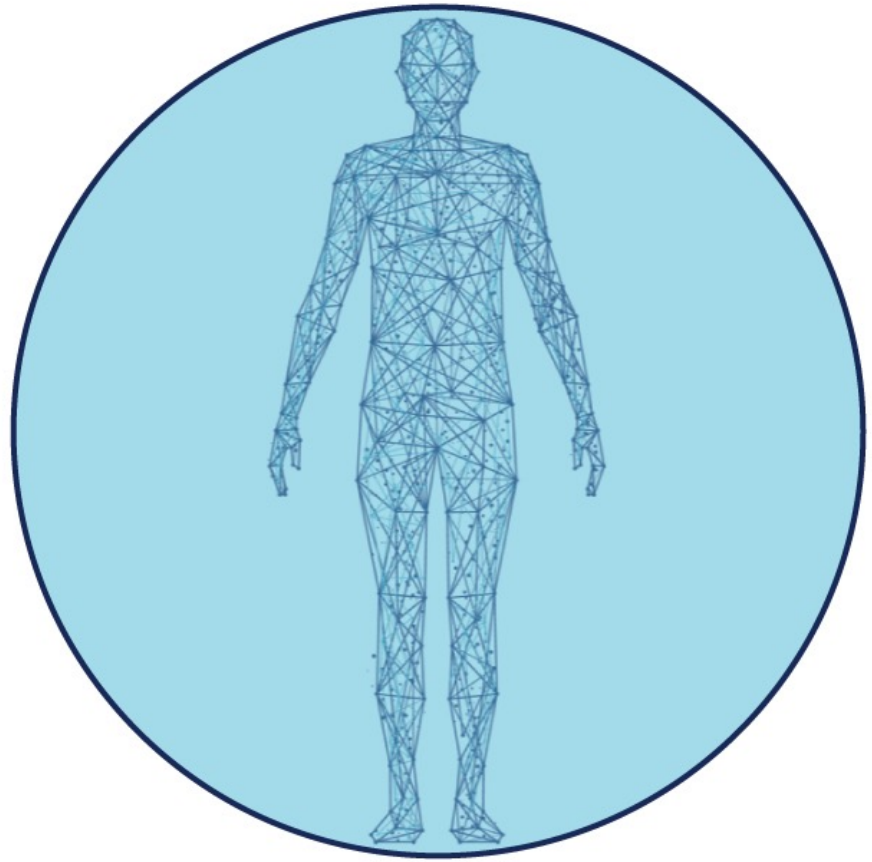
Long-term outcomes of children with suspected COVID-19 illness in Cape Town, South Africa.

COVID kids cohort, South Africa



Isabelle Dewandel, MD

Paediatrician and clinical researcher

Department of Paediatrics and Child health
Stellenbosch University, Desmond Tutu TB Centre

idewandel@sun.ac.za

Overview

- Introduction
- COVID kids cohort
- Preliminary data
- Discussion

Background

- **Children seem relatively protected from COVID-19**
  - Majority of children asymptomatic / mild disease
  - Limited data in Sub-Saharan Africa other LMICs
    - *The under-5 pneumonia mortality rate is significantly higher in LMICs compared to HICs*
    - *Effect of underlying co-morbidities such as TB, HIV, malnutrition?*

Molteni et al. Lancet 2021.

Marangu et al. Paediatr Respir Rev. 2019.

Clinical outcomes COVID-19 in LMICs

Clinical Infectious Diseases

MAJOR ARTICLE

Clinical Experience With Severe Acute Respiratory Syndrome Coronavirus 2–Related Illness in Children: Hospital Experience in Cape Town, South Africa

Marieke M. van der Zalm,[1] Juanita Lishman,[2] Lilly M. Verhagen,[2,3] Andrew Redfern,[2] Liezl Smit,[2] Mikhail Barday,[2] Dries Ruttens,[2,4] A'ishah da Costa,[2] Sandra van Jaarsveld,[2] Justina Itana,[2] Neshaad Schrueder,[5] Marije Van Schalkwyk,[6] Noor Parker,[2] Ilse Appel,[2] Barend Fourie,[2] Mathilda Claassen,[7] Jessica J. Workman,[1] Pierre Goussard,[2] Gert Van Zyl,[7] and Helena Rabie[2]

[1]Desmond Tutu Tuberculosis Centre, Department of Paediatrics and Child Health, Faculty of Medicine and Health Sciences, Stellenbosch University, Cape Town, South Africa, [2]Department of Paediatrics and Child Health, Tygerberg Hospital, Faculty of Medicine and Health Sciences, Stellenbosch University, Cape Town, South Africa, [3]Department of Pediatric Infectious Diseases Immunology, Wilhelmina Children's Hospital, University Medical Centre Utrecht, Utrecht University, Utrecht, The Netherlands, [4]Department of Paediatrics, KU Leuven University, Leuven, Belgium, [5]Division of General Internal Medicine, Department of Medicine, Tygerberg Hospital, Stellenbosch University, Cape Town, South Africa, [6]Division of Adult Infectious Diseases, Department of Medicine, Tygerberg Hospital, Stellenbosch University, Cape Town, South Africa, and [7]Division of Medical Virology, Stellenbosch University, National Health Laboratory services, Cape Town, South Africa

(See the Editorial Commentary by Marais on pages e945-7.)

