COVID-19 Update #1

MARCH 31TH 2020

ALASTAIR TEALE - INFECTIOUS DISEASES

Outline

-Review of clinical presentation/clinical manifestations including our first hospitalized patient here at NRGH

-Review admission criteria for COVID19

-Review questions surrounding diagnostic testing

-Review treatment strategies

-Review other clinical controversies

Disclaimer*

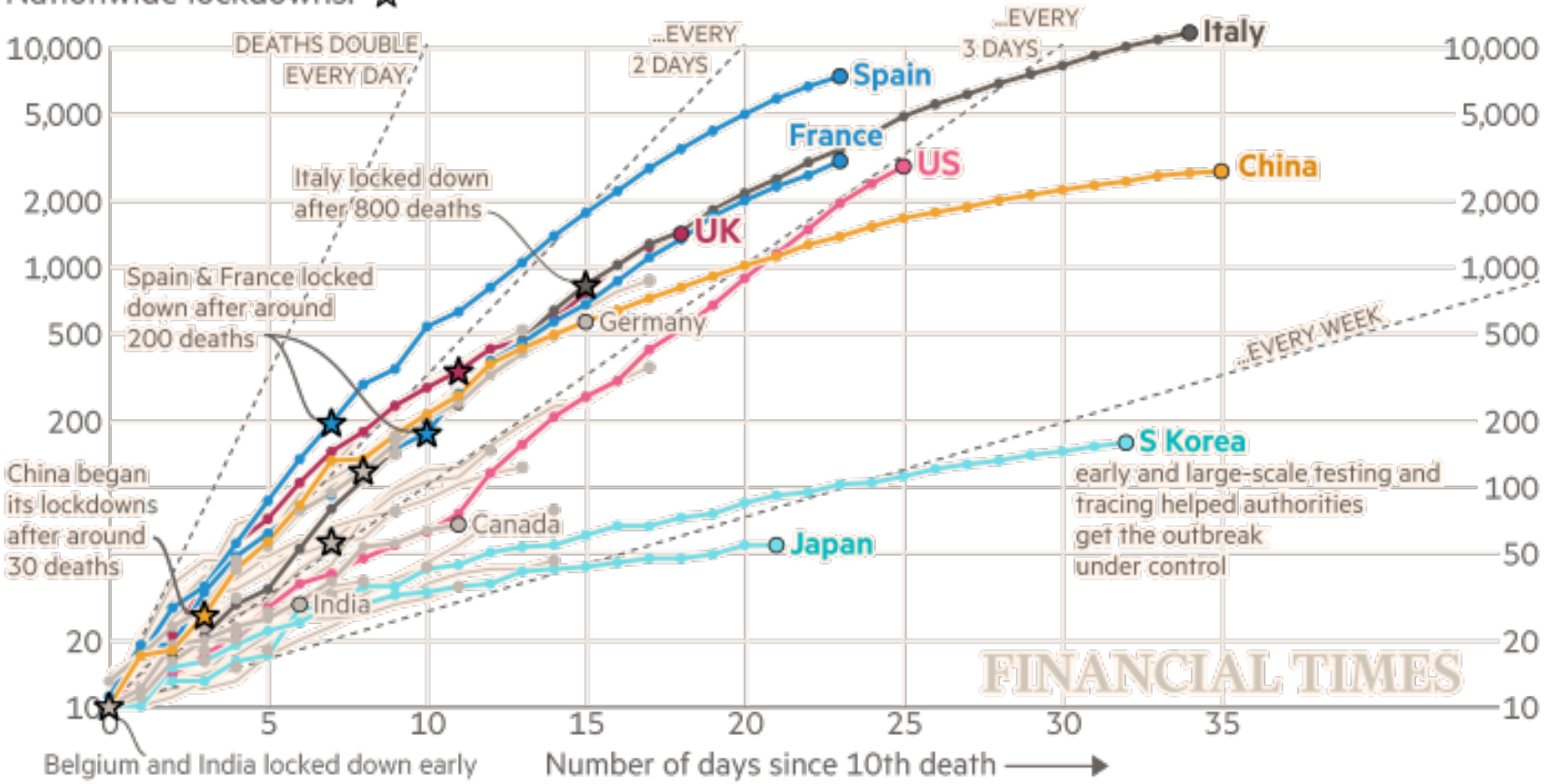
- Everything is subject to change

- Also Spectrum app has been updated with a COVID-19 section
- UTD - COVID19 article is surprisingly detailed and is free

Coronavirus deaths in Italy, Spain, the UK and US are increasing more rapidly than they did in China

