

Exploring new insights and strategies for long COVID

EU-US Conference on long COVID

13 December 2022

The European Commission, DG Health and Food Safety, hosted an online conference with over 800 participants to highlight the latest news and developments on long COVID¹ in the European Union and the United States of America.

Experts from medical, public health, and health economics disciplines as well as representatives of patient organisations and policymakers shared their experiences and insights on long COVID. Emerging evidence suggests that as many as 1 in 8 people who recover from COVID-19 will experience long COVID with a wide range of debilitating symptoms lasting weeks or months after the initial infection.

The main objectives of the conference were to exchange experiences and knowledge between the EU and the US in long COVID research, treatment and health systems' responses, and to identify key challenges and knowledge gaps in these areas.

1 Long COVID, also known as post-COVID syndrome or long-haul COVID, refers to the ongoing symptoms and health effects experienced by some individuals after recovering from COVID-19, the illness caused by the SARS-CoV-2 virus.

Introductions

Opening the conference, **Sandra Gallina, Director-General for Health and Food Safety, European Commission,**

said there was an urgent need for a concerted and coordinated international response to the challenges posed by long COVID. A recently published European Commission report had underscored the need to adapt national health systems to dealing with long COVID as well as addressing multimorbidity in the context of caring for patients with the condition. Millions of people in Europe and the United States have been affected by long COVID and they need targeted clinical care, better treatments, and support in dealing with the condition on a daily basis. This first EU-US conference on long COVID was an important starting point to share research data, policy initiatives and expertise for the benefit of those patients on both sides of the Atlantic, she said.



Admiral Rachel Levine, the Assistant Secretary for Health at the United States Department of Health and Human Services, emphasized that long COVID is a real and significant issue affecting millions of people who need help. She highlighted the efforts being made by the US government across 14 different federal agencies to address long COVID, including the publication of two recent reports and the funding of numerous research programmes. Admiral Levine explained that long COVID is not one specific condition, but rather represents a variety of potentially overlapping entities with different causes and risk factors. She also highlighted the importance of building on existing research to gain a deeper understanding of long COVID and potentially other post-infection conditions. In addition, she emphasized the importance of international collaboration and sharing of information in addressing long COVID, and mentioned the efforts being made to improve access to care and support for people with long COVID.



Keynote addresses

Sharing knowledge and strategies key to long COVID action



Professor Peter Piot, special advisor to the President of the European Commission,

discussed his personal experience with long COVID and the difficulties faced in getting others to recognize and take seriously the existence of the condition. He mentioned that primary care physicians often do not know how to handle long COVID cases and that there is still debate among some experts about whether the condition exists at all. He commended the European Commission for hosting the conference: sharing knowledge and strategies was an important part of any effort to understand and develop evidence-based treatment and prevention strategies for long COVID.

Professor Piot highlighted the importance of investing in research on long COVID, including on its definitions, incidence, aetiology, pathophysiology, clinical syndromes, diagnosis, treatment, prevention, and economic impact. He commented that there may be both biological and behavioural risk factors for long COVID, as well as social and economic impacts. He underscored the importance of multidisciplinary research and the need for clinical guidance and support in the absence of firm evidence. In terms of prevention, he said that evidence was accumulating that boosted vaccination and antiviral treatments may reduce the risk of contracting long COVID, and this needed to be considered in drawing up public health responses.

Professor Piot also noted that long COVID was not the only condition that could cause post-acute syndromes and that similar syndromes may be caused by other infections such as influenza and Ebola, though COVID-19 appears to be particularly prone to causing such complications. He stated that long COVID could affect anyone, regardless of age or the severity of their initial COVID-19 infection, and that it was still not fully understood why some people developed long COVID while others did not. He said that investments in long COVID research may also help those suffering from other similar syndromes caused by different factors. Summing up, Professor Piot emphasized the need for international collaboration and a coherent agenda on long COVID in the European Commission and Member States, involving all relevant sectors.

Take home messages

- ▶ Primary care physicians often do not know how to handle long COVID cases and some experts remain sceptical about whether the condition exists at all.
- ▶ Investing in research on long COVID, including on its definitions, incidence, causes, diagnosis, treatment, prevention, and economic impact, is important.
- ▶ Boosted vaccination and antiviral treatments may reduce the risk of contracting long COVID.
- ▶ Investments in long COVID research may also help those suffering from other similar syndromes caused by different factors.
- ▶ International collaboration and a coherent agenda on long COVID are needed in the European Commission and Member States, involving all relevant sectors.

US advocates all-of-government and all-of society approach

Dr Ashish Jha, the White House COVID-19 Response Coordinator for the United States, reflected on the progress made in understanding and managing the COVID-19 pandemic over the past three years. He emphasized that while significant advances had been made in developing highly effective vaccines and therapies to treat acute COVID-19 infections, a proportion of people continued to experience persistent symptoms which impacted directly on their quality of life and well-being.

Dr Jha identified four potential mechanisms that may be responsible for long COVID: persistent virus or antigens, immune dysfunction, initial tissue and endothelial damage, and intravascular damage. He emphasized the importance of understanding these mechanisms in order to develop effective therapeutics for the management of long COVID. Dr Jha stated that the US government was taking an all-of-government and all-of-society approach to managing long COVID, focusing on three main areas: providing medical care for people with long COVID, providing support and services for those affected by the condition, and conducting extensive research on long COVID. He added that the complexity and size of the problem required a collaborative effort between the US and EU.

Dr Jha also provided an update on the National Institutes of Health (NIH) RECOVER initiative², which thus far has been primarily focused on epidemiology and understanding the mechanisms behind long COVID. In the coming months, a series of clinical trials would be launched focusing on four key mechanisms: antivirals, immune modulation, rehabilitation, and tissue damage. He expressed hope that these trials would yield valuable insights in the next year or two on which approaches were most effective in treating long COVID.

Summing up, Dr Jha said that significant progress had been made in understanding and combating COVID-19 over the past few years, but long COVID remains a major challenge. He said that all the available evidence suggests that vaccines are effective in reducing the risk of long COVID, and antivirals may also be helpful. He was confident that more work and enhanced collaboration between the EU and the US would allow for substantial progress to be made in addressing long COVID.



Take home messages

- ▶ There are four potential mechanisms that may be responsible for long COVID: persistent virus or antigens, immune dysfunction, initial tissue and endothelial damage, and intravascular damage.
- ▶ The US government is taking an all-of-government and all-of-society approach to managing long COVID, focusing on medical care, support and services, and research.
- ▶ The NIH RECOVER initiative has focused on epidemiology and will launch clinical trials focusing on antivirals, immune modulation, rehabilitation, and tissue damage.
- ▶ Enhanced collaboration between the EU and the US will be needed to make progress in addressing long COVID.

Patient perspectives on long COVID

An 'urgent health crisis' requiring a rapid response



Ann Li, Chair of the patient organisation Long COVID Europe, said that without effective treatments, many people with long COVID would never recover, and that the illness would significantly disrupt the global economy. The condition is characterized by multisystemic somatic symptoms and impairments that often lead to chronic illness and disability.

