MORNING BRIEF

Scientific Review

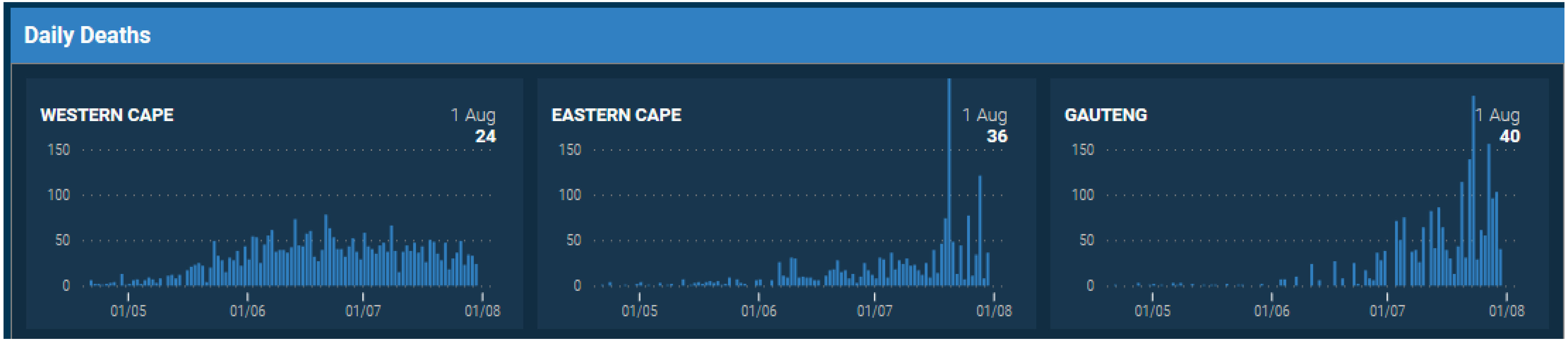
3 August 2020

The purpose of the Morning Brief is to summarize and present key information, research articles and other relevant publications pertaining to critical care and COVID-19.

Stellenbosch University Research Response Team

Content

Statistics
Longitudinal immune response Severe vs Moderate Covid-19


Daily Deaths
WESTERN CAPE
1 Aug
24
EASTERN CAPE
1 Aug
36
GAUTENG
1 Aug
40
150
100
50
0
01/05
01/06
01/07
01/08

