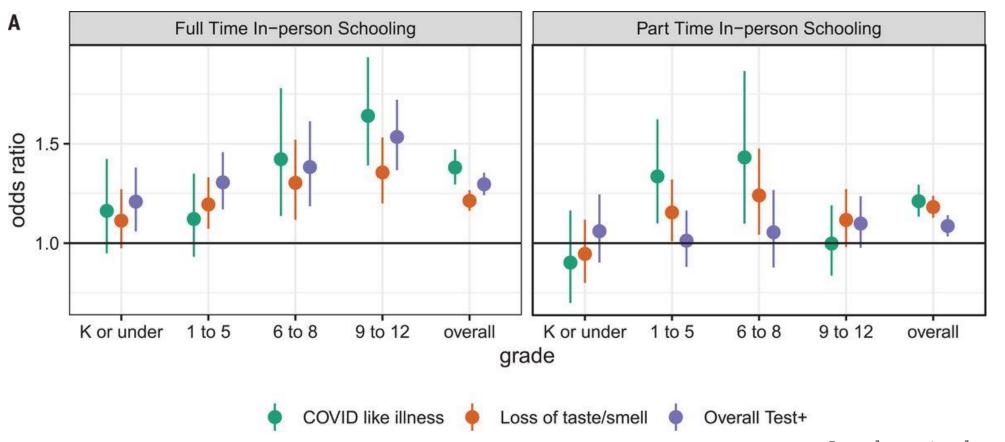
- For the original strain children are half as likely to get infected if exposed than adults.
- Children are less likely get sick if infected.
- Unclear if children are less likely to transmit if symptomatic.
- Unclear if this has changed with Alpha and Delta variants.



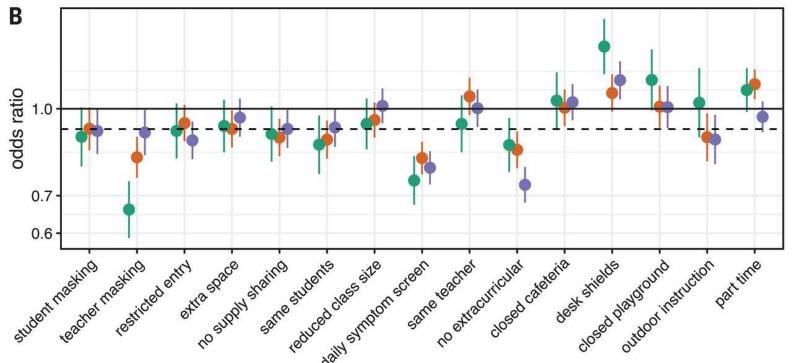
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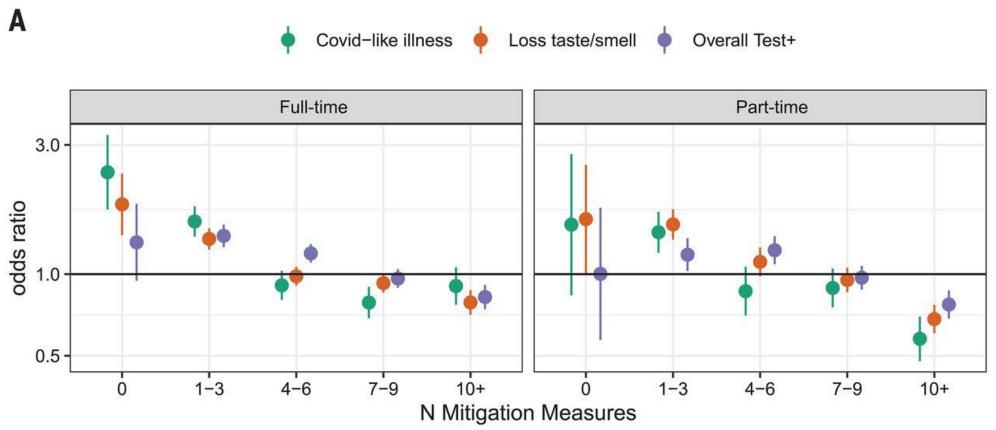
• **People living with a child in in-person** school are around 30% more likely to report COVID-19 related outcomes than those living with a child not in in-person school.



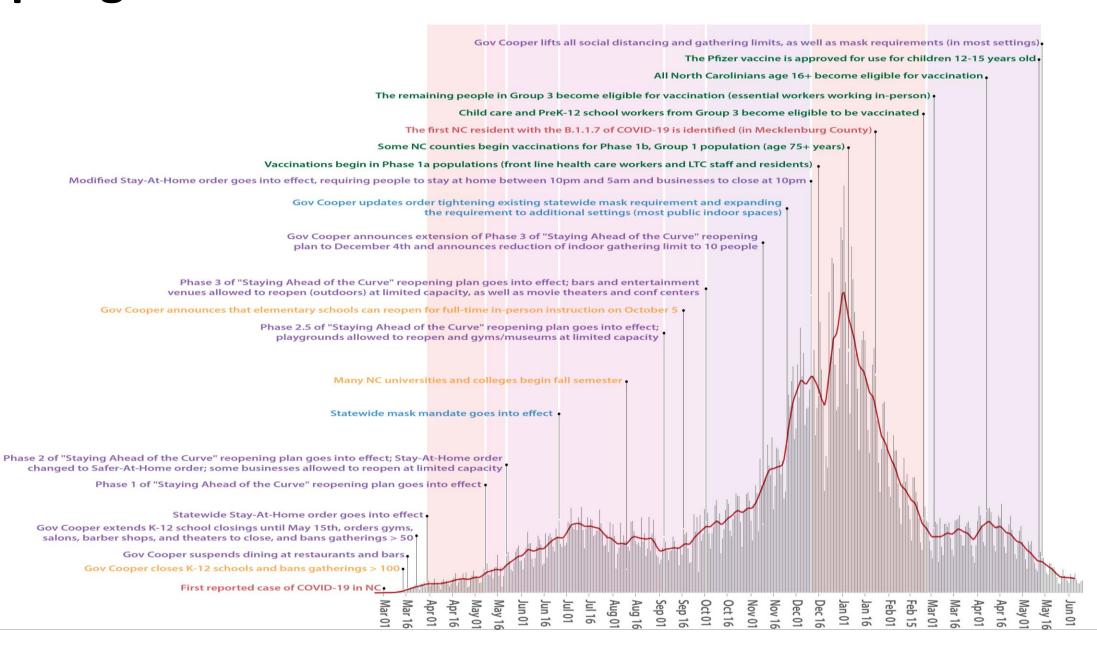
- Each additional mitigation measure put in place leads to about an 8% reduction in the chances of a household member reporting a COVID-19 related outcome.
- Teacher masking, daily symptom screens and cancelling extracurricular activities stand out as effective



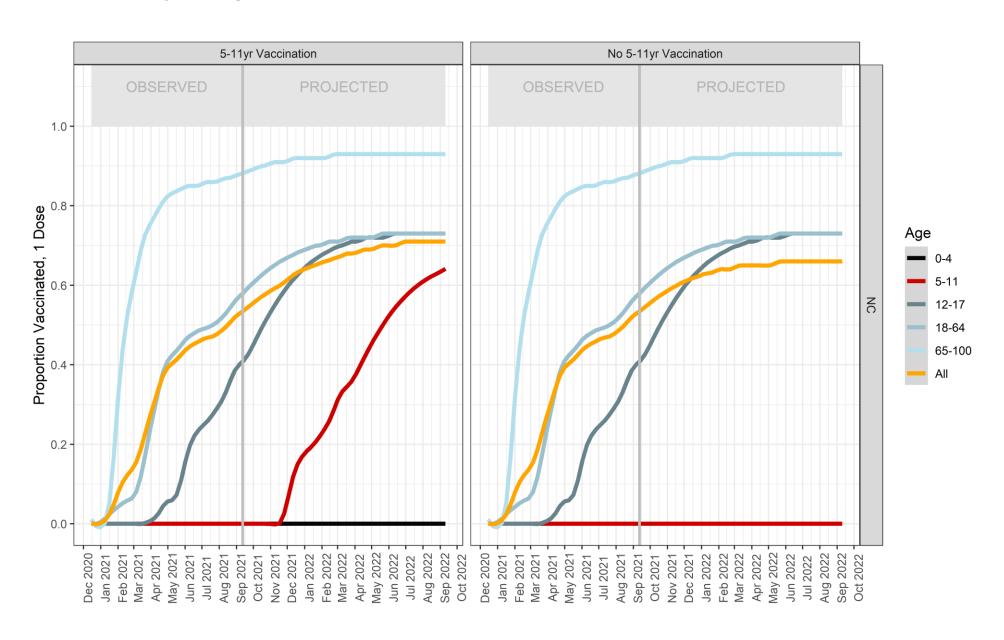
 Once 7+ mitigation measures are in place there is no excess risk of reporting COVID-19 related outcomes among household members of kids attending in-person school.



Spring to Summer 2021: Vaccination and Decline



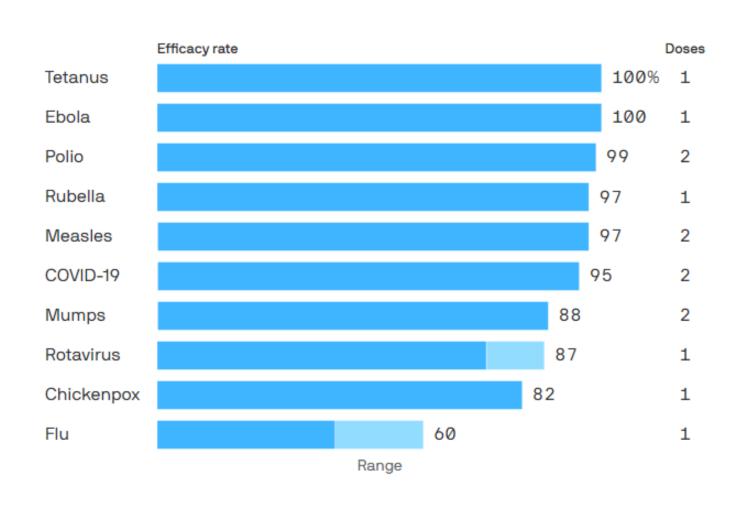
Past and projected vaccination rates in NC



How well does the vaccine work?

