Coronavirus:
Treating the Pregnant Patient with COVID-19

5th May 2020

Pharmacology & Therapeutics in COVID-19

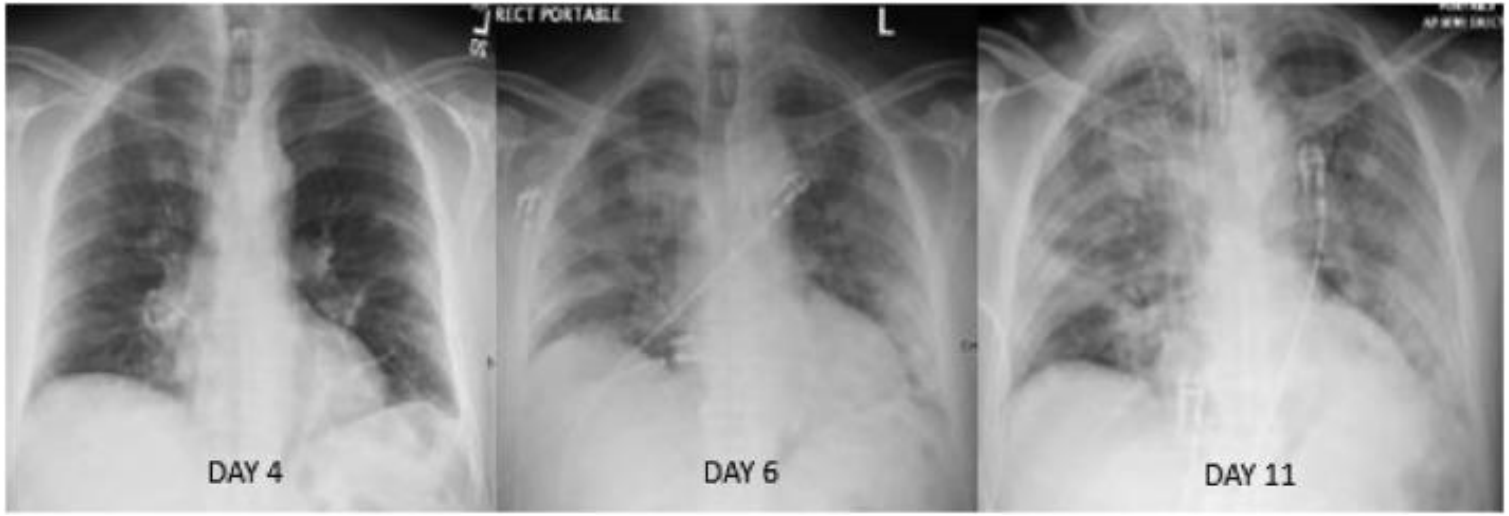
Dr David Williams

Obstetric Physician