Many of those affected by long COVID are under the age of 60 and part of the active workforce. With no effective biomedical treatments currently available, people with the condition often lose their employment and financial security. In addition to the personal impact of long COVID, it also has significant economic consequences as it decreases the total availability and productivity of the workforce, she said.

Ms Li noted that the World Health Organization estimated that 17 million people in Europe experienced long COVID in 2020 and 2021, with numbers increasing in 2022 due to the surge of the Omicron variant. In response, Long COVID Europe urged the European Commission to create a €500 million emergency fund for biomedical research and clinical trials on long COVID and related health conditions. This fund would be used to support research efforts coordinated with established patient groups and in close cooperation with partners in the United States, where over \$1 billion has been allocated for long COVID research.

Ms Li said that governments and other stakeholders need to prioritize the development of effective treatments and support services for people with long COVID. Without addressing this urgent public health crisis, the personal and economic consequences of long COVID would continue to have a significant impact on individuals and society.

Take home messages

- ▶ Long COVID is characterized by multisystemic somatic symptoms and impairments that often lead to chronic illness and disability.
- ▶ Many people with long COVID are under the age of 60 and part of the active workforce, but often lose their employment and financial security due to the condition.
- ▶ Long COVID Europe is calling for the creation of a €500 million emergency fund for biomedical research and clinical trials on long COVID and related health conditions.
- ▶ Governments and other stakeholders should prioritize the development of effective treatments and support services for people with long COVID to address the urgent public health crisis and its personal and economic consequences.

Putting patients at the heart of long COVID research



**PATIENT-LED
RESEARCH
COLLABORATIVE**

Michael Sieverts, Member of the Patient-Led Research Collaborative (PLRC) in the US, emphasised the importance of patient engagement in research, citing moral and ethical considerations, efficiency benefits, and political and practical drivers.

He explained that the PLRC is made up of people who have all experienced long COVID and whose professional backgrounds were in diverse fields such as science policy, research, and communications. Their input has had a notable impact on published papers, citations, and informing policy and guidelines. The PLRC said it was vital to have greater transparency and accountability in the decision-making process. Too often, he said, patient input was sought but not necessarily considered in decision making, leading to a perception that engagement was just for show and not a genuine collaboration.

Sieverts highlighted several key issues in long COVID research, including the importance of learning from existing research on post-viral and post-infection illnesses, the need for adequate funding for long COVID research, and the importance of collaboration and communication between researchers, clinicians, and patients. He also emphasised the need for a more tailored approach to medical testing, as standard diagnostic tests do not capture the complexity of long COVID.

Another key issue he highlighted was the difficulty in clinical trials of developing a control group of people who have never been infected with COVID-19 due to false negatives in antibody tests and the fact that most infections were not documented. It was also important in the design stage of studies to consider accessibility for patients, as this could be a significant obstacle for some. The PLRC supports increased funding for long COVID research and for greater involvement of patients at all stages of the research process. Collaboration between the US and the EU should also be bolstered. All of these measures were necessary to address the significant challenges posed by long COVID and to support the well-being of individuals affected by the condition, he concluded.

Take home messages

- ▶ Patient engagement in research is important for moral and ethical reasons, as well as for its efficiency benefits and political and practical drivers.
- ▶ The PLRC advocates for greater transparency and accountability in decision-making processes, with patients recognised as co-equals partners.
- ▶ Increased funding and support for long COVID research is required as well as greater patient involvement at all stages of the research process.
- ▶ Collaboration between the US and the EU should be strengthened to boost long COVID research and support for patients.

**Research evidence on
epidemiology, symptoms,
and treatment**

Shedding light on the many mysteries of long COVID

Professor Evelina Tacconelli, Professor of Infectious Diseases at the University of Verona and director of the Infectious Diseases Section at Verona University Hospital, Italy, summarised the latest epidemiological evidence. She noted the high number of symptoms associated with long COVID, with more than 60 already documented, and said that women have a threefold higher risk of developing long COVID than men³. People who were not hospitalized with COVID-19 still carried a risk of developing long COVID regardless of the severity of their initial infection. A recent study of over 10,000 children in Denmark with confirmed SARS-CoV-2-infection matched against controls from Danish national registers showed that infected children had higher odds of reporting at least one symptom lasting more than two months compared to control groups. Another recent study⁴ based on a primary care database of 486,149 adults in the United Kingdom concluded that females, ethnic minority groups, increasing socioeconomic deprivation, smoking and former smoking, high body mass index (BMI) and a wide range of comorbidities were all associated with an increased risk of reporting symptoms more than 2 weeks after SARS-CoV-2 infection.

Professor Tacconelli said that the introduction of vaccines had significantly changed the incidence and prevalence of long COVID. This had been clearly demonstrated in a recent study which found that patients with infected with COVID-19 after vaccination had a reduced risk of long COVID and death compared to unvaccinated patients.⁵ She also noted that the risk of long COVID varied depending on the circulating variant of the virus, with a reduced risk of long COVID with the omicron variant versus the delta variant depending on age and time since vaccination.⁶

She remarked that the stigma associated with long COVID was similar to that seen with HIV/AIDS. In a recent UK study, 95% of patients with long COVID said they experienced stigma “sometimes” while 76% said it was “often” or “always”. Professor Tacconelli said that there was a clear need for consensus on the definition of long COVID. In Europe, the World Health Organization definition of “post COVID condition” was commonly used, and denoted the presence of at least one symptom for two months that could not be attributed to any other cause. In this regard, she cited recent research by colleagues in Ireland who used machine learning to identify clusters of symptoms in patients with long COVID.⁷ Cluster 1 (joint pain, headache, myalgia) and cluster 2 (cardiovascular symptoms) showed greater functional impairment and poorer quality of life compared to cluster 3 (fewer symptoms). The results suggest that the number of symptoms should not be the determining factor in defining long COVID, she said.

Professor Tacconelli also gave an update on ORCHESTRA⁸ (Optimising Research Capacity in Health: Science, Technology and R&D for Action), a 3-year European Union-funded research project that aims to respond to the SARS-CoV-2 pandemic and other emerging health threats. The main goal of ORCHESTRA is to establish an international large-scale cohort for the conduct of retrospective and prospective studies in order to generate rigorous evidence to improve the prevention and treatment of COVID-19 and to be better prepared for future pandemics. Using machine learning and advanced statistical analysis, initial studies under the project have yielded valuable insights into the main clinical phenotypes and clusters of symptoms that are



3 Michelen M, Manoharan L, Elkheir N, et al. Characterising long COVID: a living systematic review. *BMJ Global Health* 2021;6:e005427.

4 Subramanian, A., Nirantharakumar, K., Hughes, S. *et al.* Symptoms and risk factors for long COVID in non-hospitalized adults. *Nat Med* **28**, 1706–1714 (2022). <https://doi.org/10.1038/s41591-022-01909-w>

5 Al-Aly, Z., Bowe, B. & Xie, Y. Long COVID after breakthrough SARS-CoV-2 infection. *Nat Med* **28**, 1461–1467 (2022).

6 Antonelli M. et al. Risk of long COVID associated with delta versus omicron variants of SARS-CoV-2, *The Lancet*, Volume 399, Issue 10343, 2022, pp 2263-2264.

