Health Information and Quality Authority
An tÚdarás Um Fhaisnéis agus Cáilíocht Sláinte

Health Technology Assessment (HTA) Expert Advisory Group Meeting (NPHET COVID-19 Support)		
Meeting no. 19 : Wednesday 11th August 2021 at 11:30		
(Zoom/video conference)		
(DRAFT) MINUTES		
Attendance:		
Chair	Dr Máirín Ryan	Director of Health Technology Assessment (HTA) & Deputy Chief Executive Officer, HIQA
Members via video conference	Prof Martin Cormican	Consultant Microbiologist & National Clinical Lead, HSE Antimicrobial Resistance and Infection Control Team
	Dr Ellen Crushell	Consultant Paediatrician, Dean, Faculty of Paediatrics, Royal College of Physicians of Ireland & Co-National Clinical Lead, HSE Paediatric/Neonatology Clinical Programme
	Dr John Cuddihy	Specialist in Public Health Medicine & Interim Director, HSE-Health Protection Surveillance Centre (HPSC)
	Dr Cillian de Gascun	Consultant Virologist & Director of the National Virus Reference Laboratory, University College Dublin
	Dr Vida Hamilton	Consultant Anaesthetist & National Clinical Advisor and Group Lead, Acute Hospital Operations Division, HSE
	Dr David Hanlon	General Practitioner & National Clinical Advisor and Group Lead, Primary Care/Clinical Strategy and Programmes, HSE
	Dr Derval Igoe	Specialist in Public Health Medicine, HSE- Health Protection Surveillance Centre (HPSC)
	Prof Mary Keogan	Consultant Immunologist, Beaumont Hospital & Clinical Lead, National Clinical Programme for Pathology, HSE
	Mr Andrew Lynch	Business Manager, Office of the National Clinical Advisor and Group Lead - Mental Health, HSE
	Prof Paddy Mallon	Consultant in Infectious Diseases, St Vincent's University Hospital & HSE Clinical Programme for Infectious Diseases
	Dr Grainne McNally	Workplace Health and Wellbeing Unit HSE; Occupational Medicine Fellow in Physician Health and Wellbeing, Royal College of Physicians Ireland
	Dr Michele Meagher	Medical Officer, Health Products Regulatory Authority
	Dr Deirdre Mulholland	Consultant in Public Health, National Clinical Lead for Knowledge, Evidence and Quality Improvement, Office of the National Clinical Director of Health Protection
	Ms Michelle O'Neill	Deputy Director, HTA Directorate, HIQA
	Dr Margaret B. O'Sullivan	Specialist in Public Health Medicine, Department of Public Health, HSE South & Chair, National Zoonoses Committee
	Dr Michael Power	Consultant Intensivist, Beaumont Hospital & Clinical Lead, National Clinical Programme for Critical Care, HSE
	Prof Susan Smith	Professor of Primary Care Medicine, Royal College of Surgeons in Ireland
	Dr Patrick Stapleton	Consultant Microbiologist, UL Hospitals Group, Limerick & Irish Society of Clinical Microbiologists
	Dr Conor Teljeur	Chief Scientist, HTA Directorate, HIQA
In attendance	Ms Susan Ahern	Health Services Researcher, HTA Directorate, HIQA
	Dr Christopher Fawsitt	Senior Health Economist, HTA Directorate, HIQA
	Dr Louise Larkin	HTA Programme Manager, HTA Directorate, HIQA