Cumulative number of deaths, by number of days since 10th death

Nationwide lockdowns: ★

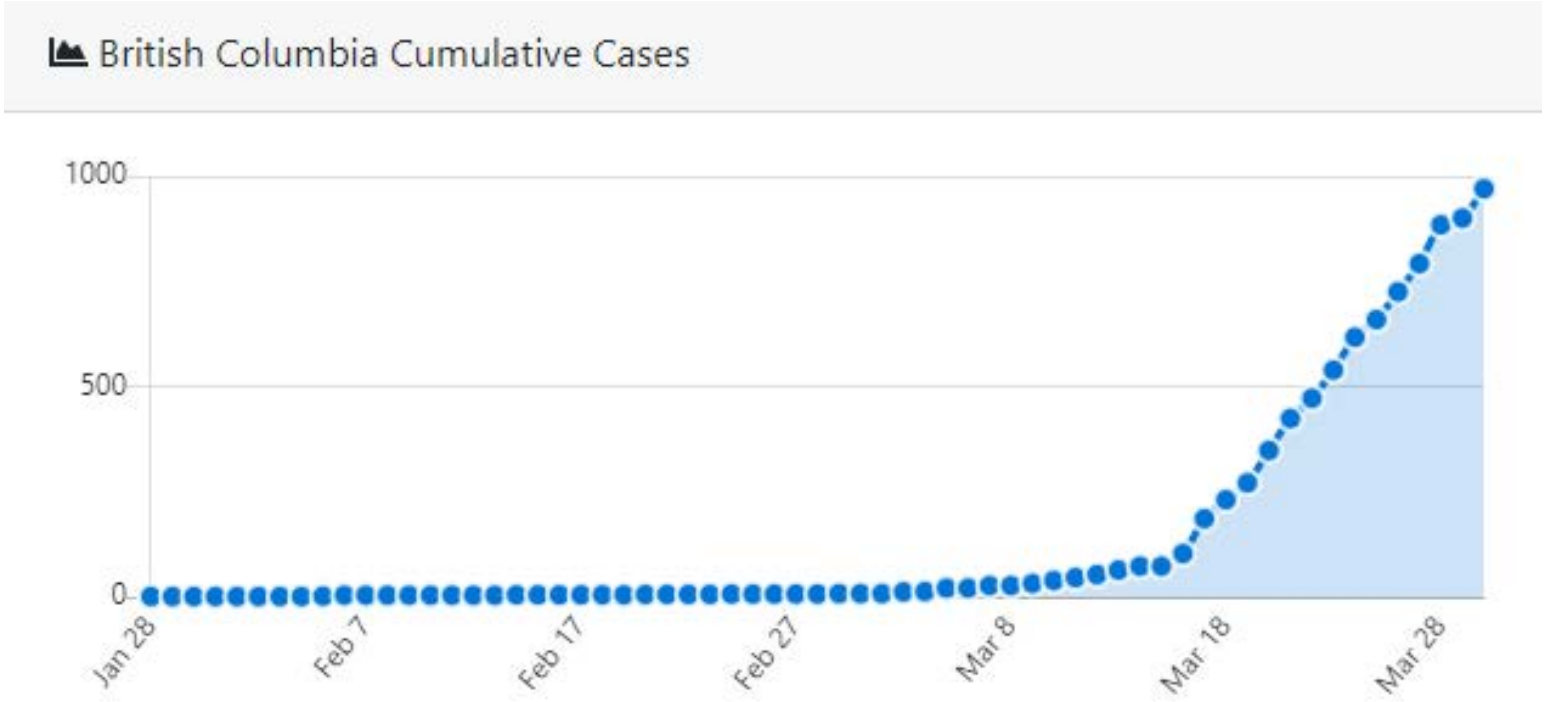


FT graphic: John Burn-Murdoch / @jburnmurdoch

Source: FT analysis of Johns Hopkins University, CSSE; Worldometers; FT research. Data updated March 30, 19:00 GMT

BC (March 30th)

- 970 total known positive cases, 19 deaths
- 100 inpatients across province – 60 in critical care
- 31 patients in HAU/ICUs across Fraser Health
- 6 inpatients on Vancouver Island, 1 so far at NRGH



Case presentation - Summary

Sx – Cough (productive/non productive), fever, malaise, atypical symptoms - diarrhea

Vitals – HD stable, afebrile or low grade fever on ER visit, hypoxic if more advanced

