

## COVID-19 Rapid Briefings



# No.5 – Vaccine Dosing Timescales

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*Produced by the Public Health Team for Stakeholders*

Dear Colleagues

### Explainer Briefings

The issue of whether it is right to extend the time between doses 1 and 2 of Covid-19 vaccination has been raised repeatedly. It has also been wrongly stated that the vaccine dose is now a single dose strategy.

At the time of writing:

- The UK strategy remains two doses
- For reasons explained in the briefing the delay between the doses has been extended to 12 weeks
- This is under regular review nationally and will be changed if the evidence makes clear it needs to be

This briefing, as part of our Covid Briefing Series, provides information on the rationale for this.

We will keep this updated.

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## Background: Changing the timing between Vaccine Doses

The Four Chief Medical Officers of the UK announced on 31<sup>st</sup> December 2020 that, based on scientific advice from the Joint Committee on Vaccination and Immunisation (JCVI), the maximum interval between the first and second doses should be 12 weeks for both the Pfizer/BioNTech and Oxford/AstraZeneca vaccines.

Read the JCVI 31 December statement and supporting documents [here](#)

Read the Updated 26<sup>th</sup> January JCVI statement [here](#)

JCVI have made a judgement on maximising population protection, and their reading of the science is that any “waning” or fall off in individual level protection from longer space between dose 1 and 2 is negligible. JCVI are an independent scientific advisory committee (aka SAGE) that advise govt on all aspects of vaccination. They have been established for about 3 decades.

Within it there is plenty of expert clinical opinion, basic immunological science (which supports the decision) and interpretation of the vaccine data.

The JCVI advice, published on 31 December 2020 and updated on 26<sup>th</sup> January, concluded that

*“The committee supports a 2-dose vaccine schedule for the Pfizer-BioNTech and AstraZeneca vaccines. Given the data available, and evidence from the use of many other vaccines, JCVI advises a maximum interval between the first and second doses of 12 weeks for both vaccines. It can be assumed that protection from the first dose will wane in the medium term, and the second dose will still be required to provide more durable protection.*

*The committee advises initially prioritising delivery of the first vaccine dose as this is highly likely to have a greater public health impact in the short term and reduce the number of preventable deaths from COVID-19.”*

This approach is a bid to provide as many people as possible with a first dose, to provide a level of protection for them and then return for a second dose.

Both vaccines currently being used in the UK were intended to be given over much shorter timescales.

## Why is this controversial?

It is controversial because it is a change, suddenly announced, to the dosing schedule. And there was an immediate level of scientific debate where a consensus was hard to discern, but the consensus is now moving in favour. At the same time the original intention of the manufacturers and regulators was not to have such a delay between doses. It was also often wrongly presented as a “people will only get one dose” strategy. At the same time, a number of commentators pointed out that it is to the commercial advantage of a number of players to keep the two doses within a shorter period schedule originally developed.

And people at present still need two doses to be get the full benefit of the vaccine. You are only really properly “vaccinated” after both doses. But again, this is only a delay to the vaccine dose schedule, not a move from two doses to one.

## **So why did we do it?**

Put simply, to reduce the numbers of people dying, and the numbers of people with very severe disease. The JCVI and Chief Medical Officers conclude that given there is a good level of protection provided by a first dose, and in the case of the Pfizer vaccine particularly, after 28 days only slightly below that conferred by two doses, it is better to give that protection to as many of those vulnerable as possible, and then give them the second dose, to reduce deaths.

## **Will it work?**

The short answer is that for now the available data suggests it is safe and will work. And it is being kept under regular review by the scientists, regulators and chief medical officers. Bear in mind the acceptable threshold for a vaccine in the UK is 50% protection of people who receive it.

