

Article

Coronavirus (COVID-19) vaccination and selfreported long COVID in the UK: 25 October 2021

Estimates of the association between coronavirus (COVID-19) vaccination and selfreported long COVID in people infected prior to vaccination, using data from the UK Coronavirus Infection Survey.

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1. Main points

- Receiving a first coronavirus (COVID-19) vaccination was associated with an initial 13% decrease in the likelihood of self-reported long COVID (symptoms persisting for at least 12 weeks after first having COVID-19 that were not explained by something else) among study participants aged 18 to 69 years in the UK who had confirmed COVID-19 prior to vaccination, using data to 5 September 2021.
- However, it is unclear from the data whether the improvement in self-reported long COVID symptoms after receiving the first vaccination was sustained over time until receiving the second vaccination.
- Receiving a second COVID-19 vaccination was associated with 9% decrease in the likelihood of selfreported long COVID, relative to having received the first vaccination, and there was statistical evidence of a sustained improvement after this.
- There was no statistical evidence of differences in post-vaccination trends of self-reported long COVID between participants who received an adenovirus vector (Oxford/AstraZeneca) vaccine and those who received an mRNA (Pfizer/BioNTech or Moderna) vaccine.
- There was also no statistical evidence of differences in trends according to socio-demographic characteristics (age, sex, ethnic group and area deprivation) or health-related factors (self-reported health status not related to COVID-19, and whether ever hospitalised with acute COVID-19).
- The observational nature of the study means that we cannot say whether COVID-19 vaccination caused subsequent changes in the likelihood of self-reported long COVID; also, study follow-up after receiving the second vaccination was limited, so long-term associations between COVID-19 vaccination and selfreported long COVID remain unknown.

If you are worried about new or ongoing symptoms four or more weeks after having COVID-19, there are resources available to help: see the <u>NHS webpage on the long-term effects of coronavirus</u> and the <u>Your COVID</u> <u>Recovery</u> website, which can help you to understand what has happened and what you might expect as part of your recovery. The time it takes to recover from COVID-19 is different for everyone, and the length of your recovery is not necessarily related to the severity of your initial illness or whether you were in hospital.

This is analysis of new, recently collected data, and our understanding of it and its quality will improve over time. Long COVID is an emerging phenomenon that is not yet fully understood. The estimates presented in this release are <u>experimental</u>; these are series of statistics that are in the testing phase and not yet fully developed.

2. Self-reported long COVID before and after vaccination

This article explores changes in the likelihood of experiencing persistent symptoms following coronavirus (COVID-19) infection, commonly known as long COVID, after COVID-19 vaccination among adults aged 18 to 69 years. This is an analysis of whether people infected before vaccination continued to experience long COVID symptoms afterwards, rather than an investigation into the likelihood of developing long COVID in people infected after vaccination. See <u>Data sources and quality</u> for details of the study data and methodology.

For this analysis, long COVD status was self-reported by study participants over the period 3 February 2021 to 5 September 2021, and defined as symptoms persisting for at least 12 weeks after first having COVID-19 that were not explained by something else.

Receiving a first coronavirus (COVID-19) vaccination was associated with an initial 12.8% decrease (<u>95%</u> <u>confidence interval</u>: 18.6% decrease to 6.6% decrease) in the odds of self-reported long COVID among participants aged 18 to 69 years in the UK. The odds presented in this analysis are adjusted for a range of characteristics; see <u>Data sources and quality</u> for details. The model specification implies that the change in the odds occurs instantly following vaccination, but in reality, this may take place over several days or weeks.

The observational nature of the study means that we cannot say whether COVID-19 vaccination caused subsequent changes in the likelihood of self-reported long COVID.

Prior to receiving the first vaccination, the odds of self-reported long COVID decreased by 0.3% (0.9% decrease to 0.2% increase) with each week from infection. Between the first and second vaccinations, this trend changed to an increase of 0.3% per week. However, the 95% confidence interval around this estimate suggests that the data are also compatible with a decrease of up to 0.6% per week or a larger increase of up to 1.2% per week. There was therefore no statistical evidence (in terms of <u>statistical significance</u>) of a change in the trend of self-reported long COVID over the period between receiving the first and second vaccinations. It is thus unclear from the data whether the initial improvement in symptoms is sustained over time until the second vaccination.