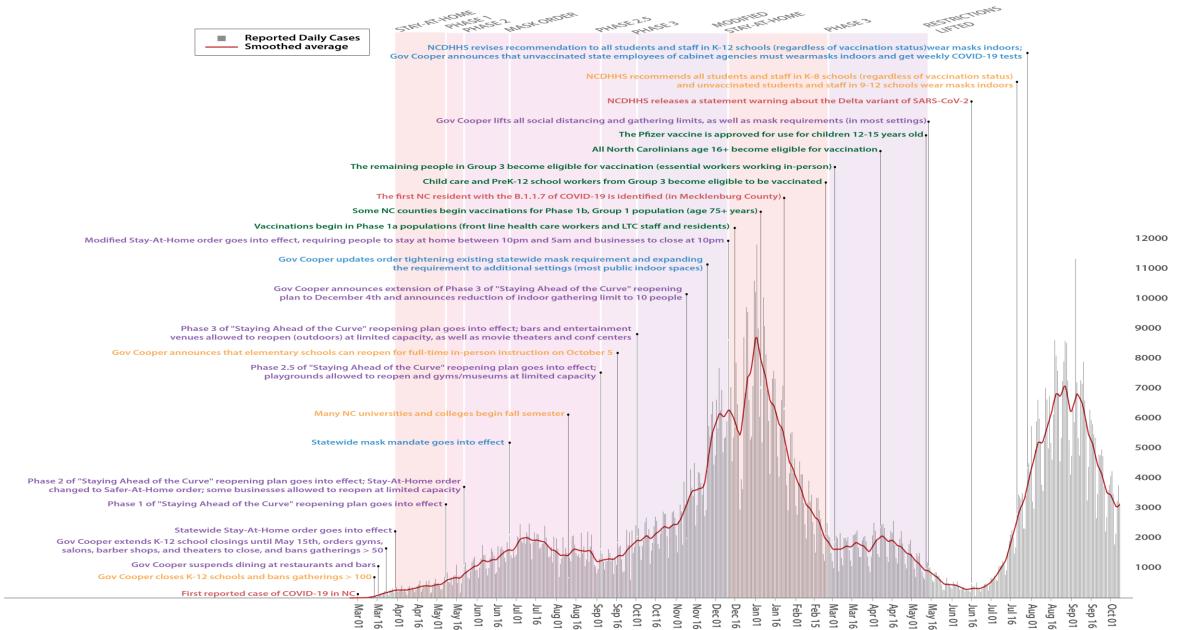
mRNA vaccines are:

- > 90% effective against hospitalization and death
- >70% effective against infection
- Declines as we get further out from vaccination
- Slightly less effective in those 65 or older.



Data: CDC, Moderna and Pfizer; Note: Flu vaccine based on yearly average from 2009-2019. Moderna and Pfizer coronavirus vaccine efficacy based on early clinical trial data. Chart: Sara Wise/Axios

Summer to Fall 2021: The Delta Wave

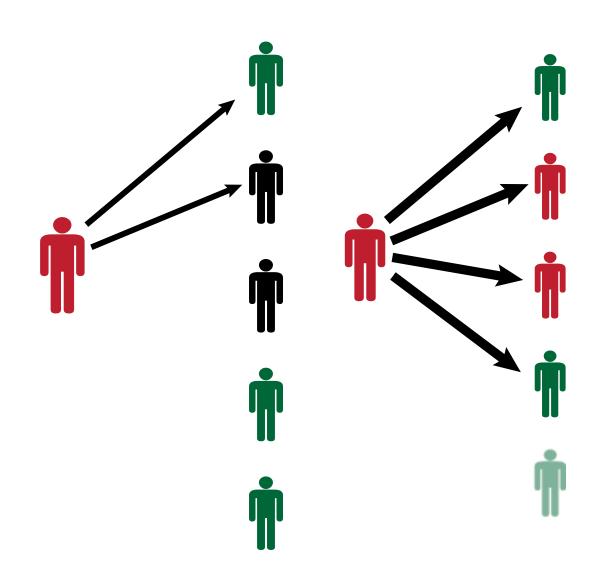


Why has Delta been so bad?

 Delta is about 1.5 times as transmissible as Alpha and over twice as transmissible as the original strain.

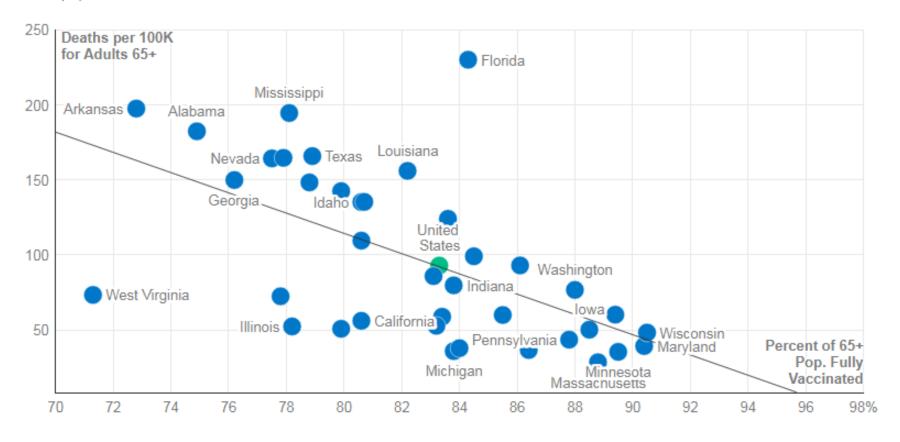
 Delta's emergence coincided with reductions in mandated control measures and voluntary changes in behavior.

 Some reductions in vaccine efficacy associated with the risk of Delta.



Vaccines blunt the impact of Delta

COVID-19 deaths for adults 65 and older per 100,000 between July 1, 2021 and September 25, 2021, among the 65 and older population of each state



NOTE: States were excluded from this analysis where there was a discrepancy of more than 10% between the total number of COVID-19 deaths by age group and the total number of deaths overall within the state. We calculated the Pearson correlation coefficient, which indicated there was a significant negative correlation between vaccination rates and death rates among older adults: r= -.59, p-value <.001. See methods for additional information.



SOURCE: KFF analysis of the CDC Provisional COVID-19 Death Counts by Sex, Age, and State data July 1 - September 25, 2021. Population estimates of adults 65 and older from each state are from the 2019 US Census Bureau. • PNG

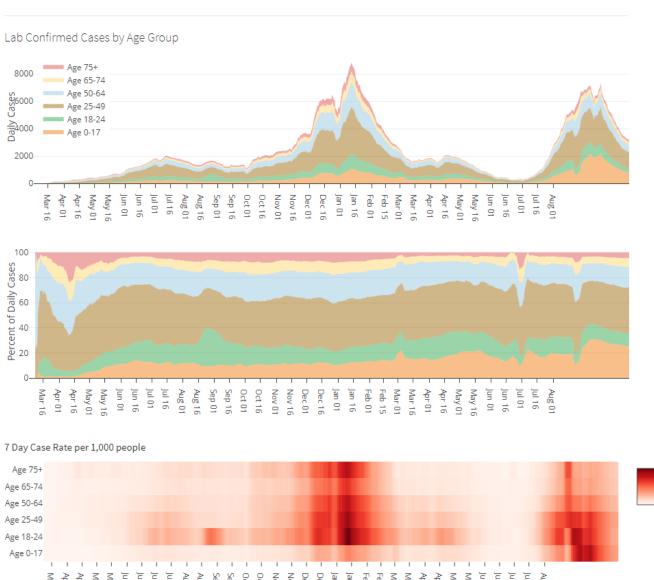
Delta and the changing epidemiology of the pandemic.

Lab Confirmed Cases by Age Group

 Cases have been younger in the Delta wave than in previous waves.

 This likely reflects the impact of a more infectious virus differential vaccination/immunity by age.

 This effect is even more stark for deaths.

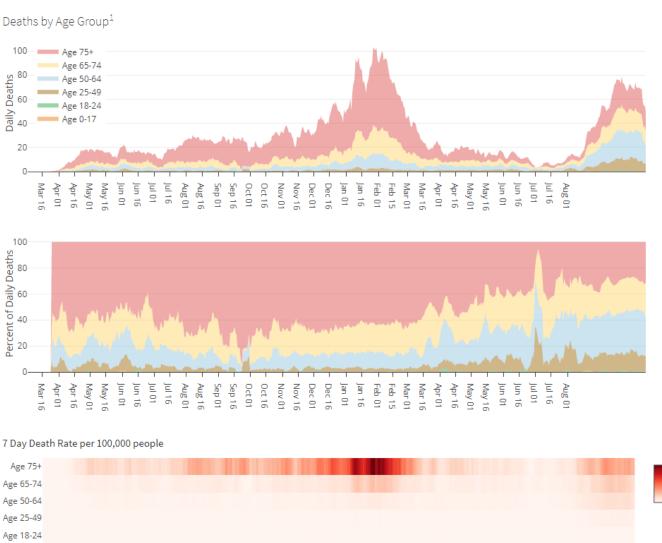


Delta and the changing epidemiology of the pandemic. Deaths by Age Group¹

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The Impact of the Pandemic in North Carolina

- 3.9 million infected (over 1 in every 3 North Carolinians)
- 1.4 million cases
 (about 1 in every 7)
- 550,000-820,000 hospitalized (about 1 in every 20 to 1 in every 12)
- 18,000 deaths (over 1 in every 600)
- About 5.6 million fully vaccinated (over 1 in every 2)



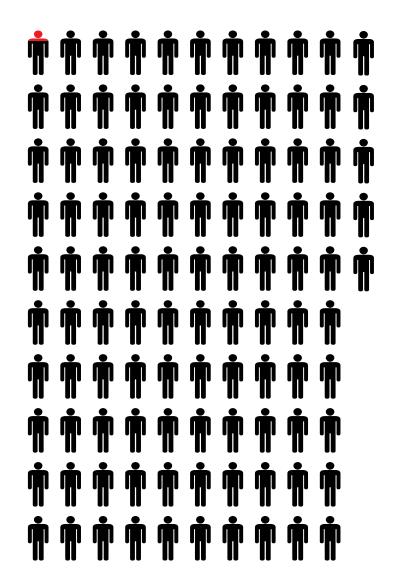
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...and the pandemic that wasn't.