CID vd Zalm et al 2021

Design

- Observational cohort South Africa
- April-July 2020

Results

- 50% of hospitalizations <1year of age
- ±75% of infants needed respiratory support
- New diagnoses of PTB - incidental? Other?
- PLHIV limited numbers, HEU

Conclusion

- Low mortality
- More severe COVID-19 respiratory illness in infants
- Long-term outcomes?

Clinical outcomes COVID-19 in LMICs

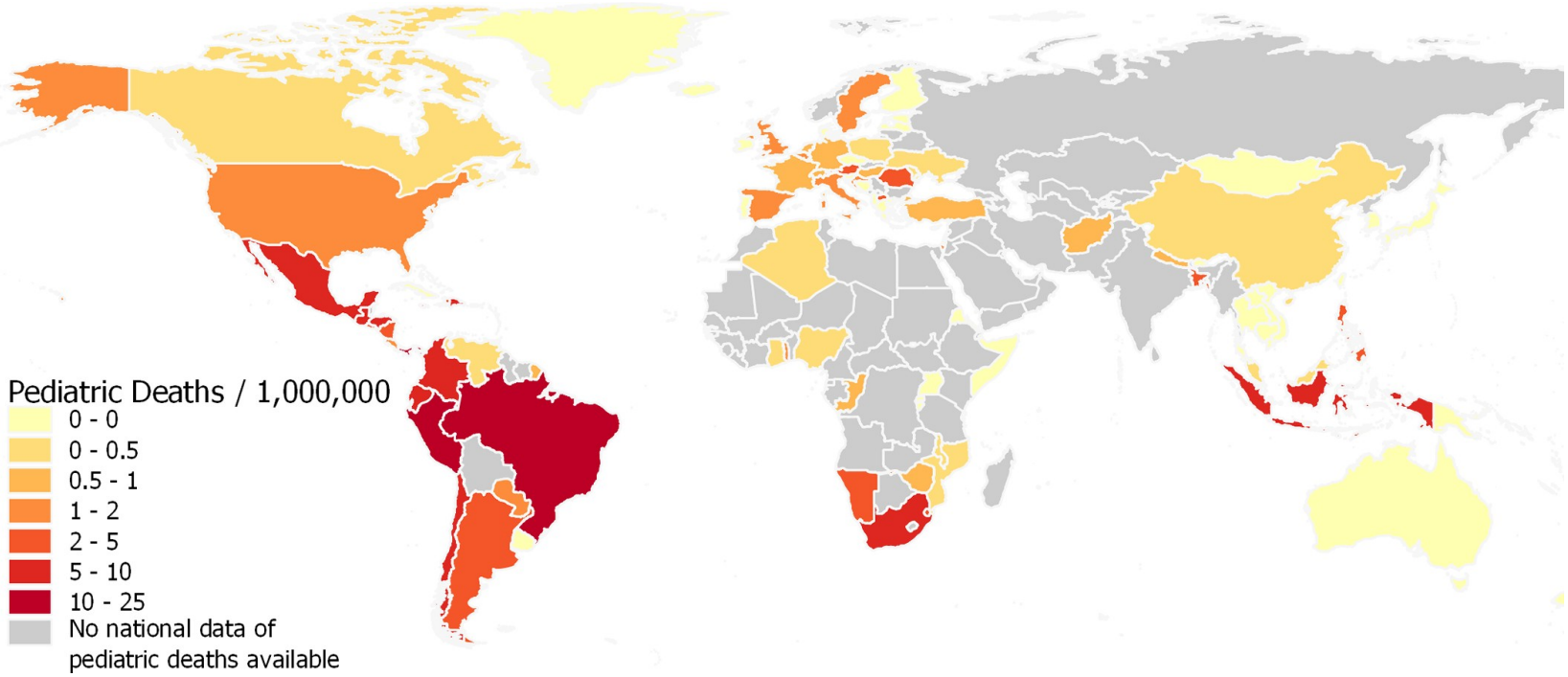


Fig 2. World map of national pediatric COVID-19 deaths (/1,000,000 children). The map was built with the geographic information system QGIS (v3.10, https://qgis.org) and the World Bank Official Boundaries Data Set (https://datacatalog.worldbank.org/dataset/world-bank-official-boundaries). Deaths are presented per million children. Countries of no pediatric case reported includes the country clearly report that there was no confirmed case in children in the national report as of December 7, 2020. National reports published more than 2 months before December 7 were included, if the countries were CDC COVID-19 Level 1 (low transmission) since the date of report.