Receiving a second COVID-19 vaccination was associated with an initial 8.8% decrease (14.1% decrease to 3.1% decrease) in the odds of self-reported long COVID. The second vaccination was also associated with a change in the trend of self-reported long COVID, with the odds decreasing by 0.8% (1.2% decrease to 0.4% decrease) per week after double vaccination, possibly indicating a sustained improvement in symptoms.

These results should be interpreted with caution because not all participants were double vaccinated by the end of the follow-up period, and follow-up time was limited to a median of 67 days after the second vaccination. Long-term associations between COVID-19 vaccination and self-reported long COVID therefore remain unknown.

We found comparable findings when focussing on self-reported long COVID resulting in limitation to day-to-day activities. We also found similar results when omitting follow-up visits within the first week of each vaccination from the analysis, suggesting that the findings are unlikely to be largely driven by post-vaccine placebo effects. Model outputs in full can be found in the <u>data tables</u>.

Figure 1 shows modelled probabilities of self-reported long COVID for a hypothetical study participant who received their first COVID-19 vaccination 24 weeks after infection and their second vaccination 12 weeks later. This illustrative example demonstrates the estimated change in the long COVID trend after each vaccination. While the estimated probabilities are specific to the profile of the hypothetical participant in the example (see note 1 under Figure 1), the proportional change in the probability after each vaccination is not specific to this profile and can therefore be generalised to participants with other characteristics.

Figure 1: COVID-19 vaccination was associated with a decrease in the likelihood of selfreported long COVID among participants 18 to 69 years, which was sustained after the second vaccination

Modelled probabilities of self-reported long COVID for a hypothetical study participant who received their first vaccination 24 weeks after infection and their second vaccination 12 weeks later (indicated by dashed lines), UK: 3 February 2021 to 5 September 2021

Notes:

- 1. Probabilities are shown for a participant of approximately mean age (50 years) and in the modal group for other covariates (female, White, living in London, in an area in the least deprived quintile group of the Index of Multiple Deprivation, not a patient-facing health or social care worker, no pre-existing health conditions, not hospitalised at the acute phase of infection, and infected on 7 September 2020).
- 2. Confidence intervals are at the 95% level.

Download the data

.xlsx

3. Post-vaccination changes in self-reported long COVID according to vaccine type and personal characteristics

There was no statistical evidence (in terms of <u>statistical significance</u>) of differences in post-vaccination trends of self-reported long COVID between participants who received adenovirus vector and mRNA vaccines.

Numerically, the first coronavirus (COVID-19) vaccination was associated with an initial 14.9% decrease (<u>95%</u> <u>confidence interval</u>: 21.8% decrease to 7.5% decrease) in the odds of self-reported long COVID among participants aged 18 to 69 years in the UK who received an adenovirus vector vaccine, and an initial 8.9% decrease (18.2% decrease to 1.4% increase) among those who received an mRNA vaccine. Decreases in the odds of self-reported long COVID after the second vaccination were numerically similar between vaccine types, at 8.7% (15.4% decrease to 1.4% decrease) for participants who received an adenovirus vector vaccine and 8.9% (17.6% decrease to 0.7% increase) for those who received an mRNA vaccine.

In the period between receiving the first and second vaccinations, the odds of self-reported long COVID numerically increased by 0.6% per week for participants who received an adenovirus vector vaccine, and numerically decreased by 0.3% per week for those who received an mRNA vaccine.

However, the 95% confidence intervals around these trend estimates suggest that the data are also compatible with a decrease in the odds of up to 0.5% or an increase of up to 1.6% per week among participants who received an adenovirus vector vaccine, and a decrease in the odds of up to 1.8% or an increase of up to 1.2% per week among participants who received an mRNA vaccine. It is therefore unclear from the data whether the initial improvement in self-reported long COVID symptoms after receiving the first vaccination was sustained over time for either vaccine type.