nature
https://doi.org/10.1038/s41586-020-2588-y
Accelerated Article Preview

Longitudinal analyses reveal immunological misfiring in severe COVID-19

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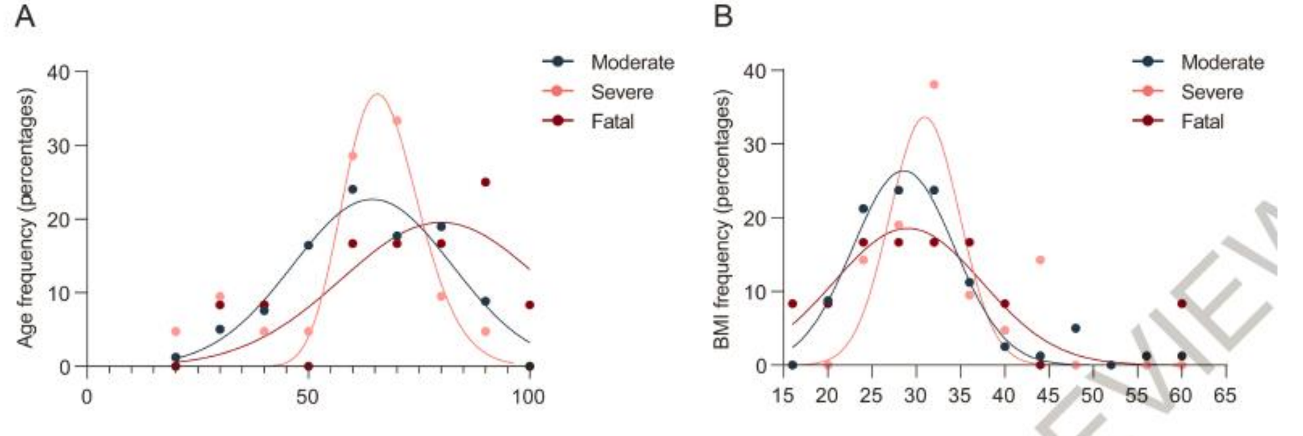
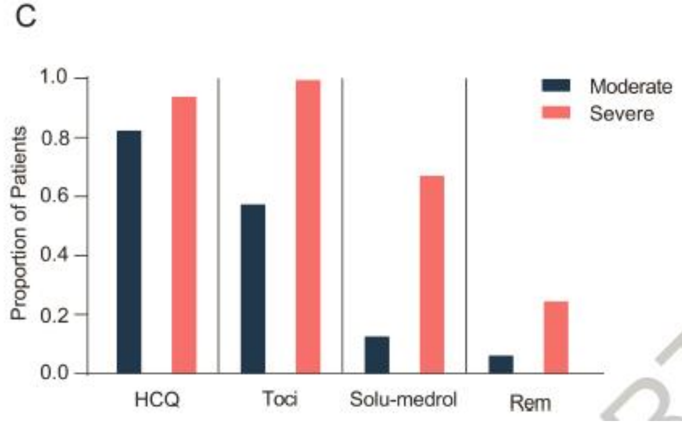
Carolina Lucas, Patrick Wong, Jon Klein, Tiago B. R. Castro, Julio Silva, Maria Sundaram, Mallory K. Ellingson, Tianyang Mao, Ji Eun Oh, Benjamin Israelow, Takehiro Takahashi, Maria Tokuyama, Peiwen Lu, Arvind Venkataraman, Annsea Park, Subhasis Mohanty, Haowei Wang, Anne L. Wyllie, Chantal B. F. Vogels, Rebecca Earnest, Sarah Lapidus, Isabel M. Ott, Adam J. Moore, M. Catherine Muenker, John B. Fournier, Melissa Campbell, Camila D. Odio, Arnau Casanovas-Massana, Yale IMPACT Team, Roy Herbst, Albert C. Shaw, Ruslan Medzhitov, Wade L. Schulz, Nathan D. Grubaugh, Charles Dela Cruz, Shelli Farhadian, Albert I. Ko, Saad B. Omer & Akiko Iwasaki

Age and sex not different in severe vs moderate in this cohort
BMI > 35 RR for mortality 1.6 (95% CI 0.81 – 3.22)
Mortality ICU vs general ward: 27.27% vs 3.75% ($p < 0.001$)

Longitudinal analysis of immune response, focused on type 1,2 and 3 response
N = 113 hospitalised, single centre, USA, prospective
Severe vs moderate based on O2 and ICU need
3 to 51 days after symptom onset
Controls – 108 healthcare workers, PCR and serology negative
Tests:
- Viral load
- Cytokines and chemokines
- Leukocyte profiles by flow cytometry





D

Changes in IL-6, according to tocilizumab, after controlling, age, ICU admission and days from symptom onset, accounting for multiple observations per person (GEE).

Covariate	Coefficient	95% CI
Tocilizumab	**0.55**	**0.07, 1.04**
ICU admission	0.48	-0.02, 0.99
Days from symptom onset	-0.02	-0.04, -0.003
Age	0.01	0.0003, 0.02

This analysis excludes two individuals whose IL-6 was measured before receiving tocilizumab.

Changes in T cell count, according to age, ICU admission and days from symptom onset, accounting for multiple observations per person (GEE).

Covariate	Coefficient	95% CI
ICU admission	-13.43	-19.32, -7.55
Days from symptom onset	-0.15	-0.41, 0.11
Age	**-0.16**	**-0.33, 0.02**

Low CD4 and CD8 T-cells, corrected for age in COVID-19 patients vs healthy controls

A group of patients with severe disease had high eosinophils, monocytes and neutrophils

Increased T-cell activation, decreased HLA-DR expression by circulating monocytes (decreased antigen presentation)

