Interim guidance on the use of Antigen Detection Tests (ADTs) in the public health system in Ireland

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Key points

- Antigen Detection Tests (ADTs) for SARS-CoV-2 detection are carried out either at the point of care, where they are known as Rapid Antigen Detection Tests (RADTs), or they can be laboratory based.
- These immunoassays detect the presence of specific antigens on the surface of the virus, and identify people who are infectious, when virus levels in the body are likely to be high
- They are less sensitive than PCR tests, but can be performed outside the laboratory and generally take less than 30 minutes to perform, providing rapid information for detection management and control of the spread of infection.
- Before implementing ADT, ECDC has advised countries to undertake independent and setting-specific validations of RADTs. This work is underway in Ireland, led by the HSE Antigen Project Evaluation Working Group.
- Based on the results of validations to date, ADTs will be used in the acute hospital setting and in outbreaks in vulnerable populations in the community
    - In the acute hospital setting, deployment will depend on local laboratory capabilities for provision of large-volume batch testing, rapid PCR testing, and staffing levels, and approaches will vary by hospital location. They may be used in a range of settings including:
        - Triage of patients in emergency departments and in ambulances arriving at the department pending admission to the emergency department;
        - To support early diagnosis in hospital outbreaks, including testing of symptomatic health care workers;
        - In identification of infectious cases in outbreaks, and also in using repeat ADTs to guide decisions on when to declare an outbreak closed.
        - In situations where ADTs can reduce pressures on the hospital's capability for rapid PCR testing.
    - In community settings they will be used for cases and close contacts in outbreaks in vulnerable populations when community transmission is high.
- An operational framework which includes national and local governance arrangements, roles and responsibilities, procedures for all aspects of the testing process, as well as specifying how to report results to the individual and to public health for contact tracing and surveillance has been developed.
- The Irish case definition for SARS-CoV-2 has been updated to include notification of positive results from ADTs undertaken in the public health system.

Introduction

This document provides guidance on the use of antigen detection tests (ADTs) for SARS-CoV-2 in the public health system in Ireland. The majority of ADTs are rapid tests undertaken at the point of care, known as Rapid Antigen Detection Tests (RADTs); antigen detection tests can also be carried out in the laboratory. This guidance was developed by the HSE Antigen Project Evaluation Working Group (membership in Appendix A), and approved by the National Public Health Emergency Team.

Given rapidly emerging information about their use in supporting public health response, ongoing validation work, and also the pace of innovation in diagnostics, it is likely that this guidance will need to be adapted and amended over time.

Background

Antigen Detection Tests (ADTs) for SARS-CoV-2 are carried out either at the point of care, where they are known as Rapid Antigen Detection Tests (RADTs), or they can be laboratory based. ADTs are immunoassays that detect the presence or absence of specific antigens on the surface of the virus, and can identify people who are at the peak of infection, when virus levels in the body are likely to be high. ADTs need a sample to contain thousands of virus particles per microlitre to produce a positive result whereas RT-PCR tests can detect very small amounts of viral RNA. ADTs are less sensitive in detecting SARS-CoV-2 infection, so, if a person has low amounts of virus in their body, the test can give a false-negative result. Antigen tests are currently designed to be performed on nasopharyngeal or nasal swab specimens placed directly into the assay's extraction buffer or reagent. Tests take between 15 and 30 minutes to perform and provide a result, and need to be carried out by trained personnel.

Benefits of ADTs

There is growing interest in the potential for ADTs to aid the public health response to COVID-19. The main potential benefits identified are shorter turnaround times, and lower reagent costs, particularly in cases with high viral loads i.e. pre-symptomatic cases shortly before symptoms develop and symptomatic cases within 5 days of onset of symptoms. Used in this way, ADTs can help reduce further transmission through early detection of highly infectious cases, enabling isolation of cases, contact tracing and restriction of movements of contacts to start quickly.

When community prevalence is high, and when there may be pressures on laboratory capacity for PCR testing, ADTs have a role in detection of symptomatic cases, particularly in settings where there is swabbing capacity on site, such as in acute hospitals. In these circumstances RADTs as well as laboratory-based ADTs might be used.

