TONY BLAIR INSTITUTE FOR GLOBAL CHANGE

Ahead of the Curve: Preventing a Third Wave of Covid-19

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Summary

The government has embarked upon a programme of easing Covid-19 restrictions on social activity as the vaccination programme builds up biological immunity among the population.

But as the prime minister reminded the country this week, the results of modelling by SAGE's epidemiological advisors suggest that once all restrictions are lifted – step 4 of the government's roadmap, currently planned for 21 June – there is expected to be a third wave of Covid-19 infections that could result in between 20,000 and 40,000 further deaths in the UK and upwards of 100,000 further hospital admissions.

This is not inevitable, however. Getting under the bonnet of the SAGE analysis, this paper describes three components of the third wave that can help us avoid that fate.

- First, the planned lifting of the final set of restrictions is at risk of running too far ahead of the vaccination rollout, leaving many soon-to-be-vaccinated people exposed to unnecessary infection.
- Second, despite impressive vaccine take-up, the population protection afforded by inoculation and past infections looks set to fall short of what will be needed to reach herd immunity even once the vaccine has been offered to all adults.
- Finally, these two facts together also make it likely that a summer surge in case numbers will cause infections to substantially overshoot the herd immunity threshold, resulting in more cases and deaths than would occur if numbers were under control.

There remains a lot of uncertainty about the path of the virus over the coming months. But if, by the time of the next SAGE assessment, the prognosis has not improved, we propose three changes to the current programme. Together, these would avoid a third wave and cut the anticipated numbers of infections and deaths by more than three-quarters between now and June 2022.

- First, **if the pace of vaccination cannot be increased towards the rates achieved in March, the government should consider delaying step 4 of the roadmap by a month** until the summer holidays when transmission is anticipated to be lower. Lifting the final set of restrictions only once all eligible people have been offered a first dose would likely prevent a summer resurgence of the virus entirely.
- Second, as planned in the US and Israel, **the vaccination programme should be extended to adolescents, subject to regulatory approval**. On its own, delaying step 4 could leave the country under-protected for a recurrence later in the year as the virus may spread more readily in winter. Offering a vaccine to a further 6.8 per cent of the population could be critical in taking population

protection levels over the winter herd immunity threshold, thereby preventing a further wave of infections in the new year.

- Third, the new guidance from the Medicines & Healthcare products Regulatory Agency (MHRA) on the use of the Oxford/AstraZeneca vaccine in younger people should facilitate a change in the composition of vaccines adopted. Shifting towards greater reliance on the mRNA vaccines – Pfizer-BioNTech and Moderna – which the SAGE modellers currently see as marginally more effective at preventing infection, could boost overall population protection (although recent studies increasingly suggest that the efficacy of the AstraZeneca and Pfizer vaccines are very similar). **Achieving a 65-35 split between AstraZeneca and Pfizer/Moderna** – compared to the 80-20 assumed in the Imperial College model – could therefore further reduce the total number of cases and deaths across the year.

Using a model designed to replicate the Imperial College results, this paper assesses the impact of combining all three of these steps. We find that this package would save around 77 per cent of the anticipated deaths between now and June 2022 – amounting to around 15,000 lives across the UK over the course of the year – relative to the central case assessment of the SAGE modellers. We recommend that the government asks its epidemiological advisors to explore these proposals and alternatives.

Inevitably there is substantial uncertainty around the path of the virus in the months ahead. The SAGE models may turn out to be too pessimistic. But if, as we approach step 3 of the roadmap next month, the modelling assessment continues to foresee a third wave over the summer, the government should act. A further surge in hospitalisations and deaths is preventable if the right policy decisions are made in good time. But the government needs to begin preparing the ground now.

Introduction

A tentative optimism has spread across the country since England moved to step 2 of the government's roadmap out of lockdown on 12 April. The Covid-19 vaccine rollout has proceeded apace, and the country is enjoying a gradual easing of restrictions imposed during the winter months. Supply hiccups and concerns about rare side effects aside, the UK now appears to be on a glide path back to normality by 21 June as vaccine coverage increases and the government's lockdown exit roadmap reaches its final stages.

But we're not out of the woods yet. The ever-present risk of a widespread outbreak of a vaccine-resistant variant – most obviously B.1.351 that originated in South Africa, and which is thought to have a foothold in the UK – could blow plans off course. But even without this, there are significant challenges ahead for the government's stated policy.

The prime minister's announcement of his decision to press ahead with step 2 in the plan last week was accompanied by a warning about what may lie ahead. According to current plans, the government's epidemiological modelling advisors expect there to be a third wave of infections causing 20,000 to 40,000 more deaths for the UK as a whole, and on more pessimistic assumptions, a number comparable to the second wave of the virus. The prime minister highlighted the risk of a third wave again earlier this week.

Media commentary suggests many were surprised to hear that the modelling indicates a third wave involving millions of infections and tens of thousands more deaths. But a closer examination of the modelling produced by SAGE's advisors shows that the assumption of a significant third wave has been baked into the easing plan from its inception. Indeed, the latest assessments from SAGE are significantly more optimistic than they were in February.

Since the government's Covid-19 policy plan is predicated on such a large number of further deaths – most of which are anticipated to occur over the next six months – it is reasonable to ask whether this is the best strategy. By getting under the bonnet of the models, we can understand what is driving the third-wave projections and consider what policy options are available to prevent it.