An uncontrolled pandemic:

Original strain:
 7.8 million infections and 47,000 deaths

Delta like:
 10.2 million infections and up to 134,000 deaths

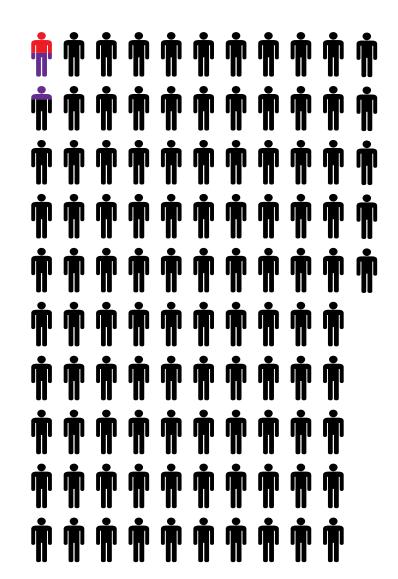


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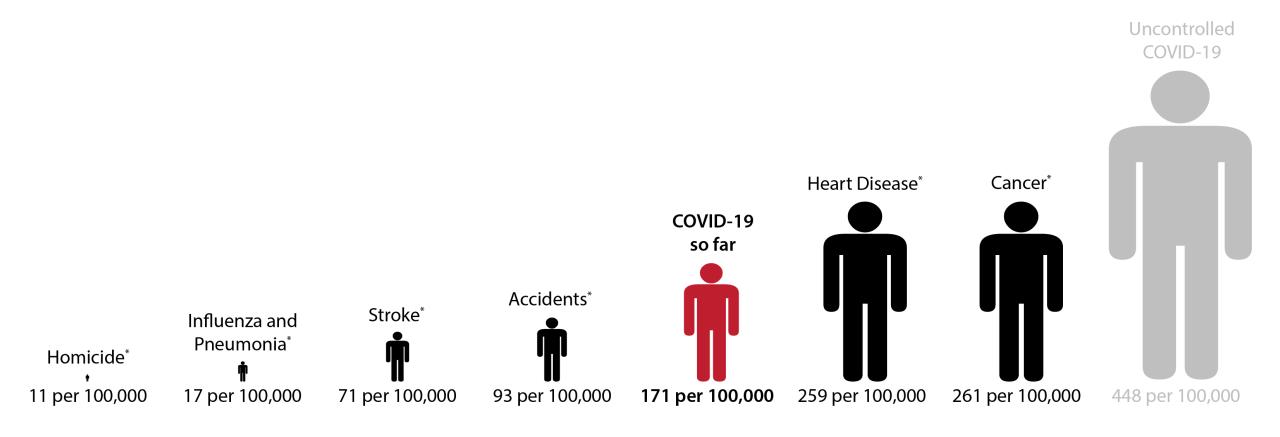
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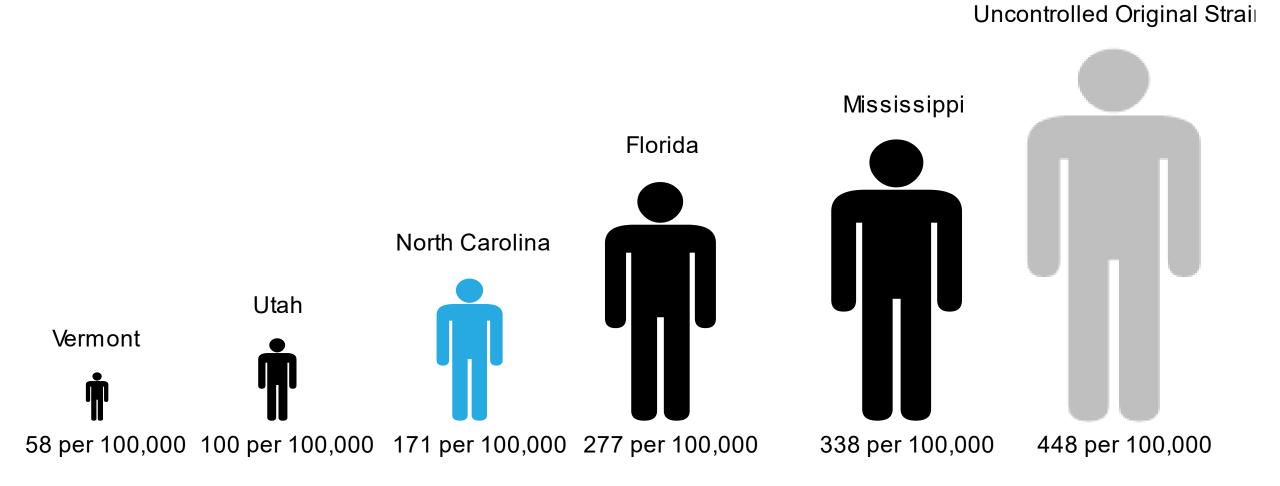


North Carolina COVID-19 deaths in context

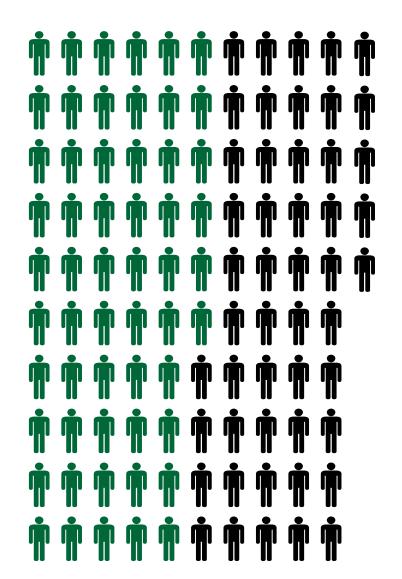


^{* -} projected deaths March 1, 2020 - October 31, 2021 based on 2017 rate.

