Statistical bulletin

Risk of death following COVID-19 vaccination or positive SARS-CoV-2 test in young people, England: 8 December 2020 to 25 May 2022

Estimates of the risk of all-cause and cardiac death in the 12 weeks after vaccination or positive SARS-CoV-2 test compared with subsequent weeks for people aged 12 to 29 years in England using two sources of mortality data: ONS death registrations and deaths recorded in Hospital Episode Statistics. Experimental Statistics.

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1 . Main points

- Several studies have reported associations between coronavirus (COVID-19) vaccination and risk of cardiac diseases, especially in young people; we assessed the impact of COVID-19 vaccination and positive SARS-CoV-2 tests on the risk of cardiac and all-cause mortality in young people (aged 12 to 29 years) in England using a self-controlled case series design.

- There was no significant increase in cardiac or all-cause mortality in the 12 weeks following COVID-19 vaccination compared with more than 12 weeks after any dose for the study population as a whole.

- There was evidence of an increase in cardiac death in young women after a first dose of non-mRNA vaccines, with the risk being 3.5 times higher in the 12 weeks following vaccination, compared with the longer-term risk.

- The subgroup who received non-mRNA vaccines was more likely to be clinically vulnerable and may be at greater risk of adverse events following vaccination than the general population.

- According to the statistical model, 11 out of the 15 cardiac deaths in young women that occurred within 12 weeks of a first dose of a non-mRNA vaccine were likely to be linked to the vaccine; this corresponds to 6 cardiac-related deaths per 100,000 females vaccinated with at least a first dose of a non-mRNA vaccine.

- We find no strong evidence of an increase in risk of cardiac or all-cause death after vaccination for young men for either vaccine type; we will continue to monitor this as more deaths are registered and more doses are administered.

- A positive SARS-CoV-2 test was associated with increased cardiac and all-cause mortality among people; the risk was higher in those who were unvaccinated at time of testing than in those who were vaccinated.

- It is important to consider the risks of vaccination in light of the benefits; this analysis of vaccine safety contributes to the growing body of scientific work on the impact of vaccinations.

Statistician's comment

"Today's analysis looks at the risk of death after COVID-19 vaccination in young people. Existing studies show that COVID-19 vaccination is linked to an increased risk of cardiac diseases.

"We find no evidence that the risk of cardiac or all cause death is increased in the weeks following vaccination with mRNA vaccines. However, receiving a first dose of a non-mRNA vaccine was associated with an increased risk of cardiac death in young women. Vaccination with the main non-mRNA vaccine used in the UK was stopped for young people following safety concerns in April 2021, and most of the young people who received it would have been prioritised due to clinical vulnerability or being healthcare workers. Therefore, these results cannot be generalised to the population as a whole.

"Whilst vaccination carries some risks, these need to be assessed in light of its benefits. Our analysis shows that the risk of death is greatly increased following a positive test for COVID-19 even in young people and many studies show that vaccines are highly effective at preventing hospitalisation or death following COVID-19 infection.

"We will continue to monitor data on vaccinations as further doses are rolled out and produce analyses such as this study that contribute to the body of knowledge on risks and benefits of vaccination."

Vahé Nafilyan, Senior Statistician, Office for National Statistics

The method used to produce these statistics and the full analysis are described in this paper published in Nature Communications.

2 . Risk of death following COVID-19 vaccination or positive SARS-CoV-2 test in young people data

Risk of death following COVID-19 vaccination or positive SARS-CoV-2 test in young people, England
Dataset | Released 27 March 2023
Estimates of the risk of all-cause and cardiac death in the 12 weeks after vaccination or positive SARS-CoV-2 test compared with subsequent weeks for people aged 12 to 29 years in England using two sources of mortality data: ONS death registrations and deaths recorded in Hospital Episode Statistics. Experimental Statistics.

3 . Glossary

Coronaviruses

The World Health Organization (WHO) defines coronaviruses as "a large family of viruses that are known to cause illness ranging from the common cold to more severe diseases such as Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS)". Between 2001 and 2018, there were 12 deaths in England and Wales because of a coronavirus infection, with a further 13 deaths mentioning the virus as a contributory factor on the death certificate.

Coronavirus (COVID-19)

COVID-19 refers to the "coronavirus disease 2019" and is a disease that can affect the lungs and airways. It is caused by a type of coronavirus. Further information is available from the World Health Organization (WHO).

Statistical significance

The term "significant" refers to statistically significant changes or differences. Significance has been determined using the 95% confidence intervals, where instances of non-overlapping confidence intervals between estimates indicate the difference is unlikely to have arisen from random fluctuation.

