TACKLING CORONAVIRUS (COVID-19)
CONTRIBUTING TO A GLOBAL EFFORT

THE ECONOMIC IMPACT OF LONG COVID IN OECD COUNTRIES:

WHAT DO WE KNOW?

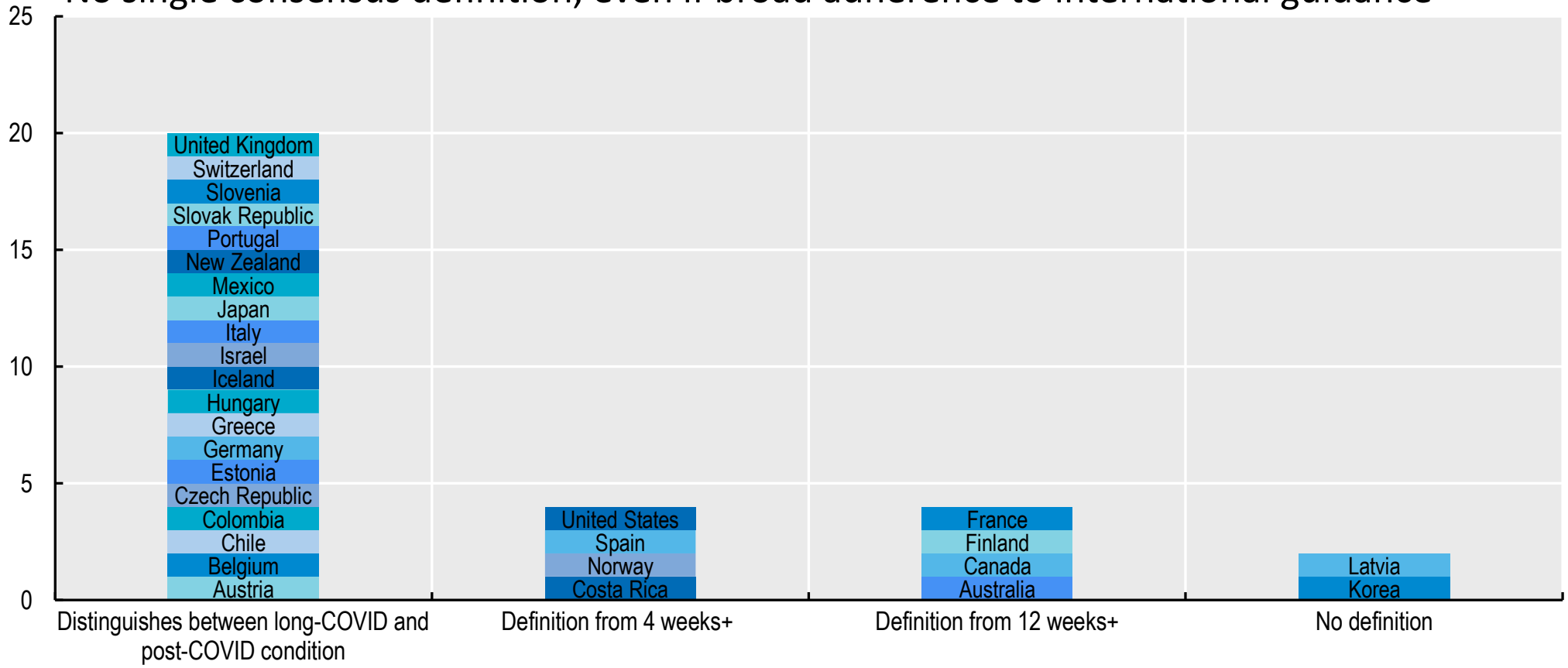
Online EU-US Conference on Long COVID
13 December 2022

