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

COVID kids cohort, South Africa

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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?

Clinical outcomes COVID-19 in LMICs

Design
- Observational cohort South Africa
- April-July 2020

Results
- 50% of hospitalizations <1 year 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

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

PLOS ONE, Kitano Jan 2021

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
Clinical outcomes COVID-19 in LMICs

What about long-COVID 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
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

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COVID kids cohort

PIs: M vd Zalm/ H Rabie/ A Redfern
COVID-19 waves in South Africa

Number of Daily Cases

- **Ancestral type variant**
  - COVID-19 + n=4
  - COVID-19 - n=51

- **Beta variant**
  - COVID-19 + n=4
  - COVID-19 - n=4

- **Delta variant**
  - COVID-19 + n=14
  - COVID-19 - n=2

**Study period**

- **22 June 2020** to **28 September 2021**

**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

**STEP 1**
Routine care data collection

COVID + cases (although ethics of COVID- too)
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- Co-morbidities
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**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

Part of larger WC data-set (DATCOV)

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COVID respiratory illnesses

Other respiratory viruses

Case-control design

Enrollment

3 months

12 months

18 months

24 months

* 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

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World Health Organization

Every breath counts

CARE

Conform
Assess
Respond
Evaluate
### Preliminary data: Demographics

#### Demographics

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

* One patient with unknown HIV exposure

#### Known comorbidities

<table>
<thead>
<tr>
<th></th>
<th>All, n=20</th>
<th>COVID-19 +, n=8</th>
<th>COVID-19 -, n=12</th>
</tr>
</thead>
<tbody>
<tr>
<td>TB</td>
<td>5 (25%)</td>
<td>3 (37.5%)</td>
<td>2 (16.7%)</td>
</tr>
<tr>
<td>HIV</td>
<td>2 (10%)**</td>
<td>1 (12.5%)**</td>
<td>1 (8.3%)</td>
</tr>
<tr>
<td>Asthma</td>
<td>2 (10%)</td>
<td>0 (0%)</td>
<td>2 (16.7%)</td>
</tr>
<tr>
<td>Oncological</td>
<td>2 (10%)</td>
<td>1 (12.5%)</td>
<td>1 (8.3%)</td>
</tr>
<tr>
<td>Other</td>
<td>10 (50%)</td>
<td>4 (50%)</td>
<td>6 (50%)</td>
</tr>
</tbody>
</table>

#### New diagnosis

<table>
<thead>
<tr>
<th></th>
<th>All, n=17</th>
<th>COVID-19 +, n=10</th>
<th>COVID-19 -, n=7</th>
</tr>
</thead>
<tbody>
<tr>
<td>TB</td>
<td>12 (70.6%)*</td>
<td>7 (70%)</td>
<td>5 (71.4%)*</td>
</tr>
<tr>
<td>Other</td>
<td>6 (35.3%)</td>
<td>3 (30%)</td>
<td>3 (42.9%)</td>
</tr>
</tbody>
</table>

* One known asthmatic patient with newly diagnosed TB
** One patient known HIV/TB
## Clinical presentation

<table>
<thead>
<tr>
<th>Clinical presentation</th>
<th>All, n=100</th>
<th>COVID-19 +, n=43</th>
<th>COVID-19 -, n=57</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular</td>
<td>2/100 (2%)</td>
<td>2/43 (4.7%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>7/100 (7%)</td>
<td>4/43 (9.3%)</td>
<td>3/57 (5.3%)</td>
</tr>
<tr>
<td><strong>Respiratory</strong></td>
<td><strong>60/100 (60%)</strong></td>
<td><strong>19/43 (44.2%)</strong></td>
<td><strong>41/57 (71.9%)</strong></td>
</tr>
<tr>
<td>Inflammatory conditions</td>
<td>13/100 (13%)</td>
<td>4/43 (9.3%)</td>
<td>9/57 (15.8%)</td>
</tr>
<tr>
<td>Other</td>
<td>18/100 (18%)</td>
<td>14/43 (32.6%)</td>
<td>4/57 (7%)</td>
</tr>
</tbody>
</table>

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

#### Clinical diagnosis

<table>
<thead>
<tr>
<th></th>
<th>All, n=100</th>
<th>COVID-19 +, n=43</th>
<th>COVID-19 -, n=57</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute pneumonia</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number</td>
<td>61 (61%)</td>
<td>19 (44.2%)</td>
<td>42 (73.7%)</td>
<td></td>
</tr>
<tr>
<td>Severe pneumonia</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number</td>
<td>27/61 (44.3%)</td>
<td>11/19 (57.9%)</td>
<td>16/42 (38.1%)</td>
<td>0.15</td>
</tr>
</tbody>
</table>

#### Imaging

<table>
<thead>
<tr>
<th></th>
<th>All, n=100</th>
<th>COVID-19 +, n=43</th>
<th>COVID-19 -, n=57</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest X-ray (baseline)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of zones</td>
<td>88 (88%)</td>
<td>35 (39.8%)</td>
<td>53 (60.2%)</td>
<td></td>
</tr>
<tr>
<td>affected (median)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2.0 (1.0-4.0)</td>
<td>3.0 (0-6.0)</td>
<td>1.5 (1.0-3.0)</td>
<td>0.50</td>
</tr>
<tr>
<td>Chest X-ray (follow up after 1 year)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of zones</td>
<td>40/88 (45.5%)</td>
<td>9/35 (25.7%)</td>
<td>31/53 (58.5%)</td>
<td></td>
</tr>
<tr>
<td>affected (median)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>12/40 (30%)</td>
<td>5/9 (55.6%)</td>
<td>7/31 (22.6%)</td>
<td>0.10</td>
</tr>
</tbody>
</table>

- **Acute pneumonia**: 61 (61%) vs 19 (44.2%) vs 42 (73.7%)
- **Severe pneumonia**: 27/61 (44.3%) vs 11/19 (57.9%) vs 16/42 (38.1%)
- **Chest X-ray (baseline)**: 88 (88%) vs 35 (39.8%) vs 53 (60.2%)
- **Chest X-ray (follow up after 1 year)**: 40/88 (45.5%) vs 9/35 (25.7%) vs 31/53 (58.5%)
## Morbidity after admission

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

*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

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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?
Collaboration – the ultimate intertwining of skills, passions, and knowledge – is what concocts the most shatterproof forms of changemaking.

- 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
- MIS-C teams (University of Cape Town / Stellenbosch University)
- Paediatric team, Desmond Tutu TB Centre (Stellenbosch University)
- NHLS virology; Prof. Wolfgang Preiser, Prof. Gert van Zyl
- All other collaborators & funders
- Family