Labs – N or L WBC, lymphopenia, N PCT

X ray – Normal or bilateral infiltrates

Table 2. Laboratory Data at Hospital Admission and Imaging Findings.*

Laboratory Data	Patients (N=24)
On admission	
White-cell count	
Median (IQR) — per mm^3	8430 (5625–12,450)
Distribution — no. (%)	
≥10,000/mm^3	9 (38)
≤4000/mm^3	1 (4)
Lymphocyte count	
Median (IQR) — per mm^3	720 (520–1375)
≤1500/mm^3 — no. (%)	18 (75)
Aspartate aminotransferase >40 U/liter — no./total no. (%)	9/22 (41)
Alanine aminotransferase >40 U/liter — no./total no. (%)	7/22 (32)
Lactate ≥1.5 mmol/liter — no./total no. (%)	8/15 (53)
Infection analyses — no. positive/total no.	
Blood cultures	0/20
Sputum cultures	0/15
Influenza A	0/23
Influenza B	0/23
Respiratory syncytial virus	0/23
Extended-spectrum respiratory viruses	0/21
Chest radiography findings — no./total no. (%)§	
Clear	0/23
Bilateral infiltrates	23/23 (100)
Pleural effusion	0/23

Bhatragu *et al* (NEJM March 30th)

Outcomes	
Median length of stay (IQR) — days	
In hospital	12 (8–18)
In ICU	9 (4–14)
In hospital, survivors	17 (16–23)
In ICU, survivors	14 (4–17)
Median duration of mechanical ventilation (IQR) — days	
Overall	10 (7–12)
In patients who were extubated	11 (7–12)
Extubated — no./total no. (%)	6/18 (33)
Died in hospital — no. (%)	12 (50)
Discharged from hospital — no. (%)	5 (21)

First NRGH case

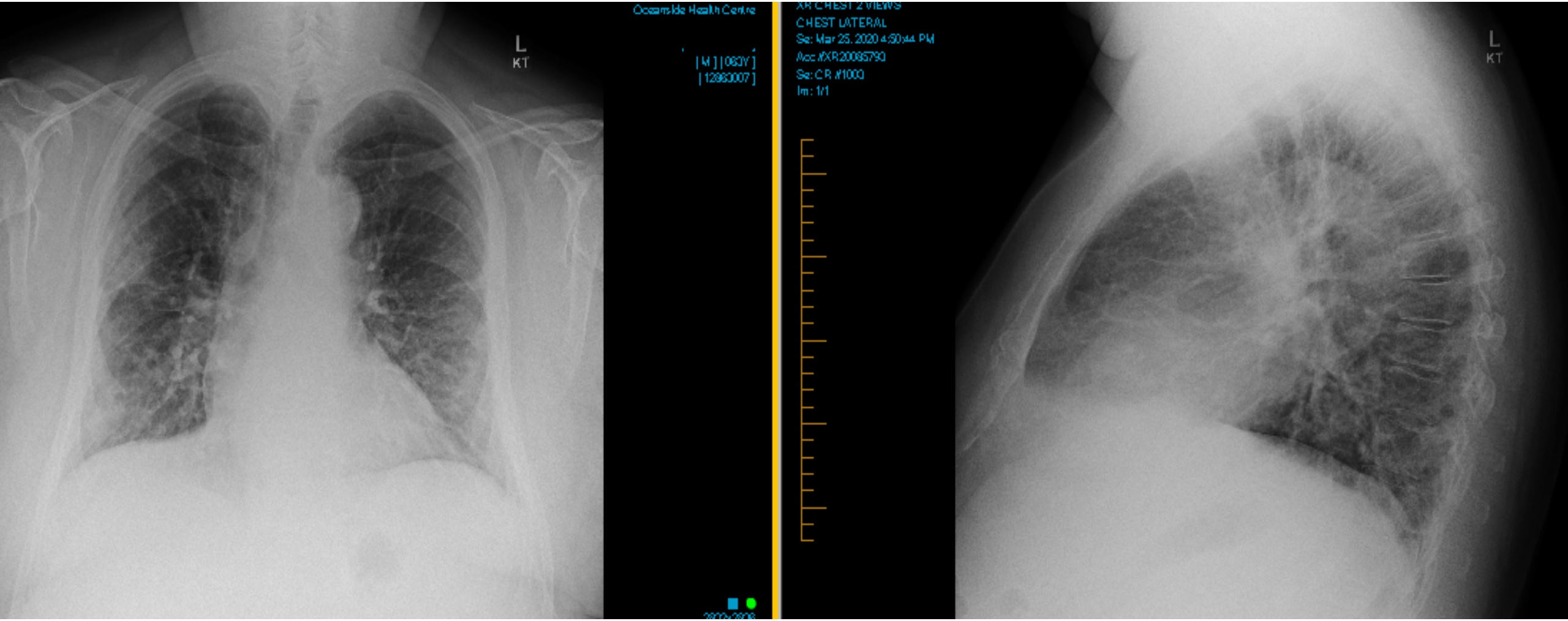
- 63 yo M from Errington
- PMH – Obesity, Borderline DM A1C 6.5, Gout
- Meds – Allopurinol
- HPI – travelled from VI to England in February visiting friends and relatives. Attended Cheltenham horse racing festival (>250K people present). Slightly vague on start of symptoms - ?March 12th – fever, malaise, cough, sore throat, one episode of diarrhea. Returned to Canada while symptomatic on March 24th . Presented to OHC on March 25th.