Francesca Colombo
Head of the Health Division

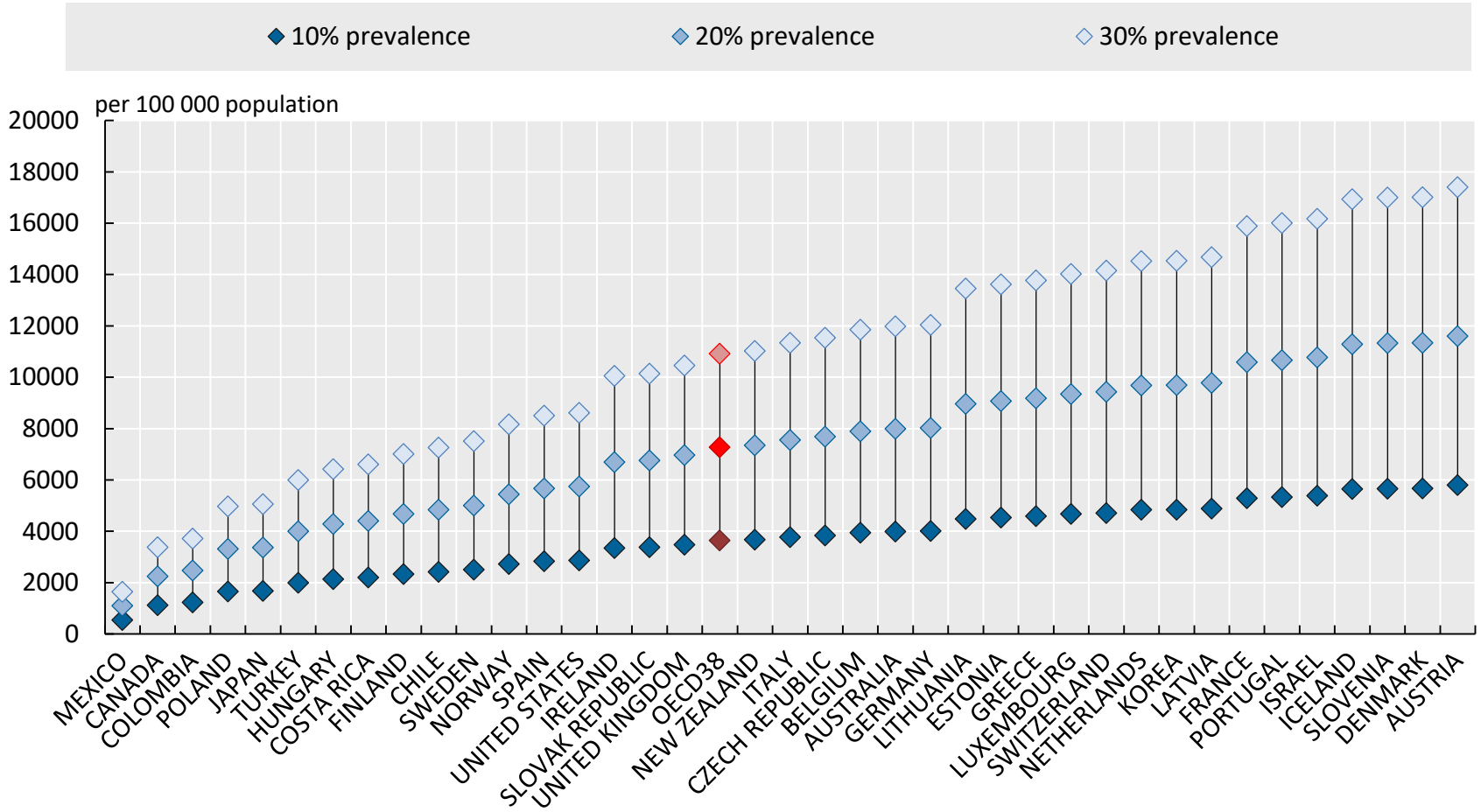
OECD
BETTER POLICIES FOR BETTER LIVES

Significant variation on the timeframe used to define long COVID

No single consensus definition, even if broad adherence to international guidance



Upwards of 39 million people likely to have/had long COVID across OECD



Less clear what proportion of the population is living with ‘long-term’ or ‘severe’ long COVID

