

In the Wake of the First Wave

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Objectives

- Review the first wave of COVID-19, and what we have learned
- Recommend preparations for preventing/managing outbreaks in LTC
- Present the role of chemo-prophylaxis and the COVID CONTROL trial

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)

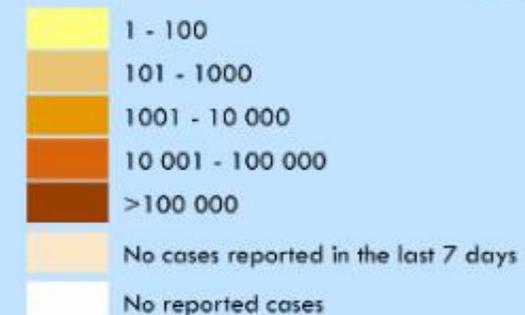


Situation in numbers (by WHO Region)

Total (new cases in last 24 hours)

Globally	15 012 731 cases (247 225)	619 150 deaths (7 097)
Africa	642 387 cases (18 536)	10 789 deaths (632)
Americas	7 948 513 cases (137 386)	317 962 deaths (4 153)
Eastern Mediterranean	1 429 084 cases (14 622)	36 118 deaths (490)
Europe	3 147 860 cases (22 909)	208 970 deaths (501)
South-East Asia	1 571 317 cases (50 537)	37 203 deaths (1 312)
Western Pacific	272 829 cases (3 235)	8 095 deaths (9)

Cases reported in the last 7 days



WHO Sitrep July 23, 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 to date, about 2% have died overall – 0.2% in younger adults, up to 30-50% in the frail elderly in nursing homes
- 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 months, but are not associated with replicating virus

<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

Choe YJ, Park O, Park SY, Kim YM, Kim J, et al. Contact tracing during coronavirus disease outbreak, South Korea, 2020.

Emerg Infect Dis. <https://doi.org/10.3201/eid2610.201315>

Age group (years)	Households		Non-Household contacts	
	No. contacts positive/no. contacts traced	% Positive (95% CI)	No. contact positive/no. contacts traced	% Positive (95% CI)
0–9	3/57	5.3 (1.3–13.7)	2/180	1.1 (0.2–3.6)
10–19	43/231	18.6 (14.0–24.0)	2/226	0.9 (0.1–2.9)
20–29	240/3,417	7.0 (6.2–7.9)	138/12,393	1.1 (0.9–1.3)
30–39	143/1,229	11.6 (9.9–13.5)	70/7,407	0.9 (0.7–1.2)
40–49	206/1,749	11.8 (10.3–13.4)	161/7,960	2.0 (1.7–2.3)
50–59	300/2,045	14.7 (13.2–16.3)	166/9,308	1.8 (1.5–2.1)
60–69	177/1,039	17.0 (14.8–19.4)	215/7,451	2.9 (2.5–3.3)
70–79	86/477	18.0 (14.8–21.7)	92/1,912	4.8 (3.9–5.8)
≥80	50/348	14.4 (11.0–18.4)	75/1,644	4.6 (3.6–5.7)

