

COVID-19: Lessons Learned, Challenges Ahead

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Objectives

- Provide an update to the status of the COVID-19 pandemic in Ontario
- Highlight some successes and failures of living with the pandemic
- Discuss prospects and timelines for vaccines
- Review expectations for the 2020/21 influenza season

Bats, Wildlife, and SARS-CoV



- Reservoir for CoVs are bats
- SARS and COVID-19 epidemics started at a Chinese wildlife markets.

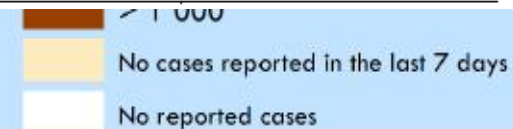
(Wang, 2018; Wang, 2007)



Table 1. Newly reported and cumulative COVID-19 confirmed cases and deaths, by WHO Region, as of 11 October 2020**

WHO Region	New cases in last 7 days (%)	Change in new cases in last 7 days	Cumulative cases (%)	New deaths in last 7 days (%)	Change in new deaths in last 7 days*	Cumulative deaths (%)
Americas	804 735 (35%)	6%	17 794 771 (48%)	20 509 (52%)	-5%	588 867 (55%)
South-East Asia	575 763 (25%)	-6%	7 911 036 (21%)	7 750 (20%)	-8%	126 917 (12%)
Europe	694 275 (31%)	34%	6 918 265 (19%)	6 172 (16%)	16%	246 709 (23%)
Eastern Mediterranean	138 751 (6%)	10%	2 605 478 (7%)	3 173 (8%)	13%	66 329 (6%)
Africa	29 169 (1%)	11%	1 227 719 (3%)	991 (3%)	27%	27 255 (3%)
Western Pacific	26 199 (1%)	6%	651 841 (2%)	633 (2%)	26%	14 265 (1%)
† Other	-	-	741 (<1%)	-	-	13 (<1%)
Global	2 268 892 (100%)	10%	37 109 851 (100%)	39 228 (100%)	<1%	1 070 355 (100%)

WHO Sitrep Oct 12, 2020



What do we know about COVID19?

- You start shedding virus 2-4 days before you get sick
 - As much as 40% of transmission may occur before symptoms
- The range of illness is wide
 - Some people get infected, but never get sick
 - Many people get a very mild “cold”
 - Some people get “influenza-like illness” with fever and cough
 - A few people get pneumonia, some of them very severe
 - Among people diagnosed, 0.4-2% have died (very steep age gradient)
- Discontinuing precautions
 - 10 days after symptom onset for mild-moderate disease, as long as fever gone
 - Consider 20 days for severe illness, testing if severely compromised
 - PCR+ve tests can persist for 3 (maybe 5??) months

<https://www.cdc.gov/coronavirus/2019-ncov/hcp/duration-isolation.html>

<https://www.cdc.go.kr/board/board.es?mid=a30402000000&bid=0030>

What do we know about COVID19? II

- Most transmission occurs in the community
 - Transmission in healthcare is predominantly from asymptomatic or presymptomatic healthcare workers
 - also from asymptomatic/pre-symptomatic or unrecognized patients
- Children under 10 are less likely to have symptomatic disease and **may be** less likely to transmit infection (but not no transmission)
- As with other infectious diseases, transmission risk is heterogeneous
 - “superspreading” events occur

Transmission

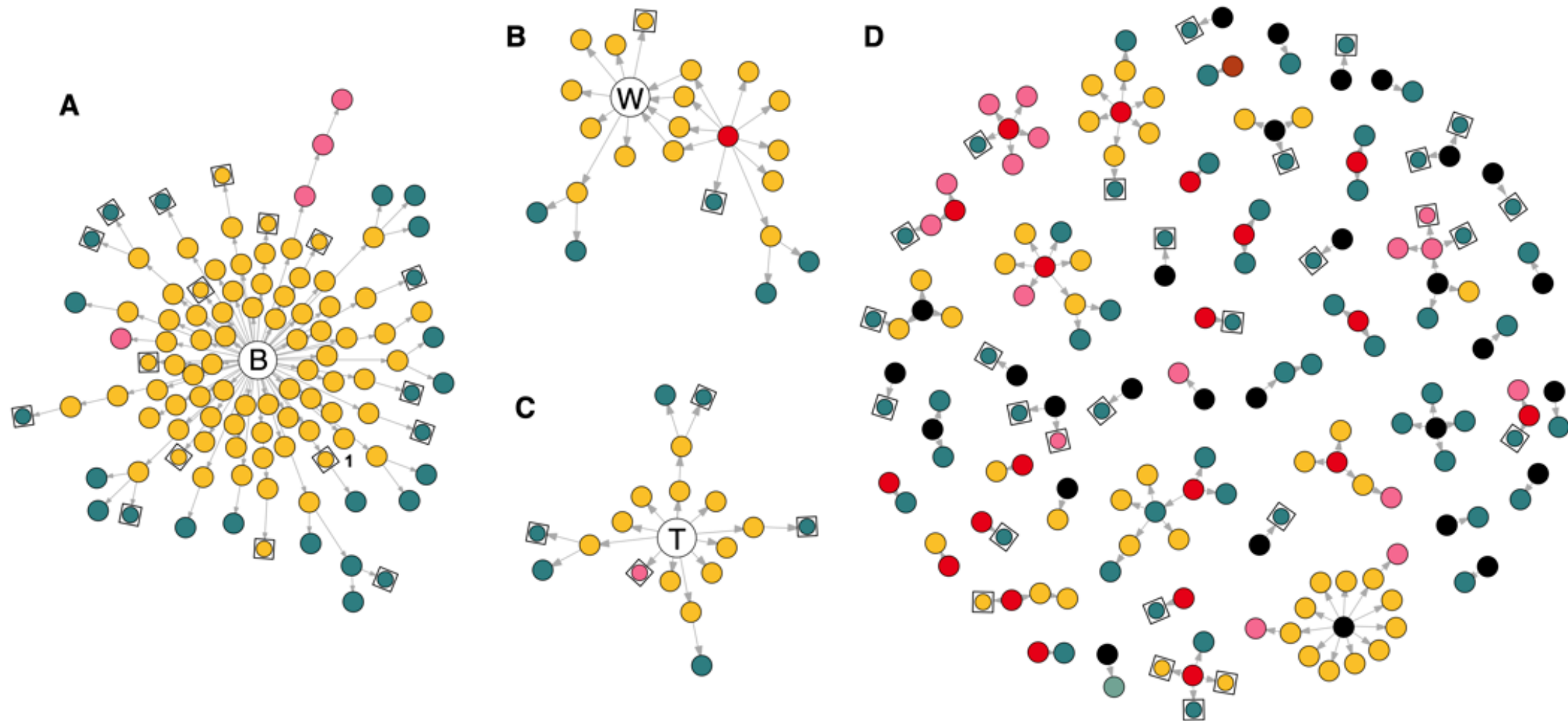
- Social
- Family
- Work
- Local Travel
- Ⓜ Wedding
- Ⓣ Temple
- Ⓟ Bar

