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Morning Brief: Scientific Review

25 May 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

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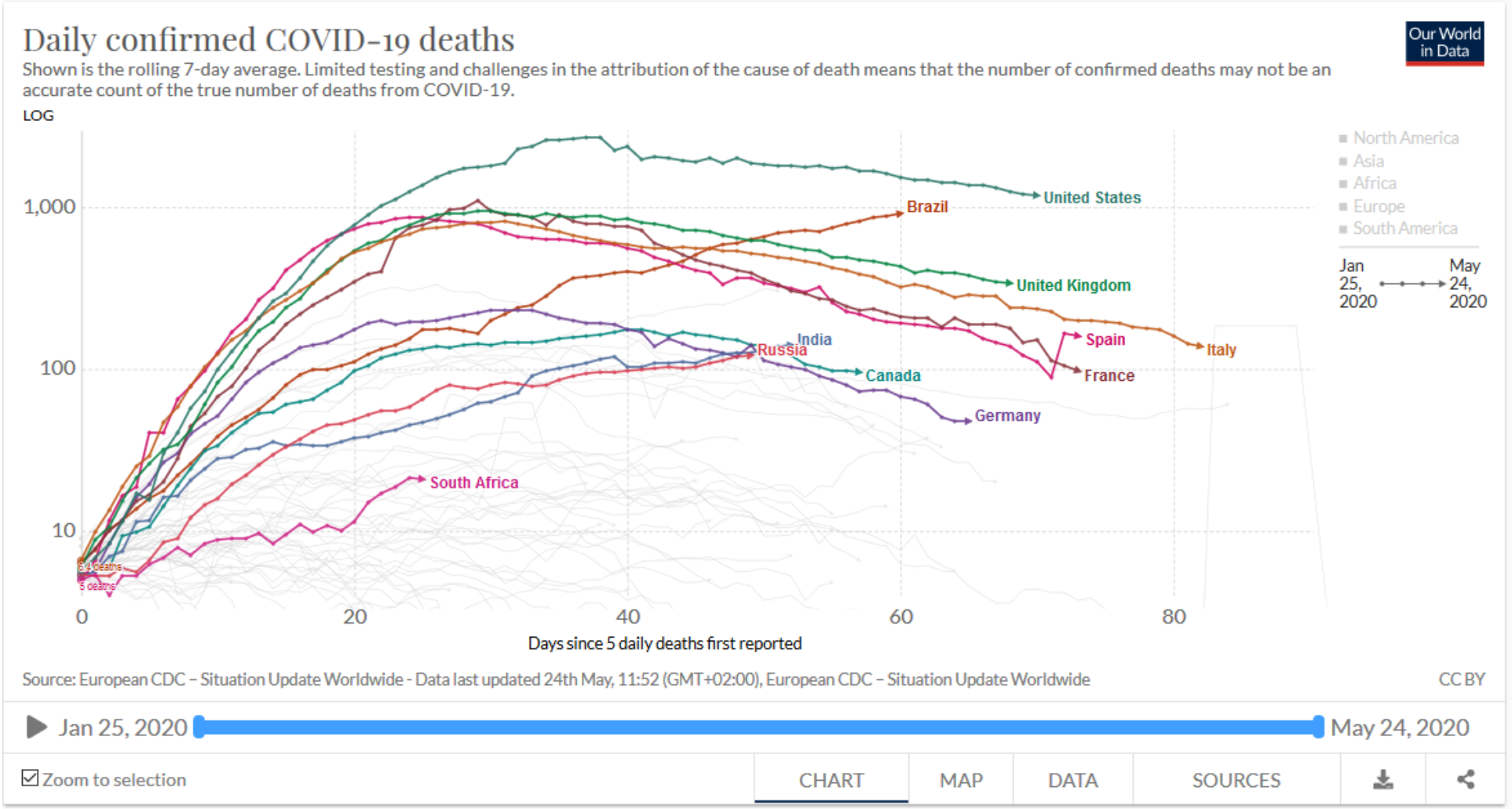
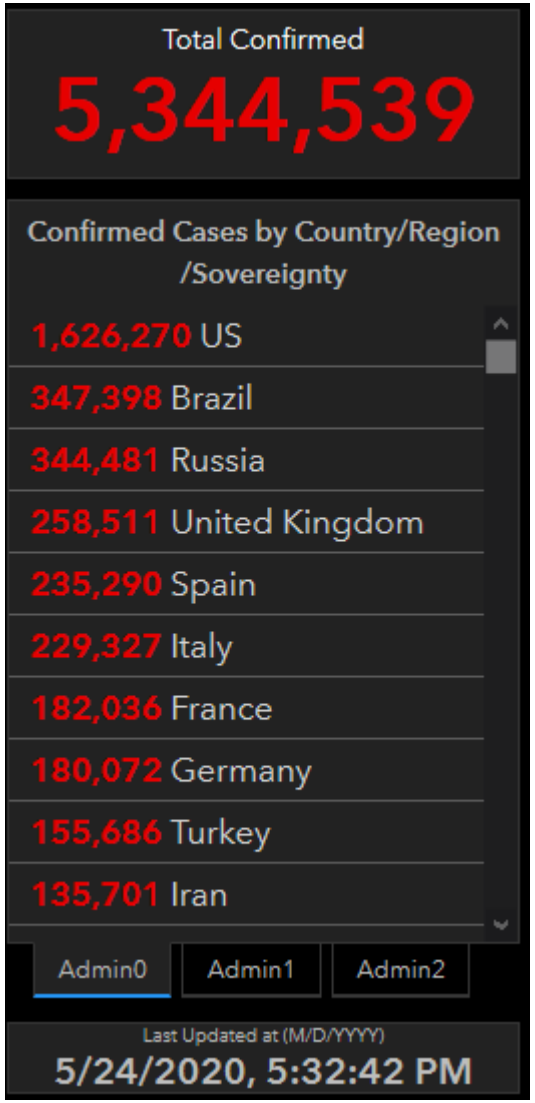
Content of the brief

