Africa CDC Interim Guidelines on Rapid Antigen Testing

Sikhulile Moyo (MSc, MPH, PhD)

22 January 2021
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.
- 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\(^1\)

![Graph showing the inverse correlation between viral load and Ct value.](image)

Percentage of samples testing positive relative to Ct value of sample\(^2\)

![Graph showing the percentage of samples testing positive relative to Ct value.](image)

**Molecular test**

**Antigen rapid diagnostic test**

**Antibody test**

**Negative test**

**Positive test**

**Infectious phase**

**Viral Load**

**Low analytic sensitivity (Ag RDT)**

**High analytic sensitivity (PCR)**

**Antibody test**

**Antigen rapid diagnostic test**

**Molecular test**

**Negative test**

**Positive test**

**Infectious phase**

**Viral Load**

**Low analytic sensitivity (Ag RDT)**

**High analytic sensitivity (PCR)**

**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.**

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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

#### Diagnosis in populations with known risk or exposure to suspected or confirmed outbreak

<table>
<thead>
<tr>
<th>Relevant Africa CDC scenarios</th>
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<tbody>
<tr>
<td>Confirmed outbreaks, suspected outbreaks, regions of widespread community transmission, asymptomatic contacts, Frontline healthcare workers, essential workers, high risk population</td>
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<tr>
<th>Location of Testing</th>
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<tr>
<td>Health facilities (clinics, hospitals, treatment centers, etc)</td>
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<tr>
<td>Contact Tracing Response teams (community or home)</td>
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<td>Closed / semi-closed settings (care homes, prisons, etc)</td>
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<th>Target populations</th>
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<tr>
<td>Patients w/ severe presentation</td>
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<td>Frontline HCWs and essential workers (symptomatic &amp; asymptomatic)</td>
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<tr>
<td>Symptomatic cases w/ high transmission risk</td>
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<tr>
<td>Contacts of confirmed cases (symptomatic &amp; asymptomatic)</td>
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</table>
Testing Strategy: General Population screening

General population screening where there is no suspected or confirmed outbreak

**Testing Scenario**

**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)

**Relevant Africa CDC scenarios**
- General population screening, monitoring disease incidence, points of entry, educational institutions, workplaces, religious institutions

*Note: The original content is provided in the image. The summary is a transcription of the key points.*
Testing algorithm for populations with known risk or exposure in suspected or confirmed outbreak (health facilities, contact tracing, and closed / semi-closed settings)

Symptomatic cases, Frontline HCWs and essential workers\(^1\), Contacts of confirmed cases\(^2\) High-risk populations in confirmed outbreaks\(^2\)

- **Antigen Negative result**
  - High degree of continued clinical suspicion?\(^3\)
  - No: Manage as Negative result
  - Yes: Isolate AND Manage as Positive result (repeat Antigen test or preferably confirm with NAAT where possible)

- **Antigen Positive result**
  - Manage as Positive result\(^4\)
    - Initiate appropriate treatment
    - Implement infection prevention and control measures
  - Negative: Manage as Negative result
  - Positive: Manage as Positive result\(^4\)

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).”  
4. Special considerations for contacts  
5. 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)

General population screening
(educational institutions, workplaces, ports of entry, religious institutions, etc)

Antigen Negative result

Manage as Negative result

Antigen Positive result

Isolate AND Manage as Positive Result
(preferably confirm with RT-PCR where possible)

Manage as Negative result
- Initiate appropriate treatment
- Implement infection prevention and control measures

Further isolation may not be required, however infection prevention and control measures should be followed

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/](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

<table>
<thead>
<tr>
<th>Product</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>WHO TPP Performance</th>
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<tbody>
<tr>
<td>Product A</td>
<td>80%</td>
<td>97%</td>
<td>Threshold performance</td>
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<tr>
<td>Product B</td>
<td>90%</td>
<td>99%</td>
<td>Desirable performance</td>
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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%.

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<tr>
<th>Example prevalence target populations</th>
<th>Prevalence (%)</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>NPV</th>
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<th>TP</th>
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sensitivity = false negatives ➔ potential transmissions

specificity = false positives ➔ suggestive (false) outbreaks
The link between performance and prevalence = predictive value

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↓ sensitivity = ↑ false negatives

↓ specificity = ↑ false positives

potential ↑ transmissions

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
Acknowledgements

We acknowledge organizations and individuals that have contributed to the development of the guidance document:

1. Nqobile Ndlovu, African Society for Laboratory Medicine (ASLM)
2. Silver Mashate, ASLM
4. Shaukat Khan, Clinton Health Access Initiative (CHAI)
5. Owen Demke, CHAI
6. Trevor Peter, CHAI
7. Jilian Sacks, Foundation for Innovative New Diagnostics (FIND)
8. Sergio Carmona, FIND
9. Yenew Kebede Tebeje, Africa CDC
10. Abebaw Kebede, Africa CDC

External review was provided by:

1. Rosanna Peeling, London School of Hygiene & Tropical Medicine
2. Adrian Puren, National Institute for Communicable Diseases
3. International Diagnostic Centre, London School of Hygiene and Tropical Medicine
4. National Institute for Communicable Diseases, South Africa
5. Fifa Rahman, Civil Society Representative
6. Wendy Stevens, National Health Laboratory Service, South Africa