



**Health
Information
and Quality
Authority**

An tÚdarás Um Fhaisnéis
agus Cáilíocht Sláinte

**Protocol: Evidence summary for use of
rapid antigen testing for screening or
surveillance of asymptomatic individuals
to limit transmission of SARS-CoV-2**

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Purpose and aim

The purpose of this protocol is to outline the process by which the Health Information and Quality Authority (HIQA) will synthesise evidence to inform advice from HIQA to the National Public Health Emergency Team (NPHE). The advice will take account of expert interpretation of the evidence by HIQA's COVID-19 Expert Advisory Group. This evidence synthesis was requested by NPHE to address the following policy question:

“What is the emerging evidence with regard to the effectiveness of rapid antigen testing of asymptomatic populations, to limit the spread of SARS-CoV-2?”

The following two research questions (RQs) were formulated to inform the policy question:

RQ1: What are the key technical characteristics of SARS-CoV-2 rapid antigen tests, in relation to their use for screening or surveillance in asymptomatic populations?

RQ2: What is the evidence that SARS-CoV-2 rapid antigen testing for screening or surveillance of asymptomatic people, reduces onward transmission?

1. Process outline

A rapid HTA of alternatives to RT-PCR was previously conducted by HIQA. This report defined testing as being performed for the purposes of diagnosis, screening or surveillance of SARS-CoV-2 infection as outlined below.⁽¹⁾

- **Diagnostic** testing for SARS-CoV-2 is intended to identify occurrence of infection at the individual level. It is performed when there is a reason to suspect that an individual may be infected, for example, where individuals are symptomatic. This includes **testing of contacts** when there is reason to suspect that an individual may be infected despite them being asymptomatic.
- **Screening** tests for SARS-CoV-2 are intended to identify occurrence of infection at the individual level even if there is no reason to suspect infection, for example, where there is no known exposure. Screening tests are intended to identify infected individuals who may be contagious, but who are without, or prior to development of, symptoms. This is performed so that infection prevention and control measures can be taken to prevent further transmission, for example, in a workplace, educational or healthcare setting. Screening may also be conducted as part of pre-admission protocols to ensure individuals who are infected with SARS-CoV-2 are identified prior to admission to events or availing of flights. This also includes serial testing

(repeated testing) to maintain access to activities (for example elite athletes) or in settings where infection is more likely to occur despite implementation of infection prevention and control measures (for example, meat processing factories, and health and social care settings).

- **Surveillance** for SARS-CoV-2 includes ongoing systematic activities, including collection, analysis and interpretation of health-related data that are essential to planning, implementing and evaluating public health practice. Surveillance testing is generally used to monitor for community or population-level infection, for example, an infectious disease outbreak, or to look back at the level of incidence and prevalence of infection that has already occurred. Surveillance testing is used to gain information at a population level rather than an individual level - for example, to evaluate the effect on the population of public health interventions such as social distancing - and usually involves testing a representative group of the population as opposed to all individuals.

In this evidence summary, only evidence relating to the use of SARS-CoV-2 rapid antigen testing for **screening** or **surveillance** of asymptomatic individuals will be evaluated. The evidence summary will not evaluate use of SARS-CoV-2 rapid antigen tests in symptomatic and or at-risk populations (including close contacts) for the purpose of diagnosing infection. In addition, the use of laboratory-based antigen tests will not be evaluated, as the focus will be on rapid antigen tests that are intended for use as self-tests or in near patient (point of care) settings.