University College London Hospitals NHS Foundation Trust

UCL EGA Institute for Women's Health

Clinical Progression of COVID-19

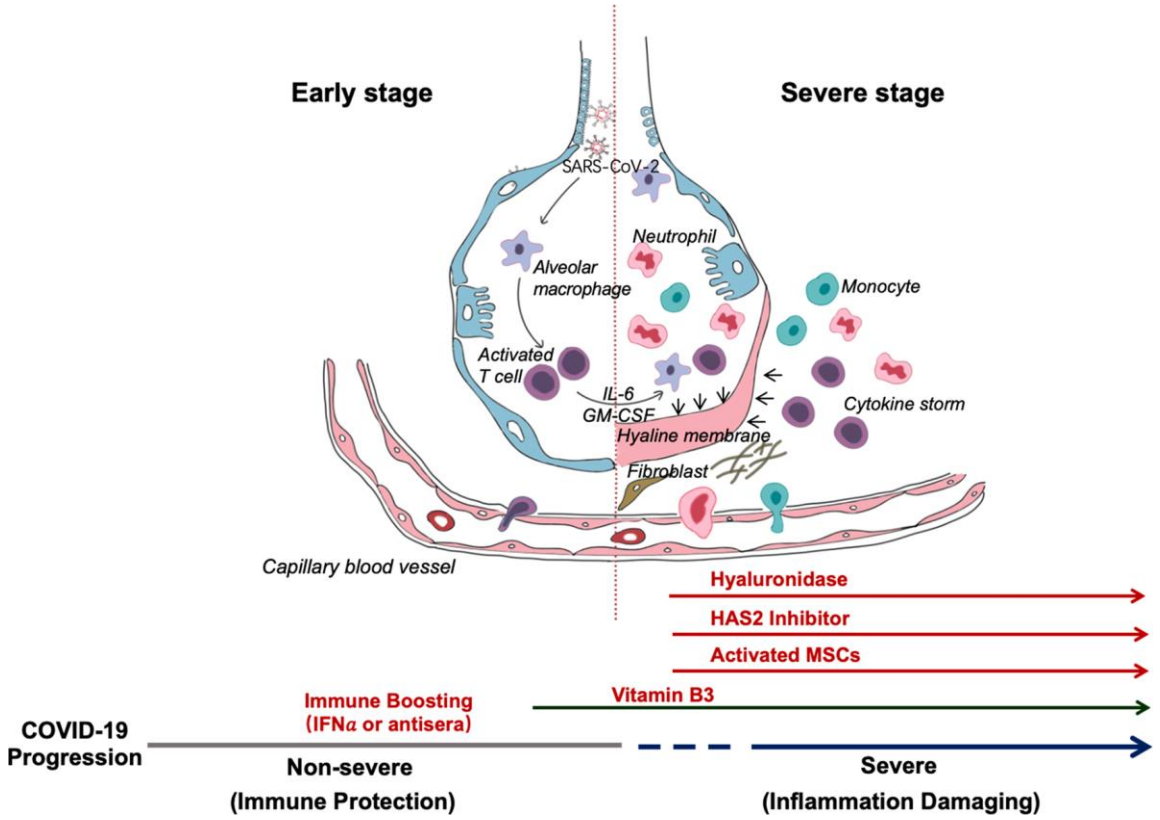


Jacobi A et al Clin Imaging 2020 64; 35-42

