Morning Brief :
Scientific Review

6 April 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. We aim to prioritise information, articles and publications released in the preceding 24-48hours.

Stellenbosch University Research Response Team

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- World Data
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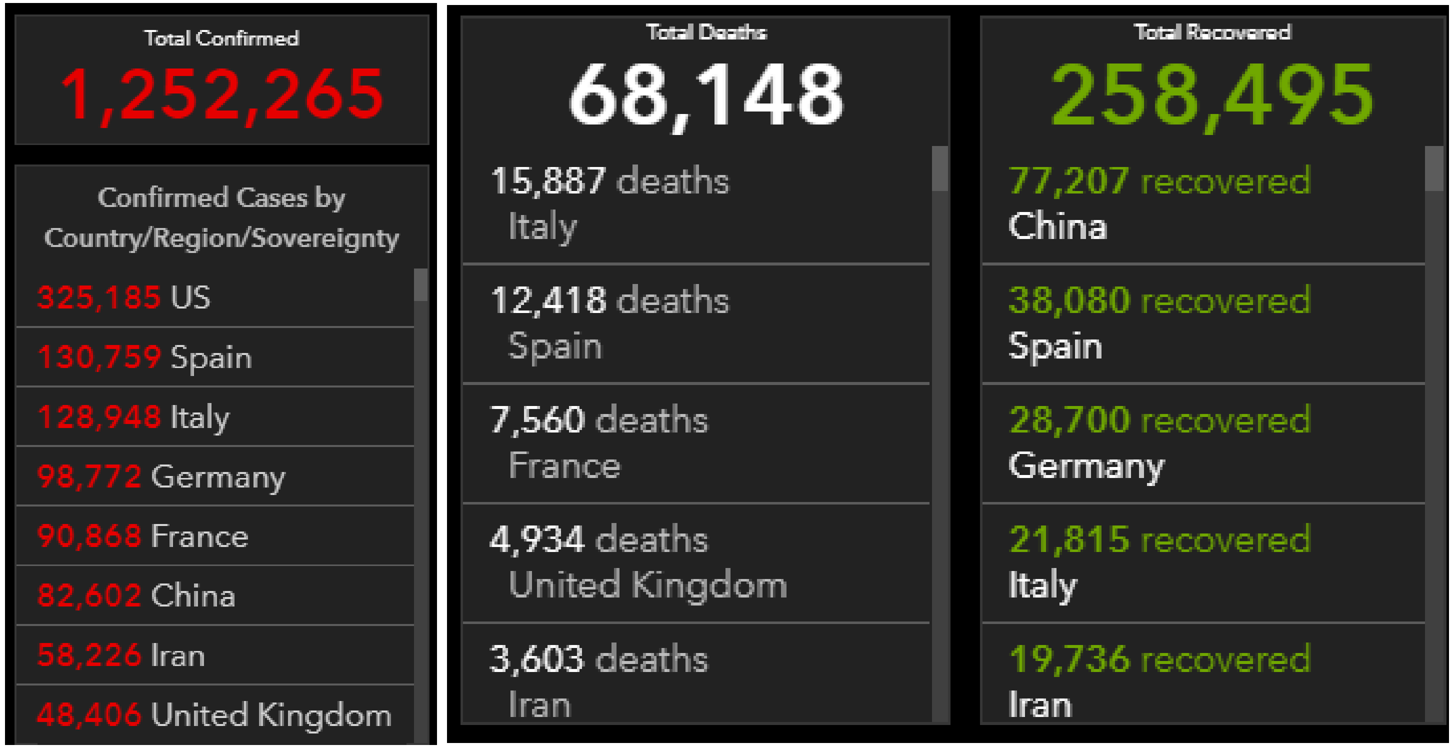
World data

- 1.2 million cases worldwide
- USA >300 000
- Tokyo reports over 100 new cases today
- France, Italy and Germany are seeing a slowly of new cases reported



Source: Johns Hopkins Corona Virus Resource Centre [https://coronavirus.jhu.edu/map.html Accessed 21h00](https://coronavirus.jhu.edu/map.html) 5 April 2020

South African Data

Total cases: 1655
Total deaths: 11

Below is a table with sex and ages of the deceased

We convey our condolences to the family of the deceased and thank the health workers who were treating these deceased patients.

NO.	PROVINCE	SEX	AGE
1	WESTERN CAPE	FEMALE	48
2	FREE STATE	MALE	85
3	GAUTENG	MALE	79
4	KWAZULU-NATAL	FEMALE	46
5	KWAZULU-NATAL	MALE	74
6	KWAZULU-NATAL	FEMALE	63
7	KWAZULU-NATAL	FEMALE	81
8	KWAZULU-NATAL	FEMALE	80
9	KWAZULU-NATAL	MALE	80
10	WESTERN CAPE	FEMALE	82
11	KWAZULU-NATAL	MALE	86

5 April 2020

As at today, the total number of confirmed COVID-19 cases is 1655. This is an increase of 70 from the previously reported cases.

