Expansion of COVID19 diagnostics in South Africa: Rapid Antigen Testing

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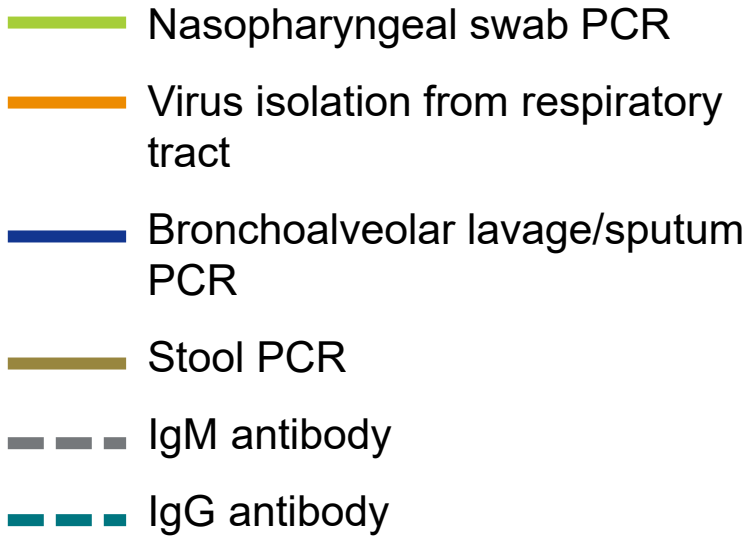
- **02 March 2021**

Contents

1. Background to Testing Context of SARS CoV-2 IN SA

Temporal Considerations for SARS CoV-2 Diagnosis

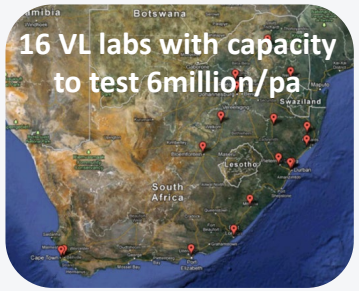
Nandini Sethuraman et al1 concluded a comprehensive laboratory testing window with different technologies based on published studies. Detection sensitivity for SARS-COV-2 antibodies and virus varies significantly from the time the specimens are taken



Context in South Africa

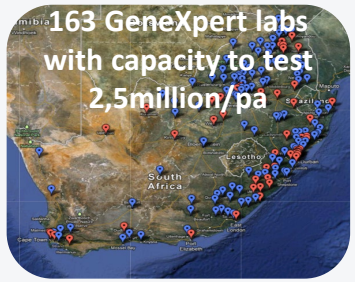
NHLS has a network of 265 laboratories across the country. By 28 February 2021, the country had conducted approximately 9 million COVID 19 tests

Capacity for COVID 19 Testing



32%

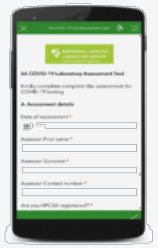
Only 6 labs receiving SARS-CoV2 testing stock



14%

24 sites ready and verified, only 15 labs receiving SARS-CoV2 testing stock

Virology capability = 54%

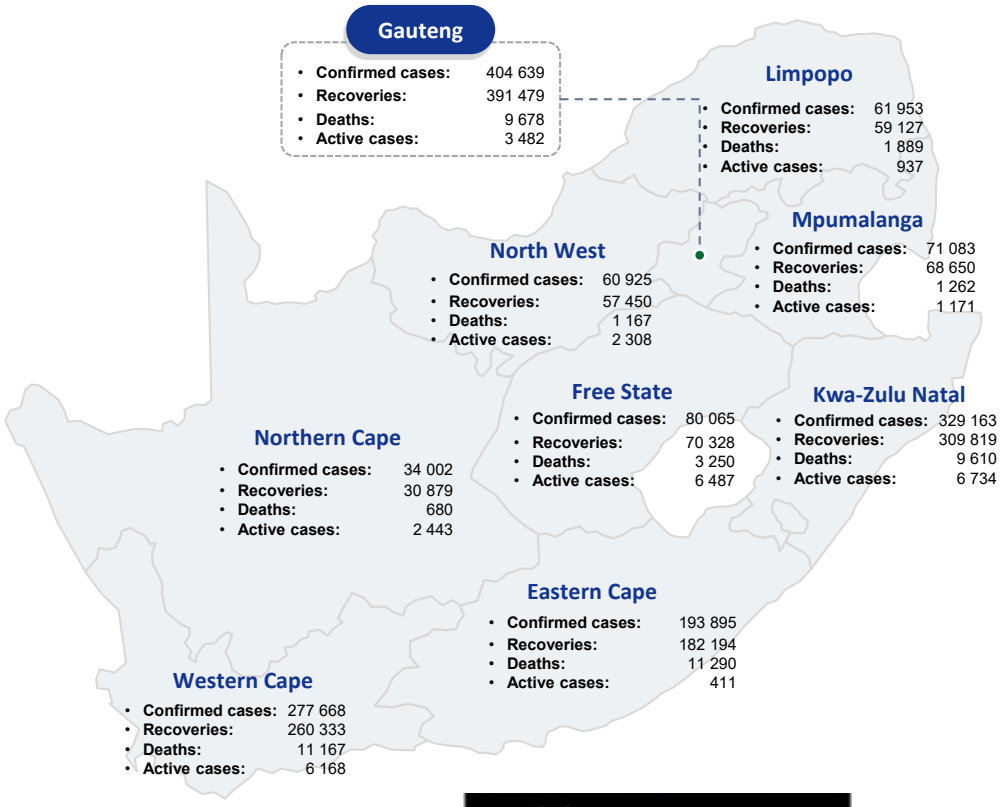


UTILISING DIGITAL HEALTH – RAPID ASSESSMENT TOOL

11 Academic, 29 private and 9 tertiary laboratories

COVID 19 National Statistics

Tests conducted	9 007 479
Positive cases identified	1 513 393
Total recoveries	1 430 259
Total deaths	49 993
New cases	1 168
Active cases	33 141



Vaccines administered
70 527

Source: NHLS Portfolio Committee Presentation, June 2020; SA Department of Health, NICD, "Update on Covid-19 (28th February 2021)" Notes: 1. Tests done by NHLS (250 tests with unconfirmed location); 2. Backlog of unprocessed specimens; 3. Capacity (equipment available) as at end May 2020, 4. Number of hospitals reporting COVID 19 cases from both public and private sector