Case presentation

- 37.3 – 82 – 139/58 – 22 – 94% RA

Speaking half sentences but denied subjective dyspnea. Exam unremarkable – no crackles or wheezes, ?slightly erythematous oropharynx.

WBC 4.5, Lymphocyte count N. Plts low at 102. Creatinine 78

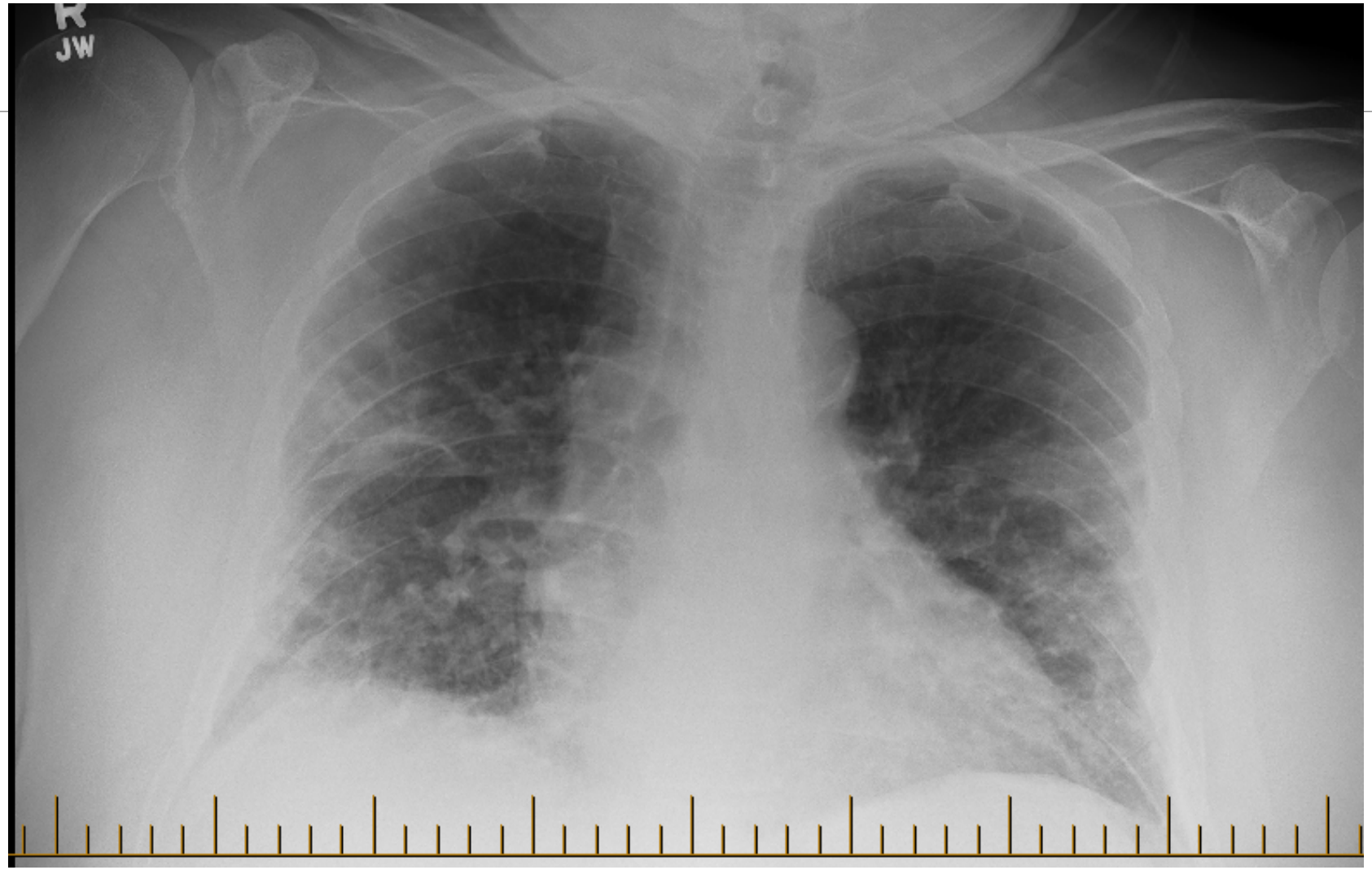


Radiology (paraphrasing) – consider pulmonary edema, interstitial pneumonitis also a possibility