- Global Statistics
- South African Statistics
- Topics:
  - Nephrology

Global Statistics





Source: https://coronavirus.jhu.edu/map.html, ourworldindata.com

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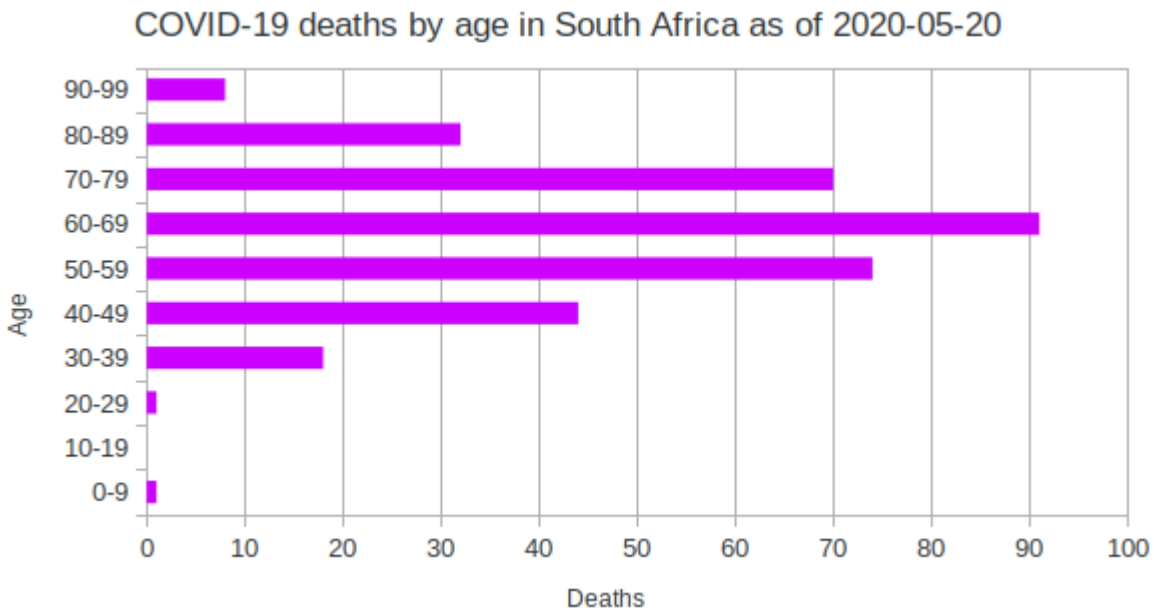
South African Statistics

24 May 2020
Number of cases 22583
Deaths 429
842 currently in hospital, 128 in ICU



Sources: Department of Health on Twitter and Wikipedia

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Articles of Interest

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Morning Brief : Selected renal aspects of COVID-19

24 May 2020

Razeen Davids and Thabiet Jardine
Division of Nephrology and Department of Medicine

Contents:

- **Does SARS-CoV-2 target the kidney?**
- **Can it be isolated from urine?**
- **Can it be isolated from peritoneal dialysis drainage fluid?**
- **What are the outcomes of COVID-19 in patients on renal replacement therapy?**

Note: Since COVID-19 is a novel illness, many of the reports are not in the form of full, peer-reviewed publications and are only available as research letters, correspondence or pre-prints on platforms such as bioRxiv and medRxiv.

