Health Technology Assessment (HTA) Expert Advisory Group Meeting (NPHET COVID-19 Support)		
Meeting no. 18 : Monday 24th May 2021 at 11:00		
(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 Karina Butler	Consultant Paediatrician and Infectious Diseases Specialist, Children's Health Ireland & Chair of the National Immunisation Advisory Committee
	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
	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 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 James Gilroy	Medical Officer, Health Products Regulatory Authority
	Dr Patricia Harrington	Deputy Director, HTA Directorate, HIQA
	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
	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 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
	Prof Susan Smith	Professor of Primary Care Medicine, Royal College of Surgeons in Ireland
	Dr Conor Teljeur	Chief Scientist, HTA Directorate, HIQA
In attendance	Ms Natasha Broderick	HTA Analyst, Health Technology Assessment, HIQA
	Dr Paula Byrne	Health Services Researcher, HTA Directorate, HIQA
	Dr Karen Cardwell	Postdoctoral Reseacher, HTA Directorate, HIQA
	Dr Eamon O'Murchu	Senior HTA Analyst, HTA Directorate, HIQA
	Mr Barrie Tyner	Information Scientist, HTA Directorate, HIQA

	Dr Kieran Walsh	Senior HTA Analyst, HTA Directorate, HIQA
Secretariat	Ms Debra Spillane	PA to Dr Máirín Ryan, HIQA
	Dr Jeff Connell	Assistant Director, UCD National Virus Reference Laboratory, University College Dublin
	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 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 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 Deirdre Mulholland	Consultant in Public Health, National Clinical Lead for Knowledge, Evidence and Quality Improvement, Office of the National Clinical Director of Health Protection
	Dr Des Murphy	Consultant Respiratory Physician & Clinical Lead, National Clinical Programme for Respiratory Medicine, HSE
	Dr Michael Power	Consultant Intensivist, Beaumont Hospital & Clinical Lead, National Clinical Programme for Critical Care, HSE
	Dr Lynda Sisson	Consultant in Occupational Medicine, Dean of Faculty of Occupational Medicine, RCPI & HSE National Clinical Lead for Workplace Health and Well Being
	Dr Patrick Stapleton	Consultant Microbiologist, UL Hospitals Group, Limerick & Irish Society of Clinical Microbiologists

Proposed Matters for Discussion:

1. **Welcome**

   The Chair welcomed all members for joining and apologised if members were unable to receive some documentation due to some remaining email issues relating to the recent ransomware attack on the public health system. As such, additional detail was given throughout presentations to assist with commentary.

   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 meeting of 19.05.2021 will be provided at the next scheduled meeting.

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	Update – Duration of protective immunity (protection from reinfection) following SARS-CoV-2 infection	Drafted	27 May 2021
3	Public health measures to limit the transmission of SARS-CoV-2 at mass gatherings	Drafted	27 May 2021
3	Review of international public policy response for update	To start 8 June 2021 - TBC	17 June 2021 - TBC
	Database	Ongoing - weekly	
	Public health guidance: - vulnerable groups - LTCFs	Ongoing	

5. **Presentation on Duration of protective immunity (protection from reinfection) following SARS-CoV-2 infection (E'OM) (*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 topics:

"How long does protective immunity (that is, prevention of antigen or RT-PCR confirmed reinfection) last in individuals who were previously infected with SARS-CoV-2 and subsequently recovered?"

and

"What is the duration of immune memory responses (T-cell and B-cell memory and or their components' responses) following SARS-CoV-2 infection?"

This evidence summary is expected to inform a range of policy questions relating to the duration of protective immunity following infection with SARS-CoV-2.

The following points were raised for clarification following this presentation:

- It was clarified that while studies consistently demonstrated low rates of PCR-confirmed SARS-CoV-2 reinfection, the included studies could not determine if natural infection prevents onward transmission of SARS-CoV-2. In addition, it was clarified that there is a lack of data on the presence and impact of mucosal immune memory.

- It was clarified that a number of included studies were subject to bias. This was particularly apparent in studies with relatively lower participation rates or low uptake of testing where testing was voluntary. These studies may be affected by outcome ascertainment bias. It was also clarified that a limitation of a number of studies was that short intervals between primary and secondary infections were allowed (such as a minimum of 45 days between infection events) thus these may be detecting persistent shedding of viral RNA in the early convalescent period rather than true reinfection.

