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Impact of Delta and calendar time on symptoms reported by individuals testing swab positive: preliminary analysis of data to 12 July 2021

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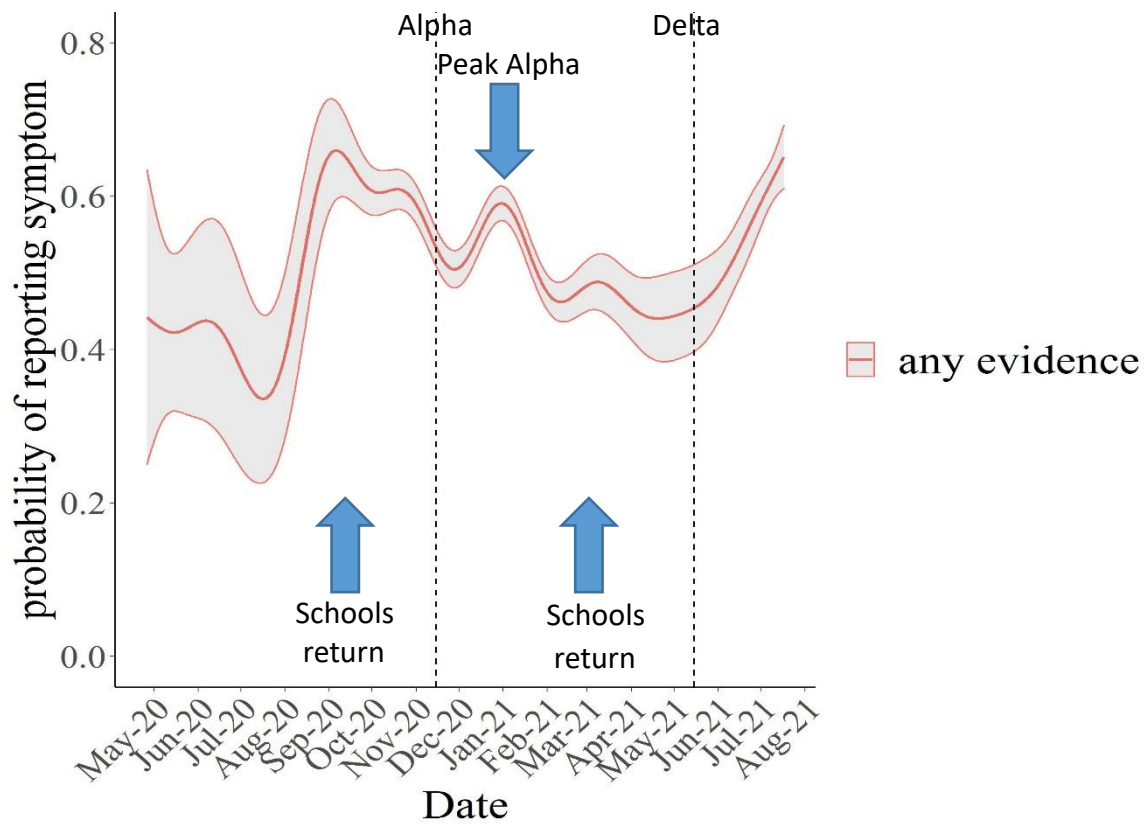
Summary

- We modelled the percentage of individuals newly testing positive or testing negative over time who reported any symptoms (positive responses to any of the 12 specific symptom questions or to the generic question about symptoms compatible with COVID-19). Of those reporting any symptoms, we also modelled the percentage reporting each specific symptom.
 - 12 specific symptoms are: loss of taste, loss of smell, fever, cough, headache, weakness/tiredness (labelled fatigue/weakness in figures), muscle ache (labelled muscle ache/myalgia in figures), shortness of breath, sore throat, diarrhoea, nausea or vomiting and abdominal pain.
 - Note: given its non-specific nature (e.g. associated with hayfever), the survey does not ask about runny nose/rhinitis.
 - Additional details are provided on p12
- In the survey, Alpha-compatible cases started to dominate from 17 November 2020 and Delta-compatible cases from 17 May 2021.
- **[p3-4]** Overall reporting of any symptoms in new positive cases varied substantially over calendar time (40-70%), reflecting both emergence and increases in new variants (Alpha and Delta), consistent with more higher viral burden (low cycle threshold (Ct)) infections being identified at (mostly) monthly visits when positivity rates are increasing, but also background incidental changes in symptom reporting (eg temporally associated with schools re-opening).
 - Variation in reporting of any symptoms at test-negative visits was much smaller, but percentages are low.
- **[p5-7]** Reporting of specific symptoms as a percentage of those reporting any symptom increased over the first 6 months of the survey in positive cases, consistent with greater awareness. Reporting of most specific symptoms in positives temporarily increased in Jan 2021, consistent with the peak in Alpha cases, then remained approximately constant through to the second half of May-21. From mid May 2021, the majority of symptoms increased in positive cases, consistent with increasing Delta cases. Increases in percentage of positive cases reporting sore throat appeared slightly earlier (from April 2021) at the same time as increases in the percentage of negative cases reporting sore throat.
 - In negatives, rates of reporting of cough and sore throat (as a percentage of negatives reporting any symptom) have increased concurrently from April 2021, and are now remaining higher than previously. This is consistent with some early reports

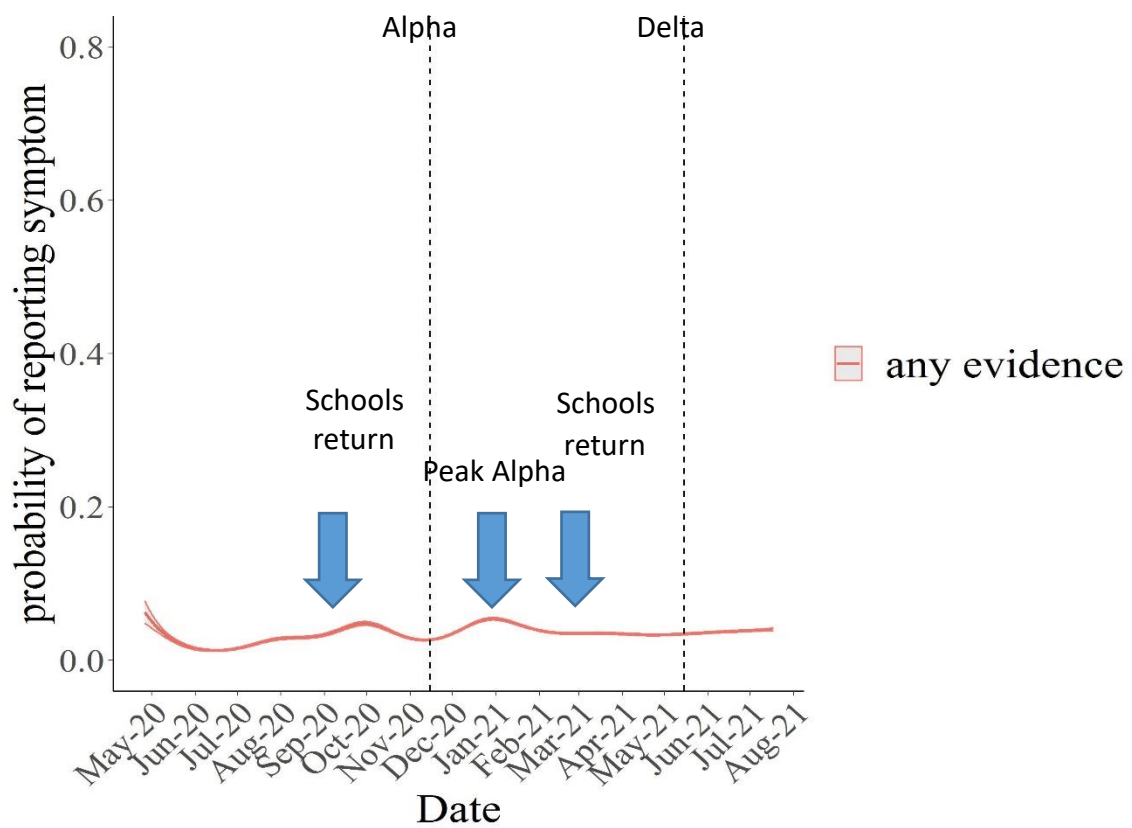
- of other respiratory viruses causing infections in hospitalised cases (RSV, parainfluenza, rhinovirus; personal communication)
- In negatives, rates of reporting of most other symptoms have generally increased slightly over time. Headache is an exception, with high rates reported Feb-April 2021 which have then declined (reasons unclear).
 - **[p8-11]** In positives, the percentage reporting any symptom increases from ~25% in the youngest children to ~50% at age 20, then increasing slightly further to ~60% at age 50 years, before dropping to ~30% by age 85 years. In negatives, the percentage reporting any symptoms is highest in under 5s and late 30s, but remains under 8%¹.
 - In positives, the pattern of reporting of specific symptoms is generally similar across the ages, with the following exceptions:
 - Fever is more commonly reported in children and adolescents.
 - Cough and fatigue are more commonly reported in older individuals (and to a lesser degree diarrhoea).
 - Shortness of breath is more commonly reported in those over 70.
 - Loss of taste or smell and sore throat are more commonly reported in young adults.
 - In negatives, several symptoms also followed a similar pattern of higher symptom reporting in young to middle-aged adults, with the following exceptions:
 - Cough and fever are more commonly reported in children and adolescents.
 - Sore throat and abdominal pain have a peak in reporting in those aged ~10y
 - Shortness of breath, myalgia and diarrhoea all increase consistently across the ages.
 - Fatigue is more common in those aged >70.
 - There is no evidence of interaction between calendar date and age on symptoms reported.
 - We therefore do not see any major shift away from the importance of the classic four symptoms in positive cases with the emergence of the Delta variant in the UK. Recent reports of associations with sore throat may reflect background increases in other respiratory infections/hayfever, potentially even with SARS-CoV-2 isolated incidentally.