Source

- Imported Source
- Local Source

Intervention

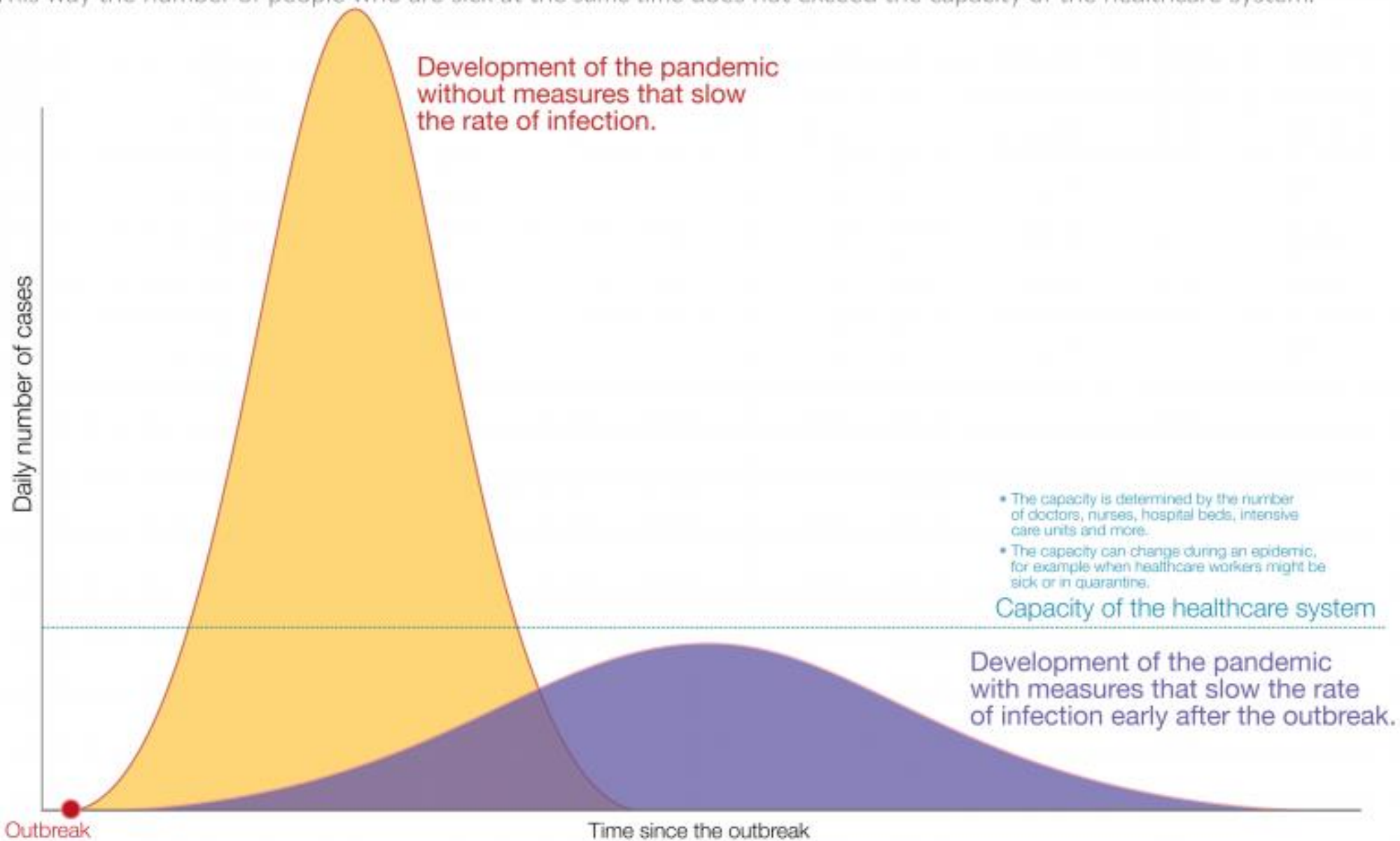
- ◻ Case Quarantined



In the outbreak of an epidemic *early* counter measures are important

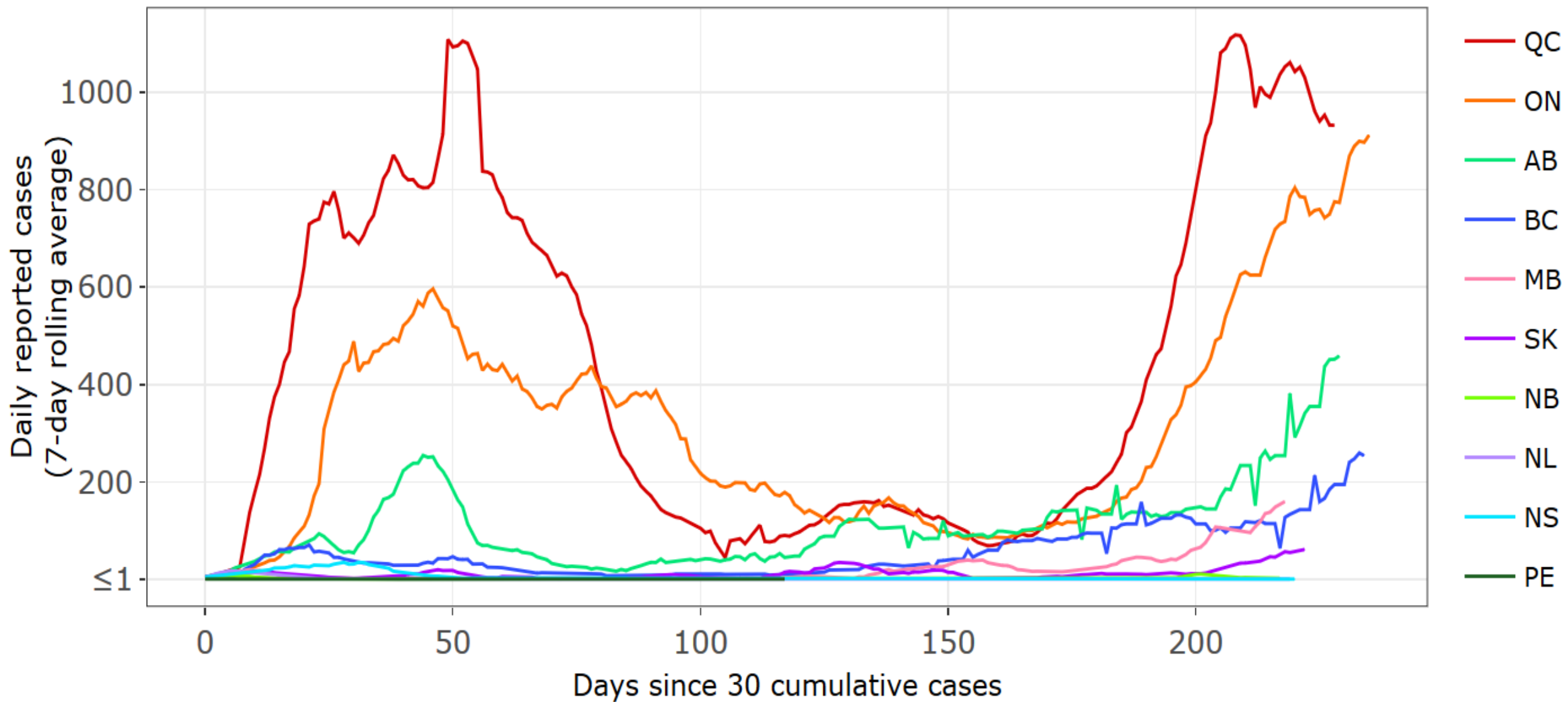
Their intention is to 'flatten the curve': to lower the rate of infection to spread out the epidemic.

This way the number of people who are sick at the *same time* does not exceed the capacity of the healthcare system.



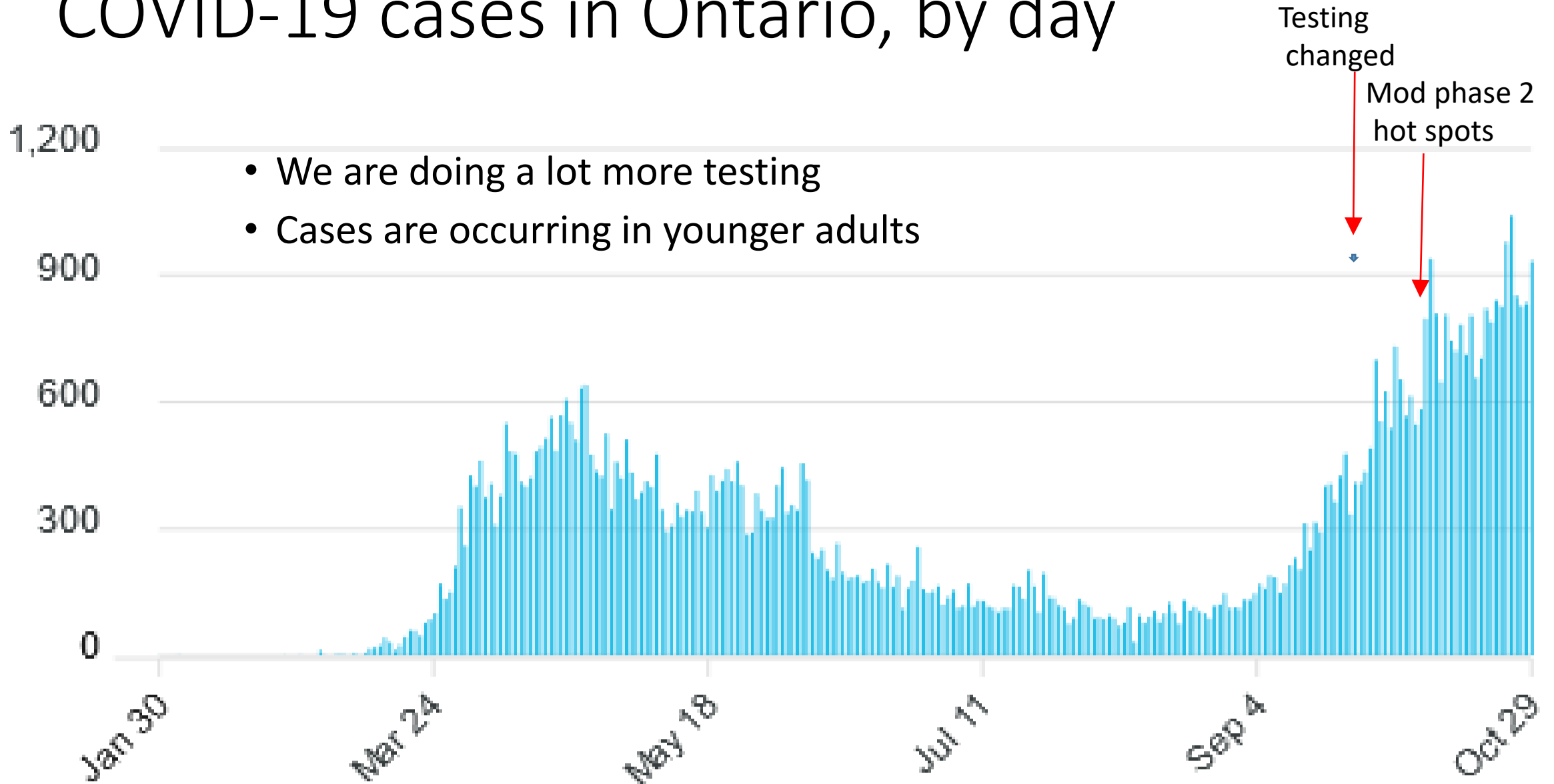
How did we “flatten the curve”?