7 Kenny, Grace et al. “Identification of Distinct Long COVID Clinical Phenotypes Through Cluster Analysis of Self-Reported Symptoms.” *Open forum infectious diseases* vol. 9,4 ofac060. 7 Mar. 2022, doi:10.1093/ofid/ofac060

8 <https://orchestra-cohort.eu/>

predictive of long COVID. Four main phenotypes have been identified thus far – respiratory, chronic pain, neurological and chronic fatigue – with a different distribution of risk factors for each phenotype. Noteworthy risk factors overall include female gender, as well as gastrointestinal and neurological symptoms at the time of diagnosis. The initial results also confirmed the hypothesis that vaccination may reduce the risk of contracting long COVID, with a specific impact on chronic fatigue syndrome. The studies also provided convincing evidence that early treatment of SARS-CoV-2 infection with monoclonal antibodies significantly reduced the risk of long COVID.

Professor Tacconelli also provided a brief update on the work of the Cohorts Coordination Board (CCB), a network focused on supporting the scientific value and impact of cohort studies in Europe and promoting their use in policy-making and the development of evidence-based guidelines and recommendations. A focus group on long COVID has been established within the CCB looking at the impact of early interventions and treatment in immunocompromised patients, among others.

In conclusion, she reiterated that the definition of long COVID needs to be improved in order to provide personalized care to patients and facilitate their inclusion in clinical trials for treatment. There was an urgent need to focus more on low-income countries and vulnerable populations, particularly females and children, where there is a lack of information about long COVID. She emphasized the importance of considering psychological and quality of life impacts in the definition of long COVID, as well as the need for legal recognition of long COVID as a disabling disease. The COVID-19 pandemic had shown the value of international collaboration and data sharing in reducing the burden of the disease and helping national health systems to respond to the crisis.

Take home messages

- ▶ There are more than 60 documented symptoms of long COVID, and women are at a threefold higher risk of developing the condition than men.
- ▶ People who were not hospitalized with COVID-19 can still develop long COVID, regardless of the severity of their initial infection.
- ▶ The incidence and prevalence of long COVID have been impacted by the introduction of vaccines, with vaccinated individuals having a reduced risk of long COVID and death compared to unvaccinated individuals.
- ▶ The risk of long COVID varies depending on the circulating variant of the virus.
- ▶ There is a high level of stigma associated with long COVID.
- ▶ There is a need for consensus on the definition of long COVID. Symptoms should not be the only factor in defining long COVID, as different symptom clusters can have varying impacts on functional impairment and quality of life.

Patient-centred approach to care vital



Professor Monica Verduzco-Gutierrez, Chair of the Department of Rehabilitation Medicine at the Long School of Medicine at the University of Texas Health Science Center in San Antonio, Texas,

discussed the pathogenesis and underlying causes of long COVID. She mentioned that there is evidence of SARS-CoV-2 viral antigen persistence in the gastrointestinal tract and other parts of the body, which may contribute to inflammation and autoimmunity. The observations of Epstein-Barr virus (EBV) reactivation in patients with long COVID means that treating EBV may be necessary for these patients due to its role in inflammation throughout the body. She said that there is increasing evidence of a link between long COVID and microthrombi, which are small blood clots that can form in the capillaries and cause inflammation. It was important to make microthrombi testing more widely available as it has been found in many patients with long COVID. The presence of microthrombi may be related to autoimmune responses and inflammation in the immune system, which may contribute to the ongoing symptoms experienced by individuals with long COVID.

She emphasized that individuals who had mild disease and were not hospitalized may also be disproportionately impacted by long COVID and should be included in treatment considerations. Possible therapeutic strategies include preventing infection through vaccines, administration of antivirals and anti-inflammatory drugs, and providing rehabilitation for patients with debility or neuromuscular weakness. Some trials have shown that vaccination may be helpful in reducing symptoms of long COVID. While antivirals were a promising treatment option, they may not be effective against certain mutated strains of the virus.

In terms of clinical management of long COVID, Professor Verduzco-Gutierrez emphasized the need for a multidisciplinary and patient-centred approach to care, and highlighted the importance of identifying red flags such as cardiac symptoms and post-exertional symptom exacerbation. She also mentioned the need to consider treatments for persistent micro-clots and endothelial dysfunction, such as anticoagulants and thrombolytics, and for inflammation, such as anti-inflammatories and antihistamines. Additionally, she highlighted the need to treat viral reactivation and dysbiosis, which is an imbalance in the microbial community in the body. Viral persistence also needed to be addressed, with a large-scale trial of Paxlovid currently under way in the United States. She said that intravenous immunoglobulin (IVIg) or B-cell directed therapies represented promising treatments for patients with autoimmune disorders. There were also ongoing trials for mitochondrial directed therapies for individuals with mitochondrial dysfunction. Overall, she emphasized the need for more research and treatment options for individuals with long COVID and the importance of bringing attention to this issue.

Take home messages

- ▶ Inflammation and autoimmunity due to SARS-CoV-2 viral antigen persistence in the body and reactivation of Epstein-Barr virus (EBV) may be linked to long COVID.
- ▶ Research shows an association between long COVID and microthrombi, small blood clots that can cause inflammation.
- ▶ Possible treatment options include vaccines, antivirals, anti-inflammatory drugs, and rehabilitation.
- ▶ Multidisciplinary and patient-centred approach to care is necessary, with consideration for red flags such as cardiac symptoms and post-exertional symptom exacerbation.
- ▶ Ongoing trials for intravenous immunoglobulin (IVIg) or B-cell directed therapies for autoimmune disorders and mitochondrial directed therapies for individuals with mitochondrial dysfunction are being conducted.

Panel discussion:

Speakers discussed the need for research on the impact of long COVID on daily life, including work time and absence from work. **Professor Tacconelli** said that there were several groups under the ORCHESTRA project, as well as dedicated patient groups, specifically focusing on the impact of long COVID on daily life, including work time and absence from work. **Professor Verduzco-Gutierrez** said studies have estimated that the economic cost of long COVID due to direct and indirect work losses could be \$3 to \$4 trillion for the United States alone. She stressed the importance of accommodating patients' recovery depending on the type of work that they do and enabling them to return to the work environment as smoothly as possible.

The speakers also noted the challenges of accessing long COVID clinics and the pressing need to transmit up-to-date knowledge to primary frontline care providers. **Professor Verduzco-Gutierrez** said that there was currently a five to six month wait for patients at her long COVID clinic, which she said was unacceptable. To enable the dissemination of knowledge to the primary frontline personnel, she noted that national long COVID societies have been instrumental in making consensus guideline papers available. She added that the fee-for-service healthcare model practised in the US makes it difficult to treat patients holistically and ensure they receive multidisciplinary care. She said it was important to support frontline clinics and primary care to ensure they had the relevant knowledge and information to conduct appropriate testing, be comfortable with diagnosis and start symptom management treatment.