SARS-CoV-2 Testing Landscape: South Africa

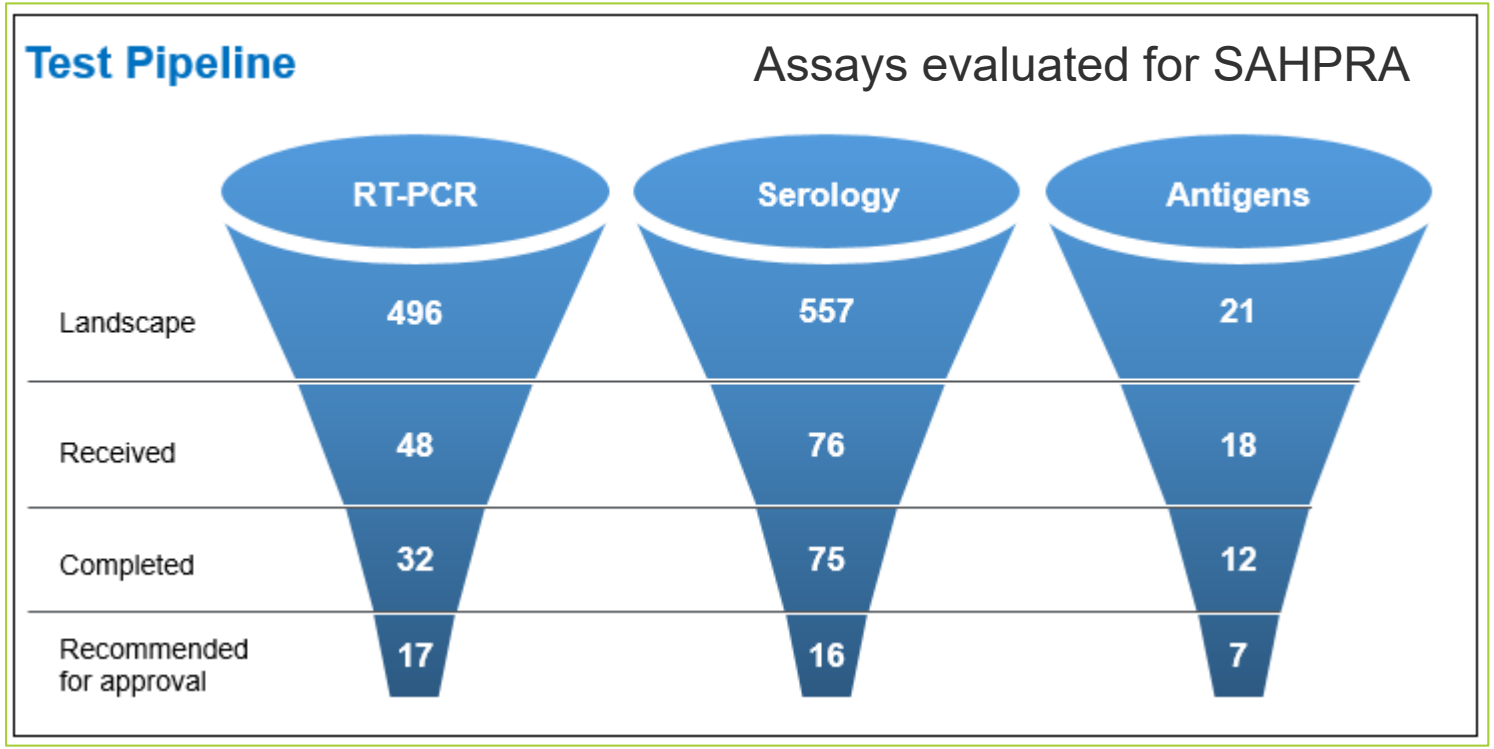


Table 1. Advantages and disadvantages of testing methods for SARS-CoV-2

TEST TYPE	ADVANTAGES	DISADVANTAGES
Nucleic acid amplification testing (NAAT)	• Detects active SARS-CoV-2 infection • High sensitivity and specificity	• Turnaround time of hours to days • Labour intensive • Requires laboratory infrastructure and skilled personnel • More expensive than RDTs
Rapid diagnostic tests: Antigen-detecting tests	• Detects active SARS-CoV-2 infection • Can be used at the point of care (outside laboratories) • Easy to perform • Quick results (typically under 30 minutes) enabling rapid implementation of infection control measures, including contact tracing • Less expensive than NAAT, e.g., RT-PCR tests	• Variable sensitivity and specificity, generally lower than NAAT • Lower sensitivity means negative predictive value is lower than for NAAT, especially in settings with high prevalence of SARS-CoV-2 • Confirmatory NAAT testing of RDT positives is advised in all low-prevalence settings and for RDT negatives in high-prevalence settings. • Negative Ag-RDT results cannot be used to remove a contact from quarantine
Rapid diagnostic tests: Antibody-detecting tests	• Ab-RDTs can be used to detect previous infection with SARS-CoV-2 • Can be used at the point of care (outside laboratories) or in higher throughput formats in laboratories • Easy to perform • Quick results (typically under 30 minutes for point-of-care testing) • Less expensive than NAAT, e.g., RT-PCR tests	• Clinical significance of a positive Ab-RDT result is still under investigation • Positive Ab-RDT results do not guarantee presence of neutralizing antibodies or protective immunity • Ab-RDTs should not be used for determining active infections in clinical care or for contact-tracing purposes • Interpretation of Ab-RDT results depends on the timing of the disease, clinical morbidity, the epidemiology and prevalence within the setting, the type of test used, the validation method, and the reliability of the results

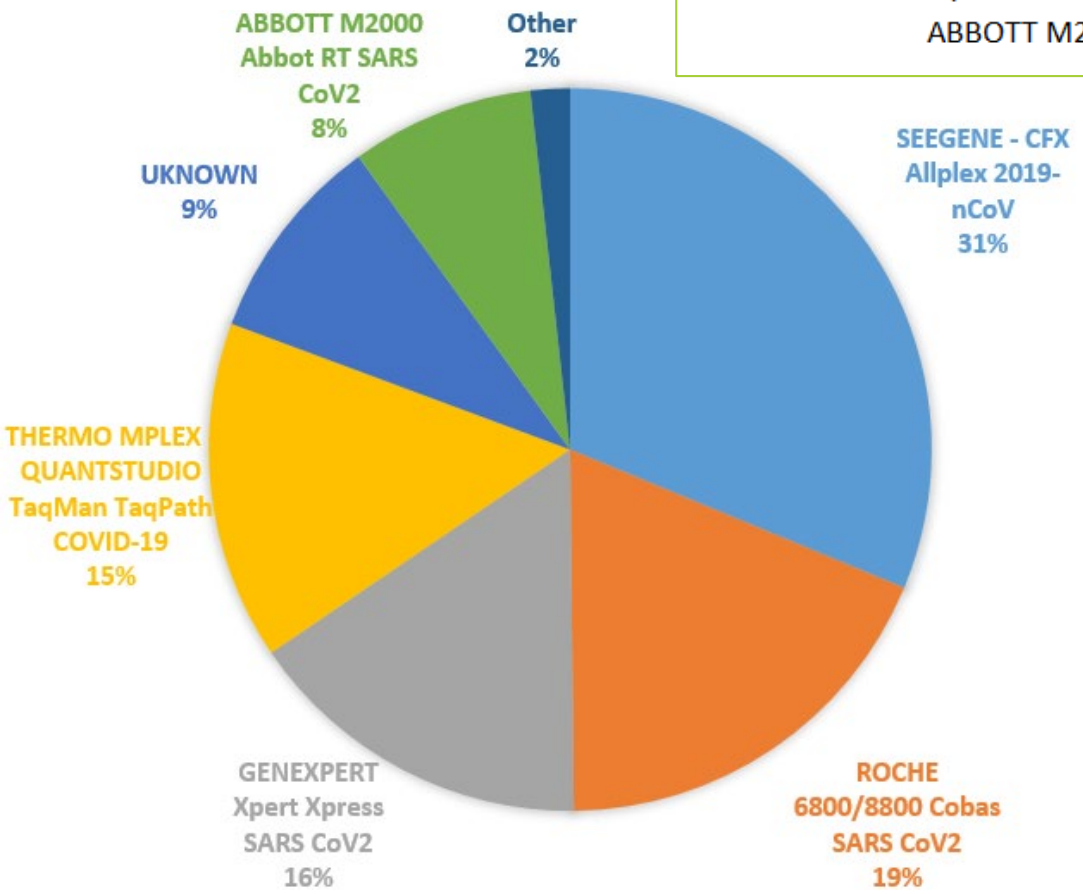
SARS-CoV-2 antigen-detecting rapid diagnostic tests: an implementation guide. Geneva: World Health Organization; 2020. Licence: CC BY-NC-SA 3.0 IGO.

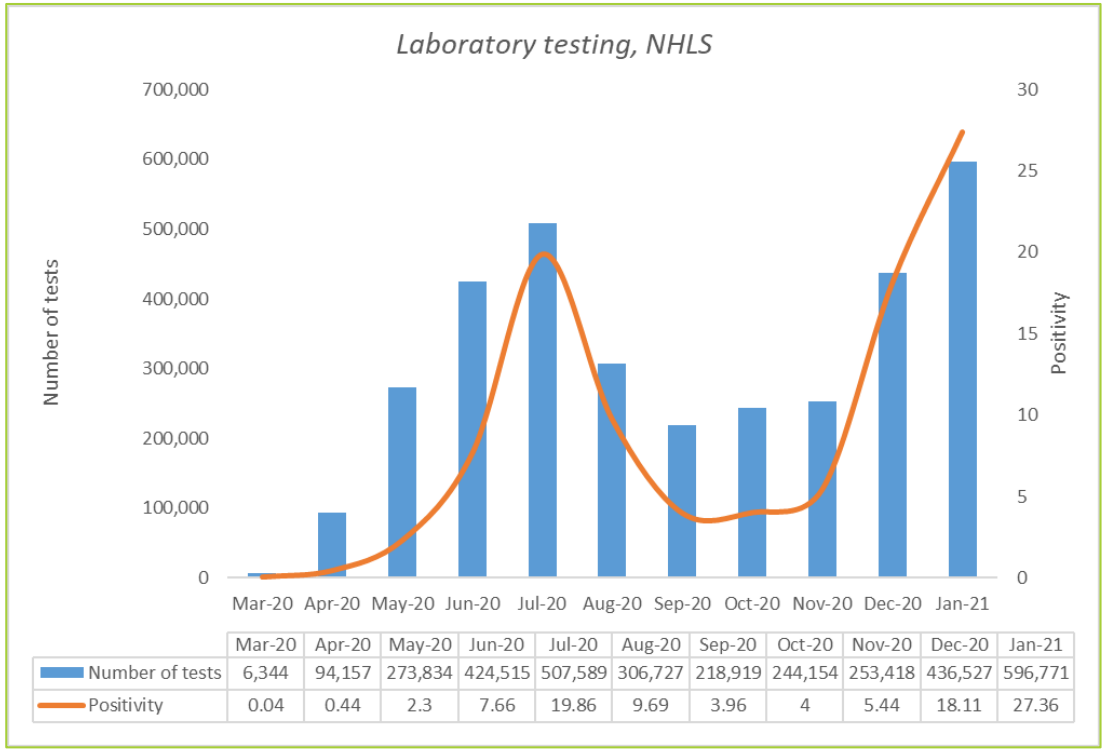
2. Molecular Testing Update

NHLS SARS-CoV-2 molecular testing platform

~3 million laboratory test results

Assay name	Assay type	n	Positive	Inconclusive	Unsuccessful
SEEGENE - CFX	open	942831	18.5%	1.1%	0.4%
ROCHE 6800/8800	closed	561069	20.0%	0.1%	0.1%
GENEXPERT	closed	472268	21.0%	0.2%	0.2%
THERMO MPLEX - QUANTSTUDIO	open	457681	18.7%	1.3%	0.2%
ABBOTT M2000	closed	247280	20.5%	0.0%	0.0%