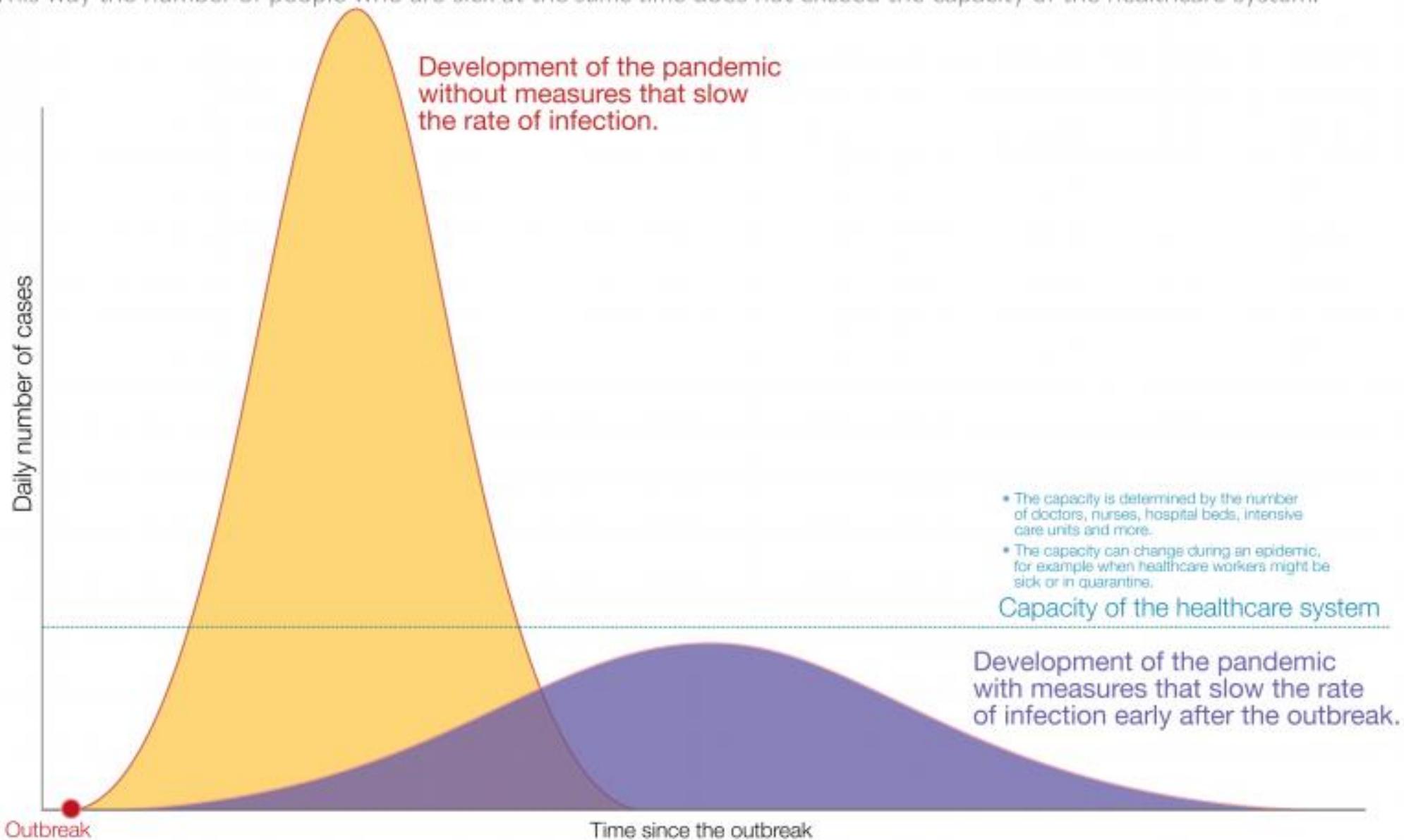
Treatment, Prophylaxis, Vaccines

- Success in two very large treatment clinical trial networks, the WHO “Solidarity” trial in 60 countries, and the UK “Recovery” trial
 - Hydroxychloroquine and Kaletra do NOT work
 - Remdesivir MAY work if used early (clinical trials on-going; supply issues)
 - Corticosteroids (dexamethasone) help severely ill people
 - ?inhaled β -interferon
 - ?Favipiravir
- Prophylaxis - no data yet (Boulware NEJM not useful)
- Vaccines
 - More than 100 possible vaccines in development, 3 with phase II trial data reported

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

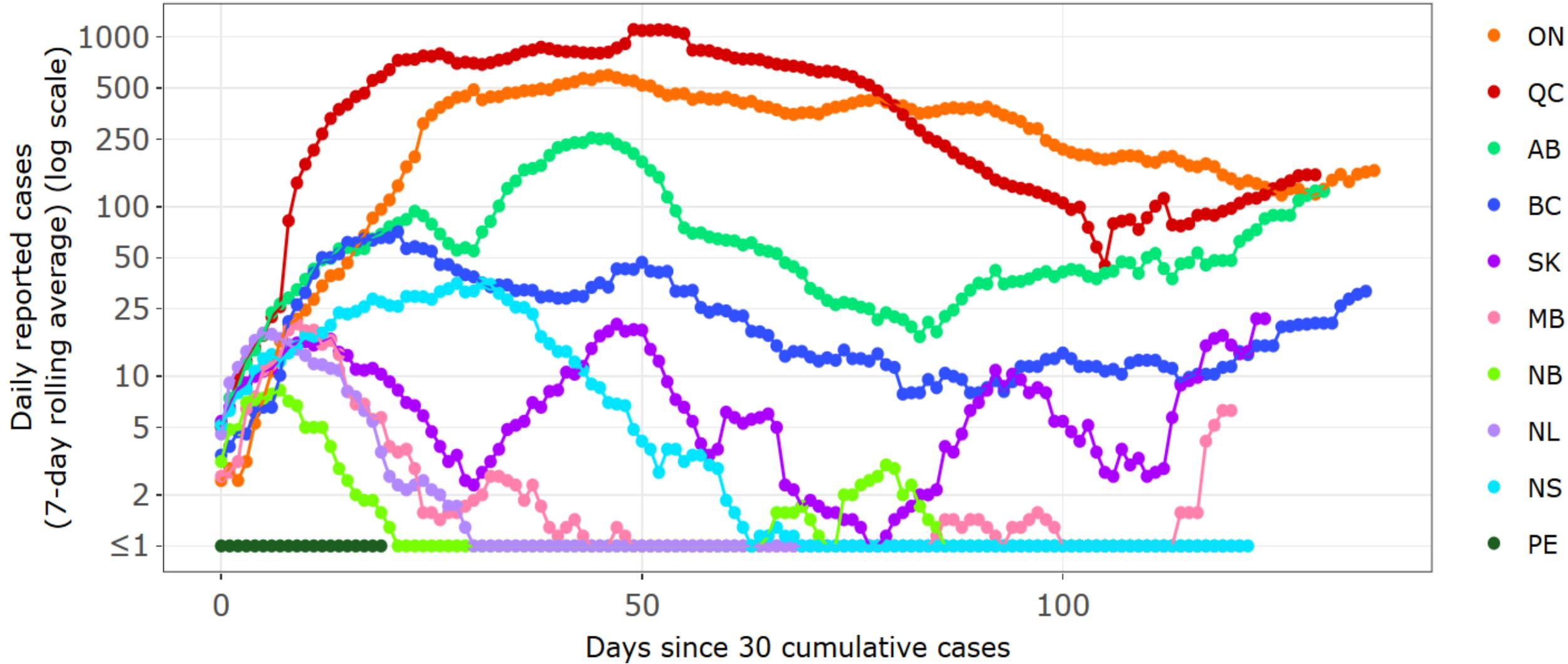
Their intention is to 'flatten the curve': to lower the rate of infection to spread out the epidemic.

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 may help too)



What happens now?

- We are trying to combine minimization of deaths from COVID19 with minimization of economic and collateral health impact
- Less than 3% of the population have been infected, and at least 50% have to be before this slows down
- Why are cases not increasing quickly as we re-open?
 - Because disease is seasonal
 - Because we did more than was necessary
 - Because it takes time for amplification to occur

What about long term care?

Early experiences with antibody testing in a Flemish nursing home during an acute COVID-19 outbreak: a retrospective cohort study.