This analysis paper outlines the prognosis for a third wave and proposes a package of measures to prevent it, including pushing back step 4 of the roadmap to July and vaccinating adolescents once regulatory approval is given.

What do government advisors expect to happen in the coming months?

Ahead of its decision to proceed with step 2 of the roadmap for easing Covid-19 restrictions, the government commissioned updates from the SAGE modelling teams to assess the likely consequences of pressing ahead with the plan. The papers from epidemiologists at the University of Warwick, Imperial College London and the London School of Hygiene & Tropical Medicine represent the best assessment we have of the likely impact of the roadmap on the number of Covid-19 cases and deaths that we might see as restrictions are eased. In this briefing, we base our analysis on the Imperial and Warwick modelling, which offers more detailed published results.

Imperial College's central case results in 5.6 million new Covid infections, 79,000 additional hospital admissions and 15,700 further deaths in England by 1 June 2022, if restrictions are eased according to the timetable set out by the government's roadmap. This assessment is very sensitive to some key assumptions. For example, if the virus is more transmissible once formal restrictions are lifted than assumed in the central case, the roadmap easing could result in 40,000 deaths in England. If vaccine take-up among younger adults reaches only 80 per cent, rather than the 90 per cent assumed in the main analysis, this would increase the number of further deaths in England to around 19,000. In all scenarios, the third-wave deaths peak in the summer, with the rate of daily cases and deaths declining into the autumn.

The University of Warwick's central case implies around 18,600 additional deaths in England in the third wave, along with around 84,000 further hospital admissions. The number of daily deaths accelerates through June and July and peaks in August. With higher levels of transmissibility, the projected third-wave death toll rises to 30,500.

Scaled up to the UK as a whole, the combined Warwick and Imperial central case estimates average around 20,300 further deaths from Covid-19 over the coming year and around 100,000 more hospital admissions.

The results of modelling by the London School of Hygiene & Tropical Medicine are significantly more downbeat than those of Warwick and Imperial, suggesting that the third wave of cases and deaths could be comparable to the first wave when some 40,000 people died. Such a wave would entail daily deaths rising to around 1,000 per day in England, comparable to the worst days of the second wave, and peaking in August and September.

Overall, with the possibility of a third wave costing around 20,000, and perhaps as many as 40,000, further lives, the pandemic in the UK is far from over and difficult decisions remain.

Three components of a third wave

How could such an outcome happen after the success of the vaccination programme so far? At the heart of the third-wave projections is the view that as restrictions on social activity are lifted, population immunity – derived either from past Covid infection or the protection afforded by vaccination – will be insufficient to prevent the spread of the virus accelerating. This could occur either because the pace of easing runs ahead of the protection generated by the vaccine rollout, or because vaccine protection is expected to be insufficient even once the rollout programme is complete. In both cases, population immunity falls short of the so-called herd immunity threshold (HIT) – the level of protection against infection across the population above which new case numbers start to fall.

The first source of new cases therefore stems from the fact that the roadmap sees **restrictions being fully lifted well before vaccine rollout is expected to be completed**. On the rollout assumptions in the latest SAGE reports (2.7 million vaccine doses per week for England or 3.2 million for the UK), we estimate that all adults who want to have a vaccine should have received at least a first dose by around mid-July, with protection against infection kicking in for those people some two to three weeks later. However, step 4 in the roadmap is planned for 21 June. At this point, we estimate population protection through either vaccination or past infection will only be around 54 per cent, well below the HIT of 66 per cent foreseen in the central case. The intervening period will therefore see cases accelerate among people who would not have caught the virus, had the removal of restrictions been linked to the end of vaccine rollout.

The second possible cause of third-wave cases comes from the fact that **even once the vaccination campaign has been fully rolled out to adults, vaccine protection is unlikely to be high enough to achieve population immunity**. The level of protection needed to reach the HIT, and prevent the exponential spread of the virus, once restrictions are removed depends on what the reproduction number, or R, would be in the absence of any immunity to the virus among the population. If the R number without any restrictions on social mixing is 3, then two-thirds of the population need to be immune from infection to prevent case numbers accelerating once restrictions are eased. This is the central assumption in the Imperial and Warwick papers, giving a HIT of 66 per cent. If the R number were 4, then the HIT would be around 75 per cent.

But, in either case, the current vaccine rollout combined with current levels of past infection looks set to fall short of these levels of protection. There are three components to the calculation of the degree of protection offered by the vaccination programme. First, vaccines are only currently planned to be rolled out to people aged 18 and over, who comprise around 79 per cent of the population. Second, with take-up among over-50s assumed by the modelling teams to be 95 per cent, and 90 per among younger adults, the average take-up rate would end up at around 92.4 per cent. Finally, while the AstraZeneca

and Pfizer vaccines appear to be highly effective at preventing severe disease, their effectiveness at preventing infections may be lower. Imperial assumes that after both doses have been administered, vaccinated people will on average have their risk of infection reduced by around 69 per cent.

Combining these numbers suggests that once the vaccination programme has offered both doses to all UK adults, only (79% x 92% x 69% =) 50% of the population will be protected from infection through vaccination alone.