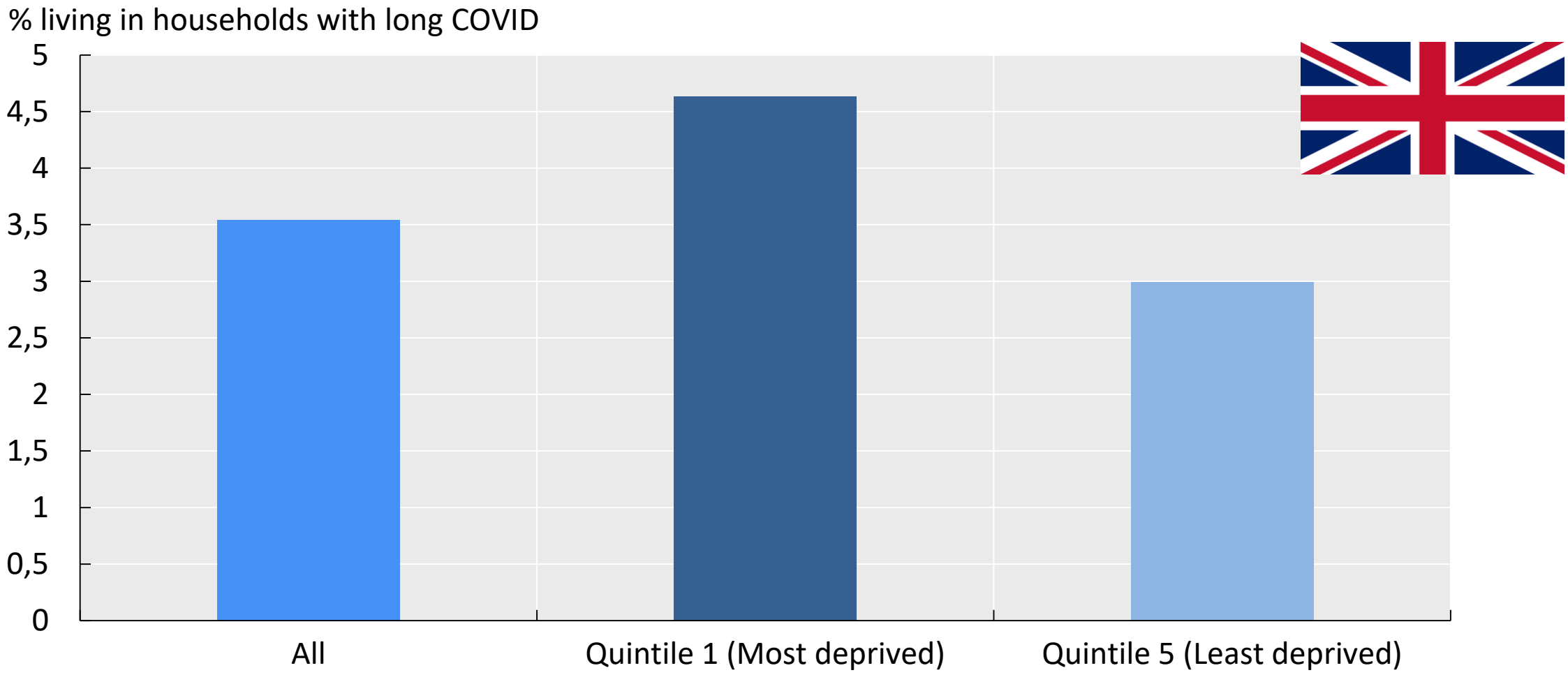
The impacts of long COVID are significant

More than 7 million QALYs may be lost annually across OECD countries due to long COVID

One-sixth to **more than one-third** of people may have persistent cognitive symptoms

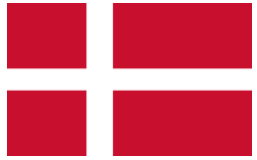
Upwards of **one-third** of people may experience poor mental health