Buntinx Frank, MD, PhD.

-University of Leuven, Department of Public Health and Primary Care, Leuven, Belgium

-Woonzorgcentrum Bessemerberg, Lanaken, Belgium.

		Antibody		
		Positive	Negative	
PCR	Positive	11 (34%)	21 (66%)	32
	Negative	4 (6%)	63 (94%)	67
	Total	15 (15%)	84 (85%)	99

Do residents develop protective immune responses?

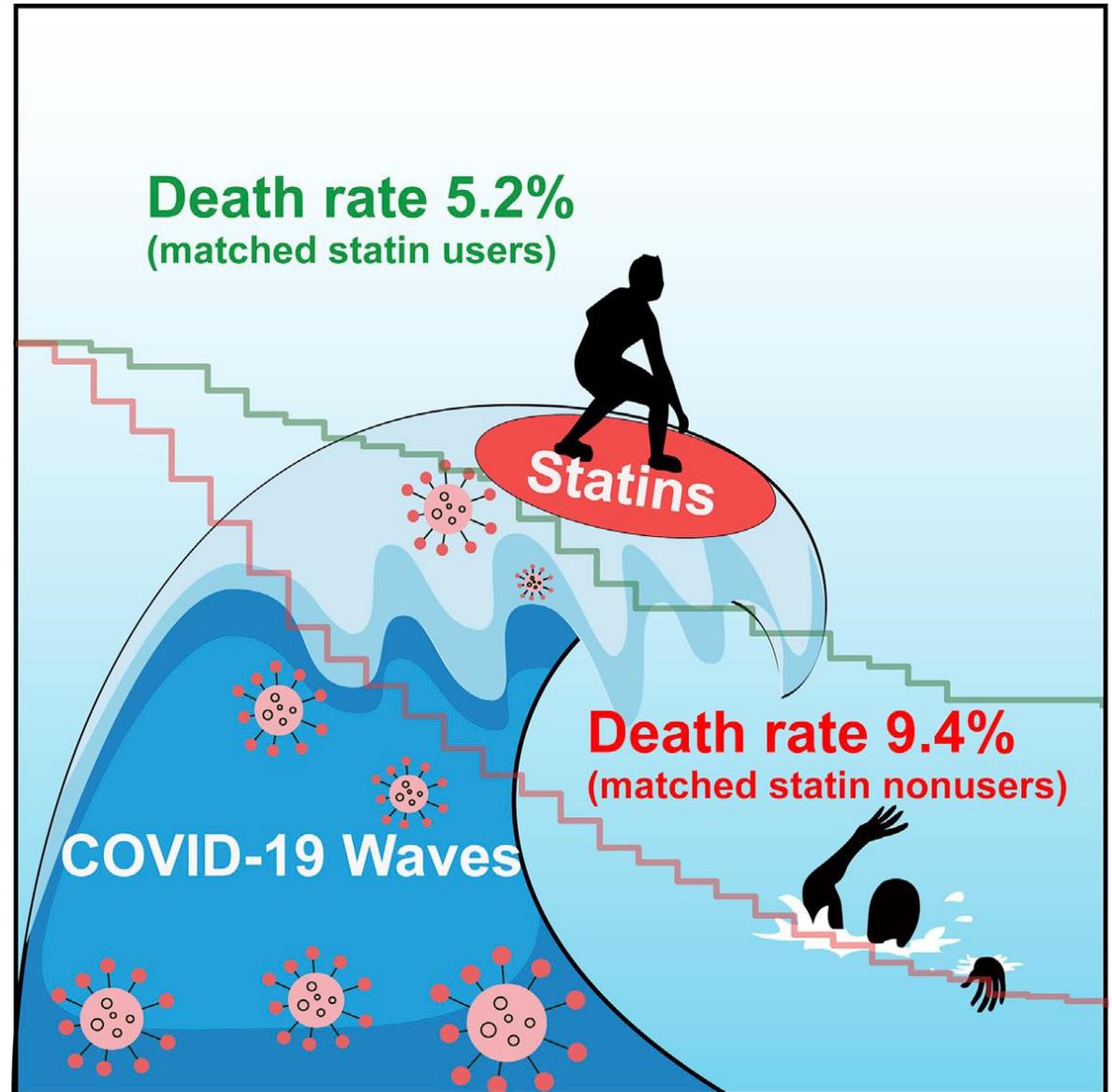
**The effects of ARBs, ACEIs and statins on clinical outcomes of
COVID-19 infection among nursing home residents**

Anton De Spiegeleer^{1,2,3*}, Antoon Bronselaer^{4*}, James T Teo⁵, Geert Byttebier⁶, Guy De Tré⁴, Luc Belmans⁷,
Richard Dobson⁸, Evelien Wynendaele¹, Christophe Van De Wiele⁹, Filip Vandaele¹⁰, Diemer Van Dijck¹¹, Dan
Bean⁸, David Fedson¹² and Bart De Spiegeleer^{1**}

Table 2. Summary of odds ratios for the asymptomatic COVID-19 infection using logistic regression with Firth's correction.