It is probably best to state this in the JCVI’s own words:

- When considering vaccination schedules JCVI often considers first principles, and regularly advises schedules which differ from the marketing authorisation. In every case, the advice of JCVI is aimed at maximising protection in the population.
- Published efficacy between dose 1 and 2 of the Pfizer vaccine was 52.4% (95% confidence interval (CI) 29.5 to 68.4%). Based on the timing of cases accrued in the phase 3 study, most of the vaccine failures in the period between doses occurred shortly after vaccination, suggesting that short-term protection from dose 1 is very high from day 10 after vaccination. Using data for those cases observed between day 15 and 21, efficacy against symptomatic COVID-19 was estimated at 89% (95% CI 52 to 97%).
- The level of protection gained from a single dose of the AstraZeneca vaccine was assessed in an exploratory analysis. Vaccine efficacy from 22 days post dose 1 was 73% (95% CI 48.79 to 85.76). High protection against hospitalisation was seen from 21 days after dose 1 until 2 weeks after the second dose, suggesting that a single dose of the AstraZeneca vaccine will provide high short-term protection against severe disease. Protective immunity from the first dose likely lasts for a duration of 12 weeks.
- With most vaccines an extended interval between the prime and booster doses leads to a better immune response to the booster dose. There is evidence that a longer interval between the first and second doses promotes a stronger immune response with the AstraZeneca vaccine.

So there is a good scientific rationale for doing this. Again, remember the acceptable threshold for a vaccine in the UK is 50% protection of people who receive it.

This is a finely balanced judgement. Give a second dose of a vaccine too soon and the body may not have built the “immune memory” needed to get the boosting effect of the second dose. Give it with a sufficient gap, and it acts as a booster, enhancing protection

[which is what we want ]. The evidence currently suggests the Pfizer vaccine works better with a delay. Leave too long a delay, however, and the virus may have a greater opportunity to build resistance to the vaccine. But the detailed monitoring strategy put in place, and the advice of expert immunologists, is that currently the 12 week delay does not increase that risk substantially. This will be monitored carefully.

## Who is questioning this strategy?

The British Medical Association (BMA) called for “a dialogue” with the government over halving the maximum interval between doses of the Pfizer/BioNTech vaccine, from 12 weeks to 6. On 21 January 2021, the US Centers for Disease Control and Prevention (CDC) updated its recommendations for intervals between the first and second dose of the Pfizer/BioNTech and Moderna COVID-19 vaccines in the US, stating that the second dose should be given within six weeks, and the European Medicines Agency has also said that the gap between the first and second doses should not exceed 42 days.

## Who is in favour of this schedule?

Besides the independent JCVI, the British Society for Immunology (the body for professional immunologists and vaccinologists) issued a [statement](#) which concluded “that a pragmatic approach in the short-term is needed, and accept the rationale for the change in dosing schedule for the Oxford/AstraZeneca and for the Pfizer/BioNTech vaccine that has been recommended by the Joint Committee on Vaccination and Immunisation (JCVI).” While at the same time calling for this to be very carefully monitored and making a number of asks of government to ensure the strategy continues to be monitored.

The Royal Pharmaceutical Society issued a [statement](#) supporting the position, and [re-iterated](#) its public support on 25<sup>th</sup> January 2021.

The Royal College of General Practitioners has also [supported](#) it.

## What does this say about the vaccine and exiting the pandemic?

The fact we have two vaccines already being rolled out and a third on the way is a tremendous achievement. But the vaccine is not a magic bullet and not the only part of a strategy to exit covid.

- We do NOT yet know whether the vaccine stops onwards transmission from one person to another. If it does this is a major bonus.
- We DO know the vaccines will reduce death and serious illness
  - People often ask what use this is? Basically what we know currently is the vaccine reduces death and serious illness, so it works in a way analogous to a seat belt in a car. Even if it doesn't stop an accident, it will save your life.
- We will still need testing, contact tracing and self-isolation
- We will still need people to take the preventive measures (hygiene, face coverings, distancing etc) until they have a good standard of protection. And if the vaccine doesn't stop transmission, then we will need to continue with some of these.

So a vaccine is an important part of our strategy to exit covid. But we need more things too. At the time of writing the Health Protection Board is developing our “route out” plan.

## Useful additional Links

- CMO statement <https://gov.uk/government/news/statement-from-the-uk-chief-medical-officers-on-the-prioritisation-of-first-doses-of-covid-19-vaccines...>
- CMO letter at new year - [CEM\\_CMO\\_2020\\_044.pdf](#)
- JCVI summary [CEM\\_CMO\\_2020\\_044\\_JCVI\\_Statement.pdf](#)
- Green book updated chapter [CEM\\_CMO\\_2020\\_044\\_GreenBook.pdf](#)

### About this briefing:

This briefing was compiled by the Director of Public Health for the Health Protection Board which comprises all eleven Councils in Hertfordshire, Police, NHS, Public Health England and Voluntary and Community Sectors.