¹ at the reference category: white, male, 1 January 2021, see p12

Percentage of new **positive** cases reporting any symptoms over calendar time (UK)



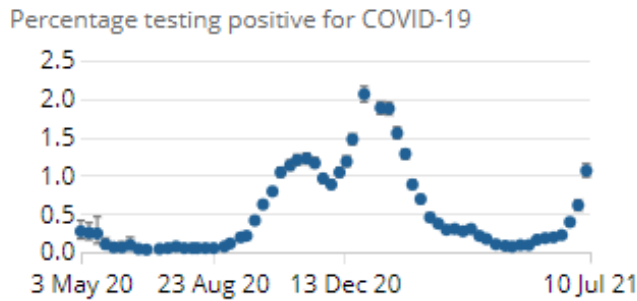
Percentage of comparator negative test visits reporting any symptoms over calendar time (UK)



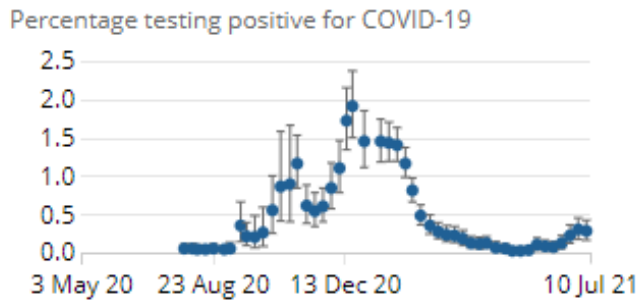
For information: positivity over time in the UK (reproduced from ONS)