95% confidence intervals

A confidence interval is a measure of the uncertainty around a specific estimate. If a confidence interval is 95%, it is expected that the interval will contain the true value on 95 occasions if repeated 100 times. As intervals around estimates widen, the level of uncertainty about where the true value lies increases. The size of the interval around the estimate is strongly related to the number of deaths, prevalence of health states and the size of the underlying population. At a national level, the overall level of error will be small compared with the error associated with a local area or a specific age and sex breakdown. More information is available on our uncertainty pages.

Incidence rate ratio

Compares the rate at which an outcome (in this case, death) occurs in the risk period to the rate at which it occurs in a reference period. An incidence rate ratio of greater than 1 indicates a higher rate of events in the risk period, whereas an incidence rate ratio of less than 1 indicates a lower rate of events in the risk period.

Self-controlled case study

The [self-controlled case series](#) (SCCS) is a method developed to study adverse reactions to vaccines. This method compares the incidence of the outcome in a risk period (here weeks 1 to 12 after vaccination) with a baseline period (weeks 13 onwards after vaccination) to assess whether there is a change in the risk of death soon after vaccination compared with later after vaccination. The technique used in this release uses an [SCCS method adapted for multiple exposures](#) (because of the multiple vaccination doses administered) and for deaths as the outcome, to take into account the fact that the vaccination cannot occur after death.

4 . Measuring the data

The method used to produce these statistics is described in this [paper published in Nature Communications](#).

Data sources

We analysed two independent sources of data on death. First, we used data from death registration registered by 8 June 2022 that occurred between 8 December 2020 (the start of the vaccine rollout in England) and 25 May 2022. Second, we used data on hospital deaths recorded in Hospital Episode Statistics for England (HES) between 8 December 2020 and 31 March 2022.

Unlike death registrations, deaths recorded in HES are not subject to delay because of coroner referrals. There were 367 records of deaths in HES (25.8% of the 1,420 total) that did not have a linked death registration, likely because of an ongoing coroner inquest.

Deaths data were linked to data on coronavirus (COVID-19) vaccination from the National Immunisation Management Service (NIMS) and a supplementary extract from NHS point of care data provided by NHS Digital. The NIMS data include most COVID-19 vaccinations administered in England since 8 December 2020. However, in rare cases, if the death was recorded on the Personal Demographics Service (PDS) before the vaccination record was sent to NIMS then the patient's vaccination registration in NIMS is not updated. The supplementary extract of NHS point of care data includes all vaccination records so affected. The NIMS and point-of-care extracts include all vaccinations recorded by 14 June 2022.

To assess the relative incidence of death following a positive test for SARS-CoV-2, we linked death records to national testing data from pillar 1 (tests in hospitals) and pillar 2 (tests in the community) recorded between 9 September 2020 (when mass testing became available) and 31 December 2021.

The linkage across databases was conducted using NHS number, which was available for 99.96% of NIMS records, 99.7% of Office for National Statistics (ONS) death registrations, 99.1% of deaths in HES, and 100% of the point-of-care extract from NHS Digital.

The study population included all people whose deaths were recorded since the start of the vaccination roll-out on 8 December 2020 and who were aged 12 to 29 years on date of death.

Statistical analysis

We used a [Self-Controlled Case Series (SCCS) approach](#) designed to handle multiple event-dependent exposures. Event-dependent exposure occurs when the event of interest influences the likelihood of exposure; death represents an extreme example in which any subsequent exposure is impossible after the event. This specific SCCS approach compares the risk of death during a predefined risk period following exposure (vaccination or positive test for SARS-CoV-2) with a reference period of all time after the risk period.

By comparing time periods within individuals, time-invariant factors such as sex and, in general, age group and comorbidity, are implicitly controlled for; time-varying factors can be controlled by the inclusion of unexposed cases in the analysis and by the inclusion of calendar time as a covariate. Participants were followed from 8 December 2020 to 25 May 2022 for death registrations and 31 March 2022 for hospital deaths and were included in all weeks up to the end of the study period, whether a death occurred or not. For the analyses of positive SARS-CoV-2 test, follow-up ended at 31 December 2021 when testing data ended. The risk period was defined as the first 12 weeks after vaccination or positive test, while the reference period was defined as all the following weeks to the end of study. In addition, all the weeks before vaccination or positive test from 8 December 2020, or all weeks throughout the follow-up time if the individual was unvaccinated or never positive, were also included in order to adjust for calendar time.

The exposure was the week since vaccination or positive SARS-CoV-2 test for each of the first 12 weeks individually, or the 12 weeks together. For vaccination, the risk weeks were further categorised by dose or considered for all doses combined.