Cytokine expression differences between moderate and severe

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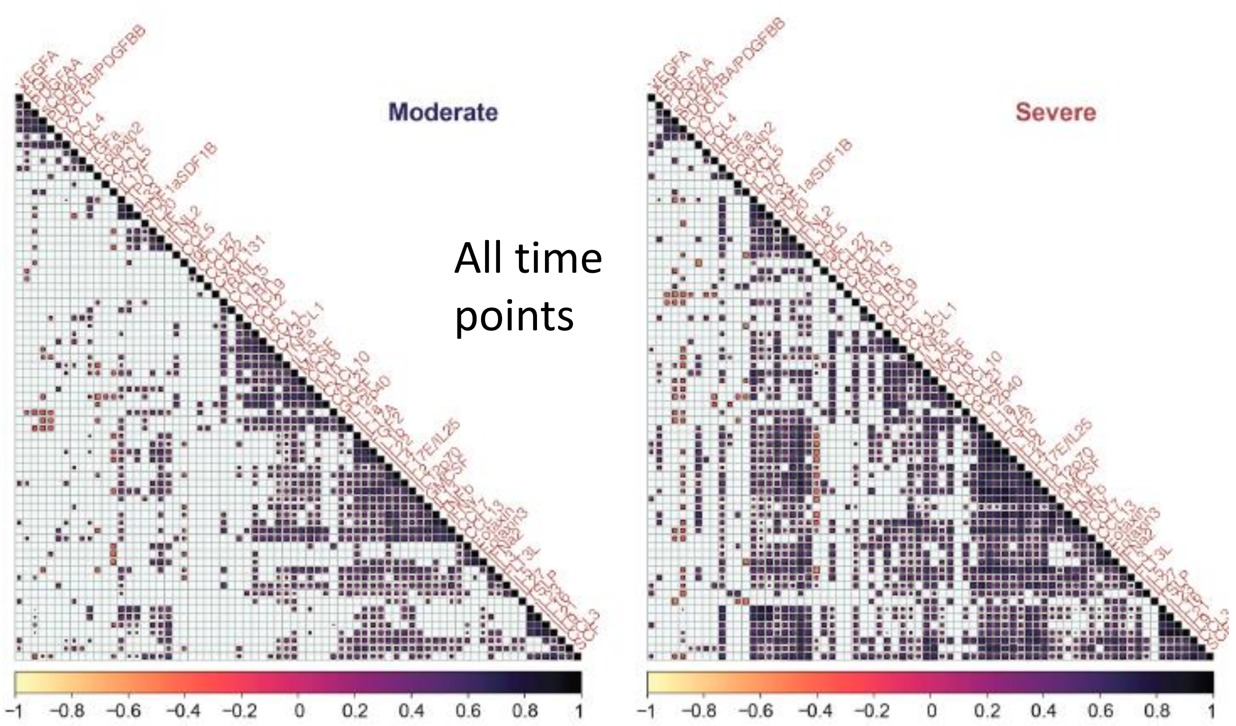