● Estimates with 95% confidence/credible intervals

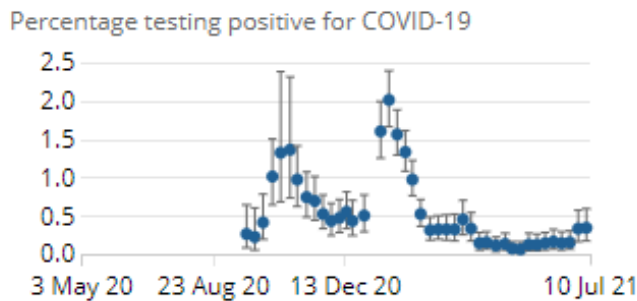
England



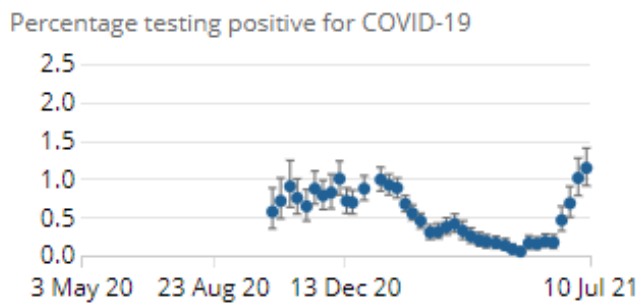
Wales



Northern Ireland

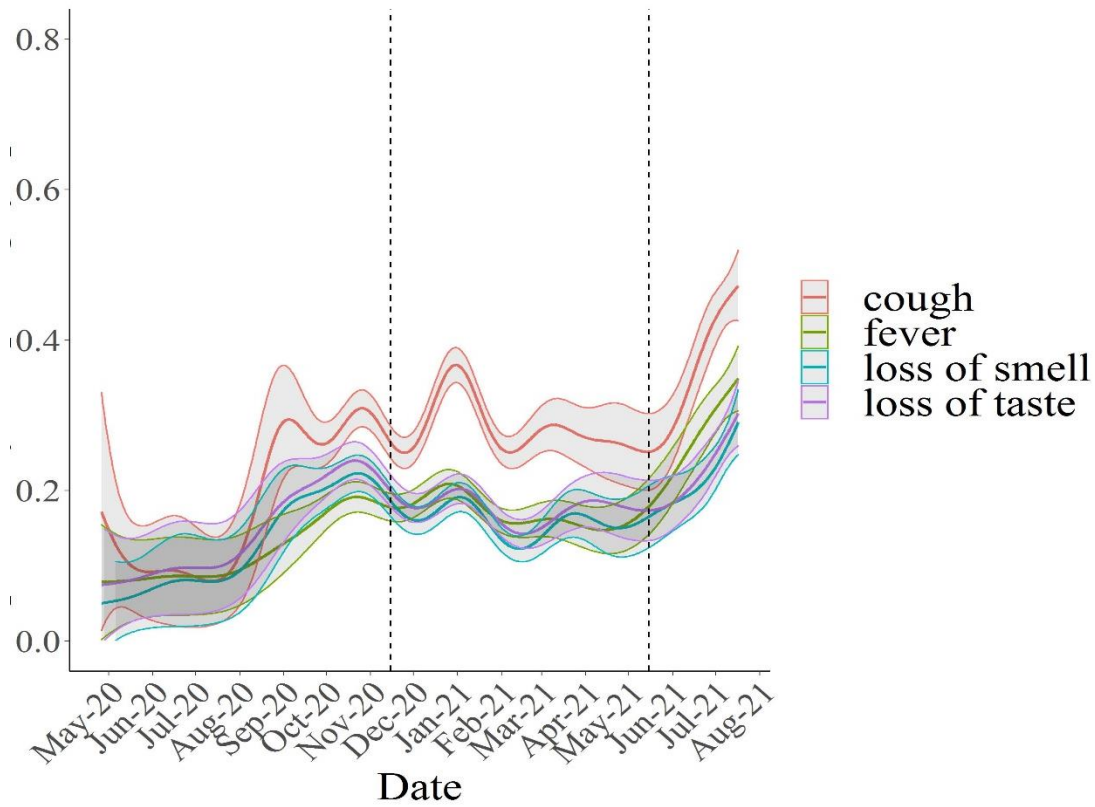


Scotland

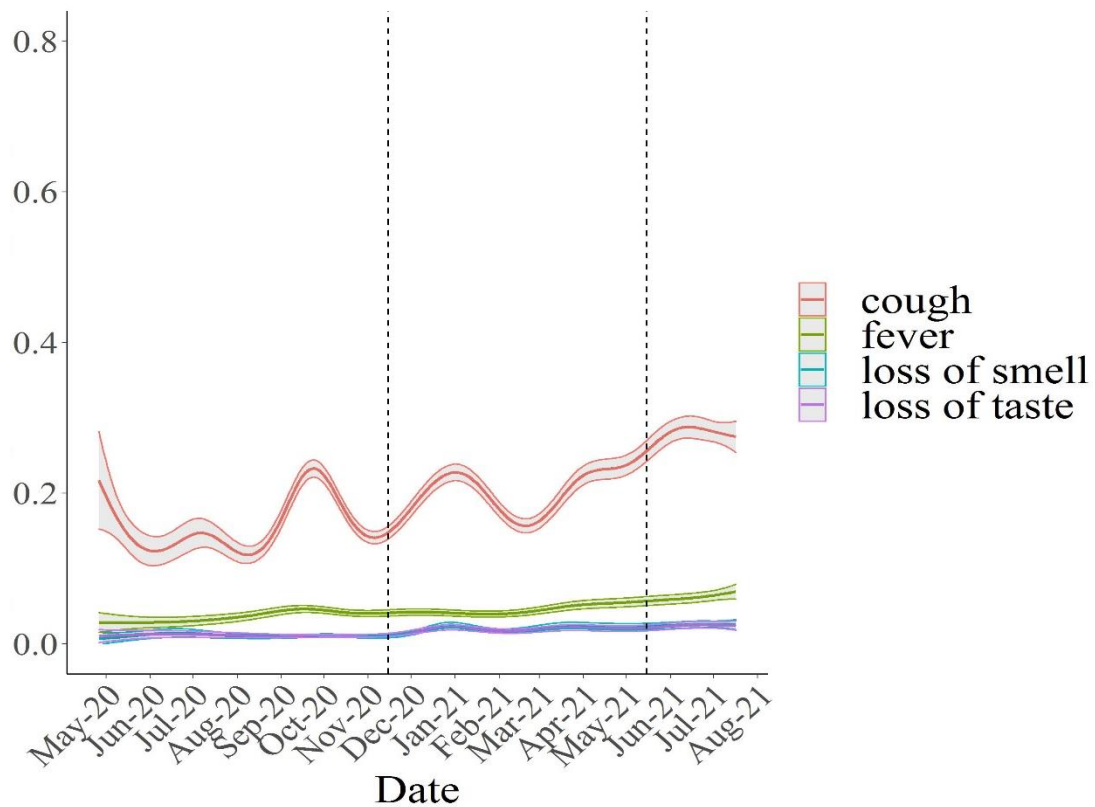


Source: Office for National Statistics

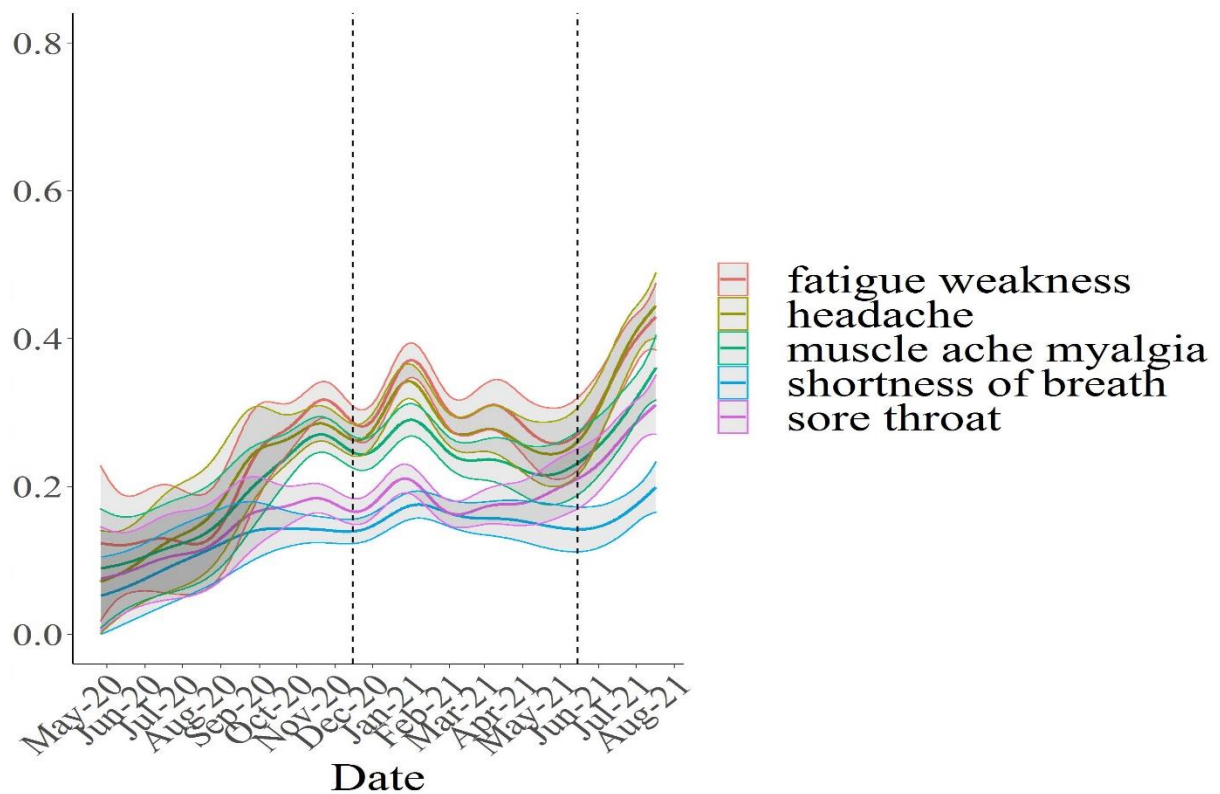
Percentage of positives reporting any symptom who report specific classic symptoms over time



Percentage of negatives reporting any symptom who report specific classic symptoms over time