For RQ1, a description of technology will be conducted in accordance with the European Network for Health Technology Assessment (EUnetHTA) Core Model guidance.⁽²⁾ The purpose of RQ1 is to provide background information as context against which RQ2 will be interpreted. A de-novo systematic review of diagnostic test accuracy (DTA) will not be undertaken as part of this evidence summary, but rather findings from published systematic reviews of DTA will be discussed as part of RQ1 to provide context. This section will provide summary information on the use of SARS-CoV-2 rapid antigen testing in asymptomatic people under the following topics:

- features of the technology (for example, what is rapid antigen testing and what are the alternatives, what is the diagnostic test accuracy (sensitivity and specificity) relative to PCR in real-world settings, and what factors impact accuracy (for example, choice and timing of test, conditions of use such as specimen type, and professionally-delivered testing or self-testing)
- regulatory status (for example, for which indications and settings have rapid antigen tests received CE marking)
- investments and tools required to use the technology (for example, what material investments are needed to use rapid antigen tests in asymptomatic

populations at scale, how antigen tests results from different modalities are incorporated into the wider public health test and trace system)

- training and information needed to use the technology (for example, what kinds of skills and training are required to use rapid antigen testing, and what impact might this have on accuracy)
- ethical concerns regarding antigen testing in asymptomatic people not known to have been exposed to or infected with SARS-CoV-2 (for example, the implications of false negative or false positive results, and the potential requirement for repeated testing).

With regard to RQ2, a rapid review on the use of SARS-CoV-2 rapid antigen testing for screening and surveillance in asymptomatic individuals to limit transmission of SARS-CoV-2 will be undertaken, with a focus on real-world evidence (including field evaluations and pilot events). The context in which rapid antigen testing is being undertaken, the testing process and test characteristics are important determinants that complicate evaluations of the effectiveness of rapid antigen testing. This is particularly the case for asymptomatic individuals, as the potential benefit may not be seen in these individuals, but rather there may be downstream effects as onward transmission may be prevented.^(3, 4) For the purpose of RQ2, rapid antigen testing will be considered in the context of a public health intervention that impacts on a population, rather than at the level of the individual, therefore effectiveness will be measured as the prevention of transmission or reduction in outbreaks in a range of settings. RQ2 will be conducted in line with standard Cochrane rapid review methodology.⁽⁵⁾

A standardised approach to the process has been developed and documented to allow for transparency and to aid in project management. Five distinct steps have been identified in the process for completion. These are listed below and described in more detail in Sections 2.1-2.5.

1. Identify document types of interest.
2. Search relevant databases and websites of relevant national and international agencies and other organisations.
3. Screen identified documents.
4. Data extraction and quality appraisal of included documents.
5. Summarise findings.

2. Review process

2.1 Identify document types of interest

Scoping of the literature was carried out in preparation for this evidence summary and based on the volume of literature available and project timelines, a technology

description and a rapid review, were considered to be the most efficient methods to address the above research questions.

Evidence to inform the two research questions will be identified from the following document categories:

- a) Reviews, technical reports, websites of regulators, manufacturer and other diagnostics specialists.
- b) Primary research studies.

2.2 Search relevant databases

- a) Description of technology

For RQ1, key information relating to the broad categories of rapid antigen tests and their use in asymptomatic individuals will be retrieved by searching websites of regulators, manufacturers and diagnostics specialists, as well as targeted searches of electronic databases for expert reviews (including relevant Cochrane reviews) and governmental and public health agency websites. The following is a non-exhaustive list of websites that will be searched:

Regulators

- www.hpra.ie
- <https://www.gov.uk/government/publications/how-tests-and-testing-kits-for-coronavirus-covid-19-work>
- www.fda.gov
- <https://ec.europa.eu/>

Public Health Agencies

- <https://www.who.int/emergencies/diseases/novel-coronavirus-2019>
- <https://www.ecdc.europa.eu/en/covid-19>
- <https://www.cdc.gov/coronavirus/2019-ncov/testing/diagnostic-testing.html>

Governmental Agencies

- https://covid-19-diagnostics.jrc.ec.europa.eu/https://ec.europa.eu/health/sites/default/files/preparedness_response/docs/covid-19_rat_common-list_en.pdf
- <https://covid-19-diagnostics.jrc.ec.europa.eu/>

Diagnostic Specialists

- <https://www.360dx.com/coronavirus-test-tracker-launched-covid-19-tests>
- <https://www.finddx.org/sarscov2-eval-antigen/>

Academic Groups systematically evaluating diagnostic test accuracy of rapid antigen tests

- <https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD013705.pub2/full>
- <https://www.klinikum.uni-heidelberg.de/diagnostics-global-health>

Input from the Expert Advisory Group (EAG) will also be sought, as appropriate.