North Carolina COVID-19 deaths in context



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The Future







University of Massachusetts Amherst

















Northeastern University







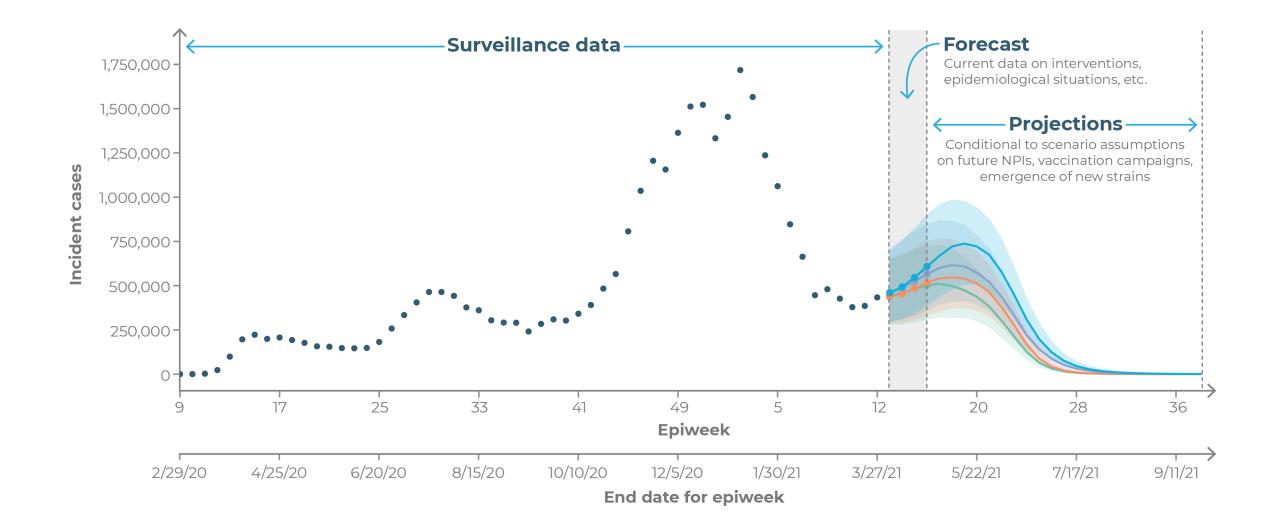


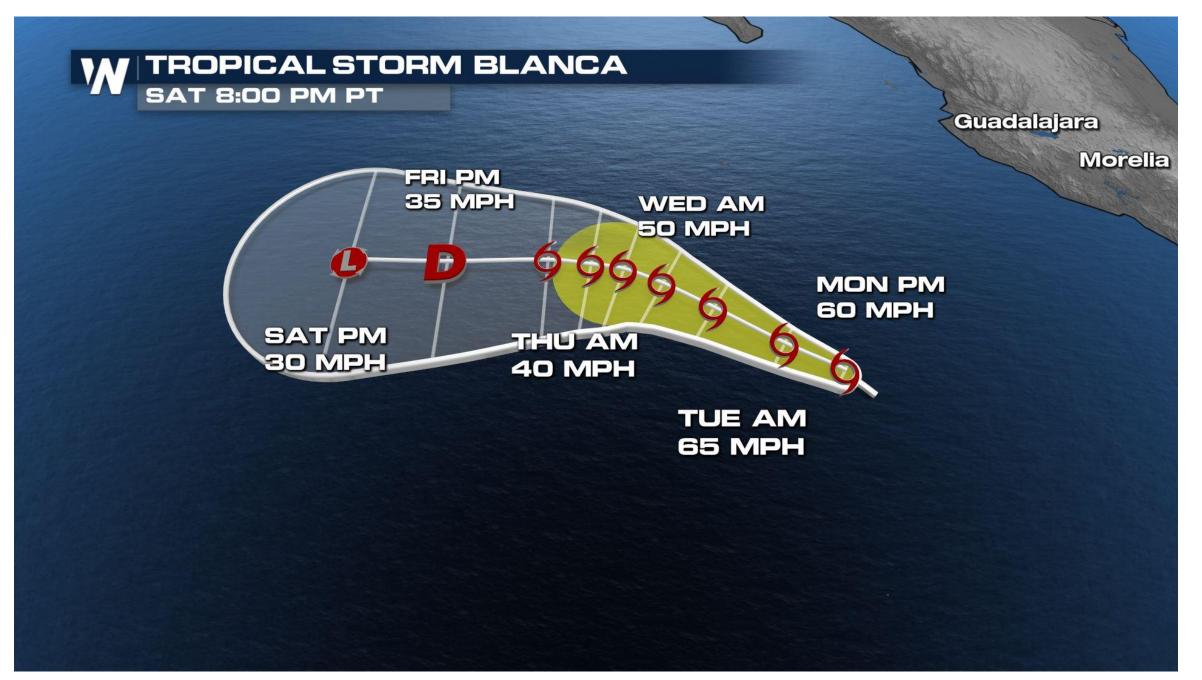




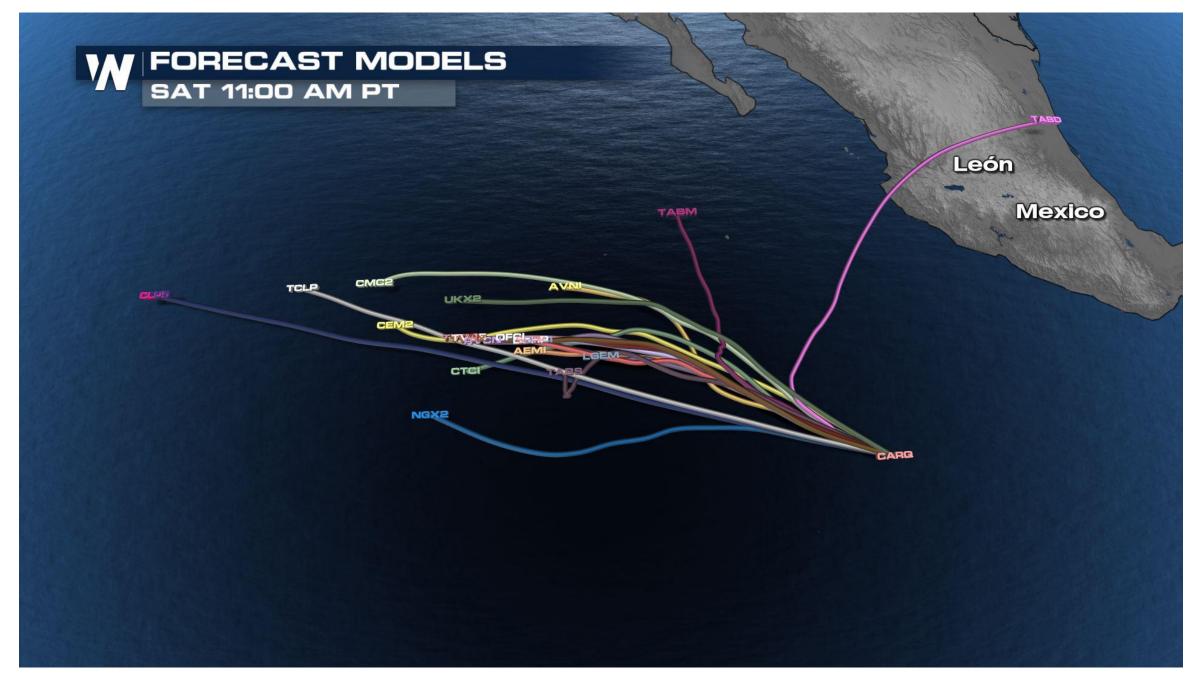
THE UNIVERSITY
of NORTH CAROLINA
at CHAPEL HILL

Planning scenarios, not forecasts!





From Tropical Storm Blanca Strengthens in the Eastern Pacific - WeatherNation (weathernationtv.com)



From <u>Tropical Storm Blanca Strengthens in the Eastern Pacific - WeatherNation (weathernationtv.com)</u> / cyclocane.com

Immunization 5-11 yrs

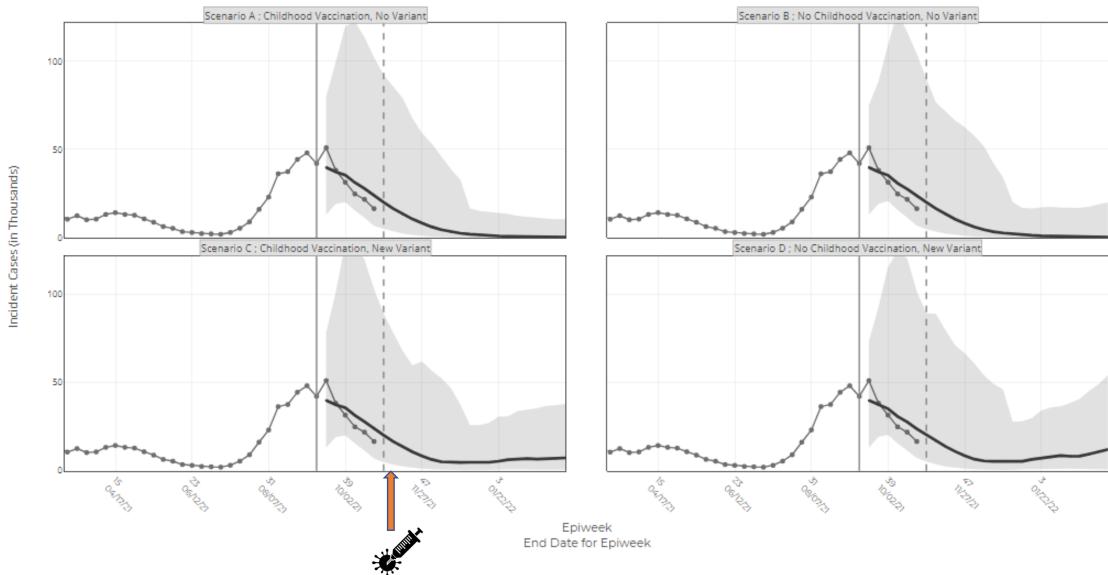
Round 9 Scenario Definitions

Variant emergence

	The same mix of variants circulate throughout the projection period. No change in virus transmissibility.	A more transmissible variant emerges, comprising 1% of circulating viruses on Nov 15 . The new variant is 1.5X as transmissible as viruses circulating at the beginning of the projection period.
Vaccination among 5-11yrs is approved and immunization begins on Nov 1. Each state's uptake rate reflects the percent coverage increases observed for 12-17-year-olds since distribution began on May 13.	A	С
No vaccination for children under 12	В	D

- Under 12 yrs immunization starts Nov 1
- Vaccine parameters at teams' discretion
- Report age-specific projections

Results, General Projections



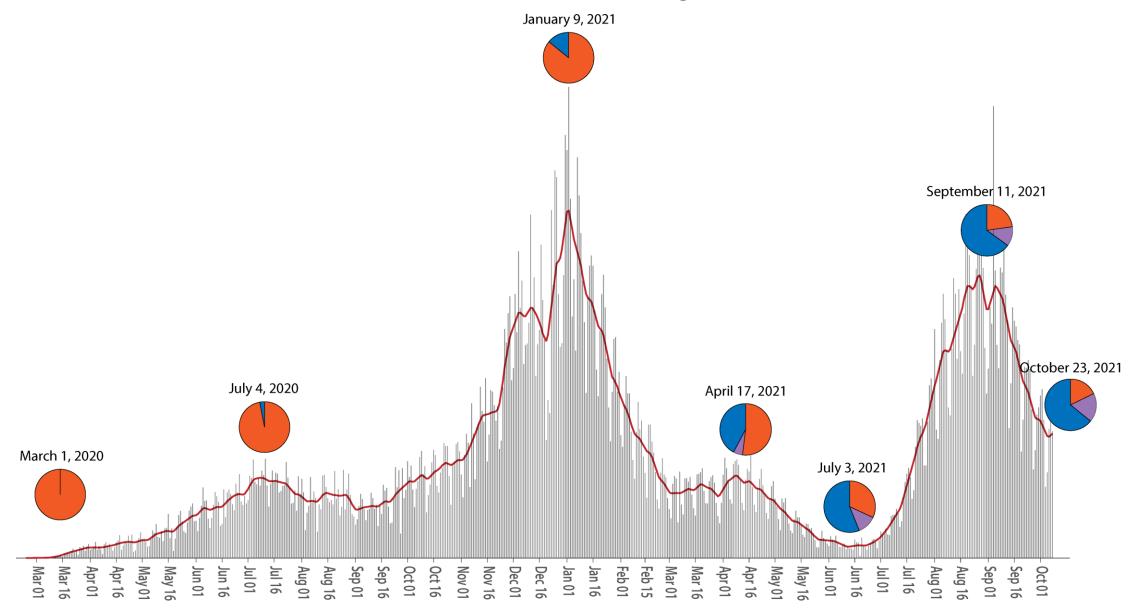
Results: The impact of vaccinating 5-11 year olds

