Symptom profiles and accuracy of clinical definitions for COVID-19 in the community. Results of the Virus Watch community cohort.

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NOTE: This preprint reports new research that has not been certified by peer review and should not be used to guide clinical practice.
Abstract

**Background:** Understanding the symptomatology and accuracy of clinical case definitions for COVID-19 in the community is important for the initiation of Test, Trace and Isolate (TTI) and may, in future, be important for early prescription of antivirals.

**Methods:** Virus Watch is a large community cohort with prospective daily recording of a wide range of symptoms and self-reporting of swab results (mainly undertaken through the UK TTI System). We compared frequency, severity, timing, and duration of symptoms in test positive and test negative cases. We compared the test performance of the current UK case definition used by TTI (any one of: new continuous cough, high temperature or loss of or change in sense of smell or taste) with a wider definition that also included muscle aches or chills or headache or loss of appetite.

**Findings:** We included results from 8213 swabbed illnesses, 944 of which tested positive for COVID-19. All symptoms were more common in swab positive than swab negative illnesses and symptoms were also more severe and of longer duration. Common symptoms such as cough, headache, fatigue, muscle aches and loss of appetite occurred early in the course of illness but were also very common in test-negative illnesses. Rarer symptoms such as fever or loss or altered sense of smell or taste were often not present but were markedly more common in swab positive compared to swab negative cases. The current UK definition had a sensitivity and specificity of 81% and 47% respectively for symptomatic COVID-19 compared to 93% and 26% for the broader definition. On average cases met the broader case definition one day earlier than current definition. 1.7-fold more illnesses met the broader definition than the current case definition.

**Interpretation:** COVID-19 is difficult to distinguish from other respiratory infections and common ailments on the basis of symptoms. Broadening the list of symptoms used to encourage engagement with TTI could moderately increase the number of infections identified and shorten delays but with a large increase in the number of tests needed and in the number of people and contacts who do not have COVID-19 but might need to self-isolate whilst awaiting results.
Introduction

The natural history of COVID-19 infection can range from asymptomatic infection in around 25% of infections\(^1\) to severe or fatal disease at a rate that is highly age dependent\(^2\). Understanding the natural history of symptomatic COVID-19 in the community is critical to the control of infection because it informs decisions about who should seek testing, whether those with symptoms should self-isolate and whether those in contact with symptomatic people should self-isolate. Understanding the normal course of symptoms is also potentially helpful to patients and clinicians assessing whether care needs to be escalated due to unexpectedly severe or prolonged symptoms. In future, symptom profiles may also trigger early use of antivirals to prevent deterioration and potentially to minimise transmission\(^3\). Finally understanding symptom profiles is important to inform syndromic surveillance.

A wide range of clinical case definitions for COVID-19 are available utilising different combinations of symptoms to alert individuals to the need for testing, isolation and contact tracing. For example, WHO include the following symptoms in the clinical case definition of a suspected case - Acute onset of fever AND cough; OR Acute onset of ANY THREE OR MORE of the following signs or symptoms: Fever, cough, general weakness/fatigue, headache, myalgia, sore throat, coryza, dyspnorea, anorexia/nausea/vomiting, diarrhoea, altered mental status\(^4\). European Centers for Disease Control define a possible case based on - at least one of Cough, Fever, Shortness of breath or sudden loss of sudden onset of anosmia, ageusia or dysgeusia\(^4\); and US Centers for Disease Control use the following clinical criteria - at least two of fever (measured or subjective), chills, rigors, myalgia, headache, sore throat, new olfactory and taste disorder(s) OR at least one of fever (measured or subjective), chills, rigors, myalgia, headache, sore throat, new olfactory and taste disorder(s)\(^5\).

In the UK, the Test Trace and Isolate Community testing programme (TTI) asks individuals to seek testing if they have any of the following symptoms - a new continuous cough, a high temperature, loss of or altered sense of smell or taste\(^6\).

Although it is clear that addition of further symptoms could increase sensitivity, this is at the cost of a loss of specificity and increasing numbers of people who require testing, isolation and contact tracing\(^7\).
For example, recent analysis of data from the REACT community survey suggests that adding 
in loss of appetite, chills, headache or muscle aches could increase the proportion of cases 
identified from 53% to 75% but at the cost of a 2.7 fold increase in required testing capacity\(^8\).  
Altering clinical case definitions will have different implications at different disease prevalences, 
since positive and negative predictive values of tests depend on disease prevalence as well as 
sensitivity and specificity.  The timing within the course of an illness at which infected people 
meet the case definition is important since early isolation of cases and contacts reduces 
transmission.