While the evaluation team will endeavour to identify the range of available tests, new tests are regularly entering the market and it may not be possible to capture all test types at the time of completing the evidence review.

b) Primary research studies

For RQ2, a systematic literature search will be conducted in Cochrane Library, Embase (OVID), Medline (EBSCO), Google Scholar and Europe PMC, to identify evidence regarding the effectiveness of SARS-CoV-2 rapid antigen testing in asymptomatic populations at reducing transmission. The search strategy is presented in Appendix 1.

A grey literature search will also be conducted for technical reports evaluating the impact of rapid antigen testing pilots in asymptomatic populations on SARS-CoV-2 transmission. The websites listed below will be reviewed to identify any such evidence. These websites were chosen based on awareness of the widespread use of rapid antigen testing and the countries being in a similar phase of pandemic response as Ireland. The list of websites for inclusion was also informed by the experience of HIQA's COVID-19 evidence synthesis team in conducting rapid reviews of public health measures.

International public health agencies:

- World Health Organization (WHO)
<https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance-publications?healthtopics=b6bd35a3-cf4f-4851-8e80-85cb0068335b&publishingoffices=aeebab07-3d0c-4a24-b6ef-7c11b7139e43&healthtopics-hidden=true&publishingoffices-hidden=true>
- European Centre for Disease Prevention and Control (ECDC)
https://www.ecdc.europa.eu/en/search?s=&sort_by=field_ct_publication_date&sort_order=DESC&f%5B0%5D=diseases%3A2942

National governments and public health agencies:

EU/EEA countries

- Austria
 - <https://www.sozialministerium.at/en.html>
 - <https://corona-ampel.gv.at/aktuelle-massnahmen/bundesweite-massnahmen/>
 - <https://metropole.at/coronavirus-updates-in-english/>
- Belgium
 - <https://www.info-coronavirus.be/en/faq/>
 - <https://www.info-coronavirus.be/en/covid/>
 - <https://www.info-coronavirus.be/en/>
 - <https://www.sciensano.be/en/health-topics/coronavirus>
- Czech Republic
 - <https://www.vlada.cz/en/media-centrum/aktualne/measures-adopted-by-the-czech-government-against-coronavirus-180545/>
 - <https://covid.gov.cz/opatreni>
 - <https://koronavirus.mzcr.cz/en/>
- Denmark
 - <https://coronasmitte.dk/en>
 - <https://www.sst.dk/da>
 - https://virksomhedsguiden.dk/erhvervsfremme/content/temaer/coronavirus_og_din_virksomhed/
- Finland
 - <https://stm.fi/en/frontpage>
 - <https://thl.fi/en/web/thlfi-en>
 - <https://valtioneuvosto.fi/en/information-on-coronavirus/current-restrictions>
- France
 - <https://www.gouvernement.fr/info-coronavirus>
 - <https://solidarites-sante.gouv.fr/>
 - <https://www.hcsp.fr/Explore.cgi/AvisRapports>
 - https://www.has-sante.fr/jcms/fc_2875171/en/resultat-de-recherche?FACET_THEME=c_64654%2Fc_64679%2Fp_3203414
- Germany
 - <https://www.bundesregierung.de/breg-en>
 - <https://www.zusammengegen corona.de/en/?articlefilter=all>
 - https://www.rki.de/DE/Home/homepage_node.html;jsessionid=360826C43D1A5736B0C0F3521211B355.internet102
- Iceland
 - <https://www.covid.is/english>
- Ireland