After receiving the second vaccination, the odds of self-reported long COVID decreased numerically by 0.8% (1.4% decrease to 0.2% decrease) per week for participants who received an adenovirus vector vaccine, and by 0.7% (1.3% decrease to 0.1% decrease) per week for those who received an mRNA vaccine.

There was no statistical evidence of differences in post-vaccination long COVID trends according to sociodemographic characteristics (age, sex, ethnic group and area deprivation) or health-related factors (self-reported health status not related to COVID-19 and whether ever hospitalised with acute COVID-19). See the <u>data tables</u> for results.

Figure 2: There was no statistical evidence that post-vaccination changes in the likelihood of self-reported long COVID differed between participants aged 18 to 69 years who received an adenovirus vector vaccine and those who received an mRNA vaccine

Modelled probabilities of self-reported long COVID for hypothetical study participants who received their first vaccination 24 weeks after infection and their second vaccination 12 weeks later (indicated by dashed lines), UK: 3 February 2021 to 5 September 2021

Notes:

- 1. Probabilities are shown for participants of approximately mean age (50 years) and in the modal group for other covariates (female, White, living in London, in an area in the least deprived quintile group of the Index of Multiple Deprivation, not a patient-facing health or social care worker, no pre-existing health conditions, not hospitalised at the acute phase of infection, and infected on 7 September 2020).
- 2. Estimates were obtained by including a binary variable representing vaccine type in the model, and interacting this with all four exposure variables of interest (changes in odds and trends after first and second vaccinations).
- 3. Confidence intervals are at the 95% level.

Download the data

.xlsx

4 . Likelihood of experiencing specific symptoms before and after vaccination

Study participants who responded positively to the question on long COVID were asked whether they were experiencing any of 21 individual symptoms attributable to long COVID at the time of the follow-up visit. For this analysis, we explored post-vaccination changes in the trends of the 10 symptoms that were most frequently reported over the follow-up period by participants aged 18 to 69 years in the UK.

The odds of experiencing symptoms initially numerically decreased after each vaccination for most symptoms included in the analysis (Figure 3). After the first vaccination, the largest numeric decreases in the odds were observed for:

- loss of smell (12.5% decrease, <u>95% confidence interval</u>: 21.5% decrease to 2.5% decrease)
- loss of taste (9.2% decrease, 19.8% decrease to 2.7% increase)
- trouble sleeping (8.8% decrease, 19.4% decrease to 3.3% increase)

After the second vaccination, the largest numeric decreases in the odds were observed for:

- weakness and tiredness (9.7% decrease, 16.5% decrease to 2.4% decrease)
- headache (9.0% decrease, 18.1% decrease to 1.0% increase)
- trouble sleeping (9.0% decrease, 18.2% decrease to 1.2% increase)

Like the overall self-reported long COVID measure, trends in the odds of individual symptoms were generally numerically upwards between the first and second vaccinations, with most returning to a declining or flat trend after the second vaccination.

However, for most symptoms, the 95% confidence intervals around the estimates suggest that the data are compatible with both initial increases and decreases, and with both upward and downward trends, in the likelihood of experiencing symptoms after each vaccination. There was therefore no statistical evidence (in terms of <u>statistical significance</u>) of post-vaccination changes in the likelihood of experiencing most of the symptoms included in the analysis. Neither was there statistical evidence of differential changes between most of the symptoms. Model outputs for all 10 analysed symptoms can be found in the <u>data tables</u>.

Confidence intervals around estimates for individual long COVID symptoms are relatively wide, so there is considerable uncertainty regarding the size and direction of post-vaccination changes in the likelihood of experiencing symptoms.

Figure 3: After an initial numeric decrease in the likelihood of experiencing most symptoms among participants aged 18 to 69 years, symptom trends were generally numerically upwards between the first and second vaccinations, with most returning to numerically declining or flat trends after the second vaccination

Modelled probabilities of individual long COVID symptoms for a hypothetical study participant who received their first vaccination 24 weeks after infection and their second vaccination 12 weeks later (indicated by dashed lines), UK: 3 February 2021 to 5 September 2021

Notes:

- 1. Probabilities are shown for a participant of approximately mean age (50 years) and in the modal group for other covariates (female, White, living in London, in an area in the least deprived quintile group of the Index of Multiple Deprivation, not a patient-facing health or social care worker, no pre-existing health conditions, not hospitalised at the acute phase of infection, and infected on 7 September 2020).
- 2. Study participants who responded positively to the question on long COVID were asked whether they were experiencing any of 21 individual symptoms. For this analysis, we explored post-vaccination changes in the trends of the 10 symptoms that were most frequently reported over the follow-up period.