The fact that RADTs can be performed outside the laboratory can be an advantage, but they need to be performed by trained personnel and each test takes time. There are significant

logistical issues to consider in introducing RADTs, including limitations in their capacity to scale up to test large volumes of patients, and the need for large numbers of trained staff to undertake higher volumes of testing.

Laboratory based antigen detection tests (ADTs) are also becoming an option as availability increases. ADTs offer greater scalability, as they avoid the need to recruit large numbers of staff required to perform antigen testing at the point of care to a significant extent. Additionally, these tests are more sensitive than RADTs.

On 20th January 2021, the European "Council Recommendation on a common framework for the use and validation of rapid antigen tests and the mutual recognition of COVID-19 test results in the EU" set out several recommendations regarding ADTs. These include the following:

- Consider using RADTs where there is limited capacity for RT-PCR, or prolonged testing turnaround times
- Ensure that ADT is conducted by trained healthcare personnel or other trained operators where appropriate and in line with national specifications, as well as in strict accordance with manufacturer's instructions, with appropriate biosafety measures in place, and subject to quality control.
- Invest in training and, if appropriate, certification of healthcare personnel and other operators to carry out sampling and testing, thereby ensuring adequate capacities as well as safeguarding the collection of good quality samples.
- Ensure that the results of rapid antigen testing are registered in the respective national data collection and reporting systems, where feasible.
- Consider their use among symptomatic cases regardless of the setting, for asymptomatic close contacts, and in outbreaks. For screening in high risk areas and closed settings, if used, they need to be repeated every 2 to 4 days if possible. ECDC will soon publish guidance on the advantages and disadvantages of population wide testing using ADTs.
- Continue to invest in conducting independent and setting-specific validation studies of rapid antigen tests, with the aim of assessing their performance against RT-PCR assays. They recommend that the Member States agree on, maintain and share with the ECDC and the Commission, a common and updated list of COVID-19 rapid antigen tests that are considered appropriate for use in the situations described above, following validation.

Work of the HSE Antigen Evaluation Working Group

On November 19th 2020 ECDC recommended that EU Member States perform independent and setting-specific validations of RADTS before their implementation[1]. Sensitivity and specificity depend on the performance characteristics of individual assays, and on the

[1] ECDC Options for the use of rapid antigen tests for COVID-19 in the EU/EEA and the UK https://www.ecdc.europa.eu/sites/default/files/documents/Options-use-of-rapid-antigen-tests-for-COVID-19_0.pdf

circumstances in which they are used. The Irish Antigen Project Evaluation Working Group was established to perform independent and site-specific validations in Ireland. It has undertaken desktop evaluations to identify assays suitable for further evaluation, and site-specific evaluations in acute hospitals, in meat plants and in the community. Some of these evaluations are still ongoing.

Validations undertaken to date by the HSE Antigen Project Evaluation Working Group have shown sensitivity above 80% and specificity >97% for some RADT assays when used in symptomatic patients. Results in asymptomatic patients however have shown significantly lower sensitivity, well below the minimum performance requirements set by WHO of >=80% sensitivity. Evaluations of laboratory-based antigen detection tests (ADTs) are also underway.

The ADT evaluation process is still underway. One test has been verified for use with nasopharyngeal swabs in symptomatic individuals. Verification of a second test, for use with nasal swabs, will conclude soon, and a third assay verification, using viral transport medium (the same sample could be used for antigen and PCR) is underway and will conclude in the coming weeks.

Details on how to order validated ADTs are available in the HSE "Operational plan for the deployment of rapid antigen detection tests for SARS-CoV-2 in acute settings".

Operational framework for implementation

An operational framework for implementing RADT within the HSE has been developed. This includes national and local governance arrangements, roles and responsibilities, procedures for all aspects of the testing process, as well as specifying how to report results to the individual and to public health for contact tracing and surveillance.

The Irish case definition for SARS-CoV-2 has been updated to include notification of positive results from ADTs undertaken in the public health system, see here.