Inequalities in the prevalence of long COVID



Data from sickness funds suggest labour market impact from long COVID

18% of Covid-19 patients on sick leave for +30 days, including 4.7% for +90 days

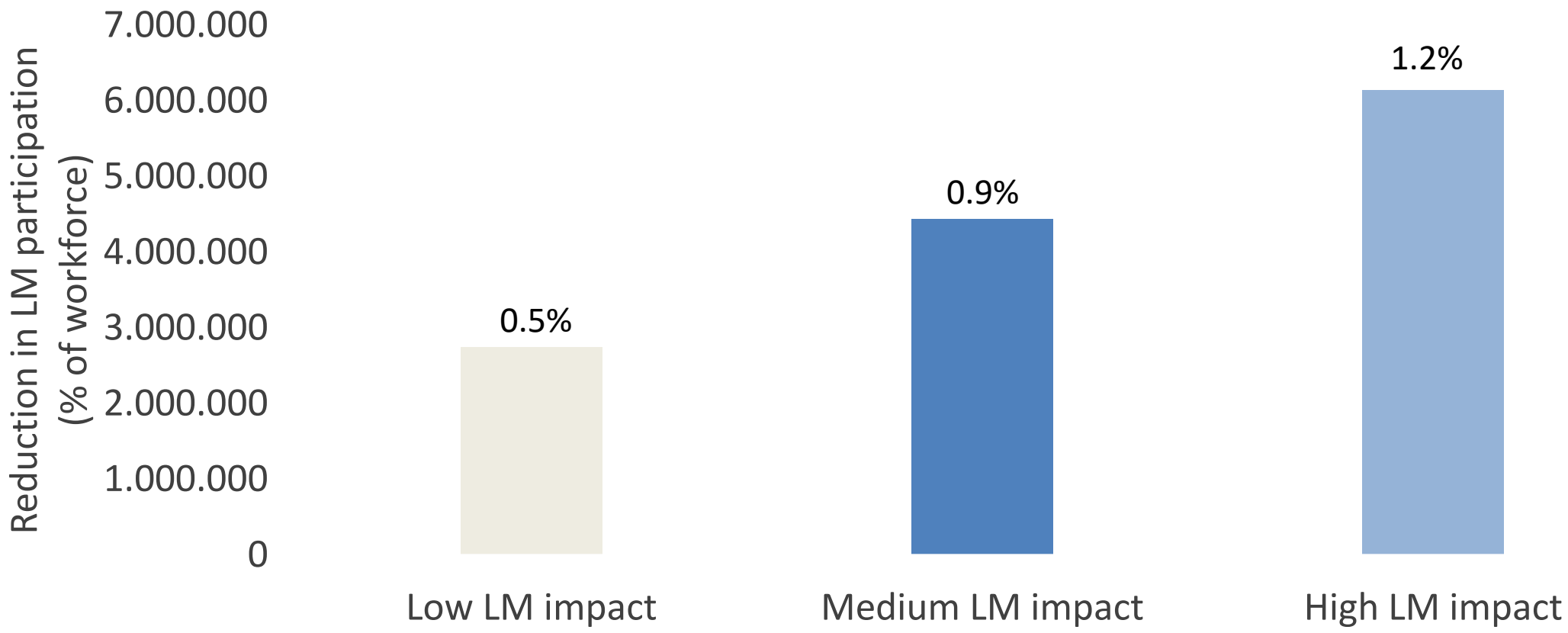


People with a positive COVID-19 test 56% more likely to take sick leave 4 weeks – up to 1 year after their positive test