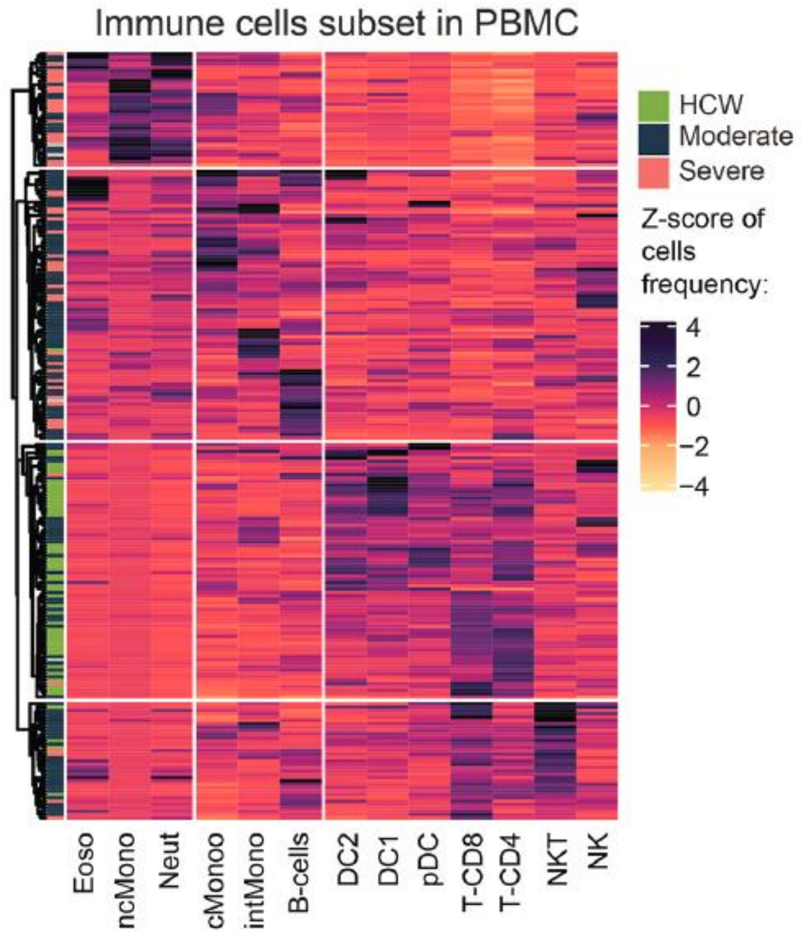

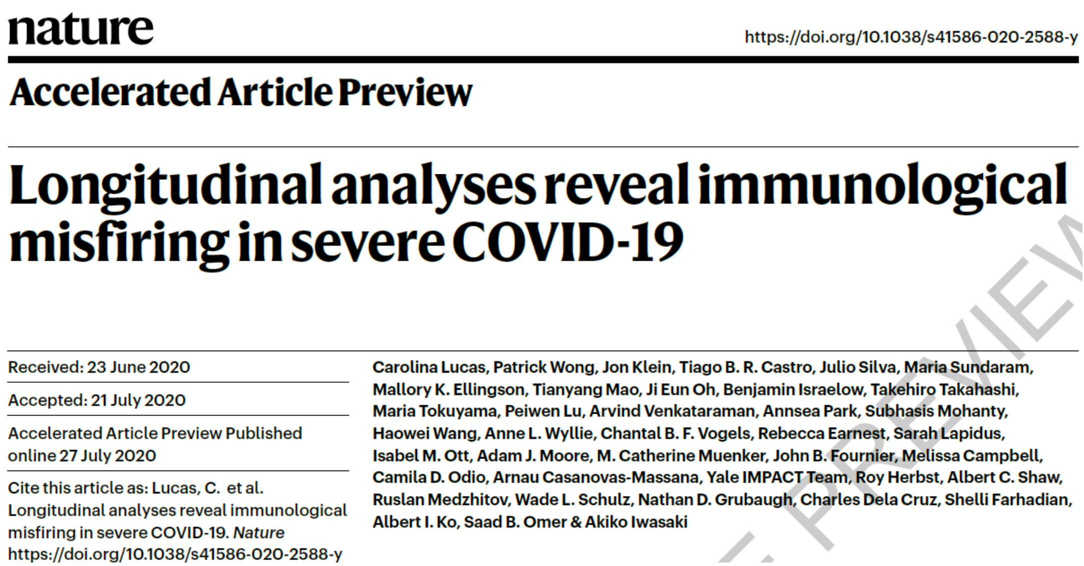
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