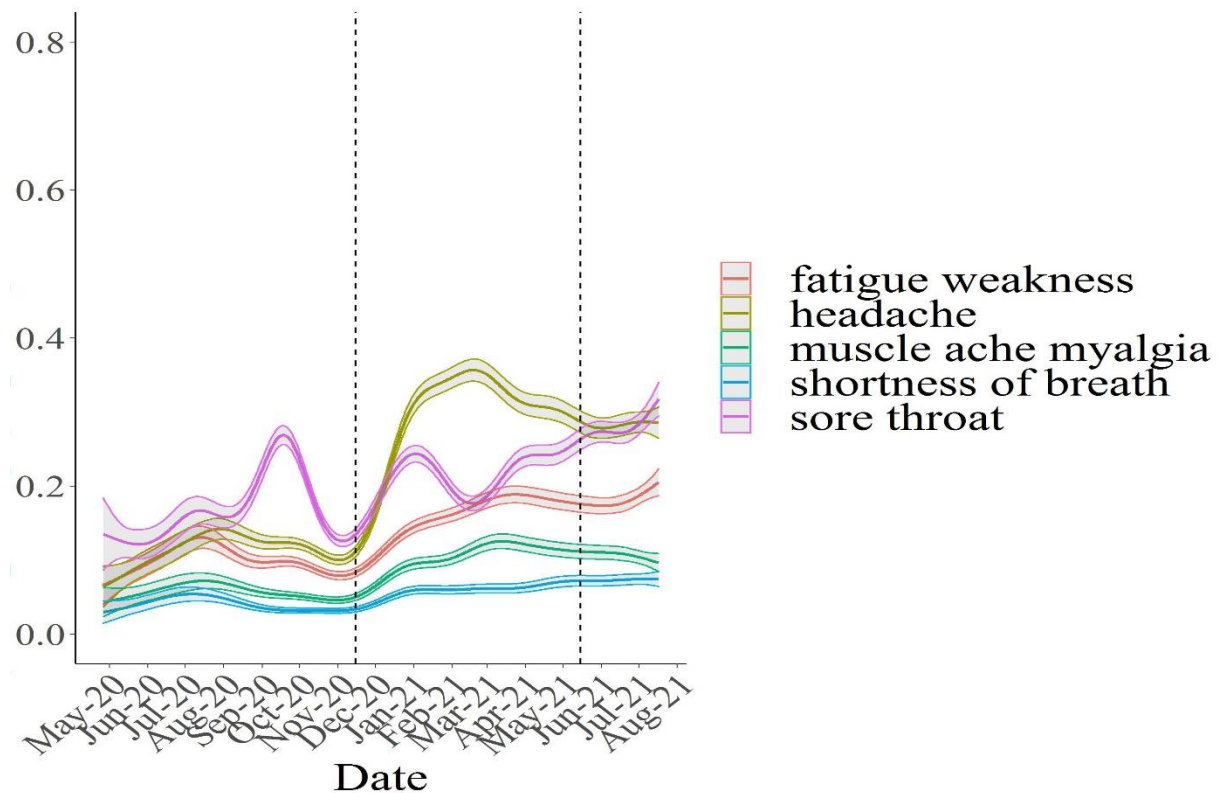


Percentage of positives reporting any symptom who report other specific symptoms over time

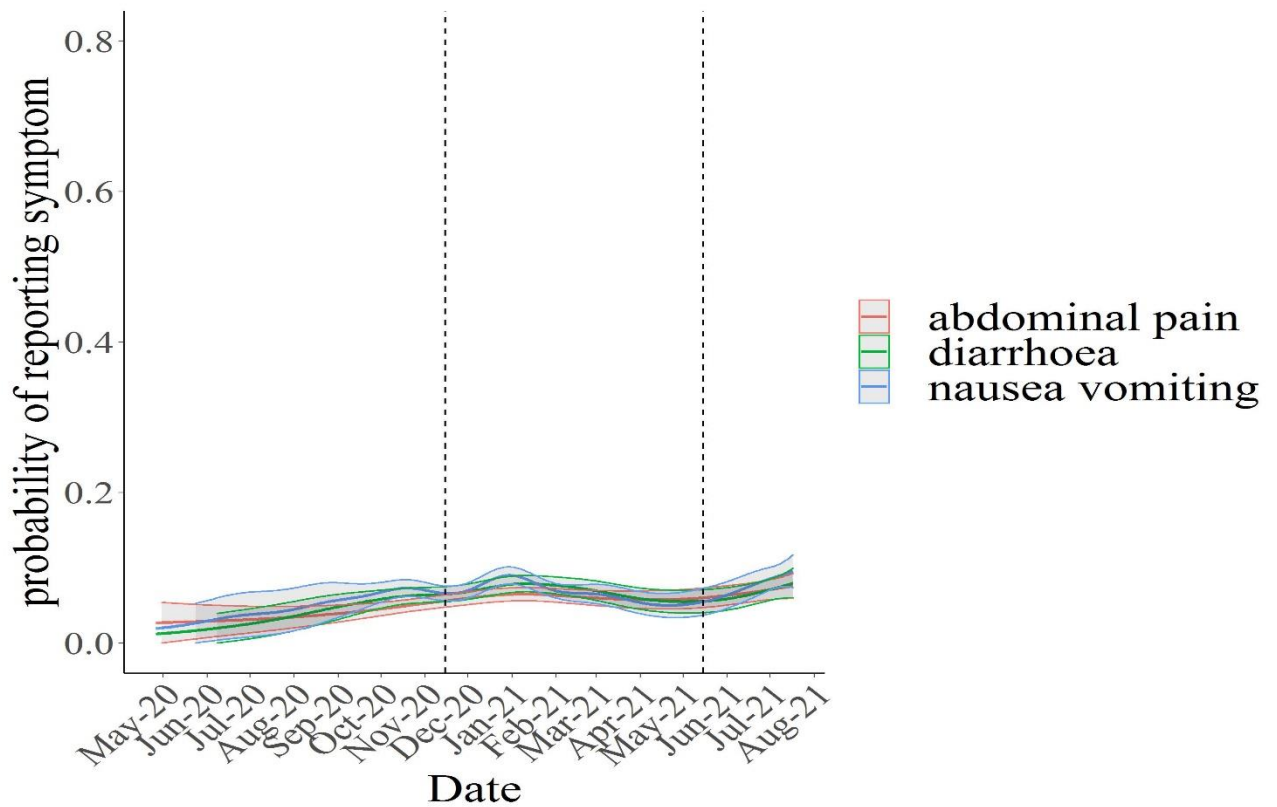


Note: question on fatigue is asked as “Weakness/tiredness”.

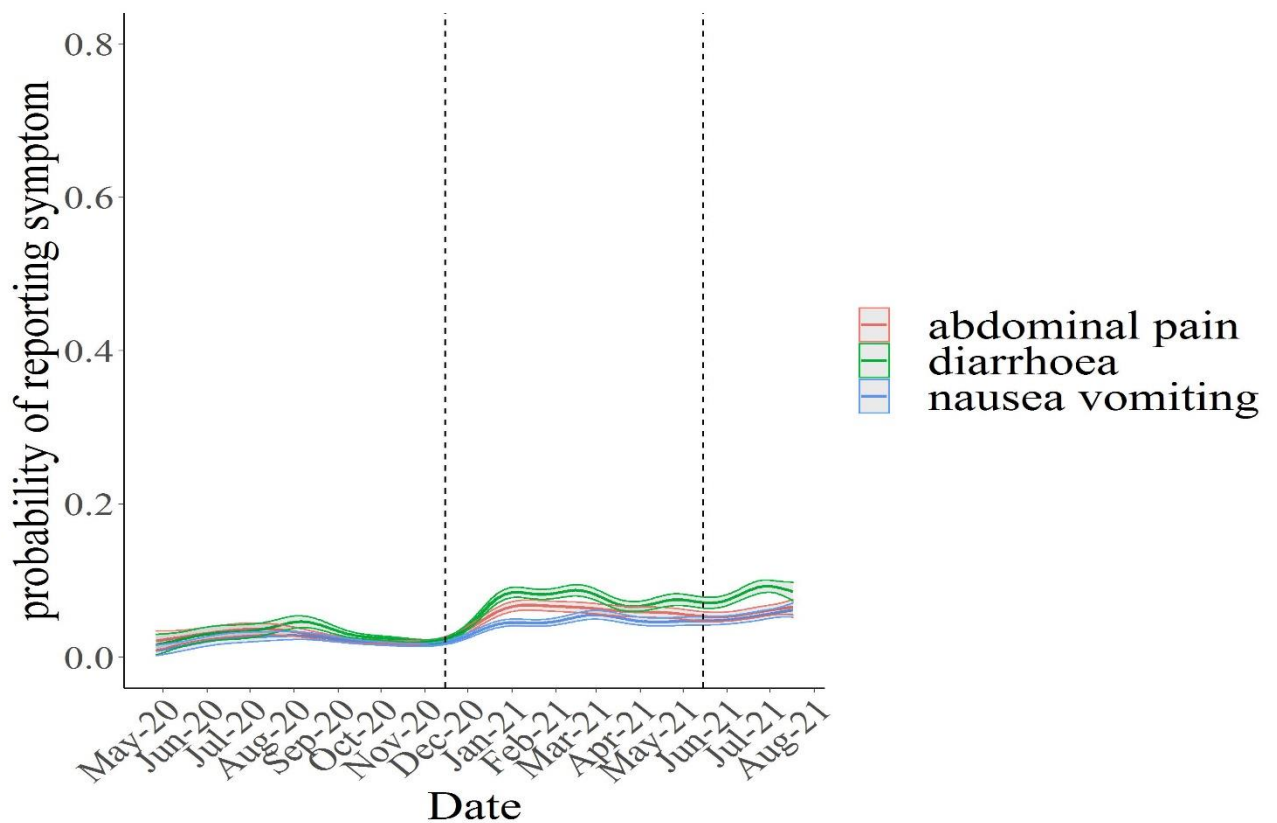
Percentage of negatives reporting any symptom who report other specific symptoms over time