Clinical course

- Admitted due to dyspnea, borderline O2 saturations. ?pneumonia vs CHF
- NP swab + COVID19, negative for influenza, RSV
- BNP normal at 74. Troponin 0.01. PCT low at 0.10. CRP moderately elevated at 53.
- Required 4 L O2 PAD1, now ranging between 2 and 5L. Two low grade fevers 38.5, 38.1
- Antibiotics stopped PAD2

X ray March 30th



Admission Criteria – Who to Keep?

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- No specific guidelines/validated scoring systems to date in Canada
- Decision for admission should be analogous to other respiratory infections.
- No specific lab test/x ray finding overtly helpful in decision to admit or send home.
- Consider a combination of patient factors (age >65, comorbidities), clinical factors (dyspnea, increased respiratory rate, borderline O2 saturations), social factors (phone, stable housing, ability to re-present if required)
- Counsel patients on the possibility of deterioration and to re-present in that situation

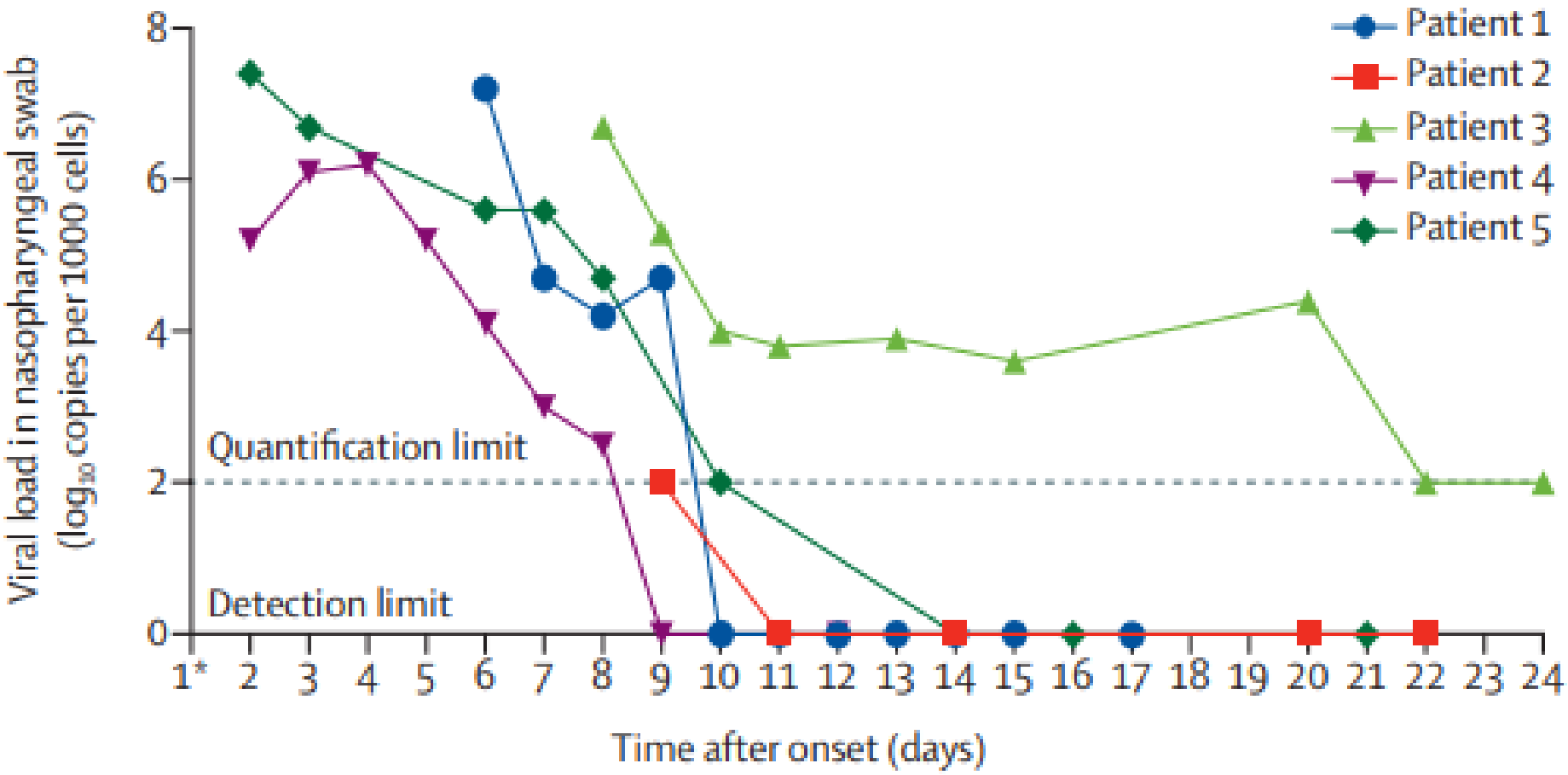
Controversies in Diagnostics

- There has been some discussion about the sensitivity of the NP swab for detection . Chinese data, non peer reviewed, has sensitivity at 62-78%. Sensitivities of influenza swabs have been reported to be ~10-20% higher.
- Lack of data from other countries at the moment – anecdotally from Europe and the US – reports of false negative tests have been prominently discussed
- What is going on with this??

Controversies in Diagnostics

- We know that PCR testing is able to detect very small burden of infection and can be overly sensitive
- We know from studies from closed systems, (Princess Diamond, some LTC homes) the assay is able to pick up asymptomatic infection – and the majority of “asymptomatic” cases were in fact, pre-symptomatic – indicating that likely the issue is not missing early infections.
- ?Technique related or lab factor
- ?Timing of presentation

Lescure *et al* (Lancet March 27th 2020)

