THE NEW ZEALAND MICROBIOLOGY NETWORK

NZMN position statement on Rapid Antigen Tests (RAT) for SARS CoV-2 in Aotearoa New Zealand

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Executive summary

- Rapid antigen tests (RAT) have lower sensitivity compared to nucleic acid amplification tests (NAAT) and can only reliably detect people with high viral load
- RAT are not suited to high throughput usage, and do not replace the need for increased laboratory-based NAAT capacity during periods of high demand, but may have a complementary role under defined circumstances
- The main benefit of RAT is fast turnaround time, which becomes most relevant during periods of high demand if NAAT turnaround times become prolonged
- Symptomatic people require NAAT in addition to RAT in the current New Zealand context
- All positive RAT require confirmation by NAAT in the current New Zealand context
- Appropriate training, ongoing quality assurance, clinical oversight and result reporting mechanisms must be well-established prior to any RAT programme rollout
- New Zealand needs to address ongoing laboratory capacity for SARS-CoV-2 NAAT; any introduction of RAT does not offer a reliable solution to this need.

The lower sensitivity of rapid antigen tests (RAT) compared with nucleic acid amplification tests (NAAT) for the detection of SARS CoV-2 has been clearly documented both in overseas populations and in smaller evaluations in New Zealand [1-5]. Sensitivity of RAT is lower than NAAT among both symptomatic and asymptomatic populations. Sensitivity of RAT has been shown to be approximately 40% among asymptomatic people in the community in the UK [1-3]. Poor sensitivity means false negative tests will occur. Widespread RAT use in a low-prevalence setting means a low positive predictive value such that false positives will outnumber true positives, despite high test specificity >99%. The risk of false negative results is particularly true for infected individuals with a relatively low viral load (e.g., approximately equivalent to Ct >25 on RT-PCR) with no RAT able to detect reliably cases with a PCR Ct >30 cycles. Test sensitivity in the real world will depend on whether the aim is to find all positive cases or just those who are most infectious. It should be noted that there is no universally agreed laboratory cut-off or correlate of infectiousness and many cases occur, including in the New Zealand context, with Ct values >25 [6]. Furthermore, RAT sensitivity has been demonstrated to be lower when used for home testing or by non-laboratory personnel as compared to testing performed within the laboratory setting.

In countries where SARS-CoV-2 has become endemic the tolerance for false negative tests is much greater than in countries where the elimination strategy remains in place, such as in New Zealand, where a single false negative test has the potential to begin or extend an outbreak.

Both the RCPA and the PHLN/CDNA have published statements about the use of RAT in Australia and New Zealand. [7,8] The WHO, ECDC, US CDC and Health Canada have also all issued guidelines for the use of rapid antigen tests [9-12].

The NZMN appreciates that the benefit of RAT lies in their ability to quickly detect people with SARS-CoV-2 who are likely to be most infectious, that this can be done in a remote setting or distant to a laboratory, and a result available in as little as 20 minutes. The NZMN also recognise that during periods of high volume surge testing, laboratory capacity for the gold-standard RT-PCR may be rapidly outstripped by demand. Under certain circumstances, the use of a less sensitive test such as RAT can be deployed as complementary to NAAT, not in place of, to bring about the ultimate aim of outbreak control and return of elimination status. However, such use needs careful consideration so as to avoid any unintended harmful consequences including missing cases of infectious SARS-CoV-2 or false positive results which unnecessarily trigger resource-intensive contact tracing efforts.