Ratio of Cases (A vs B) in Vay Period

Model			Rallo C	with 95% CI	(%)
CU-AGE-ST		_		0.95 [0.80, 1.10]	9.24
JHUAPL-Bucky		_		0.94 [0.77, 1.11]	8.26
JHU_IDD-CovidSP		-		1.00 [0.93, 1.06]	14.55
MOBS_NEU-GLEAM_COVID				0.96 [0.96, 0.96]	16.97
UNCC-hierbin				0.93 [0.91, 0.96]	16.60
USC-SIkJalpha		•		0.98 [0.54, 1.42]	2.11
UVA-EpiHiper	4	-		0.73 [0.68, 0.79]	15.38
UVA-adaptive				0.94 [0.93, 0.96]	16.89
Overall		•		0.92 [0.85, 0.99]	
Heterogeneity: $\tau^2 = 0.01$, $I^2 = 98.53\%$, $H^2 = 0.01$	67.89				
Test of $\theta_i = \theta_j$: Q(7) = 82.31, p = 0.00					
Test of $\theta = 0$: $z = 26.49$, $p = 0.00$					
	.5	1	1.5		

Random-effects REML model

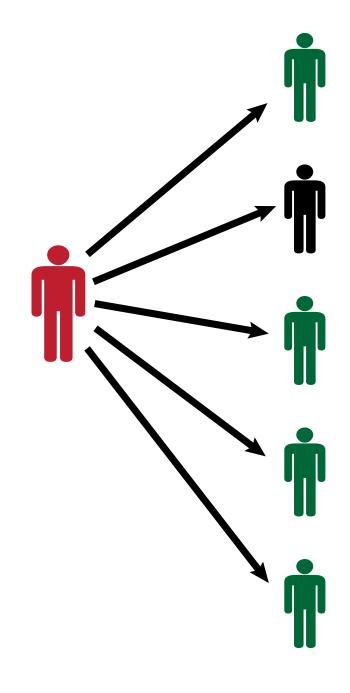
The accumulation of immunity in North Carolina



How could this all be wrong?

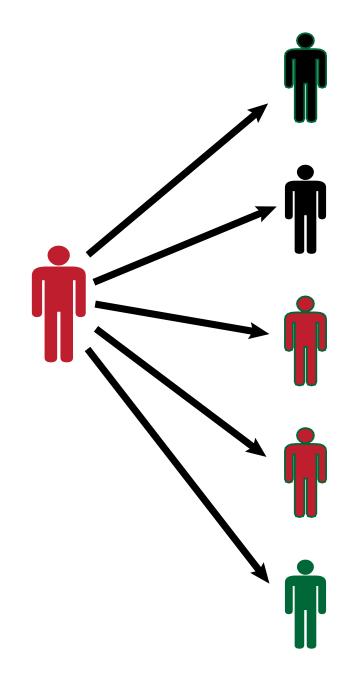
- Immune escape
- Stronger than expected behavioral or seasonal impacts

• Higher than expected COVID-19 detection/death rates.



- Immune escape
- Stronger than expected behavioral or seasonal impacts

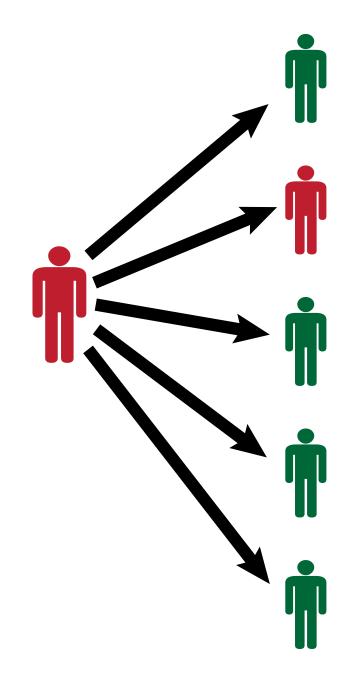
• Higher than expected COVID-19 detection/death rates.



• Immune escape

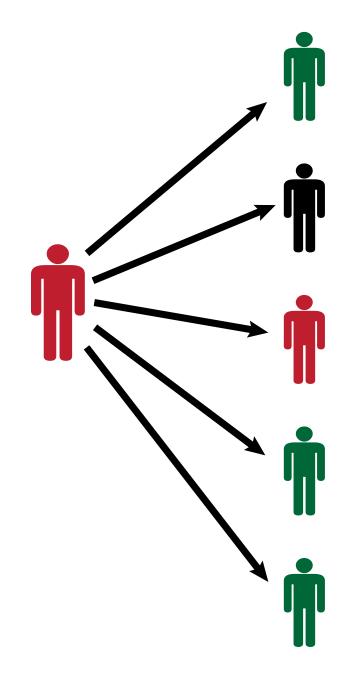
Stronger than expected behavioral or seasonal impacts

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- Immune escape
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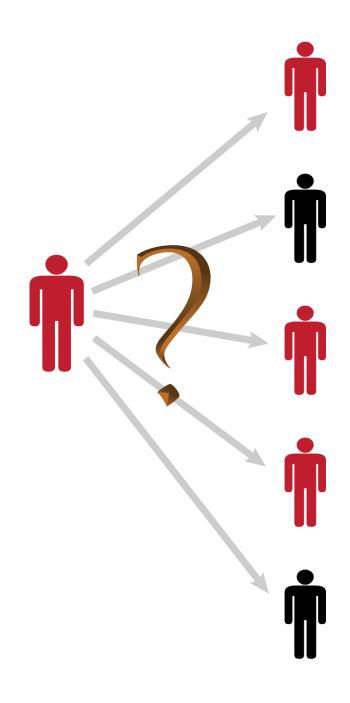
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• Immune escape

 Stronger than expected behavioral or seasonal impacts

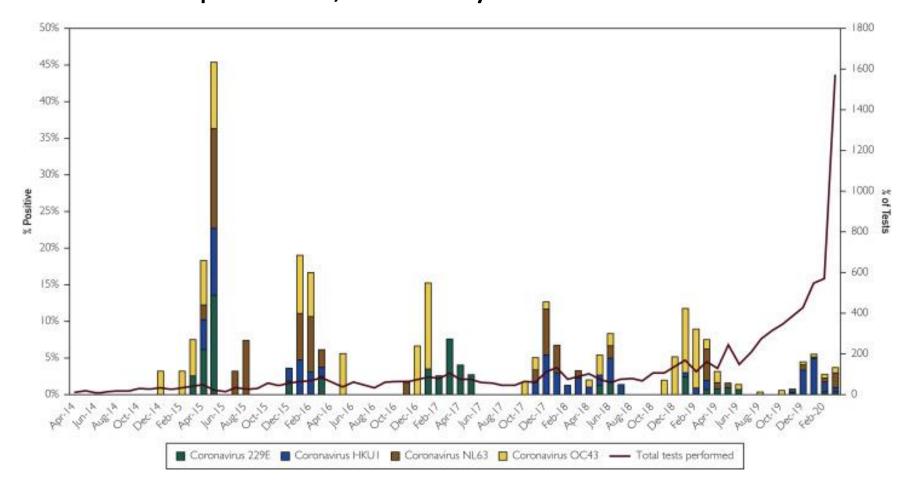
• Higher than expected COVID-19 detection/death rates.



What does COVID-19 look like in 10 years?

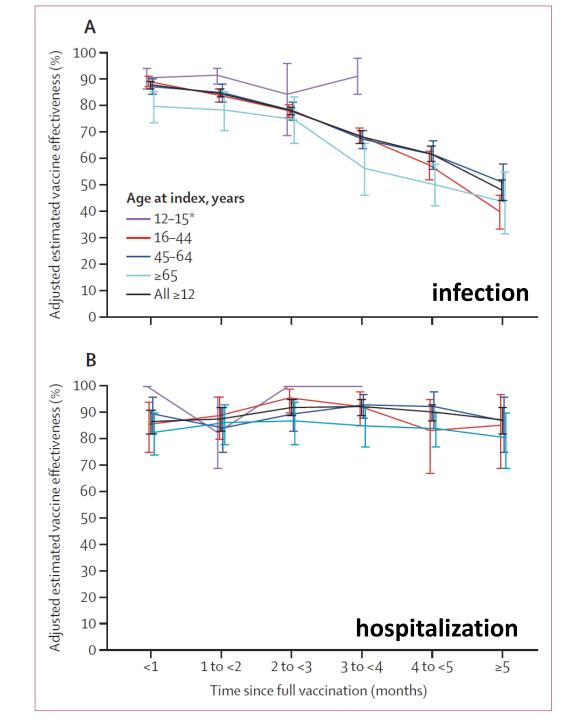
A seasonal coronavirus?

• Most coronaviruses and other respiratory pathogens settle down to cause seasonal epidemics, it is likely COVID-19 will do the same...



