PRESS RELEASE

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Multiple Types of Long COVID Identified for the First Time

All-Luxembourg study finds that Long COVID is not just a single disease but can take a variety of forms with different symptoms and potential treatments

A consortium of Luxembourgish research institutions studying the national population have been looking to identify factors that may contribute to variations in severity of COVID-19 and its associated symptoms. In their most recent study the teams were able to show that individuals who experienced moderate to severe cases of the acute COVID-19 infection were more likely to experience increased frequencies and burden of symptoms after 12 months, with a notable impact on quality of life. Furthermore, the researchers were able to identify various sub-categories of Long COVID for the first time, showing that it is not a single disease as previously thought.

The COVID-19 infection manifests itself through a diverse array of symptoms, varying in type and intensity and consequently resulting in very different outcomes for affected patients. One outcome that has become increasingly clear over the past year is the onset of persistent symptoms after the initial acute infection, which has been widely referred to as 'Long COVID'. Despite this now being a well-known potential outcome of COVID-19, little is still known about this debilitating disease, leaving researchers with many questions to answer.

The "CoVaLux" (COVID-19, Vaccination & long-term health consequences of COVID-19 in Luxembourg) study is coordinated by Research Luxembourg and a consortium of Luxembourgish research institutions, including the Luxembourg Institute of Health (LIH). Overall, this unique project is providing important results that are helping to improve the understanding and long-term impacts of COVID-19, while also leading to improvements in patient care.

In its first published work led by Dr Guy Fagherazzi, Director of the Department of Precision Health at LIH, the consortium has investigated the association between the severity of the initial COVID-19 infection, and the frequency and burden of symptoms in patients 12 months later. The hope of researchers was that this could shed more light on the nature of Long COVID, filling in crucial blanks that could ultimately help to predict outcomes and uncover more about the disease.

"An increasing number of studies report long-term health consequences across the spectrum of patients who have had COVID-19. As such, the identification of predictive markers and risk factors of the long-term sequelae of COVID-19 has been defined as a research priority. Our hypothesis is that Long COVID symptomatology may differ according to the initial COVID-19 disease severity and that symptoms can cluster and define sub-types of Long COVID," explains Dr Fagherazzi.

Among the 289 adult participants who fully completed the 12-month questionnaire, almost 60% reported at least one symptom with an average of 6 symptoms. These could range from the more commonly known fatigue and shortness of breath, to less well-known problems such as memory loss and gastrointestinal problems. When one considers that over 580 million cases of COVID-19 have been diagnosed around the

world so far, this indicates that a significant number of people could be experiencing Long COVID in some form.

Regarding the effect of the initial disease severity, the volunteers who had experienced an initial moderate or severe COVID-19 infection were found to be more than twice as likely to experience Long COVID symptoms after one year, than those who had been mild or asymptomatic at the beginning. Furthermore, moderate to severe sufferers had an average of 6 more symptoms than those who had been initially asymptomatic. These results indicate that Long COVID and its severity have strong links to the severity of the initial infection, where a worse case of COVID-19 could significantly increase your chances of having more symptoms that last for longer.

A further striking outcome of the study was the researchers' ability to see patterns in the symptoms of participants, which suggests that Long COVID is likely made up of multiple sub-categories rather than a single disease. By looking at how symptoms tended to cluster in individuals, it was possible to get some idea of how these sub-categories present themselves. For example, loss of taste and smell appears to characterise one type of Long COVID, while another could be better described by gastrointestinal symptoms including nausea, diarrhoea, stomach burns and other abdominal pain. This information could be extremely useful as researchers seek to better define the disease and hunt for effective therapies.

"Our study provides an extensive description of symptoms present 12 months after COVID-19 infection and highlights a significant burden for people living with Long COVID. With this work, we are helping to describe Long COVID and confirm that it is multisystemic and presents different clusters of symptoms. These results will ultimately help to better identify Long COVID in clinical settings and contribute to the definition of precision health strategies to improve the care of people with Long COVID," summarises the study's lead author Aurélie Fischer, Scientific Coordinator in the LIH's Deep Digital Phenotyping Research Unit.

The study was published on 5th August 2022 in Open Forum Infectious Diseases (OFID), a peer-reviewed open access journal dedicated to the intersection of biomedical science and clinical practice, under the full title "*Long COVID Symptomatology After 12 Months and Its Impact on Quality of Life According to Initial Coronavirus Disease 2019 Disease Severity*" (DOI: 10.1093/OFID-ofac-397).

Funding and collaborations

About the Luxembourg Institute of Health (LIH)

The Luxembourg Institute of Health (LIH) is a public biomedical research organization focused on precision health and invested in becoming a leading reference in Europe for the translation of scientific excellence into meaningful benefits for patients.

LIH places the patient at the heart of all its activities, driven by a collective obligation towards society to use knowledge and technology arising from research on patient derived data to have a direct impact on people's health. Its dedicated teams of multidisciplinary researchers strive for excellence, generating relevant knowledge linked to immune related diseases and cancer.

The institute embraces collaborations, disruptive technology and process innovation as unique opportunities to improve the application of diagnostics and therapeutics with the long-term goal of preventing disease.

About Research Luxembourg

Research Luxembourg is a unified, agile team of thought leaders working to learn, explore and make an impact to shape a better future. By connecting all players in Luxembourg and abroad, Research Luxembourg aims to become a leader in research and innovation focusing on four research priority areas: (1) Industrial and Service Transformation; (2) Personalised Healthcare; (3) Sustainable and Responsible Development; (4) 21st Century Education.

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