https://doi.org/10.1371/journal.pone.0246326.g002

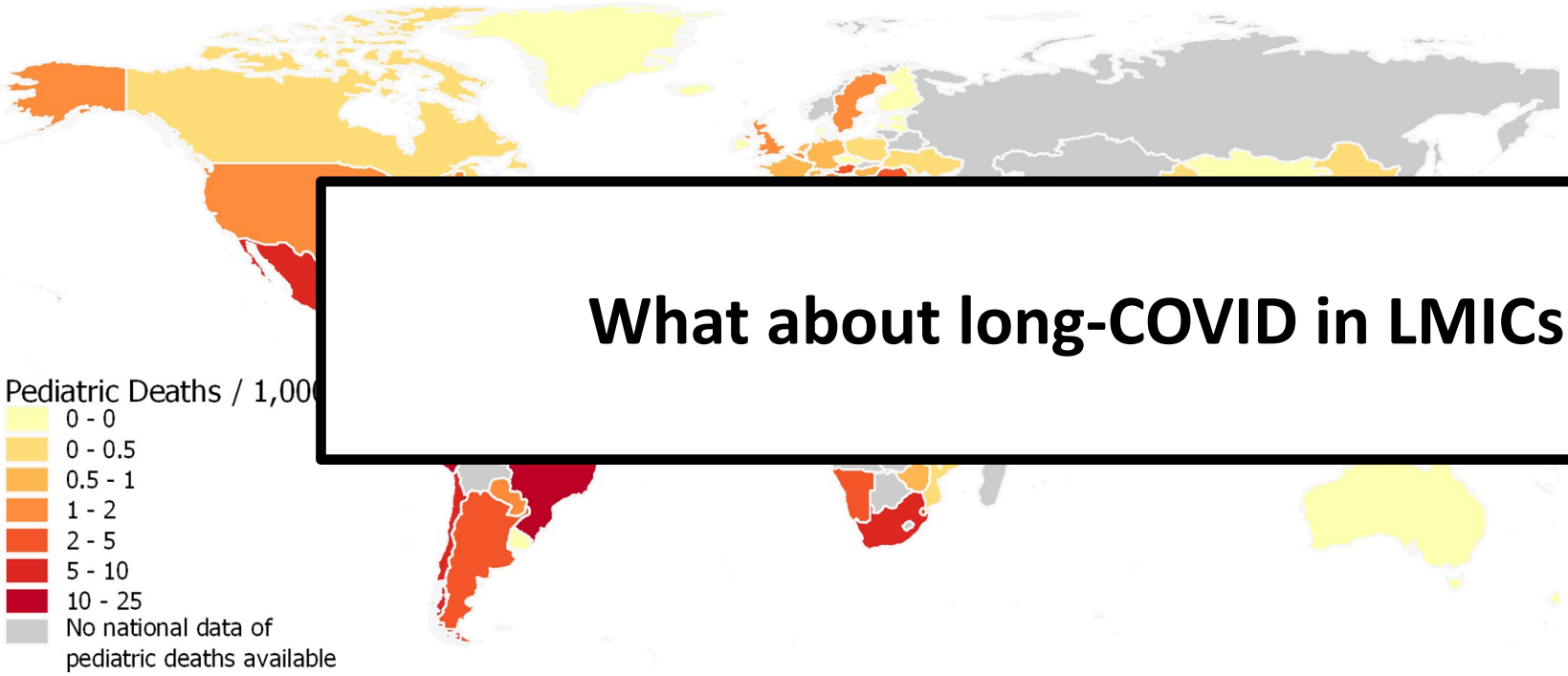
RESEARCH ARTICLE

The differential impact of pediatric COVID-19 between high-income countries and low- and middle-income countries: A systematic review of fatality and ICU admission in children worldwide

Taito Kitano[1]*, Mao Kitano[2], Carsten Krueger[1], Hassan Jamal[1], Hatem Al Rawahi[1], Rachelle Lee-Krueger[3], Rose Doulin Sun[1], Sandra Isabel[1], Marta Taida García-Ascaso[1], Hiromi Hibino[4], Bettina Camara[5], Marc Isabel[6], Leanna Cho[1], Helen E. Groves[1], Pierre-Philippe Piché-Renaud[1], Michael Kossov[7], Ikuho Kou[8], Ilsu Jon[9], Ana C. Blanchard[1], Nao Matsuda[10], Quenby Mahood[11], Anupma Wadhwa[1], Ari Bitnun[1], Shaun K. Morris[1,12]

PLOS ONE, Kitano Jan 2021

Clinical outcomes COVID-19 in LMICs



What about long-COVID in LMICs?