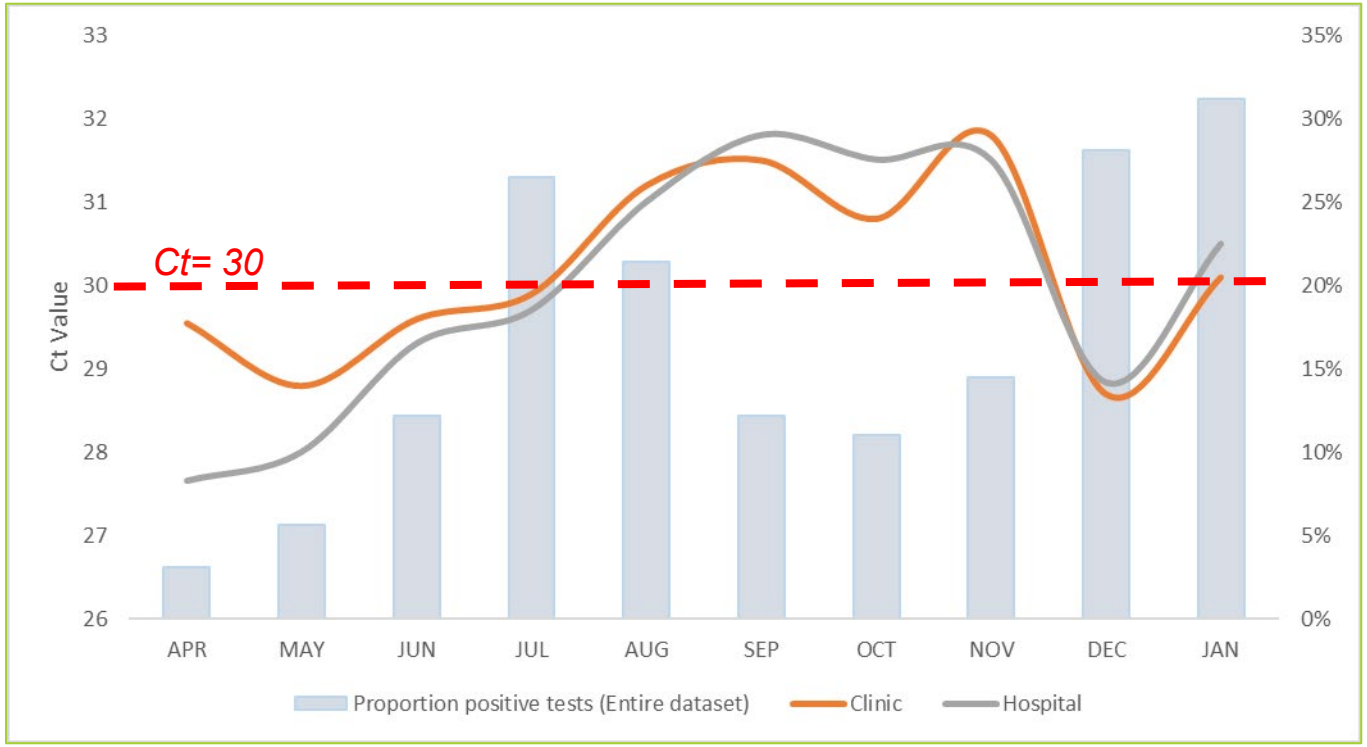


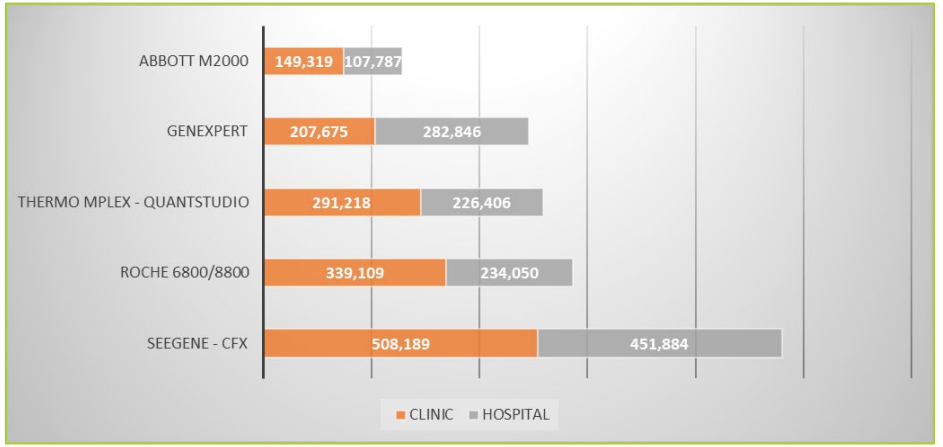
	Mar-20	Apr-20	May-20	Jun-20	Jul-20	Aug-20	Sep-20	Oct-20	Nov-20	Dec-20	Jan-21
Number of tests	6,344	94,157	273,834	424,515	507,589	306,727	218,919	244,154	253,418	436,527	596,771
Positivity	0.04	0.44	2.3	7.66	19.86	9.69	3.96	4	5.44	18.11	27.36

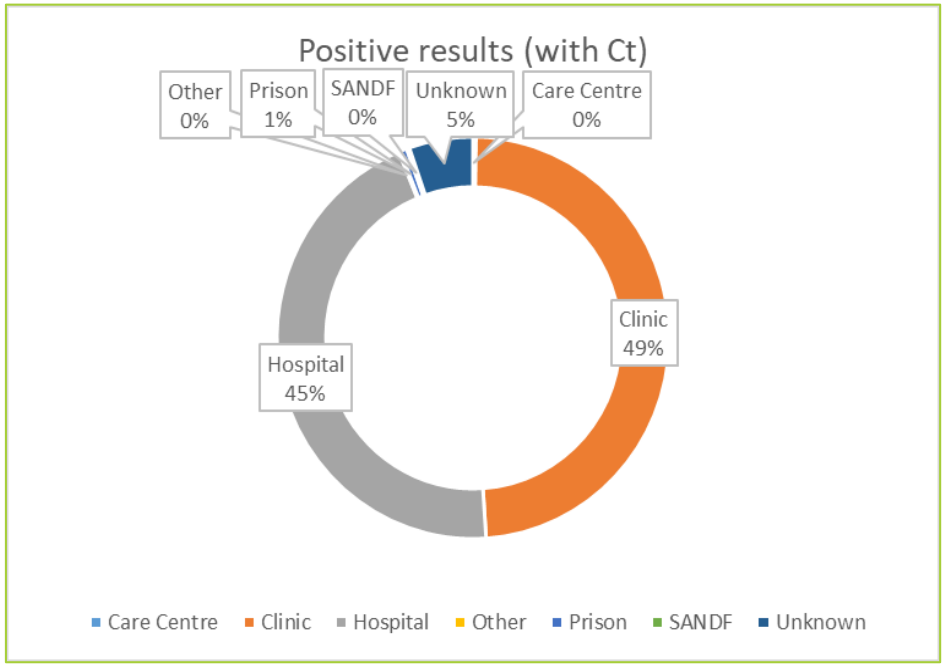
Increase in VL: Median Ct by facility type

- Similar distribution of assays receiving specimens from “clinic” and “hospital”
- Ct lower in 2nd wave
- By January in spite of increasing positivity, the Ct trend is upward (lower viral load)

Median Ct (N-Gene) by Facility Type	JUL	DEC	Delta
Clinic	29.9	28.7	1.2
Hospital	29.7	28.8	0.9

