Virus Watch

Findings so far

Symptoms by COVID-19 swab result and UK variant hotspot status.

This paper describes in further detail the methods and a-priori analysis plan behind results presented publicly by the Virus Watch study using data up to 25 January 2021.

We aimed to explore the symptom profile of confirmed COVID-19 illnesses, and to determine which symptoms may be most sensitive for identifying COVID-19 illnesses. We also wanted to explore differences in symptom profiles amongst COVID-19 illnesses by age.

Finally, we wanted to explore differences in symptom profiles caused by novel coronavirus variants of concern. The proportion of infections caused by the new variant of SARS-CoV-2 (B.1.1.7), which originated in Kent, is increasing across the U.K.. London, South East and parts of East of England, as well as Wales were initially most affected, and London and South East entered Tier 4 restrictions in December. However the new variant has spread rapidly across the country, and following substantial growth in cases and hospital admissions, a national lockdown has been imposed. An increase in transmissibility (estimated ~70%) has been demonstrated for the new variant, and lower cycle threshold (Ct) values, indicating a higher viral load in infected patients, have been observed; more recent data also suggests a potentially higher mortality rate. It remains unknown whether the symptom profile for the new U.K. variant differs from other circulating strains.

Research Questions:

1. What are the frequencies of different symptoms and symptom groupings by self-reported COVID-19 swab- positive and negative illnesses and do these vary by age group?

2. Do symptom frequencies vary between self-reported COVID-19 swab-positive and negative illnesses?

3. Do symptom frequencies within self-reported COVID-19 swab-positive illnesses vary in regions and times with high prevalence of the new UK variant of concern, compared with regions/times with lower prevalence?

Methods:

Study design and data collection

The Virus Watch study is an online, prospective, community cohort study following up entire households in England and Wales during the COVID-19 pandemic. As of 25th January 2021, 22,488 households and 45,861 people across England and Wales have joined the study. Within this larger cohort there is a nested laboratory cohort of approximately 10,000 participants who have recently started swabbing during episodes of illnesses. The analyses described here are based on the overall cohort and do not include swabs taken as part of this study as this aspect of the study has only just begun. The overall study methods have been described in detail elsewhere. In brief, after registering with the study, Virus Watch participants completed baseline surveys where detailed demographic, socio-economic and health data was collected for each household member. Participants were then asked to prospectively complete detailed daily symptom diaries recording the presence and severity of any symptoms of acute respiratory and gastrointestinal infections during periods of illness. At the end of each week participants were emailed links to a weekly survey where they reported any symptoms from that previous week as well as the dates and outcomes of any COVID-19 swabbing conducted outside of the Virus Watch study (e.g. as part of NHS Test and Trace, work-based testing schemes, other research studies, etc).

Outcome

Symptom data were gathered through the weekly survey and grouped into illness episodes. The start date of an illness episode was defined as the first day any

symptoms were reported, and the end date was the final day of reported symptoms. A 7-day washout period where no symptoms were reported was used to define the end of one illness episode and the start of a new illness episode. The data presented in this analysis includes illnesses which began between the start of the study through 10 Jan 2021. It is likely that some illnesses reported in the final weeks, and particularly the last week of data, may not have resolved yet and therefore our data will only represent the initial stages of those illnesses.

Within illness episodes, we investigated the following symptoms and symptom groupings:

- Case definition – this symptom group reflects the NHS Test and Trace criteria for someone with COVID-like symptoms. A person meets this case definition if they report one or more of the following: cough, measured fever or feeling feverish, loss of, or change to, sense of smell or taste.
- Cough - this includes any type of cough, including dry and productive.
- Fever - this includes a high temperature (≥37.8C) as measured by a thermometer, and/or 'feeling feverish'.
- Smell / taste - either a loss of, or change to, sense of smell or taste.
- Nose / throat - this includes sneezing, runny nose, blocked nose, sore throat, swollen tonsils, and sinus pain.
- Respiratory - this includes cough, loss of, or change to sense of smell or taste, wheezing, shortness of breath, chest pain on breathing, and the nose and throat symptoms listed above.
- GI - this means gastrointestinal symptoms, and includes nausea, vomiting, and diarrhoea.
- Eye - this includes red, painful, and sticky eyes, and deterioration of vision.