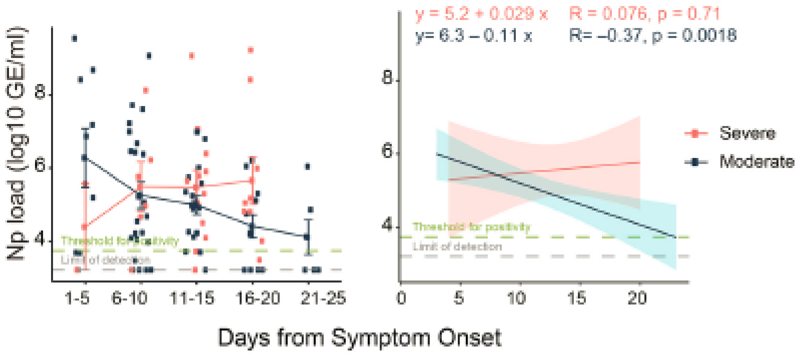
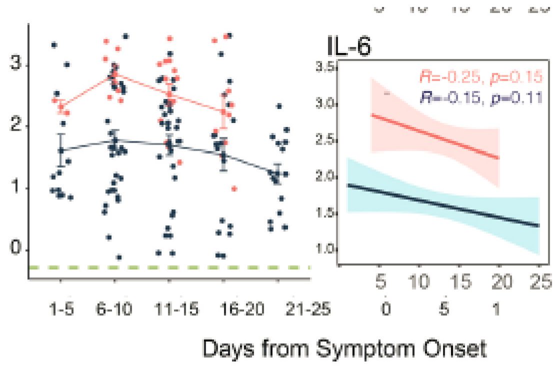
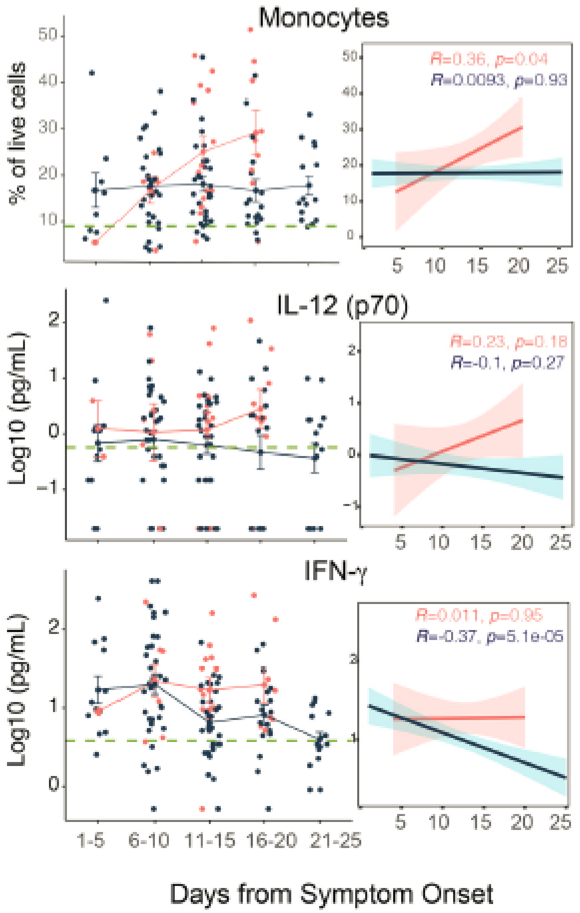