RESEARCH ARTICLE

The differential impact of pediatric COVID-19 between high-income countries and low- and middle-income countries: A systematic review CU admission in children

Carsten Krueger[1], Hassan Jamal[1], Hatem Al Rawahi[1], e Doulin Sun[1], Sandra Isabel[1], Marta Taida García-Ascaso[1], a[5], Marc Isabel[6], Leanna Cho[1], Helen E. Groves[1], Pierre-ael Kossov[7], Ikuho Kou[8], Ilsu Jon[9], Ana C. Blanchard[1], od[11], Anupma Wadhwa[1], Ari Bitnun[1], Shaun K. Morris[1,12]

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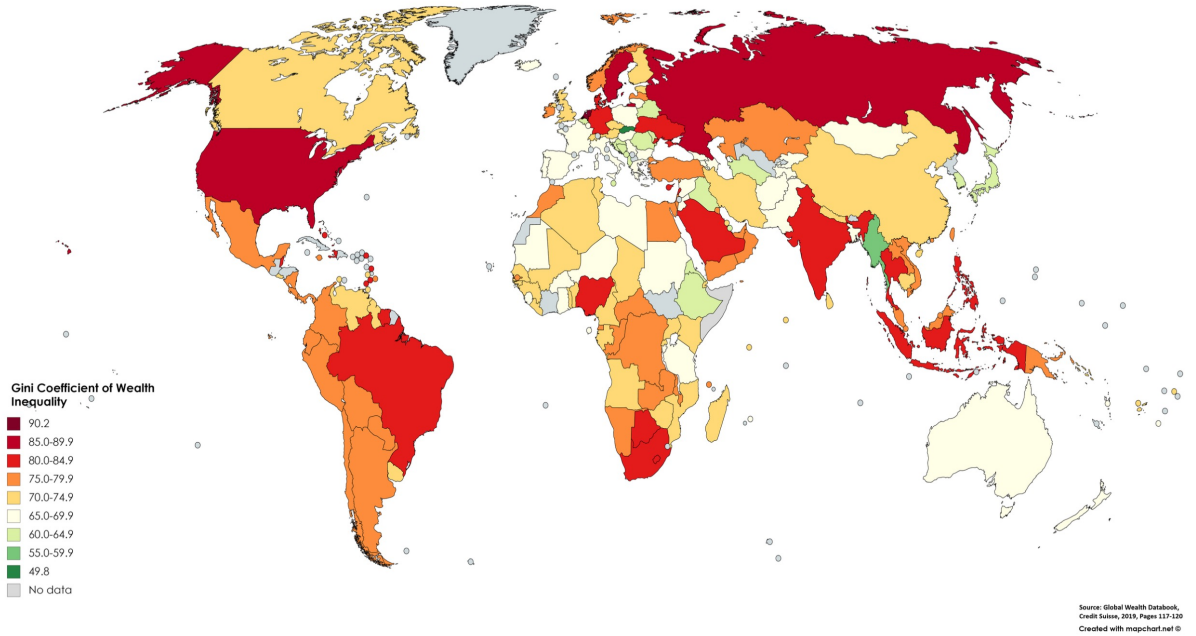
South Africa - Statistics

- Population of ±60 million people
- South Africa country of contrasts
- Considered MIC as per world bank
  - Highest GINI coefficient = inequality
- ~ 90% depend on public health care
  - ~20% PLHIV