Past infections are also understood to confer immunity, which helps take population protection closer to the HIT. The Imperial model assumes that by late March some 25 per cent of the population had immunity from past infection. Stripping out the overlap between people who have both been infected and received a vaccine, this suggests that the degree of population protection would likely be shy of 60 per cent, assuming no further infections, by the time a first dose of vaccine has been offered to all adults.

This is nevertheless well below a HIT of 66 per cent. The gap between the two will either be made up by expanding vaccine protection in some way or through at least a further unprotected 6 per cent of the population catching the virus.

There is also a third source of third-wave cases and deaths. At the point where population protection reaches the HIT, the virus will stop *accelerating* but its spread will continue. As the level of protection creeps above the HIT, the R number will fall just below 1, but at that level the number of new daily cases could take a long time to decline, causing **total infections to overshoot the herd immunity threshold**, with more people getting sick than necessary. The degree of overshoot depends on the prevalence of the virus at the time herd immunity is reached. If daily new cases are running at 50,000 when the herd immunity threshold is reached, there will be many more cases before the epidemic fizzles out than if new daily cases are running at 5,000. Converging on the HIT in a controlled way can therefore save thousands of cases and lives.

How does the government's plan measure up?

The government's current roadmap does not appear the optimal approach in the case of any of these three third-wave drivers, based on assumptions in the SAGE modelling papers. In the following analysis, we have applied the key assumptions from the Imperial model, as outlined in the 30 March report entitled *Evaluating England's Roadmap out of Lockdown*, to our own susceptible-infected-recovered (SIR) model, including: past infection rates by region, vaccine efficacy, vaccine mix, uptake by age, estimates of R under each step of the roadmap, the impact of seasonality and other parameters set out in the report. In doing so we are able broadly to replicate its results and track how population immunity is expected to evolve over the coming months.

The appendix to this paper reports a detailed comparison of the results of our model with those of the Imperial model. While our simulation is more rudimentary, the comparison shows that it matches the Imperial results reasonably closely under the various scenarios, giving confidence that it is a broadly accurate guide to the different dynamics at play. We then use our model to identify the key policy levers available to prevent a third wave. As with the SAGE models, we assume throughout that any new variants of the virus make a negligible difference to the overall efficacy of the vaccines currently being deployed.

The red line in Figure 1 traces out the herd immunity threshold – including the effects of both seasonality and any prevailing restrictions on social mixing – at different stages in the roadmap. This line is derived directly from the inputs set out in the Imperial modelling paper. For example, after step 1 and during the school Easter holidays, the modellers anticipated the R number without immunity to be around 1.3. Consequently, population immunity anywhere above (1 – 1/1.3 =) 23 per cent is sufficient to keep the effective R below 1.

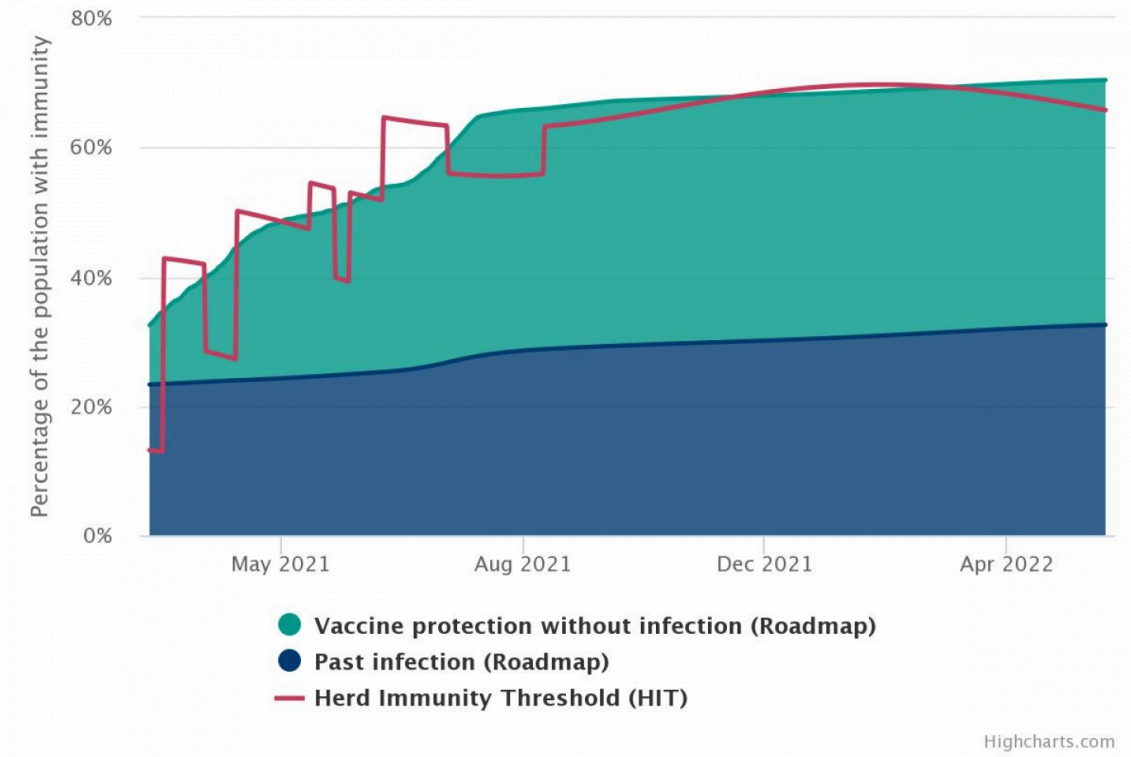
Step 2 of the roadmap, implemented on 12 April, is anticipated to take the R number without immunity to 2.0 (including the impact of seasonality), as shops and outdoor hospitality re-open and the summer school term begins. This implies population protection, either via vaccination or past infection, of around (1 – 1/2 =) 50 per cent is required to keep the virus in check. This is somewhat higher than the estimated protection level at this point, which our model suggests is 45 per cent. The protection deficit causes the spread of the virus to accelerate until the gap with the HIT closes by early May as vaccine protection grows. A similar small protection deficit is expected to open up briefly after step 3 on 17 May.

