Africa CDC Interim Guidelines on Rapid Antigen Testing

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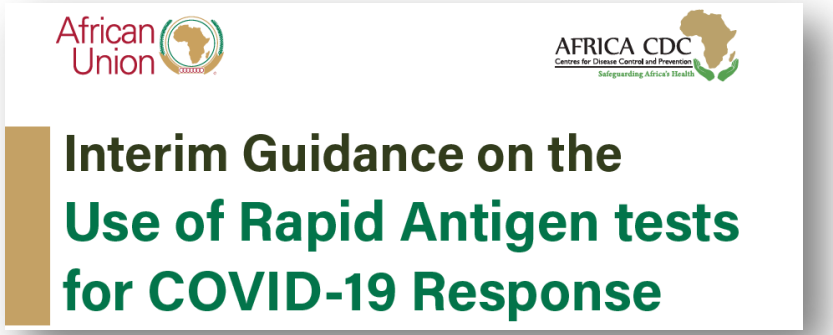
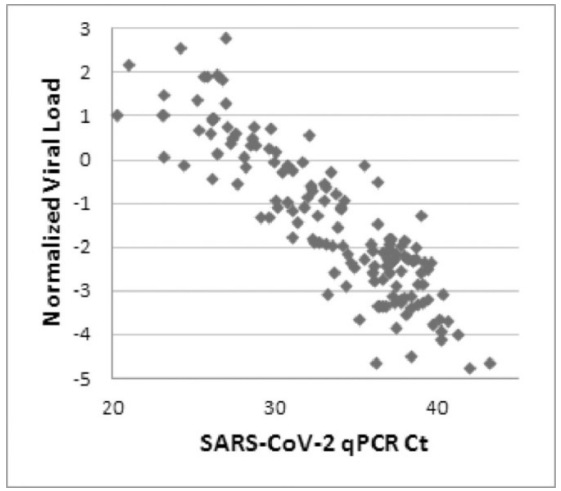
Interim Guidance on the Use of Rapid Antigen tests for COVID-19 Response (Africa CDC)

- RDTs can be used outside of laboratory conditions, at/ or near the point of care.
- Two types of COVID-19 rapid diagnostic tests (RDTs): **Antigen tests (Ag-RDT)** & **Antibody tests (Ab-RDT).**
- Ag-RDTs can be considered as alternatives to NAAT for direct detection of SARS-CoV-2 virus for diagnosis of early COVID-19.
- Africa CDC in collaboration with partners released interim guidance on antigen testing (https://africacdc.org/download/interim-guidance-on-the-use-of-rapid-antigen-tests-for-covid-19-response/)
- **The guidance in this document refers only to COVID-19 Ag-RDTs.**

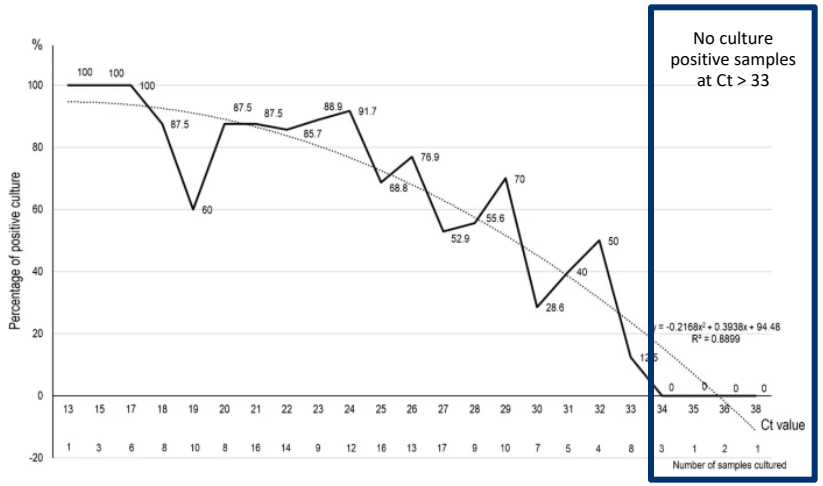


Antigen testing identifies cases at highest risk of transmission – critical for stemming the spread of the epidemic