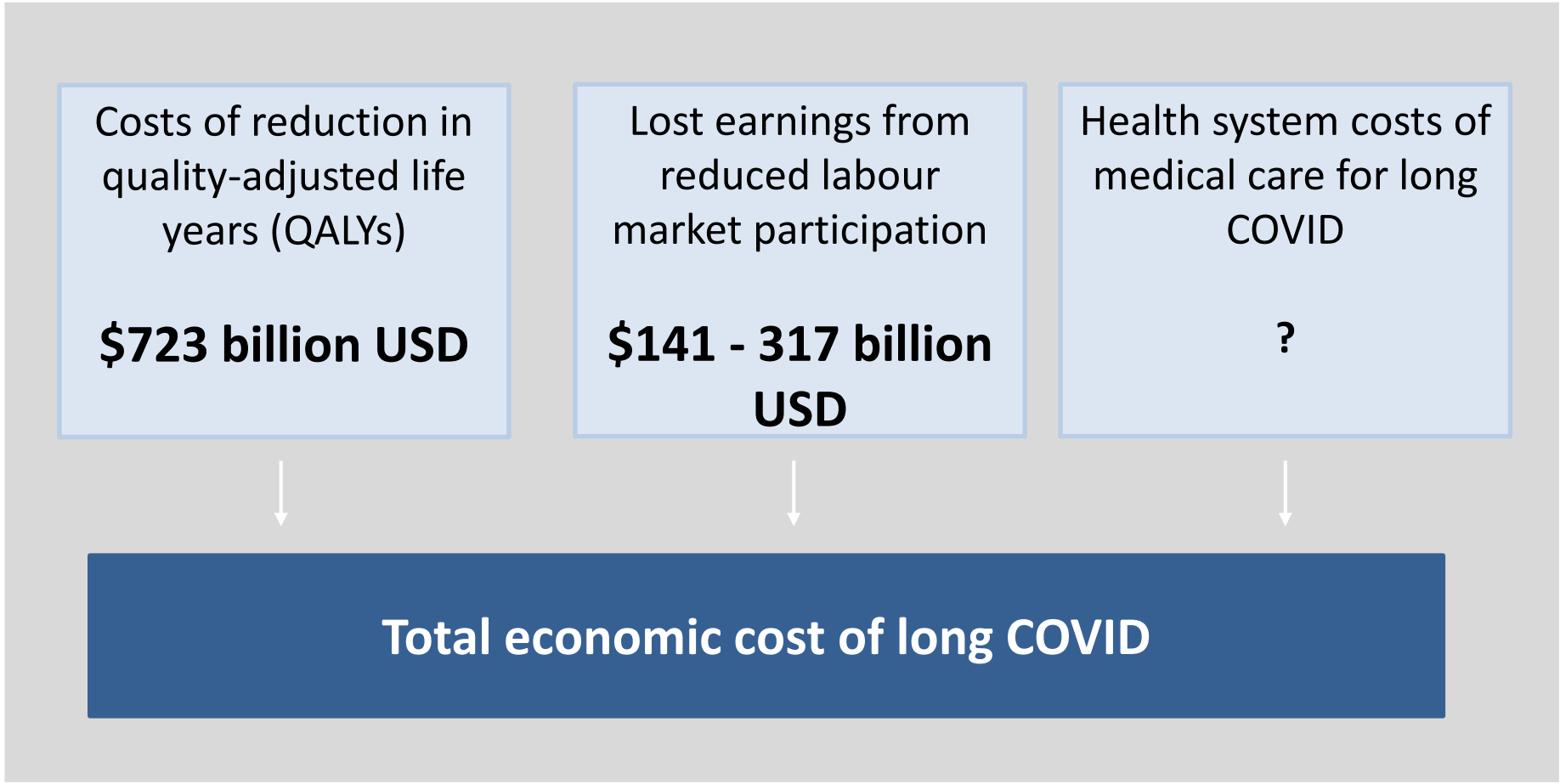
6% of people on sick leave for COVID-related illnesses remained on sick leave for 4+ weeks

10% of sick leave due to COVID lasted for 3+ months, and 2% for 6+ months

Initial estimates suggest impact on labour market participation across OECD – but prevalence and severity matter



The economic costs of long COVID are significant – even before direct health costs are considered



Better policies and practices needed to tackle long COVID

Data and measurement

Care pathways

Access to care

Patient-centred approach

Access to labour market benefits

Care coverage

In summary:

- **Definition**, **surveillance** and **measurement** remain critical challenges to understanding long COVID
- Clear **labour market impact** from long COVID – but better data needed for better estimates of effect and to design appropriate responses
- **Cost** of long COVID to OECD countries is significant
- Countries have mounted **policy responses**, but more services and integrated policy approaches are needed