Does SARS-CoV-2 target the kidney?

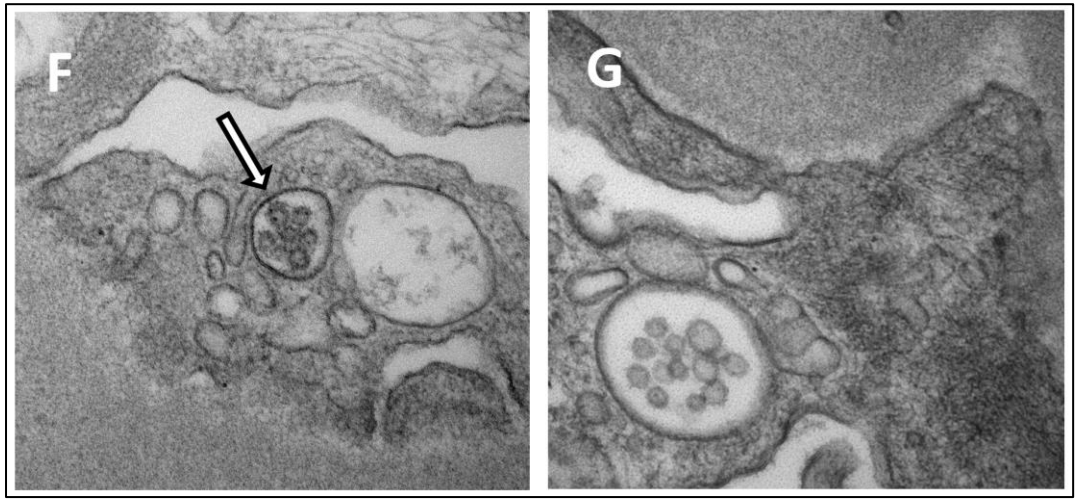
Proteinuria, haematuria and elevated creatinine are common [1,2]. Acute kidney injury is an independent risk factor for mortality.

The virus accesses cells via ACE2, also expressed in the kidney [3]. Using electron microscopy, viral particles identified in renal tubular epithelial cells [4-6], endothelial cells [7] and podocytes [5,8]. Positive immunofluorescence staining seen in tubular cells [5].

NB: Other authors dispute these findings - suggest that the virus-like particles described are clathrin-coated vesicles and microvesicular bodies [9-11,12].

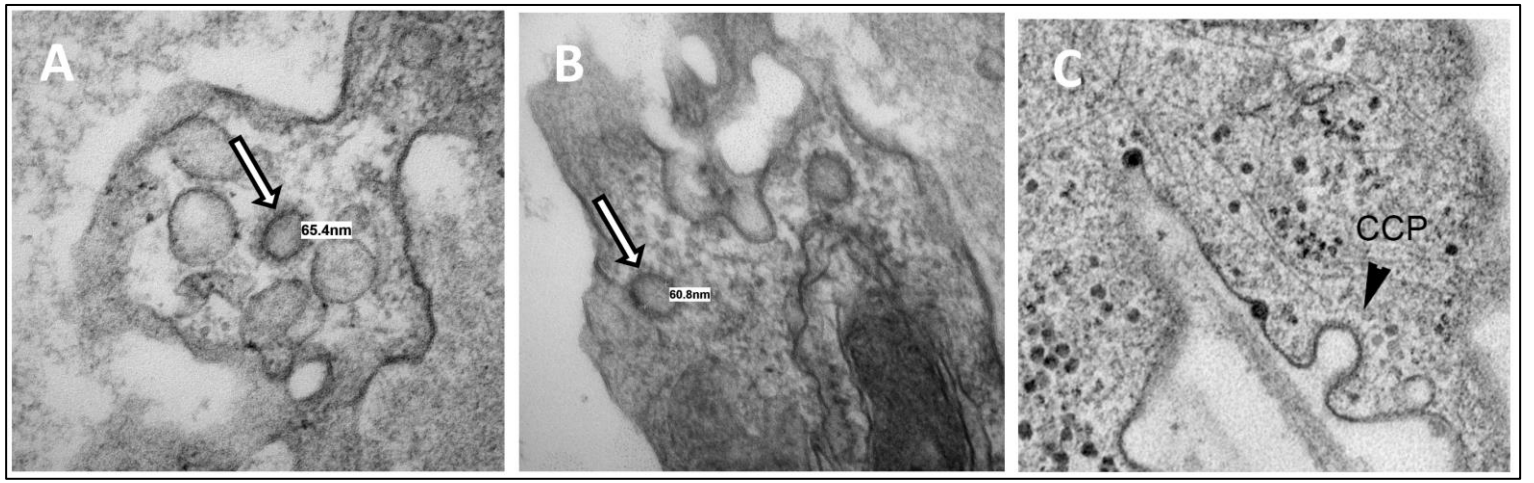
Our perspective:

