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Guidance Document 5
Rational use of PCR testing for COVID-19: informing public health recommendations (13th May 2020)

Background

- COVID-19 is caused by the SARS-CoV-2 RNA virus and spreads from person-to-person through respiratory droplets produced when an infected person coughs, sneezes or speaks, and from touching surfaces contaminated with the virus (a fomite)
- COVID-19 presents as a respiratory infection, but there is now an evidence base to indicate that there are multiple presenting symptoms which are not all related to the respiratory tract
- Many infected individuals will have no symptoms (asymptomatic) or will initially have no symptoms but will still be infectious prior to developing symptoms (pre-symptomatic)
- In general, the severity of COVID-19 infection is associated with older age groups and populations with comorbidities including immune suppression
- Children and adolescents usually exhibit mild or no symptoms and mortality is extremely rare
- The SARS-CoV-2 virus is detected by testing for viral RNA in secretions (usually from the nasopharynx) using a polymerase chain reaction test (PCR) performed in specialized laboratories
- The global standard for diagnosis is a positive PCR test for SARS-CoV-2 which confirms a diagnosis for COVID-19 disease
- Many laboratories in the public and private sector are able to conduct the PCR test for COVID-19
- The National Health Laboratory Service (NHLS) is aiming to conduct 15,000 tests daily, although it has not yet achieved this number on account of logistic issues and a lack of test reagent and viral extraction kits[1]
- Laboratory turn-around times (the time it takes from obtaining the sample to receiving the laboratory results) vary, and can range from 2 days to 7 days[1]
- Delays in receiving test results significantly hampers the ability of response teams to follow the World Health Organization (WHO) imperative to test and trace contacts as the most important measure to reduce the spread of SARS-CoV-2
- PCR testing kits developed for the different testing platforms (e.g. Roche, GeneXpert) are in increasingly short supply globally which has implications for test kit availability in South Africa[2]
- As with many countries, it is possible that SA may run out of the required test kits

[1] https://www.spotlightnsp.co.za/2020/05/08/covid-19-doctors-concerned-about-severe-testing-delays/

[2] Kavanagh MM, Erondu NA, Tomori O, Dzau VJ, Okiro EA, Maleche A, Aniebo IC, Rugege U, Holmes CB, Gostin LO. Access to lifesaving medical resources for African countries: COVID-19 testing and response, ethics, and politics. Lancet. 2020 May 7 [Epub ahead of print] https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31093-X/fulltext

- In South Africa, as of 10th May 2020, a total of 341,336 tests have been conducted with 10,015 laboratory-confirmed COVID-19 infections (2,9%)
- The percentage positivity of test samples sent to the laboratory ranges widely between provinces, and is likely partly due to different strategies and intensities in contact tracing and testing these contacts
- Guidance is required to limit PCR testing to 1) reduce unnecessary testing to preserve test kits for those environments where it is needed most; and 2) to reduce the burden on laboratories to ensure more rapid turn-around times to permit the implementation of effective test and trace measures

Current risk of community transmission of SARS-CoV-2 in South Africa

The WHO categorises the expansion of the COVID-19 spread into four categories: Stage 1 - imported by travellers; Stage 2 - sporadic transmission; Stage 3 - clustered transmission; Stage 4 - widespread community transmission[3] .

We recognize that the majority of infections are asymptomatic, and that those diagnosed within laboratories are a small fraction of the total. At 10,015 individuals with laboratory confirmed infection (10th May 2020), South Africa is moving towards Stage 4 transmission category. Within some regions, and especially focused in metro areas, there is increasing recognition that Stage 4 is already in effect.

WHO Guidelines for Rational Use of Testing

The WHO has provided guidelines for the rational use of testing with countries encouraged to consider how in-country resources and availability influence their testing strategies[4]. A table of management options linked to situational responses advised by WHO is available in the appendix.

WHO advises that in settings of limited resources in areas with community transmission, national policies should consider prioritization for testing of:

- Vulnerable populations and people at risk of developing severe disease
- Health workers (including emergency services and non-clinical staff), and contacts of confirmed cases (to protect health workers and reduce the risk of nosocomial transmission)
- The first symptomatic individuals in a closed setting (e.g. schools, long-term living facilities, prisons, hospitals) to quickly identify outbreaks and ensure containment measures
- All other symptomatic contacts may be considered probable cases and isolated without additional testing if testing capacity is limited
- Testing strategies may change where there are more severe shortages of diagnostic tests or reagents.