- Hand hygiene
- Identification of cases
- Isolation of cases and quarantine of close contacts
- **Social (physical) distancing**
- (Masks)



<https://art-bd.shinyapps.io/covid19canada/>

COVID-19 cases in Ontario, by day



What happens now?

- We are trying to combine minimization of deaths from COVID19 with minimization of economic and collateral health impact
- Less than 3% (less than 1% in most areas) of the population have been infected
- In Ontario – hopefully we are at peak hospitalizations, nursing home outbreaks
 - Over next 2-3 weeks, we find out if current restrictions are enough
 - Restrictions targeted to geography and risk

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Dexamethasone in Hospitalized Patients with Covid-19 — Preliminary Report

The RECOVERY Collaborative Group*

RECOVERY

Randomised Evaluation of COVID-19 Therapy

HAVE YOU BEEN ADMITTED TO HOSPITAL WITH SUSPECTED OR CONFIRMED COVID-19?

Are you interested in research?

There are currently no approved treatments for COVID-19.

Oxford University is running the **RECOVERY** Trial which will enable reliable assessment of the effects of multiple different treatments on major outcomes among people with suspected or confirmed COVID-19.

Some of the treatments will be drugs used for other conditions, other new drugs may become available during the trial.

All patients participating in the trial will receive usual standard of care.

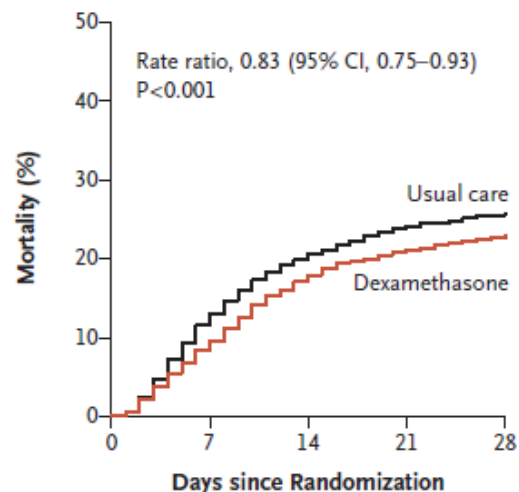


We need your help



If you are interested in joining the **RECOVERY** Trial, please ask your medical team for information about the trial.

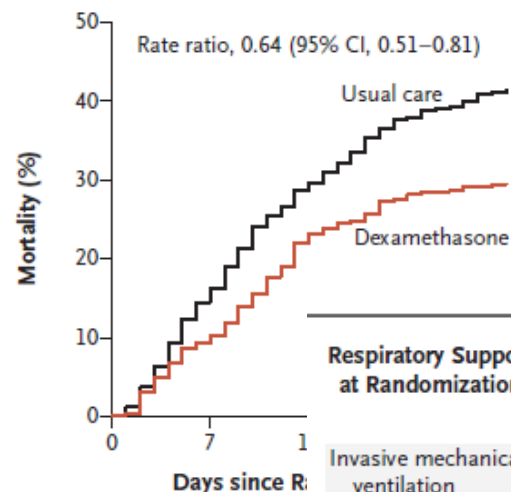
A All Participants (N=6425)



No. at Risk

	0	7	14	21	28
Usual care	4321	3754	3427	3271	3205
Dexamethasone	2104	1903	1725	1659	1621

B Invasive Mechanical Ventilation (N=1007)



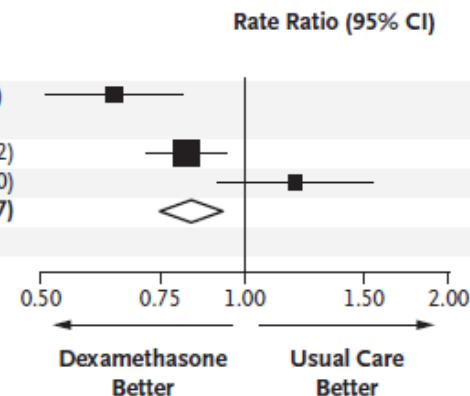
No. at Risk

	0	7	14	21	28
Usual care	683	572	449	414	401
Dexamethasone	324	290	229	212	201

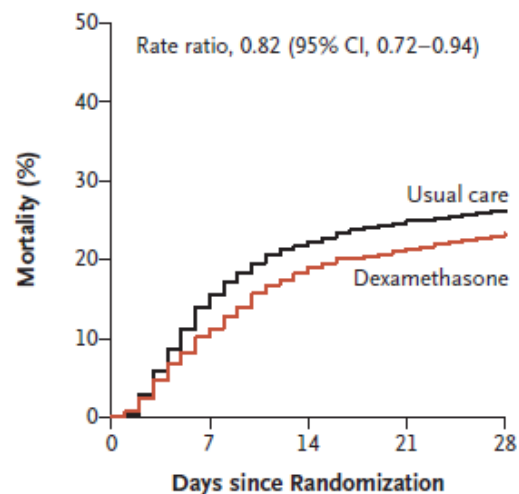
Respiratory Support at Randomization

	Dexamethasone no. of events/total no. (%)	Usual Care no. of events/total no. (%)	Rate Ratio (95% CI)
Invasive mechanical ventilation	95/324 (29.3)	283/683 (41.4)	0.64 (0.51-0.81)
Oxygen only	298/1279 (23.3)	682/2604 (26.2)	0.82 (0.72-0.94)
No oxygen received	89/501 (17.8)	145/1034 (14.0)	1.19 (0.91-1.55)
All Patients	482/2104 (22.9)	1110/4321 (25.7)	0.83 (0.75-0.93)

Chi-square trend across three categories: 11.5



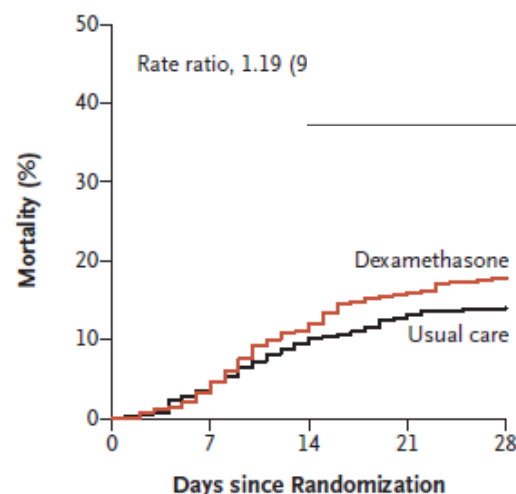
C Oxygen Only (N=3883)



No. at Risk

	0	7	14	21	28
Usual care	2604	2195	2018	1950	1916
Dexamethasone	1279	1135	1036	1006	981

D No Oxygen Received (N=1535)



No. at Risk

	0	7	14	21	28
Usual care	1034	987	928	897	889
Dexamethasone	501	478	441	421	412

Figure 3. Association Between Corticosteroids and 28-Day All-Cause Mortality Within Subgroups Defined by Patient Characteristics at the Time of Randomization