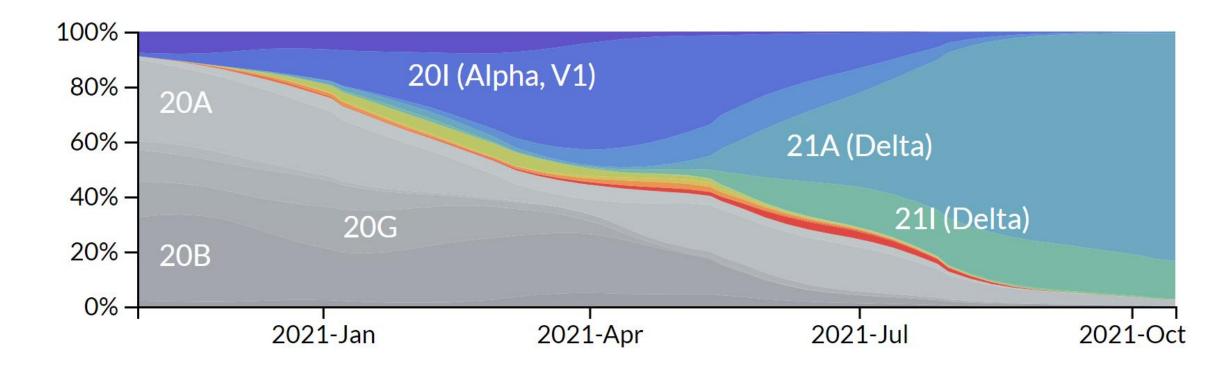
A mild childhood infection?

- Decades in the future only very young children will be seeing COVID-19 for the first time.
- Currently, young children appear to be very unlikely to have severe disease, so most of these first infections will be mild.
- Older individuals will have preexisting immunity from vaccine or previous infection, hence will have more mild symptoms if they are infected at all.



Annual vaccination?

• The variants prove that there is every possibility that SARS-CoV-2 continues to evolve away from human immunity (like influenza), and repeated vaccination will be needed.



Summing Up

 The impact of COVID-19 in North Carolina has been middling compared to all US states.

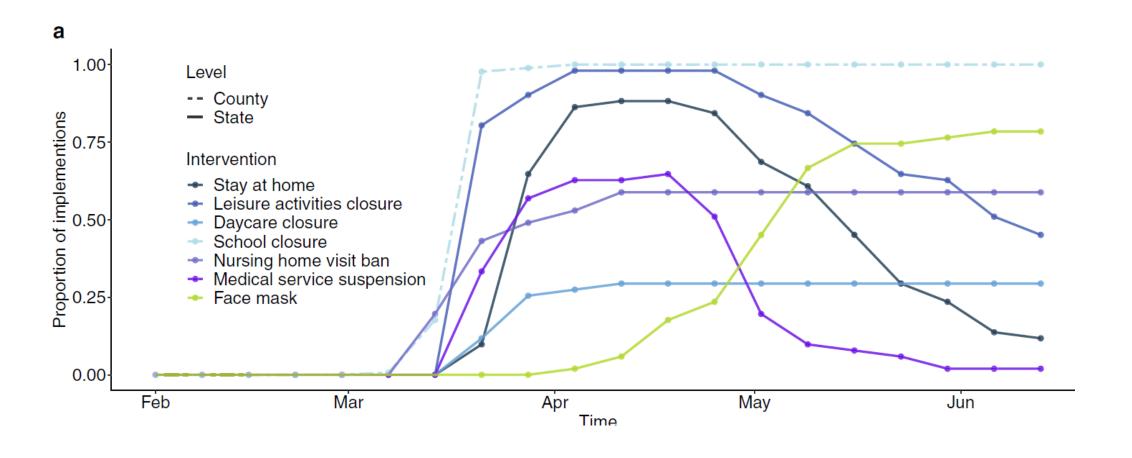
• Control measures from masks, to lockdowns, to vaccination have been effective in controlling COVID-19, but will not eradicate the disease.

 We are likely entering a new phase of the pandemic with things looking good over the short term and a long term outlook where COVID-19 remains a threat, but not a big one.

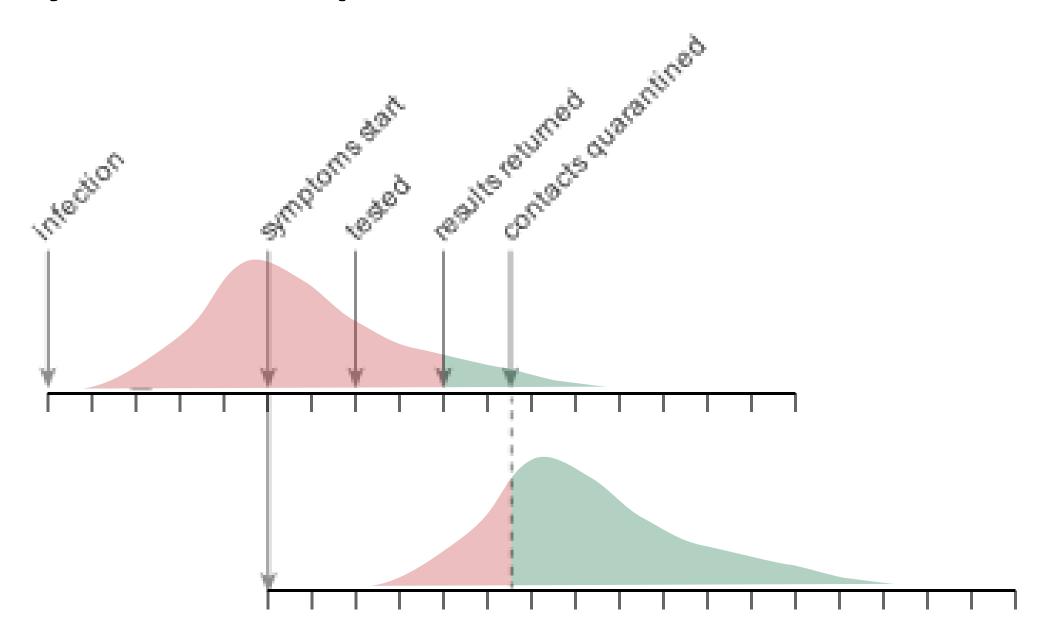
• The virus has surprised us before, and very well could again, so caution and humility are needed as we look to the future.

Backup

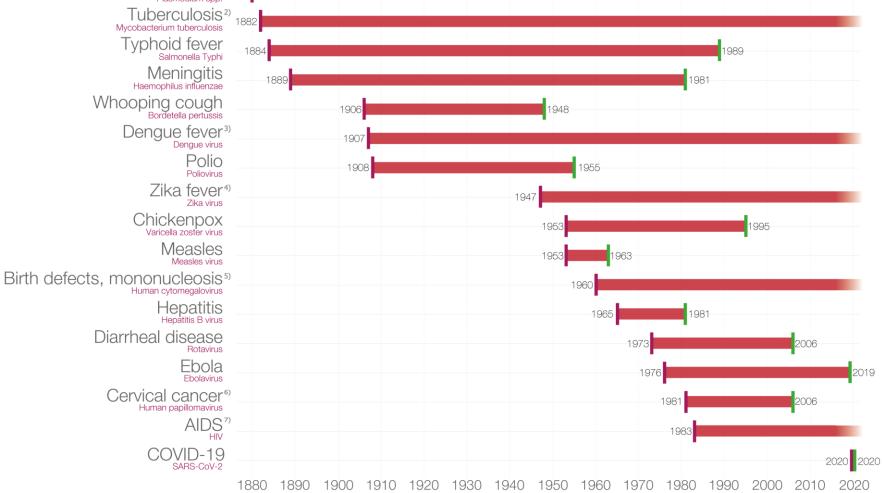
How well do "lockdowns" work?



Why should we quarantine?



Vaccination innovation, Our World Disease in Data Infectious agent from 1880 to 2020 year in which the agent year in which the vaccination was linked to the disease was licensed in the US Malaria¹⁾ Plasmodium spp. Tuberculosis²⁾ Mycobacterium tuberculosis Typhoid fever



^{1) - 2016} vaccine RTS,S undergoing pilot trials in select countries after being approved by European regulators in 2015.

^{2) –} The only approved vaccine is bacilli Calmette-Guérin (BCG), developed in 1921 but its efficacy in adults is variable. Other tuberculosis vaccines are currently in development. 3) – 2016 partially effective vaccine CYD-TDV, sold under the brand name Dengvaxia.

^{4) -} Successful first human clinical trials of a vaccine against the virus in 2016. Only in 2016 did the WHO issue statements of concern about the zika virus' links to Guillain-Barré Syndrome (GBS) and microcephaly. 5) - A number of vaccine candidates are under investigation.

^{6) -} Not all cervical cancers are caused by the HPV virus and the HPV vaccine can protecet against other cancers caused by the HPV virus.

^{7) - 2009} efficacy findings for vaccine candidate RV 144 has shown some promise. In stage III human trials.