Prospective community studies where participants record symptoms in near real time are 
needed to accurately measure COVID-19 symptom profiles with minimal recall bias.  Here we 
describe prospectively recorded symptom profiles (frequency, severity and duration) of illnesses 
that tested positive for COVID-19 and illnesses that tested negative within a large community 
cohort study (Virus Watch).  We compare the test characteristics (Sensitivity, Specificity, 
Positive and Negative Predictive Value, timing of meeting the case definition, number of tests 
needed to identify one case) for the current UK definition and a wider definition proposed 
following analysis of the REACT study, which adds headache or chills or loss of appetite or 
muscle aches to the existing UK definition. We explore how symptom profiles and case 
definition performance vary by age and stage of the pandemic. We will also publish the dataset 
from which these analyses were conducted allowing readers to explore the implications of 
different symptom combinations on case definition performance.

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 04 May 2021, 24,296 
households and 50,699 people across England and Wales have joined the study. The full study 
protocol is published elsewhere\(^9\).

In brief, after registering with the study, Virus Watch participants completed baseline surveys 
and 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 any illness occurring during follow up. 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 (mainly as part of TTI). Within the main cohort there is a nested laboratory sub-cohort of 10,766 participants who have additionally provided study-specific swab specimens tested using COVID-19 PCR from the end of December 2020 onwards.

Symptom data gathered through the weekly survey were grouped into illness episodes and matched to swab results (see appendix for further details). 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 02 May 2021. Within illness episodes, we investigated a wide range of individual symptoms (see appendix for further definition of symptoms collected) and the following symptom groupings: UK Case definition – one or more of the following: cough, measured fever or feeling feverish, loss of, or change to, sense of smell or taste. Broader case definition - one or more of the following: cough, measured fever or feeling feverish, loss of, or change to, sense of smell or taste, headache, muscle aches, loss of appetite or chills.

We present simple descriptive analyses of the frequency, severity and duration of symptoms in COVID-19 positive and negative illnesses. We calculate sensitivity and specificity for individual symptoms and, for the two case definitions we also calculate the positive predictive value (PPV), negative predictive value (NPV) number of people meeting the definition within the cohort and the numbers needed to test to identify one positive case (NNT).

We will provide a dataset with age group classified into broad categories and timing of illnesses and tests removed to preserve anonymity. This can be used to assess sensitivity and specificity of different symptom combinations.
Results

Overall, there were 29,083 illnesses (with at least one of the symptoms defined in supplementary Table S1) reported in the cohort. 8,213 illnesses were swabbed and of these 944 (11.5%) tested positive for COVID-19; 436 of these swabs were conducted as part of the study, including 22 positives. The percentage of swabbed illnesses testing positive were highest in young adults aged 16-24 and lowest in children aged 0-15, highest in London and lowest in the South East and South West regions and peaked in December 2020 (Table 1).

Supplementary appendix Table S2 shows the proportion of illnesses with swabs for each symptom - those with the symptoms recommended for swabbing by TTI are more likely to be swabbed than those with other symptoms.

Figure 1a shows the proportion of swabbed illnesses that reported each symptom according to whether they tested positive or negative for COVID-19. All of the wide range of reported symptoms were more common in illnesses that tested positive for COVID-19 than in other illnesses. Amongst COVID-19 positive illnesses the 10 most commonly reported symptoms in decreasing order of frequency were: fatigue, headache, cough, muscle ache, loss or change to sense of smell or taste, needing to spend extra time in bed, sore throat, difficulties in undertaking daily activities, feeling feverish and sneezing. The percentage showing each symptom by day of illness is shown in figure 1b and c illustrating both the higher frequency and longer duration of key symptoms in COVID-19 positive and negative cases.

Table S2 in the supplementary appendix shows the sensitivity and specificity of each symptom and the mean and median day of illness on which they are first reported. It can be seen that although constitutional symptoms such as headache, fatigue and muscle aches are common and occur early in the course of illness they are also a common feature of non-COVID illnesses and have low specificity.