[3] World Health Organization 2020. WHO reference number: WHO/2019-nCoV/Community_Actions/2020.3
https://www.who.int/publications-detail/critical-preparedness-readiness-and-response-actions-for-covid-19
[4] World Health Organization 2020. WHO/2019-nCoV/lab_testing/2020.1
https://apps.who.int/iris/bitstream/handle/10665/331509/WHO-COVID-19-lab_testing-2020.1-eng.pdf

How we make guidance

We considered the following when developing this guidance:

- We develop guidance using the overriding ethical principle of "first do no harm"
- Our guidance is based on public health principles and aims to maximise utility from testing to contain the epidemic and is informed by the WHO recommendations for laboratory testing strategies[5]
- Overarching benefits versus harms are assessed whilst also taking into account uncertainties and unknowns and issues of feasibility
- COVID-19 will not be eradicated without a vaccine; in the absence of a vaccine, public health strategies for epidemic control need to consider a longer-term, multi-year approach
- Based on international and current national experience, we presume a supply-demand mismatch with regard to PCR tests as the epidemic progresses
- While current constraints determine our guidance at this time point, we recognise that many of the obstacles facing implementing optimal testing strategies are challenges in the current South African healthcare delivery system; we actively identify where these can be improved

Understanding public health approaches to epidemic control for SARS-CoV-2

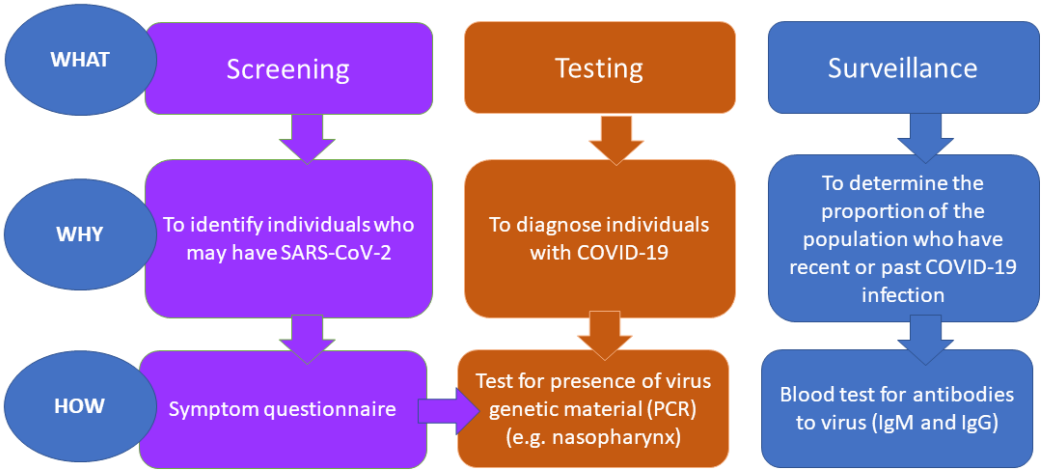
There are 3 key strategies for managing epidemics:

1. Surveillance: aims to identify infections before they become outbreaks
2. Screening: aims to identify individuals who are more at risk based on their symptoms and so require a test
3. Testing: aims to provide a laboratory diagnosis for COVID-19 in an individual

While screening is done primarily for clinical reasons, surveillance by contrast is done primarily for epidemiological reasons, to assess programmes for prevention and control of disease. We currently only have tests which assess incidence of active SARS-CoV-2, and do not have reliable tests to measure immunity to COVID-19. It is therefore difficult to assess the COVID-19 epidemic by direct surveillance, as we would do with other diseases. Once approved antibody tests are available, improved surveillance will be possible.