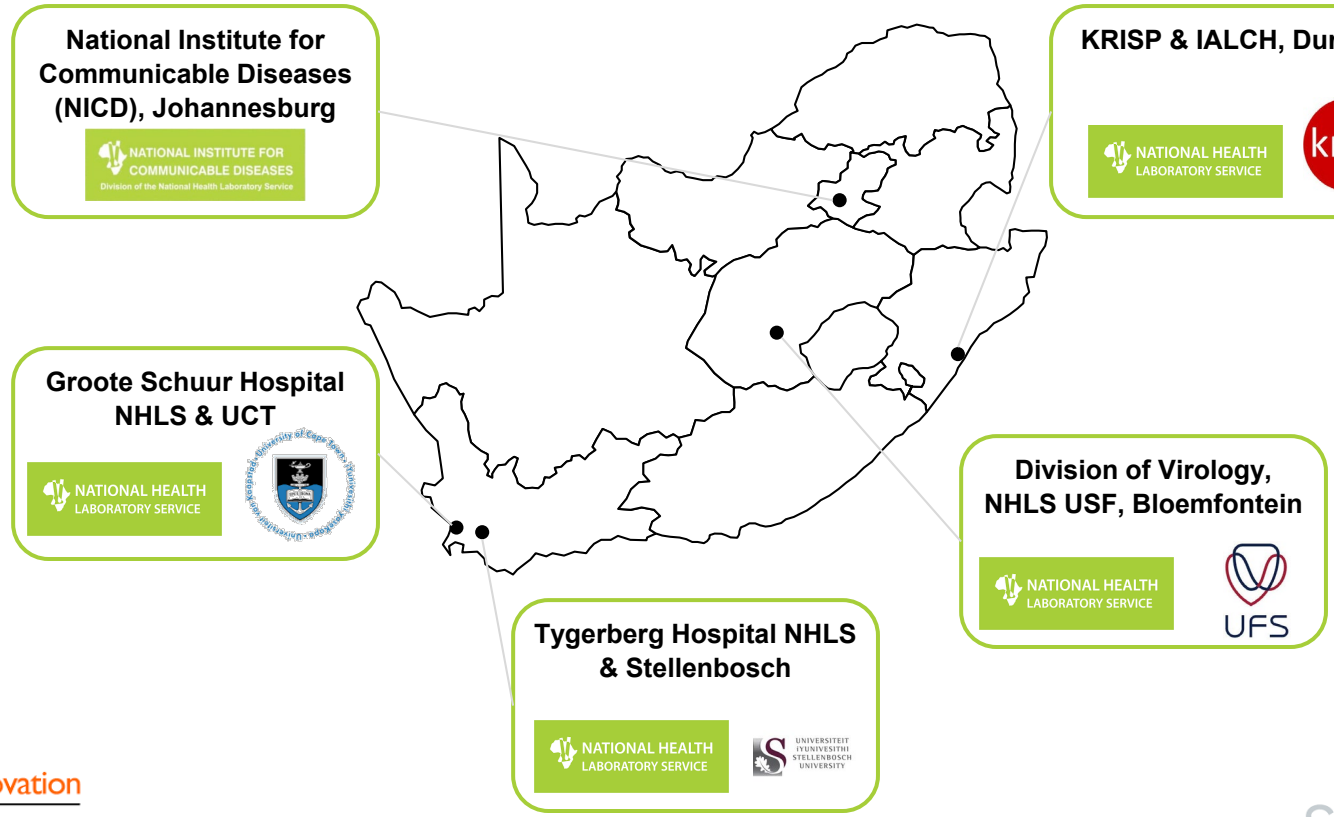






3. Discovery of new variant

Network for Genomic Surveillance in South Africa



science & innovation
Department:
Science and Innovation
REPUBLIC OF SOUTH AFRICA

Supported by the DSI and the SA MRC

saMRC advancinglife

Msomi N, Mlisana K, *et al.* Lancet Microbe 2020

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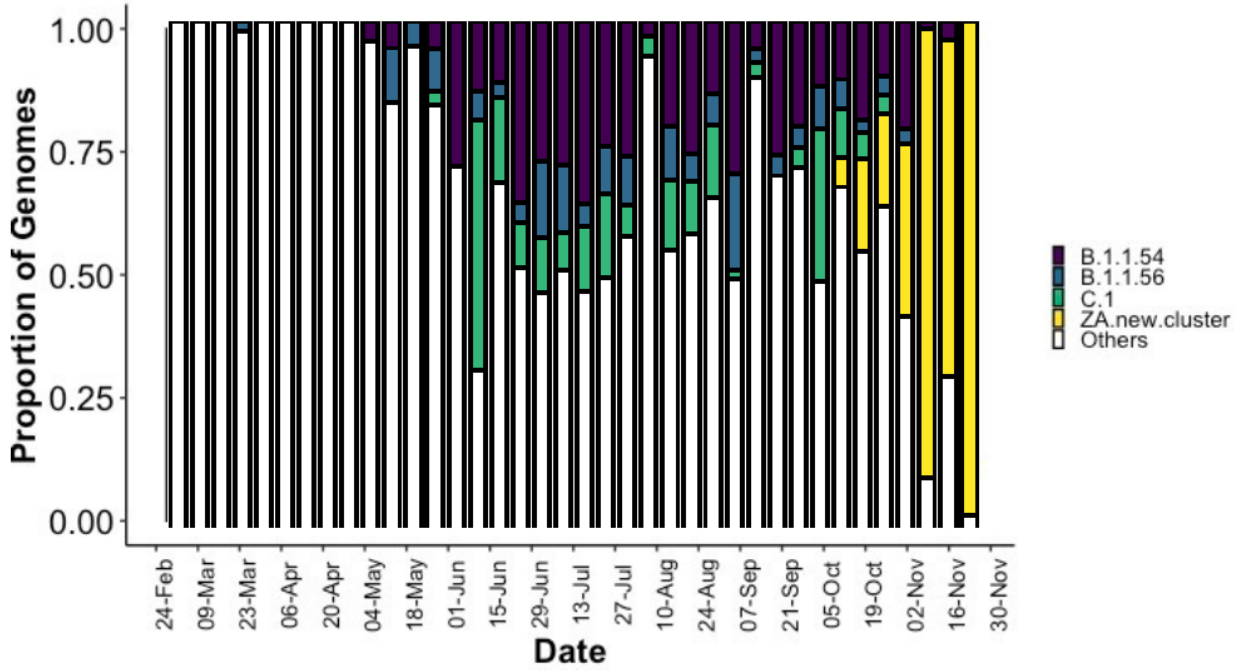
NATIONAL INSTITUTE FOR COMMUNICABLE DISEASES
Division of the National Health Laboratory Service

Identification and tracking of novel SARS-CoV-2 lineage in South Africa

New lineage rapidly become the dominant



Since early November, the new lineage has rapidly become the **dominant lineage** in the sampled locations
(>90% of sequences in week beginning 16 Nov)

UKZN INSPIRING GREATNESS

UNIVERSITY OF KWAZULU-NATAL
INYUVESI YAKWAZULU-NATALI

krisp

A NEW SARS-COV-2 LINEAGE WITH MULTIPLE SPIKE MUTATIONS EMERGE AND SPREAD FAST IN SOUTH AFRICA

Prof. Tulio de Oliveira on behalf of the NGS-SA
Director: KZN Research Innovation & Sequencing Platform (KRISP)
Professor: Nelson R Mandela School of Medicine, UKZN
Associate Professor: University of Washington & CAPRISA

Dr. Tulio de Oliveira, KRISP Minsterial and Media Briefing, 18 December 2021

South African variant

United Kingdom variant

S.501Y.V2

Gene	Nucleotide	Amino Acid
orf1ab	1059C>T	T265I
	5230G>T	K1655N
	10323A>G	K3353R
spike	21614C>T	L18F
	21801A>C	D80A
	22206A>G	D215G
	22287T>A*	L242H*
	22286-22294 deletion*	L242_244L deletion*
	22299G>T	R246I
	22813G>T	K417N
	23012G>A	E484K
	23063A>T	N501Y
	23664C>T	A701V
orf3a	25563G>T	Q57H
	25904C>T	S171L
E	26456C>T	P71L
N	28887C>T	T205I

Summary:
15 lineage defining mutations
8 in spike
1 deletion

B.1.1.7

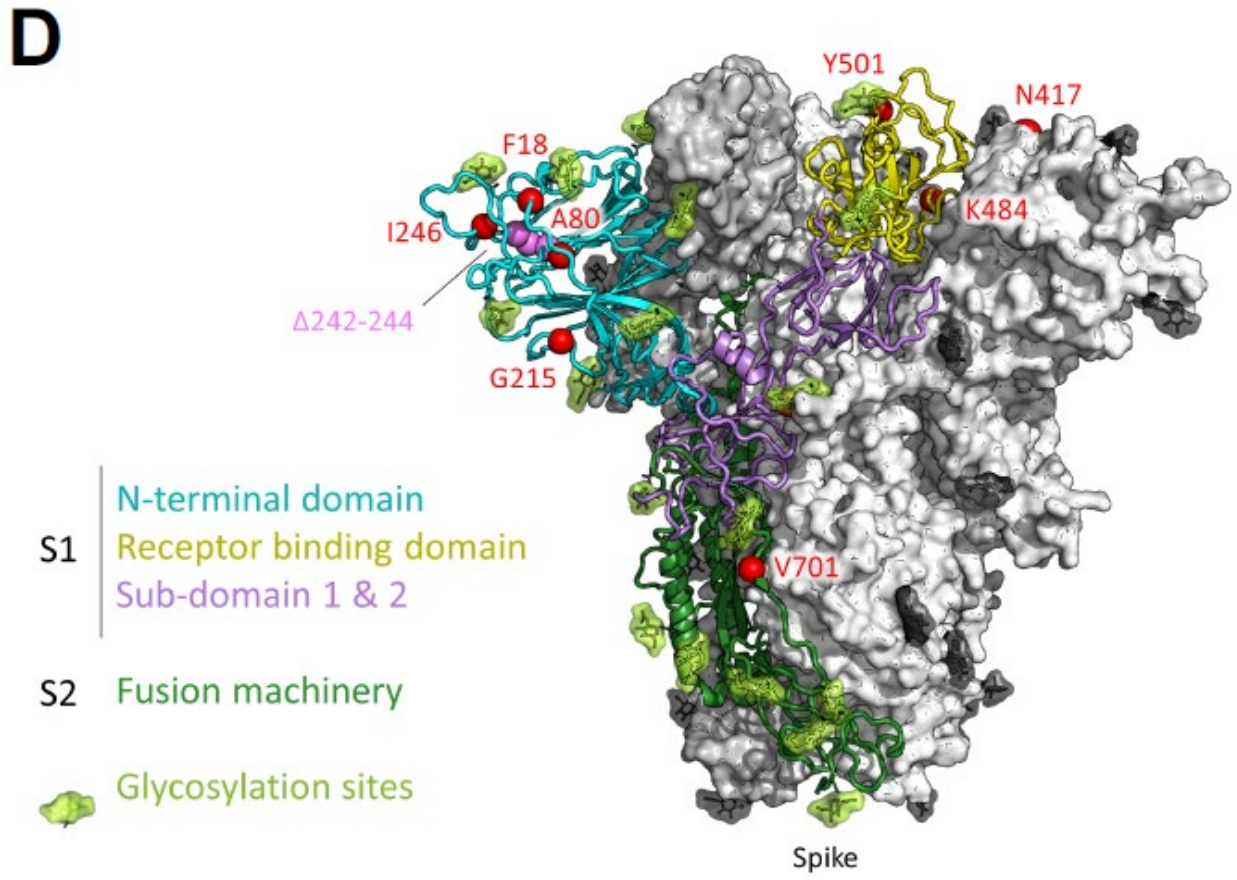
gene	nucleotide	amino acid
ORF1ab	C3267T	T1001I
	C5388A	A1708D
	T6954C	I2230T
	11288-11296 deletion	SGF 3675-3677 deletion
spike	21765-21770 deletion	HV 69-70 deletion
	21991-21993 deletion	Y144 deletion
	A23063T	N501Y
	C23271A	A570D
	C23604A	P681H
	C23709T	T716I
	T24506G	S982A
	G24914C	D1118H
Orf8	C27972T	Q27stop
	G28048T	R52I
	A28111G	Y73C
N	28280 GAT->CTA	D3L
	C28977T	S235F