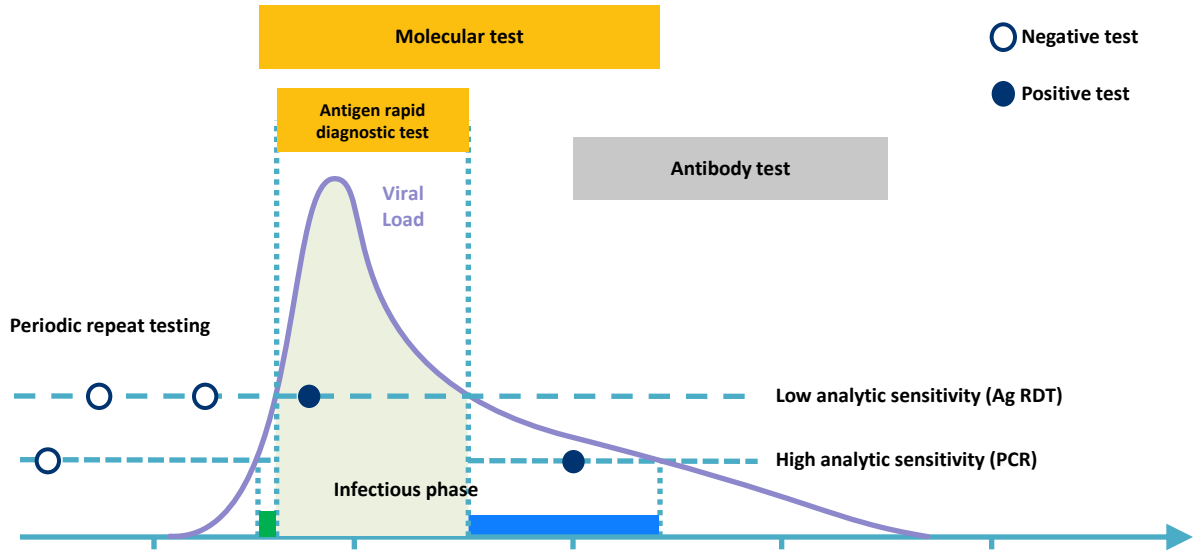
Viral load inversely correlated with Ct value[1]



Percentage of samples testing positive relative to Ct value of sample[2]



Antigen test sensitivity highest at peak viral concentration



Antigen testing most sensitive when viral concentration is high (low Ct value) - **identifies samples with the highest risk of transmission.**

Antigen sensitivity lower for low viral concentration (high Ct value) correlated with negative cultures – **lowest risk for transmission.**

1. Dahdouh, E. et al. Ct values from SARS-CoV-2 diagnostic PCR assays should not be used as direct estimates of viral load. Journal of Infection. (2020).

2. La Scola, B. et al. Viral RNA load as determined by cell culture as a management tool for discharge of SARS-CoV-2 patients from infectious disease wards. Eur J Clin Microbiol Infect Dis 39, 1059-1061 (2020).

Africa CDC guidance on SARS-Cov-2 Ag-RDTs allows for their use in any setting, subject to certain conditions such as minimum performance standards

- SARS-CoV-2 Ag RDTs >80% sensitivity and >97% specificity should be used, with a broader number of use cases and settings accessible for higher performing products
- Introduction of high specificity tests (>99%) is preferred in all settings and is particularly important in low prevalence settings
- SARS-CoV-2 Ag RDTs can be deployed in any setting, though use cases with the greatest impact on epidemic management goals should be prioritized
- SARS-CoV-2 Ag-RDTs should be deployed as first-line test in contexts where NAAT is not feasible (e.g. long TAT or lack of access) or where turnaround times are too long for clinical utility (e.g. >24 – 48 hours)

Considerations Context is CRITICAL in Ag-RDT implementation

- COVID-19 Ag-RDT with ***high specificity (>99%) can be deployed in any setting*** but may be of increased importance in settings where the consequences of a false positive are impactful, either due to needs for epidemic management or economic consequences.

- **Proper interpretation of antigen results** within these use cases is important for clinical management of cases and for assessing them SARS-CoV-2 epidemic.

- The **accuracy of results depends largely on the context** within which the results are interpreted.

