Deep-Dive on the Future of COVID-19

Scottish Government COVID-19 Advisory Group / Standing Committee on Pandemics
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Via Microsoft Teams

The Chair welcomed attendees to this session and welcomed Professor David Nabarro, WHO Special Envoy on COVID-19. The purpose of today's session is to outline the possible future evolution of the SARS-CoV-2 virus and the resilience and preparedness tools that will form part of the response to this and future pandemics and novel pathogens.

Introduction

Looking ahead – the pandemic is not finished. The virus is the problem and people are the solution. The goal looking ahead is for people to choose to do the right thing at the right time because they want to, and shift from behaviours being changed as a result of strong regulations unless these are absolutely necessary. The people of the UK have been incredibly responsive to the demand being placed on societies as a result of COVID-19. Looking ahead cannot be focussed on planning for future measures or restrictions. There is a need to make and maintain the social contract between the people and state to facilitate positive behaviour change.

The relation between people and state is shaped by people, and the necessary partnership between people and the state. The four key components of this (the '4Ps') are:

1. People and partnership with government;
2. Preventing transmission – physical distancing, hygiene, face protection, ventilation.
3. Protecting all those at high risk of severe illness and long term consequences of illness, for example by using vaccination;
4. Preparing for future surges which will come.

Mandates more likely to lead to political disputes and stigmatisation. The aim is to try to minimise the use of mandates and maximise the emphasis on partnership.

Protecting people should include protecting people from the impact of long covid, which is likely to be currently underestimated and the potential costs of long covid will begin to become more apparent over time. Because of this, preventing transmission should be focus when there are high levels of the virus circulating. Vaccination does not play a primary role in preventing transmission but plays a role in preventing serious illness and death. Vaccination should not be marketed as a primary means of stopping the pandemic but does reduce its impact.

Surges are likely to come roughly every 3 months, even with Omicron, due to waning immunity both from vaccination and natural immunity, particularly in older people. In

preparing for surges we should prepare for surges of variants we know as well as new variants.

The state should play the leading role in detecting potential surges and in communicating this to the public and local officials, even before there is granular data available on these. Waiting for certainty can lead to missed opportunities to get the virus under control.

Public health should be at the centre of the future response. This needs to be part of the discourse, not focussing only on healthcare capacity but the resilience of local-level systems, surveillance, support for isolation etc.

The only way to communicate about COVID-19 is to be authentic. Five key words to explain what really matters here:

1. Pandemic is about all of humanity, not about a particular country or subset of this. Attempting to deal with the pandemic in isolation without reference to other countries will not work.
2. To respond to the pandemic we have to be aware we are dealing with a virus that is new that is not fully understood. Because of this, we should be humble about what is not known.
3. We must deal with the pandemic by looking at all aspects of humans, how they live, how they socialise – dealing with the response in a holistic way and remembering the most vulnerable will often suffer the most.
4. We must be hopeful about what we are learning from the pandemic.
5. We must be honest. Promises about what might happen risks making promises that cannot be kept. Promises about dates are not realistic, we must be prepared for having to change course.

The discussion noted the importance of working in partnership with populations, moving away from restrictions and mandates. A challenge here is how to keep a population engaged when the public perception might be that the risk is diminished despite levels of hospitalisation being back similar levels to the omicron peak. The whole of the population does not need to remain engaged but those key groups responsible for the well-being of society: law and order, education, local authorities etc. should continue to be engaged. There are groups in every community that need to be engaged and encouraged to have regular dialogue as well as coming together for simulations to play out how to handle different eventualities. Vulnerabilities and gaps can be identified through these, which can touch on public health but also other aspects of administrations. There needs to be low intensity but regular engagement between those who need to be kept engaged.

Viral Evolution

Each wave of C-19 has shown an incremental increase in immune evasion. For the Omicron variant, genetic sequencing indicated this would be associated with vaccine and natural immunity escape.

There is significant heterogeneity associated with different variants. We were lucky with Omicron that although there was marked immune evasion there was markedly

reduced clinical severity due to changes in the biology of the virus. Omicron has reduced cell-to-cell fusion and a propensity to divide in nasal cells rather than lung cells. The key issue here is that we cannot expect new variants to be associated with lower clinical severity.

There are significant unknowns about where new variants originate from. It is possible these have emerged from patients with suppressed immune systems and this is an area that is possibly not being monitored at the level it should or could be. It may also be linked to zoonotic reservoirs.

There are a number of tools used to gather more information on severity, transmission, and growth rates. Newer technologies could be incorporated into monitoring going forwards. Genomic sequencing can be used to detect immune evasion but we are less good at detecting changes in the biology. With Omicron this was only done with live virus work. Although this was not predicted from genetic sequencing for Omicron, this may be possible in the future as our understanding of the role of the Spike protein develops.

A key challenge in monitoring variants is that enhanced data linkage is required. Data linkage between clinical and epidemiological data and genomic sequencing data.

Horizon scanning work being done with genomics is focussing on looking at variants that could pose challenges.

Future Scenarios

The discussion considered the SAGE and Scottish Government scenarios for the future of COVID-19. In the SAGE 'Central optimistic scenario' and the SG's 'waning world' scenarios the impact of COVID-19 is driven by waning immunity. In the SAGE 'Central Pessimistic scenario' and the SG's 'variant with vaccine escape world' scenario the emergence of new variants would lead to future large waves of infections which may be of similar severity as previous variants. These scenarios help with planning at the Scottish, UK and international levels. Detection of infection and sequencing of new variants will require surveillance within Scotland and elsewhere. Details of these scenarios, which are not predictions, were provided in meeting papers.