However RAT are utilised, during low prevalence of COVID-19, three important principles must be adhered to:

1. For symptomatic testing, **all RAT should be accompanied by a NAAT**
2. For asymptomatic or symptomatic testing, **all positive RAT results should be confirmed by a NAAT**
3. For asymptomatic screening, **sensitivity should be augmented by increased frequency of testing**

Considerations for implementation of RAT

1. In symptomatic people, or asymptomatic travellers from SARS-CoV-2 endemic areas, a negative result does not mean the individual is not infected or infectious with SARS-CoV-2 and a NAAT must also be performed. This will require 2 samples to be taken.
2. Respiratory tract sample collection must still be performed with all necessary IP&C considerations, including a suitable sample collection environment and safe disposal of waste [13]. Currently most RAT still require a nose and throat or nasopharyngeal swab and not saliva, which may affect tolerability. Home/self-testing may not produce reliable results. Self-sample collection with independent operator performing RAT itself may partially mitigate these issues.
3. Appropriate validation and registration of the RAT must be met, as well as minimum performance standards (WHO states ≥80% sensitivity and ≥97% specificity, while ECDC suggests aiming to use tests with a performance closer to RT-PCR in areas of low prevalence, i.e., ≥90% sensitivity and ≥97% specificity [9-10]),

4. A quality assurance programme is needed for the RAT and ongoing oversight ideally from a laboratory-based point-of-care coordinator.
5. Operators must be appropriately trained in performing and interpreting the RAT and require demonstration of ongoing competency, noting that RAT do not contain controls for confirmation of adequacy of sample. Training could be supported by online training tools and simple to follow instructions for use.
6. Data on testing and results must be accurately collated and reported electronically to public health units (PHU) and ESR. RAT will not be interfaced into current laboratory information systems in the way that current laboratory based NAAT are. IT solutions for accurate data capture would need to be developed, such as online or App based reading and reporting.
7. Large scale testing will be limited – each operator can process at most 15-20 samples/hour. This is not suited to the central laboratory setting which are best to focus on upscaling of high throughput molecular technology. May be suited for use in smaller or remote laboratory settings, or non-laboratory settings with suitable processes in place.
8. A positive result must be reported immediately to the PHU, the individual isolated and contact tracing begun, while confirmation by a repeat sample by NAAT is performed.
9. RAT should be used in a way that compensates for lower test performance, such as repeated testing (e.g., daily to twice weekly) for screening purposes (with confirmation of positive test results by NAAT) or by improving access to testing which otherwise would not have been undertaken or where critical results would otherwise be significantly delayed
10. Careful consideration of the expected sample volumes, availability of resources (including personnel), equipment and logistical arrangements would be needed.
11. The risks and benefits of introducing RAT in New Zealand are untested. New Zealand should perform careful evaluation prior to any implementation since, for example, it is not yet known whether community mass testing can reduce transmission of SARS-CoV-2 even in an endemic setting. The NZMN would support pilot projects to assess suitability.
12. RAT do not allow for genomic analysis of positive cases; a repeat sample would be required.

The NZMN acknowledges that RAT may be considered alongside (but not as a replacement for) NAAT in the situations outlined below.

Asymptomatic screening

- When NAAT testing by labs has surpassed capacity, turnaround times (TAT) are too long, or testing would not otherwise be done. Under such circumstances, NAAT resource should be prioritised towards diagnosis of symptomatic individuals or testing of close contacts.
- Lower test sensitivity is mitigated by increased frequency of testing, e.g., daily or several times per week [14-16]
- Testing of individuals at increased risk of SARS-CoV-2 or where the consequences of unrecognised asymptomatic/presymptomatic infection could be catastrophic and NAAT is not available
    a. HCW during periods of community transmission of SARS-CoV-2, noting that staff caring directly for COVID patients (and symptomatic staff) should preferably have testing performed using NAAT, or possibly frequent RAT and interval NAAT.
    b. Essential workers during periods of community transmission of SARS-CoV-2 and who work in environments where physical distancing is difficult e.g., supermarket workers, aged residential care (ARC) workers, pharmacies, police, prisons
    c. Border workers, Air NZ, international shipping crew, only under circumstances where laboratory NAAT TAT is too long, noting RAT would need to be added to NAAT.