- o <https://www.gov.ie/en/campaigns/c36c85-covid-19-coronavirus/>
- o <https://www.hpsc.ie/a-z/respiratory/coronavirus/novelcoronavirus/>
- Italy
 - o <http://www.salute.gov.it/portale/nuovocoronavirus/homeNuovoCoronavirus.jsp>
 - o <https://www.governo.it/it/articolo/domande-frequenti-sulle-misure-adottate-dal-governo/15638>
- The Netherlands
 - o <https://www.government.nl/topics/coronavirus-covid-19>
 - o <https://lci.rivm.nl/richtlijnen/covid-19>
 - o <https://www.rijksoverheid.nl/>
- Norway
 - o <https://www.fhi.no/sv/smittsomme-sykdommer/corona/>
 - o <https://www.helsedirektoratet.no/>
 - o <https://www.regjeringen.no/en/topics/koronavirus-covid-19/id2692388/>
- Portugal
 - o <https://covid19estamoson.gov.pt/>
 - o <https://www.visitportugal.com/en/node/421175>
 - o <https://covid19.min-saude.pt/>
- Slovakia
 - o <https://www.health.gov.sk/Clanky?tlacove-spravy>
- Spain
 - o <https://www.lamoncloa.gob.es/lang/en/Paginas/index.aspx>
 - o <http://www.exteriores.gob.es/Portal/es/Paginas/inicio.aspx>
 - o <https://www.mscbs.gob.es/profesionales/saludPublica/ccayes/alertasActual/nCov/documentos.htm>
- Sweden
 - o <https://www.government.se/government-policy/the-governments-work-in-response-to-the-virus-responsible-for-covid-1/>
 - o <https://www.folkhalsomyndigheten.se/smittskydd-beredskap/utbrott/aktuella-utbrott/covid-19/>
 - o <https://www.krisinformation.se/>

UK countries

- England
 - o <https://www.gov.uk/coronavirus>
- Northern Ireland
 - o <https://www.nidirect.gov.uk/campaigns/coronavirus-covid-19>
 - o <https://www.publichealth.hscni.net/>

- Scotland
 - <https://www.gov.scot/coronavirus-covid-19/>
 - <https://www.hps.scot.nhs.uk/a-to-z-of-topics/covid-19/>
- Wales
 - <https://gov.wales/coronavirus>
 - <https://phw.nhs.wales/topics/latest-information-on-novel-coronavirus-covid-19/>

Non-EU/EEA/UK countries

- Israel
 - https://www.gov.il/en/departments/ministry_of_health
 - <https://www.gov.il/en/Departments/Guides/ramzor-cites-guidelines?chapterIndex=1>
- Switzerland
 - <https://www.bag.admin.ch/bag/en/home/krankheiten/ausbrueche-epidemien-pandemien/aktuelle-ausbrueche-epidemien/novel-cov.htm>
- US Centers for Disease Control and Prevention (CDC)
 - <https://www.cdc.gov/coronavirus/2019-ncov/whats-new-all.html>

2.3 Screen identified documents

For RQ1, all relevant information will be screened for relevance and summarised with the aim of providing a description of SARS-CoV-2 rapid antigen tests, specifically their use in asymptomatic populations.

For RQ2, all potentially eligible primary research studies identified in the database search will be exported to Covidence systematic review software (available at www.covidence.org) and single screened against the Population, Intervention, Comparator, Outcome and Study design (PICOS) framework with any uncertainty checked by a second reviewer. Relevant governmental reports identified through RQ1 will also be included. The PICOS framework specifying the inclusion and exclusion criteria for RQ2 is detailed in Table 1 below.