6. **Advice: Duration of protective immunity (protection from reinfection) following SARS-CoV-2 infection (PH) (*for discussion*)**

The following points were raised for discussion following this presentation:

- The evidence regarding immunity up to 10 months post-infection was considered robust.

- Regarding immune memory, it was noted that studies investigating serological samples may underestimate immunological memory as measures of immune memory cells in the blood are not representative of the larger proportion of these cells that may be resident in tissues.

- Extrapolating the findings regarding immune memory from laboratory studies to real-world settings should be done with caution, as assays that measure immune memory are still undergoing standardisation. Additionally, samples from patients included in studies may not be representative of the broader population.

- The included studies do not determine if natural infection prevents onward transmission of SARS-CoV-2. To date previously infected individuals have not been observed to amplify outbreaks in Ireland. Further data specifically on the presence and impact of mucosal immune memory will be required to determine the potential for onward transmission of the virus following recovery from infection.

- It was noted that post-pandemic population immunity may depend on the endemic presence of SARS-CoV-2 in conjunction with vaccination.

- Regarding the cohort studies that investigated the risk of reinfection in individuals who had knowledge of prior SARS-CoV-2 infection, the EAG noted the potential for outcome ascertainment bias and selection bias, in particular in studies where testing was voluntary and in studies with low participation in follow-up testing. Knowledge of prior infection may alter an individual's behaviour, which may result in bias in outcome measurement.

- The EAG noted a recent study by Public Health England and updated results from the SIREN study (published 23 and 24 May 2021). While not specific to reinfection, these studies provide updated evidence that vaccination is effective at preventing infection with the variants B.117 and B.1.617.2 (Indian variant).

- The potential advantages of changing the current advice (as in, extending the period of presumptive immunity from six months), were discussed. This would have a number of practical implications and would be welcomed by the health system.

    - At present, individuals are considered to have immunity for six months after their initial positive SARS-CoV-2 PCR test; therefore, a person who becomes an asymptomatic contact of a case and has had a positive test result within the previous six months does not need to restrict their movements and does not require testing.

    - The duration of presumptive immunity would be important to the implementation of 'green certificates' that provide proof of either full vaccination, recent negative test result or recovery from COVID-19.

    - Current advice from NIAC is that those with laboratory-confirmed COVID-19 within the last six months, who are under 50 years of age and who are immunocompetent, only require a single vaccine dose to be considered fully vaccinated. Extending the period of presumptive immunity would increase the number of individuals considered fully vaccinated with a single one dose. However, it was noted that implementing the one dose vaccine schedule for those previously

infected was problematic as it has been difficult to ascertain previous infection status.

- The EAG acknowledged that it would be meaningful to people if the period of presumptive immunity is extended. While the impact of SARS-CoV-2 variants is uncertain, it is reassuring that to date reinfection rates have remained low. This is a positive message that is important to communicate.

- Based on the evidence review there was general agreement within the EAG that the period of presumptive immunity should be extended to nine months.

7. Presentation on Public health measures to limit the transmission of SARS-CoV-2 at mass gatherings (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 question:

"What public health measures are necessary to enable mass gatherings to occur safely in both indoor and outdoor settings?"

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

RQ1: What public health measures are advised internationally to limit the transmission of SARS-CoV-2 at mass gatherings (including both indoor and outdoor settings)?

RQ2: What is the evidence that public health measures aimed at limiting the transmission of SARS-CoV-2 at mass gatherings (including both indoor and outdoor settings) are effective?

<u>The following points were raised for clarification following this presentation:</u>

- It was clarified that the English Events Research Programme involves mandatory pre-event mandatory lateral flow device (antigen) testing for entry. While attendees are also asked to take pre- and post-event home PCR tests these are not mandatory, but rather are being undertaken to inform the research. During the event physical distancing and mask requirements are generally eased.
- It was suggested that providing the COVID-19 incidence rates for the location and date of each of the included studies may help provide some useful context.
- It was suggested that it would be helpful to provide further discussion on the differences between PCR and antigen testing in the report.
- The ambiguity of the WHO mass gathering definition was discussed. It was suggested that if there is no agreed international definition, then developing a

new definition might help, as people's understanding of what constutitues a mass gathering likely differs.