Drug treatment	Adjustments	OR (95% CI) on drug vs. no drug	P-value
ACEi/ARB	-	1.52 (0.62-3.50)	0.339
	Age, sex	1.61 (0.65-3.80)	0.283
	Age, sex, functional status	1.35 (0.51-3.31)	0.521
	Age, sex, functional status, diabetes mellitus, hypertension	2.72 (0.59-25.1)	0.242
Statins	-	2.91 (1.27-6.71)	0.011
	Age, sex	2.88 (1.26-6.83)	0.013
	Age, sex, functional status	2.87 (1.23-7.07)	0.016
	Age, sex, functional status, diabetes mellitus, hypertension	2.65 (1.13-6.68)	0.028

Zhang et al., 2020,
Cell Metabolism 32, 1–12
August 4, 2020 © 2020 Elsevier Inc.
<https://doi.org/10.1016/j.cmet.2020.06.015>

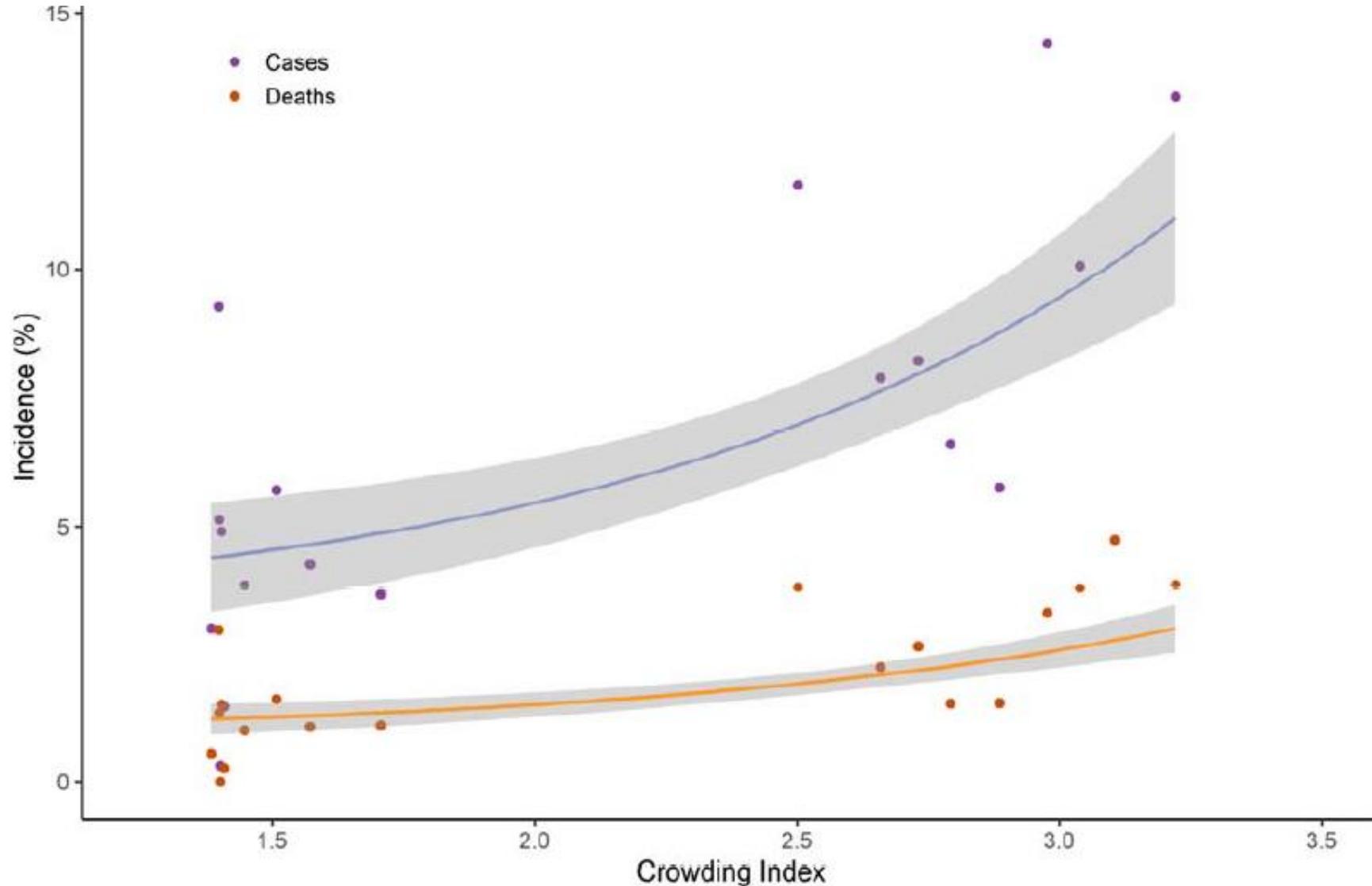


Why challenges in long term care?

- 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

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^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***