Download the data

.xlsx

5. Comparison with other studies

Although existing evidence is limited, our main finding, of reduced odds of experiencing long COVID symptoms after double coronavirus (COVID-19) vaccination, is broadly coherent with those from other studies. A <u>study of 455 participants with pre-existing long COVID</u> found reduced symptom burden and double the rate of remission at 120 days post-vaccination compared with unvaccinated controls. A <u>descriptive analysis of 900 social media users</u> with long COVID found that over half had experienced an improvement in symptoms after vaccination while just 7% reported a deterioration. In a <u>study of 44 vaccinated patients and 22 unvaccinated controls previously</u> hospitalised with COVID-19, there was no evidence of a worsening in long COVID symptoms or quality of life after vaccination.

In addition to research into vaccination and pre-existing long COVID symptoms, evidence suggests that the incidence of long COVID is reduced in those infected after vaccination. In a <u>study of 906 fully-vaccinated mobile</u> <u>phone app users</u>, the odds of having symptoms for at least 28 days post-infection were approximately halved after vaccination compared with unvaccinated controls.

6 . Coronavirus (COVID-19) vaccination and self-reported long COVID in the UK, 25 October 2021 data

Coronavirus (COVID-19) vaccination and self-reported long COVID in the UK: 25 October 2021

Dataset | Released 25 October 2021

Estimates of the association between coronavirus (COVID-19) vaccination and self-reported long COVID in people infected prior to vaccination, using data from the UK Coronavirus Infection Survey.

7. Glossary

Coronavirus and COVID-19

Coronaviruses are a family of viruses that cause disease in people and animals. They can cause the common cold or more severe diseases, such as COVID-19. COVID-19 is the name used to refer to the disease caused by the SARS-CoV-2 virus, which is a type of coronavirus. The Office for National Statistics (ONS) takes COVID-19 to mean presence of SARS-CoV-2 with or without symptoms.

Date of COVID-19 infection

Date of COVID-19 infection was taken to be the earliest of: date of first positive swab for COVID-19 infection or blood test for antibodies (ignoring positive blood tests after the first COVID-19 vaccination), obtained either as part of study follow-up or self-reported outside of the study; and the date when the participant first thought they had COVID-19.

Logistic regression

Logistic regression is a statistical technique for modelling associations between a binary dependent variable and a set of independent variables. The model can be used to estimate the size and direction of the relationship between an outcome (such as self-reported long COVID status) and an exposure (such as vaccination status) while holding other characteristics (such as age or sex) fixed at reference levels, thus isolating the relationship of interest from other confounding factors.

8. Data sources and quality

Study data

This analysis was based on data from Coronavirus (COVID-19) Infection Survey (CIS) participants aged 18 to 69 years in the UK. Further information can be found in the CIS <u>methodology guide</u>, <u>study protocol</u> and <u>survey</u> <u>questionnaire</u>.

For participants in England, we gathered vaccination information from self-reported CIS responses and linked National Immunisation Management System (NIMS) records, with NIMS being prioritised where data conflicted. Administrative records were not available for participants in Wales, Scotland and Northern Ireland, so we gathered vaccination data for these individuals from the CIS alone.

