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.2: Tuesday 6th October 2020 at 12:00

(Zoom/video conference)

MINUTES

Attendance:

Chair	Dr Máirín Ryan	Director of Health Technology Assessment & Deputy Chief Executive Officer, HIQA
Members via video conference	Dr Niamh Bambury	Specialist Registrar in Public Health Medicine, HSE- Health Protection Surveillance Centre (HPSC)
	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 Adjunct Professor of Global Health and Development, National University of Ireland, Galway
	Prof Martin Cormican	Consultant Microbiologist & National Clinical Lead, HSE Antimicrobial Resistance and Infection Control Team
	Ms Sinead Creagh	Laboratory Manager at Cork University Hospital & Academy of Clinical Science and Laboratory Medicine
	Dr Cillian de Gascun	Consultant Virologist & Director of the National Virus Reference Laboratory, University College Dublin
	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 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 Patricia Harrington	Head of Assessment, Health Technology Assessment, HIQA
	Dr Muiris Houston	Specialist in Occupational Medicine, Clinical Strategist – Pandemic, Workplace Health & Wellbeing, 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
	Dr Siobhán Kennelly	Consultant Geriatrician & National Clinical & Advisory Group Lead, Older Persons, HSE
	Mr Andrew Lynch	Business Manager, Office of the National Clinical Advisor and Group Lead - Mental Health, HSE
	Dr Gerry McCarthy	Consultant in Emergency Medicine, Cork University Hospital & National Clinical Lead, HSE Clinical Programme for Emergency Medicine
	Dr Eavan Muldoon	Consultant in Infectious Diseases, Mater Misericordiae University Hospital, National Clinical Lead for CIT and OPAT programmes & HSE Clinical Programme for Infectious Diseases
	Dr Desmond Murphy	Consultant Respiratory Physician & National Clinical Lead, HSE Clinical Programme for Respiratory Medicine
	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
	Ms Michelle O'Neill	HRB-CICER Programme Manager, 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, Beaumount Hospital & National Clinical Lead, HSE Clinical Programme for Critical Care
	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, Health Technology Assessment, HIQA
	Ms Anne Tobin	Assessment and Surveillance Manager, Medical Devices, Health Products Regulatory Authority
In attendance	Dr Christopher Fawsitt	Senior Health Economist, HIQA
	Dr Eamon O'Murchu	Senior HTA Analyst, Health Technology Assessment, HIQA
	Ms Karen Jordan	HTA Analyst, Health Technology Assessment, HIQA
	Ms Natasha Broderick	Health Economics Intern, Health Technology Assessment, HIQA
	Dr Laura Comber	HTA Research Analyst, Health Technology Assessment, HIQA
	Ms Susan Ahern	Health Services Researcher, Health Technology Assessment, HIQA
	Dr Susan Spillane	Senior HTA Analyst, Health Technology Assessment, HIQA
Secretariat	Ms Debra Spillane	PA to Dr Máirín Ryan, HIQA
Apologies	Prof Karina Butler	Consultant Paediatrician and Infectious Diseases Specialist, Children's Health Ireland & Chair of the National Immunisation Advisory Committee
	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)
	Ms Sarah Lennon	Executive Director, SAGE Advocacy
	Prof Paddy Mallon	Consultant in Infectious Diseases, St Vincent's University Hospital & HSE Clinical Programme for Infectious Diseases
	Dr Mary O'Riordan	Specialist in Public Health Medicine, HSE- Health Protection Surveillance Centre (HPSC)
	Dr Lynda Sisson	Consultant in Occupational Medicine, Dean of Faculty of Occupational Medicine, RCPI & HSE National Clinical Lead for Workplace Health and Well Being

Proposed Matters for Discussion:

1. **Welcome**
   The Chair welcomed all members to the meeting. An updated membership list was circulated; new members were asked to check their names and titles for accuracy.
2. **Apologies**
   Noted above.
3. **Conflicts of Interest & Minutes of Meeting 29.09.2020**
   Conflict of interest and confidentiality statements are required for all members with new potential conflicts to be discussed with the Chair in advance of meetings. Completed statements have been received from all members, with no new conflicts raised in advance of this meeting.
   The minutes of 29.09.2020 were accepted as a fair and accurate representation of the discussion.
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.	Rapid HTA of diagnostic tests for SARS-CoV-2	Drafted	8/10/2020
2.	RQ 22 Testing at day 7 and 10 to reduce duration of restriction of movement	Ongoing	22/10/2020
3.	RQ 9 – Long term immune response and reinfection post SARS-CoV-2 infection	Ongoing	22/10/2020
4.	RQ 20 – Conditions that are at very high risk (extremely medically vulnerable) from COVID-19	Ongoing	5/11/2020
5.	RQ 21 – High risk settings for transmission of SARS-CoV-2	Scoping to begin 5/10/20	
6.	Database	Ongoing	
7.	Public health guidance: - vulnerable groups - LTCFs	Ongoing	

5. Presentation of rapid HTA of alternatives to laboratory-based RT-PCR for the detection of SARS-CoV-2

It was noted that the HIQA evaluation team was requested by NPHET to update the rapid HTA submitted to NPHET in April 2020. The focus of the update was alternative tests and testing methods to laboratory-based real time RT PCR (rRT-PCR) that could be used to detect current infection with SARS-CoV-2. As per the agreed deliverables document, four key research questions (RQs) were addressed in the updated report. The Chair thanked the members for reviewing the draft HTA circulated last week and the initial feedback received. Presentations were provided on key points for each of the chapters of the HTA that addressing the following four RQs:

a) *RQ1: What are the potential tests or testing methods that can detect SARS-CoV-2?*

b) *RQ2: What testing methods are currently being used internationally for the detection of SARS-CoV-2?*

c) *RQ3: What is the diagnostic accuracy of alternatives to laboratory based real-time RT-PCR testing, for the purpose of diagnosis of current infection with SARS-CoV-2?*

d) *RQ4: What are the potential organisational considerations and resource implications that might arise from the use of alternative tests for direct detection of SARS-CoV-2 infection in Ireland?*

The following points were raised as matters for clarification or discussion by the EAG:

- The types of healthcare professionals performing rapid testing internationally was queried. The team noted that no details were provided in the international documents reviewed. Current CE-marking of rapid tests including rapid antigen detection tests

(RADTs) limits their use to healthcare professionals, that is, they are not authorised for self-testing.

- The EAG enquired as to whether there was evidence of patient charges or out-of-pocket expenses for testing. The team clarified that this appeared limited to travel-related testing, for example in airports, most of which was noted to be laboratory-based RT-PCR.
- The meaning of the term 'hard to reach' populations in country-specific testing strategies was queried. The team clarified that, in the context of the international evidence, this related to geographical distances rather than vulnerable groups (homeless etc).
- It was queried whether cross-reactivity in antigen detection tests, with respect to seasonal coronaviruses, was addressed in any studies included in RQ 3. It was noted that this was not reported in the diagnostic accuracy studies identified. The EAG stressed the importance of data to confirm the absence of cross-reactivity with other coronaviruses in the context of the coming months.
- Nasal swabs have been accepted by NPHET as an alternative to combined nasopharyngeal/oropharyngeal swabs for children in Ireland. Laboratory validation of saliva samples is ongoing and it was hoped that a clinical validation study in the community will be up and running in a couple of weeks.
- WHO has announced that 120 million RADTs will be made available for low and middle income countries; costs are to be set at a maximum of $5 per kit. The WHO has endorsed two particular RADTs for this purpose.
- There are significant limitations with the CE-marking process for diagnostic tests, which is based on self-certification by the manufacturers. Applicability to other clinical scenarios is limited if reported analytical performance is based only on hospitalised patients or on a very symptomatic population. Also, sample numbers were noted often to be small, so there is substantial uncertainty associated with the reported estimates. Clinical validation for all tests is required, which takes consideration of the planned use of the test (purpose, population, setting) with performance measured relative to the accepted standard (laboratory-based rRT-PCR).
- Consideration should be given to the usefulness of a potential study on the utility of faster turnaround time of tests (that is, the utility of fast turnaround in aiding public health interventions) versus higher diagnostic sensitivity.
- Clinical validation studies with parallel testing of a RADT and rRT-PCR would help to identify accuracy of RADT in asymptomatic as well as symptomatic populations. Due to the current lack of comparative evidence, a study which compares the clinical performance in parallel of a number of test approaches (RADT, RT-LAMP) with laboratory-based rRT-PCR would help establish their comparative values.
- For logistical reasons, the use of RADTs that could support rRT-PCR confirmatory testing on the same patient sample should be considered.
- An assay that could indicate current infectiousness of confirmed COVID-19 cases, or lack thereof, could be helpful in allowing de-isolation to improve patient flow in hospitals. Noted that testing to inform this decision is not currently in place.
- In the event that near-patient testing (NPT) sites are established as part of the COVID-19 national testing strategy:

a) there would be a requirement for an ongoing quality assurance programme. Consideration should be given to establishing a link with local hospital pathology services to provide support to NPT sites, however the resource capacity of laboratories will need to be considered. It was noted that many healthcare facilities are currently working towards full ISO accreditation, but that there is no legislative requirement for this.
b) Connectivity between disparate computer systems and COVID-19 NPT devices would be necessary to facilitate efficient exchange of results and disease surveillance.
c) Consideration needs to be given to how the results of rapid tests are managed and how they might be used to inform contact tracing efforts.

- Concern was noted regarding potential quality issues with a significant number of commercial entities offering testing for COVID-19 on an array of platforms and including use of RADTs of uncertain diagnostic accuracy.
- Pooling of validation data from different laboratories could expedite the validation process, and conserve limited laboratory consumables.
- Increased use of sample pooling in selected groups with low prevalence of SARS-CoV-2 could be deployed as an immediate measure that can be taken to increase test capacity, but this is logistically challenging and not suitable for NPT.

Some notes of clarification will be made to the draft report where necessary based on the above points. The draft was otherwise accepted by the EAG as a fair reflection of the evidence synthesis that was undertaken.

6. Advice from Rapid HTA of diagnostic tests for SARS-CoV-2

The current laboratory capacity was noted to be approx. 115,000 rRT-PCR tests per week. It was noted that demand for testing could exceed this capacity in the coming months. Based on the evidence presented in relation to potential tests or testing methods that could detect SARS-CoV-2, the potential organisational issues and resource implications that might arise from their use, and their knowledge of this area, the EAG were asked to consider what alternatives to laboratory-based rRT PCR could be deployed in Ireland immediately (coming weeks) and in the near future (e.g., Q1 2021 / Q2 2021). Key points discussed were as follows:

- Discussion around the use of sample pooling strategies in high-throughput laboratories if local laboratory directors consider it an appropriate approach to increase test capacity, particularly in asymptomatic populations such as planned admissions for elective surgery. Pooling could be implemented immediately without the need for additional investment.
- In terms of deployment of RADT:
  - Clinical validation studies will be necessary prior to deployment; concern was expressed that if there is not immediate investment in these studies with resources