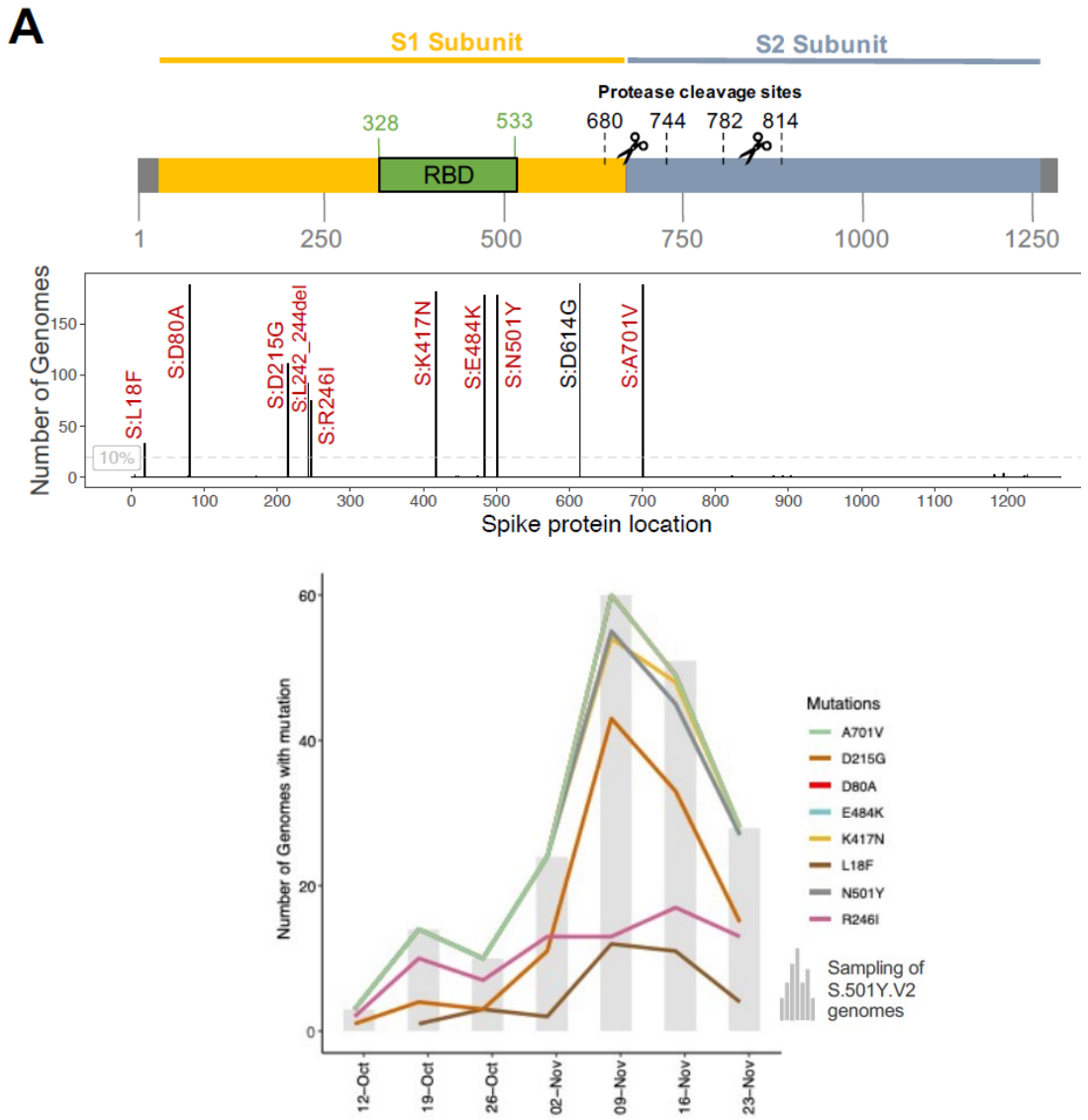
Summary:
14 lineage defining mutations
6 in spike
3 deletions (1 in spike)

Receptor binding domain (RBD). Some experimental data on enhanced binding and nAb resistance.

Thermo Fisher assay S-target dropout

501Y.V2 Structure: Tegally et al, 2021





Source: https://www.medrxiv.org/content/10.1101/2020.12.21.20248640v1

4. Antigen testing overview

Available WHO approved COVID-19 Antigen RDTs

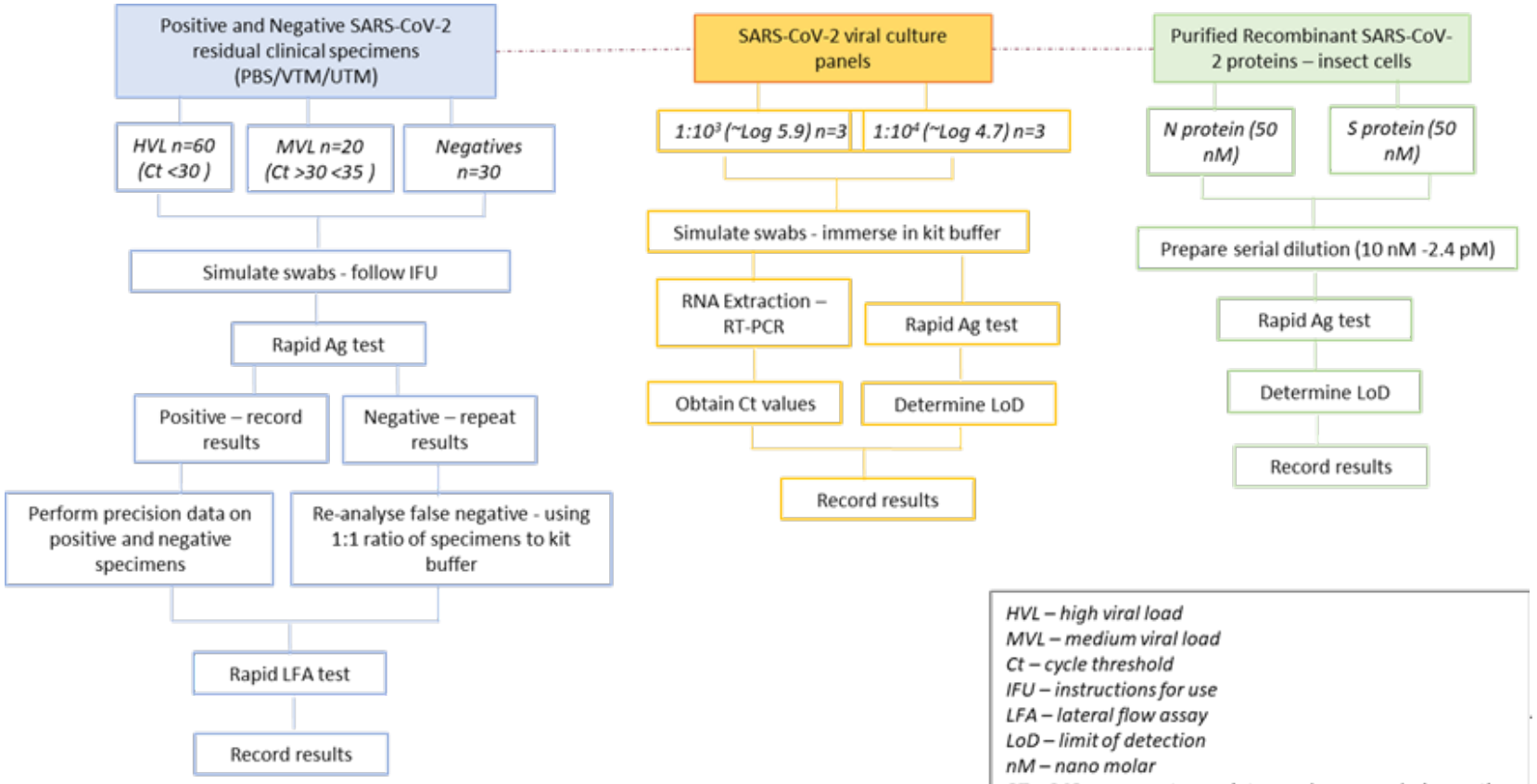
- High-performance SARS-COV-2 antigen tests are flexible tests to deploy across settings to reduce COVID-19 transmission
- There are currently three antigen (Ag) tests for SARS-CoV-2 that are being marketed in Low- and Middle-Income Countries **("LMICs")**
- WHO recommends use of Ag rapid tests for COVID-19 diagnosis if they **meet minimum performance standards (≥97% specificity and ≥80% sensitivity)**

Approved COVID-19 diagnostics[1]	*Test type*	*Test characteristics[2]*
Abbott	• **Ag-RDT**	• Spec: 99.8%, Sen: 91.4% • TAT[3]: ~15 min/test
SD Biosensor	• **Ag-RDT**	• Spec[4]: 97.6[B] - 99.3%[G] Sen[4]: 76.6[G] - 88.7%[B] • TAT: ~15 min/test
Lumira	• **Ag POC device**	• Spec: 96.6%, Sen: 97.6% • TAT: ~12 min/test • Throughput: 5 tests/hr
Various suppliers	• **NAAT (PCR)**	• Gold standard, but high TATs limit usefulness of results[5]

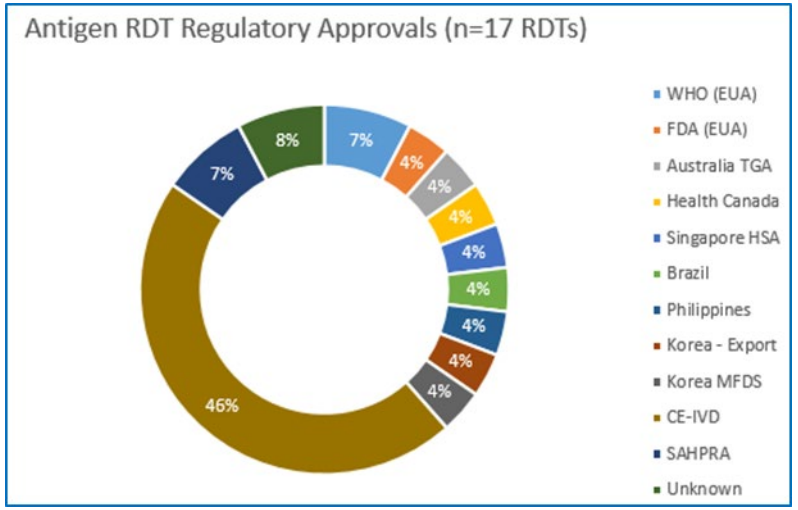
1. Includes COVID-19 tests approved by a stringent regulatory authority (WHO, US FDA, and/or CE) as of Sept-2020.
2. Source: Data from manufacturer IFU.
3. TAT = turnaround around time.
4. Ranges represent data from Germany (low-prevalence) and Brazil (high-prevalence), respectively; performance expected to fall within this range.
5. Data suggests that TATs >2 days have little to no impact on reducing transmission, however in many SSA countries average turnaround times are 2-5 days or more (further detail on slide 10).