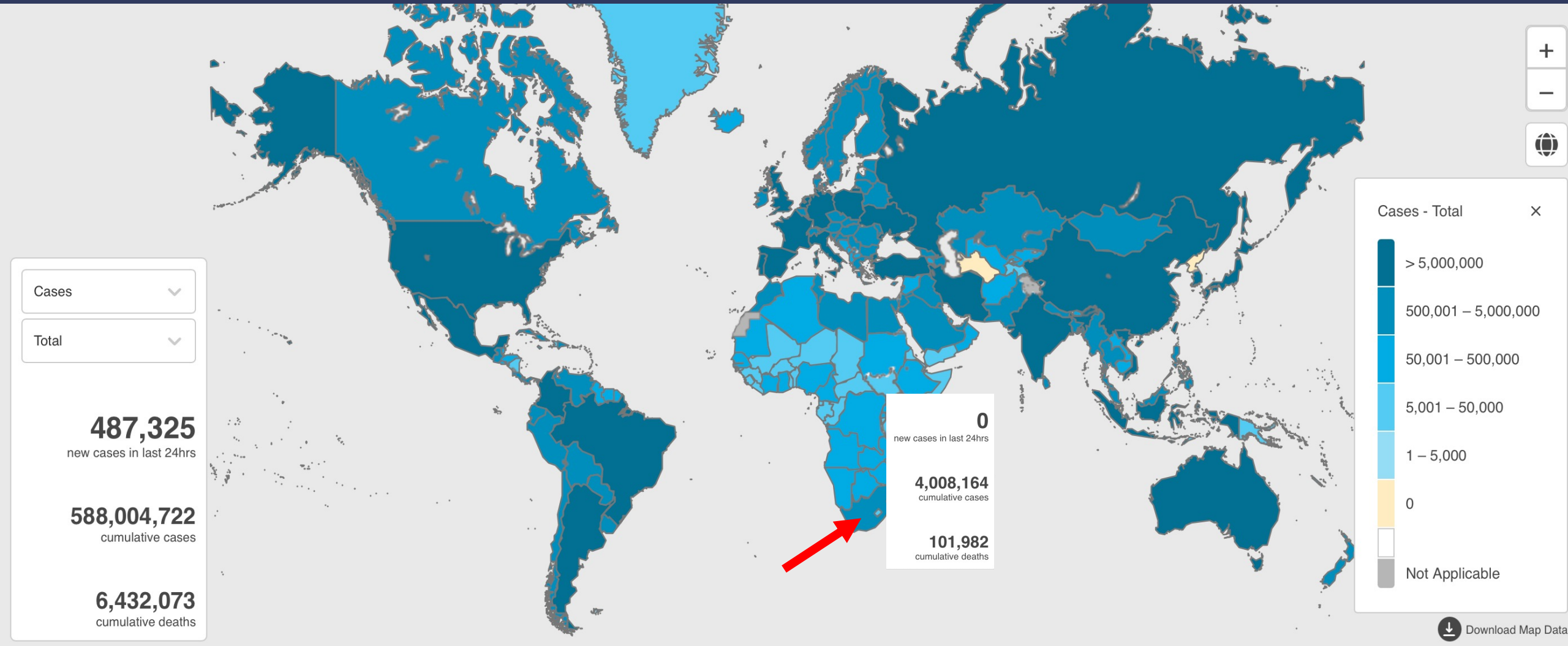


** WHO COVID-19 dashboard*

Tygerberg Hospital

- Public- sector health care service
  - Tertiary referral hospital
- Drainage area in the Western Cape
  - ~4,5 million residents
  - >100 primary care health facilities
  - ~ 400 paediatric beds
  - ~ 5000 paediatric admissions / year