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THANK YOU

@OECD_social @FranColombo2019

OECD
BETTER POLICIES FOR BETTER LIVES

Online EU-US Conference on Long COVID

RECOVER Initiative Update

Tuesday 13 December 2022

Joseph Breen, PhD, NIAID

RECOVER
Researching COVID to Enhance Recovery

NIH National Institutes of Health
Researching COVID to Enhance Recovery

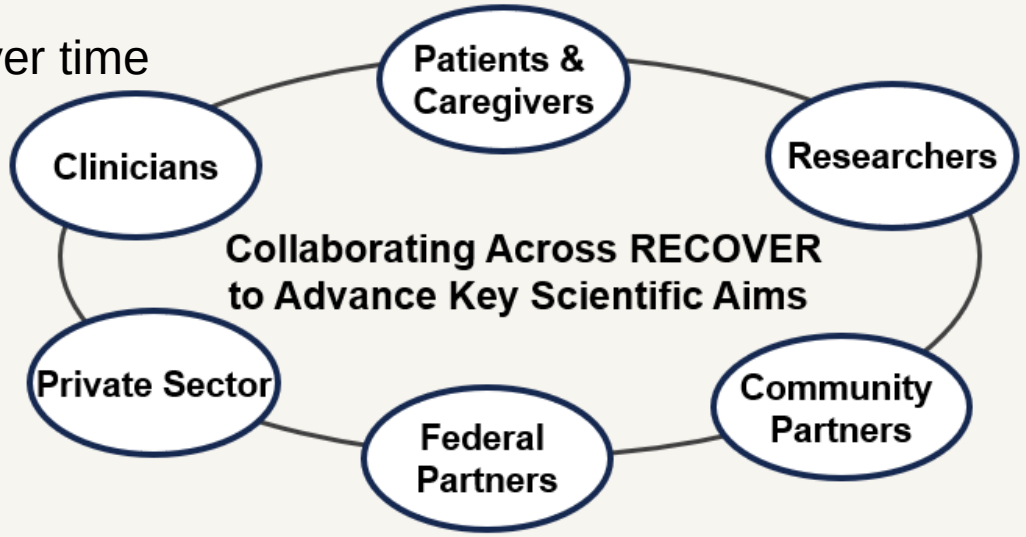
NIH RECOVER Initiative

Goal

Rapidly improve our **understanding** of and ability to **predict, treat, and prevent** PASC

Key Scientific Aims

1. Understand clinical spectrum/biology underlying recovery over time
2. Define risk factors, incidence/prevalence, and distinct PASC sub-phenotypes
3. Study pathogenesis over time and possible relation to other organ dysfunction/disorders
4. Identify interventions to treat and prevent PASC



Guiding Principles

Patient-centered, participants as partners

National Scale with Inclusive, **diverse** participation & community engagement

Platform protocols, standardized methodologies, and common data elements

Adaptive approaches based on emerging science

NIH RECOVER Initiative: Research Components

Patient-Centered. National Scale. Common Protocols. Standardized Methods/Data. Adaptive to Emerging Science.

RECOVER Cores

Patient Engagement Core	Administrative Coordinating Center	Clinical Trial Data Coordinating Center	Clinical Science Core	Data Resource Core	Biorepository Core

Research Studies

RECOVER Clinical Trials

Adaptive Platform
Multi-therapeutic domains

RECOVER Longitudinal Cohort studies

~40,000 participants

EHR/ Health Systems Studies

60 million+ records;
~7 million+ COVID cases

Pathobiology Studies

Mechanistic studies of pathogenesis

Tissue Pathology Studies

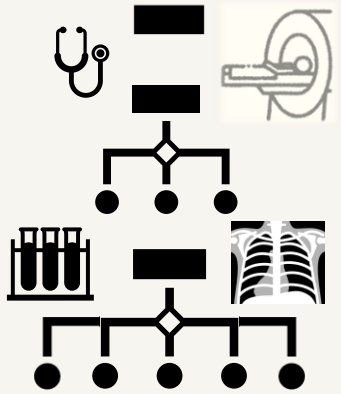
50+ tissue types
Neuro-imaging

Data Resources

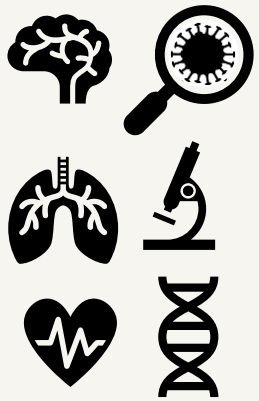
Clinical	Imaging	Mobile and Digital Health	EHR / Other Real-World Data	Pathology

Key Progress in 2022 *(as of December)*

Over 13,000 new patients enrolled since Jan 2022 [22 reports (21 draft manuscripts, 1 submitted)]



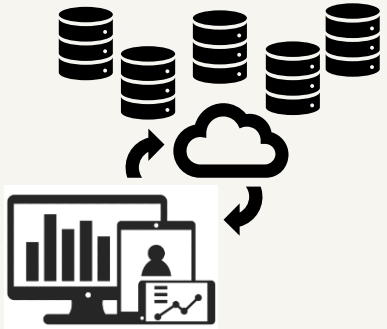
8 longitudinal clinical cohort studies and related sub-studies



42+ pathobiology studies

5 master protocol-driven platform clinical trials under development

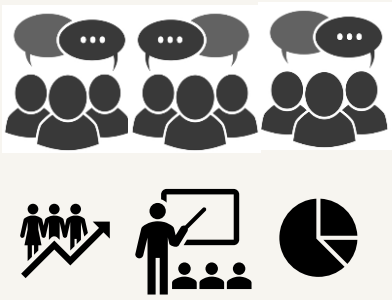
EHR study results: ~45 reports (20 draft, 11 submitted, 8 preprint, 6 published)