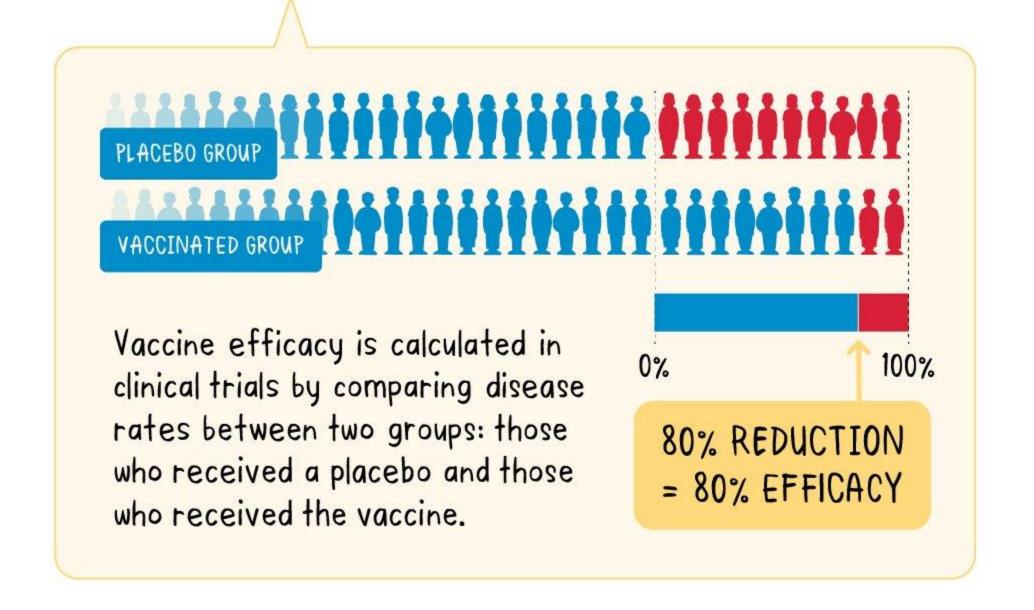
Vaccine-preventable diseases in the US Shown is the reduction of cases and deaths after the introduction of the vaccine Our World in Data



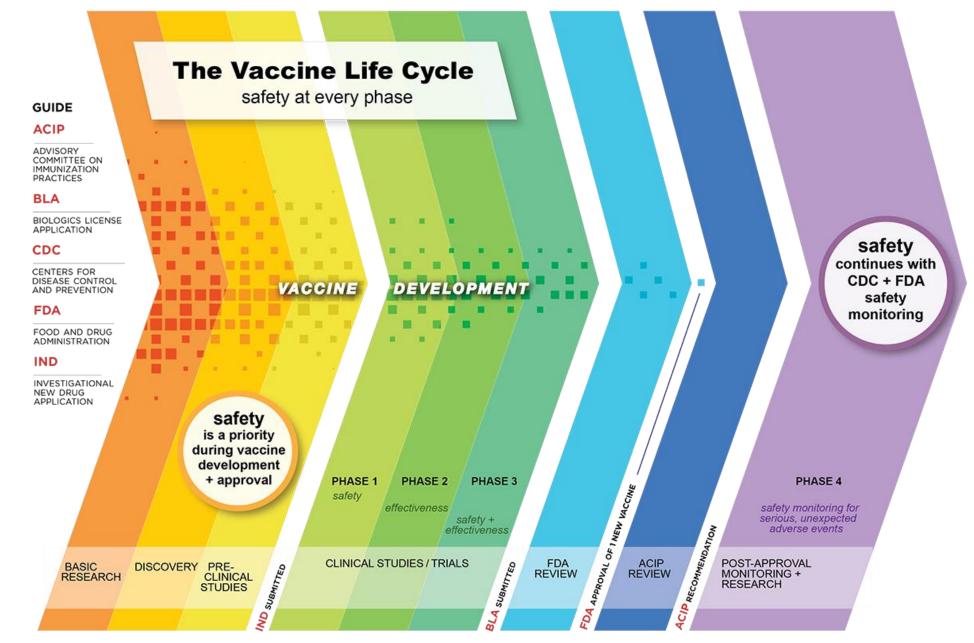
		Cases	All post-vaccine cases refer to 2006	[Deaths	All post-vaccine deaths refer to 2004
Diphtheria	Pre-vaccine: 158 cases per million per year (1936-45)	100% Reduction	Post-vaccine: 0 cases per million per year	Pre-vaccine: 13.7 deaths per million per year (1936-45)	100% Reduction	Post-vaccine: 0 deaths per million per year
Measles	Pre-vaccine: 3044 cases per million per year (1953-62)	99.99% Reduction	Post-vaccine: 0.2 cases per million per year	Pre-vaccine: 2.5 deaths per million per year (1953-62)	100% Reduction	Post-vaccine: 0 deaths per million per year
Mumps	Pre-vaccine: 830 cases per million per year (1963-68)	97.4% Reduction	Post-vaccine: 22 cases per million per year	Pre-vaccine: 0.2 deaths per million per year (1963-68)	100% Reduction	Post-vaccine: 0 deaths per million per year
Pertussis	Pre-vaccine: 1534 cases per million per year (1934-43)	96.6% Reduction	Post-vaccine: 52 cases per million per year	Pre-vaccine: 30.8 deaths per million per year (1934-43)	99.7% Reduction	Post-vaccine: 0.09 deaths per million per year
Acute Poliomyeltis	Pre-vaccine: 141 cases per million per year (1941-50)	100% Reduction	Post-vaccine: 0 cases per million per year	Pre-vaccine: 10 deaths per million per year (1941-50)	100% Reduction	Post-vaccine: 0 deaths per million per year
Paralytic Poliomyeltis	Pre-vaccine: 103 cases per million per year (1951-54)	100% Reduction	Post-vaccine: 0 cases per million per year	Pre-vaccine: 11.8 deaths per million per year (1951-54)	100% Reduction	Post-vaccine: 0 deaths per million per year
Rubella	Pre-vaccine: 242 cases per million per year (1966-68)	99.98% Reduction	Post-vaccine: 0.04 cases per million per year	Pre-vaccine: 0.09 deaths per million per year (1966-68)	100% Reduction	Post-vaccine: 0 deaths per million per year
Congenital Rubella Syndron	Pre-vaccine: 0.76 cases per million per year (1966-69)	99.6% Reduction	Post-vaccine: 0.003 cases per million per year	Pre-vaccine: no data (1966-69)	no data	Post-vaccine: 0 deaths per million per year
Smallpox	Pre-vaccine: 250 cases per million per year (1900-49)	100% Reduction	Post-vaccine: 0 cases per million per year	Pre-vaccine: 2.9 deaths per million per year (1900-49)	100% Reduction	Post-vaccine: 0 deaths per million per year
Tetanus	Pre-vaccine: 4 cases per million per year (1947-49)	96.6% Reduction	Post-vaccine: 0.14 cases per million per year	Pre-vaccine: 3.2 deaths per million per year (1947-49)	99.6% Reduction	Post-vaccine: 0.01 deaths per million per year
Hepatitis A	Pre-vaccine: 465 cases per million per year (1986-95)	89% Reduction	Post-vaccine: 51 cases per million per year	Pre-vaccine: 0.5 deaths per million per year (1986-95)	88.7% Reduction	Post-vaccine: 0.06 deaths per million per year
Acute Hepatitis B	Pre-vaccine: 273 cases per million per year (1982-91)	83.9% Reduction	Post-vaccine: 44 cases per million per year	Pre-vaccine: 1 death per million per year (1982-91)	83.6% Reduction	Post-vaccine: 0.16 deaths per million per year
Haemophilus Influenza type b	Pre-vaccine: 84 cases per million per year (1980s)	99.8% Reduction	Post-vaccine: 0.17 cases per million per year	Pre-vaccine: no data (1980s)	no data	Post-vaccine: 0.02 deaths per million per year
Pneumococca Disease	Pre-vaccine: 233 cases per million per year (1997-99)	40.5% Reduction	Post-vaccine: 139 cases per million per year	Pre-vaccine: 24 deaths per million per year (1997-99)	31.3% Reduction	Post-vaccine: 16.5 deaths per million per year
Varicella	Pre-vaccine: 16018 cases per million per year (1990-94)	87.2% Reduction	Post-vaccine: 2046 cases per million per year	Pre-vaccine: 0.41 deaths per million per year (1990-94)	84.3% Reduction	Post-vaccine: 0.06 deaths per million per year

Data source: Roush and Murphy (2007) - Historical comparisons of morbidity and mortality for vaccine-preventable diseases in the United States. In The Journal of the American Medical Association, 298, 18, 2155--2163. Licensed under CC-BY by the author Max Roser

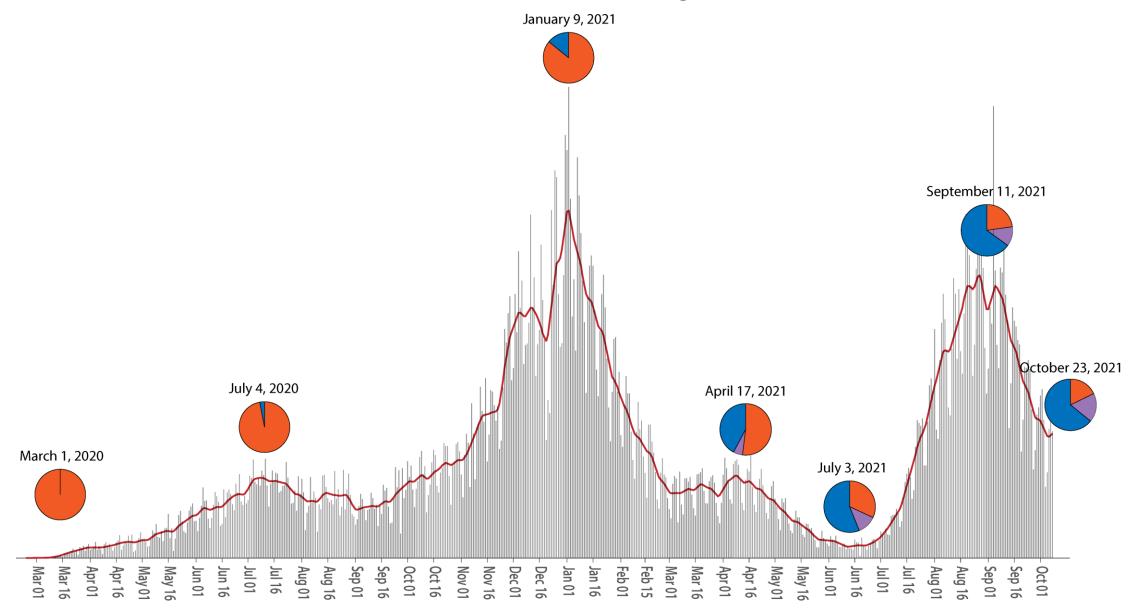
How well does the vaccine work?