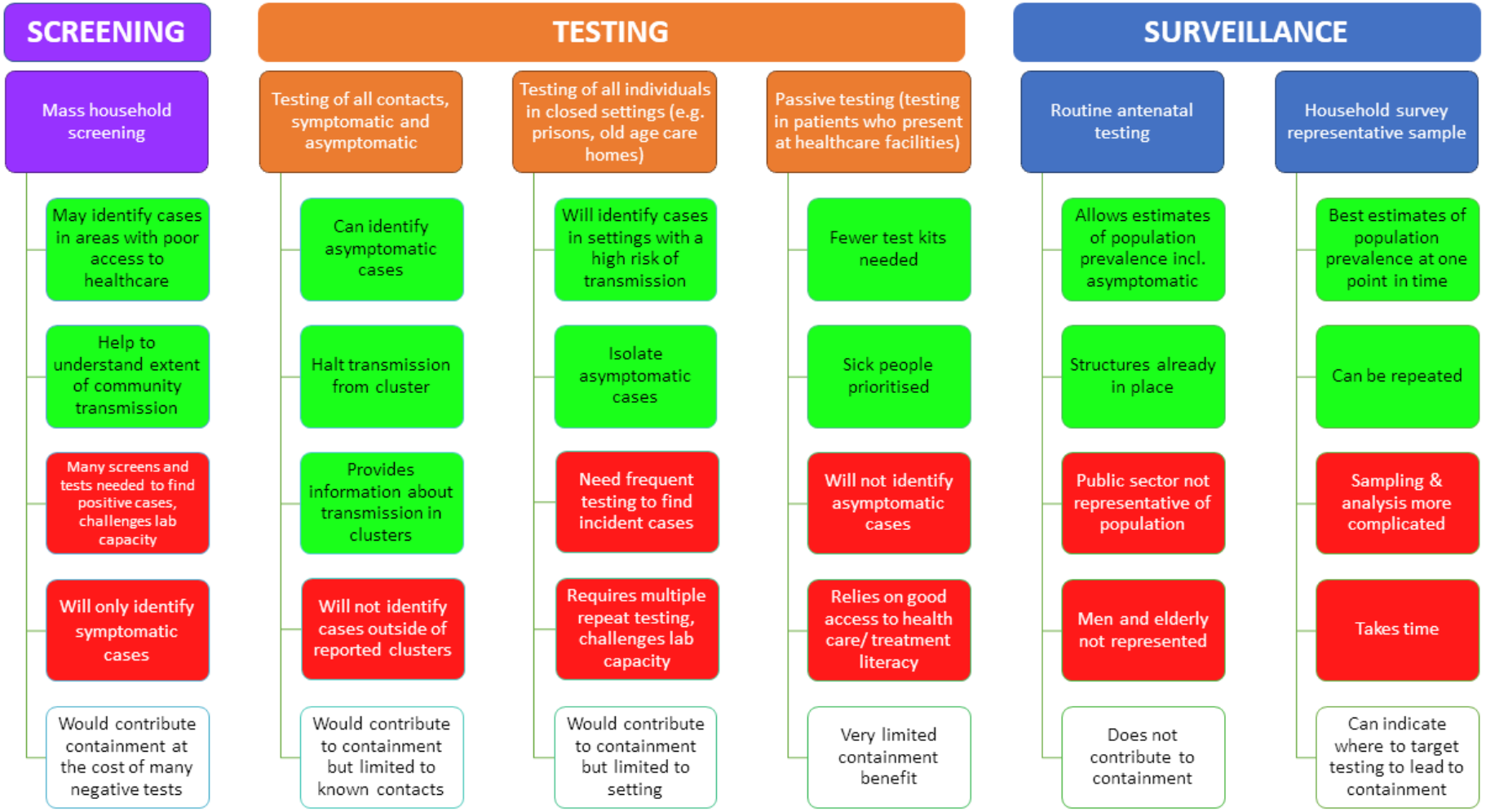
This can be best represented in the figure overleaf:

[5] World Health Organization 2020. WHO/2019-nCoV/lab_testing/2020.1
https://apps.who.int/iris/bitstream/handle/10665/331509/WHO-COVID-19-lab_testing-2020.1-eng.pdf



In addition to the different purposes of screening, testing and surveillance, there are additional targeted strategies within the three broad categories. We outline them on the following page and recognize that there may be some overlap.

As a Task Team, we have interrogated each strategy and identified the advantages, disadvantages and overall containment benefit versus the cost of number of tests for each strategy.



LEGEND: Green denotes advantages and Red denotes disadvantages

Recommendations regarding rational testing for COVID-19 in the setting of limited resources

The single biggest improvement that could enhance the South African response over the long-term would be to reduce the turn-around time for testing results while maintaining appropriate levels of testing.

Prerequisite for a successful Testing Strategy

Laboratory capacity, resources and management should urgently focus on improving the turn-around time for laboratory results. This can be done by:

- Streamlining and optimising public, private and academic laboratory resources
- Urgently investing in additional testing capacity including human resources
- Explore enhanced communication systems (e.g. results via SMS) for immediate result notification
- Negotiating more robust supply chain security at more affordable prices and/or develop in-house manufacturing capacity using voluntary or compulsory licensing as required[6]

The following recommendations are specific to our current setting with limited resources.