Interim recommendations for use of ADTs in Ireland

ADTs are proposed for use in the following circumstances and settings:

1. **Use in community outbreak response and control in vulnerable populations**

The procedure for NAS deployment in outbreaks is yet to be finalised. There is an agreement in principle and, pending process finalisation and training, the use of ADT in outbreak settings is as follows:

On notification of a potential outbreak in the community (PCR tests not yet carried out), **OR** in the early stages of management of a PCR confirmed COVID-19 outbreak, as part of the Public Health Risk Assessment, RADTs can be considered for use as part of the response if the following 3 criteria are met:

1. There is evidence of widespread community transmission (>10% positivity in the local community)

2. There are symptomatic person(s) on site

3. The outbreak involves a vulnerable population, including among staff and/or residents of long-term care facilities, homeless hostels, residents of direct provision centres, prisons, Irish Travellers etc

If these criteria are met, then

FOR CASES

(a) Ask the National Ambulance Service (NAS) to use RADTs to test all persons with symptoms suggestive of COVID-19 with onset within the last 5 days. Persons with symptom onset more than 5 days ago should be tested with PCR tests. If numbers of symptomatic cases are large, RADTs may be undertaken on a subset of cases, as advised by the Outbreak Control Team. In this instance, all those with similar symptoms but who have not been tested will be presumed to be COVID-19 positive.

(b) If the RADT result is positive, treat the person as having confirmed COVID-19.

(c) If the RADT result is "not detected", and the pre-test probability of infection is high in this instance (i.e. symptomatic person and high community prevalence), take a second sample for PCR testing and continue with infection control precautions until the second result comes back as "not detected".

(d) At least one person in the outbreak should be tested using PCR to confirm that this is a PCR confirmed COVID-19 outbreak. This can be done in parallel with RADT testing.

(e) Positive RADTs are to be reported to the COVID Care Tracker so that close contacts outside the vulnerable setting can be identified to the Contact Management Programme and contact traced.

(f) All cases detected during the outbreak either by RADT or PCR need to be notified to the Medical Officer for Health through CIDR.

FOR CLOSE CONTACTS

(g) Test asymptomatic close contacts using RADTs

(h) If the RADT is "not detected" in the close contact, repeat the test using PCR

(i) If the RADT is positive, then treat as a confirmed case, report to the COVID care tracker to identify and manage close contacts outside the outbreak setting and notify to CIDR

Clinical governance of this testing: In this instance, the testing is ordered by Public Health, as a response to an outbreak, and governance of who is to be tested, informing patients, and advising on actions based on the results rests with Public Health and the outbreak control team. Governance of undertaking the tests in a supervised manner, and in a quality management system rests with the NAS working with the local Clinical Microbiologist.

2. In the acute hospital setting

Within the acute hospital setting, deployment of ADTs will depend on the local laboratory capabilities for provision of large-volume batch testing, rapid PCR testing, and staffing levels. Approaches will vary by hospital location. The clinical director of diagnostics will be responsible for overall clinical governance with input from clinical microbiology.

Within the acute hospital setting, and as advised locally, they can be used in a range of settings including:

- Triage of patients in emergency departments and in ambulances arriving at department pending admission to the emergency department;
- To support early diagnosis in hospital outbreaks, including testing of symptomatic health care workers;
- In identification of infectious cases in outbreaks, and also in using repeat ADTs to guide decisions on when to declare an outbreak closed.
- In situations where ADTs can reduce pressures on the hospital's capability for rapid PCR testing.

Many acute hospitals have sufficient rapid PCR testing capacity and may decide for operational reasons not to use ADTs, but ADTs have a role in preserving capacity if PCR testing is under pressure or overwhelmed.

Use in other HSE settings:

Validation work on the use of ADTs for serial testing in healthcare workers is ongoing, and guidance will be updated in this area when results are available.

Validation work is ongoing in relation to the use of RADT in symptomatic people and asymptomatic close contacts in the community who are tested in community testing centres. Guidance will be updated when this work has been completed.

Appendix A Members of the HSE Antigen Project Evaluation Working Group

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