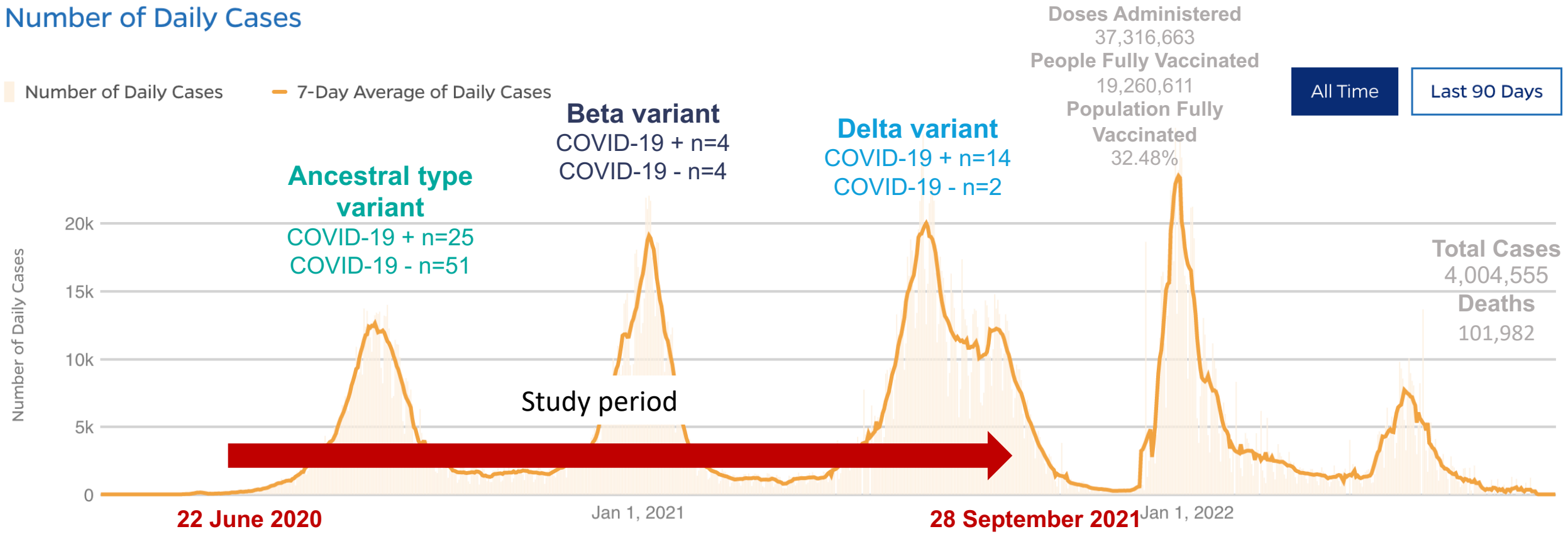
COVID-19 Statistics in South Africa



COVID kids cohort

PIs: M vd Zalm/ H Rabie/ A Redfern

COVID-19 waves in South Africa



Data Sources: Cases and deaths data from JHU CSSE; testing and vaccine data from JHU CCI; and hospitalization data from the U.S. Department of Health and Human Services.

Children (0-13y) with respiratory illnesses or COVID PUI, presenting to Tygerberg Hospital

↓

STEP 1
Routine care data collection

↓

COVID + cases (although ethics of COVID- too)
- Demographics
- Co-morbidities
- Clinical presentation
- Laboratory findings
  - Hematology and chemistry
  - COVID testing, Ct values
  - Respiratory panel, RV16
- Imaging as per routine care
- Outcomes

↓

Part of larger WC data-set (DATCOV)

Children (0-13y) with respiratory illnesses or COVID PUI, presenting to Tygerberg Hospital

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Part of larger WC data-set (DATCOV)

STEP 2
Prospective observational cohort (**COVID+ and -)**

- **As step 1 PLUS additional aims**
- Immune response: serum, paxgene, saliva
- Respiratory morbidity: non-invasive lung function
- Quality of life: effects of lockdown
- Virus: SARS-CoV-2 infectiousness and evolution
- *Household data transmission*

COVID respiratory Illnesses

Other respiratory viruses

Case-control design

*** Demographics/ comorbidities**
*** Clinical data + outcome**
*** Radiology**
*** QoL data**
*** Biorepository:**
- Serum/ saliva/ paxgene child
- Saliva/ serum caregiver

*** Questionnaires**
- Health care use
- LRTIs/ COVID reinfection

*** Lung function**
*** QoL data**
*** Biorepository**
- serum/ saliva child

*** Questionnaires**
*** Radiology**
*** Lung function**
*** QoL data**

Enrollment **3 months** **12 months** **18 months** **24 months**

Preliminary data: Demographics

Demographics	All, n=100	COVID-19 +, n=43	COVID-19 -, n=57	P-value
Age (months)	7 (2.0- 32.5)	8 (2.0-48.0)	7 (2.0-25.5)	0.59
Age subgroups • 0-3 months • 3-12 months • >12 months	 36 (36%) 28 (28%) 36 (36%)	 15 (34.9%) 10 (22.7%) 18 (40.9%)	 21 (36.8%) 18 (32.1%) 18 (32.1%)	
Gender (male)	61 (61%)	26 (60.5%)	35 (61.4%)	0.92
Living with HIV	2 (2%)	1 (2.3%)	1 (1.8%)	1.00
HIV exposed	25/99 (25.3%)*	11/43 (26.2%)*	14 (24.6%)	0.85
SARS-CoV-2 exposure	20 (20%)	11 (25.6%)	9 (15.8%)	0.23
SARS-CoV-2 antibodies	43/85 (50.6%)	26/36 (72.2%)	17/49 (34.7%)	**0.0006**
Underlying comorbidities	37 (37%)	18 (41.9%)	19 (33.3%)	0.38

* One patient with unknown HIV exposure

Known comorbidities	All, n=20	COVID-19 +, n=8	COVID-19 -, n=12
TB	5 (25%)	3 (37.5%)	2 (16.7%)
HIV	2 (10%)**	1 (12.5%)**	1 (8.3%)
Asthma	2 (10%)	0 (0%)	2 (16.7%)
Oncological	2 (10%)	1 (12.5%)	1 (8.3%)
Other	10 (50%)	4 (50%)	6 (50%)
New diagnosis	**All, n=17**	**COVID-19 +, n=10**	**COVID-19 -, n=7**
TB	12 (70.6%)*	7 (70%)	5 (71.4%)*
Other	6 (35.3%)	3 (30%)	3 (42.9%)