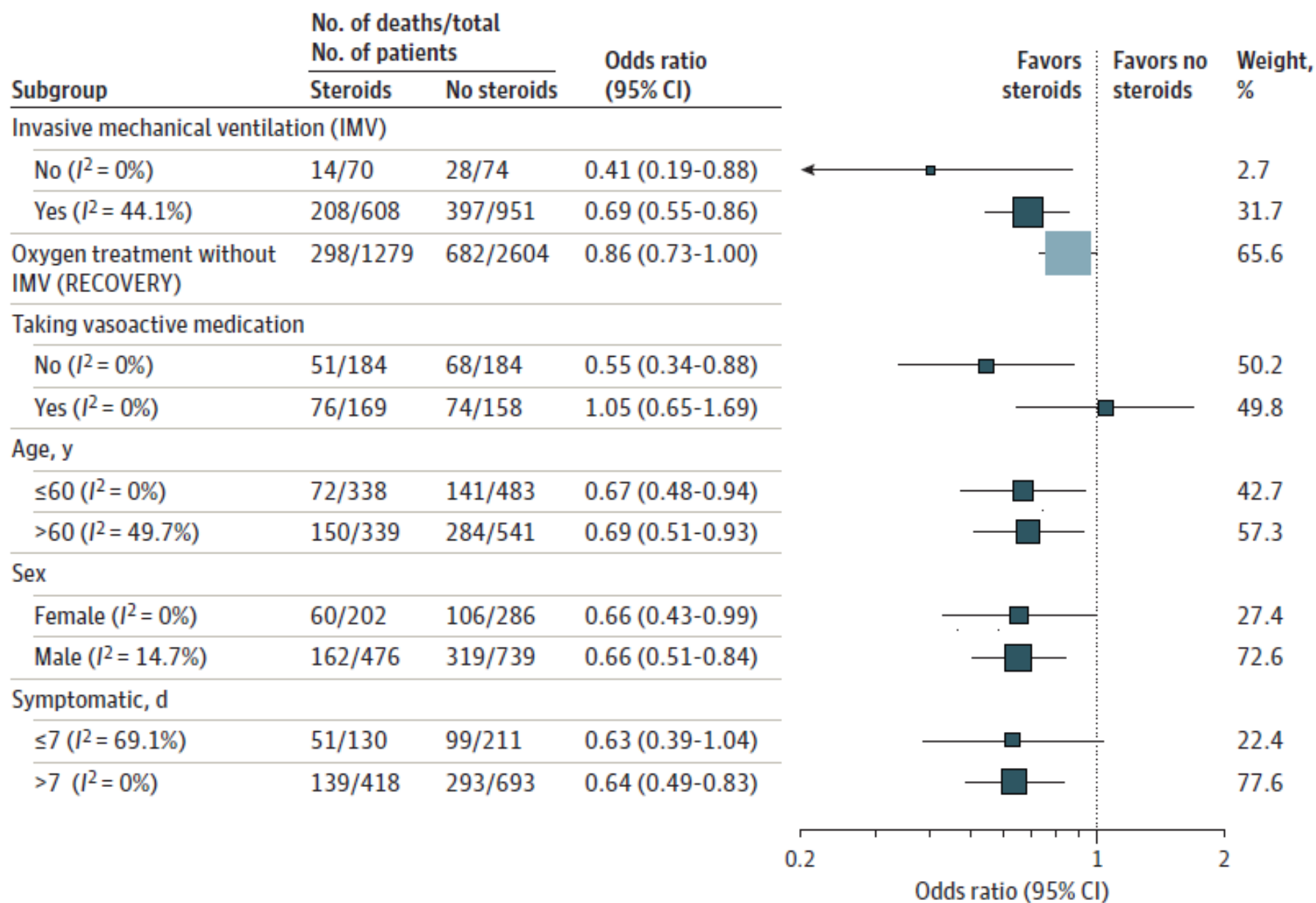
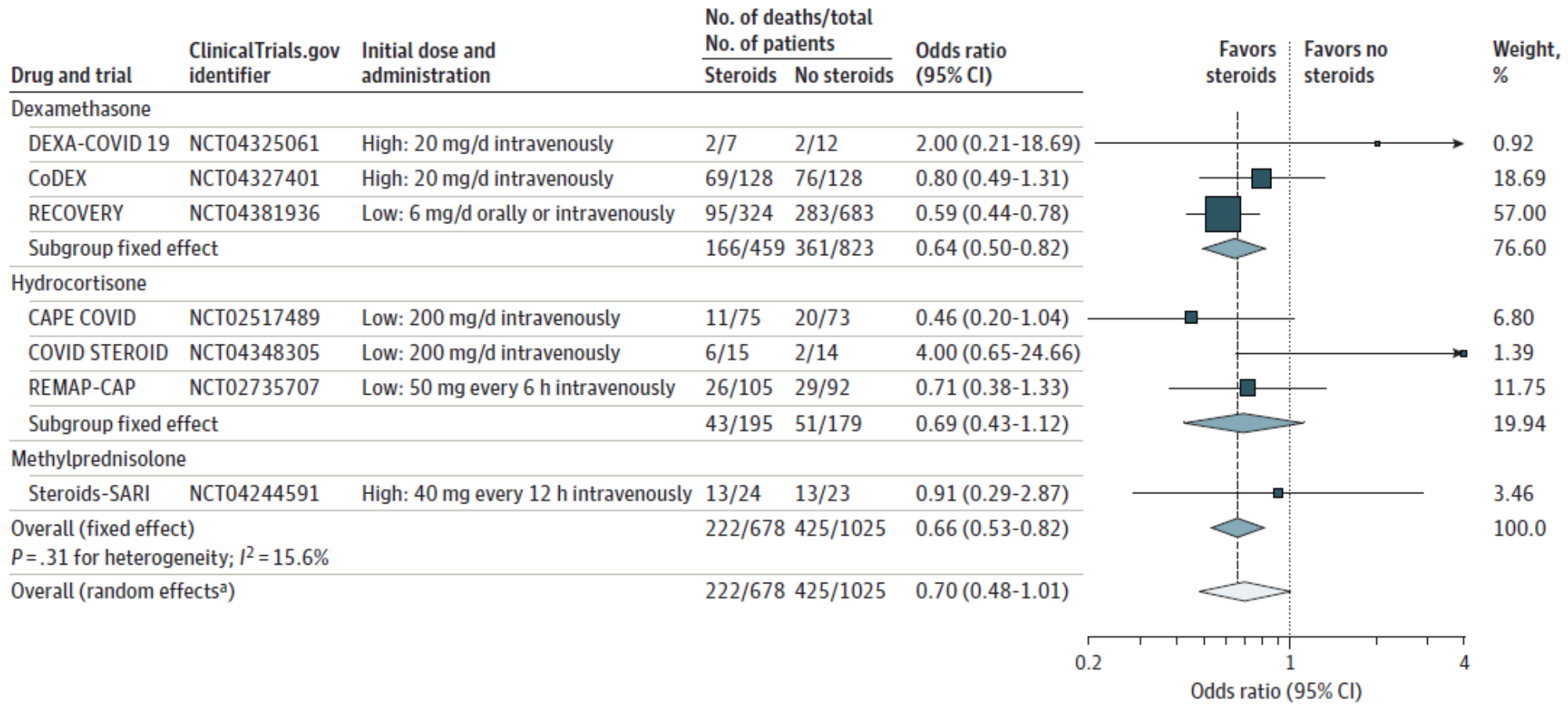


Figure 2. Association Between Corticosteroids and 28-Day All-Cause Mortality in Each Trial, Overall, and According to Corticosteroid Drug