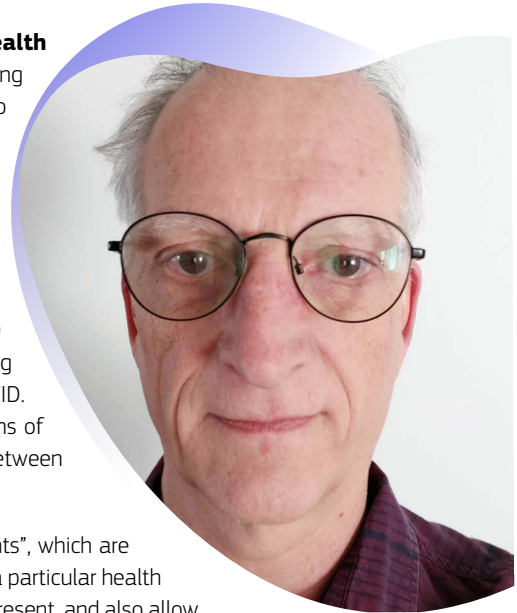
Professor Tacconelli said that one of the key learning points from the COVID pandemic was the importance of ensuring clear lines of communication to frontline workers and general practitioners. She hoped that such work would continue and be strengthened in the future. She added that it would be desirable to include more experts in infectious disease education to ensure that important information was correctly conveyed to general practitioners.

Research agenda

Getting to grips with the burden of long COVID

Professor Theo Vos, Professor of Health Metrics Sciences at the Institute for Health Metrics and Evaluation (IHME) at the University of Washington, discussed ongoing

research on quantifying long COVID as part of the global burden of disease. In order to identify the most common symptom clusters of long COVID, Prof. Vos and co-workers conducted a systematic review of data for 1.2 million individuals, including 44 published articles from 44 cohort studies and data from two large administrative databases: the PRA Health Services and Veterans Affairs (VA) data systems.⁹ However, the team found that the yield from the published articles was low and that the data was often not comprehensive enough to be useful for quantifying long COVID at a global level. As a result, the researchers sought out cohorts with access to individual record data and collated information from 10 ongoing cohort studies. This allowed them to quantify the frequency and overlap of disabling symptom clusters and make estimates on the expected duration for a new case of long COVID. Four of these cohorts were able to provide information on the health status and symptoms of individuals prior to COVID-19 infection, which allowed the team to compare the difference between those who had contracted COVID-19 and those who had never been infected by the virus.



Prof. Vos explained the methodology of determining disease burden using “disability weights”, which are numbers between 0 and 1 to indicate the amount of health loss experienced by a person in a particular health state. These weights allow for cases to be graded by severity based on the symptoms they present, and also allow for the positioning of long COVID relative to other conditions in the study. Using this approach, the results showed that approximately 1 in 10 women experience any of three common symptom clusters – respiratory problems, fatigue, cognitive symptoms – three months after COVID-19 infection, with a lower risk in men and children. The overlap between the symptom clusters was common, with around 30% to 40% of people affected by more than one cluster. He noted that the average disability weight of long COVID was 0.23, which he said was a similar score to that attributed to complete hearing loss or the long-term consequences of moderate to severe traumatic brain injury. Prof. Vos said there was a lack of follow-up data for long COVID patients beyond the one-year mark, but he estimated that around 15% of individuals who qualified for a diagnosis of long COVID at three months were still experiencing symptoms of the condition at 12 months. Based on the available data, there were an estimated 145 million new cases of long COVID globally in 2020-2021, 90% of which came from non-hospitalised cases and 64% of which were females. Current evidence suggests that the Omicron variant may lead to a one-third lower incidence of long COVID compared to previous variants of the virus, and the risk is further lowered by vaccination. Based on the high rate of infections with Omicron, around 94 million new cases of long COVID could be expected globally in 2022, with 8 million in European Union countries, he added.

Summing up the implications of the research, Prof. Vos said there was a considerable risk of ongoing symptoms after SARS-CoV-2 infection, especially for females. The majority of cases are in people of working age, and while most cases of long COVID recover within a year, a large number (15% of many millions) continued to experience debilitating symptoms at 12 months. This situation will require significant support, including rehabilitation and income assistance, not only during the most severe phase of long COVID but also as patients transition back into the workforce or education system, he said. He added that the attention on long COVID may help improve our understanding of the mechanisms behind the condition and also benefit those with other post-viral or post-infection syndromes, such as chronic fatigue syndrome.

⁹ Global Burden of Disease Long COVID Collaborators. Estimated Global Proportions of Individuals With Persistent Fatigue, Cognitive, and Respiratory Symptom Clusters Following Symptomatic COVID-19 in 2020 and 2021. *JAMA*. 2022;328(16):1604–1615. doi:10.1001/jama.2022.18931

Take home messages

- ▶ Symptom clusters of respiratory problems, fatigue, and cognitive symptoms affected approximately 1 in 10 women, 1 in 20 men, and 1 in 40 children three months after COVID-19 infection.
- ▶ Overlap between symptom clusters was common, with around 30-40% of people affected by more than one cluster.
- ▶ An estimated 145 million new cases of long COVID occurred globally in 2020-2021, with 90% from non-hospitalized cases and 64% being females.
- ▶ The Omicron variant may lead to a one-third lower incidence of long COVID compared to previous variants and vaccination further lowers the risk.
- ▶ An estimated 94 million new cases of long COVID can be expected globally in 2022, with 8 million in the European Union.
- ▶ Attention on long COVID may improve understanding of the condition and may also benefit those with other post-viral or post-infection syndromes such as chronic fatigue syndrome.

Taking a comprehensive approach to long COVID



Dr Joseph Breen, Immunoregulation Section Chief of the National Institute of Allergy and Infectious Diseases (NIAID), National Institutes of Health (NIH), in Bethesda, Maryland, United States,

described the efforts of the NIH's RECOVER Initiative to address long COVID. The basic idea behind the initiative is to improve understanding of the clinical spectrum of the condition, define risk factors, study disease recovery and pathogenesis over time, and identify interventions to treat and prevent long COVID and other similar disorders. The RECOVER initiative is being carried out through a collaborative network that includes clinicians, the private sector, industry partners, federal partners, community partners, and researchers, with a focus on a patient-centred approach and standardized methodologies across clinical trials, he said. The programme aims to deliver on a national scale with platform protocols using standardized methodologies and common data elements across the trials in order to compare results with multiple endpoints. He stressed the need for health authorities and researchers to be adaptive in the face of a pandemic which continued to evolve.

The research components of RECOVER has several core elements, including patient engagement, administrative coordination, clinical trial data coordination, clinical science, data resources, and a biorepository core for samples. One of the first tasks of the initiative was to focus on understanding health records to try to determine the incidence and prevalence of long COVID at a national level, particularly in underserved communities that have been disproportionately affected by the severity of COVID-19. Dr Breen said that over 13,000 new patients have been enrolled in the initiative since January 2022, and there were a number of reports in progress on the cohort. The initiative has also focused on pathobiology studies and clinical trials, and has made progress in the study of potential biomarkers for long COVID. RECOVER has also engaged in key collaborative efforts with the patient community. As part of the initiative, 42 multidisciplinary pathobiology studies are currently under way to investigate the underlying causes of long COVID symptoms. These studies are diverse and cover a range of areas, including basic immunology, autoimmunity, metabolomics, imaging, and neurology, in order to better understand the clinical observations and symptoms seen in long COVID patients and prioritize and design interventions, said Dr Breen. He noted that the initiative has already prioritized interventions based on patient input, but said that the focus may shift as more is learned about the pathobiology of long COVID. The therapeutic clinical trials reflected the input of clinicians, researchers, patients, and regulatory personnel to address key areas of concern for long COVID patients, including immune dysregulation, viral persistence and reactivation, neurologic and cognitive dysfunction, autonomic dysfunctions, sleep disorders, and cardiopulmonary exercise intolerance and fatigue. The clinical trials would test a range of interventions, including drugs developed with industry partners, biologics, devices, rehabilitation, cognitive behavioural therapy, and complementary and integrative medicine approaches.