Figure 2 and Table S3 (in the supplementary appendix) shows the maximum reported severity for a range of key symptoms in COVID-19 positive and negative illnesses. It can be seen that when symptoms do occur, they are more likely to be severe in COVID-19 illnesses than in test negative illnesses. Figure 3 shows the distribution of the duration of illnesses in COVID-19 positive and negative illnesses. It can be seen that the duration of illness is longer in COVID-19 illnesses than in other illnesses. Table S4 shows how illness duration varies by age and gender.
in COVID-19 positive and negative illnesses and Figure S1 shows the distribution of duration of illnesses among COVID-19 illnesses by age group. Illnesses tend to be of longer duration in older cases.

Table 2 shows the mean and median day of meeting the current and broader case definition, Sensitivity, Specificity, Positive predictive value (PPV), Negative predictive value (NPV) and numbers needed to test to identify a case (NNT). The numbers meeting the case definition and how many fold higher this is for the broader case definition are shown (multiplication factor). These results are stratified by age and calendar time.

Sensitivity of the current case definition (i.e. the proportion of all those illnesses testing COVID-19 positive who met the definition) was 81% compared to 93% for the broader case definition. Specificity (i.e. the proportion of all those illnesses testing COVID-19 negative who did not meet the case definition) was 47% for the current case definition and was 26% for the broader case definition. Sensitivity and specificity of both case definitions was lower in children age 0-15 than in older age groups. Sensitivity of case definitions remained stable over time. Specificity of the current UK definition appeared lower in August/September (coinciding with a large national outbreak of Rhinovirus in children). The PPV (the proportion of those meeting the clinical case definition who test positive for COVID) was 17% for the current UK case definition and 15% for the broader definition. PPV was substantially lower during August/September when disease rates were low (8% for current UK definition and 7% for the broader definition). NPV (the proportion of those with illnesses not meeting the clinical case definition who test negative for COVID-19) was 95% for the current UK case definition and 96% for the expanded case definition. The number of illnesses meeting the broader case definition was 1.7 fold higher than those meeting the current definition.

Discussion

We characterised the symptom profiles and estimated the accuracy of clinical case definitions for COVID-19 among community cases arising in a large, prospective population-based cohort study based in the UK. All symptoms asked about were more frequently reported and when present were generally more severe and longer lasting in COVID-19 positive illnesses compared to COVID-19 negative illnesses. Individually, cough and some constitutional
symptoms including headache, muscle ache and fatigue presented early in illness and had moderate sensitivity and specificity as they were common in both COVID-19 positive and COVID-19 negative illnesses. In contrast, fever and loss or change to smell or taste presented slightly later in illness and had a lower sensitivity but higher specificity as they were not as common in COVID-19 positive illnesses but were even less common in COVID-19 negative illnesses. The combination of symptoms in the current UK TTI case definition had a higher sensitivity (81%) than any individual symptom, with a specificity of 47%. Adding additional symptoms to the case definition can lead to earlier case identification and higher sensitivity but at the cost of specificity and consequently, a substantial increase in the number of illnesses eligible for testing. For example, when we compare the broader case definition to the current UK case definition, cases on average met the case definition one day earlier and there was a moderate increase in sensitivity to 93% but at a much lower specificity of 26%. It would also lead to 1.7 times more illnesses eligible for testing.

Strengths of this work include the prospective daily recording of a wide range of symptoms across a large community cohort and linkage of these to self reported swab results ascertained on a weekly basis. This should maximise the accuracy of symptom data amongst swabbed participants. Our sample is not fully representative of the population of England and Wales but includes participants in every local authority area. There is a moderate overrepresentation of those aged over 65 and an underrepresentation of those in more deprived areas. Whilst we collected information on a very wide range of symptoms testing primarily relied on that conducted through the national TTI programme meaning that those meeting the current case definition are more likely to be tested. This is likely to lead to an overestimation of the sensitivity of the current UK case definition. A further strength is that we will publish the dataset online to enable replication of analyses and for others to explore the test characteristics of various combinations of symptoms for case definitions.