It is still unclear whether the kidneys can be considered target organs of SARS-CoV-2 infection



Arrow: microvesicular bodies

Roufosse et al. [9]



CCP: clathrin-coated pits

Can SARS-CoV-2 be isolated from urine?

Early, informal report from Guangzhou of the successful isolation of SARS-CoV-2 from the urine of an infected patient [13]; however, in a study in JAMA on the detection of SARS-CoV-2 in different clinical specimens, no virus was identified in the urine of 72 patients [14]. Kim et al. [15] reported identifying viral mRNA in just 2 of 247 samples in 74 patients with COVID-19. They were not able to isolate live virus by cell culture from the positive samples.

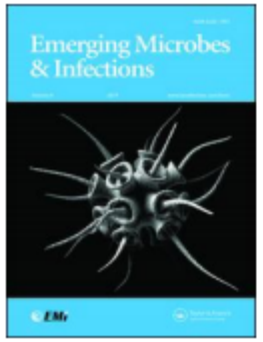
NB: Just recently, however, Sun et al. [16] have described the isolation of SARS-CoV-2 from urine using RT-PCR and the inoculation of Vera E6 cells.

No virus in urine of 72 samples using RT-PCR

Table. Detection Results of Clinical Specimens by Real-Time Reverse Transcriptase–Polymerase Chain Reaction

Specimens and values	Bronchoalveolar lavage fluid (n = 15)	Fibrobronchoscope brush biopsy (n = 13)	Sputum (n = 104)	Nasal swabs (n = 8)	Pharyngeal swabs (n = 398)	Feces (n = 153)	Blood (n = 307)	Urine (n = 72)
Positive test result, No. (%)	14 (93)	6 (46)	75 (72)	5 (63)	126 (32)	44 (29)	3 (1)	0
Cycle threshold, mean (SD)	31.1 (3.0)	33.8 (3.9)	31.1 (5.2)	24.3 (8.6)	32.1 (4.2)	31.4 (5.1)	34.6 (0.7)	ND
Range	26.4-36.2	26.9-36.8	18.4-38.8	16.9-38.4	20.8-38.6	22.3-38.4	34.1-35.4	
95% CI	28.9-33.2	29.8-37.9	29.3-33.0	13.7-35.0	31.2-33.1	29.4-33.5	0.0-36.4	

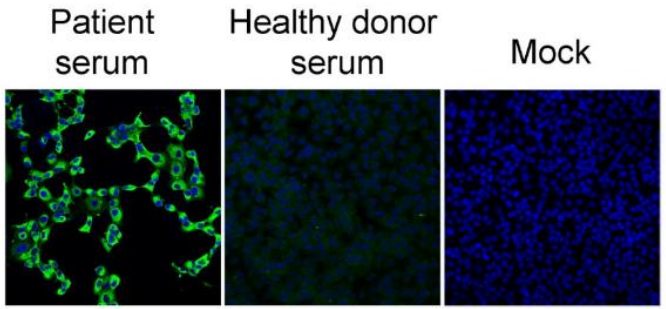
Wang et al. JAMA 2020 [14]