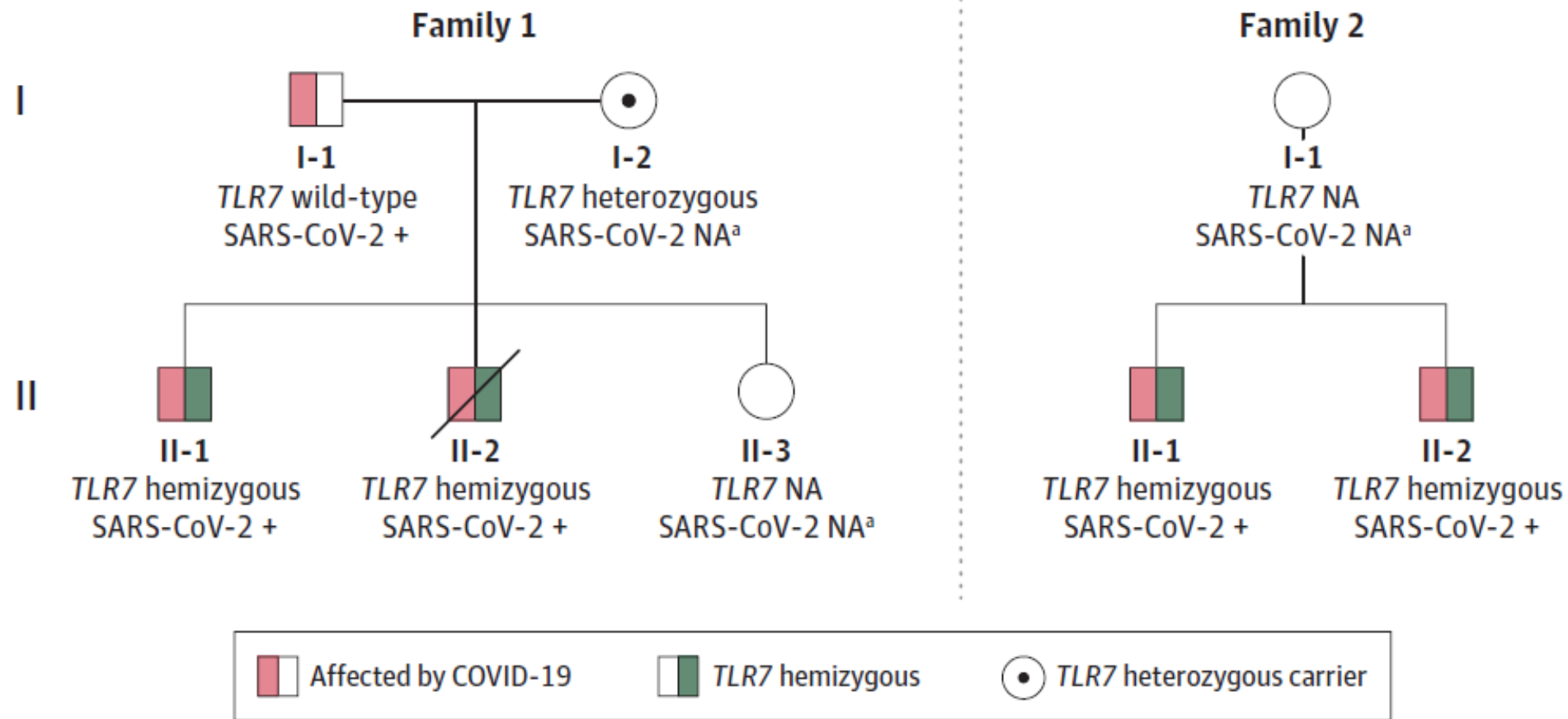
JAMA | **Preliminary Communication**

Presence of Genetic Variants Among Young Men With Severe COVID-19

Caspar I. van der Made, MD; Annet Simons, PhD; Janneke Schuurs-Hoeijmakers, MD, PhD;
Guus van den Heuvel, MD; Tuomo Mantere, PhD; Simone Kersten, MSc; Rosanne C. van Deuren, MSc;
Marloes Steehouwer, BSc; Simon V. van Reijmersdal, BSc; Martin Jaeger, PhD; Tom Hofste, BSc; Galuh Astuti, PhD;
Jordi Corominas Galbany, PhD; Vyne van der Schoot, MD, PhD; Hans van der Hoeven, MD, PhD;
Wanda Hagmolen of ten Have, MD, PhD; Eva Klijn, MD, PhD; Catrien van den Meer, MD; Jeroen Fiddelaers, MD;
Quirijn de Mast, MD, PhD; Chantal P. Bleeker-Rovers, MD, PhD; Leo A. B. Joosten, PhD; Helger G. Yntema, PhD;
Christian Gilissen, PhD; Marcel Nelen, PhD; Jos W. M. van der Meer, MD, PhD; Han G. Brunner, MD, PhD;
Mihai G. Netea, MD, PhD; Frank L. van de Veerdonk, MD, PhD; Alexander Hoischen, PhD

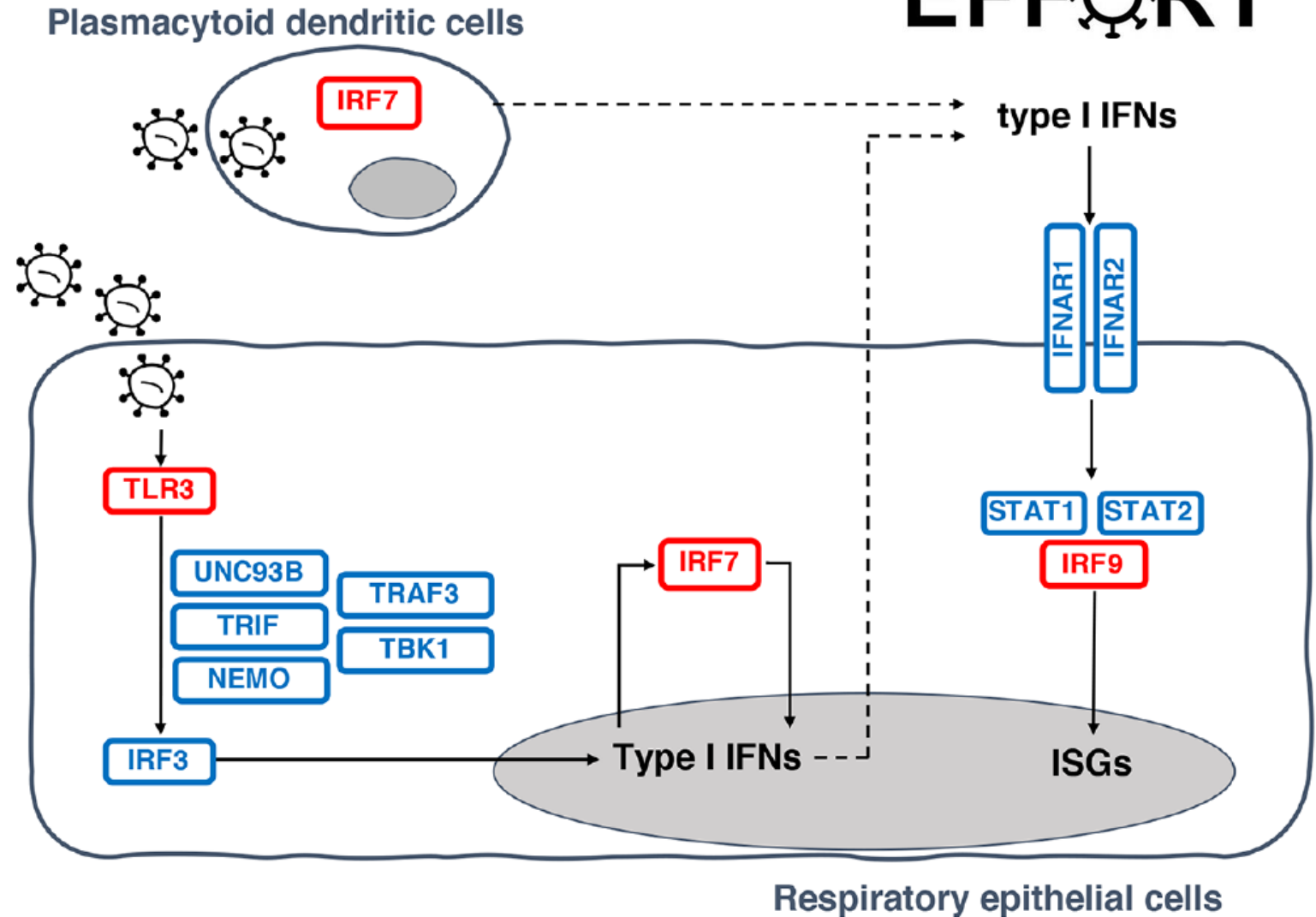
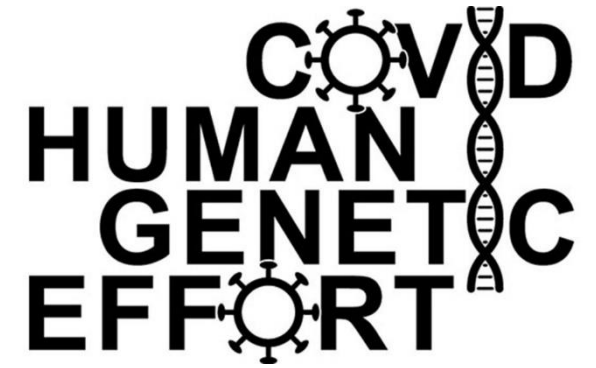
Figure 1. Identification of *TLR7* Variants in 4 Patients From 2 Families With Severe Coronavirus Disease 2019 (COVID-19)

A Pedigrees of family 1 and family 2

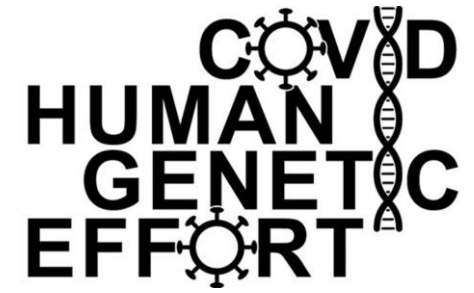


Cite as: Q. Zhang *et al.*, *Science* 10.1126/science.abd4570 (2020).

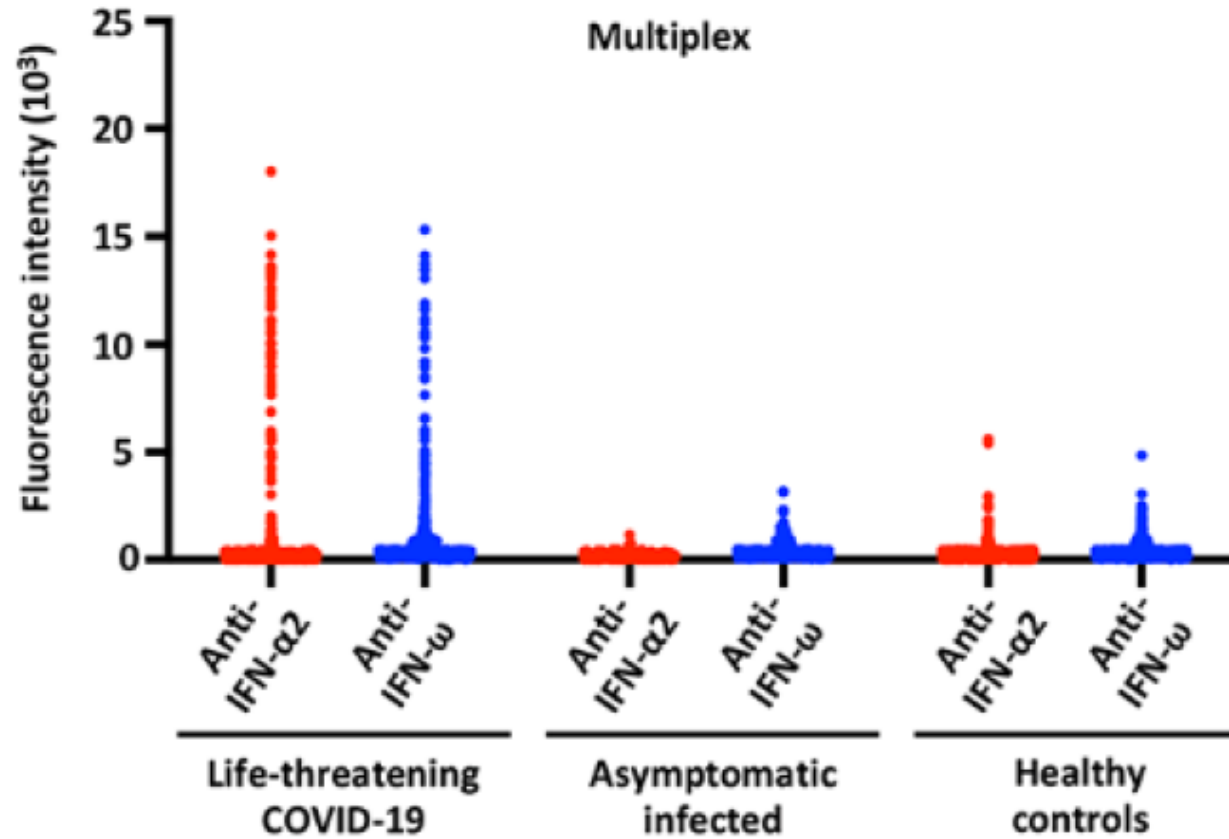
Inborn errors of type I IFN immunity in patients with life-threatening COVID-19