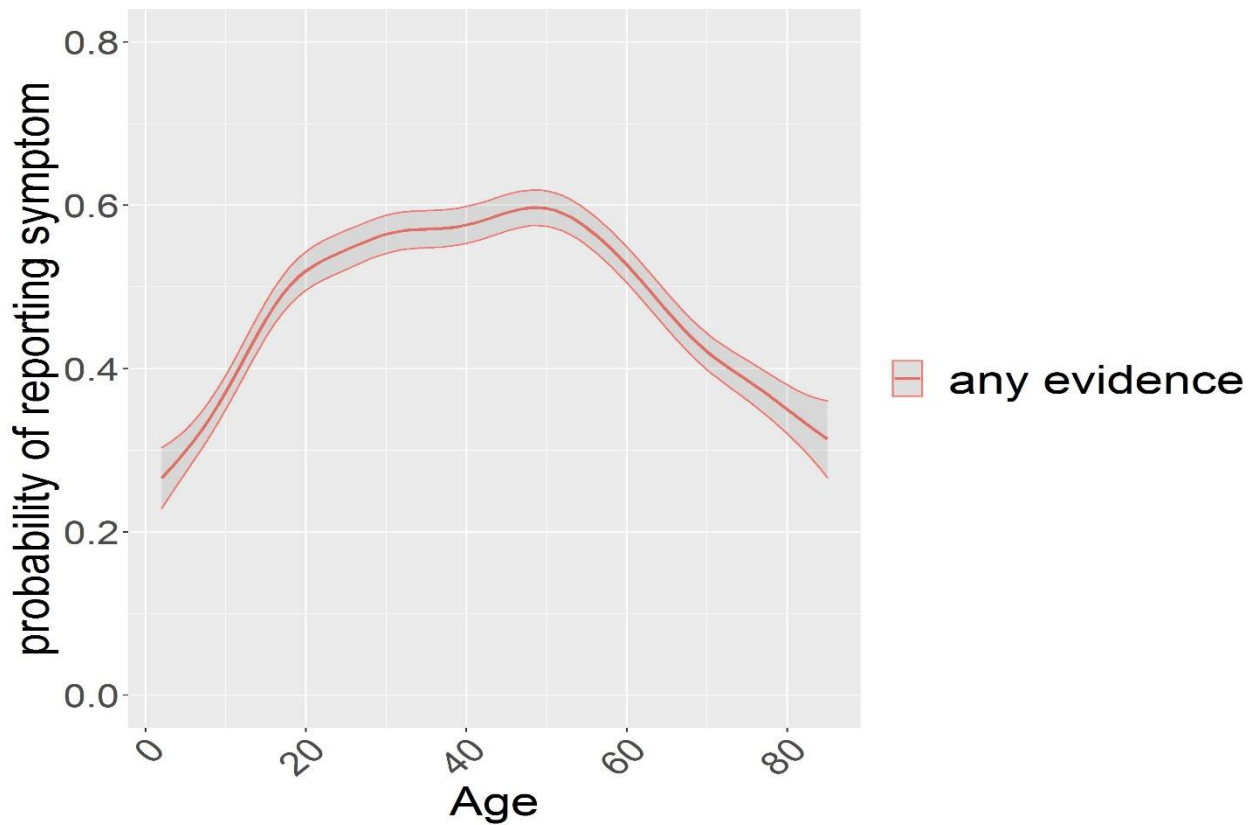
Percentage of positives reporting any symptom who report specific gastrointestinal symptoms



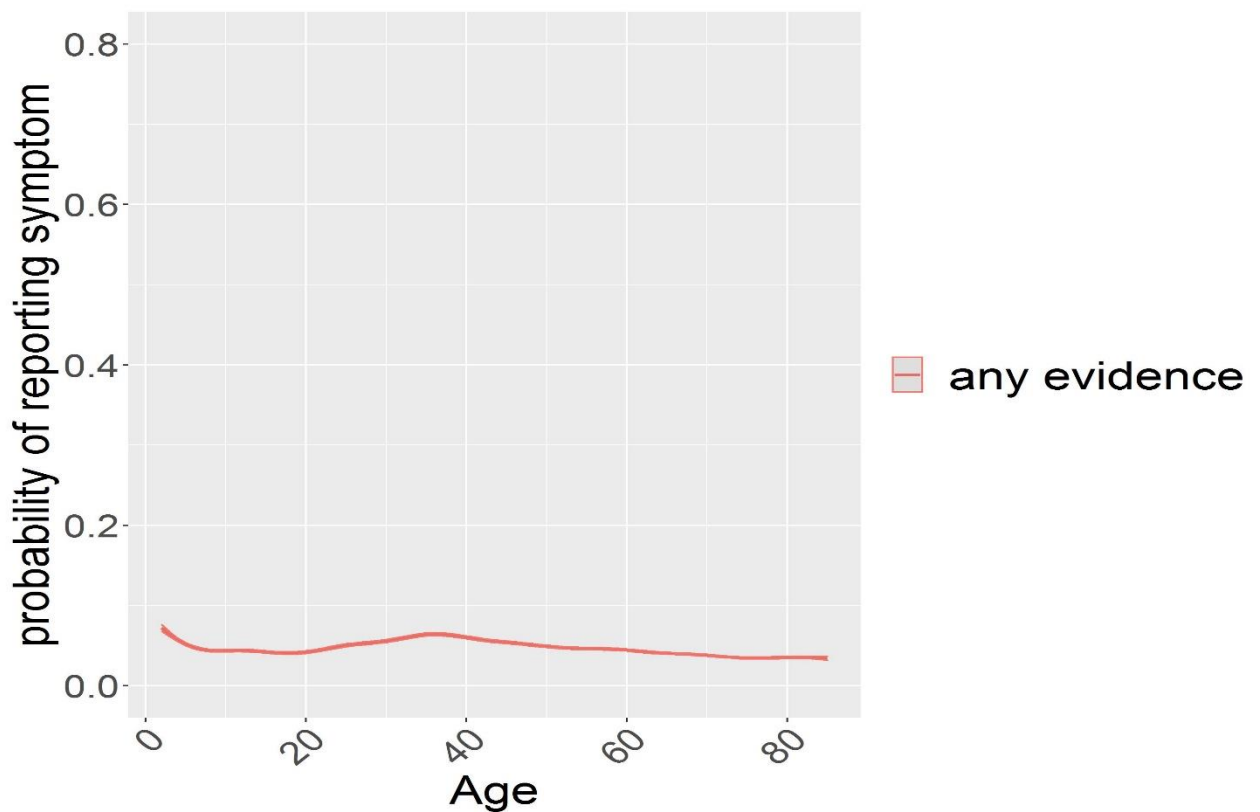
Percentage of negatives reporting any symptom who report specific gastrointestinal symptoms



