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Covid-19 beyond spring

SARS-CoV-2 will remain a major public health issue globally for the foreseeable future. This note examines some of the exogenous factors that will shape the path of the SARS-CoV-2 pandemic in the medium to long-term - beyond this Spring, 2021 vaccine rollout and the anticipated lifting of NPIs.

1. Vaccine performance

There are several important unknowns with respect to aspects of vaccine performance that could make things much harder or much easier, this year and beyond:

Real-world effectiveness: The vaccines developed so far are remarkably good at stopping serious disease, but data are as yet limited on how well and for how long they work on the most vulnerable cohorts such as the over 80s. This will affect re-vaccination schedules. New variants may mean more frequent vaccine boosting is required. Understanding the impact of vaccination on long Covid will also be important.

Impact of vaccination on transmission: It is not yet clear the extent to which vaccines stop recipients being infected and, if they are infected, from infecting others. Early results from studies of natural infection and vaccines suggest that some reduction overall in transmission is likely. If the reduction of transmission is high (>>50%), this will have a dramatic impact on the course of the epidemic this year and in the future.

Optimal revaccination strategy: with multiple different vaccines at our disposal, it will be important to understand how best to deploy them, including (i) how soon a booster will be needed (ii) whether it is better for one person to receive the same vaccine for repeat inoculations vs changing from one to another (iii) how best to design new vaccines to protect against variants. It is possible that vaccines using the adenovirus platform may only be useable once if recipients develop immunity to the vector. All currently approved vaccines target the virus Spike protein whereas targeting other viral proteins may help avoid immune escape by new variants. Oral or intranasal vaccine delivery would simplify logistics and may stimulate better immunity in airways.

2. Characteristics and frequency of new variants

New variants will undoubtedly emerge in or reach the UK. Initially it will be those that transmit more readily; then, as the number of people with immunity rises, variants that can evade this immunity will be at an advantage. High prevalence creates the right conditions for variants to emerge and spread. Infection of other species can create zoonotic reservoirs in which new strains develop and cross back to humans. Infection can persist for a long time in immunocompromised people, which also creates favourable conditions for immune escape variants to emerge. It is possible to delay new variants coming from overseas but we are unlikely to be able to stop them completely and some will arise domestically.

More transmissible variants may or may not be more dangerous. B.1.1.7 may cause higher mortality but other variants may not – for example, if a variant tends to infect the upper airway rather than the lungs it may spread more by coughing and sneezing but cause less serious disease. It is possible that the virus will mutate to become more transmissible and less dangerous over time.

Variants that can escape vaccine-induced immunity are clearly a worry. Vaccines so far seem to provoke a very strong immune response (at least in terms of antibodies), which may diminish the impact of mismatches between vaccines and variants. Nevertheless, having vaccines that correspond to the currently dominant variant or variants is preferable. Immune escape is not a major issue for B.1.1.7 overall although this it may be for some individuals. The B.1.351 and P.1 lineages, first detected in South Africa and Brazil/Japan are much more concerning and there is now evidence of reduced vaccine efficacy against these variants. Novavax data suggest effectiveness was 50% with B.1.351 compared to 90% for other lineages; the new J&J vaccine also appears less effective against this variant.

It is unclear how many new variants we will see or how often. It depends on how many novel ways the virus can change while still remaining viable. It is notable that we are seeing the same mutations arising

independently in different countries although there is experimental evidence of other changes in the virus not yet seen in circulation but which could increase binding, transmission and/or immune evasion.

3. Therapeutics and antivirals

Several effective treatments are already available, either repurposed drugs (Remdesivir) or older therapeutics (dexamethasone). Some SARS-CoV-2 specific monoclonal antibodies have been developed that look to be highly effective to prevent infection and may have use in treatment as well. They are, however, expensive for widespread use and some appear ineffective against variants.

The next area in which we can hope for significant advances will be specific antiviral drugs, such as viral protease, helicase and polymerase inhibitors, developed to block SARS-CoV-2 activity. These would probably be most useful early in infection or as prophylactics in an outbreak setting, or for individuals who have not been vaccinated for whatever reason, or who did not develop a strong immune response. It seems probable that we will get the first antivirals some time in 2021.

4. What the future will look like?

How the factors above play out will determine how bumpy the road ahead will be. There are, however, some things about which we can be reasonably sure:

SARS-CoV-2 will be with us indefinitely. It will become endemic and its impacts will diminish, though not to zero, and this may take several years. Once this becomes endemic it may become predominantly a mild disease of childhood (but carry risk to the most elderly as annual flu does).

Vaccines will remain key to managing the transition from pandemic to endemic. But therapeutics, antivirals and NPIs will all have a role to play.

There will be new variants that will escape immunity though the impact or new variants may diminish over time, albeit years. New variants may cause “bad years” from time to time as occurs with flu.

Next winter at the very least is likely to be difficult, probably at very best like a bad flu year. The fact that there has been little flu this year – and so less immunity – may mean a tough flu season as well.

SARS-CoV-2 is a global problem needing global solutions – surveillance of new variants and design and development of vaccines will require an international approach and system (there is something like this flu already which provides a template) Ultimately, we are not safe until everyone is safe.

5. What will we need to do?

It is also clear that in all eventualities, there are several essential, no-regrets actions to prioritise:

Vaccine updates will be needed, this year and beyond. We need to know how best to do this, both in terms of the vaccines themselves (e.g. new, single variant vaccines to match emerging lineages vs an approach against a cocktail of variants) and the process for surveillance and variant selection. A multi-year strategy "from eyes to arm" - surveillance, updates, manufacture, delivery - is required. This will need to be both a UK and a global effort and is needed now.

Accelerate development of therapeutics and antivirals. Although slower to emerge, they will be an important complement to vaccines. The UK should aim to become a place to do the trials and get early access to the medicines. Stockpiling may become an option.

Plan for a difficult winter for the NHS in 2021/22 and in future years.

Normalise Covid-secure behavioural changes, for example don’t to work with a sniffle but get tested; wear masks and minimise higher risk contacts in winter or during outbreaks.

Engineer in resistance to this and future respiratory disease pandemics, as was done for faeco-oral infections with sewers and clean water, for example by improvements to the hospital estate to allow better management of infectious patients, or to workplaces, venues and housing to improve ventilation.