Through analysing new data collected through an app, **Professor Sebastien Ourselin** and colleagues have gained new insights into COVID-19 symptoms.

A s the story of the COVID-19 pandemic continues to unfold, the science and research around the virus, its spread and symptoms is also accelerating at an unprecedented pace. All sorts of new lessons are being learned – not least the vital importance of up-to-date data and the use of digital technology. It was a point made by a team from King's College London in a letter in *The Lancet*, entitled "Quantifying additional COVID-19 symptoms will save lives".

Looking at the data from more than three million UK app users, the team found that, as of 19 May, 76,260 had been tested for COVID-19: "71.5% of the 13,863 individuals testing positive indicated fever or cough, suggesting that only isolating and screening those reporting fever or cough could have missed almost 30% of positive cases... loss of smell and taste was reported overall by 64.5% of those testing positive; and by 15.9% of those not suffering from either fever or cough."

The UK Government added the loss of smell and taste (anosmia) to the list of key COVID-19 symptoms on 18 May, long after many EU countries and the US. Until that point, they had argued that anosmia alone accounted for fewer than 2% extra cases. "Our data suggest this not to be the case," said the King's College researchers.

LOSS OF SMELL

A new understanding

The data quoted in the letter was collected by the COVID-19 Symptom Study app, which is the work of the health science company ZOE and is endorsed by the Welsh Government and NHS Wales, the Scottish Government and NHS Scotland. By mid-June, almost four million people were using the app to report on their health. The developers claim it is "the largest public science project of its kind anywhere in the world". All the anonymised data are being analysed by teams at ZOE as well as the researchers at King's College. By filtering the data through software algorithms, they say they are able "to predict who has the virus and so track COVID-19 infections across the UK and now other countries". The results are also being used to "generate new scientific understanding of the very different symptoms the virus causes in different people. We are also studying the way that risks vary between individuals because of their own personal characteristics".

One of the authors of the letter is

Professor Sebastien Ourselin is Head of the School of Biomedical Engineering and Imaging Sciences at King's. He outlines the key problem that data have posed during the COVID-19 response. "When you are in this situation of having a pandemic, you will have trouble trying to get real-time information about how your population is affected by this. You can run large statistical analyses but it will be roughly on mostly retrospective data, so you will struggle to get important on-the-fly daily information about your population."

Revealing numbers

The COVID-19 Symptom Study app has changed that by managing to reach out to millions of people across the UK, and also to participants in the US and Sweden. "So now we can reach those people and are able to assess on a daily basis what is happening to their health," says Ourselin. "For instance, we can see how the behaviour of self-isolation is going to affect the spread of the virus. We have also really been able to learn much more about the symptoms associated with COVID-19. This has been a bit of a controversial situation, and we have been seeing that a lot of scientists were not always recognising anosmia as an important symptom, but the numbers were quite revealing. And of course something else that has come out of this is that you can identify new symptoms, and identify and predict from those symptoms who is likely to have COVID-19."

By using machine learning and prediction modelling, the researchers have extracted key insights from the data. "One of the biggest findings is that we are able to identify five days in advance if a patient will need to be hospitalised. That is before they are even going to call emergency services. And this is all coming from understanding how the clusters of symptoms change over time."

Looking ahead, the team hopes the app will eventually have more than 60 million daily users, though Ourselin is wary about potential bias. "People who are young, who have an appetite for digital technology and access to it will be more interested in giving their data online. People who have symptoms might also be more interested. A lot of the work we are doing now is to understand this bias. This is vital if it is to become not only a diagnostic tool but also a recruitment tool for new trials."

Understanding patterns

For the moment, the data collected via the app are revealing that COVID-19 is a

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more multifaceted and subtle disease than initially suspected – and it is doing it quickly. "For instance, we have been asking participants about skin rashes," says Ourselin. "We have seen a specific pattern of skin rashes that are associated with COVID, but this would have taken perhaps four or five months in a standard study just to start to see those patterns. It would take a long time just to recruit those patients, and get them to the hospital and have their symptoms recorded. So approaching them via digital health apps is a fantastic opportunity to get real-time feedback and predictions of what could happen to those people in a much safer way."

It might also be the route to more precise treatment. "We have more evidence that anosmia is one of the most widely frequent symptoms. With better data and understanding such as this, we can see how COVID-19 can take a different path into the body, affecting a different part of the immune system. The more we understand these patterns of symptoms, the better we will be able to deliver appropriate treatment." BMS