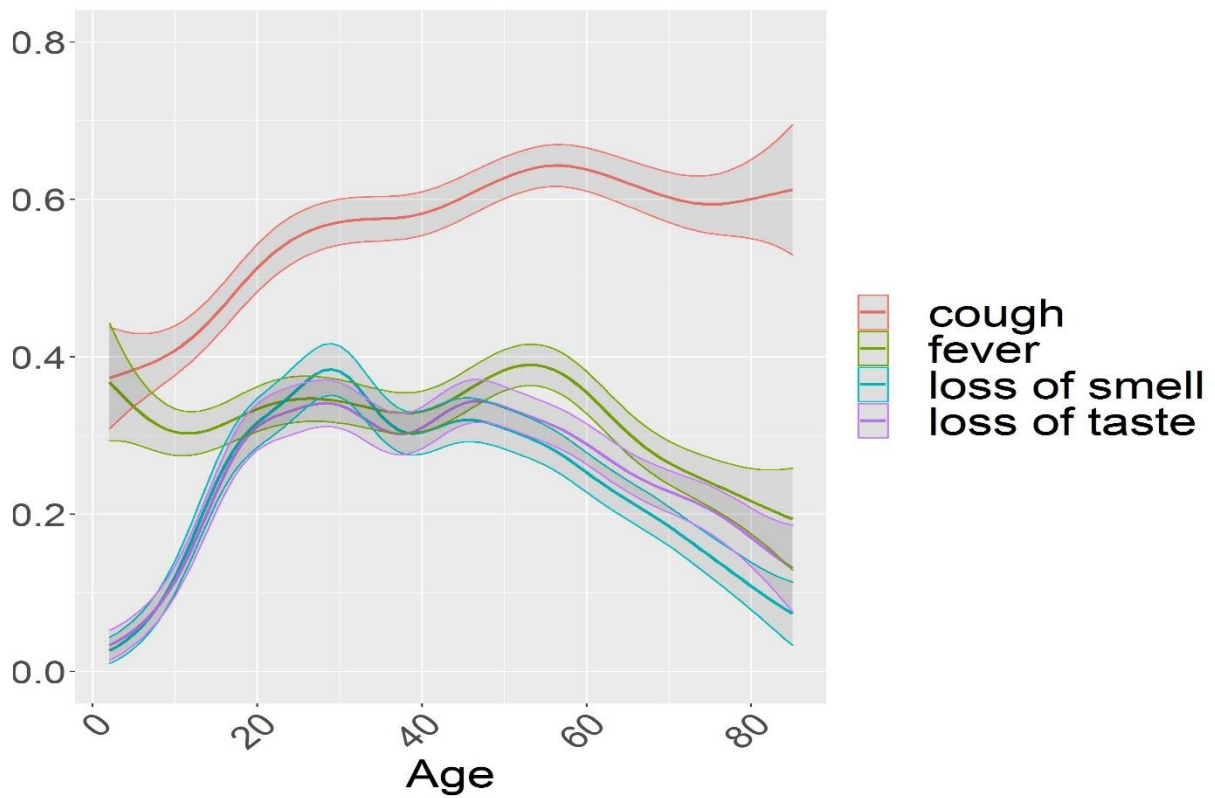
Percentage of new **positive** cases reporting any symptoms over age



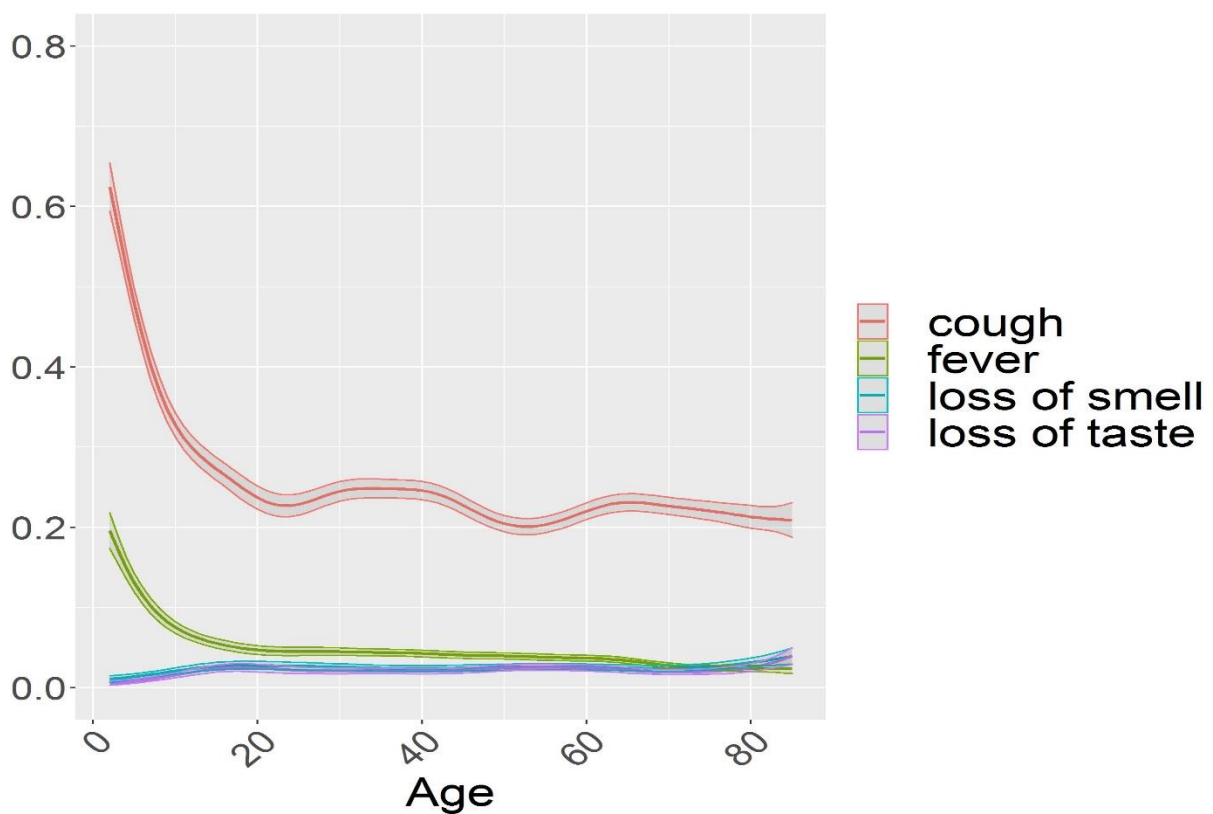
Percentage of comparator negative test visits reporting any symptoms over age