8. **Advice: Public health measures to limit the transmission of SARS-CoV-2 at mass gatherings (M'ON) (*for discussion*)**

The following points were raised for discussion following this presentation:

- There was a general welcome among the EAG for the cautious reopening of society as this was felt to be important for the mental health of the nation as well as the economic recovery. It was discussed how some European countries were proposing a gradual approach to easing mass gathering restrictions. There was general consensus among the EAG that a gradual and cautious approach to reopening should be followed in Ireland.
- It was noted that the World Health Organization (WHO) recently updated their guidance to acknowledge that SARS-CoV-2 can be transmitted via long range (greater than 1 metre), and that this transmission risk is particularly elevated in poorly ventilated and or crowded indoor settings, where people tend to spend longer periods of time. The avoidance of mass gatherings in indoor, crowded and poorly ventilated settings was felt to be crucial to prevent superspreading events, considering the updated WHO advice and the findings provided in the evidence summary. Particular concerns were raised about holding mass gathering events in such settings without face masks and physical distancing.
- A clear preference was stated, in the first instance, for outdoor, seated events, involving relatively small numbers, and for a short period of time, with no eating or drinking permitted. Thereafter, an incremental, step-wise approach to easing restrictions was suggested as a means to enable mass gatherings to recommence safely in all settings, while population vaccination coverage increases.
- While the stringent public health measures that were implemented for the Hajj pilgrimage were noted to be very successful in reducing the risk of SARS-CoV-2 transmission to an extremely low level, there was a general consensus that such onerous measures would not be acceptable or feasible in an Irish context.
- Concerns were raised about the impartiality of some of the major pilot event studies conducted to date, given that they were mostly funded and or supported by the events industry. The limited follow-up data in these studies were also noted as a particular limitation. It was suggested that there may be a bias due to under-reporting and low compliance to follow-up testing in some studies as individuals may not want to officially attribute their symptoms to the event, should they view the reopening of such events as important.
- Serious ethical concerns were raised in relation to pilot mass gathering events, particularly where these target or are likely to predominantly include a younger

population who are unlikely to be eligible for vaccination until later this year. It was noted that mass gatherings involving a largely unvaccinated younger population is not without risk. The high incidence of SARS-COV-2 infection in this cohort was noted. Although this population may be at low risk of severe disease from COVID-19, the potential for developing long-COVID was highlighted.

- The purpose of many of the pilot events conducted to date was viewed to be unclear, as the epidemiological impact of the mass gathering was not measured or considered in most of them. While superspreading events may be rare, they can have significant consequences, and this was felt to be a critical issue that needs to be considered in future pilots. It was highlighted that pilot events should be carefully planned and there must be clear public health involvement to mitigate risks as much as possible. A cautious approach should apply to any pilot event, with smaller more manageable events, in lower risk settings, being piloted first.
- The importance of conducting independent research with clear protocols, robust study design, ethics review and transparent and timely reporting was stressed. It was suggested that public health expertise should direct and inform any pilot events in Ireland, given the potential impact on public health.
- There is a sense of urgency in terms of conducting these pilot studies given the movement to significantly ease restrictions and the need for high quality data to inform decision-making. Coordinated action was emphasised in order to conduct these pilot studies within the short time frame in which the data would be useful. The challenges of conducting such high quality research in the short term were discussed in the context of severe capacity restrictions facing the health service, particularly in light of the recent cyber attack on the HSE. It was suggested that universities' expertise could be leveraged in such projects, with the aim of obtaining good quality, timely and informative data.
- It was questioned where ethics approval of such studies would sit given that these types of studies would be outside the remit of institution-level research ethics committees.
- It was stated that Ireland is currently at a critical juncture in terms of reopening and there will be pressure to allow mass gatherings to occur. In the absence of well-designed pilot studies, an alternative is to continue with the current measures that are in place and wait until there is sufficient vaccination coverage in the population before permitting mass gatherings. However it was acknowledged that this may not be acceptable.
- The relative advantages and disadvantages of PCR-based and antigen-based pre-event testing were discussed. While PCR tests were acknowledged as having higher sensitivity than antigen tests, it was suggested that antigen tests