	Dr Katie O'Brien	Health Services Researcher, HTA Directorate, HIQA
	Dr Helen O'Donnell	Senior Health Economist, HTA Directorate, HIQA
	Dr Kieran Walsh	Senior HTA Analyst, HTA Directorate, HIQA
Secretariat	Ms Natsha Broderick	HTA Analyst, HTA Directorate, HIQA
Apologies	Ms Avril Aylward	IVD Operations Manager, Medical Devices Department, Health Products Regulatory Authority
	Prof Karina Butler	Consultant Paediatrician and Infectious Diseases Specialist, Children's Health Ireland & Chair of the National Immunisation Advisory Committee
	Dr Jeff Connell	Assistant Director, UCD National Virus Reference Laboratory, University College Dublin
	Dr Eibhlín Connolly	Deputy Chief Medical Officer, Department of Health
	Prof Máire Connolly	Specialist Public Health Adviser, Department of Health and Professor of Global Health and Development, National University of Ireland, Galway
	Ms Sinead Creagh	Laboratory Manager at Cork University Hospital & Academy of Clinical Science and Laboratory Medicine
	Dr Desmond Murphy	Consultant Respiratory Physician & Clinical Lead, National Clinical Programme for Respiratory Medicine, HSE
	Dr Lorraine Doherty	National Clinical Director Health Protection, HSE- Health Protection Surveillance Centre (HPSC)
	Ms Josephine Galway	National Director of Nursing Infection Prevention Control and Antimicrobial Resistance AMRIC Division of Health Protection and Surveillance Centre
	Dr Gerry McCarthy	Consultant in Emergency Medicine, Cork University Hospital & National Clinical Lead, HSE Clinical Programme for Emergency Medicine
	Dr Muiris Houston	Specialist in Occupational Medicine, Clinical Strategist – Pandemic, Workplace Health & Wellbeing, HSE
	Dr Siobhán Kennelly	Consultant Geriatrician & National Clinical & Advisory Group Lead, Older Persons, HSE
	Ms Sarah Lennon	Executive Director, SAGE Advocacy
	Dr Des Murphy	Consultant Respiratory Physician & Clinical Lead, National Clinical Programme for Respiratory Medicine, HSE
	Dr John Murphy	Consultant Paediatrician & Co-National Clinical Lead, HSE Paediatric/Neonatology Clinical Programme
	Dr Sarah M. O'Brien	Specialist in Public Health Medicine, Office of National Clinical Advisor & Group Lead (NCAGL) for Chronic Disease
	Dr Gerard O'Connor	Consultant in Emergency Medicine, Mater Misericordiae University Hospital HSE Clinical Programme for Emergency Medicine

Proposed Matters for Discussion:

1. **Welcome**

   The Chair welcomed the EAG members to the meeting and thanked everyone for all their feedback and contributions to the report.

   Apologies recorded as per above.

2. **Conflicts of Interest**

   No new conflicts raised in advance of this meeting.

3. **Minutes**

   The minutes of the previous meetings of 19th and 24th May 2021 were approved as an accurate reflection of the discussions involved.

4. **Work Programme**

   The group was provided with an overview of the current status of the work programme including:

No.	Review Questions	Status of work	NPHET date
1	RADT asymptomatic populations	Drafted	17th August 2021
2	Face masks in children (update)	Commences 17th August	25th August 2021
3	Review of PPE Models	Commences 16th August	AMRIC 3rd September
4	Duration of immunity post vaccination	Ongoing	23rd September 2021
5	Reinfection rate post infection with SARS-CoV-2 (update)	Commences 7th September	7th October 2021
	Nursing home analysis	Ongoing	
	UNICOV	Ongoing	
	Database	Ongoing - weekly	
	Public health guidance: -vulnerable groups -LTCFs	Ongoing -biweekly -monthly	

5. Presentation on Evidence summary for use of rapid antigen testing for screening or surveillance of asymptomatic individuals to limit transmission of SARS-CoV-2 (KW) (*for discussion*)

The EAG were reminded that NPHET had requested that the HIQA conduct an evidence summary and formulate advice with input from the EAG to address the following policy topic:

"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 points were raised for clarification following this presentation:

- Clarification was sought on how the testing of close contacts had been classified in this report. It was confirmed that for the purpose of the evidence summary contact tracing had been categorised as diagnostic testing and subsequently fell outside the scope of the report. It was suggested that close contact testing and outbreak management should from a group separate from diagnostic testing, as there is testing of asymptomatic individuals with known or suspected exposure. It was agreed that this amendment would be done for clarity.
- It was suggested that the ability of RADTs to detect those that are most infectious needs to be highlighted more in the report as this underpins its potential role as a screening tool, as it was proposed that it is the identification of contagious individuals in society that is key to reducing onward transmission.
- There was a discussion on the scope of the project. There was a suggestion that it was potentially too narrow. Others found the scope appropriate and felt that the evidence summary satisfactorily addressed the policy question provided by NPHET, as it focused on whether RADTs work in real life at reducing onward transmission. It was felt that the issues regarding technical details and comparisons of RADTs (which are debated at length in the literature) are not central to this evidence summary. Caution was also urged with regard to retrospectively expanding the scope of an evidence synthesis as this could introduce additional biases.
- It was suggested that additional information on new near-patient technologies could be added to one of the tables in the report to describe alternatives to lab-based RT-PCR and RADT.
- There was a discussion on superspreading events that occurred in the Netherlands. It was clarified that the evaluation team were aware of these events through the media, however the official Fieldlab reports for these events have not yet been published and so were not included in the current review. It was agreed that a note would be added to the discussion section with reference to these events given their importance to this topic.