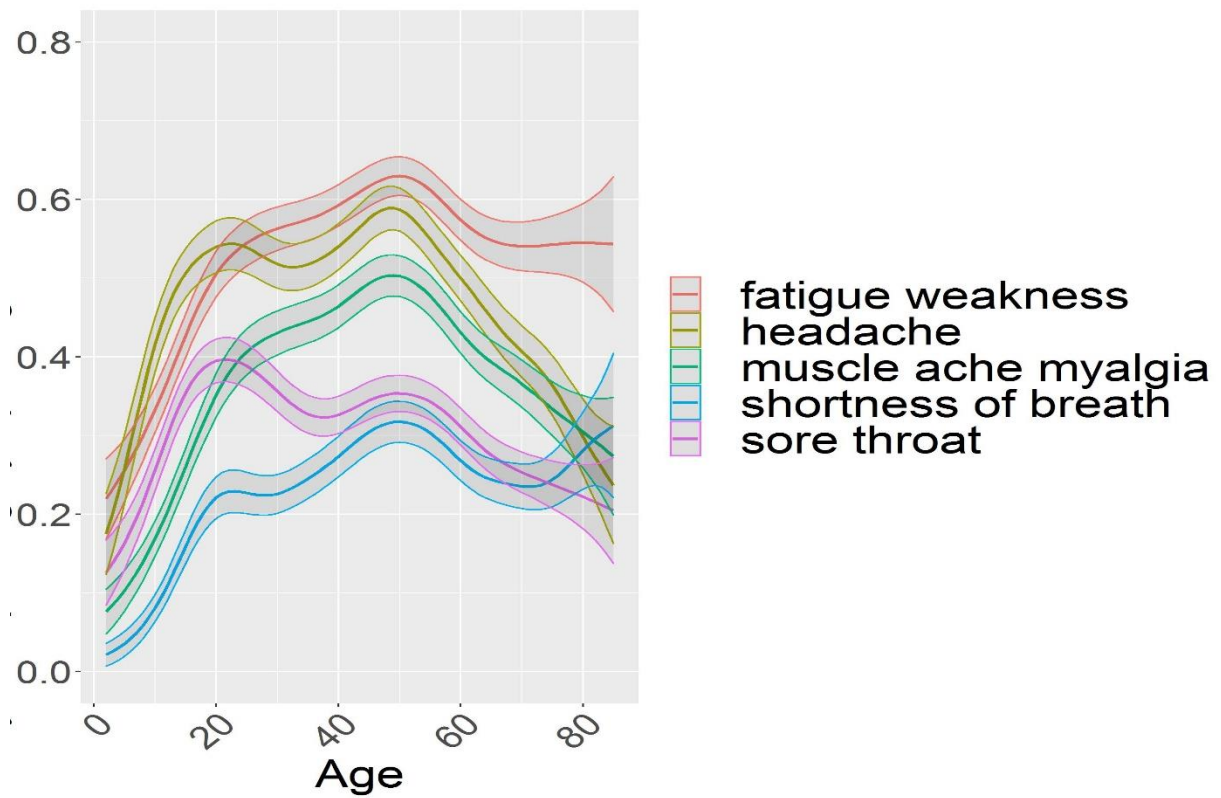
Percentage of positives reporting any symptom who report specific classic symptoms over age



Percentage of negatives reporting any symptom who report specific classic symptoms over age

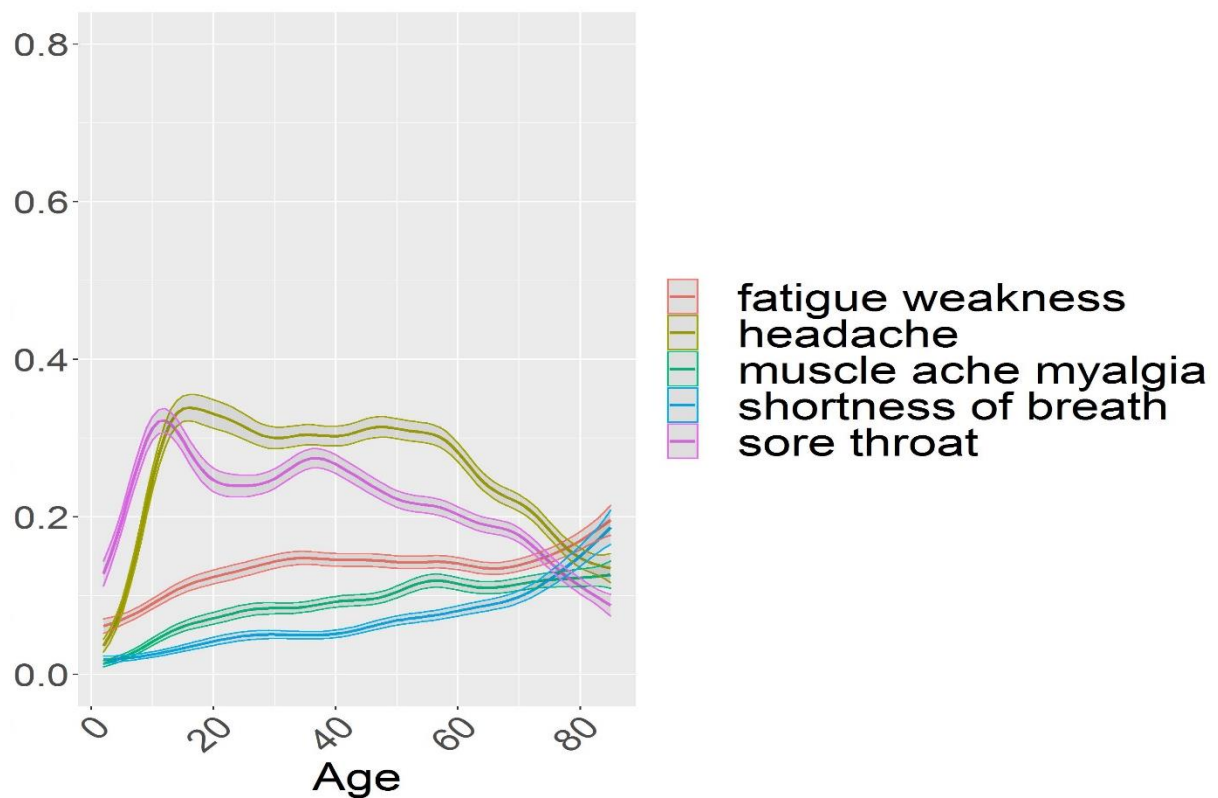


Percentage of positives reporting any symptom who report other specific symptoms over age