1. **Reduce mass screening and testing programmes**

   Rationale:
   The predictive value of a test is low when background prevalence is low, so mass screening is unlikely to yield benefit for containment (although it may benefit the few individuals who are diagnosed with COVID-19).
   Screening may be house to house or held at events. Bringing people together poses a transmission risk to community members and community healthcare workers so that the potential benefits of these events may not outweigh the potential harms. This may be especially weighted against mass screening events where many community members attend and physical distancing is not well maintained.

   Improvement:
   Any screening should have a clear aim which is defined in a *publicly accessible* protocol.
   Should resources permit, screening should:
   - ✓ Not put community members and screeners at risk
   - ✓ Adequate physical distancing, hygiene and personal protective equipment to be implemented and available at screening site
   - ✓ Should target areas where there is known high prevalence of COVID-19
   - ✓ Planning should include timeous return of results (WHO specifies within 24 to 48 hours) and contact tracing
   - ✓ Screening should use standardised tools to allow clearer interpretation of data

[6] https://www.wto.org/english/tratop_e/trips_e/public_health_faq_e.htm

2. Stop the legal imperative for negative testing for workers recovered from COVID-19 to return to work and amend regulations that requires negative testing for de-isolation

Rationale:
The diagnostic test accuracy is variably reported and both false positive and false negative tests are noted; it is also not clear how well the presence of virus correlates with infectiousness. Return to work should be based on the recommended guidelines from Department of Health which specify 14 days since tested positive or 14 days after symptoms.

Improvement:

- ✓ Amend the Department of Employment and Labour Regulations no. 43257[7] published in notice 479 on 29 April 2020, that currently state

  "*24. If a worker has been diagnosed with COVID-19 and isolated in accordance with the Department of Health Guidelines, an employer may only allow a worker to return to work on the following conditions: 24.1 The worker has undergone a medical evaluation confirming that the worker has been tested negative for COVID-19*"

  Regulations should remove the requirement for a negative test prior to return to work.

- ✓ This would be aligned with NDOH COVID-19 Disease: Infection Prevention and Control Guidelines[8] (published 1 April 2020), as well as NDOH Guidelines for symptom monitoring and management of essential workers for COVID-19 related infection[9] (published 14 April 2020).

3. **Target testing in closed settings with confirmed cases**

Rationale:
Given the close proximity of individuals to each other in closed settings (e.g. care homes, health facilities, boarding schools, prisons, health facilities) these are considered high-risk transmission environments. Because of the likely higher background prevalence in these environments when more than one individual is diagnosed with COVID-19, targeted testing within a facility is likely to yield a greater percentage of positive individuals per number of tests done. This permits efficient identification of individuals who are confirmed with COVID-19 and their close contacts[10] and should guide further screening and testing. Grouping of individuals can be done according to illness or exposure with isolation of those who are ill (cases) and quarantine for those who are exposed (contacts).

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[7] https://www.gov.za/sites/default/files/gcis_document/202004/43257gon479.pdf
[8] https://www.nicd.ac.za/wp-content/uploads/2020/04/Covid-19-Infection-and-Prevention-Control-Guidelines-1-April-2020.pdf
[9] https://www.nicd.ac.za/wp-content/uploads/2020/04/Guidance-for-symptom-monitoring-and-management-of-essential-staff-with-COVID-19-related-illness-final-2.pdf
[10] Close contact: A person having had face-to-face contact or was in a closed environment with a COVID-19 case; this includes, amongst others, all persons living in the same household as a COVID-19 case and, people working closely in the same environment as a case. A healthcare worker or other person providing direct care for a COVID-19 case, while not wearing recommended personal protective equipment or PPE (e.g., gowns, gloves, NIOSH-certified disposable N95 respirator, eye protection). https://www.nicd.ac.za/wp-content/uploads/2020/03/NICD_DoH-COVID-19-Guidelines-10March2020_final.pdf

Improvement:

- ✓ Test all initial individuals presenting with suspected COVID-19 symptoms and consider all other symptomatic individuals as probable COVID-19 and follow the guidance for isolation and quarantine
- ✓ Closed settings to retain clear line lists to facilitate testing as soon as symptoms appear
- ✓ Facilities bear responsibility for assisting health authorities with contact tracing

4. Special case for exposed asymptomatic healthcare worker to allow to return to work

Rationale:
Given limited human resources in the healthcare sector, and to avoid unnecessary reduction in the healthcare workforce, healthcare workers who have had high risk exposure to confirmed COVID-19 case, and remain asymptomatic after 7 days in quarantine, may be tested on Day 8, and if negative, may return to work. Alternatively, the healthcare worker should remain in quarantine for 14 days post exposure.