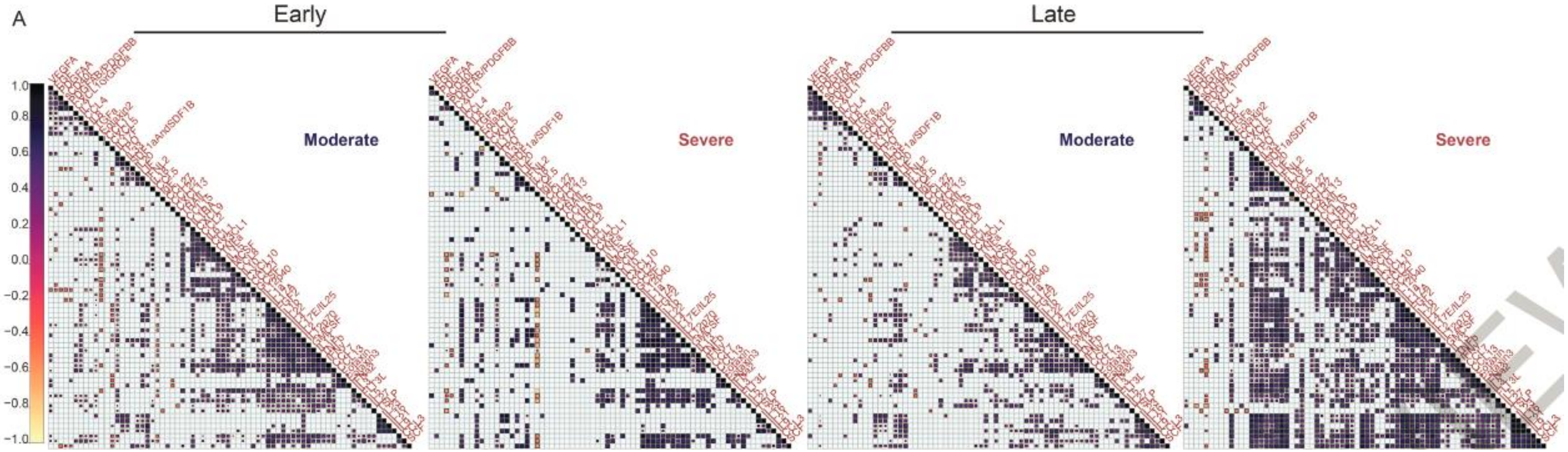
Moderate and severe picture diverge after day 10