Pregnant women appear to be at similar risk from COVID-19 as non-pregnant women

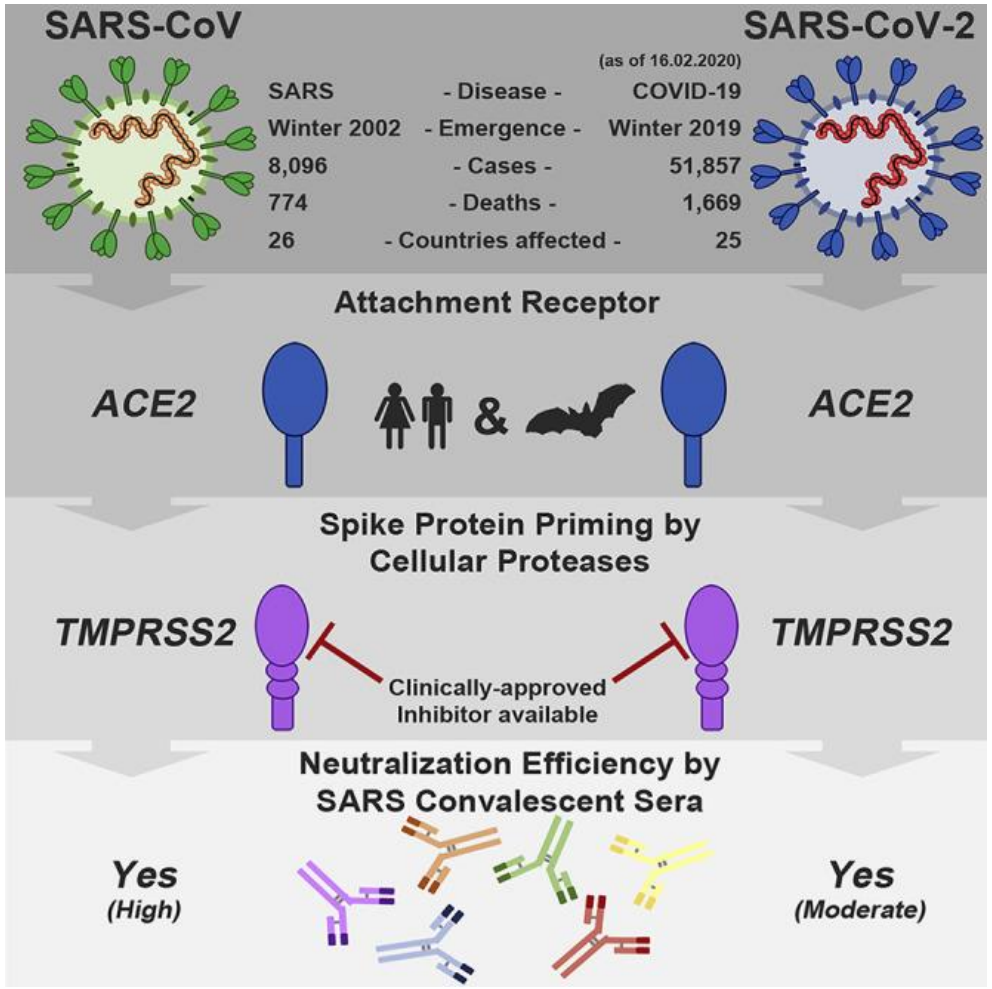
Chen et al NEJM

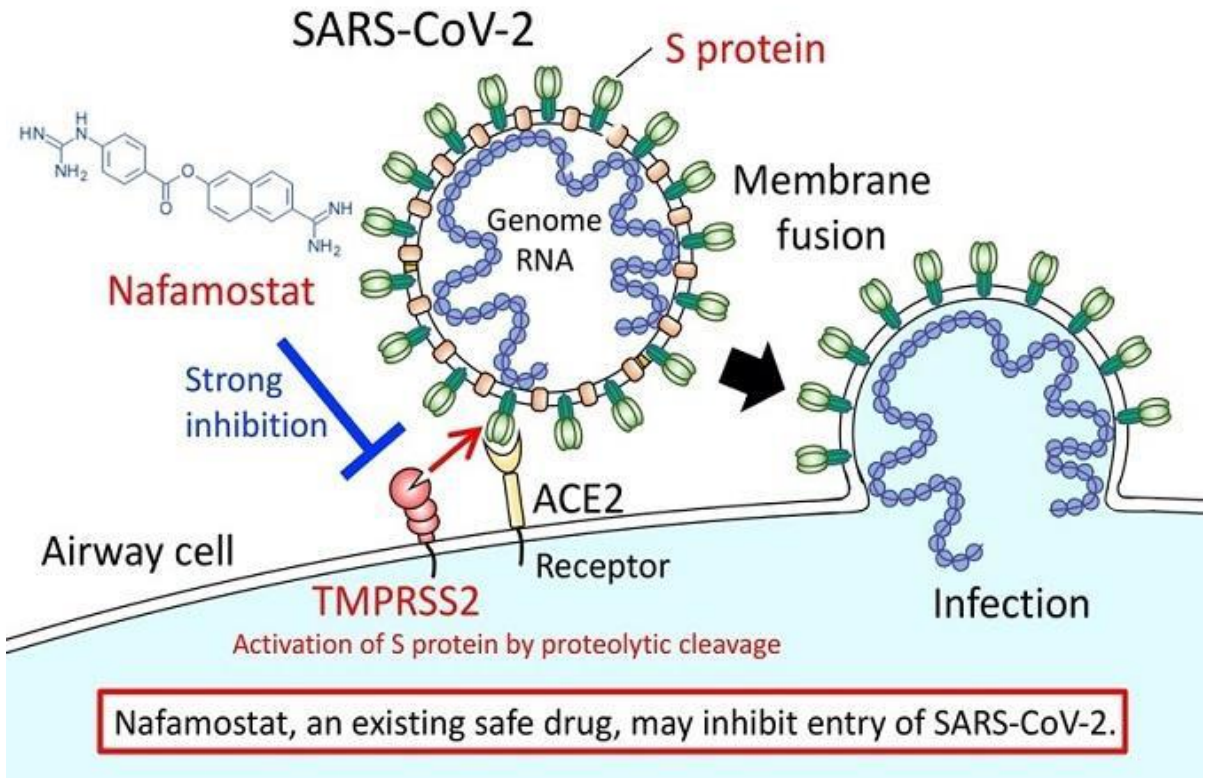
DOI: 10.1056/NEJMc2009226