Surveillance

The integration of COVID and general respiratory surveillance is now being looked at in Scotland. Real-time detection of incidents and outbreaks is central to this. As part of this, being able to describe disease severity, mortality and reinfection is crucial to informing the continued response. There have been a number of positive developments in public health surveillance, with programmes such as EAVE-II, programmes examining treatments such as antivirals and monoclonal antibodies. Consideration should be given to the infrastructure that enables this surveillance activity and how this is maintained outside of the acute response to the current pandemic.

Going forward there is a need to be pragmatic regarding how changes in surveillance and testing will impact on the speed with which new problems such as the identification of new variants can emerge.

Triggers

There are a number of potential drivers of the resurgence of COVID-19 in Scotland. The arrival of a new variant is the most likely factor that will require a rapid response to mitigate for a potential rapid surge. Our response time has improved over the course of the pandemic from months to weeks in the case of Omicron.

The speed at which biological, clinical and epidemiological data on new variants is available means that often this may not be available before decisions are required. The experience and timeline of this for Omicron was outlined in the presentation. Expert input should be sought at the earliest possible time to inform actions.

It is unlikely a single fixed set of trigger points can be identified for all scenarios. Earlier action can however mean less radical action. While fixed triggers cannot necessarily be set out, the actions and countermeasures that would be considered, the order and timing of these countermeasures, the criteria for lifting these, and steps to ameliorate knock-on effect can be outlined.

Data

There is now an opportunity for Scotland to think of data as infrastructure. It is important that this should be in near real-time, that cross-sectoral data should be considered, with diversity of datasets, and a central focus on trustworthiness of data.

The EAVE-II project is a longitudinal study of the entire country which is almost unique in the world. Three core aims of EAVE-II were:

1. Epidemiology of COVID-19
2. Patterns of healthcare utilisation and outcomes
3. The effectiveness and safety of vaccines and treatments

The first real-world evidence on the first dose of the COVID-19 vaccines came from the EAVE-II project in Scotland. This project was also the first to describe risks from new variants, vaccine escape, and vaccine waning. Recently this data has been used to highlight specific vulnerable groups such as vaccination rates in pregnant women. There has also been a concerted effort to work with health correspondents in the media to ensure the data is accurately represented.

EAVE-II data has been central to national decision making in Scotland and Internationally. There is a phenomenal capability in Scotland to do this, and we are one of only a few countries in the world to do this. There is still scope for improvement and there are still data gaps. It took 10 months to get EAVE-II up and running, having been dormant since H1N1. There would be benefit in keeping the platform active and using it beyond the pandemic to support responses to issues such as substance abuse, cancer etc., which would also enable it to be used to respond to any future pandemics.

Discussion

The discussion considered how to improve the role and use of scientific developments to inform policymaking and decision-making. The challenge is the speed at which changes and new variants can occur, leading to acute changes in circumstances and the need for rapid decision-making.

Early warning systems that can allow for decisions that have positive impact while minimising harms are vital going forwards. How are we picking things up earlier? How quickly can we determine that something is likely to be a variant of concern? Is there a way to predict how future variants may appear, based on what we have seen from variants to date?

Predicting new variants emerging – gain of function experiments can be done but there is a risk with these of releasing harmful variants. Another option is to use the backbone and spine of virus in a safe system and test mutations of these. These are experiments that probably should be done but there is no guarantee these can pick up on future variants. The speed of in-vitro work could be accelerated, to be able to give phenotypic information at an earlier point.

Improving early-warning – for rapid data that has been used on hospitalisation, ensuring the data quality of the first records from hospitalisation can allow an earlier determination of whether there is something new affecting that population. This is currently a significant challenge. Pseudo viruses – research into preferential binding sites for viruses is ongoing. There is some information on this available for Omicron and BA.2 showing where the virus is binding in the respiratory track. Whether this is reproducible remains to be seen.

Global early warning can be enabled by supporting global genomic sequencing. Half the sequences in Africa over the course of the pandemic to date have come from a programme called TIBA from the University of Edinburgh.

Genomic surveillance, data linkage – rapid phenotypic characterisation of viruses in labs will give us a lot of information on how concerned we should be about specific variants ahead of time. It is important to create systems that are linked up and there is capacity in Scotland but not always supportive legal frameworks and resources for this.

Mutations can be predicted but the problem of the evolution of this virus are sets of mutations that have emerged and understanding the collective effect of these. The following four points will determine the future of COVID:

- Behaviour
- Waning immunity
- New variants
- Efficacy of antivirals

What should we be doing now?

1. We must not forget what we have already learnt.

2. Surveillance – EAVE-II, whole genome sequencing is set up at an impressive scale, wastewater sampling systems are set up. These systems can be pivoted to tackle other challenges.
3. Large number of unresolved questions, around immunity and many other areas. It is crucial we continue research into these.

What can be done to increase the uptake of public health recommendations without having to reintroduce protective measures? Dialogue and engagement, as well as networks that keep key players at local levels engaged should be kept in place to allow for rapid engagement and dissemination of these recommendations.

From a behavioural change perspective:

- Information is key – providing clear information and avoiding conflicting messages, not just from government but also in wider media such as talking about being 'post-pandemic' when we clearly are not.
- Responsibility – information that reemphasises acting in ways that are supporting those in your community
- Support – there needs to be support in place to enable people to follow recommended behaviours (e.g. support for self-isolation). Dialogue is key, and support for mutual aid, providing the scaffolding and resources to support local groups contributes to building resilience and maintaining partnerships
- Preparing to mitigating harms – opposition to measures stems from where harms have been suffered as a result of measures. This includes public health.

The Chair thanked all attendees for their participation in today's session and their contribution to discussion. The discussions today will inform the development of the work of the Standing Committee on Pandemics which will be providing an interim report of recommendations to Ministers in the summer.