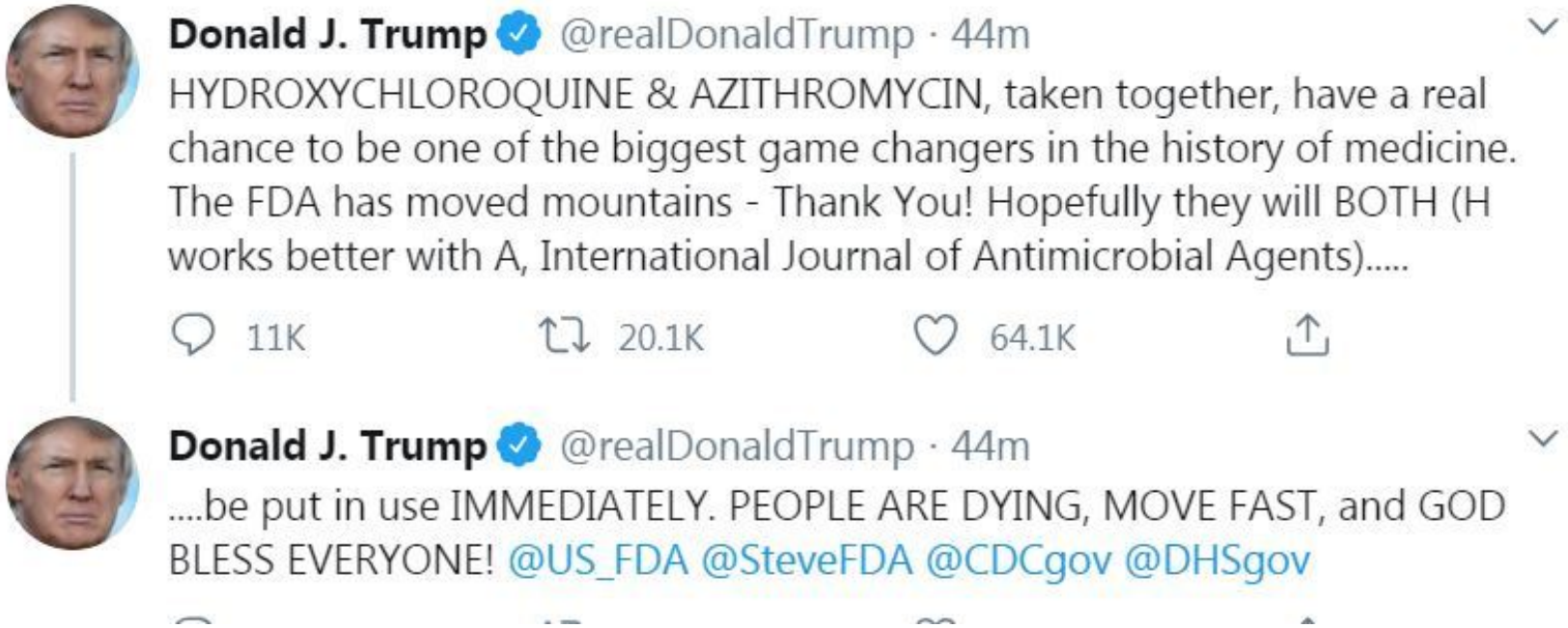


Controversies in Diagnostics

- ?decrease in NP sensitivity around when patients may be presenting in their illness (Day 7-12)
- Use clinical judgement. NP swab likely not able to rule out. If low clinical pretest probability of COVID and alternate explanation found, consider other diagnosis. If high clinical pretest probability, typical history, X ray/CT scan findings consistent, no other explanation, negative test does not rule out COVID19.
- Consider resending deeper samples, sputum or ETT tube aspirate for repeat COVID PCR
- Suggest syndromic approach to precautions

Controversies in Treatment

- Last week, antiviral expert Donald Trump tweeted on experimental therapies for COVID19