More problematic is step 4 in the roadmap. On current timing, this step is anticipated to take the HIT well above the level of population protection our model suggests at that time, triggering a sustained acceleration of case numbers from 21 June until the close of the school summer term at the end of July.

This happens largely because in the SAGE modelling, the pace of vaccine rollout is assumed to slow significantly from what was achieved in March.

Consistent with the Imperial model, we find that by September population immunity reaches the herd immunity threshold – but only through approximately a further 2.5 million Covid-19 infections between the start of May and end of August. The seasonality factor in the Imperial model indicates that the HIT starts to rise as we head into winter, which in our replication takes it slightly above the protection level during these same months, causing new daily cases to rise slightly.

Figure 1 – Projected population protection versus the herd immunity threshold based on the government's current roadmap



Source: TBI, Imperial College

Who is vulnerable to a third wave? Vaccination of the most high-risk groups is now complete and take-up rates have been impressively high. It may be tempting to think that the people most vulnerable to a further surge of infections are the few who are hesitant about having the jab and that no further infringements of other people's liberties should be entertained in order to protect them.

But despite apparently high rates of vaccine efficacy against severe disease and death, it remains vaccinated older people who would be most at risk. According to Warwick's analysis, at the peak of the third wave, around 80 per cent of deaths would be among over-50s who had received both of their doses. We cannot therefore dismiss the consequences of a third wave as the result of personal decisions to forgo the vaccine.

Many assumptions underpin the SAGE models, and some or many of them may turn out to be either too pessimistic or too optimistic. But based on those assumptions, it is possible to identify changes to the current plans that would prevent a third wave.

What can be done to avert a third wave?

The results of the SAGE models imply a substantial chance of 20,000 to 40,000 further Covid-19 deaths. But this is not inevitable. To understand the options that policymakers have to avert another wave, here we use our replica of the Imperial model to explore what can be done to tackle the three sources of cases outlined above.

Coordinate easing steps with vaccine rollout

As described above, a significant part of the projected third wave results from the fact that the timing of step 4 of the roadmap, on 21 June, takes the herd immunity threshold well above the degree of population protection achieved by vaccine rollout at this point. If the pace of vaccine rollout can be increased from the projection of 2.7 million jabs per week to something closer to the late March rates of 3.3 million, this problem would largely disappear. Failing that, pushing step 4 back by a month to coincide with the start of the school summer holidays, would minimise that problem and prevent the acceleration of case numbers in June and July.

We find that, based on the Imperial assumptions, this delay would prevent any acceleration in case numbers over the summer, with the remaining restrictions and then the school holidays holding down transmission until September by which time the vaccine rollout will be complete.

In our earlier proposals for the exit roadmap, we championed the advantages of a policy that explicitly aimed to keep R below 1 until all adults had been offered the vaccine. Delaying step 4 by a month would largely have this effect. Not only would this save cases and lives among currently unvaccinated people, it would also minimise the scale of overshooting once restrictions are finally lifted at the end of the vaccination programme.

It is important to consider the costs associated with such a delay alongside the potential benefits. In practice these are limited in economic terms for two reasons. First, the restrictions that would be extended cover activities that are of limited economic importance. Preventing multiple households mixing indoors for a further month would have no detectable economic impact. Meanwhile, nightclubs would remain shuttered and large events subject to capacity constraints but the economic costs would be minimal.

Second, as we at TBI have argued before, while restrictions reduce economic activity, so does the uncontrolled spread of the virus. Surging infection rates while large numbers of young people remain

unvaccinated could hamper the economic recovery if people remain afraid to return to pre-pandemic behaviour.

Avoiding a summer surge in cases does not mean the risk of a future wave goes away, however. On Imperial's modelling assumptions, Covid-19 transmissibility increases in the winter. So, without further population protection built up over the summer through a third wave, we end up with a slightly bigger wave of infection in the winter. To save lives, therefore, delaying step 4 needs to be combined with a widening of the vaccination programme.

Expand the vaccination programme to include adolescents

People over the age of 18 make up just under 79 per cent of the UK population. Extending the vaccination programme to children aged 12 and above would cover a further 6.8 per cent of the population. Based on the central SAGE modelling assumptions, this would keep the level of population protection above the HIT throughout the winter. It therefore addresses the winter wave problem created by delaying step 4.