Data repositories and shared analytic workbench; initial RECOVER data release to consortium in process

Study of potential PASC biomarkers

Launched mobile health platform; developed patient registry

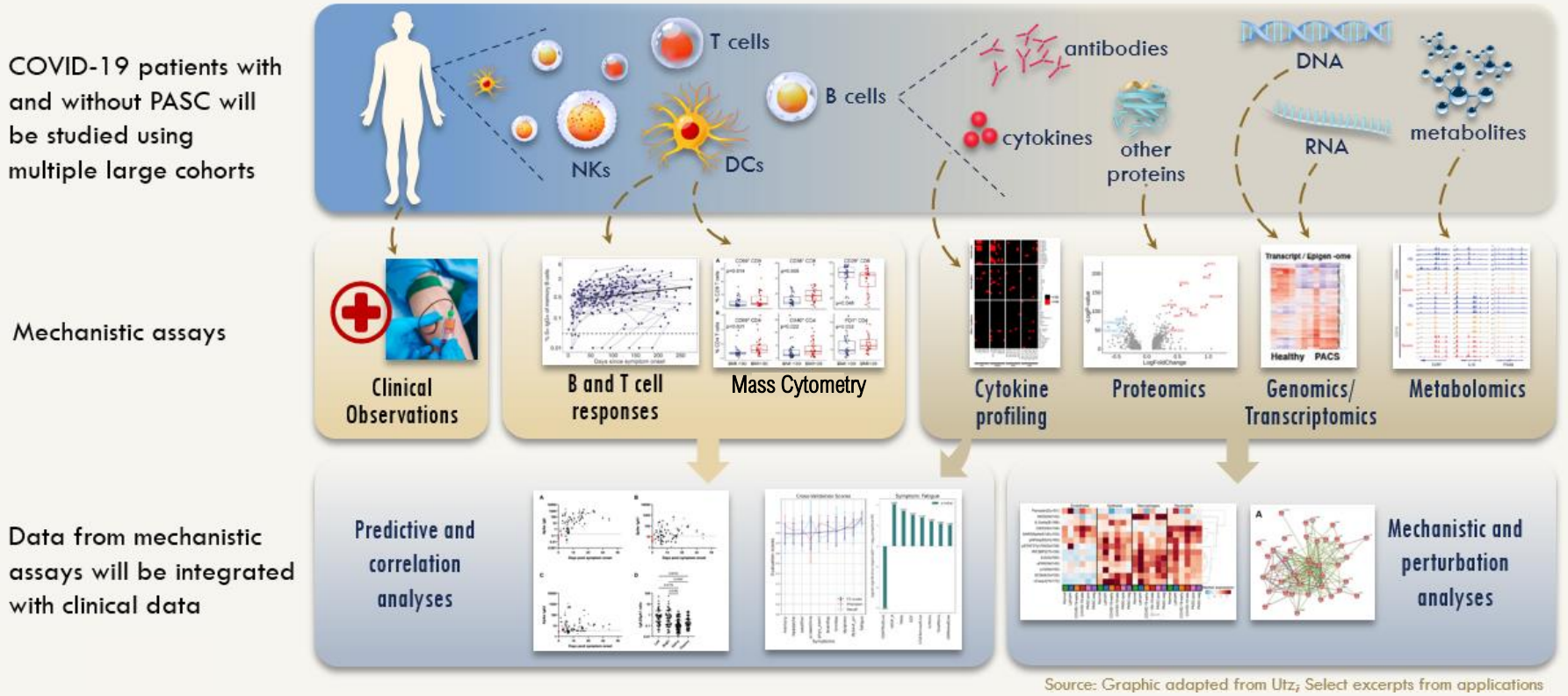


Collaborative patient community engagement and research seminar series

RECOVER-All of Us precision medicine collaboration

- Rigorously evaluate potential specific disease/biologic pathways leading to PASC, such as:
  - Viral persistence/ reactivation
  - Immune dysregulation, autoantibodies
- Mechanistic and ancillary studies critical for biomarkers discovery, informing clinical trials, and improving care and treatment of patients by enabling:
  - Patient stratification
  - Deeper sub-phenotyping
  - Identification of therapeutic targets
  - Diagnosis
  - Monitoring