may be more appropriate for short term events as these correlate well with infectivity, may be more feasible to deploy at events given their rapid turn around time, and are cheaper. However, a point was raised that while the reagents for antigen tests may be cheaper, the logistics of organising teams of trained professionals to obtain or supervise samples and administer antigen tests at events (as occurred in some of the included studied) would be challenging and costly. It was suggested that PCR-based pooled sample testing of households or friend groups/bubbles may be a potentially useful option for pre-event testing. Importantly, it was acknowledged that any pre-event testing will not detect 100% of cases and as such it would need to be combined with other measures. Particular importance was placed on adequate ventilation, face mask use, physical distancing and transport to and from mass gathering events.

- The use of trained professionals to collect and process samples, will increase the reliability of any pre-event testing. Self-testing[1] (or unsupervised self-sampling[2]) for pre-event testing may not be the preferred approach given the potential for the sub-optimal quality of specimen collection, which may undermine the reliability of the entire testing process.
- In relation to the stated policy question, instead of "what are the minimum public health *measures* necessary", it was suggested that it could be framed as "what are the public health *conditions* necessary" for mass gatherings to safely occur. It was stated that decisions on the easing of mass gathering restrictions should not be separated from the level of infection in the community and the level of vaccination coverage in the population.
- While the lifting of mass gathering restrictions in Israel was viewed as a clear outlier, it was noted that England, France and Finland are also proposing relatively rapid lifting of mass gathering restrictions over the coming weeks. Caution was urged with regards to following our neighbours' lead given that in Ireland the younger population, who have a higher COVID-19 incidence, may not be vaccinated until September. Additionally differences in the epidemiological situation between Ireland and these other countries may explain different strategies. It was suggested that there may also be legal consequences from easing mass gatherings too quickly should this prompt another wave of infections.

[1] Self-test requires an individual to collect a specimen from their nose or throat (can be a nose swab, throat swab, saliva or a combination of all), conduct the test and interpret the results according to the instructions provided. This is done using a single-use self-test kit that can be used at home (or in another setting) and without any specialised laboratory equipment or training.
[2] Self-sampling refers to an individual collecting their own swab, or specimen, for a SARS-CoV-2 test. This test could be performed using a self-test or could be performed in a laboratory (or other healthcare setting) by a trained person

- It was noted that COVID-19 cases are commonly associated with activities that occur before and after the mass gathering event (for example, due to shared transport or social events), and that this was observed by public health teams in previous outbreaks, particularly in relation to sporting events.
- It was reiterated that not all mass gatherings carry the same level of risk. While transmission can occur at any gathering, the risk of transmission differs (for example, indoor vs outdoor, seated vs unseated, short vs long duration etc.). It was felt that there should not be a blanket ban on all mass gatherings and that this should be clearly communicated.
- The recent cyberattack on the HSE was discussed in relation to its impact on the operation of the entire health service. The laboratory and radiology services were identified as being particularly affected, and another wave of COVID-19 cases, for whatever reason, may completely overwhelm the system. This further emphasises the need to proceed with caution.
- The possibility of using vaccination and or immunity status to complement pre-event testing as a requirement for accessing mass gatherings was discussed. It was suggested that this policy may result in legal challenges. Proof of vaccination was viewed as a potential incentive for many young people to get vaccinated, if it was the only means of accessing events. However, given the European Commission recently stated that those who have not been vaccinated should not be at a disadvantage, it was felt there would have to be an option for testing.
- The use of EU digital green certificates that provides proof of either full vaccination, recent negative test result or recovery from COVID-19, to gain access to mass gatherings, was discussed. It was clarified that certain EU countries such as Italy plan to use these green certificates domestically to allow individuals to access mass gathering events.
- While restricting movements before or after mass gatherings to limit potential onward transmission has been implemented in some of the included studies, it was noted that such a measure may not be feasible or enforecable and could only be advisory. However, it was suggested that vulnerable populations may be advised not to attend mass gatherings.

9. Meeting Close

The Chair thanked the EAG members for their contributions and would follow up with members with the next date of the EAG in the following weeks.

a) AOB – none.
b) Date of next meeting: TBD

Meeting closed at 12:56