Vaccinating people under 18 is not currently part of the plan for Phase 2 of the rollout. Interim guidance given by the Joint Committee on Vaccination and Immunisation (JCVI) from March indicates that a decision on this remains under consideration. [1] At present, only the Pfizer vaccine is authorised for use in people aged between 16 and 18, with the MHRA's recent guidance now suggesting other vaccines are preferred to AstraZeneca for use among under-30s.

Those aged under 16 are currently not eligible for vaccination, both because of the very low incidence of serious Covid-19 infection among children in the UK and a lack of trial data on vaccine efficacy in children under 16. [2] But there have been reports that the government was considering starting vaccination for children from August 2021 onwards, and one JCVI member has highlighted that a decision to roll out vaccines to adolescents should depend, in part, upon whether or not the current plans are sufficient to reach herd immunity. Pfizer also recently announced the completion of phase III trials in children aged between 12 and 15, reporting 100 per cent vaccine efficacy in the treatment group. They have since filed for authorisation with the FDA.

Elsewhere, plans to vaccinate older children are already in train. In the US, Chief Medical Advisor to the President Anthony Fauci has suggested that vaccinations for people aged between 12 and 15 could begin by September 2021, with younger children becoming eligible by the first quarter of 2022.

The Israeli Ministry of Health, too, expects to begin vaccinating children aged 12 and 15 in the next few weeks pending FDA emergency approval, as the first-dose vaccine rollout to the over-16s in Israel nears completion.

Clearly any such extension of the vaccination programme to under-18s would be dependent upon regulatory approval. But assuming this is ultimately granted, vaccinating adolescents could play an important role in preventing further deaths.

Shift the vaccine mix towards Pfizer

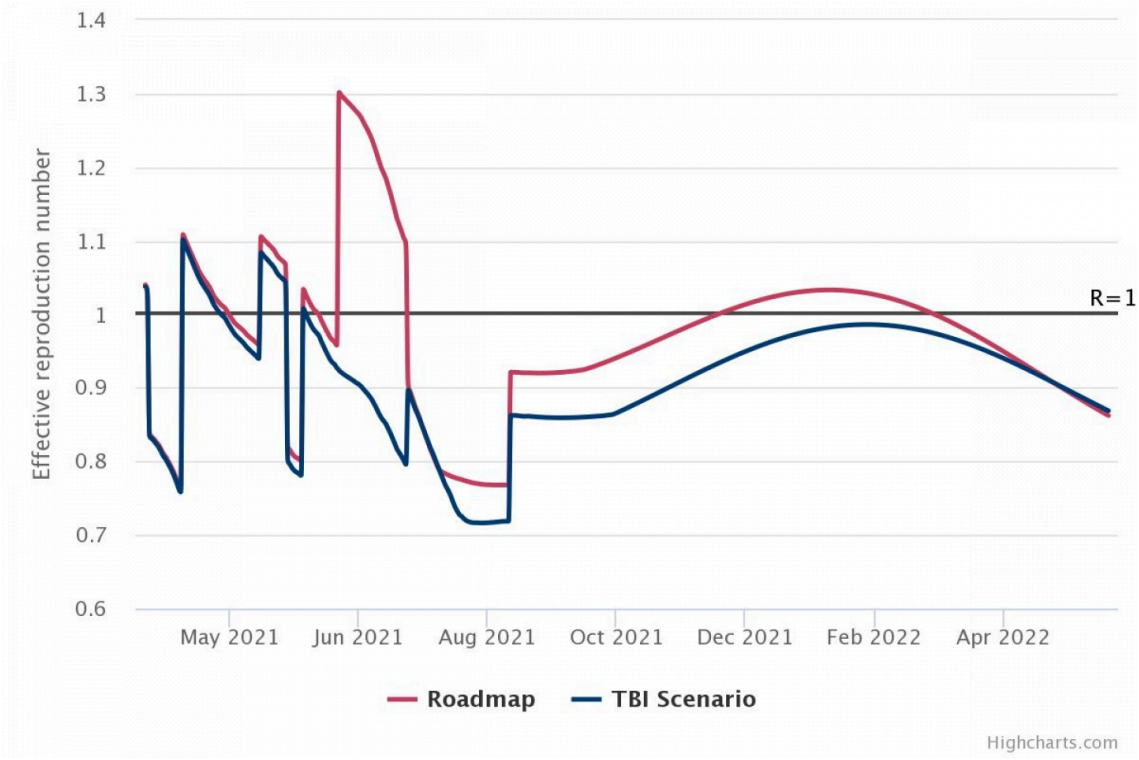
As discussed above, in response to concerns about possible rare side effects with the AstraZeneca vaccine, the MHRA has indicated that other vaccines – most likely Pfizer or Moderna – should be preferred for younger people. While all the approved vaccines are highly effective at preventing severe disease, the SAGE modelling assumes that Pfizer's vaccine may have somewhat higher efficacy against infection (94 per cent) than AstraZeneca's (65 per cent). For the purposes of replicating the SAGE analysis we take these assumptions, however it should be noted that recent studies appear to suggest that there is very little difference in efficacy between these two vaccines.