Shi Y et al Cell death and Differentiation 2020; 27: 1451-54

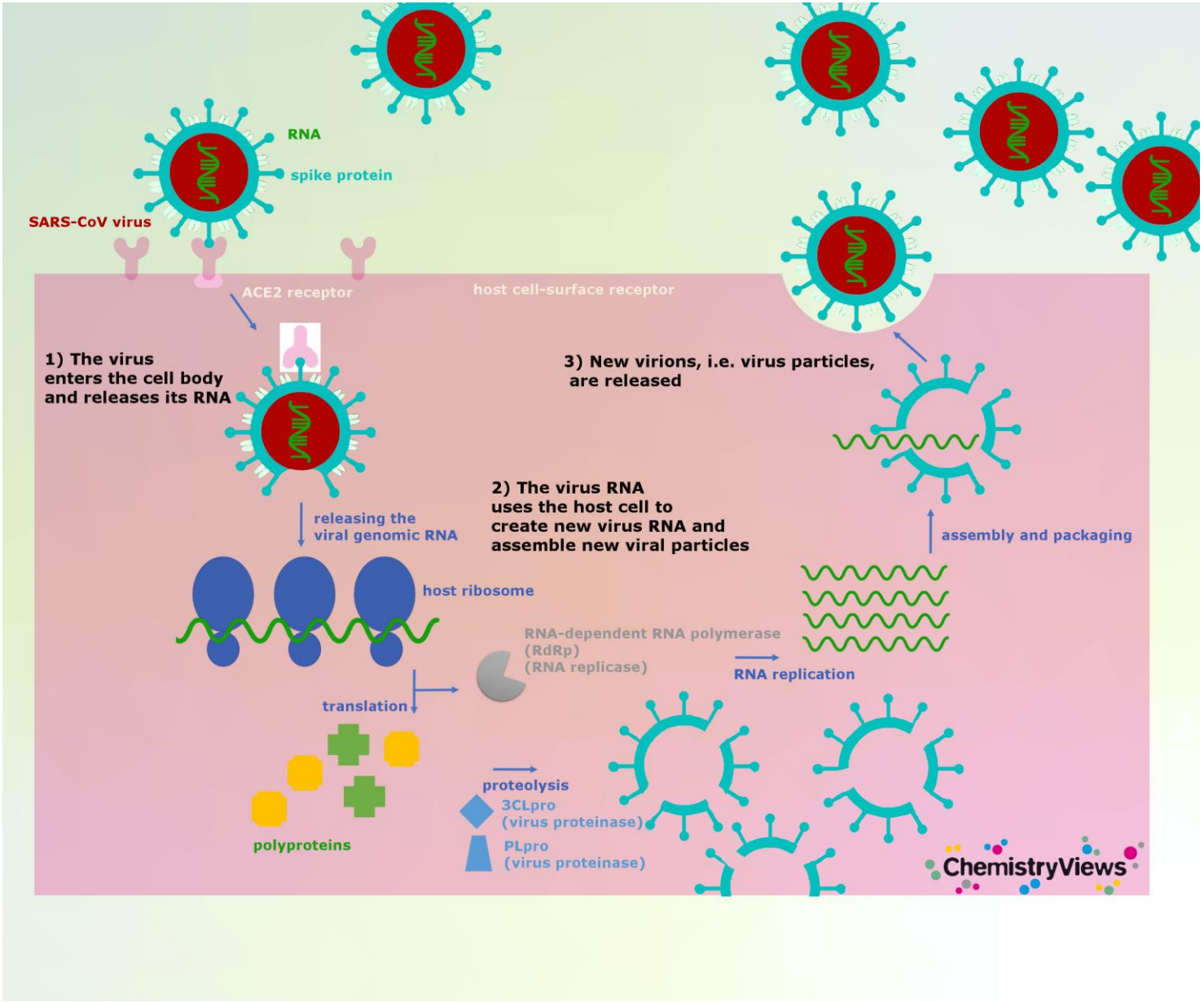
SARS-CoV-2 enters the host cell via ACE2 receptor and serine protease TMPRSS2 and can be blocked by protease inhibitors