Summing up the key challenges ahead, Dr Breen said that long COVID is a global and urgent issue, with a heterogeneous clinical presentation and many unknowns in terms of pathogenic pathways. Multiple clinical trials would be necessary to identify safe and effective treatments for both adults and children, and ancillary studies and longer term follow-up of cohort participants would also be important to identify and refine biomarkers, improve diagnostics, and understand the impact of long COVID on comorbidities, disabilities, and social determinants of health. The initiative would continue to work closely with patient partners to design interventions and improve the overall health and well-being of long COVID patients.

Take home messages

- ▶ The NIH's RECOVER initiative aims to improve understanding of long COVID, define risk factors, study disease recovery and pathogenesis over time, and identify interventions to treat and prevent long COVID and other similar disorders.
- ▶ The initiative has initially focused on understanding health records to determine the incidence and prevalence of long COVID at a national level, particularly in underserved communities.
- ▶ 42 multidisciplinary pathobiology studies are currently under way to investigate the underlying causes of long COVID symptoms.
- ▶ Clinical trials will test a range of interventions for long COVID, including drugs, biologics, devices, rehabilitation, cognitive behavioural therapy, and complementary and integrative medicine approaches.
- ▶ Key challenges for the RECOVER initiative include the heterogeneity of long COVID, the need for multiple clinical trials to identify safe and effective treatments, and the importance of ancillary studies and longer term follow-up of cohort participants.

Economic impact of long COVID

Long COVID taking a huge toll on labour markets

Dr Gopi Shah Goda, Senior Fellow at the Stanford Institute for Economic Policy Research (SIEPR), Stanford University, California, United States, discussed the impact of long COVID on the labour market, noting that the US labour force participation rate was currently about 1% lower than it was before the COVID-19 pandemic, which translated to about 3 million workers. While some of the reduction was attributable to population ageing, about 1.5 million workers were unexplained. Other rough estimates using survey data have suggested labour force losses in the range of 2 to 4 million people.¹⁰

In order to obtain a more precise estimate of the reduction in labour force participation due to COVID-19 illness, Dr Goda conducted a study using a large, nationally-representative household survey, the Current Population Survey (CPS), to develop a proxy for probable COVID-19 illness and then compared labour market outcomes for those who did and did not become ill with COVID-19 before and after illness.¹¹ The proxy used in the CPS showed a significant increase in the number of people absent from work due to illness after the COVID-19 pandemic. This increase appeared to be closely related to the number of reported COVID-19 cases in the United States. Additional research on this topic also supported this conclusion, she said. The researchers then looked at two groups of workers: those who were absent from work due to illness and a control group of workers who did not experience a health-related absence from work. They found that the labour force participation of both groups was similar before the illness occurred. However, after the illness, the labour force participation of the group that experienced an illness-related absence dropped significantly and these results remained consistent for up to 14 months after the illness occurred.

Overall, Dr Goda concluded that the number of illness-related absences increased during the COVID-19 pandemic and that on average, illness reduced labour force participation by about 7 percentage points. Based on these findings, she estimated that the loss in labour force participation due to COVID-19 illness was approximately 0.2 percentage points. She noted that while this might seem insignificant, it nevertheless equated to approximately 500,000 workers who could be out of the labour force. The impact of this loss was equivalent to one additional year of population aging (the natural progression of labour force participation as the baby boom generation ages and retires) or to roughly \$62 billion in forgone earnings, which is about half the burden of cancer or diabetes.

In summary, she said that health-related work absences continued to be elevated relative to pre-COVID levels, suggesting an enduring impact of the pandemic. The labour losses have a direct impact on the economy as well as potential implications for social insurance programmes and COVID-19 mitigation strategies.



10 Bach, Katie, "Is 'Long Covid' Worsening the Labor Shortage?," Report, Brookings Institution 2022; Cutler DM, Summers LH. The COVID-19 Pandemic and the \$16 Trillion Virus. JAMA. 2020;324(15):1495-1496. doi:10.1001/jama.2020.19759; Domash A & Summers LH, 2022. "How Tight are U.S. Labor Markets?," NBER Working Papers 29739, National Bureau of Economic Research, Inc.

11 Goda, Gopi Shah and Soltas, Evan, The Impacts of COVID-19 Illnesses on Workers (September 2022). NBER Working Paper No. w30435, Available at SSRN: <https://ssrn.com/abstract=4216221>

Take home messages

- ▶ The labour force participation rate in the US is about 1% lower than it was before the COVID-19 pandemic, equating to around 3 million workers.
- ▶ A study using the Current Population Survey in the US found that labour force participation dropped significantly after experiencing an illness-related absence, remaining consistent for up to 14 months after the illness occurred.
- ▶ The loss in labour force participation due to COVID-19 illness was estimated to be around 0.2 percentage points, or approximately 500,000 workers.
- ▶ The impact of this loss is equivalent to one additional year of population aging or roughly \$62 billion in forgone earnings.
- ▶ Health-related work absences remain elevated relative to pre-COVID levels, suggesting an enduring impact of the pandemic with potential implications for the economy, social insurance programmes, and COVID-19 mitigation strategies.

A massive impact on quality of life and productivity



Francesca Colombo, Head of the Health Division of the Organisation for Economic Co-operation and Development (OECD) observed that the significant variation in the definition of long COVID among countries made it difficult to accurately estimate its economic impact. She said that most OECD countries divide long COVID into two groups: ongoing symptomatic cases following an acute infection and a longer post-COVID condition phase. However, there were still many differences in the definitions used by different countries which made it difficult to accurately gauge the economic impact of long COVID.

She explained that prevalence estimates for long COVID typically converge on a range of 10-30% of patients who had COVID-19, which equates to at least 39 million people across the 38 OECD member countries who have or have had long COVID. However, she noted that the real prevalence could be actually be much higher if one calculated on the basis of the higher 30% estimate, especially considering a likely underestimation of COVID prevalence in many countries.

She noted that the economic impact of long COVID included health spending, reduced quality of life, and loss of productivity. By using “quality-adjusted life year” (QALY) scores, the OECD was able to estimate the impact of long COVID on both the length of time that a person lives and the overall quality of that person’s life during that time. The data showed that more than 7 million QALYs may be lost annually across OECD countries due to long COVID, one-sixth to one-third of people may have persistent cognitive symptoms and over one-third may also experience poor mental health. It was also important to bear in mind, potential differences across different population groups in terms of the prevalence of long COVID. Data from the UK, for instance, showed that people in the most deprived socioeconomic group were 50% more likely to report living in a household with at least one person experiencing symptoms of long COVID compared to those in less deprived groups. These differences among population groups should be taken into consideration when looking at the socioeconomic costs of long COVID, she said.