The provincial breakdown is as follows:

GAUTENG	704
WESTERN CAPE	454
KWAZULU – NATAL	246
FREE STATE	87
EASTERN CAPE	31
LIMPOPO	19
MPUMALANGA	18
NORTH WEST	11
NORTHERN CAPE	8
UNALLOCATED	77

Source: Media Briefing by Health Minister Dr Zwelini Mkhize www.sacoronavirus.co.za Accessed 21h40 5 April 2020

Western Cape Data

Western Cape:

Hospitalised with COVID19 = 20

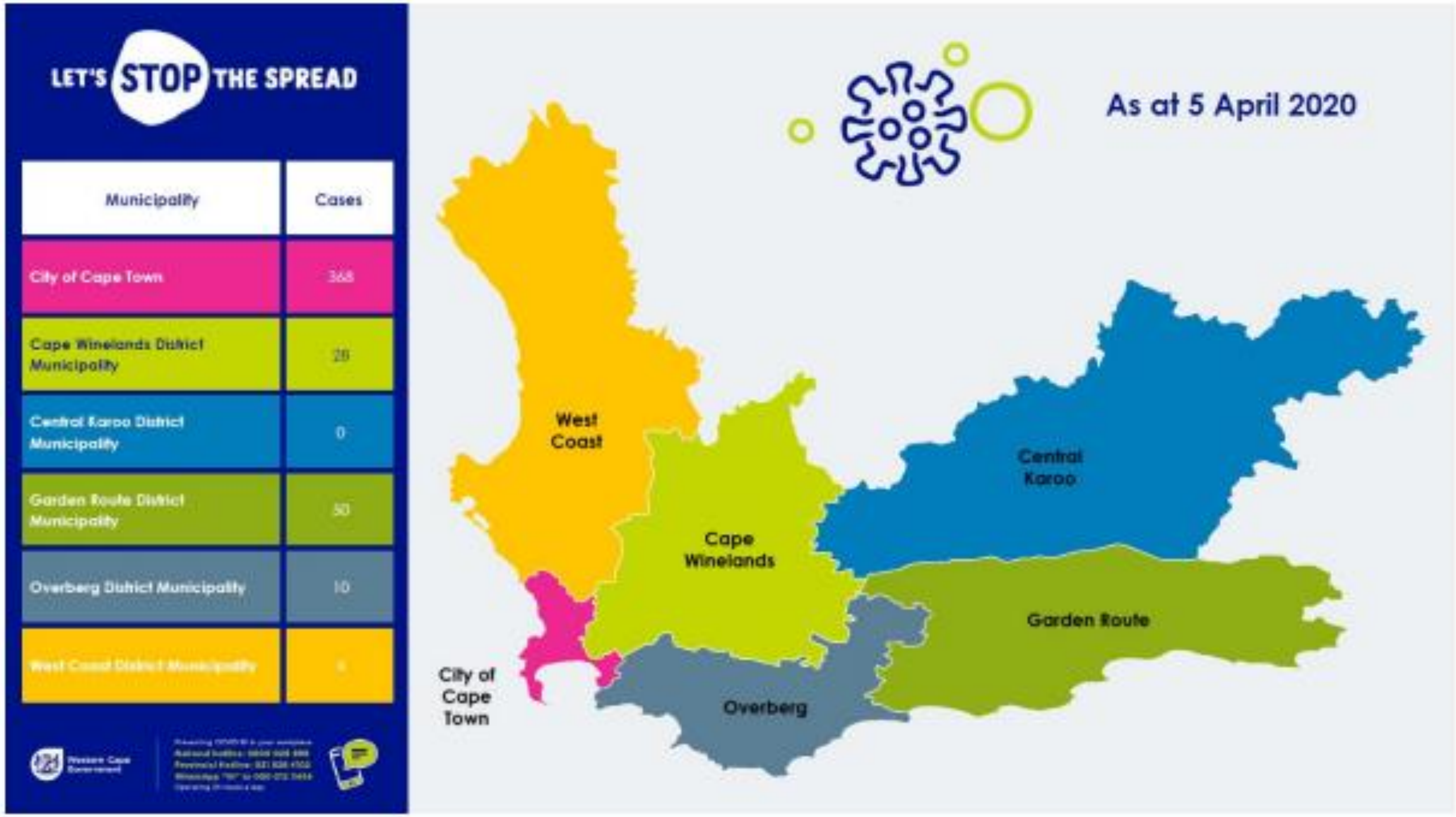
ICU admissions = 9

As of (5/4/2020)

<u>Total WC cases = 464</u>

Cape Town Metro = 368

Non- metro = 96



Source: Media Briefing by WC Premier Alan Winde https://www.westerncape.gov.za/department-of-health/coronavirus Accessed 5 April 2020

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What we do and do not know currently about COVID-19

Prevalence
We do not know true prevalence.