- Therefore, the management of results within a given setting should consider the tolerance and **consequences of misdiagnosis, either false positive or false negative**.

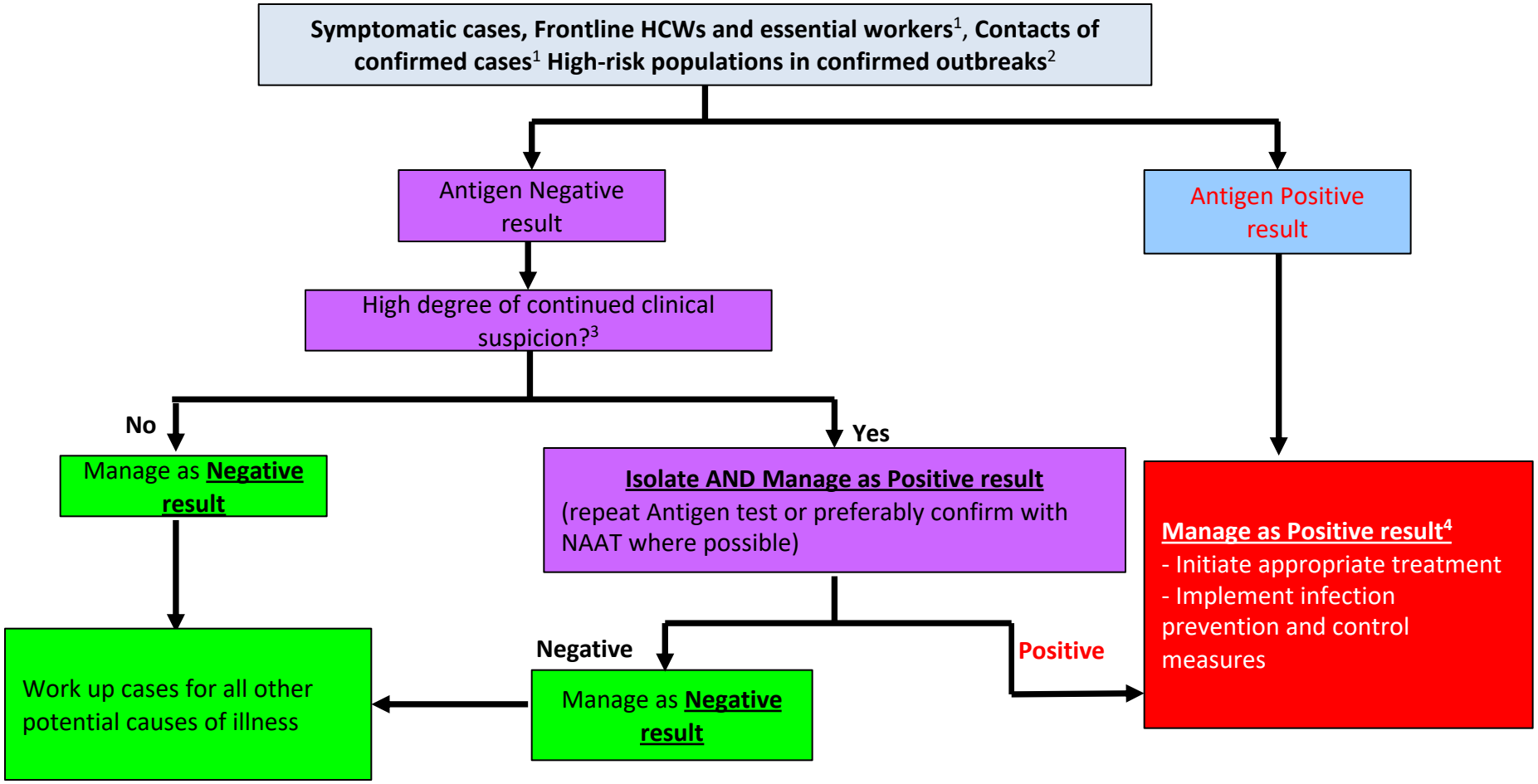
Testing Strategy: Population with known risk or exposure