Table 1: PICOS for RQ2

Population	<p>Asymptomatic (or pre-symptomatic) populations, in any setting.</p> <p>Contexts of interest:</p> <ul style="list-style-type: none"> ▪ general population (for example, a national screening programme) ▪ education and child care facilities (including, pre-school, creches, schools and universities) ▪ workplaces (for example factories)
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	<ul style="list-style-type: none"> ▪ sports programmes (for example, elite athletes) ▪ social and sporting events (for example, spectators at events) ▪ travel (for example, flight passengers) ▪ entertainment venues and hospitality (for example, restaurants and bars) ▪ health and social care settings (for example, nursing homes).
Intervention	SARS-CoV-2 rapid antigen testing for the purpose of screening (including serial testing) and surveillance.
Comparator(s) (if relevant)	No testing, or laboratory-based PCR.
Outcome	<p>Primary outcomes</p> <ul style="list-style-type: none"> ▪ transmission outcomes (for example, infection rates, onward transmission (as measured by whole genome sequencing or contact tracing)). <p>Secondary outcomes</p> <ul style="list-style-type: none"> ▪ biological outcomes (for example, concordance with PCR or viral culture positivity) ▪ mortality ▪ healthcare utilisation outcomes (for example, hospitalisation, ICU rates) ▪ behavioural outcomes (for example, adherence to self-isolation, uptake of testing, knowledge, attitudes and beliefs) ▪ costs, resources and cost-effectiveness outcomes (for example, cost per quality-adjusted life year (QALY) gained) ▪ time in quarantine/isolation (for example, as a result of being identified as a positive case or close contact) ▪ time present for in-person education (for example, for second and third level students).
Study design	<p>Include:</p> <ul style="list-style-type: none"> ▪ Primary research studies including interventional studies, observational studies, ecological studies, and epidemiological investigations, of SARS-CoV-2 rapid antigen testing, where the aim of testing was screening or surveillance. ▪ Single or serial rapid antigen testing studies. <p>Exclude:</p> <ul style="list-style-type: none"> ▪ animal studies ▪ mathematical and statistical modelling studies ▪ diagnostic test accuracy studies (except where these have

	<p>relevant transmission outcomes)</p> <ul style="list-style-type: none">▪ studies without the primary outcome of interest▪ studies where rapid antigen testing was used for diagnosis (that is, in symptomatic individuals or close contacts)▪ studies relating to non-SARS-CoV-2 infectious diseases▪ reviews (but included studies will be screened for relevance)▪ media reports and press releases (but attempts will be made to identify any linked research article)▪ editorials and opinion pieces.
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2.4 Data extraction and quality appraisal of included documents

Data extraction and quality appraisal will be performed by one reviewer, and double checked by a second reviewer. Data extraction templates are detailed in Appendix 2.

The following data will be extracted for RQ2:

- Study descriptors.
- Sample size.
- Population demographics.
- Setting.
- Aim of rapid antigen testing (for example screening, serial testing, surveillance).
- Other public health measures in place at time of study
- Epidemiological and vaccination situation (including information on predominant variant of concern).
- Rapid antigen test process (for example, test kit used, specimen site, testing process [self-test, supervised self-sample/self-test, provider-based sample/test], number of tests performed).
- Outcomes (the primary outcomes of interest will be transmission-related), the secondary outcomes will be biological (for example, concordance with PCR positivity), mortality, healthcare utilisation outcomes (for example, hospitalisation, ICU admission), behavioural (for example, adherence to self-isolation) and cost-effectiveness (for example, cost per QALY).
- Author conclusions.

The relevant National Heart, Lung and Blood Institute (NIH) Quality Assessment Tool will be used for the quality appraisal of included studies.⁽⁶⁾

2.5 Summarise findings

A descriptive overview of the identified evidence and information to date for both review questions will be compiled. A PRISMA flow chart will be presented for RQ2.

3. Quality assurance process

Each research question will be led by an experienced analyst. A minimum of four team members will conduct the evidence summary. This will permit confirmation that the report accurately reflects the body of literature, and will help expedite the process given the short turnaround time. All reports will be further reviewed by two members of the senior management team, to ensure standard operating processes are followed and quality maintained.

4. Review and update

Given the rapidly changing environment, this protocol will be regarded as a live document and amended when required to ensure it reflects any changes made to the outlined processes.

5. Timelines

This rapid evidence synthesis will be conducted in line with the processes and timelines outlined for Phase 2 of HIQA's COVID-19 response. Work will commence on 12 July 2021 and a final draft will be completed by 5 August 2021. Draft outputs from the rapid evidence synthesis will be circulated to HIQA's COVID-19 Expert Advisory Group for review, with a view to providing advice to NPHET on 12 August 2021.