With some 11 million people in the UK having received Pfizer so far, if all under-30s were to be offered Pfizer (or Moderna, which appears to have similar levels of efficacy), this would change the vaccine mix that has been assumed in the March SAGE models. A more Pfizer-heavy vaccine mix would lead to a higher degree of population protection, taking it clear of the estimated HIT and accelerating the decline in case numbers. For the purposes of this analysis we model this as a shift from an 80-20 AstraZeneca-Pfizer split to a 65-35 one.

Combined impact of the alternative strategy

Combining these three changes to the plan would avoid a third wave this summer while also reducing the risk of a surge in the winter, by holding the effective R number at or below 1 for longer than the government's current plan. Most notably, in the chart below, our alternative scenario (see the blue line in the chart below) removes the June-July spike in the R number that drives the third wave.

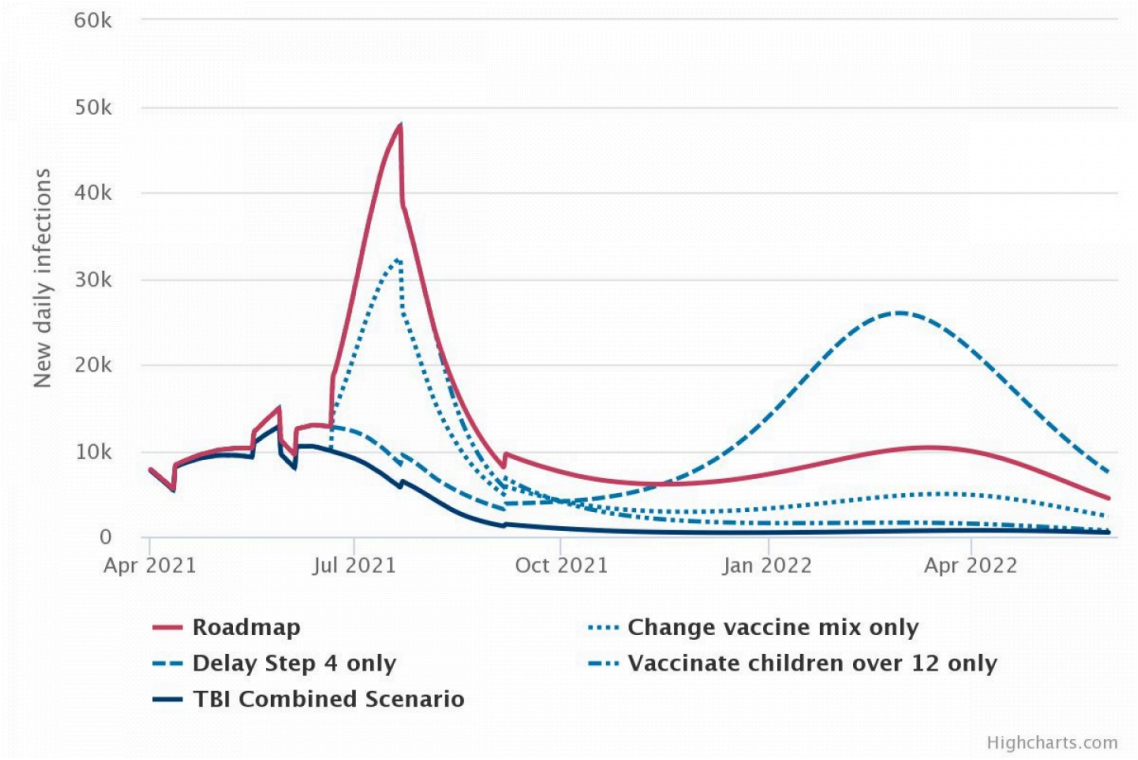
Figure 2 – Modelling our alternative scenario against the government's current plan



Source: TBI, Imperial College

The separate effects of each aspect of the plan on the path of daily cases across the year are illustrated in Figure 3 below, along with the combined effect. Changing the vaccine mix reduces the scale of infections throughout the year; delaying step 4 removes the summer wave; extending vaccination to adolescents then tackles any winter resurgence. While no one of the three measures is sufficient to prevent a further large wave of infections, the combined package achieves that aim.