COVID-19 is difficult to distinguish from other respiratory infections or common ailments on the basis of symptoms alone. Also, a high proportion of infections are asymptomatic or have a pre-symptomatic phase when transmission can occur. As such, systems to identify symptomatic cases, test them and isolate them and their contacts can only ever reduce, rather than prevent all transmission. These programmes, when part of a broader programme of Non-Pharmaceutical Interventions, can however contribute to control of infection and may be particularly effective when introduced at very low levels of infection. For example, countries that combined early and strict border controls, intensive testing and rapid introduction of lockdowns
have had substantially lower COVID-19 transmission and mortality than other countries such as the UK\textsuperscript{11}.

The success of testing and isolation programmes is dependent on public understanding and engagement. Data from behavioural surveys in England show only 51\% of participants knew the symptoms that testing is recommended for, only 18\% sought testing if they had the symptoms and only 42.5\% fully adhered to self-isolation. Engagement was lower in younger people and amongst those in financial hardship\textsuperscript{12}. Engagement with population level asymptomatic testing using lateral flow testing has also been shown to be low, particularly in socioeconomically disadvantaged areas\textsuperscript{13}.

Policy makers, considering which symptoms might prompt testing, tracing and isolation need to balance the availability of testing capacity at different stages of the pandemic, the speed with which samples can be taken and results returned, the harms incurred by asking large numbers of people who do not have COVID-19 and their contacts to self-isolate whilst awaiting test results, the consistency and simplicity of public health messaging and the likely public engagement with the system. Alteration of symptom profiles triggering testing and isolation may have less impact than other approaches to increase uptake and engagement with programmes and to ensure timely and effective contact tracing of household and non-household contacts.

The fact that COVID-19 may present as any of a very wide range of symptoms or with no symptoms at all is one of the key challenges in implementing successful TTI systems. Low levels of engagement also limit effectiveness. This emphasises the importance of not placing undue reliance on such systems as a mechanism to allow relaxation of other social distancing measures and the critical importance of protecting populations globally through immunisation.

**Ethics:**

This study has been approved by the Hampstead NHS Health Research Authority Ethics Committee. Ethics approval number - 20/HRA/2320.
Funding:

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Conflicts of interest

ACH serves on the UK New and Emerging Respiratory Virus Threats Advisory Group. AMJ was a Governor of Wellcome Trust from 2011-18 and is Chair of the Committee for Strategic Coordination for Health of the Public Research.
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## Tables and Figures

Table 1. Characteristics of illnesses by demographics and swab outcome

|                                | All illnesses | Swabbed illnesses | Swab+ illnesses |
|--------------------------------|---------------|-------------------|-----------------|
|                                | N             | % of all illnesses (column %) | N       | % of swabbed illnesses (row %) |
| Overall                        | 29083         | 100.0%            | 8213   | 11.5%           |
| **By Age Group***              |               |                   |        |                |
| 0-15                           | 4110          | 14.3%             | 1114   | 6.8%            |
| 16-24                          | 877           | 3.0%              | 300    | 18.0%           |
| 25-44                          | 6637          | 23.0%             | 2153   | 12.5%           |
| 45-64                          | 10350         | 35.9%             | 3158   | 12.0%           |
| 65+                            | 6859          | 23.8%             | 1425   | 11.4%           |
| **By Sex**                     |               |                   |        |                |
| Male                           | 9864          | 35.8%             | 2604   | 13.8%           |
| Female                         | 17713         | 64.2%             | 5197   | 9.9%            |
| **By Region***                 |               |                   |        |                |
| East Midlands                  | 2535          | 9.0%              | 787    | 11.8%           |
| East of England                | 4861          | 17.3%             | 1332   | 11.1%           |
| London                         | 4039          | 14.4%             | 1255   | 15.1%           |
| North East                     | 1505          | 5.4%              | 368    | 11.7%           |
| North West                     | 3225          | 11.5%             | 981    | 13.4%           |
| South East                     | 5394          | 19.2%             | 1520   | 7.8%            |
| South West                     | 2281          | 8.1%              | 529    | 9.3%            |
| Wales                          | 746           | 2.7%              | 165    | 11.5%           |
| West Midlands                  | 1793          | 6.4%              | 521    | 10.6%           |
| Yorkshire and The Humber       | 1661          | 5.9%              | 470    | 12.6%           |
| **By Month**                   |               |                   |        |                |
| Jun-Aug                        | 1871          | 6.4%              | 203    | 2.5%            |
| Sep                            | 5646          | 19.4%             | 694    | 7.5%            |
| Oct                            | 3897          | 13.4%             | 876    | 12.0%           |
| Nov                            | 3412          | 11.7%             | 968    | 12.4%           |
| Dec                            | 4164          | 14.3%             | 1647   | 21.6%           |
| Jan                            | 2866          | 9.9%              | 1239   | 17.4%           |
| Feb                            | 2499          | 8.6%              | 809    | 6.7%            |
| Mar                            | 2740          | 9.4%              | 979    | 3.0%            |
| Apr                            | 1902          | 6.5%              | 773    | 1.2%            |
| May                            | 86            | 0.3%              | 25     | 0.0%            |