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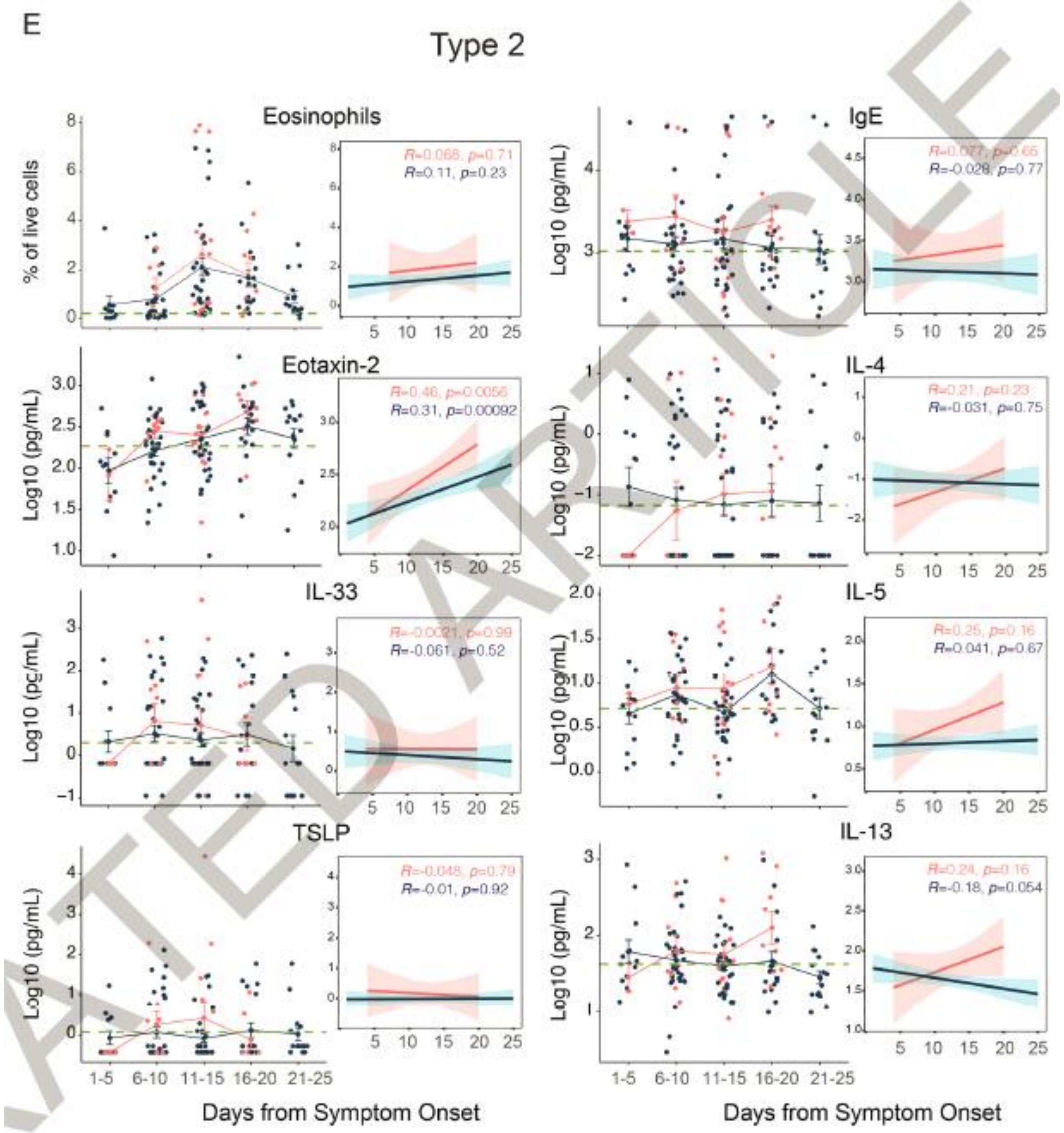
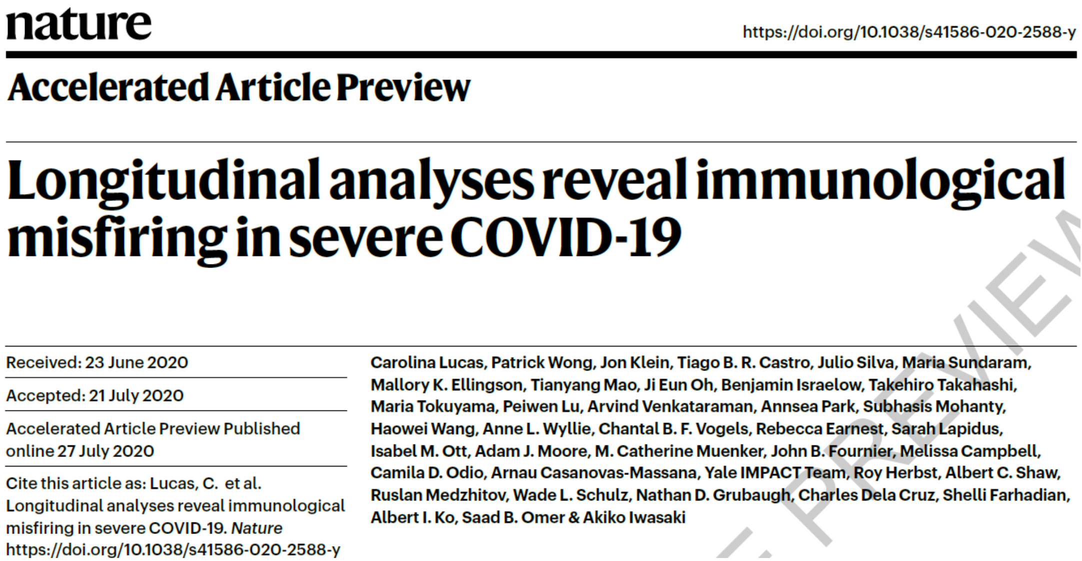
Authors discuss a difference in type 2 immune response between severe and moderate – not very convincing, see fig. on the right