A prevalence study done in Los Angeles, where all nasal swabs sent for Influenza and RSV, in patients with mild influenza-like illnesses, were also tested for SARS-CoV-2, found a 5% prevalence in one centre in 131 tests over 4 days. (Spellberg et.al).

Incubation period
Medians range from 5 to 7 days (Backer 2020)
99^{th} percentile estimate 9.7 – 17 days (Backer 2020)
This informs the 14 day quarantine period that is being used.

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Clinical presentation

What we know about the clinical presentation is from symptomatic cases severe enough to present to healthcare facilities.

43% to 80% present with **fever** (Chan et al., 2020, Chen et al., 2020, Guan et al., 2020.

67% to 80% with **cough** (as above)
Cough may be **dry or productive** (many studies).

Atypical presentations are reported, e.g. vomiting, diarrhoea, no fever, asymptomatic.

High level of suspicion should be maintained by clinicians, with community transmission now clearly established in South Africa, exposure to confirmed cases could be unknown, clinical presentation may be atypical.

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Duration of symptoms
Data from China, 191 patients

Median time from illness onset to death or discharge 21 days IQR (17 - 25)

Median time to death was 18·5 days IQR (15·0–22·0)

Hospital stay median 11 days IQR (7 - 14)

ICU stay 8 days IQR (4 - 12)

Time from symptom onset to ICU admission 12 days IQR (8 - 15)

The median time from illness onset to invasive mechanical ventilation was 14·5 days IQR (12·0–19·0)

(Zhou et al)

PCR Test accuracy

Unknown.

Probably varies by sample type, e.g. nasopharyngeal or oropharyngeal swab, sputum, bronchoalveolar lavage fluid, anal swabs.

False negatives reported.

It seems likely that there is a window period when virus is present, but below the limit of detection of PCR, leading to false negative tests.

False positives more unlikely.

Detection of viral RNA by PCR does not necessarily mean live virus. (Lippi et. al and Patel et. al).

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Progression to severe disease – who?
15 – 20% of those we are testing – severe or critical (Wu, 2020)

We know age is associated with more severe disease.

We know COPD is associated with severe disease. In a meta-analysis including 1592 COVID-19 patients, 314 of which (19.7%) had severe disease – OR for COPD was 5.69 [95:CI:2.49–13.00], (Lippi et al).

We know diabetes mellitus is associated with severe disease. (Fadini, et al). In a meta-analysis of 1687 patients, the pooled risk ratio of diabetes among patients with severe disease as compared to those with non-severe disease was 2.26 (95% CI 1.47–3.49).

Hypertension (HR 1.58, 95%CI 1.07–2.32)
Malignancy (HR 3.50, 95%CI 1.60–7.64) (Guan et al)
Cardiovascular disease (OR 3.42, 95% CI: 1.88-6.22)(Yang et al.)

TB/HIV co-infection: Currently, we have little data on TB and HIV.

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Progression to severe disease – what?

Systematic review:

20.3% (95%CI 10.0–30.6%) required ICU

Among those:

32.8% with ARDS (95%CI 13.7–51.8)

13.0% with acute cardiac injury (95%CI 4.1–21.9%)

7.9% with acute kidney injury (95%CI 1.8–14.0%)

6.2% (95%CI 3.1–9.3%) with shock

13.9% (95%CI 6.2–21.5%) had fatal outcomes

(Rodriguez-Morales)

Death – who?

From more than 44000 cases in China:

- 2.3% (1023 of 44 672 confirmed cases) died

- 14.8% of patients aged >80 years (208 of 1408)
- 8.0% of patients aged 70-79 years (312 of 3918)
- 49.0% of critical cases (1023 of 2087)

Of those who died:

10.5% had cardiovascular disease,

7.3% had diabetes

6.3% had chronic respiratory disease,

6.0% had hypertension

5.6% had cancer

(Wu et al)

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Antiviral Treatment

At least 25 trials registered for testing treatment for COVID-19.
Very little data available from randomised trials currently.

Immunity in recovered cases

We do not know whether people who recovered from COVID-19 are immune to the disease. There have been reports of convalescent plasma from recovered patients used as treatment, but the numbers are small and not randomised.
There have been reports of viral "reactivation" in patients whose symptoms improved and whose PCR became negative, but this happened within days of their first episode and they remained clinically well.

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Viral loads

Viral loads have been measured, and some correlation with severity of disease have been shown, but not in properly controlled studies. It may play a role in monitoring improvement of patients, but at the moment we are not sure what viral loads mean exactly. (Joynt et al)

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Pregnant women

No data currently to highlight pregnant women as particularly at risk of contracting the disease or of developing severe disease. We do not know whether in-utero transmission is possible, nor whether the virus can be isolated from breast milk.

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Health care workers
3.8% of cases in China were health care workers.
60% of HCWs infected were in Hubei (Wu et al).

Proportion of severe cases and death same as general population in China.

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This summary was prepared by

Dr Elizna Maasdorp

as part of the daily brief to the TBH ICU team