Testing Scenario	**Diagnosis in populations with known risk or exposure to suspected or confirmed outbreak**
Relevant Africa CDC scenarios	***Confirmed outbreaks, suspected outbreaks, regions of widespread community transmission, asymptomatic contacts, Frontline healthcare workers, essential workers, high risk population***
Location of Testing	• **Health facilities** (clinics, hospitals, treatment centers, etc) • **Contact Tracing Response teams** (community or home) • **Closed / semi-closed settings (care homes, prisons, etc)**
Target populations	• **Patients w/ severe presentation** • **Frontline HCWs and essential workers** (symptomatic & asymptomatic) • **Symptomatic cases w/ high transmission risk** • **Contacts of confirmed cases** (symptomatic & asymptomatic)

Testing Strategy: General Population screening

Testing Scenario	**General population screening where there is no suspected or confirmed outbreak**
Relevant Africa CDC scenarios	***general population screening, monitoring disease incidence, points of entry, educational institutions, workplaces, religious institutions***
Location of Testing	• **Ports of entry** (e.g. land borders, airports, etc) • **Educational institutions** • **Religious institutions** • **Workplaces** • **Targeted population screening**
Target populations	• **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)

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



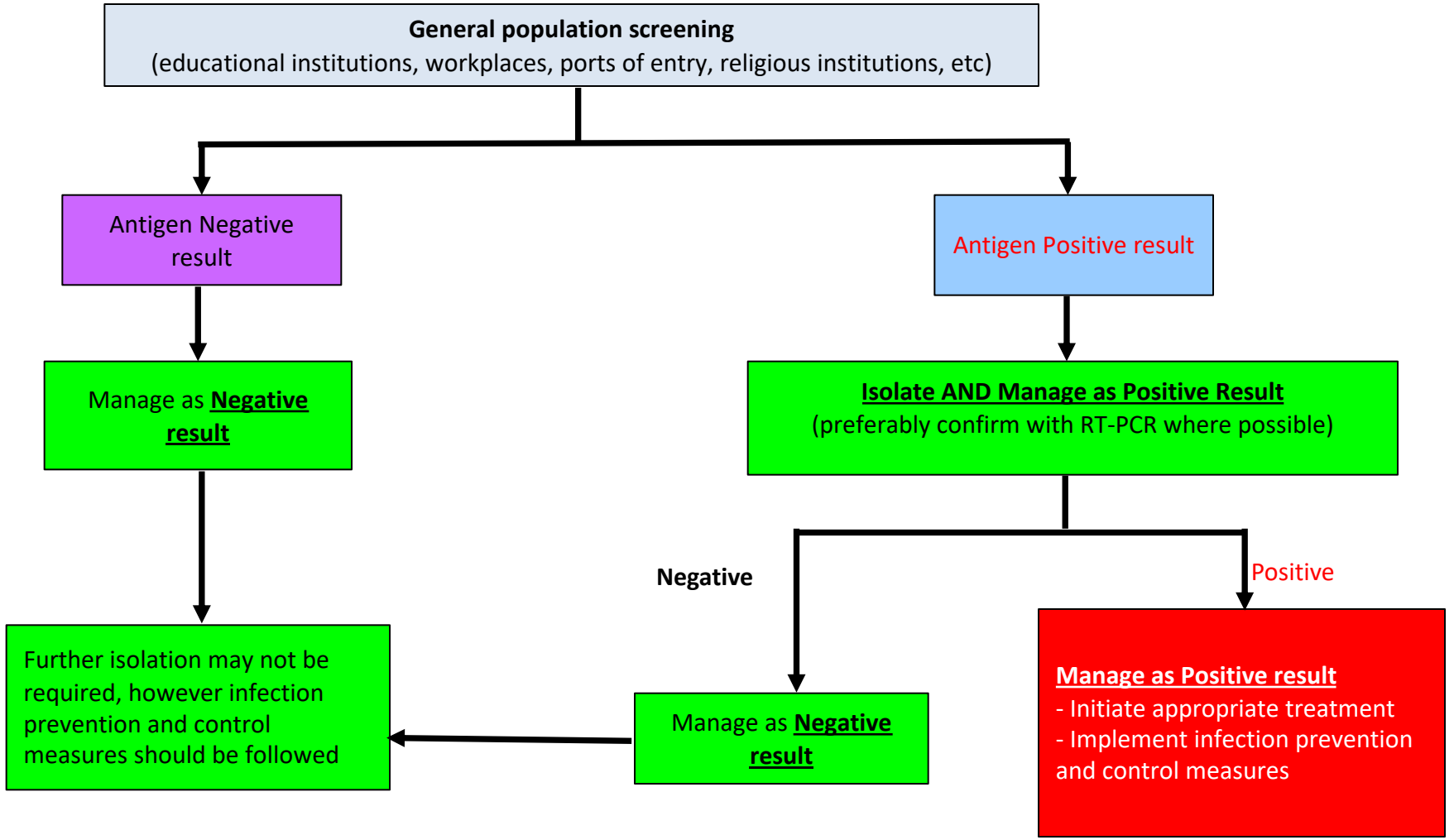
1. Symptomatic & asymptomatic 2. Includes elderly, people with comorbidities, populations in closed-settings (prisons, care homes, etc) 3. As determined by clinician based on patient clinical history. As per WHO "Continued clinical suspicion can, for example, be the absence of another obvious etiology, the presence of an epidemiological link, or suggestive clinical finding (e.g. typical radiological signs)." Special considerations for contacts 4. Special considerations for healthcare workers and frontline workers