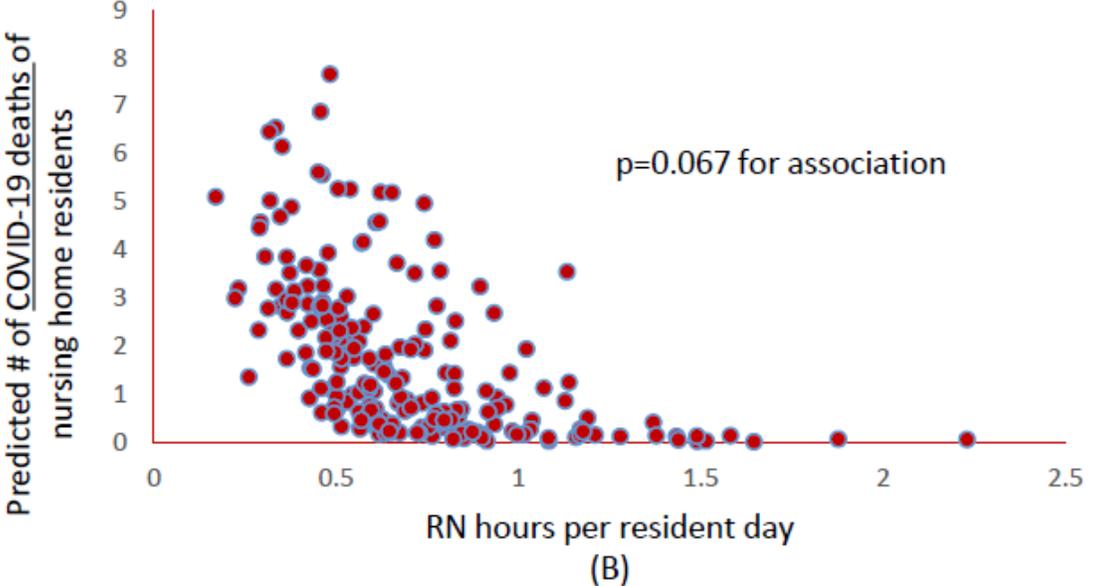
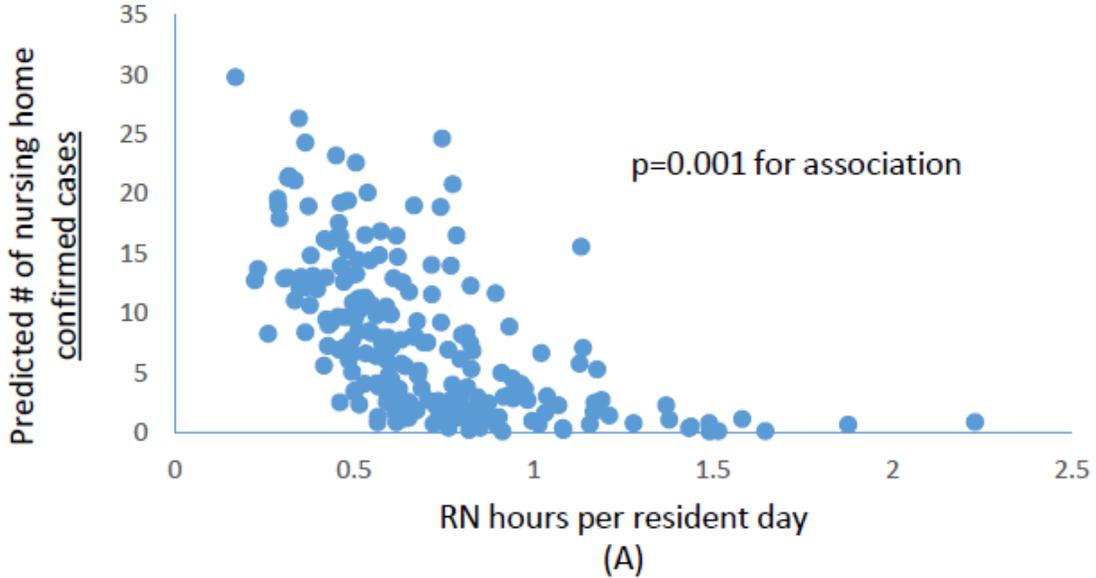
Note. ANOVA = analysis of variance; CMS = Centers for Medicare & Medicaid Services; hprd = hours per resident day; RN = registered nurse.

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

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

Li et al

JAGS (epub ahead of print)



“Abandoning this broken system of care for our nation’s older adults and developing a new system that is responsive to current realities is the only substantive alternative we have.”

Laxton CE, Nace DA, Nazir A; AMDA–The Society for Post-Acute and Long-Term Care Medicine. Solving the COVID-19 Crisis in Post-Acute and Long-Term Care. *J Am Med Dir Assoc*. 2020;21(7):885-887.
doi:10.1016/j.jamda.2020.06.017

The Hong Kong experience

- No country is spared – except Hong Kong
- Why success in Hong Kong?
 - Very effective control of community spread
 - Early interventions in LTC (first issued in January)
 - Funding for PPE and disinfection supplies for residential care homes
 - 10% pay increase for residential care service providers for 4 months; funding for added staff
 - Provision of face masks
 - Introduction of temporary isolation wards
 - Masking of staff and residents
 - Non-essential visiting banned; support for virtual visits (sponsored); 1 visitor at a time
 - Discontinuing non-essential group activities, in-room dining where possible
 - Physical distancing of staff, residents and visitors (all at all times)
 - Cohorting of staff and residents
 - Daily temp checks for residents and staff; temp check and symptom screening for visitors
 - Isolate residents discharged from hospitals