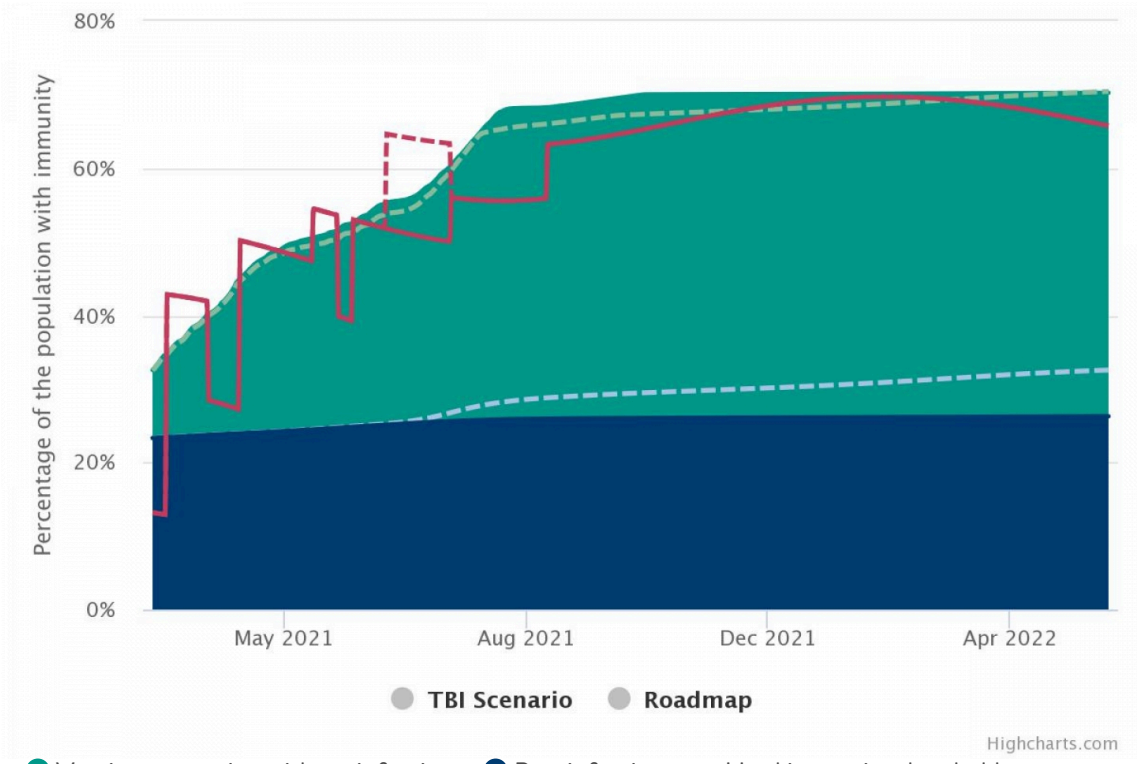
Figure 3 – Cumulative effect of each aspect of the alternative scenario on new daily infections



Source: TBI, Imperial College, Cambridge MRC Biostatistics Unit

Based on Imperial's central assumptions, our alternative strategy keeps the level of population protection (represented by the height of the light green areas in the chart below) much closer to the prevailing herd immunity threshold over the coming months, resulting in far fewer cases. By May 2022, the level of population protection is similar under the current plan and the scenario described here, but the current one achieves that with the help of 33 per cent of the population having caught the virus, compared to just 26 per cent in our alternative scenario – a difference of around 3.6 million additional cases of Covid-19.

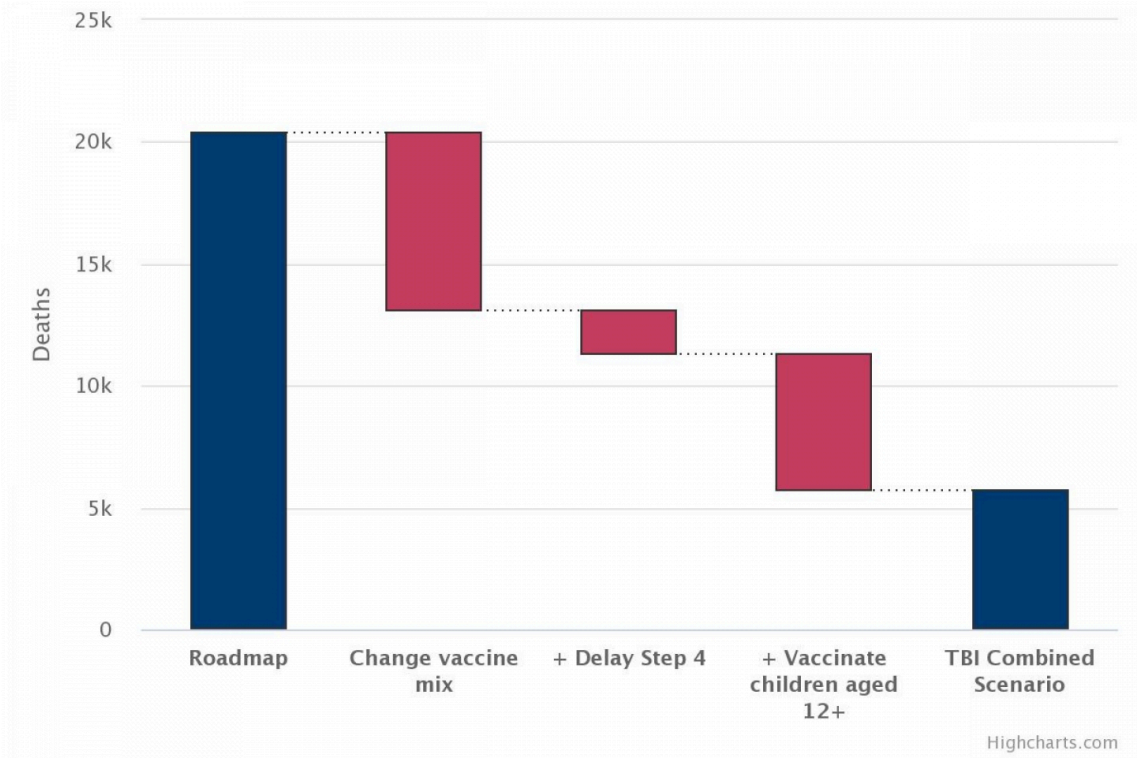
Figure 4 – Population protection versus herd immunity threshold in our alternative strategy compared to the current plan



Source: TBI, Imperial College

What might this mean for the number of lives saved? Applying the proportionate reduction in case numbers in our scenario compared to the current policy, we can make an assessment of how many of the 20,300 deaths across the UK, implied by the Warwick and Imperial analyses, could be saved. We estimate the total number of deaths would fall by around 72 per cent to 5,700 between late March 2021 and the end of May 2022. From the planned date of step 4 on 21 June to the end of May 2022, the scenario reduces total deaths by 86 per cent compared to current plans.