Cite as: P. Bastard *et al.*, *Science*
10.1126/science.abd4585 (2020).



Auto-antibodies against type I IFNs in patients with life-threatening COVID-19



What about vaccines?

COVID-19 Vaccines(WHO registry) – Oct 29

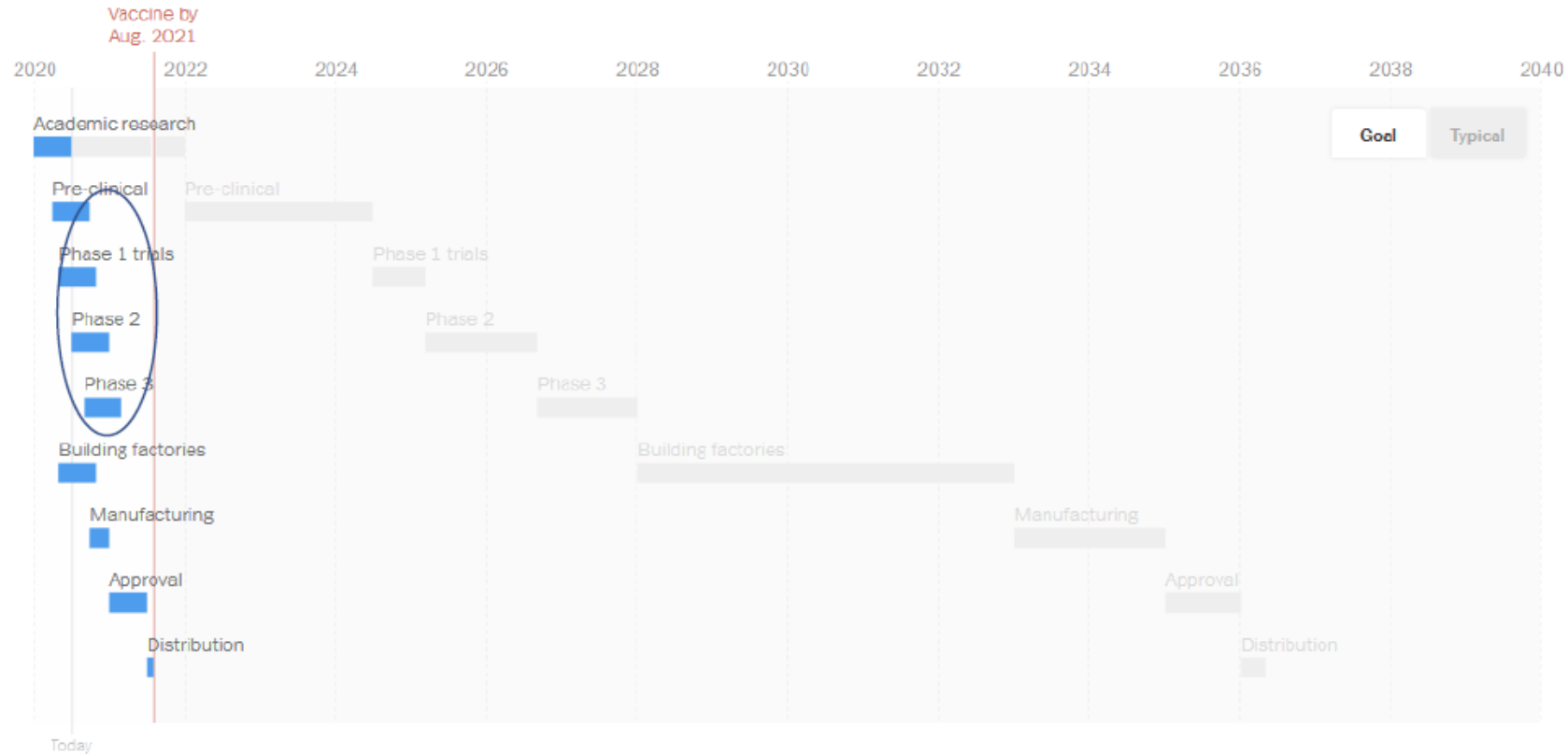
- 201 candidates
 - 45 in clinical evaluation: 10 in phase III trials
 - >10 vaccines in Canada
- 7 platforms
 - Inactivated (N=16)
 - Live-attenuated (N=3)
 - Virus-like particles (N=17)
 - Vectors (N=23 replicating, N=28 non-replicating)
 - Viruses – adenovirus (human and chimpanzee), vaccinia, yellow fever.....
 - Bacteria – Salmonella
 - Protein subunit/peptide (N=68)
 - RNA/DNA (N=42)
 - T cell based (N=1)

New York Times

Opinion

How Long Will a Vaccine Really Take?

By [Stuart A. Thompson](#) April 30, 2020



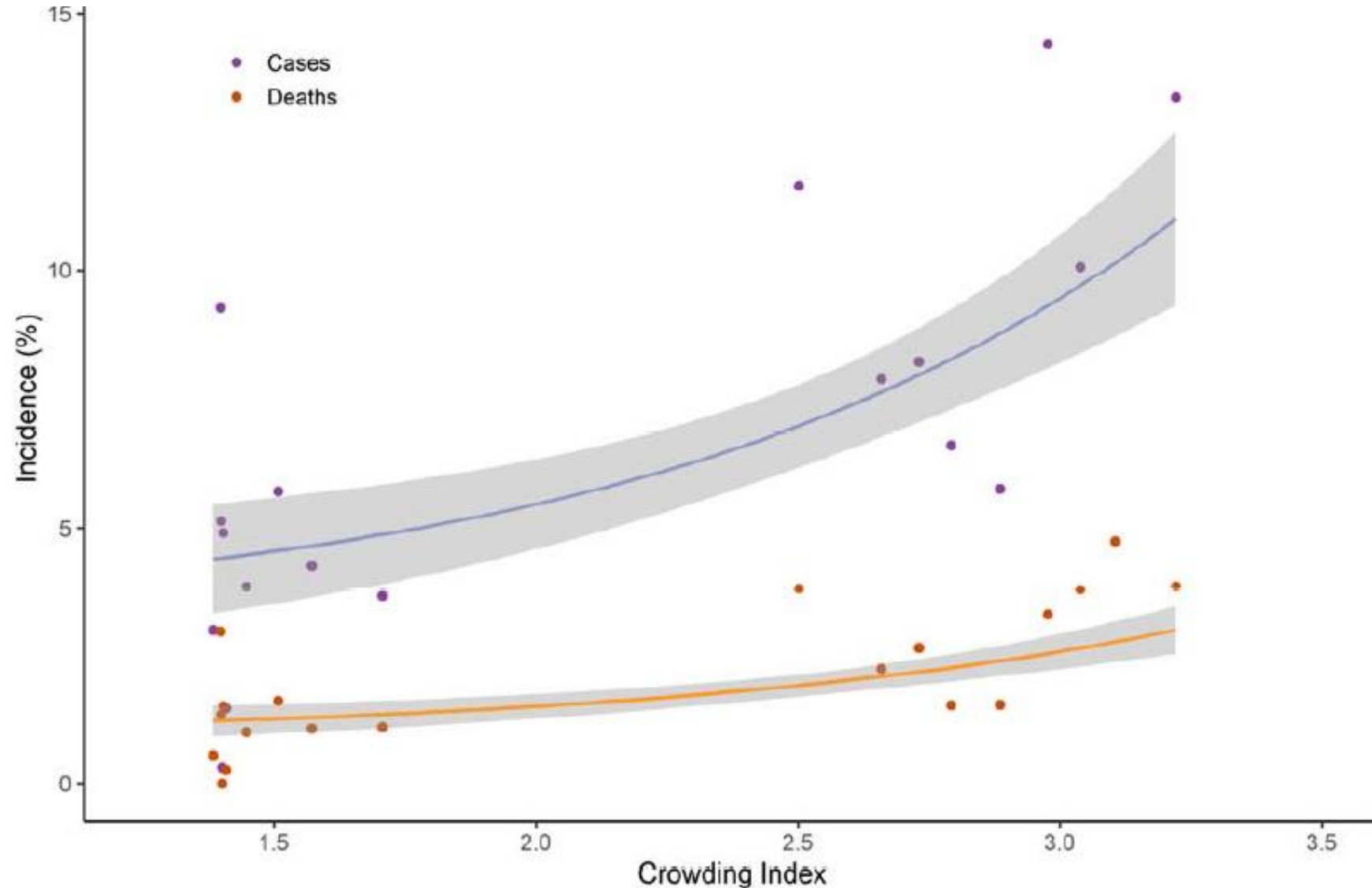
What about long term care?