6. Advice: Evidence summary for use of rapid antigen testing for screening or surveillance of asymptomatic individuals to limit transmission of SARS-CoV-2 (M'ON) (*for discussion*)

The following points were raised for discussion following this presentation:

- The three different testing scenarios outlined in the evidence summary (diagnostic,[1] screening[2] and surveillance)[3] were discussed. It was suggested that testing of close contacts and testing in the management of outbreaks could form a separate category, distinct from diagnostic testing, given that these involve testing in asymptomatic individuals with a known or suspected exposure to SARS-CoV-2. It was felt to be important to distinguish between testing symptomatic and asymptomatic individuals, even if there is known exposure to SARS-CoV-2 and hence a higher pre-test probability.[4]

- The absence of evidence for the use of RADTs for surveillance was noted. It was agreed that there was unlikely to be a particular role for their use in this regard. It was felt that screening rather than surveillance is where the use of RADTs in asymptomatic populations could provide potential benefit.

- It was felt that screening is where the use of RADTs in asymptomatic populations may be potentially beneficial. It was suggested that the ability of RADTs to detect those that are most infectious underpins their potential role as a screening tool. It was highlighted that it is the identification of contagious individuals in society that is key to reducing onward transmission. It was stated that case detection differs from detection of infectiousness and this is where the two tests (RT-PCR and RADT) fundamentally differ.

- It was acknowledged that this is a polarised area (lab-based RT-PCR vs. RADT). It was noted that there are new molecular technologies that can be used, such as LAMP and near patient PCR that are providing promising results with fast turnaround.

- There was a discussion on the appropriate comparators for RADT. The possible options considered were:

    - RADT versus RT-PCR
    - RADT versus infectivity assays
    - RADT versus no testing

[1] Diagnostic testing is intended to identify infection at an individual level and is performed when a person has signs or symptoms consistent with COVID-19, or when an individual is asymptomatic but has recent known or suspected exposure to SARS-CoV-2

[2] 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.

[3] Surveillance testing is used to gain information at a population level rather than an individual level - and usually involves testing a representative group of the population as opposed to all individuals.

[4] Pretest probability is the chance that the patient has the disease, estimated before the test result is known.

- RADT plus public health measures versus public health measures alone
- RADT without public health measures versus public health measures.

- While diagnostic test accuracy studies tend to use RT-PCR as the reference standard, it was argued that this may not be appropriate in the context of using RADTs to screen for infectiousness in asymptomatic populations, and that infectivity assays may be more appropriate. However, in terms of resource use, it was argued that RT-PCR may be a useful comparison as it illustrates the resources required and ethical issues relating to mass testing asymptomatic individuals, regardless of the test used. It was suggested that no-testing may be the most relevant comparator as currently in Ireland, unlike the UK for example, there are no mass screening programmes for asymptomatic populations. Another suggestion was that the comparison should be RADT in conjunction with usual public health measures versus the same public health measures without any RADT. Such comparisons could highlight the potential additional benefits from implementing RADTs on top of the usual public health measures. It was also suggested that the comparator might be screening with RADTs as an alternative to more restrictive measures, as some real world studies are trialling screening with RADTs as a way to replace other measures (for example, quarantining due to close contact in schools, face masks and physical distancing at concerts).

- With regard to the use of RADTs to replace existing public health measures, it was felt that the current evidence summary finds no strong evidence to support this approach. Anecdotal evidence was provided of the impact of the Delta variant on viral load kinetics, with a big change in Ct values (from weakly positive to strongly positive) observed from one day to the next in some pre-symptomatic patients. It was suggested that RADTs may not have detected these individuals in time. In this context, it was felt that replacement of current public health measures with RADTs could potentially lead to a significantly increased risk of transmission at this time.

- Poor adherence to serial testing using RADTs, as described in some of the included studies, was acknowledged as a particular issue. It was noted that there was a recent Irish publication on this topic. This questionnaire-based study by UCD Veterinary Hospital evaluated staff and students' satisfaction with an RADT pilot programme and examined their reasons for participating, or not, in the programme.[5] While participation was high among staff (75-90% on the two audited days), participation among students was low (average of 19%). The consequences of a positive test result (for example, inability to sit final examinations) was one of the main factors reported for the low participation rates among students.