Special Considerations for close contacts

- **Close Contacts**:
  - A negative result may not imply that there is no infection as they can still be in the pre-infectious phase,
  - thus they should be considered as high-degree clinical suspicion and isolated accordingly.

- **HCW (Including Lab staff)**:
  - Regular screening recommended where community spread is detected
  - Areas with limited-to-no suspected or confirmed outbreaks, a positive result should be interpreted with caution due to low likelihood of positive results
    - Re-test with Ag-RDT or preferably confirm with NAAT where possible
    - If neither is possible, then isolate and manage as presumptive positive case

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

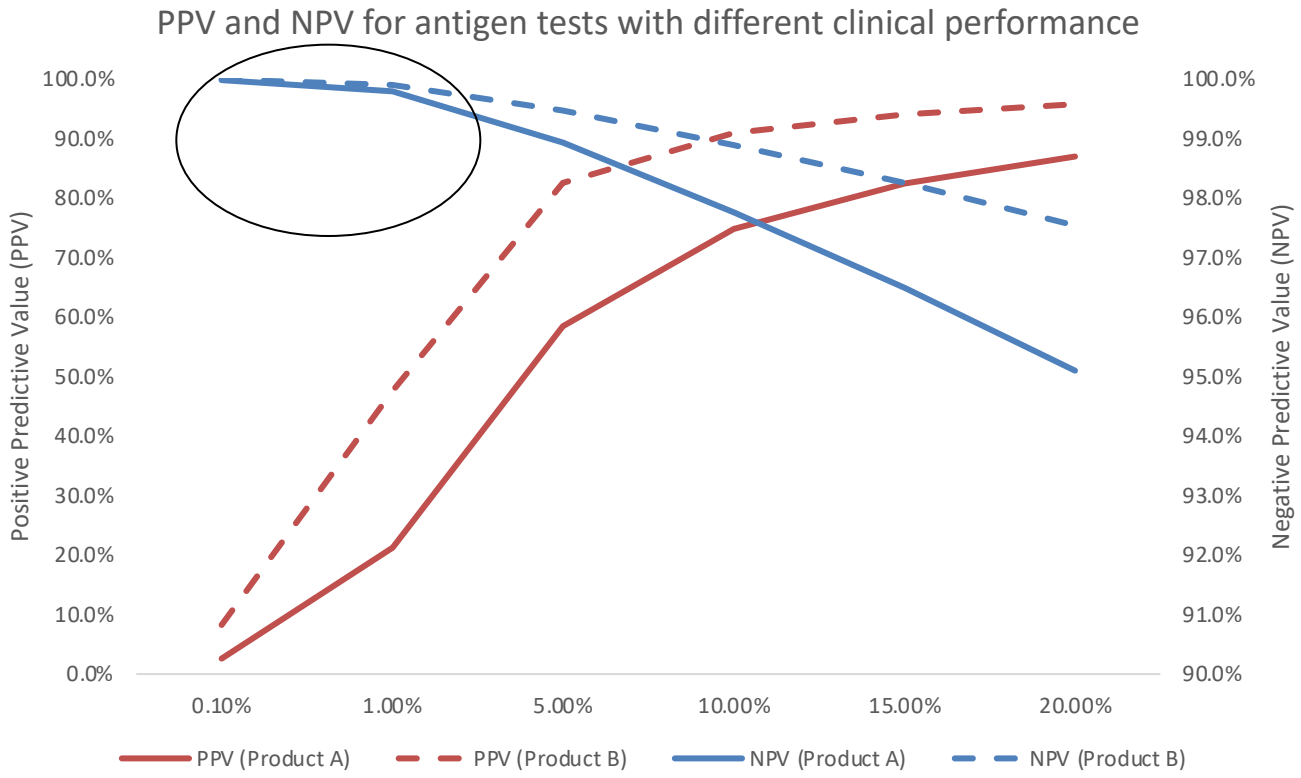


[1]More evidence is needed in support of serial testing for antigen tests and maybe an option. Follow country guidelines.

Other Special considerations

- Routine screening in semi-closed settings (high-risk environments)
  - Education Institutions
  - Workplaces that provide critical services and are important for economic activity
- Public health indicators for decision making to inform mitigation strategies
  - Positivity rate WHO recommends 5% threshold; or as low as 3%)
- Quality Assurance and Test performance assessment
- Role of existing RT-PCR programmes
- Training (Africa CDC & ASLM developed training
    - https://aslm.org/courses/covid-19-antigen-training-materials/
- Data Management
- Continuous Learning

With low prevalence, higher probability of false positives, however, at higher prevalence, higher probability of false negatives – dependent on performance



	Sensitivity	Specificity	WHO TPP Performance
Product A	80%	97%	Threshold performance
Product B	90%	99%	Desirable performance

The link between performance and prevalence = predictive value

Annex

Annex : Positive predictive value (PPV) and negative predictive value (NPV) and the number of true positive (TP), false positive (FP), true negative (TN) and false negative (FN) tests in a population of 10 000 with the prevalence of COVID-19 estimated at 5, 10, 20, 30% prevalence and based on recommended performance criteria: sensitivity of 70, 80%, 90% and specificity of 98% and 100%.

