COVID-19 Rapid Antigen Testing in Omicron Phase three

- Rapid Antigen tests (RATs) are now the primary form of testing[1]
- A person whose RAT is positive will be considered a probable case and does not need to be verified through a PCR test[2]
- MOH authorised RATs report a range of sensitivity (84-97%) and specificity (99-100%)[1]

Considerations when using RATs in Phase three

- As prevalence of COVID-19 increases:
  - The positive predictive value of RATs will improve
  - However, the negative predictive value reduces, this means we can be less assured a negative test is a true negative
  - This is especially so when used in populations with a high pre-test probability of COVID-19 (e.g. symptomatic household contact)
- People who return a negative RAT should be advised no test is 100%
  - Advise to isolate and retest according to current MOH guidance

Clinical Quality and Education Team comment:
RATs are being used to detect COVID-19. They are a useful tool for providing quick information and reducing the system demand for PCR testing. As with any test, there is a chance of both true or false positive and negative results. It is important all health professionals understand the predicted test performance in the populations using these tests to be able to have informed discussions with patients. As the prevalence of COVID-19 changes, so will the positive predictive value.

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Background

In December 2021 Canterbury had a very low prevalence of COVID-19; at that time the use of rapid antigen tests (RATs) was introduced to determine COVID-19 status prior to flying. RAT use was problematic at that stage when prevalence and hence positive predictive value were low. This meant false positives tests were an issue. Since then, the prevalence of COVID-19 has increased as Omicron has spread. It is therefore important to understand the effect this has on interpretation of RAT results.

In Omicron phase three RATs are used in the community as the primary method to detect COVID-19[2]. Symptomatic people and/or asymptomatic close contacts whose RAT is positive are considered a case and do not need to be verified through the gold standard polymerase chain reaction (PCR) test.[1] The aim of RAT use is to reduce PCR testing load on laboratories, and improve access to tests.[1]

RATs are front of nose swabs. They are currently funded for:

- People with symptoms
- Household contacts
- Critical workers through the Close Contact Exemption Scheme
- Surveillance testing e.g., in border workers

Their accessibility and funding are under constant review. For latest advice on RAT use see MOH guidance or HealthPathways.

The Ministry of Health has evaluated and currently approved for import eleven RATs to test for COVID-19[1]. The WHO recommend RATs meet minimum performance requirements of ≥80% sensitivity and ≥97% specificity[3]; all RATs available in Aotearoa NZ meet these standards[1], however in practice sensitivities may vary (see below).

Recap of Sensitivity, specificity, and predictive values

Sensitivity, specificity, positive and negative predictive value are important concepts in testing.

- **Sensitivity**: The proportion of people with the condition who return a positive test
- **Specificity**: The proportion of people who don't have the condition who return a negative test
- **Positive predictive value** (PPV): The proportion of people with a positive test who actually have the condition
- **Negative predictive value** (NPV): The proportion of people with a negative test who truly do not have the condition
- **Prevalence**: the proportion of people in a population who have the condition at a given point in time
- **Pre-test probability**: the probability a person has the condition estimated before the test result is known

Sensitivity and specificity relate to the *test* itself; for a given disease and test, they stay the same, regardless of prevalence or who is being tested.

However, PPV and NPV depend on sensitivity, specificity *AND* prevalence. For a given disease and test, they change depending on the prevalence in the population being tested.

Sensitivity of RATs in COVID-19

Evidence is rapidly evolving for the use of RATs but care must be taken in interpretation of the data as there are many factors that impact on their 'real-life' diagnostic ability. These include timing of the swab relative to the onset and/or presence of symptoms, patient factors (viral load, vaccination and immune status) and test factors (shipping, storage and shelf life) plus swabbing practices and test procedures (especially when not performed by trained health care professionals).[3,4]

To date the evidence is mixed about the ability of different RATs to detect the Omicron variant[4,5].

A Cochrane review found estimates of sensitivities varied across different situations and brands[6]:

- When used in *symptomatic* participants sensitivity was **72%** (95% CI 64 to 79% from 37 evaluations; 15,530 samples and 4410 cases) and in *asymptomatic* participants sensitivity was **58%** (95% CI 40 to 74% from 12 evaluations; 1581 samples, 295 cases)
- With *varying viral load*, RAT sensitivity was higher in the first week of illness at **78% (**95% CI 71% to 84% from 26 evaluations; 5769 samples, 2320 cases) than in the second week at **51%** (95% CI 41% to 61% from 22 evaluations; 935 samples, 692 cases)
- Specificity on average was higher than sensitivity across brands and in both symptomatic and asymptomatic patients

Positive and Negative Predictive Values

- As with any test, the PPV is lower when the test is used in low prevalence settings (e.g., Canterbury December 2021). See table below
- As the prevalence of Covid-19 increases (Canterbury March 2022) the PPV of the RAT will increase but the NPV will reduce. See table below
    - I.e., in the current higher prevalence situation, we can be less assured a negative RAT is a true negative
    - Symptomatic people have a higher pre-test probability so are being asked to re-test if they have a negative RAT result

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Table One: An illustrative example

Test performance in different scenarios			
Pre-test probability of COVID-19	Low (0.001%)[x]	Medium (5%)	Very High (50%)[y]
PPV	<1%	83%	99%
NPV	>99%	>99%	91%

(assuming sensitivity 90% and specificity 99%)[7]

x: for example, an asymptomatic traveller in Canterbury Dec 2022 with very low COVID-19 prevalence in the community

y: for example, a household contact with COVID-19 symptoms

In the current setting in Canterbury, for people with a high pre-test probability of having COVID-19 e.g., a household contact with COVID-19 symptoms, the NPV will likely be less re-assuring, there will be a higher number of false negatives.

Serial RAT testing

It has been proposed that serial testing will increase the sensitivity of RATs;[8] evidence to support this is in its infancy. In the United States in early 2021 when COVID-19 prevalence was high, serial RAT testing was found to be effective in allowing healthy staff to continue to work and avoiding asymptomatic positive cases entering the workplace.[9]

False negative RATs can occur in COVID-19 cases tested in the pre-symptomatic phase when viral load is low,[10,11] they may also occur in symptomatic people early in their illness. A single test that is a false negative may wrongly reassure people leading to further onward transmission. This is why MOH has provided further protocol for critical workers who are asymptomatic household contacts to follow to reduce the risk of asymptomatic transmission.[12] Evidence is emerging that serial RAT testing may help compensate for reduced sensitivity in the early phase of the infection when people are asymptomatic and have low viral load,[13] the ideal frequency of testing is yet to be established.[13]

Impacts of test outcomes

False positive test:

- The person will be directed to self-isolate despite being uninfected and safe to work or socialise

False negative test:

- An infected person remains in the community and does not receive any care[14]
- People may be falsely reassured and wrongly attribute new symptoms to hay fever or a cold
- Contributes to further transmission

Asymptomatic people who return a negative RAT should be reminded:

- No test is 100% accurate
- A *negative RAT does not rule out* COVID-19: especially if they have a high pre-test probability of having Covid-19 (e.g., they are household or close contacts of a known case)
- They need to repeat a test if symptoms develop or as instructed to by their health care team or workplace

Similarly **symptomatic** people who return a negative RAT should be reminded as above and:

- Re-test in 48 hours when there is potentially more viral load
- Stay at home as instructed by public health officials[15]

Current RAT testing protocols are available on the website: Unite against Covid-19

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