The models were fitted using a conditional Poisson regression model using a pseudo-likelihood method on a person-week level dataset. The calendar day of the start of each week was included in the model using a restricted cubic spline. Adjusting for calendar time is a way to capture the impact of increasing registration delays over time (more recent deaths being more likely to be under coroner review), as well as of seasonal mortality trends and changing SARS-CoV-2 infection rates. Similar analyses were conducted focusing on unvaccinated and vaccinated individuals for deaths after positive test for SARS-CoV-2.

Where the incidence rate ratio (IRR) was significantly different from 1, we derived estimates of absolute effects using an established method for the self-controlled case series. We used the total number of people who tested positive in pillar 1 and pillar 2 stratified by vaccination status on date of test registration over the period of interest as a measure of exposed cases.

5 . Strengths and limitations

Strengths

A major strength of this study is that we used death registration records and deaths that had occurred in hospital for the whole of England, linked to all vaccination records, including those that were not registered in the National Immunisation Management Service (NIMS) vaccination database because people died shortly after vaccination. Secondly, using a self-controlled case series, our estimates account for between-person differences, which is crucial because young people who were clinically extremely vulnerable were prioritised for vaccination.

Limitations

The main limitation in our analysis of death registration data is delay because of coroner referrals, which are common when young people die. As a result, not all deaths that occurred in the period had been registered.

While adjusting for calendar time can account for more recent deaths being less likely to have been registered, it cannot account for any increase in coroner referral related to time since vaccination. For instance, if deaths occurred very soon after vaccination they are more likely to be investigated by a coroner than deaths occurring at any other time. Our analysis using deaths recorded in hospital records, which are not affected by registration delays, was consistent with the analysis of registered deaths, suggesting that differential coroner referral in the period immediately post-vaccination did not substantially affect analysis of registered deaths. However, a further limitation of the Hospital Episode Statistics for England (HES) analysis is that sudden cardiac deaths, which would have occurred out of hospital, would not be captured.

Another limitation is the selective administration of the vaccines. Vaccination with the main non-mRNA vaccine used in the UK was stopped for young people following safety concerns in April 2021. Young people who had been vaccinated up to this point were mostly those prioritised, for example, because of clinical vulnerability or being a healthcare worker. The young people who were clinically vulnerable are therefore likely to be at higher risk of mortality than the general population and more vulnerable to the SARS-CoV-2 virus.

Of the 15 deaths that occurred within 12 weeks of vaccination among women who had had at least a first dose of a vaccine, 2 had a coroner inquest, which would imply that most of the deaths were not unexpected, as might be the case for a population with clinical vulnerabilities who had a high mortality risk. This difference in populations means that results for this subpopulation, such as the increase in risk of cardiac-related deaths for females after the first dose of an mRNA vaccine, may be influenced by the characteristics of this group, and may not be generalisable to the population as a whole.

6 . Related links

COVID-19 vaccine effectiveness estimated using Census 2021 variables, England: 31 March 2021 to 20 March 2022
Bulletin | Released 8 March 2023
Estimates of the risk of hospital admission for coronavirus (COVID-19) and death involving COVID-19 by vaccination status, overall and by age group, using anonymised linked data from Census 2021. Experimental Statistics.

Deaths involving COVID-19 by vaccination status, England: deaths occurring between 1 April 2021 and 31 December 2022
Bulletin | Released 21 February 2023
Age-standardised mortality rates for deaths involving coronavirus (COVID-19) by vaccination status, broken down by age group. Deaths occurring between 1 April 2021 and 31 December 2022 in England.

Coronavirus (COVID-19) latest insights
Interactive tool | Updated regularly
The latest data and trends about the coronavirus (COVID-19) pandemic from the Office for National Statistics and other sources.

Deaths registered weekly in England and Wales, provisional
Bulletin | Released weekly
Provisional number of deaths registered in England and Wales, including deaths involving coronavirus (COVID-19), in the latest weeks.

Coronavirus and vaccination rates in people aged 18 years and over by socio-demographic characteristic, region and local authority, England
Dataset | Released 9 December 2022
Coronavirus (COVID-19) vaccination rates for people aged 18 years and over in England. Estimates by socio-demographic characteristic, region and local authority.

Coronavirus (COVID-19) Infection Survey, UK
Bulletin | Released weekly
Percentage of people testing positive for coronavirus (COVID-19) in private residential households in England, Wales, Northern Ireland and Scotland. Thissurveyis being delivered in partnership with University of Oxford, University of Manchester,UK Health Security Agency (UKHSA)and WellcomeTrust, working with the University of Oxfordand partner laboratories tocollect and test samples.

7 . Cite this statistical bulletin

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