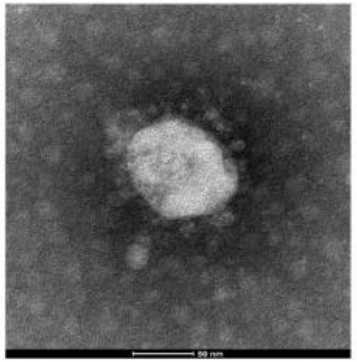


Emerging Microbes & Infections

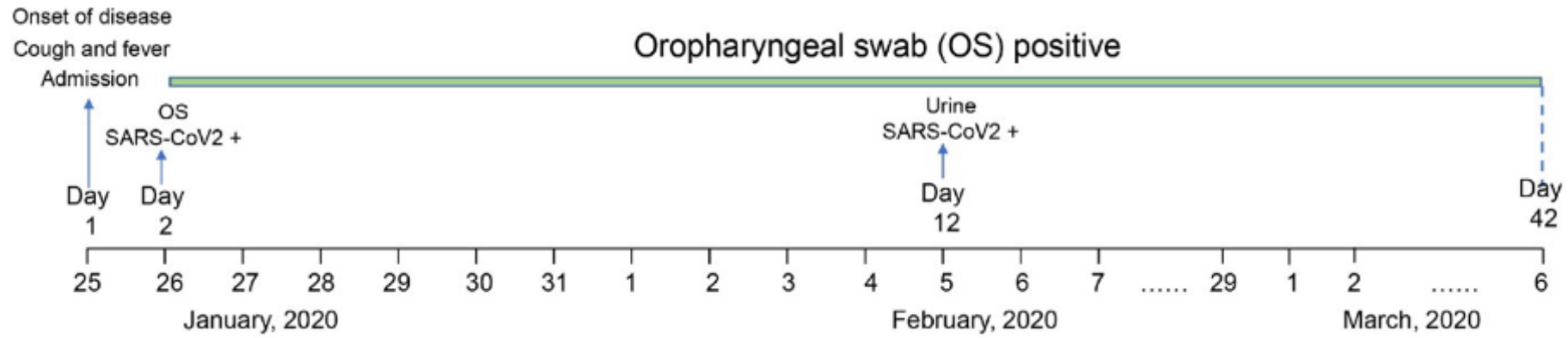
Isolation of infectious SARS-CoV-2 from urine of a COVID-19 patient

ISSN: (Print) 2222-1751 (Online) Journal homepage: https://www.tandfonline.com/loi/temi20





First convincing report of isolation of intact virus from urine using RT-PCR and inoculation of Vero E6 cells [16]



Our perspective:

There is a very low rate of detection of SARS-COV-2 in urine samples and the risk of viral transmission via urine is expected to be low.

Can SARS-CoV-2 be isolated from peritoneal dialysis drainage fluid?

Coccilini et al. [17] reported the first case where SARS-CoV-2 mRNA was detected in peritoneal fluid. This was not in a patient on chronic PD but in an elderly patient with intestinal obstruction and flu-like symptoms. The nasal swab was positive. At laparotomy, free, clear fluid was found in the abdomen and tested positive by RT-PCR. Remained positive even after 10-fold dilution. Isolation of live virus not performed.

Can SARS-CoV-2 be isolated from peritoneal dialysis drainage fluid?

Regarding patients on PD, a French study which was the first to report identifying SARS-CoV-2 in PD drainage fluid has since been retracted [18].

NB: There has just been a letter by Vischini et al. [19] reporting the finding of SARS-CoV-2 mRNA in the peritoneal drainage fluid in a patient treated with PD.

Local perspectives:

We have tested PD fluid in one patient with COVID-19 - the PCR was negative.

The Coccilini paper is important as it suggests that abdominal surgical procedures may result in aerosolization of virus.

PD is an important RRT modality in South Africa, 26% of public sector patients and 5% of private sector RRT patients on PD [20].

We need to provide guidelines for our patients on the disposal of drained dialysate and used bags and lines. There are currently no reports of viable SARS-CoV-2 isolated from drainage fluid and it is unclear whether a positive PCR means that there is contagious virus present.

International guidelines:

The International Society for Peritoneal Dialysis guideline on COVID-19 in patients on PD [21] states that there are varying opinions regarding the disposal of drained dialysate from patients with confirmed or suspected COVID-19, ranging from no additional measures to disinfection by adding a chlorine-containing solution to the drainage bags for one hour before pouring into the toilet.

To prevent accidental splashing when disposing of drained dialysate, the toilet lid should be closed when flushing. The empty bags and lines should be disposed of in accordance with local regulations.

What are the outcomes of COVID-19 in patients on renal replacement therapy?