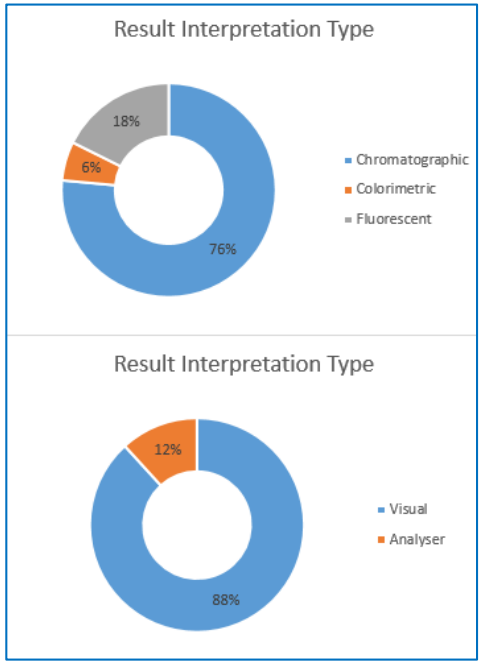
5. Antigen RDT Validations

Lab Antigen Testing Validation Streams for SAHPRA



HVL – high viral load
MVL – medium viral load
Ct – cycle threshold
IFU – instructions for use
LFA – lateral flow assay
LoD – limit of detection
nM – nano molar
RT – PCR – reverse transcriptase polymerase chain reaction



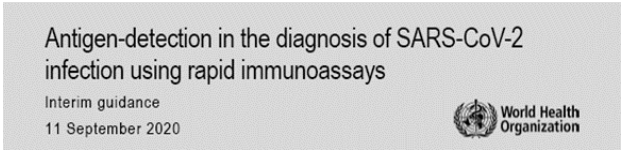


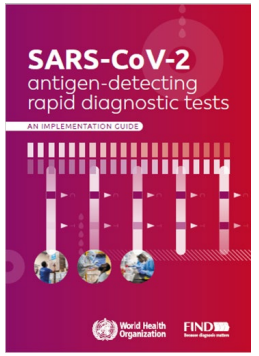
iLEAD
INNOVATION: LAB ENGINEERED ACCELERATED DIAGNOSTICS

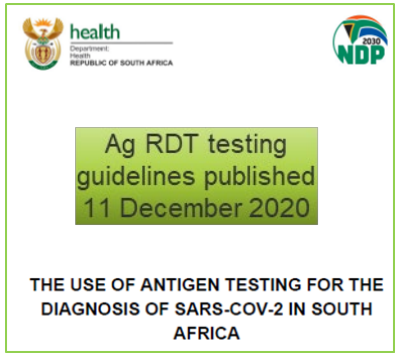
Antigen test evaluations in progress

Antigen testing evaluations conducted at NHLS	Update
Reports completed and submitted to SAHPRA (n=7)	• SD Biosensor • Rapigen (Biocredit) • Abbott Panbio • PCL Antigene • Nowcheck COVID-19 Ag test • BD Veritor Ag assay • Camtech COVID-19 Ag test \
Validations in progress (n=5)	• Sienna COVID-19 Antigen Rapid Test Cassette • Vivacheck SARS CoV-2 rapid antigen test • LumiraDx • Nanjing Norman Biological Technology Co., Ltd • Zhejiang Orient Gene Biotech
Pending evaluations (using existing panels) n=8	• BIOHIT Healthcare (Heifei) • GENEDIA W COVID-19 Ag • AMP SARS CoV-2 Rapid antigen test • Boson Biotech • Humasis COVID-19 Ag Test • Nadal Covid-19 Antigen rapid test • OnSite ® COVID-19 Ag Rapid Test • Rapigen (SAHPRA requested evaluation)

6. Antigen testing use cases and testing algorithms







Ag Testing Use Cases

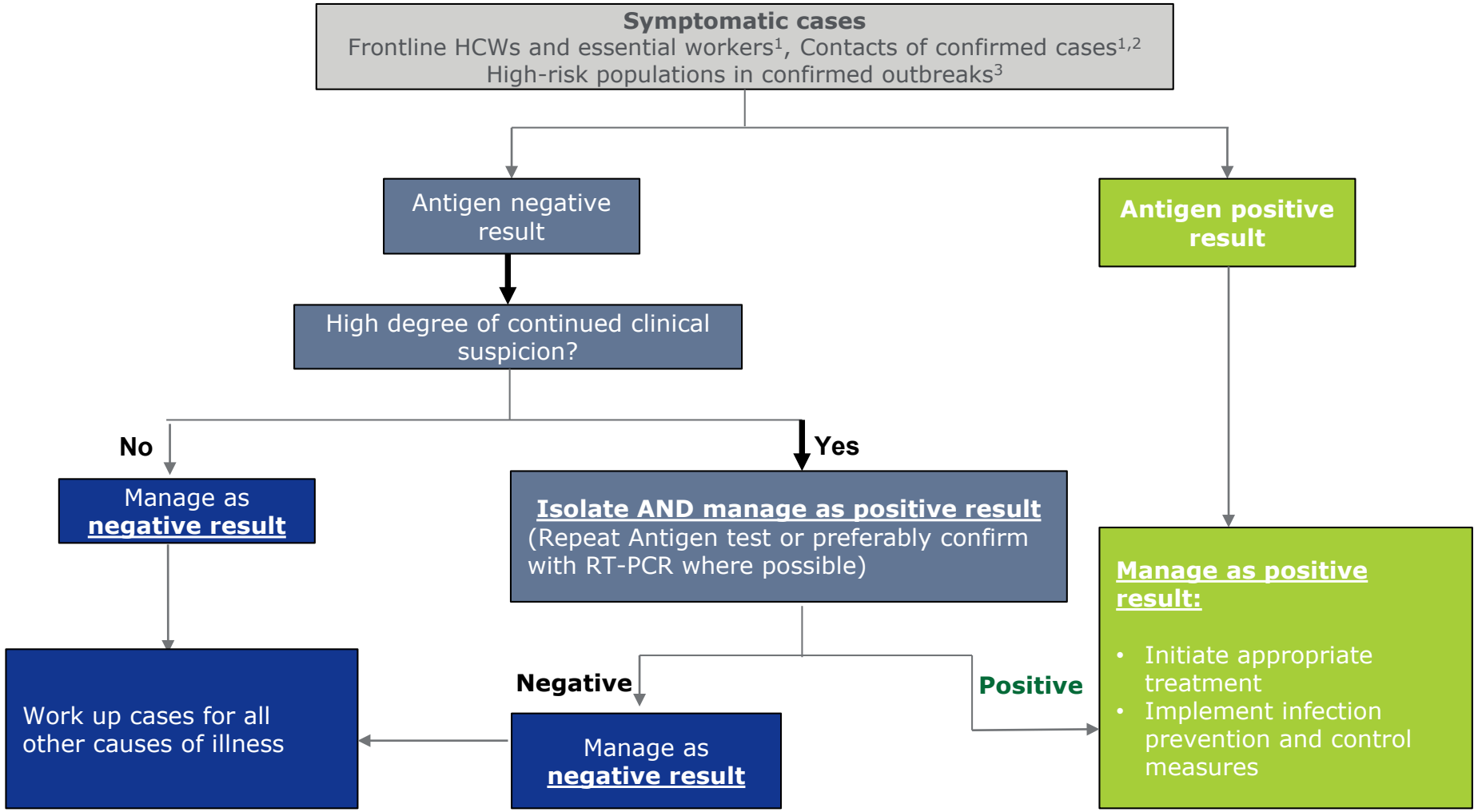
Use cases with the greatest impact on epidemic management goals should be prioritized

Algorithms in place

Testing Scenario	**Diagnosis in populations with known risk or exposure**	**General population screening**
Relevant WHO scenarios	*Confirmed outbreaks, suspected outbreaks, regions of widespread community transmission, asymptomatic contacts*	*Low-prevalence / general population screening, monitoring disease incidence, points of entry, etc.*
Location of Testing	• **Health facilities** (clinics, hospitals, treatment centers, etc.) • **Contact tracing** (community or home) • **Closed / semi-closed settings (care homes, prisons, etc.)**	• **Ports of entry** (e.g. land borders, airports, etc.) • **Schools and workplaces** • **Targeted population screening** • **Surveillance**
Target populations	• **Patients with severe presentation** • **Frontline HCWs and essential workers** (symptomatic & asymptomatic) • **Symptomatic cases w/ high transmission risk** • **Contacts of confirmed cases** (symptomatic & asymptomatic)	• **Travelers** • **Teachers, students, and administrative staff** • **Factory workers, government employees, etc.** • **Non-COVID inpatients** (e.g. elective surgeries, hospitalized non-COVID patients, etc.) • **Other general populations** (e.g. random community screening, surveillance)