Hoffmann M et al Cell 2020 Apr 16: 181 (2): 271-280

Coronavirus Entering and Replicating in a Host Cell



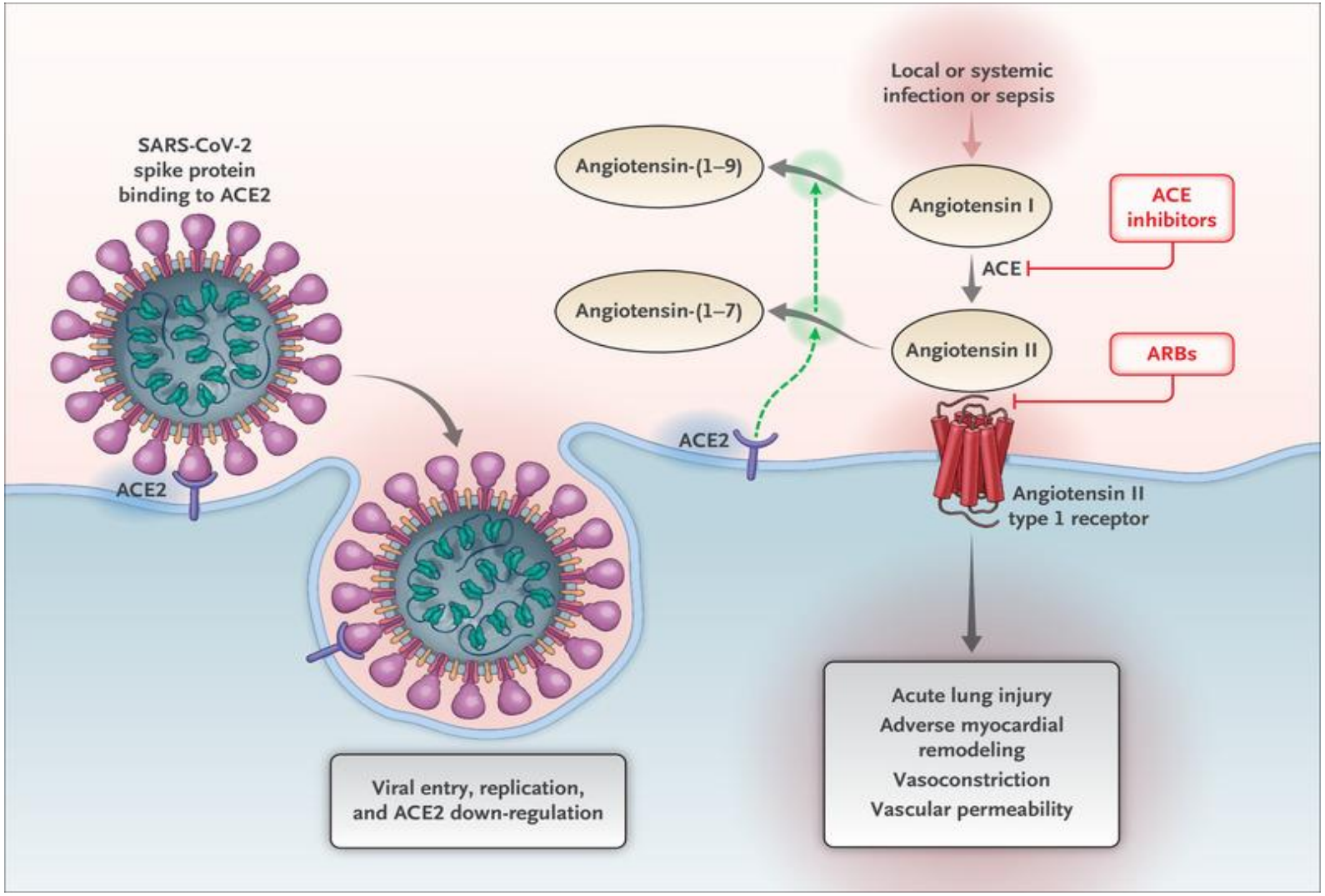
Symptoms
Fever
Dry Cough
Fatigue

Then,

Dyspnoea
Sputum
Pneumonia
Diarrhoea

Vera Koestner
Chemistry Views 3.3.20

Renin-Angiotensin-Aldosterone System Inhibitors in Patients with COVID-19



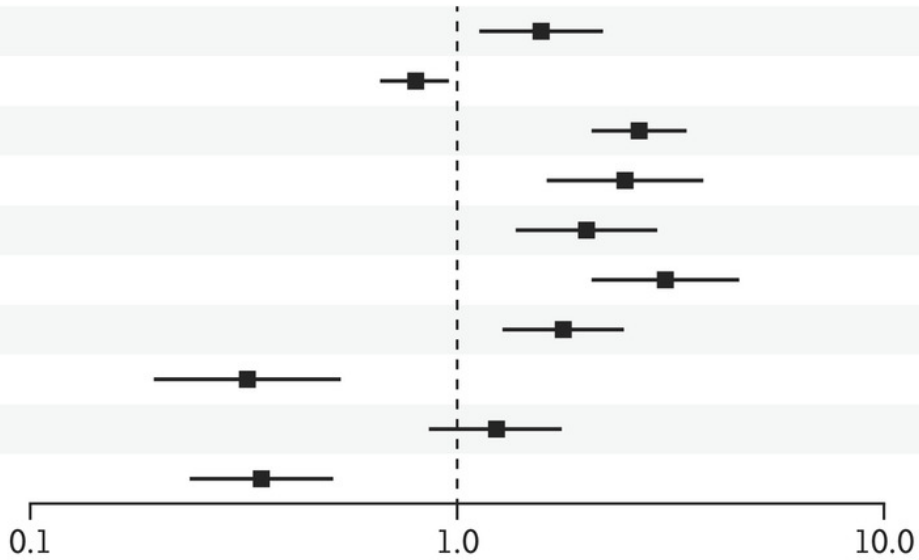
Vaduganathan M
NEJM April 23, 2020

Independent Predictors of In-Hospital Death

(Multivariable Logistic-Regression Analysis)

8910 Covid-19 patients: 515 died (5.8%) and 8395 survived

Risk Factor	Risk Factor Present	Risk Factor Absent	Odds Ratio (95% CI)
	no. of patients who died/total no. (%)		
>65 yr of age	147/1474 (10.0)	368/7436 (4.9)	1.93 (1.60–2.41)
Female sex	179/3571 (5.0)	336/5339 (6.3)	0.79 (0.65–0.95)
Coronary artery disease	103/1010 (10.2)	412/7900 (5.2)	2.70 (2.08–3.51)
Congestive heart failure	29/189 (15.3)	486/8721 (5.6)	2.48 (1.62–3.79)
Arrhythmia	35/304 (11.5)	480/8606 (5.6)	1.95 (1.33–2.86)
COPD	32/225 (14.2)	483/8685 (5.6)	2.96 (2.00–4.40)
Current smoker	46/491 (9.4)	469/8419 (5.6)	1.79 (1.29–2.47)
Receiving ACE inhibitor	16/770 (2.1)	499/8140 (6.1)	0.33 (0.20–0.54)
Receiving ARB	38/556 (6.8)	477/8354 (5.7)	1.23 (0.87–1.74)