Symptomatic testing

- When NAAT testing by labs has surpassed capacity or TAT are too long or testing would not otherwise be done.
    a. Remote/smaller laboratory settings if access to NAAT is delayed. Samples for NAAT would be required to be taken concurrently but the speed of RAT result helps expedite public health response
    b. Deployed in the field by mobile public health teams for local cluster/hot spot investigation or testing of contacts where rapid results are required and access to NAAT delayed. Any positive results in this situation would indicate the syndromic cluster is due to CoV2 and individual negative results would not be considered. Samples for NAAT would be required to be taken concurrently.
    c. Outbreaks in facilities where multiple people are affected and a rapid result is required, e.g., prisons, ARC, ships. Any positive results in this situation would indicate the syndromic cluster is due to CoV2 and individual negative results would not be considered. Samples for NAAT would be required to be taken concurrently
    At CBACs for individuals with no High Index of Suspicion (HIS) criteria to divert NAAT resource to people with a higher pre-test probability of infection. Training and competency for staff at CBACs would be a major limitation since this would add to

workload. Individuals with HIS would need samples for NAAT to be taken concurrently. During a community outbreak this could mean all individuals would need samples for NAAT to be taken concurrently but contact tracing could begin immediately for RAT-positive cases.

If SARS-CoV-2 becomes endemic in New Zealand in the future, more general widespread surveillance testing may become warranted, especially if there is no longer an essential work only policy.

It would be important to consider how to recognise and measure potential harm from implementation of RAT e.g., inappropriate use in place of NAAT, failure to confirm false negative tests leading to transmission, cost of following up false positives, stigmatisation etc.

New Zealand needs to urgently address ongoing laboratory capacity constraints if the nation wishes to continue to pursue elimination and for future planning for border opening. Introduction of RAT does not offer a solution to this need. Redundancy in the system, including workforce, will be required to allow for rapid escalation of NAAT testing capacity in times of increased demand.

Some examples of considerations for use of RAT in NZ under different possible circumstances:

	Elimination strategy & unvaccinated population & largely closed borders		**Vaccinated population & some quarantine-free travel, outbreaks occur.**	**Endemic SARS CoV-2 in NZ, vaccinated population**
	No community transmission	Community transmission		
Asymptomatic surveillance of travellers at the border	Could be piloted in conjunction with simultaneous NAAT testing. Positive results acted on immediately, negative and positive results would need NAAT confirmation. Probably better for higher risk travellers.		Depends on results of previous pilot. If that went well and suitable rapid NAAT tests are not available, may be useful.	Yes, if considered necessary to identify most infectious cases.
Frequent asymptomatic surveillance of healthcare and aged care workers	Only needed for those caring for patients with COVID-19, should be done by NAAT, in same was as for border workers.	Frequent saliva testing by NAAT likely to be more sensitive and may be better tolerated. Consider RAT as alternative or addition to NAAT if lab capacity constrained	NAAT would perform better. Consider as alternative or addition to NAAT if lab capacity constrained	Could be considered depending on characteristics of available tests at the time. Poor negative predictive value.
Patients presenting with symptoms	No – not sensitive enough.	If rapid result required and access to laboratory-based testing delayed, in which case both RAT and NAAT could be performed simultaneously.	Yes, for triage purposes if faster result than NAAT. NAAT test still needed as well.	Yes, if benefit of rapid test outweighs the limitations including poor negative predictive value, or if lab capacity constrained. NAAT also required.
Outbreak investigation in a remote setting e.g., on a container ship in NZ waters	Yes, if NAAT not available – any positive result would be assumed outbreak is SARS-CoV-2. Negative results would still need NAAT.		Yes, if NAAT not available – any positive result would be assumed outbreak is SARS-CoV-2. Negative results would still need NAAT.	Yes, if NAAT not available – any positive result would be assumed outbreak is SARS-CoV-2. Negative results would still need NAAT.
For entry to mass gatherings such as concerts, sporting events, funerals, schools, universities	Not necessary in setting of no community transmission	Mass gatherings not occurring in lockdown	Rapid NAAT would be better. RAT better than no test at all.	Could be considered depending on characteristics of available tests at the time. RAT better than no test to avoid superspreading.
Widespread access to self-testing at home	No – not sensitive enough. Performance of operator may not be reliable. (Not currently allowed in Australia under TGA rules)		Could be considered depending on appropriate tests being available and appropriate support for people testing both positive and negative.	

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