- Special threat to chronic dialysis or kidney transplant patients
- Increased risk of risk of infection and transmission of infection, including to hospital staff and family members

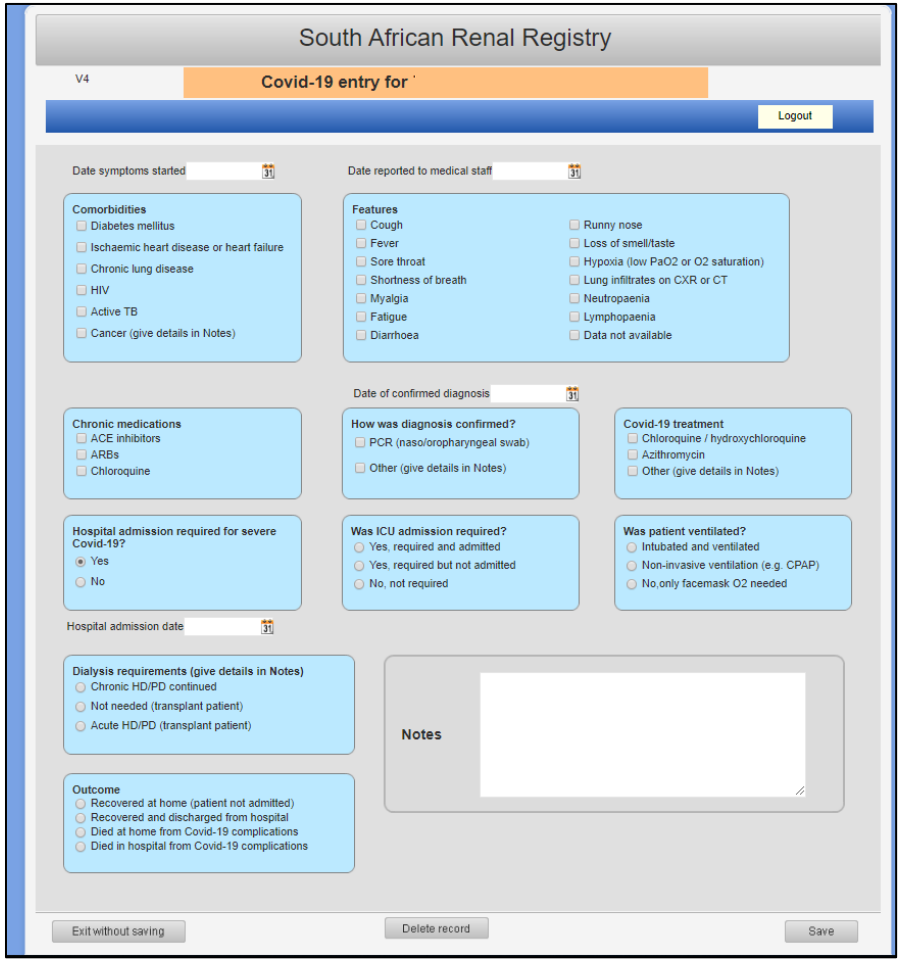
  - immunocompromised
  - often older, multiple comorbidities
  - frequent hospital visits therefore close contact with staff and other patients (transport, waiting rooms, dialysis unit, transplant clinic)
  - average mortality 20-30%

COVID-19 in patients on renal replacement therapy

Study	No. of patients	RRT	Median follow up	Mean/median age (years)	Outcome at end of follow up period					
					Died in hospital	Discharged	Still in hospital	Outpatient, recovered	Outpatient, died at home	Mortality (%)
Banerjee, UK [23]	7	KT	21 days	54	1		4	2		14
Nair, USA [24]	10	KT	25 days	57 (IQR 47-67)	3	6		1		30
Akalin, USA [25]	36	KT	21 days	60 (IQR 32-37)	8	10	10	6	2	28
Ma, China [22]	37	HD			6	31				19
Zhu, China [26]	10	KT	Not reported	49.5 (IQR 30-56)	1	8	1			20
Alberici, Italy [27]	21	KT	13 days	Not reported	5	3	13			24
	20	HD	Not reported	Not reported	5	4	11			25
Trujillo,Italy [28]	26	KT	13 days	64 ± 15	6	7	13			23
	23	HD			7	7	9			30
	2	PD					2			
Goicoechea, Spain [29]	36	HD	Not reported	71 ± 12	11	7	18			31

Local perspectives

- Six TBH patients infected
- HD 3, PD 1, TX 2
- One ICU admission (HD), since d/c to ward
- One death (TX)



Countrywide data being captured via the SA Renal Registry. We hope that our outcomes may be better as we have a younger RRT population, especially in the public sector.

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This summary was prepared by Prof Razeen Davids and Dr T Jardine as part of the daily brief to the TBH ICU team.