Receiving statin	36/860 (4.2)	479/8050 (6.0)	0.35 (0.24–0.52)



Mehra MR et al NEJM May 1st 2020

The RECOVERY Trial
(Randomised Evaluation of COVID-19 Therapy)
University of Oxford

The RECOVERY Trial is testing the following drugs against COVID-19:

1. **Lopinavir-Ritonavir** (used to treat HIV)
2. **Low-dose Dexamethasone**
3. **Hydroxychloroquine** (related to an anti-malarial drug)
4. **Azithromycin** (a commonly used antibiotic)
5. **Tocilizumab** (anti-IL-6 monoclonal, given by injection, Inflammatory Arthritis)

Data is reviewed regularly

Promising new drugs will be added to the trial

Remdesivir: antiviral used against Ebola

- April 29 2020:
- Adaptive COVID-19 Treatment Trial (ACTT); NIH Allergy Infectious Diseases
- 1063 patients with advanced COVID19 and lung involvement were randomised to daily Remdesivir for 10 days or placebo.
- Those who received Remdesivir had a 31% faster time to recovery ($p<0.001$) 11 days v 15 days compared with those who received placebo
- Remdesivir also associated with improved mortality 8.0% v 11.6% ($p=0.059$)

- Gilead Sciences subsequently showed, **a 5-day course achieved similar improvement in clinical status as a 10-day course**