Data drawn from health insurance systems across different OECD countries showed a wide variation in the duration of sick leave taken for COVID-related illness. In Germany, for instance, 6% of people on sick leave for COVID-related illness remained on sick leave for over 4 weeks, while in Spain 10% of sick leave lasted for over 3 months and 2% for over 6 months for people with COVID-related illness. Initial estimates of the impact of long COVID on the labour market across OECD countries ranged from 0.5% (low) to 0.9% (medium) and high (1.2%) which equated to anywhere between 2.7 and 6 million workers missing from the labour force, she said. The economic costs of long COVID are significant even before direct health costs are considered. The costs of reduction in quality-of-life-years is estimated at \$723 billion while the estimated figures for lost earnings from reduced labour market participation is anywhere between \$141 to \$317 billion.

Summing up, Ms Colombo said that better policies and practices were needed to effectively address the issue of long COVID, including improved definitions and data collection at the national level. Access to care for those with long COVID due to financial barriers was generally not the principal issue, but there was a need for better care pathways and a patient-centred approach. There was also a need for improved access to different types of services, including labour market benefits and rehabilitation. The economic impact of long COVID on OECD countries was significant, and more comprehensive policy responses and services were needed to address the issue.

Take home messages

- ▶ The definition of long COVID varies among countries, making it difficult to accurately estimate its economic impact.
- ▶ Prevalence estimates for long COVID range from 10-30% of patients who had COVID-19, or approximately 39 million people across 38 OECD member countries.
- ▶ The economic impact of long COVID includes health spending, reduced quality of life, and loss of productivity.
- ▶ The OECD estimates that over 7 million quality-adjusted life years (QALYs) may be lost annually across OECD countries due to long COVID.
- ▶ Data from health insurance systems shows wide variation in the duration of sick leave taken for COVID-related illness among OECD countries.

Health systems' response to long COVID

A forum for exchange, advice and best practices

Petronille Bogaert, Head of Unit of EU Health Information System at Sciensano, the national institute of public health in Belgium outlined the work of the EU Health Information Systems Unit which coordinates the Population Health Information Research Infrastructure (PHIRI)¹² project. The three-year EU-funded project brings together 41 partners across 30 countries to generate the best available evidence for research and exchange best practices on health and well-being of populations as impacted by COVID-19 in order to support decision making.

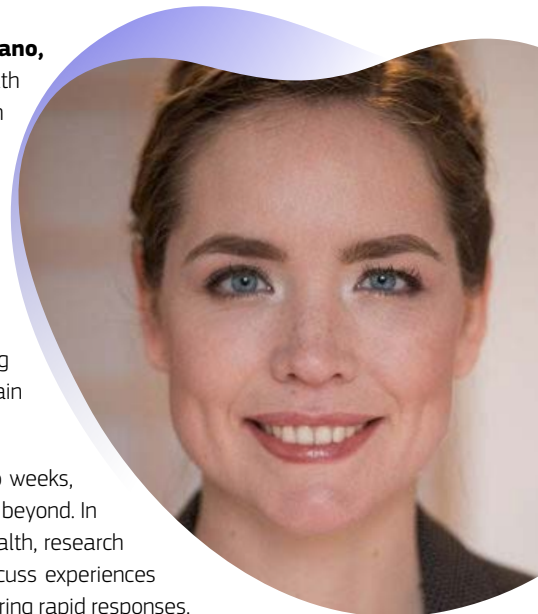
The main objectives¹³ of PHIRI are to provide a COVID-19 health information portal based on FAIR principles (Findable, Accessible, Interoperable, and Reusable). The portal offers an overview of COVID-19 population health data sources, studies, and capacity building exercises, with the goal of sharing data across countries and providing an overview of main data sources for population health in Europe.

She explained that within PHIRI, a Rapid Exchange Forum¹⁴ (REF) is organized every two weeks, addressing current developments in population health during the COVID-19 pandemic and beyond. In the meeting, participants belonging to European public health institutes, Ministries of Health, research institutions and universities as well as EU-level stakeholders answer questions and discuss experiences from their own countries related to the pandemic and other population health issues requiring rapid responses. The REF enables the rapid exchange of information and the dissemination of agreed standards, guidelines, and best practices. She said that the forum operates in a trusted environment where the different partners already know each other, allowing for quick responses to questions on a variety of topics related to COVID-19, such as risk level indicators and thresholds for stricter restrictions, mental health issues, and treatment and management of long COVID.

The PHIRI project has addressed several questions about measures taken to manage long COVID in different countries including data collection and studies on long COVID, guidelines and recommendations for its definition, diagnosis, and treatment, and whether specialized organizations have been developed to follow up on long COVID care and what professional groups and disciplines are involved. Other questions addressed how individuals can access clinics for long COVID care and whether these clinics are standalone entities or part of larger institutions, and also what tools, standards, treatment pathways, and patient information materials exist for the coordinated management of long COVID care, as well as the existence of registries for long COVID patients. She added that the responses to these questions could be found on the Health Information Portal.¹⁵

The PHIRI project recently asked for an update on long COVID management in different countries, including any major changes in processes for coordinating care for long COVID patients and the tools and treatment pathways that exist for diagnosing and treating long COVID. The responses revealed that only Italy currently maintains a long COVID registry for adults. Most countries have the general practitioner as the first point of entry for long COVID care, with referrals to specialized centres if necessary. Some countries have set up specialized centres or services specifically for long COVID care, while others have integrated long COVID care into their general hospital activities. Some countries have also set up conventions to cover the costs of primary care for long COVID patients and appointed care coordinators to help manage the care of these patients. Surveys have been used in some countries to collect data on long COVID patients. The organization of long COVID care varies greatly between countries and is influenced by factors such as the definition of long COVID, the availability of resources, and the need to coordinate care across different disciplines.

Summing up, Ms Bogaert said that the partners in the PHIRI project have indicated that an international exchange on best practice models for systematically registering patients with long COVID in medical care would be beneficial. They also emphasized the importance of continuing epidemiological and clinical studies, as well as basic research, to better understand the underlying disease mechanisms and clinical manifestations of long COVID and to improve the care of these patients.



12 <https://www.phiri.eu/>

13 <https://www.phiri.eu/project>

14 <https://www.phiri.eu/wp8>

15 <https://www.healthinformationportal.eu/rapid-exchange-forum>

Take home messages

- ▶ The Population Health Information Research Infrastructure (PHIRI) project is a project designed to gather evidence for research and exchange best practices on the health of populations as impacted by COVID-19.
- ▶ PHIRI has established a COVID-19 health information portal that offers an overview of COVID-19 population health data sources, studies, and capacity building exercises.
- ▶ PHIRI has established a Rapid Exchange Forum (REF) to enable the rapid exchange of information and the dissemination of agreed standards, guidelines, and best practices between partners.
- ▶ The organization of long COVID care varies greatly between countries and is influenced by factors such as the definition of long COVID, the availability of specialized centres, and the health system structure.
- ▶ PHIRI plans to continue collecting data on long COVID as more responses to the REF may be provided. Based on the needs of EU countries, the PHIRI REF will continue to address urgent questions on population health on COVID and beyond.