* One known asthmatic patient with newly diagnosed TB
** One patient known HIV/TB

Clinical presentation

Clinical presentation	All, n=100	COVID-19 +, n=43	COVID-19 -, n=57
Cardiovascular	2/100 (2%)	2/43 (4.7%)	0 (0%)
Gastrointestinal	7/100 (7%)	4/43 (9.3%)	3/57 (5.3%)
Respiratory	60/100 (60%)	19/43 (44.2%)	**41/57 (71.9%)**
Inflammatory conditions	13/100 (13%)	4/43 (9.3%)	9/57 (15..8%)
Other	18/100 (18%)	14/43 (32.6%)	4/57 (7%)

0-3 months:
75% Lower respiratory tract infections
COVID-19 + (60.0%)
COVID-19 - (85.7%)

Severity of respiratory disease

Clinical diagnosis ⟷ **Imaging**

	All, n=100	COVID-19 +, n=43	COVID-19 -, n=57	P-value
Acute pneumonia	61 (61%)	19 (44.2%)	42 (73.7%)	
Severe pneumonia	27/61 (44.3%)	11/19 (57.9%)	16/42 (38.1%)	0.15

	All, n=100	COVID-19 +, n=43	COVID-19 -, n=57	P-value
Chest X-ray (baseline)	88 (88%)	35 (39.8%)	53 (60.2%)	
Abnormal %	61 (69.3%)	27 (77.1%)	34 (64.2%)	0.20
Severity - Unilateral - Bilateral	27 (44.3%) 34 (55.7%)	7 (25.9%) 20 (74.1%)	20 (58.8%) 14 (41.2%)	**0.01**
Number of zones affected (median)	2.0 (1.0-4.0)	3.0 (0-6.0)	1.5 (1.0-3.0)	0.50
Chest X-ray (follow up after 1 year)	40/88 (45.5%)	9/35 (25.7%)	31/53 (58.5%)	
Abnormal %	12/40 (30%)	5/9 (55.6%)	7/31 (22.6%)	0.10

Morbidity after admission

Morbidity after admission	All, n=100	COVID-19 +, n=43	COVID-19 -, n=57	P-value
1 year visits	55 (55%)	18 (41.9%)	37 (64.9%)	
Readmissions	15/55 (27.3%)	3/18 (16.7%)	12/37 (32.4%)	0.34
• Respiratory	9/15 (60%)	3/3 (100%)	6/12 (50%)	0.23
Clinic visits	28/55 (50.9%)	13/18 (72.2%)	15/37 (40.5%)	**0.03**
• Respiratory	12/28 (42.9%)	5/13 (38.5%)	7/15 (46.7%)	0.66
Persistent or recurrent symptoms	18/55 (32.7%)	8/18 (44.4%)	10/37 (27%)	0.20
• Respiratory	12/18 (66.7%)	5/8 (62.5%)	7/10 (70%)	1.00
1.5 year visits	41 (41%)	12 (27.9%)	29 (50.9%)	
Readmissions	7/41 (17.1%)	5/12 (41.7%)	2/29 (6.9%)	**0.02**
• Respiratory	2/7 (28.6%)	1/5 (20%)	1/2 (50%)	1.00
Clinic visits*	18/40 (45%)*	6/12 (50%)	12/28 (42.9%)*	0.68
• Respiratory	9/18 (50%)	1/6 (16.7%)	8/12 (66.7%)	0.13
Persistent or recurrent symptoms*	10/40 (40%)*	5/12 (41.7%)	5/28 (17.9%)*	0.13
• Respiratory	4/10 (40%)	1/5 (20%)	3/5 (60%)	0.52
2 year visits	21 (21%)	9 (20.9%)	12 (21.1%)	
Readmissions	4/21 (19%)	4/9 (44.4%)	0 (0%)	**0.02**
• Respiratory	2/4 (50%)	2/4 50%)	0 (0%)	NA
Clinic visits**	9/19 (47.4%)**	5/8 (62.5%)**	4/11 (36.4%)**	0.37
• Respiratory	5/9 (55.6%)	1/5 (20%)	4/4 (100%)	**0.05**
Persistent or recurrent symptoms	4/21 (19%)	3/9 (33.3%)	1/12 (8.3%)	0.27
• Respiratory	3/4 (75%)	2/3 (66.7%)	1/1 (100%)	1.00
*One unknown **Two unknown				