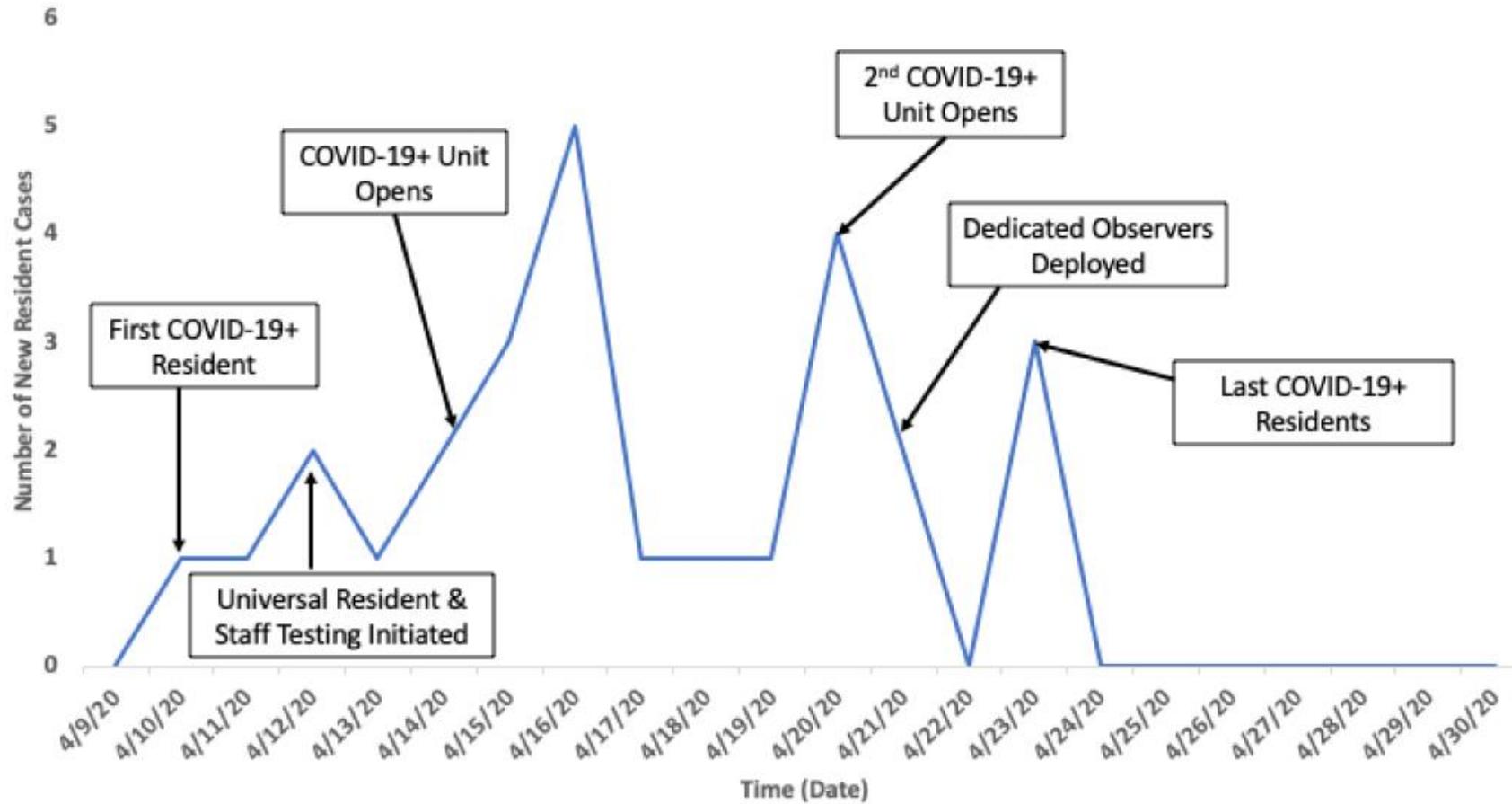
Mitigation of a COVID-19 Outbreak in a Nursing Home Through Serial Testing of Residents and Staff

Daniel J. Escobar MD^{1,2}, Maria Lanzi MS MPH ANP-BC COHN-S³, Pouné Saberi MD MPH^{2,3,4}, Ruby Love RN BSN MBA⁵, Darren R. Linkin MD MSCE^{1,2,6}, John J. Kelly MD MBA^{1,2,6}, Darshana Jhala MD MBBS^{2,7,8}, Valerianna Amorosa MD^{1,2,6}, Mary Hofmann MD^{2,5,9}, Jeffrey B. Doyon MD PhD^{1,2,6}

- Screening residents and staff Q3-5 days
- Masking all residents and staff
- In-room quarantine for residents; attempted cohorting of staff
- Eye protection for staff
- Cohorting of diagnosed residents
- Daily multidisciplinary rounds (IPAC/QI/geriatrics)
- QI team with dedicated observers auditing infection control practice

Mitigation of a COVID-19 Outbreak in a Nursing Home Through Serial Testing of Residents and Staff

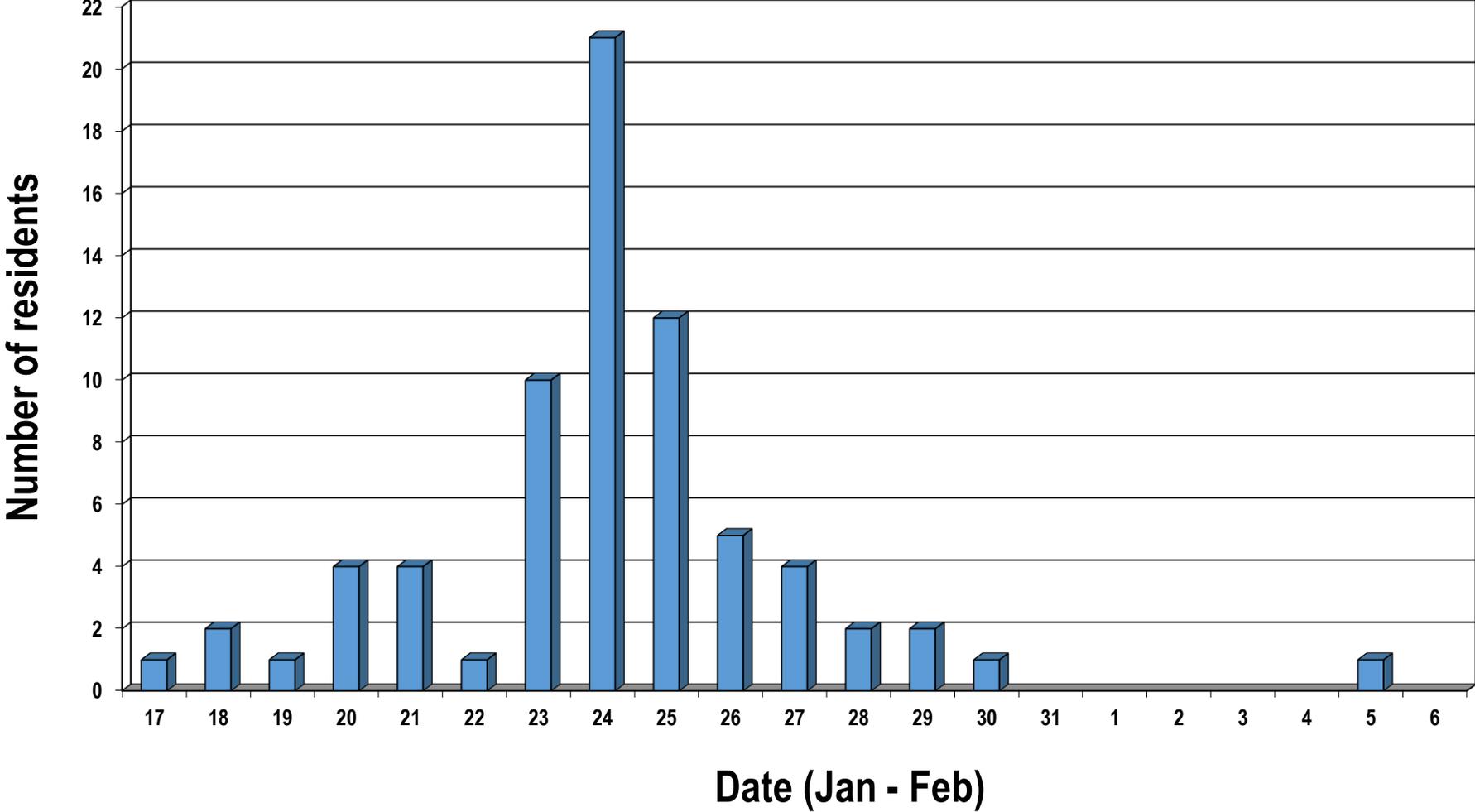
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What do we need to do to be ready?