Patient engagement critical to advance research



Dr Arlene Bierman, Chief Strategy Officer, US Agency for Healthcare Research and Quality (AHRQ), discussed the importance of addressing long COVID as an opportunity for improving health systems, increasing innovation, and advancing health equity. She emphasized the need to engage with people living with long COVID and their communities in co-designing and co-producing interventions and evidence, and to include their voices in the development of standardized data elements for long COVID to facilitate real-world research.

Dr Bierman also highlighted the challenges of providing long COVID care in the context of multimorbidity, where most people with long COVID also have underlying chronic conditions. She emphasized the need for models of whole person or person-centred care that can provide comprehensive, coordinated care to people with long COVID and manage their coexisting illness, social needs, and the context of their lives.

To support primary care in preventing, diagnosing, and managing long COVID, Dr Bierman stressed the importance of providing infrastructure, access to the latest research and guidance, and models of care that foster shared and collaborative care with specialists and multi-specialty long COVID clinics.

She also mentioned the importance of conducting living evidence reviews, developing living clinical guidelines, and implementing clinical decision support to keep pace with advances in science and help transmit this evidence to frontline providers. She said that the United States would play an active role in the EU-sponsored partnership for transforming health and care systems, which will allow for cross-border learning about approaches to delivering effective, equitable, and high-quality care. Although many challenges lay ahead, addressing long COVID represented an opportunity for improving health systems, increasing innovation, and advancing health equity, she said.

Take home messages

- ▶ Engaging with people living with long COVID and their communities in co-designing and co-producing interventions and evidence will facilitate real-world research.
- ▶ Providing long COVID care in the context of multimorbidity requires models of whole person or person-centred care to manage coexisting illness, and social needs.
- ▶ Supporting primary care in preventing, diagnosing, and managing long COVID requires infrastructure, and access to the latest research and guidance.
- ▶ Conducting living evidence reviews, developing clinical guidelines, and implementing clinical decision support will help keep pace with advances in science and transmit evidence to frontline providers.
- ▶ The United States would play an active role in partnerships for transforming health and care systems to foster cross-border learning and deliver effective, equitable, and high-quality care for long COVID patients.

Long COVID exposes weaknesses in healthcare systems

Dr Jelka Zaletel, National Institute of Public Health of Slovenia and Rapporteur of the European Commission Expert Panel on effective ways of investing in health presented the main recommendations of a recent report¹⁶ of the European Commission Expert Panel on long COVID. She explained that the European Commission established the Expert Panel to provide non-binding, independent advice on matters related to effective, accessible, and resilient health systems.

During the COVID-19 pandemic, the Expert Panel observed that long COVID highlighted weaknesses in healthcare systems. These weaknesses reflected the organizational characteristics and professional boundaries of specific healthcare systems and may be resistant to change due to the distribution of power within the system.

The panel advised that more research was needed on the wider impact of long COVID, including its effects on the labour force, economy, and social circumstances. The importance of involving patients in co-producing and co-creating long COVID research, particularly in understanding the reactions of healthcare systems to the condition was also emphasised. Dr Zaletel said that the panel strongly supported the principle that all patients should have the opportunity to participate in clinical trials and research activities related to long COVID. The panel also recommended a coordinated programme of surveillance, including data from each EU Member State and potentially other countries, using consistent case definitions and methodologies, to evaluate the impact of long COVID on health, employment, and the economy.

In addition, the panel advocated that person-centred care was necessary for managing long COVID and that care models should be coordinated in primary care with appropriate mechanisms in place to ensure rapid referrals to specialist teams. However, the panel also cautioned against placing patients with long COVID in silos, as this could negatively impact the health and well-being of individuals with comorbidities.



Take home messages

- ▶ Long COVID has highlighted weaknesses in healthcare systems, reflecting the organizational characteristics and professional boundaries of healthcare systems.
- ▶ More research is needed on the wider impact of long COVID, including its effects on the labour force, economy, and social circumstances.
- ▶ All patients should have the opportunity to participate in clinical trials and research activities related to long COVID.
- ▶ A coordinated programme of surveillance is needed using consistent case definitions and methodologies to evaluate the impact of long COVID on health, employment, and the economy.
- ▶ Person-centred care is necessary for managing long COVID and care models should be coordinated in primary care with rapid referrals to specialist teams.

¹⁶ https://health.ec.europa.eu/publications/facing-impact-post-covid-19-condition-long-covid-health-systems_en

International cooperation and solidarity vital



Dr Tomas Zapata from the World Health Organisation Regional Office for Europe (WHO/Europe) highlighted the increased demand for health services due to the COVID-19 pandemic and the increasing number of long COVID patients in Europe. During the COVID-19 pandemic, the workload and burden of disease had increased, leading to backlogs and waiting times for essential health services in many European countries. This was further compounded by an aging population and the increasing prevalence of non-communicable diseases. A recent study by the WHO and the Institute for Health Metrics and Evaluation (IHME) at the University of Washington's School of Medicine estimated that there were around 17 million patients with long COVID in the 53 WHO European countries.¹⁷

In order to meet the increased demand for healthcare services and respond to the needs of long COVID patients, the healthcare workforce must be strengthened, said Dr Zapata. This included improving working conditions, mental health and well-being, and upskilling healthcare workers. Many of these recommendations had been included in a recent WHO report on the healthcare workforce in Europe.¹⁸ He noted that primary healthcare, with a focus on the individual and multidisciplinary care pathways, could play a key role in managing long COVID symptoms and other health issues. Coordination between primary care and other levels of the healthcare system, as well as within secondary or tertiary care, could also be beneficial in providing patient-centred solutions.

The prioritization of mental health services was also important, as long COVID could affect the mental health of patients.

To achieve all of these goals, resources and investment would be necessary, particularly in the context of the ongoing conflict in Ukraine and a difficult global economic climate. Dr Zapata emphasized the importance of international cooperation and solidarity in supporting healthcare systems and addressing the needs of long COVID patients.

Take home messages

- ▶ The COVID-19 pandemic has increased the demand for health services, leading to backlogs and an increased workload and burden of disease.
- ▶ The healthcare workforce must be strengthened, including by improving working conditions, mental health and well-being, and upskilling healthcare workers.
- ▶ Primary healthcare with a focus on individual and multidisciplinary care pathways can play a key role in managing long COVID symptoms and other health issues.
- ▶ Mental health services should be prioritized as long COVID can affect the mental health of patients.
- ▶ Resources and investment are necessary to achieve these goals, particularly in the context of ongoing conflict in Ukraine and a difficult global economic climate.