After 1 year:
COVID-19 +
20% UAO
60% cough
20% cough and wheeze

After 1.5 year:
COVID-19 +
100% cough

After 2 years:
COVID-19 +
50% cough
50% cough and wheeze

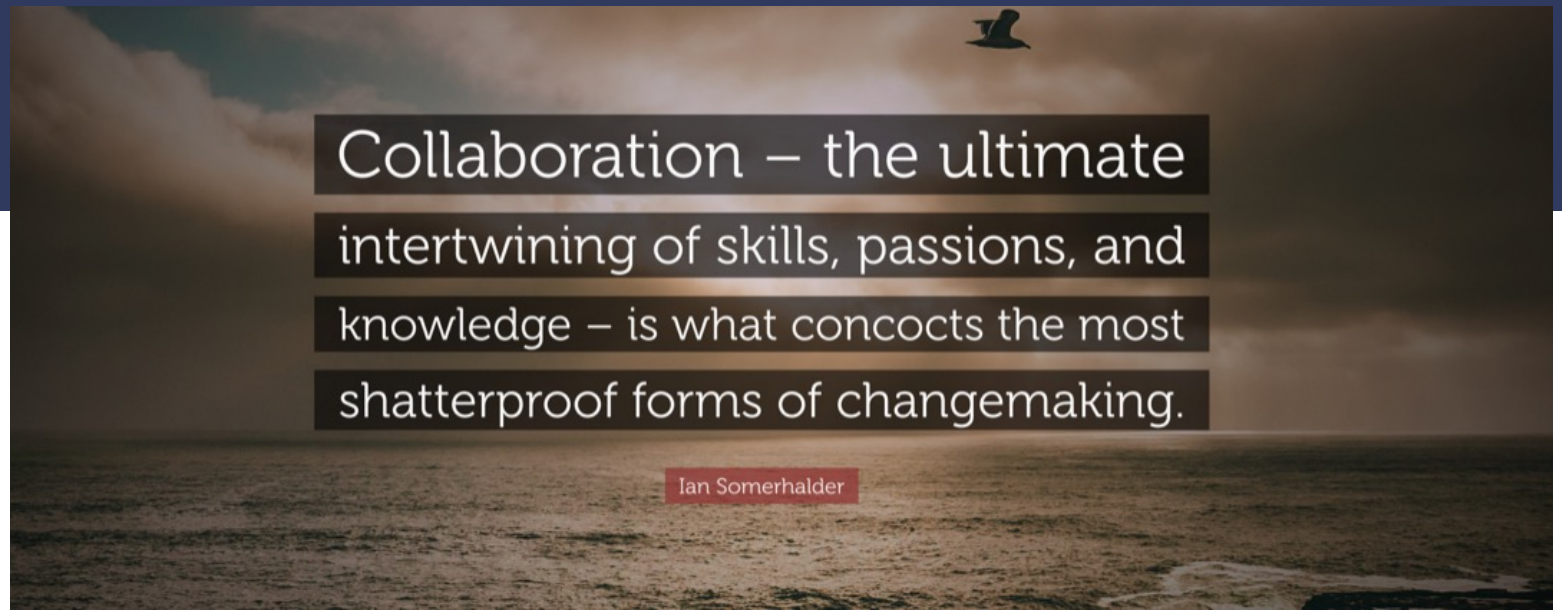
Discussion

- Our cohort is a young cohort – not typical as defined long COVID
  - *Too young to show typical long COVID symptomatology as per case definition – separate case definitions in different age groups?*
- Unknown role of immunosuppressive conditions such as tuberculosis/CLHIV in long COVID
- COVID-19 negative control group interesting comparison group – viral analysis ongoing
- Possible long-term lung health consequences? Data to follow

Conclusion

- Young children with COVID-19 mainly present with respiratory symptoms
  - *SARS-CoV-2 infected children with pneumonia presented more frequently with radiologically more severe pneumonia*
- COVID-19 positive children are more likely to be readmitted or seem to be more prone to seek medical care long-term
- Persistent symptoms are more often seen in COVID-19 positive children; mostly cough
- More follow up is needed to assess long-term outcomes
- The outcome of COVID-19 infection in children with underlying illness should be explored further
  - *Focus on TB and children living with HIV*

Questions?



- Dr. Carien Bekker, Dr. Carla Mckenzie, Prof. Pierre Goussard (Stellenbosch University)
- Prof. Marieke van der Zalm / Prof. Helena Rabie / Dr. Andrew Redfern (Stellenbosch University)
- Dr. Lilly Verhagen (Radboud Nijmegen)
- Prof. Mark Cotton (Stellenbosch University)
- Department of Paediatrics and Child Health, Tygerberg Hospital
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