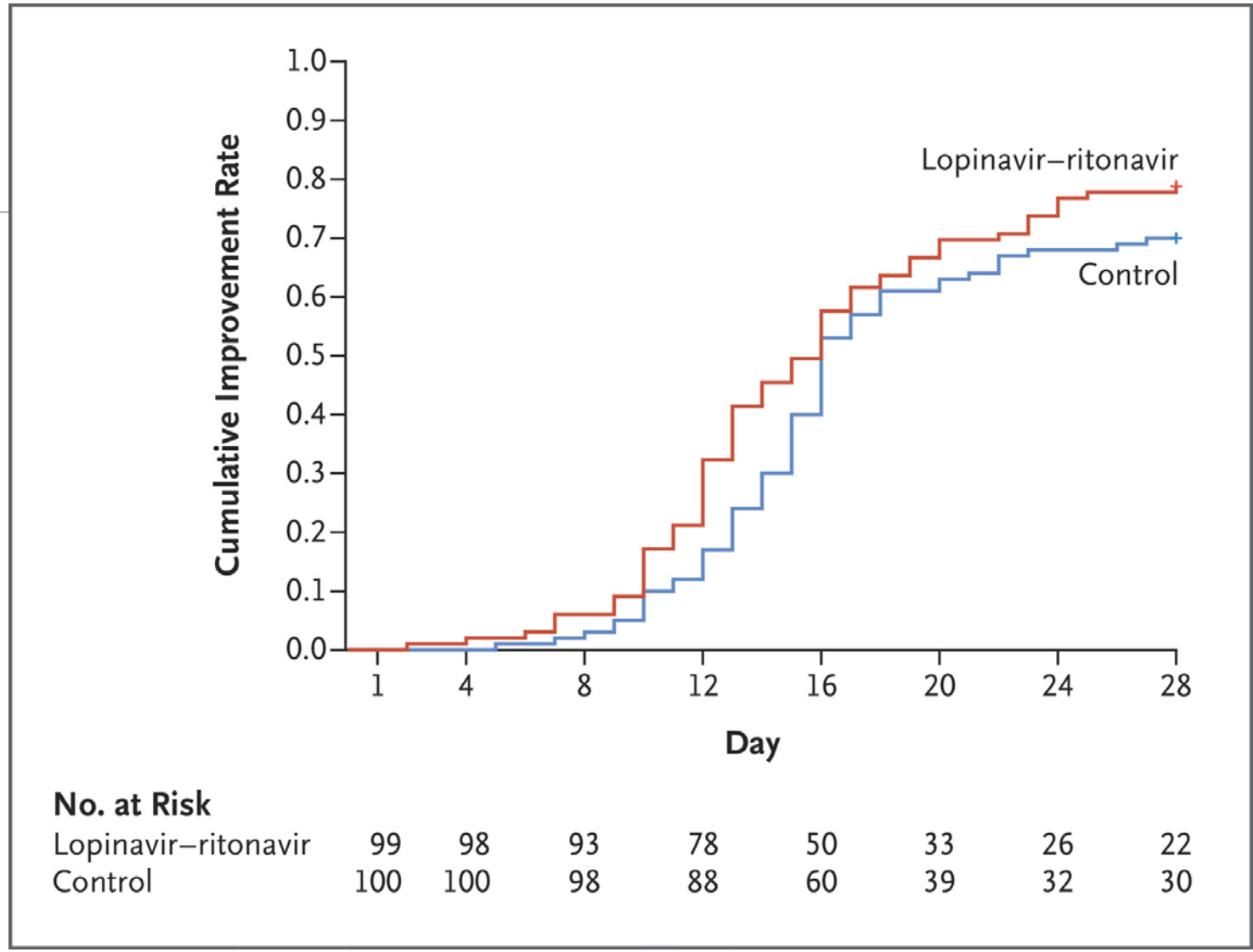


Controversies in Treatment

- This naturally caused a run on HCQ. A pharmacy in Victoria was advertising this as a prophylactic agent to HCW.
- In vitro activity as previously mentioned, but no significant clinical data to date.
- Tweet was based off of a French study with 20 patients with incomplete that showed decrease in viral load with patients with treatment. No randomization. The French primary investigator has a history of data manipulation in the past.
- Currently, the ID groups across BC are not recommending any specific therapy outside of clinical trials. The hope is that Dave and I will be able to participate in the BC arm of the CATCO clinical trial.

Cao *et al* NEJM

- Open label, Randomized trial, 200 patients, 100 patients in each arm – SOC vs Lopinavir-ritonavir
- Did not show clinical benefit of therapy – however late randomization, 13 days since beginning of symptoms. Has the horse left the barn?