An amazing accomplishment

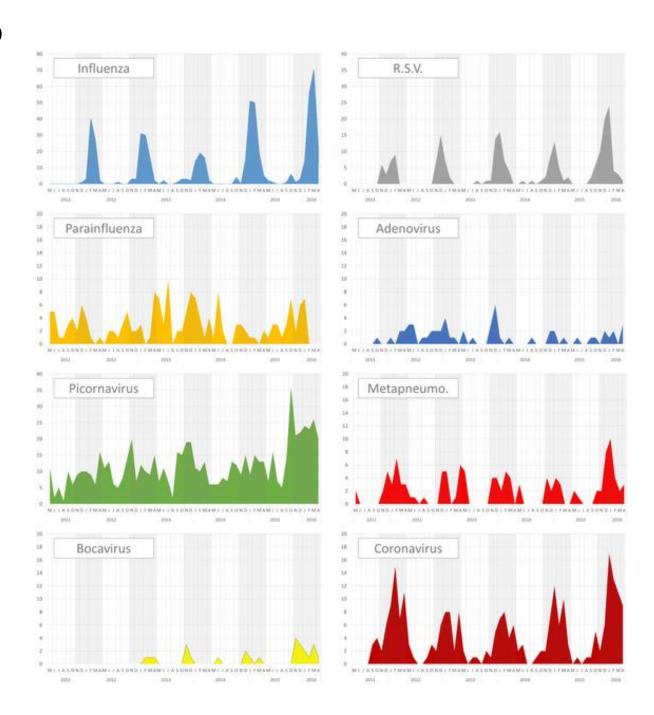


The accumulation of immunity in North Carolina

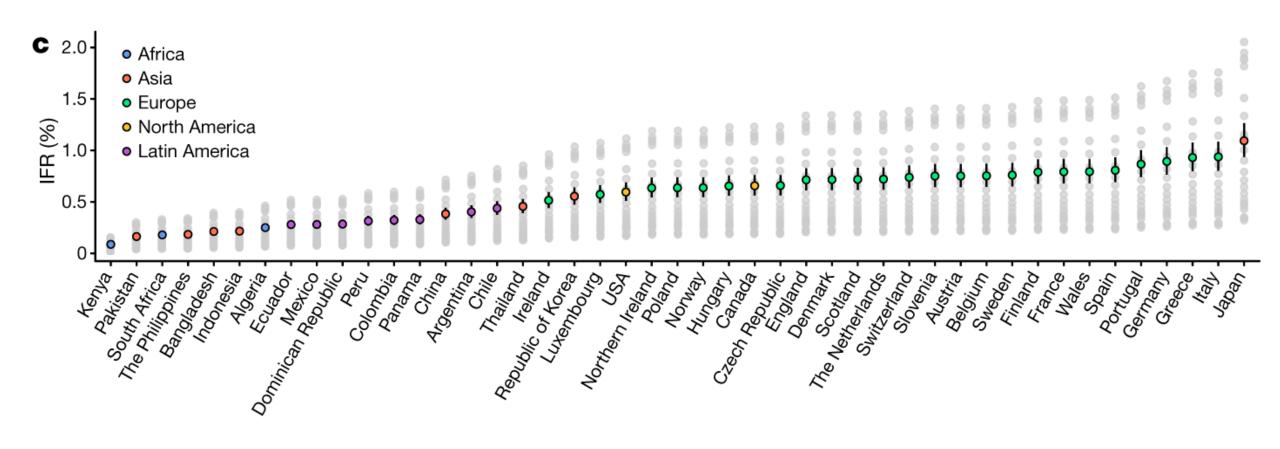


A seasonal coronavirus?

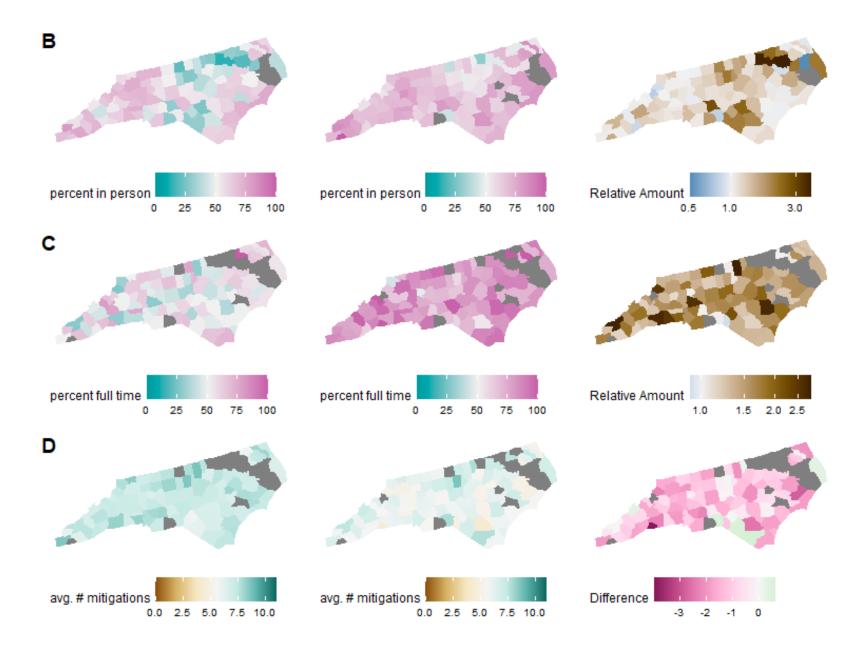
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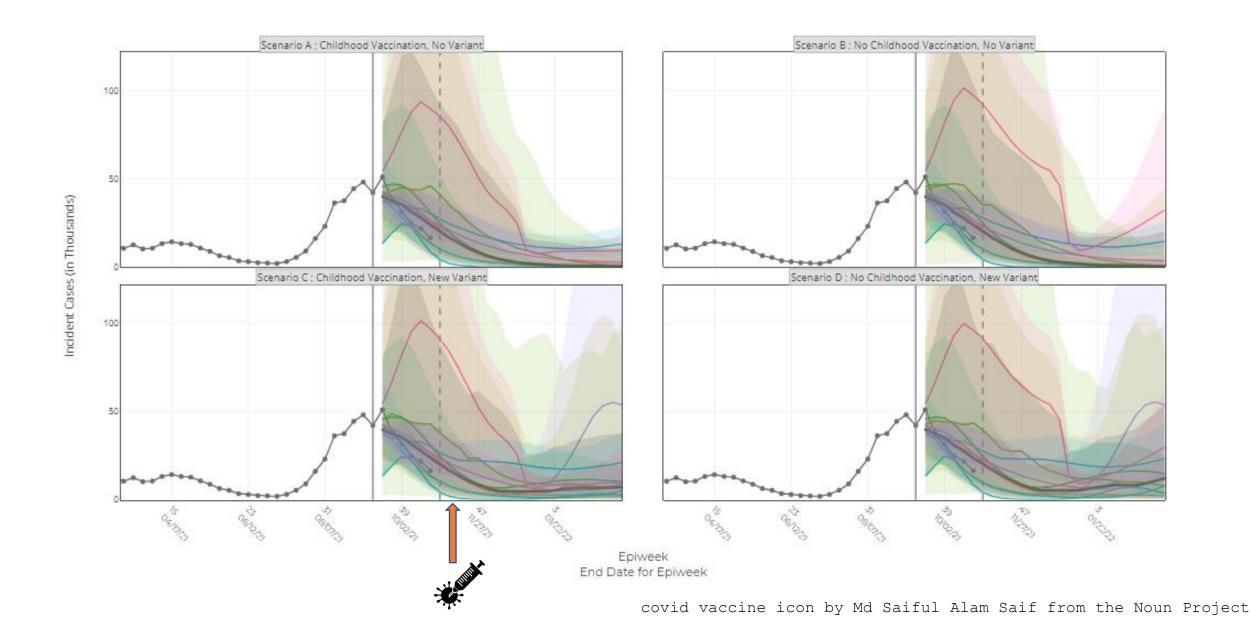
Older populations have higher death rates.



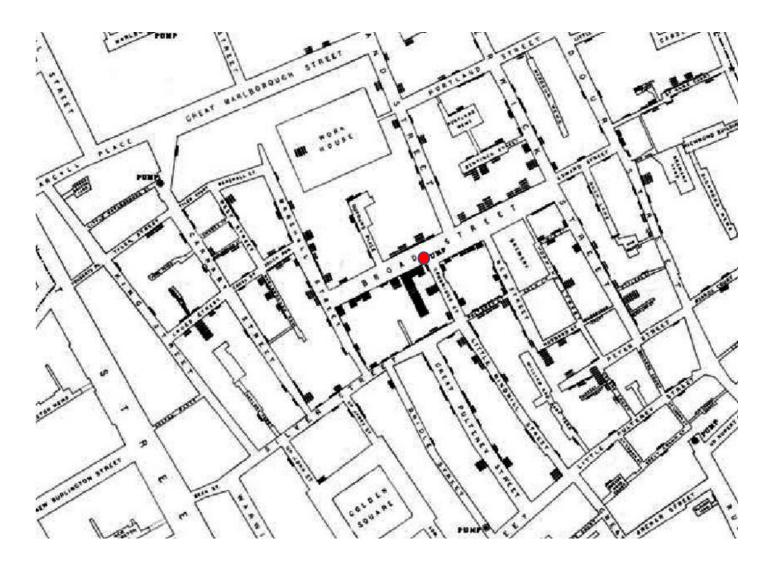
Schools and COVID-19 Transmission



Results, General Projections



John Snow and the Broad Street Pump





An amazing accomplishment