Algorithm - Populations with known risk or exposure

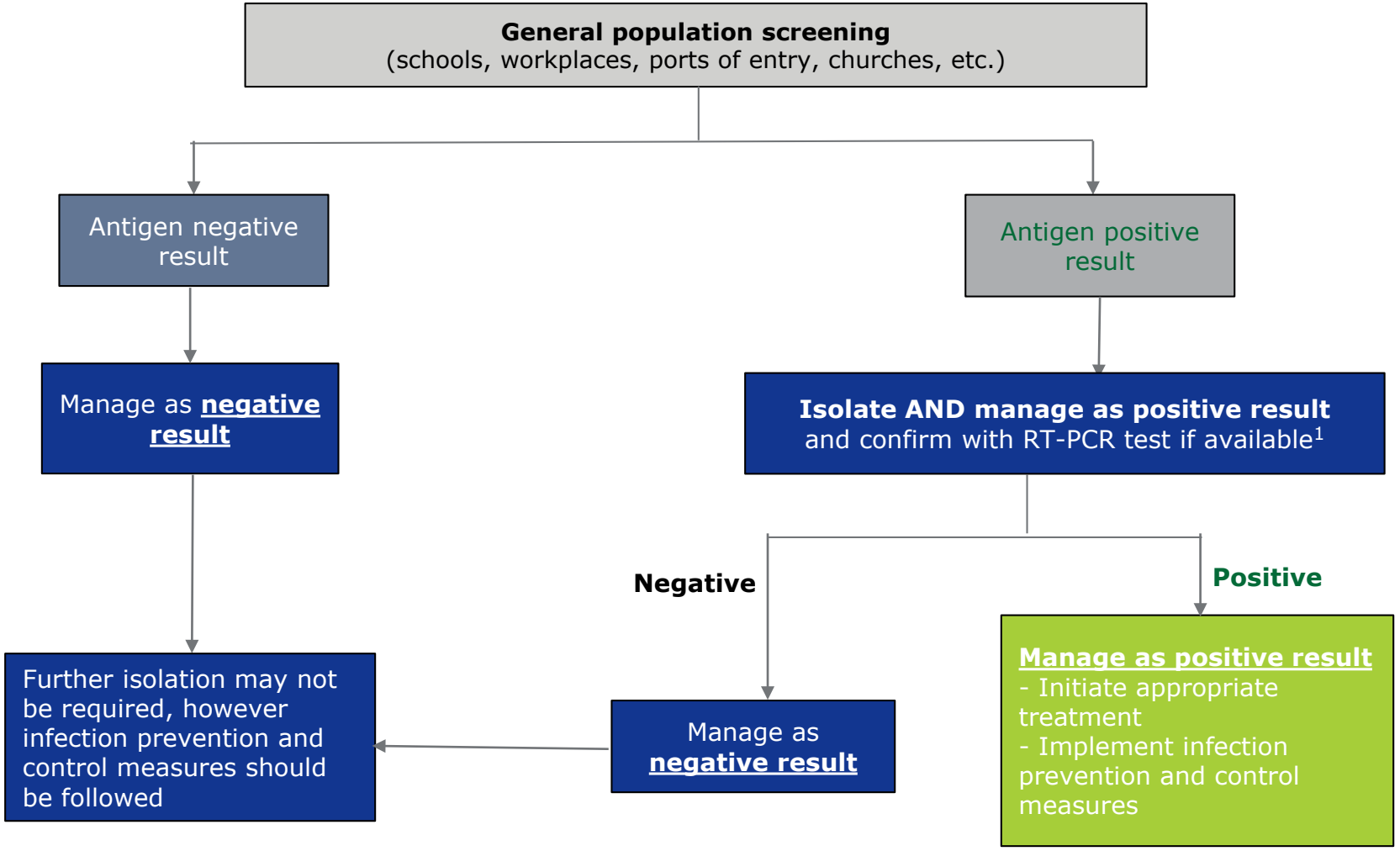
Algorithm for populations with known risk or exposure in suspected or confirmed outbreak (health facilities, contact tracing, and closed / semi-closed settings)



- [1.] Symptomatic & asymptomatic
- [2.] Follow local guidelines on isolation of contacts
- [3.] Includes elderly, people with co-morbidities, populations in closed-settings (prisons, care homes, etc.)
- [3.] As determined by clinician based on patient clinical history. As per WHO "Continued clinical suspicion can, for example, be the absence of another obvious etiology, the presence of an epidemiological link, or suggestive clinical finding (e.g. typical radiological signs)."

Algorithm - General population screening

Algorithm for general population screening where there is no suspected or confirmed outbreak (schools, workplaces, ports of entry, churches, etc.)



- [1]More evidence is needed in support of serial testing for antigen tests and maybe an option. Follow country guidelines.

Antigen testing at open border posts

NHLS COVID Mobile Laboratory

- 72 ports of entry in the country (land, sea and air) that open and close according to lockdown restrictions.
- Mobile laboratories are used for testing at all open ports: **agile system**
  - Of 53 land ports, 20 are currently open with mobile laboratories deployed to provide on-site antigen testing.
  - Of 11 airports, 2 are currently open with both PCR and antigen provided by the mobile laboratories.
    - 3 airports are reopening and being brought online.
- ALL mobile laboratory results (PCR and antigen) are reported in real time
- Travelers receive results immediately via Short Message System (SMS)

OR Tambo International Airport

Limpopo Beit Bridge border posts testing station

Approach to Antigen testing beyond PCR

NHLS COVID Mobile Laboratory

NHLS Mobile Laboratory

Generator

Sample collection station 1

Sample collection station 2

LIS Registration Station

Province	Distribution
Eastern Cape	13
Free State	10
Gauteng	12
KwaZulu Natal	10
Limpopo	6
Mpumalanga	4
North West	4
Northern Cape	6
Western Cape	5
Grand Total	70

PCR Testing – GeneXpert and BioFire

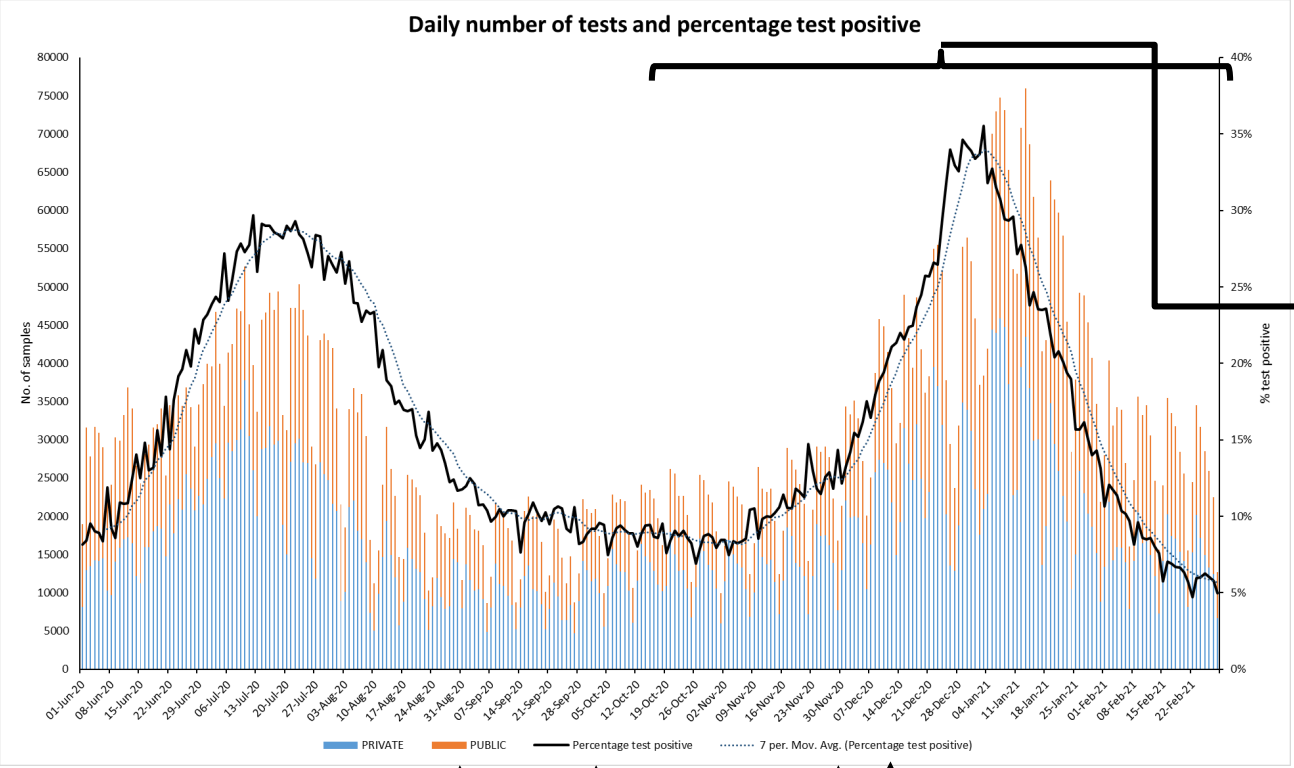
Antigen Testing – SD Biosensor and Panbio

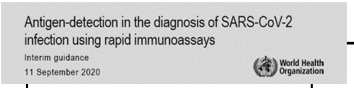
All mobile laboratories have **full connectivity**

Mobile staffing: driver-clerk and two nurses per van. Mobiles with PCR testing also have a technologist.