Exposures

SARS-CoV-2 swab test result

Throughout the study, participants reporting symptoms in the previous week were also asked to report the outcome of any NHS COVID-19 swab test for that illness. From the week commencing 28 September 2020, participants could also report the results of any swab testing in the previous week, regardless of whether they were also reporting symptoms for that week. This was to ensure that all swab test results could be reported regardless of when the test results arrived or whether the swab was taken asymptomatically.

To differentiate COVID-19 from non-COVID-19 illnesses, we matched illness episodes and self-reported swab test results that were within 1-2 weeks of each other. Matching was undertaken in a stepwise manner, for both symptomatic swabbing and asymptomatic swabbing, on a week-by-week basis, based on the likely sequence of symptoms and swab positivity. First, all available swab test results were matched to illnesses occurring in the same week as receipt of the swab result. Following that, any symptomatic test results that had not yet been linked to an illness, were sequentially matched to illness episodes that had finished in the week prior (-1 week), then finished two weeks prior (-2 weeks), and then commenced in the following week (+1 week). Asymptomatic test results were sequentially matched to an illness episode that had commenced in the following week (+1 week), then finished in the week prior (-1 week), then finished two weeks prior (-2 weeks). Illnesses commencing 2 weeks after a swab result were not matched as these were considered unlikely to be related. For each round of the sequential matching, only test results not yet matched to an illness were used.

Some illness episodes continued for several weeks, and the associated swab test may have been completed any time during the episode, or shortly before or after it. If more than one swab test result matched to an illness episode, any positive swab test result superseded any negative swab test result. Any illness episode matching to a positive swab result was taken to be a confirmed COVID-19 illness. Any illness episode matching to negative swab test results only, was taken to be a non-COVID-19 illness. Illness episodes not matching any swab test results, and swab test results not matching to any illness episodes, were not included in these analyses.

UK variant hotspots

A classification system was developed for English regions, based on week, to determine the likely hotspots for the U.K. variant that emerged in Kent (B.1.1.7).

To determine time and place 'hotspots' of the new U.K. variant of concern, we referred to region-level data from PHE (published 14th of January). The data is based on a proxy indicator for the new UK variant of concern, known as Spike-gene target failure (SGTF) which can be picked up on most PCR assays used in Pillar 2 testing.

Hotspots were defined as weeks in a particular region when SGTF was observed in >50% of PCR tests, starting from the week when SGTF % had already exceeded 50% at the beginning of the week, rather than the week during which it first crossed 50%.

The week cut-off was determined visually and verified by two independent researchers, based on graphs published by PHE.

'Hotspots' remain so from the first week they are classified as such, and do not revert to non-hotspots, as we assume the variant prevalence to be rising in all areas, and not falling in any areas.

Covariates

Age - this was taken as the participant's age on entry to the study. Ages in years were grouped into the following categories: 0-15, 16-24, 25-44, 45-64, and 65+ years.

Region - this was determined using the household's postcode as per the baseline survey.

Week - for both swab results and symptoms, this was taken as the week prior to the survey week as respondents' answers to the weekly surveys pertain to the preceding 7 days.

Statistical Analysis:

We calculated the proportion and 95% confidence interval of COVID-19 swab test positive and swab test negative illnesses reporting each symptom and symptom grouping at some point during their illness. We then stratified these calculations by age group.

We also calculated the proportion and 95% confidence interval of COVID-19 positive illnesses where each symptom and symptom group were reported, stratified by new variant hotspot vs. non-hotspot (as described above). This analysis excluded 19 COVID-19 illnesses from Wales because of a lack of data needed to determine hotspot timing in Wales.