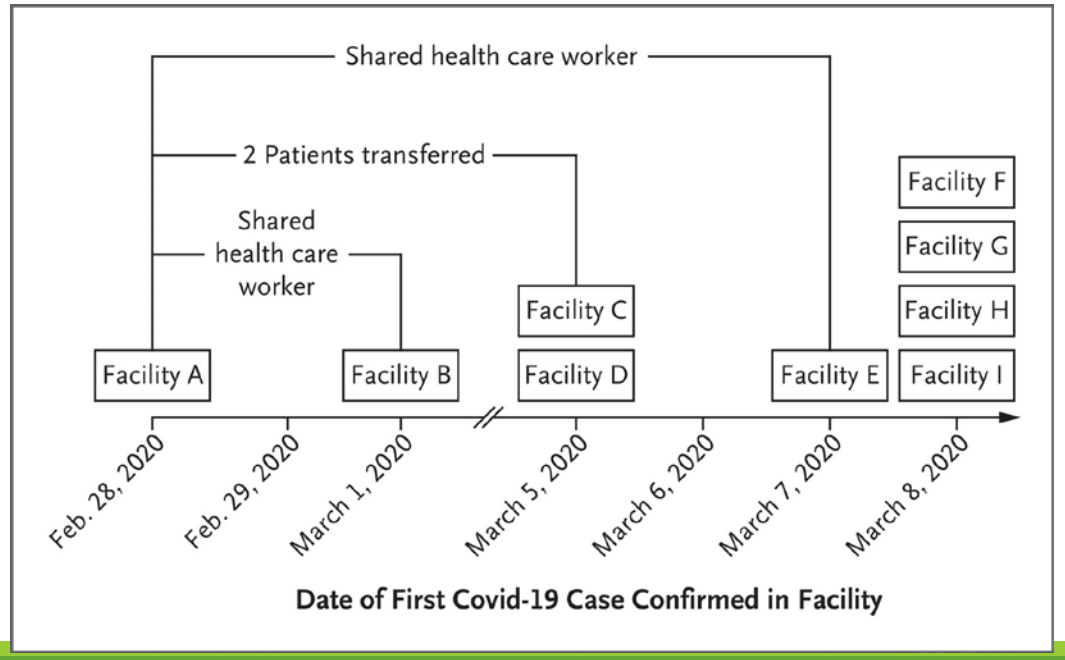


COVID19 and ACE inhibitors

- In the interim since the last presentation, multiple societies have released statements noting no evidence of harm of patients with RAS blockade. They have suggested against switching patients to alternative agents.
- No evidence in humans that RAS blockade actually increases ACE2 levels in human cells
- Hypothetical benefit of RAS blockade?
- Awaiting more clinical data – for now, ad hoc post analysis has not shown an association with poorer outcomes

COVID19 and Nursing Homes

- 13 Nursing homes affected on the Lower Mainland currently
- Outbreak in Washington described by *McMichael et al,* NEJM



Characteristic	Residents (N = 101)
Median age (range) — yr	83 (51–100)
Sex — no. (%)	
Male	32 (31.7)
Female	69 (68.3)
Hospitalized — no. (%)	
Yes	55 (54.5)
No	9 (8.9)
Unknown	37 (36.6)
Died — no. (%)	
Yes	34 (33.7)
No	67 (66.3)

Questions?

There is no emergency in a pandemic.