Why challenges in long term care?

- Non-modifiable
 - Frail elderly population with very high case fatality rate
 - COVID-19 (like other infections) may present atypically, and many residents cannot describe and/or have other reasons for symptoms
 - Hands on care with close contact required
 - Contact and socialization are very important
- Modifiable
 - Many buildings are old and crowded
 - High degree of mixing of large populations
 - Staffing shortages are chronic, and there is intense pressure for staff to come to work
 - Inadequate education, training, policies, PPE supply

Association Between Nursing Home Crowding and COVID-19 Infection and Mortality in Ontario, Canada

Kevin A. Brown, PhD, Aaron Jones, MSc, Nick Daneman, MD, MSc, Adrienne K. Chan, MD, MPH, Kevin L. Schwartz, MD, MSc, Gary E. Garber, MD, Andrew P. Costa, PhD, Nathan M. Stall, MD



Is There a Link between Nursing Home Reported Quality and COVID-19 Cases? Evidence from California Skilled Nursing Facilities

Mengying He PhD^{a,*}, Yumeng Li PhD^b, Fang Fang PhD^a

^aDepartment of Management, College of Business and Economics, California State University, Los Angeles, CA

^bBiogen, Inc, Cambridge, MA

Multivariate Logistic Regression Results

Covariates	COVID-19 Cases		COVID-19 Deaths	
	OR	95% CI of OR	OR	95% CI of OR
Ownership				
NFP	Reference			
FP	1.49*	0.97, 2.34	1.69*	1.01, 3.00
Quality ratings				
3	Reference			
1	0.83	0.52, 1.33	1.04	0.64, 1.69
2	1.02	0.68, 1.53	1.23	0.80, 1.87
4	0.66**	0.44, 0.98	0.65*	0.42, 1.01
5	0.41***	0.27, 0.62	0.30***	0.18, 0.48
Bed occupancy	1.009***	1.006, 1.012	1.006***	1.003, 1.009
White resident percentage				
≥59.5%	reference			
<59.5%	1.95***	1.49, 2.55	1.64***	1.21, 2.23
Facility age (y)	1.006	0.995, 1.017	1.006	0.993, 1.019

*** $P < .01$; ** $P < .05$; * $P < .10$

1107 complete cases contribute this logistic model.

Nurse Staffing and Coronavirus Infections in California Nursing Homes

Charlene Harrington, PhD, RN¹ , Leslie Ross, PhD¹,
Susan Chapman, PhD, RN¹, Elizabeth Halifax, PhD, RN¹,
Bruce Spurlock, MD¹, and
Debra Bakerjian, PhD, FAAN, FAANP, FGSA¹

	Nursing homes with COVID-19 residents (N = 272)		Nursing homes without COVID-19 residents (N = 819)		Total nursing homes (N = 1,091)		ANOVA
	Mean		Mean		Mean		
	<i>n</i>	(SD)	<i>n</i>	(SD)	<i>n</i>	(SD)	<i>F</i>
RN staffing hprd	265	0.56 (0.52)	770	0.66 (0.64)	1035	0.64 (0.61)	5.788*
Total nurse staffing hprd	265	4.20 (0.94)	770	4.39 (1.20)	1035	4.34 (1.14)	5.409*
CMS medicare-five-star nurse staffing rating	263	2.69 (0.95)	771	2.95 (1.10)	1034	2.88 (1.07)	11.681***
CMS medicare five-star RN staffing rating	263	2.30 (1.05)	771	2.61 (1.20)	1034	2.53 (1.17)	14.522***
Number of health deficiencies	271	15.4 (8.1)	814	12.4 (8.0)	1,085	13.1 (8.1)	29.175***
Number of beds	272	118.1 (70.5)	819	92.4 (48.8)	1,091	98.8 (56.1)	44.650***

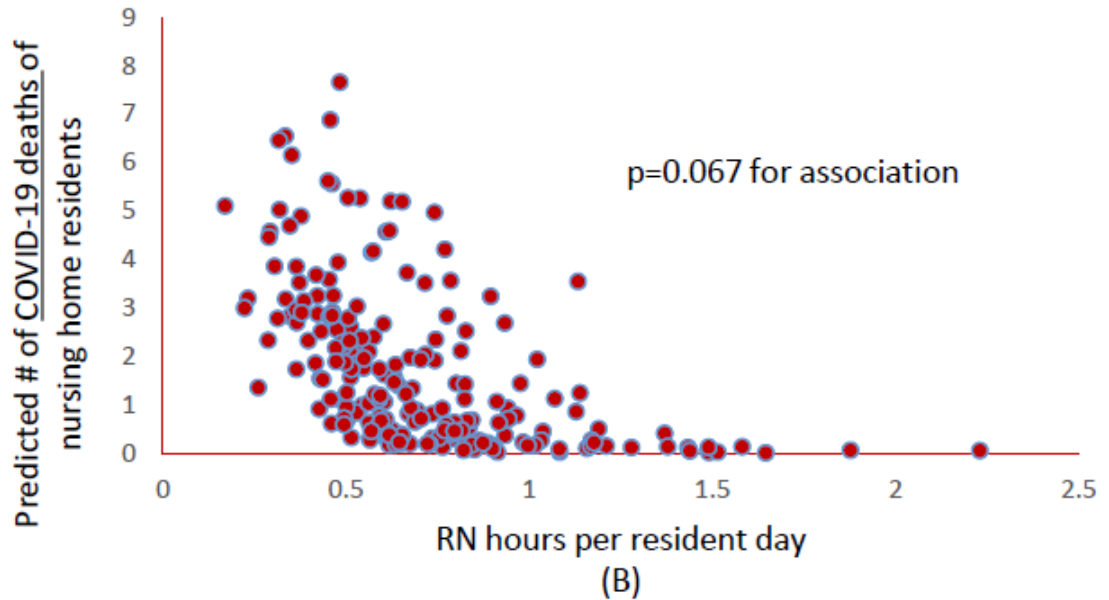
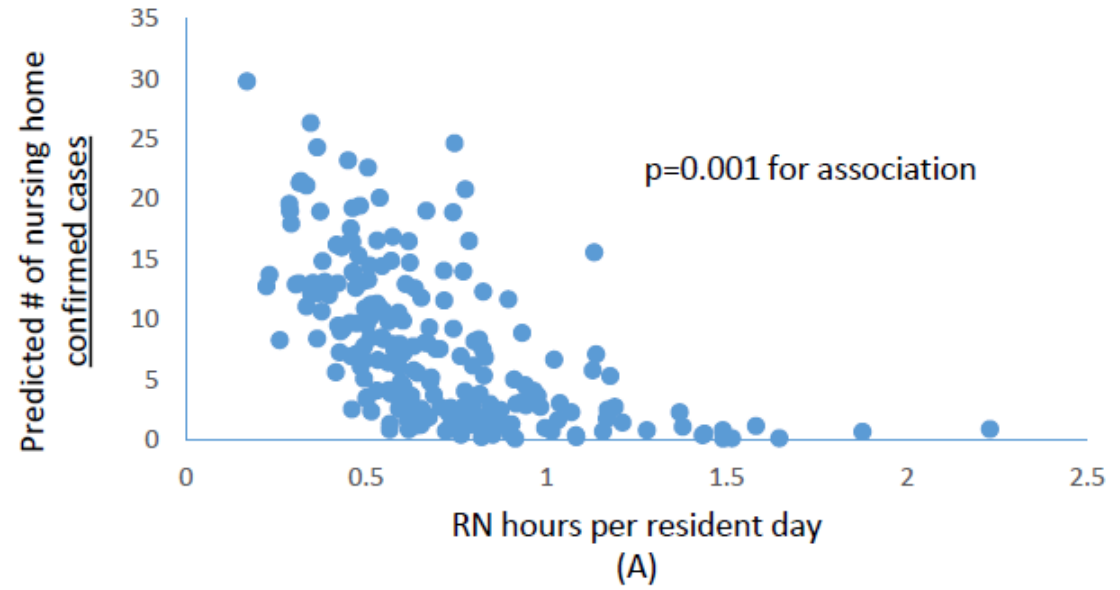
Note. ANOVA = analysis of variance; CMS = Centers for Medicare & Medicaid Services; hprd = hours per resident day; RN = registered nurse.