17 <https://www.healthdata.org/news-release/who-least-17-million-people-who-european-region-experienced-long-covid-first-two-years>

18 <https://www.who.int/europe/publications/item/9789289058339>

Building a comprehensive and equitable strategy

Sharon Arnold, the Associate Deputy Assistant Secretary for Science and Data Policy at the Office of the Assistant Secretary for Planning and Evaluation (ASPE) in the United States, provided information on the US government's policy stance on long COVID and how it is supporting the healthcare system in responding to the condition. In April 2022, President Biden issued a memorandum¹⁹ on addressing the long-term effects of COVID-19, leading to the production of two reports on existing federal supports and services available to individuals with long COVID²⁰ and on a research action plan for long COVID.²¹

Ms Arnold explained that a long COVID Coordination Council had also been established with leadership from 14 different departments across the US government to communicate and coordinate on long COVID issues. One of the strategies for the first year of the Coordination Council was to convene a national forum to align terms and definitions for long COVID research and clinical care. The US government was also supporting research into prevention, diagnosis, treatment, and the provision of services for long COVID, and had established the Health Plus programme to co-create patient-centred solutions for those impacted by long COVID.

Ms Arnold said that the US government was also focusing on improving clinical care and reimbursement for long COVID, including expanding COVID clinics at the Veterans Affairs (VA) and developing updated clinical care guidelines. It was also promoting provider education and clinical supports through existing channels and launching targeted campaigns to raise awareness of long COVID among both the general public and healthcare providers. Finally, the government was working on improved data collection and analysis to better understand the prevalence and impact of long COVID, including through the establishment of a national registry and the use of electronic health records.



Take home messages

- ▶ The US government is supporting the healthcare system in responding to long COVID with a wide range of policy initiatives.
- ▶ These initiatives include two reports on existing federal supports and services available to individuals with long COVID and a research action plan for long COVID.
- ▶ A long COVID Coordination Council has been established with leadership from 14 different departments across the US government.
- ▶ The government is supporting research into prevention, diagnosis, treatment, and the provision of services for long COVID.
- ▶ The US government is also working on improved data collection and analysis to better understand the prevalence and impact of long COVID.

19 <https://www.whitehouse.gov/briefing-room/presidential-actions/2022/04/05/memorandum-on-addressing-the-long-term-effects-of-covid-19/>

20 <https://www.covid.gov/assets/files/Services-and-Supports-for-Longer-Term-Impacts-of-COVID-19-08012022.pdf>

21 <https://www.covid.gov/assets/files/National-Research-Action-Plan-on-Long-COVID-08012022.pdf>

Questions and answers highlights

On what constitutes a good standard of care in terms of long COVID

A good standard of care for long COVID patients should involve a combination of primary care, multidisciplinary specialty care, and an integrated care plan that addresses both the patient's ongoing chronic conditions and the effects of COVID, noted **Dr Arlene Bierman**. She said it was important to have the latest evidence and resources to manage the spectrum of illness in long COVID patients, and to develop a shared care or collaborative care relationship to effectively address their needs. There was also an opportunity to gather evidence on how to make the healthcare system work most effectively for long COVID patients through the use of implementation science and health services research.

On patient advocacy at an international level

Ann Li said that Long COVID Europe was scaling up its activities internationally and was now representing long COVID patients in nearly 18 countries within the WHO Europe region. She noted that the organization had been actively coordinating efforts and exchanging information about long COVID initiatives in Europe for the past year and was now ready to expand across the Atlantic. The organization would be holding its first meeting with the patient-led research initiative next year and was welcoming members from other countries to join its community.

On efforts to counteract claims of long COVID being primarily a psychosomatic condition

Petronille Bogaert said that multiple actions were being taken across Europe to address long COVID as a serious disease. These actions included developing care pathways and long COVID guidelines, as well as altering reimbursement and healthcare costs in some countries to take long COVID into consideration. From the perspective of public health institutes, she said that long COVID was being taken seriously and efforts were being made to address it.

On gender differences in long COVID prevalence and the implications for women

Dr Arlene Bierman said it was well established that there are significant gender differences in health and epidemiology, with women more likely to have autoimmune diseases and to experience myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) as well as long COVID. She added that women also tended to have a higher burden of multimorbidity and functional impairments and that it was important to design care delivery that takes these factors into account. However, she added that more research is needed to understand why long COVID disproportionately affects women and how this may impact management of the condition. **Dr Jelka Zaletel** underscored the significant gender and age differences in the prevalence of long COVID, with women and older individuals more likely to experience the condition. She said that while the specifics of these differences were not yet well understood, it was important for healthcare systems to be able to respond to the needs of all individuals, including women who are caring for families and multiple generations.

On the stigmatisation and discrimination faced by long COVID patients

Ann Li said that long COVID patients often face stigma in various areas of their lives, including within their own homes, in the workplace, and within the medical community. Some people do not believe that long COVID symptoms are real or are caused by the virus, and may even end relationships or lose employment because of this. She emphasised that long COVID is a complex condition with symptoms that can evolve over time, and it can be difficult for patients to describe their experiences. Peer support groups could be helpful for patients to talk to others who understand their situation and to maintain their mental health. However, she noted that these groups are often run by volunteers who are also struggling with long COVID and may need better support and recognition from national governments for their efforts. **Michael Sieverts** also urged action to tackle stigma and discrimination, and said that measures were needed to prevent gaslighting in the media and healthcare system in relation to long COVID. Media coverage too often promoted the idea that long COVID was psychosomatic, and some doctors were also reportedly telling patients that their long COVID was not a real medical condition. It was important to address gaps in health providers' education, as too many patients continued to encounter disbelief and invalidation on their initial visits to primary care providers.

Closing remarks and conclusions

Bringing the conference to a close, **Sandra Gallina**, Director-General for Health and Food Safety, European Commission, thanked the speakers and attendees for their contributions and for sharing their experiences with long COVID.

Summarising some of the key points to emerge from the day's presentations and debates, she said it was impossible to ignore the real and devastating impact of long COVID on millions of people across the globe. She stressed the importance of understanding, defining, and measuring the condition in order to manage, treat, and possibly prevent it. She emphasized the need to implement promising treatments and options that are currently available and to develop evidence-based guidelines to ensure that frontline workers could deliver targeted clinical care to affected patients.

She pointed out that the lack of studies on long COVID did not mean that there was a lack of patients suffering from the condition, and called for more research to be conducted on the subject. She also highlighted the impact that long COVID has on economies and health systems, and stressed the need for systems to adapt to this type of long-term disease. Gallina said that investing in long COVID was not a sunk cost, and that it could even lead to the discovery of treatments and insights that might be useful for managing other complex conditions such as chronic fatigue syndrome and autoimmune diseases. She emphasized the need for a multidisciplinary approach to long COVID, and suggested that the condition could serve as a catalyst for addressing multi-morbidity. She also mentioned the progress that had been made in clustering symptoms of long COVID, and the potential for using targeted therapies to treat the various clusters. She highlighted the importance of using patient-reported outcomes and digital health tools to better understand and manage long COVID.

Summing up, Gallina said it was critical to prioritize and focus on the needs and experiences of patients in addressing the issue of long COVID, as their symptoms and experiences may vary. She also emphasized the importance of multidisciplinary research and international cooperation in addressing the issue and finding solutions for those affected by long COVID. She said that long COVID required a whole-of-government approach that took account of its social and economic impacts and which was committed to not leaving anyone behind. She pledged to provide ongoing support to ensure that exchanges and collaboration between the European Union and the United States continued to be actively pursued for the benefit of the millions of patients dealing with the effects of long COVID.

END