- Some recent large superspreading events that occurred in Fieldlab pilot events in the Netherlands were discussed. These particular pilot events took place when the Delta variant was dominant. A negative antigen test was required for entry, but face mask and physical

[5] Barry, Gerald, et al. "Rapid antigen testing for SARS-CoV-2 infection in a university setting in Ireland: learning from a 6-week pilot study." medRxiv (2021).

distancing measures were relaxed. In one of the festivals attended by over 20,000 individuals in Utrecht, at least 1,000 people are known to have become infected. In another event involving 650 attendees at a disco, at least 180 are known to have become infected. It was noted that the official Fieldlab reports for these events have not yet been published and so were not included in the evidence summary. In contrast, the earlier Fieldlab events, which favoured the use of pre-screening antigen tests have been published, highlighting the issues with potential publication bias where such studies are more likely to be published in the academic literature than those with negative findings.

- In light of high vaccination coverage in Ireland, it was suggested that routine testing of asymptomatic individuals should be scaled back, rather than expanded. It was argued that testing should not be viewed as a control measure of itself, but rather as part of a suite of public health measures. In the context of high vaccination coverage and continued face mask usage, it was felt that RADTs may not currently have a large role to play, but it was acknowledged that this may change if the epidemiological situation deteriorates in the future.

- While there was agreement that RT-PCR is the gold standard test for detection of SARS-CoV-2 and should not be replaced by any other test, it was suggested that use of RADTs may be better than no-testing in certain circumstances. The utility of RADT testing was agreed to be context-specific, and it was suggested that any decision to use RADTs for screening purposes should consider the following issues:

    - prevalence of SARS-CoV-2 infection in specific populations (and whether there are outbreaks involved)
    - proportion of the population that have adequate immunity
    - type and number of potential close contacts
    - public health measures in place
    - the potential adverse consequences (for example, the risk of severe COVID-19 in the population or setting involved)
    - ethical considerations.

- Preparedness was considered to be an important factor in terms of RADT screening programmes. While it may not currently be considered high priority to roll out a mass testing programme for asymptomatic individuals due to high vaccination coverage, it was suggested that preparing for such programmes may allow for a successful implementation later on if needed. Implementation and feasibility issues, as highlighted by the included studies, could be considered presently. The UK asymptomatic mass testing programme was cited as a good example of preparedness.

- The regulatory status of RADTs was discussed by a representative of the Health Products Regulatory Authority (HPRA). It was stated that there is currently no control of supply for in-vitro diagnostic devices (IVDs) once they are CE-marked, though this may change under new Directives coming into force in 2022.[6] It was clarified that there is currently no centralised database of CE-marked tests on the European market. Though there are plans for such a database (Eudamed) to be established under the new Directives, this will not be fully available for another two to three years. Although there are some lists that have attempted to collate all known RADTs on the EU market, these lists are not necessarily up-to-date or comprehensive, and information on their indications and the populations in which their use is intended (for example, symptomatic versus asymptomatic) is generally not reported. It was acknowledged that the availability of information on IVDs, including RADTs, has been less than satisfactory to-date, but this should improve under the new Directives.

- Additional considerations were discussed including effectiveness of self-testing compared with professionally administered tests (as self-tests are generally found to have lower sensitivity than those that are professionally administered) and the opportunity costs (that is the diverting of staff and or resources) associated with RADT screening, which were viewed to be substantial. There was a call for economic evaluations to be conducted alongside mass testing programmes, given the uncertainty regarding the cost-effectiveness of such resource-intensive programmes.

7. Interventions in the community setting, prior to diagnosis of COVID-19, to prevent or minimise progression to severe disease (KC) (for discussion)

The EAG were remined of a previous evidence summary that had been published by HIQA's COVID-19 evidence synthesis team on the following topic:

What is the evidence on the effectiveness of pharmacological interventions in the community, prior to a diagnosis of COVID-19, aimed at preventing or minimising progression to severe disease?

Since the publication of this report, an included study has been redacted. It was acknowledged that the redacted paper, although had been included in the report, was deemed to have a high risk of bias and that its redaction didn't change the conclusion of the report. A footnote has been added to the report wherever the paper is referred to and the published version will be updated accordingly.

No points were raised for clarification following this presentation.

[6] Health Products Regulatory Authority. Key aspects specific to the in-vitro Diagnostics Regulation (IVDR) Dublin, Ireland: HPRA
http://www.hpra.ie/homepage/medical-devices/regulatory-information/new-eu-device-regulations/key-aspects-specific-of-(in-vitro-diagnostics-regulation)-ivdr

8. Meeting Close

The Chair thanked the EAG members for their contributions and highlighted the next meeting will take place on Monday 23rd August. It was acklowledged that this was Vida Hamilton's last meeting and she was thanked for all her contributions since joining the EAG.

a) AOB – none
b) Date of next meeting: Monday 23rd August 2021

Meeting closed at 13:03