* $p < .05$. ** $p < .01$. *** $p < .001$.

COVID19 cases and deaths in Connecticut nursing home residents:
Facility correlates

Li et al

JAGS (epub ahead of print)



What are our **modifiable** challenges now?

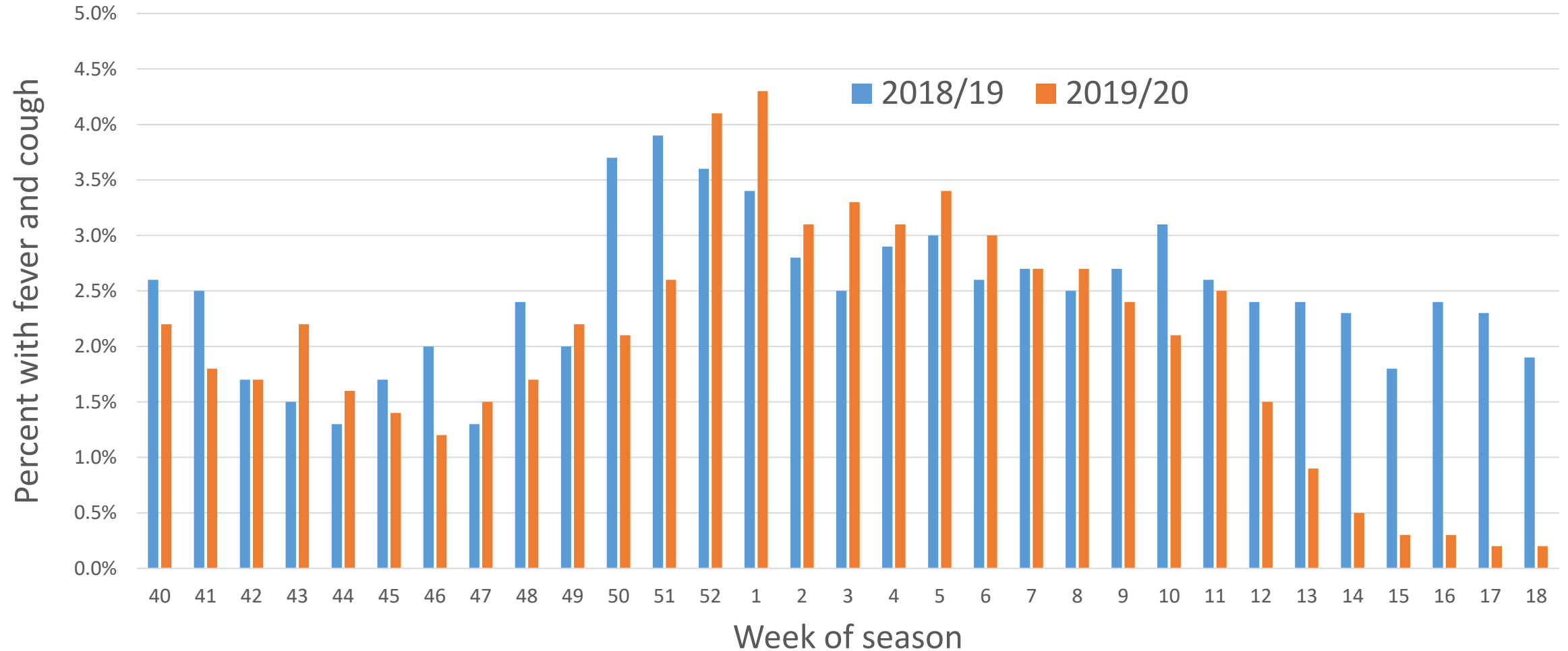
- Staffing is critical to managing outbreaks
- PPE/alcohol handrub/other supplies still challenging to manage
- Detection and transmission prevention errors are still being made
 - Staff working sick, residents not tested promptly
 - Face shields and gowns being re-used
- Testing is taking too long
 - Value of cohorting limited if cases are not identified until 4-6 days into illness
- Support remains fragmented and overstretched
 - Particularly an issue for retirement homes

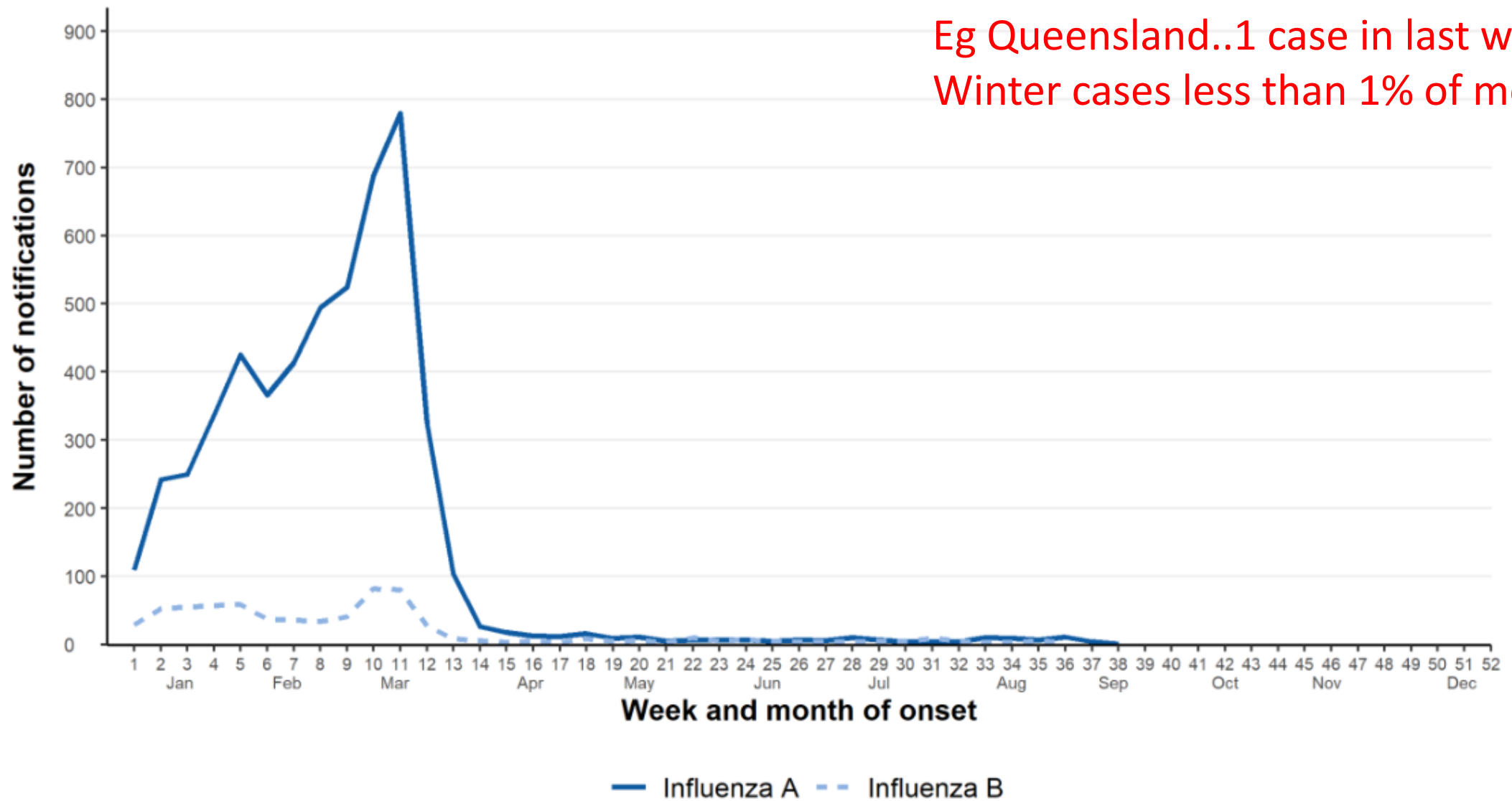
What can improve outcomes?

- Investing in IPAC
 - Disposable face shields, changing PPE between patients, on-going auditing, cohorting staff to units prior to outbreaks
 - Staff understanding critical to adherence
- Faster screening results
- Waste-water surveillance
- Treatment with steroids for those who require oxygen
- Favipiravir
 - Outbreak control trial, individual level prophylaxis trial pending
- Other treatment and/or prophylaxis
 - Interferon-lambda, MK4482,

What about influenza?

Participatory syndromic surveillance 2019/20 compared to 2018/19





Eg Queensland..1 case in last week..
 Winter cases less than 1% of mean

Figure 2: Queensland weekly influenza notifications by type, week and month of onset, 1 Jan to 20 Sep 2020.

What are we expecting for 2020/2021?

- We hope that travel restrictions and physical distancing measures (?and maybe masks?) will substantially reduce influenza transmission
- BUT, we are not on an island, and our travel restrictions and quarantine are not as draconian as Australia/New Zealand
- *Hope for the best, prepare for the worst*