Improvement:
Retain current guidelines [NDOH Guidelines for symptom monitoring and management of essential workers for CVOID-19 related infection. Published 14 April 2020][11]

5. Cease baseline testing to determine negative status

Rationale:
There is no benefit to test employees or healthcare workers to obtain a baseline of current infectivity and/or to determine fitness for work. While the benefit may be to individuals who test positive and to their contacts, the risk of transmission is dynamic and repeated tests would be required to make this a useful ongoing exercise. The utility of test to benefit ratio is very low.

Improvement:
We do not see any reason for this practice to continue.

A note about serology

Serological testing for SARS-CoV-2 antibodies is not currently used for diagnosis because antibodies are only detectable as late as the second week of symptoms. These tests are likely to become useful for surveillance in the future, however, currently available tests are of variable quality, and their specificity limits their use in low prevalence settings. This may change in the future and guidance will require updating.

[11] https://www.nicd.ac.za/wp-content/uploads/2020/04/Guidance-for-symptom-monitoring-and-management-of-essential-staff-with-COVID-19-related-illness-final-2.pdf

Summary statement

Testing kits for SARS-CoV-2 are limited and use therefore need to be rationed to optimise the use of each test, such that the greatest number of infected individuals can be identified to enhance contact tracing, and epidemic containment.

We recommend that managing the COVID-19 epidemic is viewed using a long-term approach. To this end immediate consideration should be given to enhancing laboratory capacity, resources and management to improve the turn-around time for laboratory results.

We provide five key recommendations for strategic use of testing kits in the current resource-constrained setting:

- ✓ Reduce mass screening and testing
- ✓ Stop the legal imperative for all testing of employees with confirmed COVID-19 to test negative prior to returning to work (align Department of Labour and Department of Health regulations)
- ✓ Target testing to closed settings with confirmed cases
- ✓ Retain current Department of Health guidelines for testing for exposed, asymptomatic healthcare workers
- ✓ Cease baseline testing to confirm negative status

Released by the College of Public Health Medicine COVID-19 Evidence-based Guidance Task Team[12] & the CEO for the CMSA, Prof Eric Buch
Version 4, 13th May 2020

The Task Team recognises that the response to COVID-19 is rapidly changing as new evidence comes to light. We welcome feedback on our guidance and will attempt to address criticisms in future versions.

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[12] The CPHM COVID-19 Evidence-based Guidance Task Team comprises CPHM Fellows: Kerrin Begg, Mary-Ann Davies, Rene English, Bernice Harries, Dishiki Kalonji, Alishka Rajman, Kate Rees, Nandi Siegfried, Jim teWaterNaude. Contact: Dr Nandi Siegfried nandi.siegfried@gmail.com; Dr Kerrin Begg, kerrin@begg.co.za.
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Table from WHO[13] of example situations and management alternatives if testing capacity is overwhelmed

Table 2. Example situations and management alternatives if testing capacity is overwhelmed

Situation	Alternatives if system is overwhelmed and testing is not possible
Suspected case, mild, with no risk factors	Register as a suspected case, home isolate according to WHO guidance, and do not test
Suspected case requiring admission to health care facility regardless of severity	Strongly recommended to test. If testing is not possible, implement isolation measures warding against nosocomial transmission (thus no cohort isolation possible)
Symptomatic health care worker identified as a contact	Strongly recommended to test
Symptomatic health care worker with no known COVID-19 contact	In areas with COVID-19 community transmission, test
Increased number of suspected cases in a specific demographic group (potential cluster)	Test a subset of the cases
Closed settings, including schools, hospitals, long-term living facilities	Test initial cases. Consider all other symptomatic individuals as probable cases
Recovering patient who has tested negative twice	If clinically recovered, discharge after an additional 14 days in self-isolation
Contact tracing in areas of community transmission	Quarantine contacts for 14 days, If symptomatic, assume COVID-19 and extend quarantine

Footnote: This table was constructed on 21st March 2020 earlier in the epidemic when testing constraints were not as great as now. For this reason, the Task Team would not recommend testing recovering patients to obtain two negative tests, as this would contribute to unnecessary use of testing

[13] World Health Organization 2020. WHO/2019-nCoV/lab_testing/2020.1
https://apps.who.int/iris/bitstream/handle/10665/331509/WHO-COVID-19-lab_testing-2020.1-eng.pdf