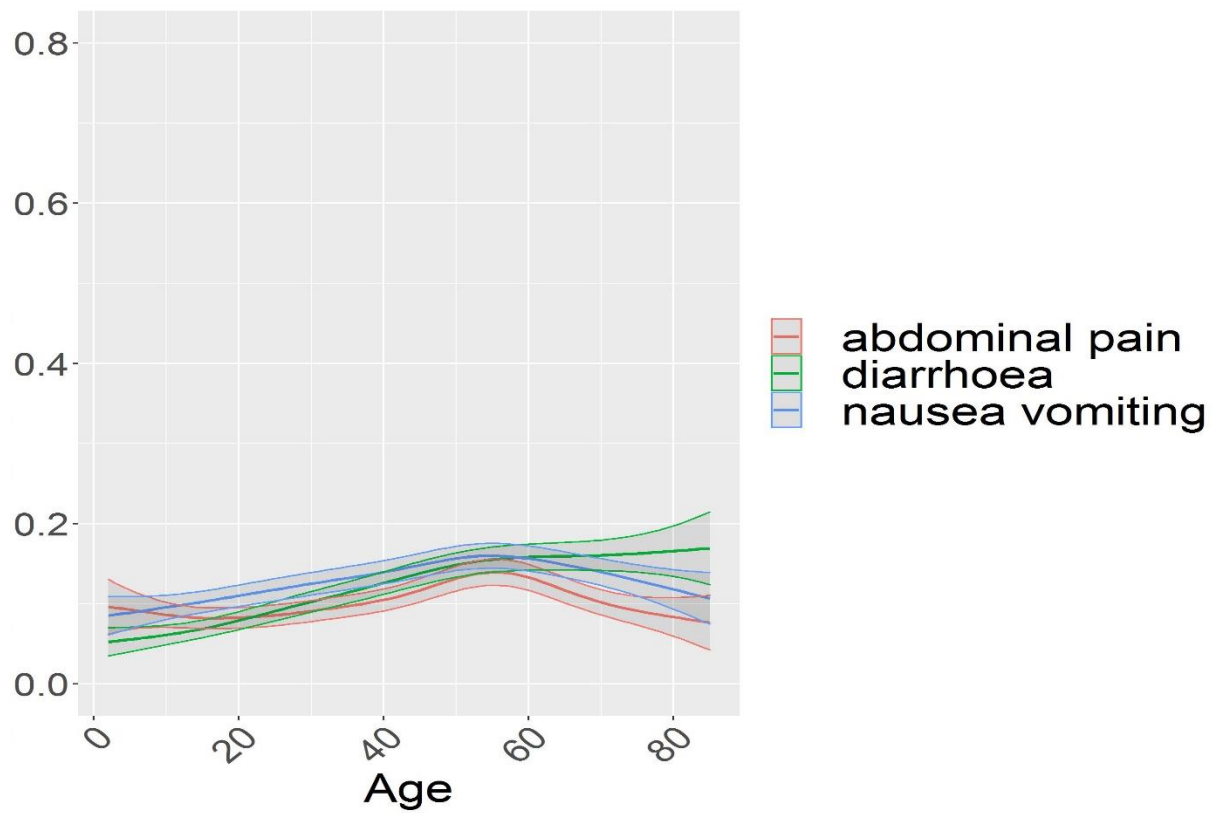


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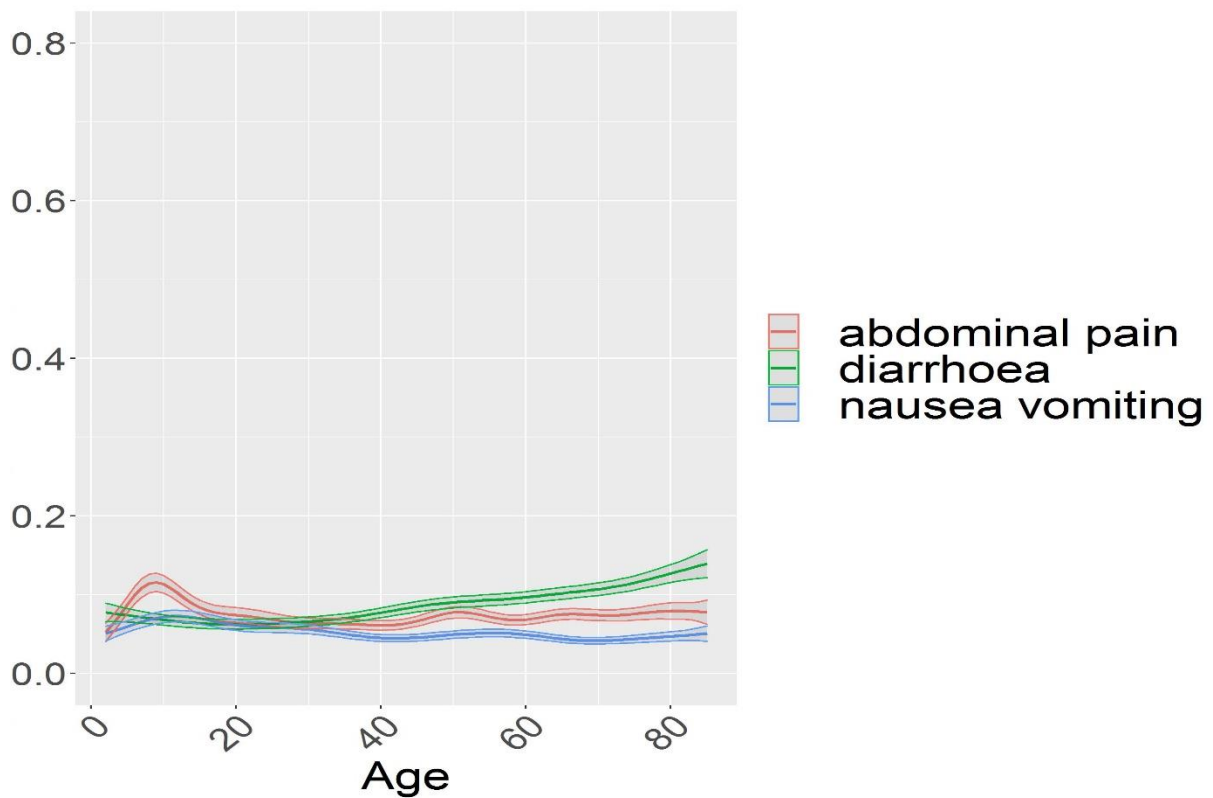
Percentage of negatives reporting any symptom who report other specific symptoms over age



Percentage of positives reporting any symptom who report specific gastrointestinal symptoms



Percentage of negatives reporting any symptom who report specific gastrointestinal symptoms



Additional information on Methods

We used flexible generalised additive models to model how percentages reporting any or specific symptoms changed over calendar time.

Positive cases

We included in analyses the first positive test in each 'positive episode', (arbitrarily) defined as a new positive >120 days after an index positive with the preceding test being negative, or a new positive after 4 consecutive negative tests. Presence or absence of specific symptoms and any self-reported symptoms overall (i.e. including the generic symptoms question) included reports at any (test positive or negative or failed) visit within [0,+35] days of the first positive per episode (i.e. spanning [-7,+35] days given the question timeframe (over the last 7 days)).

Negative cases

As a comparator group, we initially included all visits where PCR tests were negative, and then excluded visits where symptoms could plausibly be related to ongoing effects of long COVID, short-term effects of vaccination or where there was a high pre-test probability that the participant actually had a new COVID-19 infection that had not been detected in the survey. Specifically we excluded all negative visits:

1. **From -90 days before** the first antibody positive test in the study prior to vaccination, where antibody results are likely to represent previous undetected infection;
2. **From -35 days before** the first positive onwards from individuals who ever tested PCR positive in the study or in the linked English testing programme (to avoid ongoing long COVID symptoms, and symptoms shortly before the positive test);
3. **From -35 days before** any self-reported positive swab test result onwards (for the same reason; reflecting the fact that individuals may have obtained tests elsewhere);
4. From a small number of individuals who reported either loss of taste or loss of smell at their first study visit and had no national testing programme result within [-21,+21] days (all before 1 July 2020), given the high specificity of this symptom for COVID-19 infection, the fact that it would have been impossible for these individuals to get an external test and the potential for subsequent symptoms to represent long COVID;
5. Where participants reported self-isolating OR contact with **definite** positives in the preceding 28 days (since these individuals have much higher risk of SARS-CoV-2 infection which may not have been detected) and the **previous and the next visit** (because of higher risk of unidentified positivity, and because they may have been contact traced through the national testing programme they may be more likely to report symptoms through recall bias, regardless of status);
6. Occurring within [-7,+14 days] of either first or second vaccination date, to avoid the inclusion of common symptoms caused by vaccination in the test-negative comparator group and to reflect the possibility of small inaccuracies in reported date of vaccination for some participants

Plots

These are presented at a reference category of 1 January 2021, white, male, aged 45 years.