Appendix 1 Search strategy

Embase (OVID) Search Strategy Completed 19 July 2021

Database(s): from **Embase** 1974

Search Strategy:

#	Searches
1	exp coronavirus disease 2019/
2	(COVID-19 or coronavirus or "corona virus").ab,ti.
3	(wuhan adj3 virus).ab,ti.
4	("2019-nCoV" or "2019 ncov").ab,ti.
5	"severe acute respiratory syndrome coronavirus 2".ab,ti.
6	("2019" and (new or novel) and coronavirus).ab,ti.
7	SARS-CoV-2.ab,ti.
8	1 or 2 or 3 or 4 or 5 or 6 or 7
9	limit 8 to yr="2019 -Current"
10	(antigen* adj3 test*).ab,ti.
11	(rapid adj3 test*).ab,ti.
12	"lateral flow test*".ab,ti.
13	exp virus antigen/
14	exp immunoassay/
15	10 or 11 or 12 or 13 or 14
16	exp mass screening/
17	screening.ab,ti.
18	((daily or area or pilot or repeat* or serial or mass or population or community or surveillance) adj3 (screening or test*)).ab,ti.
19	testing pilot.ab,ti.
20	testing protocol.ab,ti.
21	16 or 17 or 18 or 19 or 20
22	9 and 15 and 21
22	limit 21 to (conference abstract or conference paper or "conference review" or editorial)
23	21 not 22

Medline (EBSCO) Search Strategy Completed 19 July 2021

#	Query
S19	S17 NOT S18
S18	PT editorial
S17	S4 AND S10 AND S15
S16	S4 AND S10 AND S15
S15	S11 OR S12 OR S13 OR S14
S14	TI pilot N3 test* OR AB pilot N3 test* OR TI "testing protocol" OR AB "testing protocol"

S13	TI ((daily or area or repeat* or serial or mass or population or community or surveillance) N3 (screening or test*)) OR AB ((daily or area or repeat* or serial or mass or population or community or surveillance) N3 (screening or test*))
S12	TI screening OR AB screening
S11	(MH "Mass Screening+")
S10	S5 OR S6 OR S7 OR S8 OR S9
S9	(MH "Immunoassay+")
S8	(MH "COVID-19 Serological Testing")
S7	TI lateral flow test* OR AB lateral flow test*
S6	AB rapid N3 test* OR TI rapid N3 test*
S5	TI (antigen* N3 (test* OR screening)) OR AB (antigen* N3 (test* OR screening))
S4	S1 OR S2 OR S3
S3	(MH "COVID-19")
S2	(MH "SARS-CoV-2")
S1	TI COVID-19 OR coronavir* OR "corona virus" OR (Wuhan N2 virus) OR "2019 nCoV" OR "severe acute respiratory syndrome 2" OR SARS-CoV-2 OR (2019 AND (new OR novel) AND coronavirus)) OR (AB COVID-19 OR coronavir* OR "corona virus" OR (Wuhan N2 virus) OR "2019 nCoV" OR "severe acute respiratory syndrome 2" OR SARS-CoV-2 OR (2019 AND (new OR novel) AND coronavirus

Appendix 2 Data extraction template for primary research studies for RQ2

First author Country Design DOI	Sample size Demographics (<i>age, sex, vaccination/previous infection status</i>) Timing of study	Setting Aim of antigen testing (<i>e.g. screening, serial testing, surveillance</i>)	Public health measures and restrictions in place (<i>e.g. stay at home, curfews, face coverings, hand sanitiser, physical distancing</i>)	Epidemiological situation (cases and variants), vaccination coverage	Testing process (– self-test/ supervised self-test/ self-sample and HCP test/HCP sample and test, PCR confirmation testing). Assay Frequency of testing	Outcomes (<i>transmission, behavioural, mortality, healthcare utilisation, biological, costs, resource utilisation, cost-effectiveness</i>)	Author conclusions
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References

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