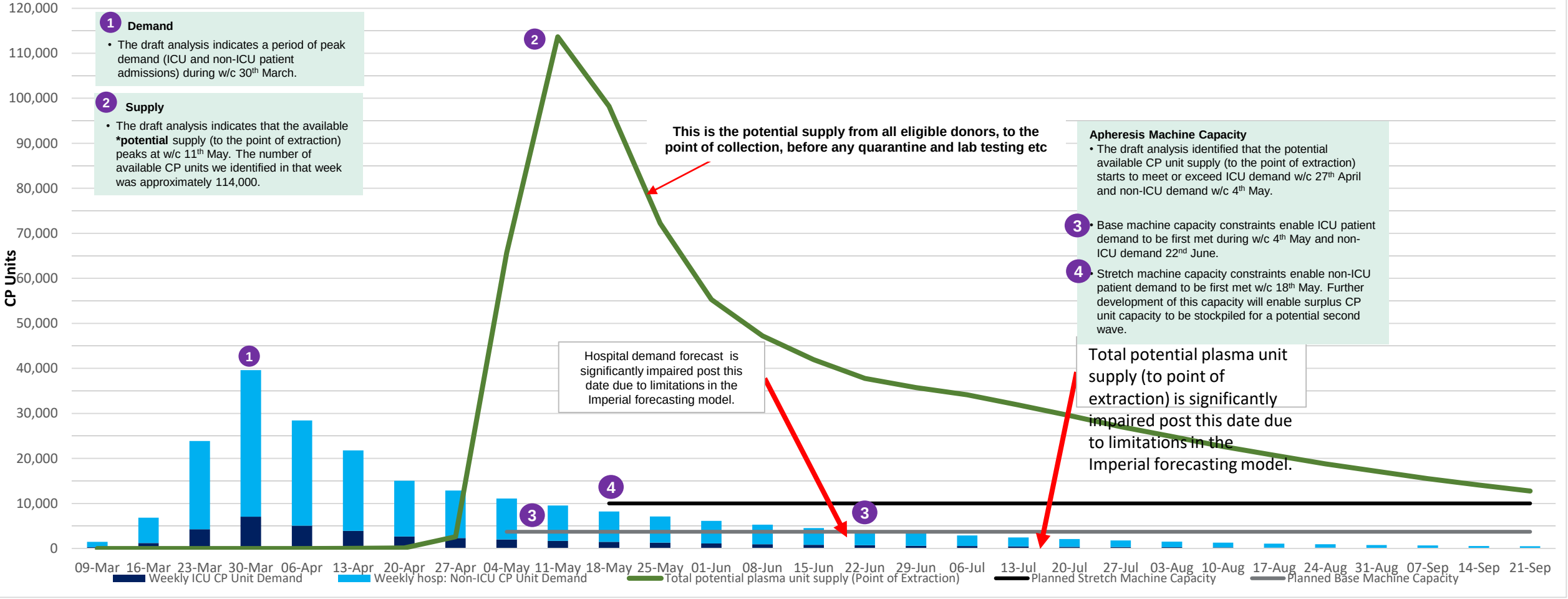
Convalescent Plasma Therapy

- Passive Immunisation Therapy: Blood drawn from people recovered from COVID19 and those with a high titre of neutralizing
- NHS Blood and Transplant Service is recruiting people who have recovered from COVID19 (no sooner than 28 days after recovery)
- Plasma apheresis takes 45 minutes (healthy, non-pregnant donors).
- Plasma will be given to treat patients on intensive care units, including pregnant women
- Rajendran et al: Reviewed 5 observational studies of convalescent plasma (4 from China) with 27 patients. It is safe, patients do well, but not controlled
- Trial in Oxford, and REMAP-CAP

15th April – Model Output, initial refresh

Key assumptions 95% sufficient titre, latest Imperial infection rates, 28 days from recovery to donation, 2% of infections hospitalised, 14% of hospitalised require ICU, ongoing lockdown, regional supply/capacity aligned, sufficient testing / manufacturing capacity is available

Subject to change as data is refreshed, additional actuals are included and assumptions amended



NHS Blood and Transplant Service

What are pharmaceutical Companies doing to tackle COVID-19?

- Over 20 companies have potential medicines, at least 4 in late phase trials
- Over 50 projects working on vaccines
- **BUT**, only 1:10 vaccine developments make it through regulatory approval
- **If one or two of the first vaccines enter development it will be 12-18 months before a vaccine is widely available!**

Therapeutic treatment of COVID-19 during pregnancy

- **Supportive measures**
- Oxygen support; nasal, mask, CPAP, ventilation
- IV Fluid,
- Thromboprophylaxis
- Antibiotics if likely secondary bacterial infection
- Pregnant women can be entered into clinical trials e.g RECOVERY Trial
- Consideration for early childbirth if severe respiratory distress requiring ventilation