Study participants

We analysed monthly survey responses over the follow-up period 3 February 2021 to 5 September 2021 from 28,356 study participants who had responded to the CIS question on long COVID at least once since it was introduced on 3 February 2021, and had both:

- received a positive swab or blood test for COVID-19, either as part of CIS follow-up or reported testing
 positive outside of the study, before COVID-19 vaccination
- received at least one vaccination of an adenovirus vector (Oxford/AstraZeneca, AZD1222) or mRNA (Pfizer /BioNTech, BNT162b2; Moderna, mRNA-1273) COVID-19 vaccine before or during the follow-up period

The analysis does not include participants:

- aged under 18 years, because very few of these participants had received their first vaccination by the end of the follow-up period
- aged 70 years or older, because nearly all of these participants had already received their first vaccination by the start of the follow-up period
- who had not received at least one vaccination by the end of the follow-up period, because these participants are likely to differ from those who were vaccinated according to characteristics that may not be measured in the CIS data (for example, personal considerations related to vaccine hesitancy)

The mean age of the study sample was 46 years at the end of follow-up and 55.6% of participants were female; see the <u>data tables</u> for a detailed description of the sample characteristics. By design, all study participants received their first COVID-19 vaccination by the end of follow-up, and 12,971 (45.7%) within the follow-up period. Some 23,753 (83.8%) participants were double vaccinated by the end of follow-up, with 20,335 (71.7%) receiving their second vaccination within the follow-up period.

Definition of long COVID

Long COVID status was self-reported by CIS participants by answering the question: "Would you describe yourself as having long COVID, that is, you are still experiencing symptoms more than four weeks after you first had COVID-19, that are not explained by something else?" This definition is based on self-classification of long COVID, and reflects participants' perception of whether their lived experience is consistent with what they understand of the syndrome.

Participants who responded positively to the long COVID question were then asked: "Does this reduce your ability to carry-out day-to-day activities compared with the time before you had COVID-19?" The possible responses were: "Yes, a lot", "Yes, a little" and "Not at all".

Although long COVID was defined as symptoms persisting for at least four weeks from infection in the CIS survey question, for this analysis we used a longer 12-week threshold, which is consistent with the <u>clinical case definition</u> <u>of post-COVID-19 syndrome</u>. We therefore only considered follow-up visits that took place at least 12 weeks after the date of infection.

Statistical techniques

We estimated how the likelihood of self-reporting long COVID changed after participants were vaccinated and then varied over time from vaccination. Binary variables indicated whether participants had been vaccinated at each follow-up visit, with separate variables for the first and second vaccinations. We estimated post-vaccination trends in the odds of self-reported long COVID using variables equal to the number of days since each vaccination at each follow-up visit (set to 0 for visits before vaccination).

Associations between long COVID status and vaccination were estimated using logistic regression models, with robust (clustered) standard errors to account for possible intra-participant correlation induced by the longitudinal nature of the data.

Statistical models were adjusted for a range of characteristics that may be related to both vaccination status or type and the probability of experiencing long COVID symptoms:

- days since infection: we explored various specifications for modelling the time trend, finding that a linear time trend minimised the value of the Bayesian Information Criterion
- calendar day of infection: calculated as the number of days from 24 January 2020 (when the first COVID-19 cases were reported in the UK) and date of infection; and modelled as a restricted cubic spline, with boundary knots at the tenth and ninetieth percentiles and an interior knot at the median of the distribution
- age: modelled as a restricted cubic spline, with boundary knots at the tenth and ninetieth percentiles and an interior knot at the median of the distribution
- sex
- ethnic group: the study sample size did not permit disaggregation beyond White and Non-White groups
- country or region
- Index of Multiple Deprivation (IMD) quintile group
- patient-facing health or social care worker
- health status: based on the survey question: "Do you have any physical or mental health conditions or illnesses lasting or expected to last 12 months or more (excluding any long-lasting COVID-19 symptoms)?"
- hospitalisation with acute COVID-19: self-reported on the survey rather than derived from medical records

Strengths

The CIS comprises a large sample of private households randomly sampled from the UK population (excluding communal establishments such hospitals, care homes, schools, halls of residence and prisons). All household members aged two years or over from sampled households are invited to enrol. Since the CIS began in April 2020, over 500,000 individuals from over 250,000 households have participated in the study.

All CIS participants, including those who do not have COVID-19 or who carry the virus but have no symptoms, are asked to provide swab samples at every follow-up visit. This analysis is therefore applicable to all people with COVID-19, not just those with symptoms during the acute phase of infection.