- Improve staffing/staff pay
- Ensure adequate PPE supplies
- Continue infection prevention training
- Get a system to isolate infected residents
- If possible, keep hospitals linked to LTCHs
- Figure out essential (care-providing) visitors
- Ask if sewage screening might work better than q2week NP swabs
- Figure out how to get rapid test results back to LTCHs
- Ask if antiviral prophylaxis works

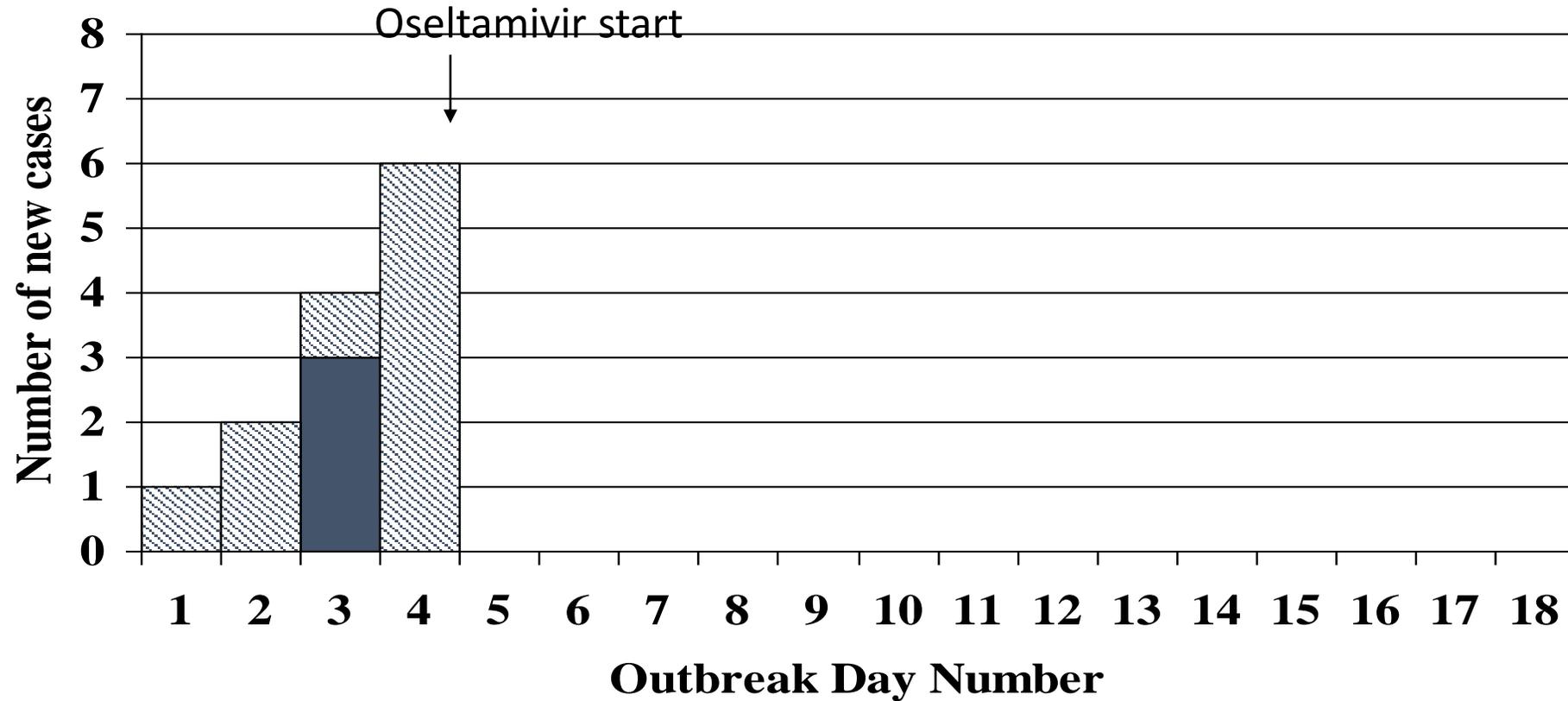
Influenza A outbreak, 2005



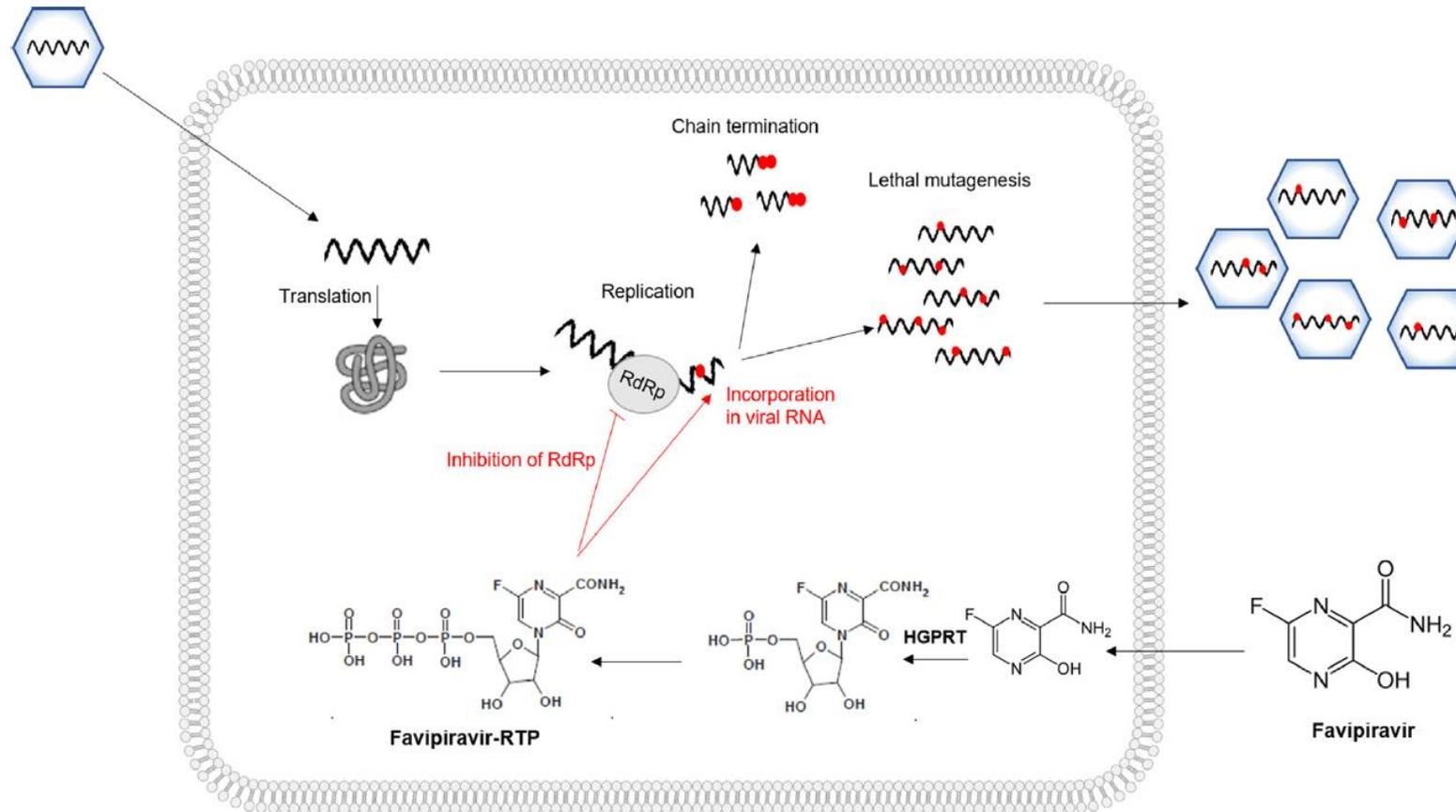
70 of 114 residents

12 deaths

Oseltamivir compassionate use program, Ontario, 2000 (outbreak B4)



- Nucleoside analogue: Inhibits RNA-dependent RNA polymerase



Favipiravir

- Laboratory activity against:
 - Influenza
 - Ebola + (agents of viral hemorrhagic fever)
 - SARS-CoV-2 (COVID-19)
- Approved in Japan for treatment of influenza
- Effective against Ebola in clinical trials (not as good as monoclonal antibodies)
- Multiple COVID19 studies current
 - Reported positive results in RCTs (news articles) from India, Russia
 - Reported negative result, observational trial in Japan (news article)

Favipiravir – Safety

- Favipiravir is considered a safe drug
- > 40 clinical studies with Favipiravir
 - No related serious adverse events
- Well tolerated in adults and elderly patients with influenza
- 1-3% risk of nausea/vomiting, diarrhea, headache
 - Transient elevation triglycerides, uric acid
- Theoretical risk of teratogenicity

Favipiravir – Exclusions

1. Pregnancy

- Females < 55 years of age require a negative urine pregnancy test, and either menopause or two concurrent reliable methods of contraception need to be confirmed

2. Previously diagnosed liver cirrhosis

3. Known abnormality of uric acid metabolism (other than gout)

4. Hypersensitivity to remdesivir or favipiravir

5. Medications, which cannot be discontinued for the study duration:

- Pyrazinamide
- Hydralazine
- > 3000 mg of acetaminophen per day

Favipiravir – Trial

- Pragmatic Cluster RCT: 1:1 favipiravir vs. placebo
 - In an outbreak, does favipiravir treatment/prophylaxis control transmission?
 - Steps
 - Outbreak identified
 - Staff and residents/SDM consented
 - Prophylaxis for 25 days
 - Follow outbreak course (no other intervention)
 - Assess: Is outbreak terminated?
- Preparation
 - Communication
 - Reassurance
 - Logistics