made available to move things forward quickly that current rRT-PCR capacity would be exceeded before evaluations can be completed.
    - Noted that when used to detect norovirus, antigen testing is far less sensitive than molecular detection, but it is useful when there are suspected cases in groups. Therefore in the context of some at-risk settings (for example, nursing homes, food processing industry and university student populations) rapid detection of an outbreak, using an appropriately validated test, could facilitate rapid initiation of public health interventions to prevent and manage viral transmission.
    - Urgent work is required for parallel testing for rRT-PCR in situ with antigen testing to assess the feasibility and performance of RADT in investigating outbreaks in settings for which this has been an issue (e.g., nursing homes, food processing settings).
    - Consideration should be given to deployment of RADT in community testing centres for symptomatic patients and testing close contacts. Clinical validation studies will be required. It would also be of interest for the local public health teams to evaluate the public health benefits of decreasing the turnaround time for positive tests (within 15 minutes vs currently > 24 hours).
    - Noted that ECDC recommendation on serial testing on an ongoing basis of healthcare workers presents significant challenges in terms of current RT-PCR capacity, so this may be an important area to consider for use of RADT. However the lack of performance data in asymptomatic populations was noted, emphasising the need for validation studies to confirm utility in this setting.
    - Settings in which serial testing has already been deployed (e.g. nursing homes, food processing factories) may also be relevant for RADT use. Again, clinical validation is required. While test sensitivity is lower than that of rRT-PCR, noted that it might be possible to compensate for this to some extent by testing more frequently.
    - The minimum acceptable performance of the RADT must be considered. It should be based on the more stringent WHO specifications (desirable minimum sensitivity and specificity, noting that the lower bound of the confidence interval should equal or exceed the stated threshold).
    - Careful selection of RADT will be required given the substantial variation between tests. Noted also that available commercial tests differ in their pre-test handling and ease of use. Initial essential criteria should be met in selecting RADT for clinical validation studies.
    - There may be merit in looking at use of RADT for patients moving between wards if the pre-test probability is high, as can indicate if urgent action required. Additionally it could remove pressure on the laboratory to do molecular testing.
    - Noted that it would be helpful to deploy a medical scientist with experience in NPT during the clinical validation phase. This would ensure oversight of the system, quality and training and facilitate coordination with the hospital laboratory systems.
- The work of the Irish coronavirus CPC Consortium was noted in terms of genome sequencing for surveillance purposes, and for tracking outbreaks. Using sequencing at scale to identify where transmission is happening, and to identify potentially what types of strains are circulating in the country. This may not be relevant until back down to low levels of community transmission.

- Care required around the use of the term 'screening' given the standard required of screening in recent judgements. The terms 'testing' or 'serial testing' were considered more applicable to this context.
- Key as part of validation would also be to look at situations where repeat testing has been done amongst contacts.
- In terms of test selection, acute unscheduled care is typically divided into COVID suspected versus non-COVID streams; desirable test characteristics for testing in acute unscheduled COVID and non-COVID care were discussed.
- Concerns were expressed around substantial commercial and private testing outside the National Test and Trace programme, particularly the performance, governance and reporting of this testing, the potential adverse implications for contact tracing, and the potential for significant confusion for stakeholders. Suggested that there is a requirement for a multi-agency communication campaign to highlight to the public and other stakeholders the risks identified.

7. Testing at day 7 and 10 to reduce duration of restriction of movement

NPHET has requested that the evaluation team undertake a modelling exercise to estimate the proportion of potentially infectious people entering the community, and the potential number of infections, resulting from a number of scenarios involving testing of close contacts that is carried out with the goal of reducing the duration of restriction of movements. The request stemmed from the HIQA advice to NPHET (meeting date 01/10/2020) in relation to the duration of restriction of movements. It was agreed that the evaluation team will meet members of ECDC evaluation team to understand the evidence base underpinning the ECDC advice in relation to use of day 10 testing to inform early release from quarantine. It was noted NPHET had asked the HSE to audit compliance with their restrictive movement requirements for contacts, but that it is unlikely that this audit data will be ready in time to inform the EAG meeting on 20 October 2020.

An update on the progress of the review was provided, and it will be discussed in full at the EAG meeting on the 20 October 2020.

8. Long term immune response and reinfection post SARS-CoV-2

This is the fourth iteration of the report, updating versions published on 13 May, 9 June and 6 August 2020. In the course of the updates, the research questions and methodology used have been refined. This fourth update is limited to studies investigating reinfection with SARS-CoV-2 and the long term (≥60 days) immune response to SARS-CoV-2

Research question:

- What is the rate of reinfection/duration of immunity in individuals who recover from a laboratory-confirmed coronavirus infection?

An update on the progress of the review was provided, and it will be discussed in full at the EAG meeting on the 20 October 2020.

9. Meeting close

a) *AOB*
No further matters.

b) *Date of next meeting:*
Tuesday 20th Oct 12pm by video conference.