"Broad elevation in type 1, 2 and 3 responses" in severe patients.





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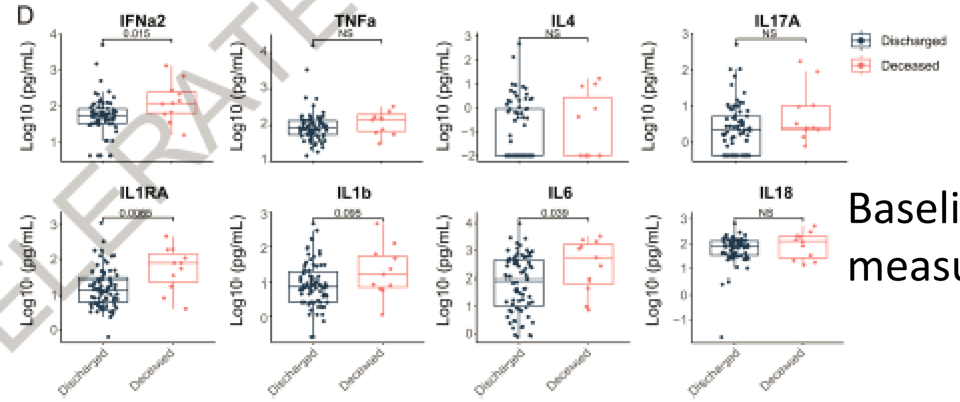
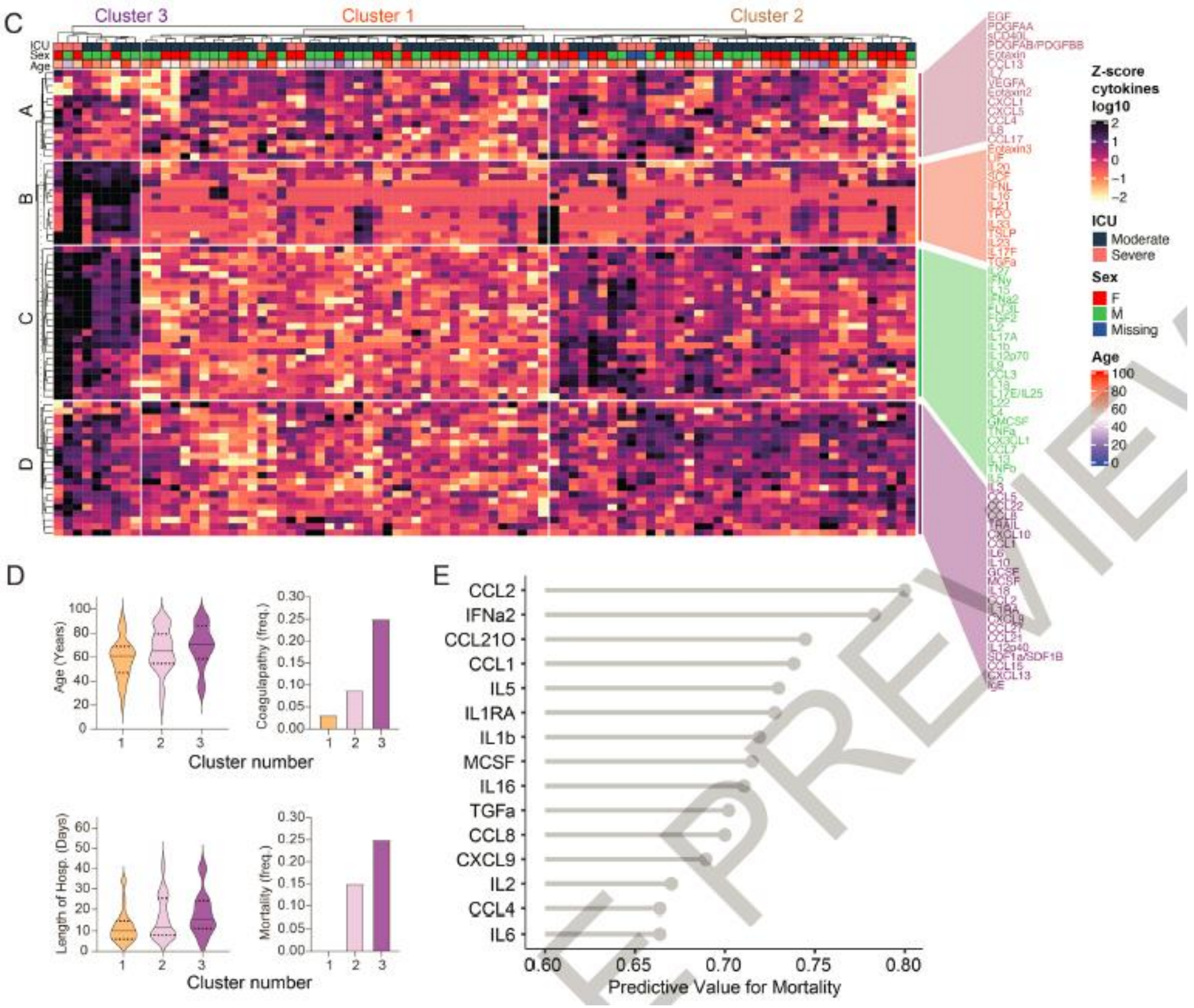
Early cytokine response show distinct clusters that correlate with severity, mortality, coagulopathy (no definition), but do not perfectly discriminate severe from moderate

Cluster 1 (~50%) – no mortality, very little coagulopathy
Cluster 2 and 3 – more inflammation and coagulopathy



Baseline measurements



Before day 12 from symptom onset

This summary was prepared by Dr E Maasdorp as part of the daily brief to the TBH ICU team.