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Covid-19: Study reveals six clusters of symptoms that could be used as a clinical prediction tool

Jacqui Wise

An analysis of data obtained from a symptom tracker app has shown that there are six distinct "types" of covid-19, each distinguished by a cluster of symptoms. The researchers said that these types could be used to predict the need for respiratory support in severe covid-19.

The study is available online as a preprint and has been submitted to a scientific journal for rapid peer review and publication.[1]

The Covid Symptom Study app was developed by King's College London in conjunction with the health technology company ZOE and has more than 4 million users.

Users of the app are asked to log their health and any new potential symptoms of covid-19 daily. A machine learning algorithm analysed data from a subset of 1653 users of the app in the UK and US with confirmed covid-19 who had regularly logged their symptoms in March and April. Of the sample, 383 reported at least one hospital visit and 107 reported respiratory support.

The algorithm revealed six distinct groupings of symptoms. This was then tested by running it on a second independent dataset of 1000 users in the UK, US, and Sweden who had logged their symptoms in May. The six clusters are:

- "Flu-like" with no fever—headache, loss of smell, muscle pains, cough, sore throat, chest pain, no fever
- "Flu-like" with fever—headache, loss of smell, cough, sore throat, hoarseness, fever, loss of appetite
- Gastrointestinal—headache, loss of smell, loss of appetite, diarrhoea, sore throat, chest pain, no cough
- Severe level one, fatigue—headache, loss of smell, cough, fever, hoarseness, chest pain, fatigue
- Severe level two, confusion—headache, loss of smell, loss of appetite, cough, fever, hoarseness, sore throat, chest pain, fatigue, confusion, muscle pain
- Severe level three, abdominal and respiratory—headache, loss of smell, loss of appetite, cough, fever, hoarseness, sore throat, chest pain, fatigue, confusion, muscle pain, shortness of breath, diarrhoea, abdominal pain.

The researchers found that 1.5% of people in cluster 1 and 4.4% of people in cluster 2 required respiratory support. Cluster 3 has stronger gastrointestinal symptoms and a need for respiratory support in 3.7%. The associated rate of hospital visits, however, was high in cluster 3 (23.6%) compared with clusters 1 and 2 (16.0% and 17.5%). Clusters 4, 5, and 6 included participants reporting more severe symptoms of covid-19 with 8.6%, 9.9%, and 19.8% requiring respiratory support, respectively. Nearly half of the patients in cluster 6 ended up in hospital (45%), compared with just 16% of those in cluster 1.

The study found that people with cluster 4, 5, or 6 symptoms tended to be older and frailer and were more likely to be overweight and have pre-existing conditions such as diabetes or lung disease than those with type 1, 2, or 3 symptoms.

The researchers then developed a model combining information about age, sex, body mass index and pre-existing conditions together with symptoms gathered over the first five days of onset of the illness. This was able to predict which cluster a patient fell into and their risk of needing hospitalisation and breathing support.

Most people who need respiratory support come to hospital around 13 days after their first symptoms, so the researchers said this extra eight days was a significant "early warning" of those most likely to need intensive care.

Claire Steves, consultant geriatrician and a member of the team working on the study, said, "If you can predict who these people are at day five, you have time to give them support and early interventions such as monitoring blood oxygen and sugar levels and ensuring they are properly hydrated—simple care that could be given at home, preventing hospitalisations and saving lives."

Tim Spector, the study lead, said: "Data is our most powerful tool against covid-19. We urge everyone to get in the habit of using the app daily to log their health over the coming months, helping us to stay ahead of any local hotspots or a second wave of infections."

One limitation of the study is that it relied on self-reported information collected from people who used smartphone devices. Additionally, some individuals might have become too unwell to record their symptoms

later in the disease course, so it may not have accounted fully for the peak of the disease. To tackle this limitation, reporting by proxy was included on the app in late April 2020.

The Covid Symptom Study has now identified skin rash as a key symptom of covid-19 in up to one in 10 cases. But it was not recognised as a symptom at the time of analysis so it is not currently known how skin rashes map onto the six clusters.

1 Sudre C, Lee K, Lochlainn M, et al. Symptom clusters in covid19: a potential clinical prediction tool from the COVID Symptom study app. MedRxiv 2020.06.12.20129056 [Preprint]. https://www.medrxiv.org/content/10.1101/2020.06.12.20129056v1.