Limitations

The observational nature of the study means that causality cannot be inferred, and it is possible that side and placebo effects of the vaccine, the <u>fluctuating nature of long COVID symptoms</u> and other factors may have contributed to our findings. Also, the self-controlled study design implicitly controls for time-invariant confounding, but time-dependent confounding by unmeasured factors, such as those related to take-up of the second vaccination given receipt of the first, may remain. Post-vaccination follow-up time was limited, particularly after the second vaccination, so long-term associations remain unknown.

The CIS data did not allow us to disaggregate long COVID according to its possible constituent syndromes, such as <u>post-intensive care syndrome</u>, <u>post-viral fatigue syndrome and long-term COVID syndrome</u>, which may not all exhibit the same relationship with vaccination. Moreover, long COVID status was self-reported rather than clinically diagnosed. Self-reported measures are subjective and may reflect systematic differences between socio-demographic groups. This can be in terms of their likelihood to report symptoms given an underlying level of severity, as well as differences in severity.

The study sample was restricted to participants aged 18 to 69 years, so our findings may not be generalised to children or older adults. They may also not be applicable to people who had not received a vaccine by the end of the follow-up period, in particular those who are vaccine-hesitant because of their long COVID symptoms.

Like all household surveys, not all sampled households invited to participate in the CIS enrol. This analysis is based on unweighted data without imputation for non-response, so bias may be introduced if response rates are related to long COVID symptoms or vaccination response.

The initial CIS sample for England, selected in April 2020, achieved a response rate of 51%. More recently, the response rate has dropped to 13%. This is because the initial sample came from households that had already participated in other Office for National Statistics (ONS) surveys and had agreed to be approached for future research. After this, addresses were selected at random from address lists. Detailed information on response rates, including for other countries of the UK, which joined the study later than England, can be found in Tables 2a to 2f of the technical datasets accompanying the latest CIS statistical bulletin.

Participants might also miss scheduled visits or drop out of the study after enrolment. Bias may be introduced if missed visits and loss-to-follow-up are related to long COVID, for example participants being more willing, or less able, to continue in the study because of their symptoms.

Collaboration

This analysis was produced in collaboration with Professor Sarah Walker and Doctor Koen Pouwels from the University of Oxford, and Doctor Nisreen Alwan from the University of Southampton.

9. Related links

Prevalence of ongoing symptoms following coronavirus (COVID-19) infection in the UK

Statistical bulletin | Updated monthly

Estimates of the UK population prevalence of self-reported long COVID and associated activity limitation, using Coronavirus (COVID-19) Infection Survey data.

Technical article: Updated estimates of the prevalence of post-acute symptoms among people with coronavirus (COVID-19) in the UK: 26 April 2020 to 1 August 2021

Technical article | Released 16 September 2021

Experimental estimates from three approaches to estimating the percentage of people testing positive for coronavirus (COVID-19) and who experience symptoms four or more weeks after infection, broken down by demographic and viral characteristics, using UK Coronavirus Infection Survey data.

Coronavirus (COVID-19) Infection Survey, UK

Statistical bulletin | Updated weekly

Estimates forEngland, Wales, Northern Ireland and Scotland. This survey is being delivered in partnership with the University of Oxford, University of Manchester, Public Health England andWellcomeTrust. This study is jointly led by the ONS and the Department for Health and Social Care (DHSC) working with the University of Oxford and Lighthouse laboratory to collect and test samples.

Coronavirus (COVID-19) Infection Survey technical article: analysis of positivity after vaccination, June 2021

Technical article | Released 17 June 2021

This release provides data about positivity after vaccination from the Coronavirus (COVID-19) Infection Survey. This analysis has been produced in partnership with the University of Oxford.

COVID-19 Infection Survey: methods and further information

Methodology article | Last updated 24 August 2021 Information on the methods used to collect the data, process it, and calculate the statistics produced from the Coronavirus (COVID-19) Infection Survey.

Coronavirus (COVID-19) latest insights

Interactive tool | Updated as and when data become available Explore the latest data and trends about the coronavirus (COVID-19) pandemic from the ONS and other official sources.