Horizon
The EU Research
& Innovation Magazine

European Commission

Long Covid: the pandemic's testing aftermath

By tracking Covid-19 patients, doctors in Europe are in search of treatments for a lingering sickness that is both debilitating and puzzling.

17 August 2023 - By ANTHONY KING

Evelina Tacconelli, an Italian infectious diseases specialist, is seeking cures for a coronavirus-induced illness that's playing havoc with the lives of millions of people in Europe and elsewhere.

Though Covid-19 itself is no longer deemed a global emergency by the World Health Organization, many infections have been followed by a malady called "long Covid". This disorder is taking a particularly hard toll on otherwise healthy women.

Unresolved symptoms

'There is no proven treatment for long Covid,' said Tacconelli, a professor of infectious diseases at the University of Verona in Italy.

One study estimated that almost half of all people who caught the coronavirus had unresolved symptoms after about four months, with one in 10 suffering from long Covid. That leaves at least 65 million people with what can be a life-changing illness.

Long Covid has a lengthy list of symptoms and scientists struggle to understand why some people suffer ill health well after they've overcome the coronavirus. Nonetheless, various elements are becoming clearer as doctors look at large groups of patients.

'There is no one long Covid,' said Tacconelli. 'It includes several diseases.'

She coordinates a project that received EU funding to compile the medical information of tens of thousands of people from across Europe. These include participants both with and without Covid-19 to allow for comparisons.

The research initiative, called ORCHESTRA, is due to wrap up in November 2023 after three years. It has received almost €30 million in funding, most of which – nearly €28 million – has been from the EU.

Four strands

There are at least four types of long Covid, all with different symptoms, according to Tacconelli.

One is a respiratory form that can make it hard for people to exercise or run and sometimes even to walk or sleep properly.

A second form involves muscle pains that people didn't have before Covid-19.

A third type resembles chronic fatigue characterised by severe tiredness and an inability to return to activities done before the infection.

The fourth version is predominantly neurological, with the major symptoms being headaches and forgetfulness.

Research surprise

The ORCHESTRA researchers have sought to answer two key questions: whether there were long-term health effects after the viral infection and what the results were of vaccination and early treatment over time.

A surprise in the project so far relates to women.

'What was very much unexpected was that women with no other disease were at higher risk of post Covid-19 syndrome,' said Tacconelli.

One reason this result was unforeseen is that elderly men were most at risk of dying from the infection itself.

Often the afflicted women are between 40 and 50 years old and have chronic fatigue symptoms followed by the neurological form of long Covid.

Women are long known to suffer more from autoimmune conditions – for reasons still debated by experts – and this could partly explain the prevalence of long Covid in female patients.

In any case, the initial coronavirus infection seemingly influences the form of long Covid. For example, people who complained mostly of headaches or stomach symptoms when ill with Covid-19 are at greater risk of the neurological form.

Revealing records

The ORCHESTRA team has tapped into the medical information of 70 000 healthcare workers who have had their condition checked every few months since 2020. Such workers were chosen because they were at high risk of Covid-19 transmission and are routinely screened for transmissible diseases.

The project scope also includes “patient cohorts” – groupings of individuals with common traits – in, for example, France and Germany.

And it includes thousands of vulnerable patients watched closely by hospital doctors.

‘All these medical records reveal that vaccinated people and vulnerable hospital patients who received antiviral drugs or antibody therapy soon after being infected have less risk of long Covid,’ said Tacconelli.

In March 2023, European Health Commissioner Stella Kyriakides said that 17 million people in the EU had been affected by long Covid and the number was rising. Kyriakides has promised more research into its causes, consequences and treatments.

Long Covid is a growing challenge for health systems in Europe and elsewhere. In December 2022, an online conference brought together 800 health experts and patient groups from the EU and US to tackle the matter, including through greater cooperation.

Quicker access

A European health-system weakness that the coronavirus pandemic exposed was difficulty in rapidly accessing real-world data needed to assess the effect on patients and to find effective treatments.

Had clinical information on patients in different hospitals been compared quickly, the ineffectiveness of an antibiotic called azithromycin and the very early effect of cortisone on survival would have been noticed, according to Tacconelli.

To address this, the ORCHESTRA researchers have established Europe-wide information on patient cohorts. This collection of data is based on existing and new large-scale cohorts in the EU and in non-European countries.

The project integrated epidemiological, clinical, microbiological and genotypic information on patient groups with common environmental and socioeconomic traits.

Major support for ORCHESTRA came from another EU-funded research project: unCoVer, which ended in May 2023 after two and a half years including a six-month extension.

This initiative sprang into action when Dr José Luis Peñalvo at the Institute of Tropical Medicine in the Belgian city of Antwerp foresaw the benefits of collating information on patients from different hospitals.

‘At the beginning of the pandemic, it was not clear what type of treatment should be used and it was not clear whether we should discontinue treatments for chronic patients once they got admitted to the hospital,’ said Peñalvo, an epidemiologist who worked in his native Spain and in the US before moving to Belgium in 2018.

Patient care

He sought to gather information quickly.

Peñalvo began by recruiting Antwerp University Hospital into the network before contacting former colleagues at medical centres in Madrid.

His interest is in patients with type 2 diabetes, high blood pressure and cardiovascular disease. Such people suffered more from Covid-19.

‘I had an interest in taking better care of these patients, but also in collecting data on patients and on how to analyse this data,’ said Peñalvo.

Dozens of hospitals – including in Croatia, Ireland, Italy, Norway and Portugal and as well as non-European countries such as Brazil and Colombia – joined the network.

The hope is that hospitals will be better prepared to handle a future pandemic or to answer medical questions using patient information from a number of health centres, all while preserving privacy by ensuring the anonymity of the people whose data gets used.

Meanwhile, Tacconelli of ORCHESTRA says possible cures for long Covid are being developed.

‘New treatments are in the pipeline,’ she said. ‘Maybe one year from now, if we are very lucky, we will have some answers from the studies now underway.’

Research in this article was funded by the EU. If you liked this article, please consider sharing it on social media.

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- ORCHESTRA
- unCoVer
- EU-funded coronavirus research and innovation