* Age missing for 250 illnesses  
** Sex missing for 1506 illnesses  
*** Region missing for 1043 illnesses
Figure 1. COVID symptoms. a, Self-reported symptoms by swab-confirmed COVID positive and COVID-illnesses. b-c, Proportion of COVID+ve illnesses (b) and COVID-ve illnesses (c) experiencing symptoms on a given day of illness within the first three week of illness. Day 1 represents the onset of symptoms.
Figure 2. Severity of symptoms among swab-confirmed COVID positive and negative illnesses reporting the symptom.
Figure 3. Distribution of illness duration by COVID swab status
Table 2. Speed of identifying cases, proportion of all community illnesses requiring testing and test characteristics for the current and proposed UK Test and Trace case definitions

| Case Definition | Strata          | Onset Mean | Onset Median | Sensitivity | Specificity | PPV* | NPV* | NNT* | N illnesses eligible for testing | Multiplication factor |
|-----------------|-----------------|------------|--------------|-------------|-------------|------|------|------|---------------------------------|-----------------------|
| Current Case Definition | Overall         | Overall    | 3.315        | 1           | 81%         | 47%  | 17%  | 95%  | 5.8                             | 1.00                  |
|                  | by age group    | 0-15       | 2.435        | 1           | 61%         | 28%  | 6%   | 91%  | 16.9                            | 1.00                  |
|                  |                 | 16-44      | 3.079        | 1           | 83%         | 47%  | 20%  | 95%  | 5.0                             | 1.00                  |
|                  |                 | 45-64      | 3.458        | 1           | 82%         | 52%  | 20%  | 95%  | 5.0                             | 1.00                  |
|                  |                 | 65+        | 3.171        | 1           | 81%         | 50%  | 19%  | 95%  | 5.3                             | 1.00                  |
|                  | by time period  | Aug-Sep    | 3.81         | 1           | 80%         | 29%  | 8%   | 95%  | 13.2                            | 2258                  |
|                  |                 | Oct-Nov    | 2.783        | 1           | 84%         | 41%  | 18%  | 94%  | 5.6                             | 2434                  |
|                  |                 | Dec-Jan    | 2.612        | 1           | 82%         | 46%  | 28%  | 91%  | 3.5                             | 2781                  |
| Proposed Case Definition | Overall         | Overall    | 2.312        | 1           | 93%         | 26%  | 15%  | 96%  | 6.7                             | 1.69                  |
|                  | by age group    | 0-15       | 2.179        | 1           | 81%         | 21%  | 7%   | 94%  | 14.2                            | 1.963                 |
|                  |                 | 16-44      | 2.305        | 1           | 93%         | 26%  | 17%  | 96%  | 6.0                             | 4552                  |
|                  |                 | 45-64      | 1.988        | 1           | 94%         | 26%  | 16%  | 97%  | 6.3                             | 6482                  |
|                  |                 | 65+        | 2.413        | 1           | 95%         | 29%  | 16%  | 97%  | 6.2                             | 4002                  |
|                  | by time period  | Aug-Sep    | 2.583        | 1           | 89%         | 17%  | 7%   | 96%  | 14.0                            | 3686                  |
|                  |                 | Oct-Nov    | 2.474        | 1           | 94%         | 21%  | 15%  | 96%  | 6.5                             | 4144                  |
|                  |                 | Dec-Jan    | 1.888        | 1           | 94%         | 27%  | 25%  | 94%  | 4.0                             | 4267                  |

* PPV and NPV calculated at a study COVID prevalence of 12.2%