Example prevalence target populations	Prevalence (%)	Sensitivity	Specificity	NPV	PPV	TP	FP	TN	FN	No. with disease	No. positive tests	Total
Symptomatic general population; contacts of index case	5	70	98	98	60	350	238	9263	150	500	588	10000
		70	100	98	88	350	48	9453	150	500	398	10000
		80	98	99	63	400	238	9263	100	500	638	10000
		80	100	99	89	400	48	9453	100	500	448	10000
		90	98	99	65	450	238	9263	50	500	688	10000
		90	100	99	90	450	48	9453	50	500	498	10000
Community transmission: Symptomatic patients presenting to health care facilities; contacts of index cases; institutions & closed communities with confirmed outbreaks	10	70	98	97	76	700	225	8775	300	1000	925	10000
		70	100	97	94	700	45	8955	300	1000	745	10000
		80	98	98	78	800	225	8775	200	1000	1025	10000
		80	100	98	95	800	45	8955	200	1000	845	10000
		90	98	99	80	900	225	8775	100	1000	1125	10000
		90	100	99	95	900	45	8955	100	1000	945	10000

sensitivity = false negatives → potential transmissions

specificity = false positives → suggestive (false) outbreaks

The link between performance and prevalence = predictive value

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		90	100	99	95	900	45	8955	100	1000	945	10000

⇩ sensitivity = ⇧ false negatives → potential ⇧ transmissions

⇩ specificity = ⇧ false positives → suggestive (false) outbreaks

Conclusion

- Ag-RDT are likely to have high impact containing the spread of COVID-19
- Africa CDC guidance on SARS-Cov-2 Ag-RDTs allows for their use in any setting, subject to certain conditions such as minimum performance standards
- The accuracy of results depends largely on the context within which the results are interpreted.
- Achieving true herd immunity with vaccinations may take >2 years and thus diagnostics and particularly antigen testing would be needed for managing of the epidemic
- Training, Quality Assurance and Data Management are critical in rolling out Ag-RDTs

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