SARS-CoV-2 Testing: South Africa

SARS-CoV-2 diagnostic tests: June 2020-March 2021

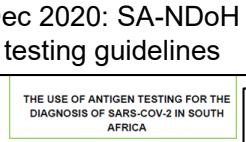




11 Sept 2020: WHO interim guidance on Ag-testing

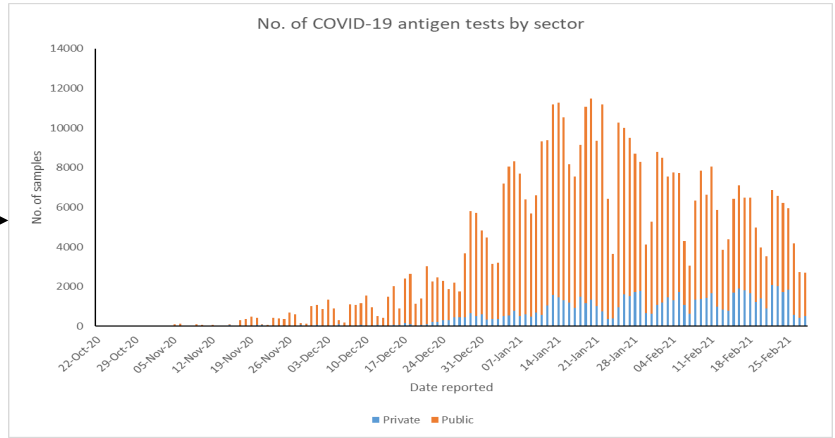
11 Oct 2020: Rollout of Ag testing at points of entry to SA

11 Dec 2020: SA-NDoH Ag testing guidelines



21 Dec 2020: WHO-FIND Ag testing implementation guidelines

SARS-CoV-2 Ag tests: October 2020-March 2021



- Private 15%
- Public 85%

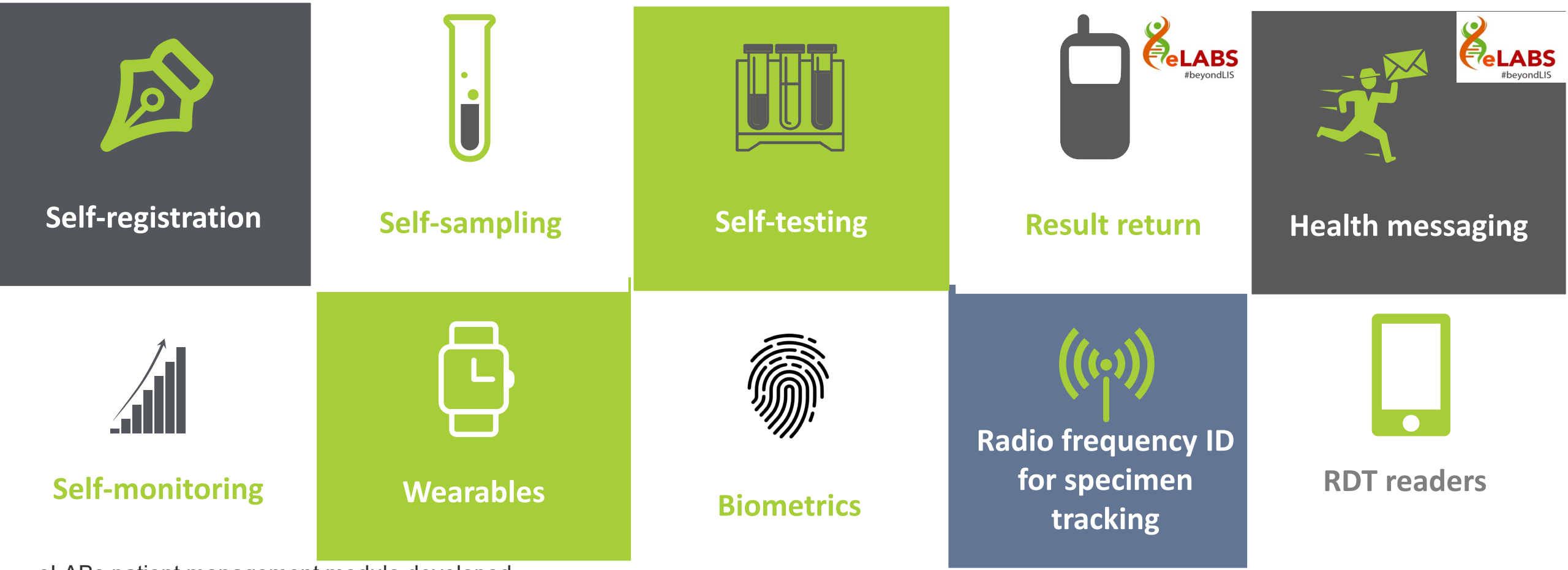
	Total tests			
Province	No. tests	Percentage tested	No. positive	Percentage test positive
EASTERN CAPE	68 479	14%	7 570	11,1%
FREE STATE	23 081	5%	1 877	8,1%
GAUTENG	46 366	10%	3 613	7,8%
KWAZULU-NATAL	221 325	46%	24 440	11,0%
LIMPOPO	6 889	1%	408	5,9%
MPUMALANGA	38 973	8%	938	2,4%
NORTH WEST	22 496	5%	2 624	11,7%
NORTHERN CAPE	4 415	1%	205	4,6%
WESTERN CAPE	35 817	8%	5 959	16,6%
UNKNOWN	9 286	2%	447	4,8%
Grand Total	477127	100%	48081	10,1%

7. Challenges with Antigen Testing

Implementation

Stakeholder Engagement	• Delays at CLI phase; responsibility/re-imbursement
Training	• Alignment on Used TOT ASLM modules: 23 certified, >160 master trainers • Modified to local context, videos
Quality Indicators	• Understanding training requirements and implementing the training programmes across all sites nationally
Supply chain	• Challenges getting materials and reagents into the country due to movement restrictions and logistics issues • Regulatory delays
HR	• Critical staff (lab technical and supporting) contracting COVID-19, amidst the current shortages of people • Data admin issues delay
Scaling up and capability	• Different lab /clinical groups may need assistance in scaling up and building capabilities required

Future-proofing testing: digital patient-centric care



- eLABs patient management module developed
- eLABS Ag-testing module developed
- eLABS scale up in over 1500 facilities in SA and 900 facilities in Zambia
- RDT reader study published
- MVP for COVID-19 self-registration and self-sampling scoped with BMGF

Future of testing

1. Remain agile and flexible with testing profiles
2. Rapid Expansion of testing: through public and private sectors
3. Use of spare capacity for HPV, STIs, oncology: Improved agility
4. Expansion of POCT strategy: Best use case
5. Maintenance of laboratory sites: Multi-disciplinary testing
6. Ongoing quality monitoring: Real-time
7. Re-evaluation of certain assays as variants emerge
8. Rapid PCR development as variants emerge
9. Increased genomic testing capacity
10. Patient centric, own data, own monitoring, O_2 sats monitoring
11. Self-collection and self-testing: Healthcare worker safety

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- National Department of Health
- Ministerial Advisory Committee
- NHLS and the National Priority Program
- NHLS QAD
- Department of Molecular Medicine and Haematology, Wits University,
- Virology and TB Expert working groups
- Funders
- Clinical partners
- Commercial collaborators
- Innovators

SARS-CoV-2 B.1.351 (501Y.V2)

Molecular

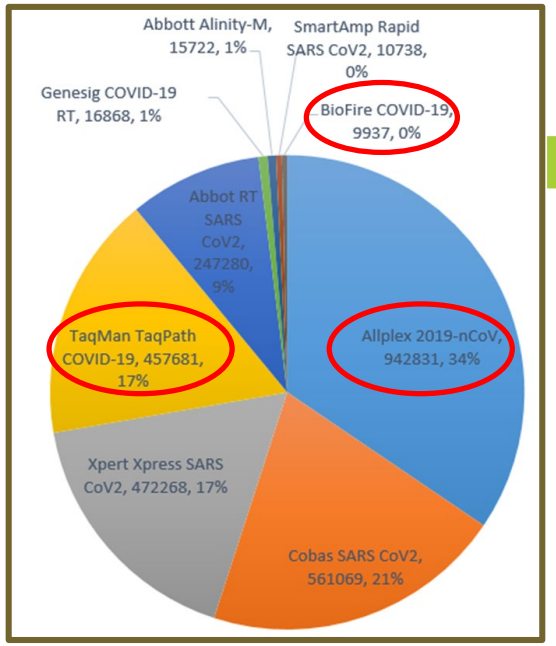
- Variant isolates to be sent from AHRI (mid-February) and will be cultured at CBTBR
- 2 variants
  - 001 with the full complement of mutations including L18F
  - 002 with a deletion in the Furin site from Vero E6 passage
- Culture panels (dilution; original and novel variants) will be shared with testing laboratories
- Impact of variants on diagnostic assays in use will be assessed
  - Novel assay evaluations will include original and novel culture isolates
- CQM of Ct values and gene-dropout
- Sharing of patient specimens for genomic studies

Serology

- Assess approved tests using residual serum/plasma (vaccine group)
- Increase serology specimen biorepository (national)

Antigen

- Currently no Ag tests use the S-protein
- Discussions with PATH re use of protein panels



MRC Variant Consortium

NHLS VEC

- Vaccines
- Immunology & Virology
- Genomics
- **Diagnostics**
- Epidemiology

Key Variant Diagnostics Collaborators

NHLS virology expert committee

National Institute of Communicable Diseases

Kwazulu-Natal Research Innovation and Sequencing Platform

Africa Health Research Institute

CBTBR – Bavesh Kana and team

Private laboratories

PATH

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