Figure 5 – Deconstructing the reduction in fatalities from our alternative strategy



Source: TBI, Imperial College

Conclusion

There is huge uncertainty over the path of the virus in the next six months, ranging from no further widespread outbreak at all to another wave that exceeds the one of the past six months in terms of fatalities. The central cases of the government's epidemiological advisors are somewhere in the middle of that spectrum, suggesting that there is a significant chance of a third wave causing upwards of 20,000 further deaths across the UK in the coming months.

This is not inevitable, however. It may be that the modelling projections turn out to be too pessimistic. But if they do not, the government has the power to avoid or substantially reduce a third wave. A revised strategy of shifting the mix of vaccines, delaying the final step in the government's roadmap out of lockdown until the school summer holidays, and expanding the vaccination programme to people aged 12 and upwards, once regulatory approval is given, could eliminate a third wave at minimal cost in terms of freedom – and potentially create net economic benefits. We urge the government to commission analysis from their epidemiological advisors to test these proposals and explore alternatives.

But if we are to avoid a further wave of entirely preventable deaths, the government would need to begin preparing the ground now. As the first two waves demonstrated, there are significant political difficulties associated with acting early to stop a surge in infections. By the time of the step 3 assessment, early next month, the government should be prepared to revise its subsequent plans if the central epidemiological assessment has not improved, so that those agonising decisions don't arise again.

Appendix – methodology and results

The TBI replication of the Imperial model matches the key assumptions set out in the paper submitted to SAGE on 30 March 2021, entitled *Evaluating England's Roadmap out of Lockdown*. We assume the same vaccine efficacies against infection and, in keeping with Imperial's central scenario, do not model additional vaccination effects on the risk of onward transmission. In the baseline replication we match the assumption of an 80-20 split between Pfizer and AstraZeneca vaccines, and associated efficacy numbers, and replicate Imperial's vaccine rollout speed of 2.7 million doses per week until 2 August, and 2 million doses per week thereafter. We assume efficacy after vaccination begins 21 days after the first dose and 7 days after the second, and we factor an 11-week gap between first and second doses into the rollout schedule. Figures for the R number without immunity align with Table 2 in the Imperial paper, and we replicate the study's seasonality factor, adjusting transmission rates +/-10% from winter to summer.

In keeping with the Imperial approach, we model vaccination rollout and the spread of the disease in each of the seven NHS England regions separately before combining figures to arrive at England-wide totals. This is because Imperial estimates different prior infection rates across regions at the start of the modelled period (26 March 2021), which results in different subsequent transmission dynamics. Our starting values for infection numbers are calibrated to match estimates provided in the Imperial paper, as well as Cambridge MRC Biostatistics Unit and Office of National Statistics estimates of historical infection rates.

Following Table 2 in the Imperial paper, we assume the same R excluding immunity rates for all regions during the modelled period and distribute vaccines proportionately by population. Unlike Imperial, we do not use an age-stratified, stochastic model but rather a parametric SIR model where vaccination rollout proceeds by age group priority until the eligible adult population in a region willing to be vaccinated has received two doses. We assume a constant disease recovery rate of 0.15 across all demographics based on prior literature. Finally, fatalities are calculated based on scaling the average results of the Imperial and Warwick studies according to the proportionate change in case numbers in our scenario compared to the baseline replication.

The first half of the table below compares the total projected new infections between 26 March 2021 and 1 June 2022 from the Imperial paper to the results from TBI's equivalent scenarios. The comparison shows that the TBI central case and sensitivity tests project similar numbers of cases as the Imperial ones, suggesting that the model behaves as expected. The second half of the table details the reduction in total projected cases produced by each element of the package of measures proposed, and all three measures together.

Scenario description	**Imperial Paper** Millions of cases 26 March 2021 to 1 June 2022	**TBI results** Millions of cases 26 March 2021 to 1 June 2022	**TBI results** Millions of cases 1 May 2021 to 1 June 2022
Central case	5.6	5.0	-
Low uptake	6.6	6.8	-
Higher R w/o NPI	12.6	12.3	-
Slower rollout	5.8	5.2	-
No seasonality	6.2	5.3	-
Lower efficacy	8.3	9.7	-
Proposed interventions (change versus central case)			
Delay step 4	-	5.2 (+3%)	4.9 (+4%)

Vaccinate 12+	-	3.4 (-32%)	3.1 (-34%)
Shift mix to 65/35 AZ	-	3.2 (-36%)	2.9 (-38%)
Delay S4, 12+, vaccine mix shift	-	1.4 (-72%)	1.1 (-77%)

Charts created with Highcharts unless otherwise credited.

Footnotes

1. ^ https://gov.wales/covid-19-vaccination-strategy-update-march-2021
2. ^ The Green Book, Chapter 14a, p. 15 (12 February 2021).

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