Suite of 42+ Multi-disciplinary Pathobiology Studies Underway



Source: Graphic adapted from Utz; Select excerpts from applications

Consequences of Acute Infection

Viral Persistence Viral Reservoirs

Secondary Damage Reprogramming of Host Tissue/Organ

Immune Response, Inflammation, Autoimmunity

Residual Tissue Organ Damage Injury

Risk, Epigenetics

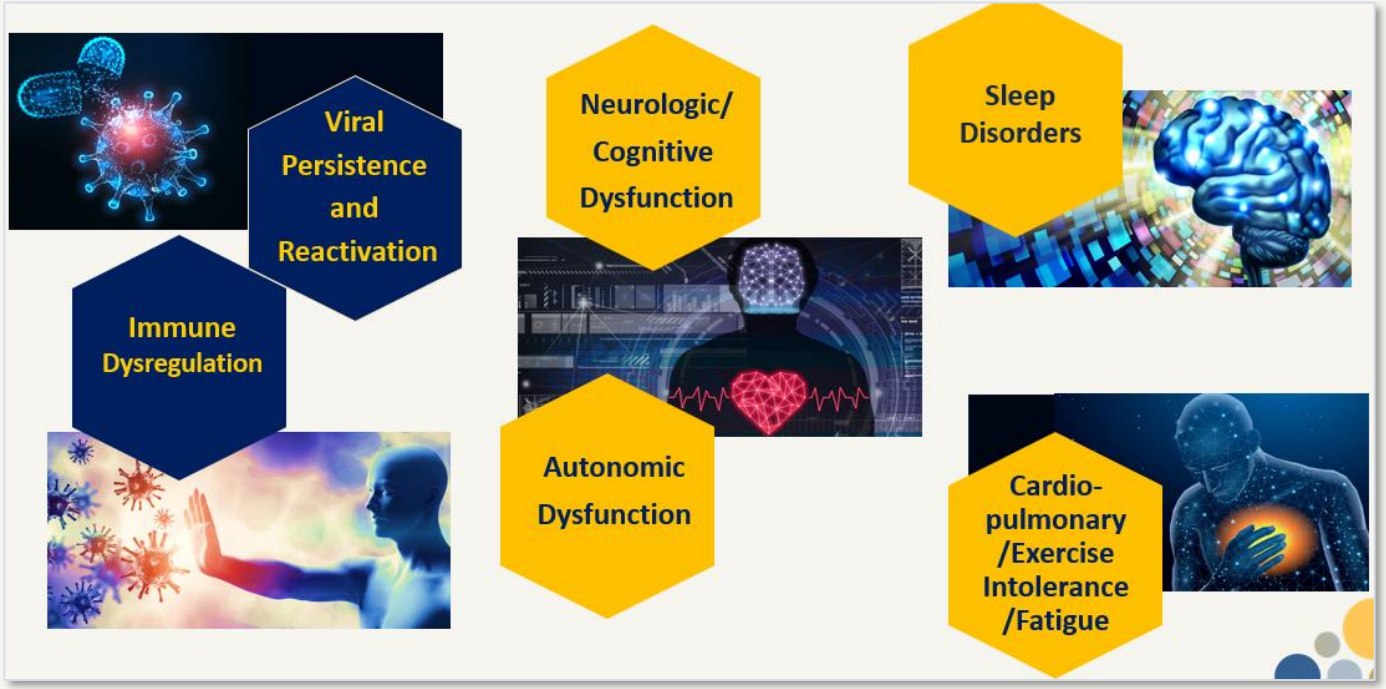
RECOVER Master Protocol-Driven Platform Therapeutic Clinical Trials: Span Dominant Symptom Clusters and Proposed Etiologic Pathways

- Trials reflect **input from clinicians, researchers, and patients and regulatory**
- Trial design and endpoints **informed by analyses of RECOVER clinical cohort data and patient surveys**

➢ **5 platform master protocols**
  - **Spanning major PASC symptom clusters and proposed etiologic pathways**
  - **Under development and, as appropriate, regulatory review**

- **Interventions include: a broad array of approaches including drugs, biologics, devices**
- **Platforms designed to efficiently test successive rounds of interventions** based on findings and as new targets are identified

RECOVER Clinical Trial Platforms Portfolio



Launching Staged Roll-out of 5 Master Protocol-Driven Randomized Controlled Trials

Challenges/Opportunities

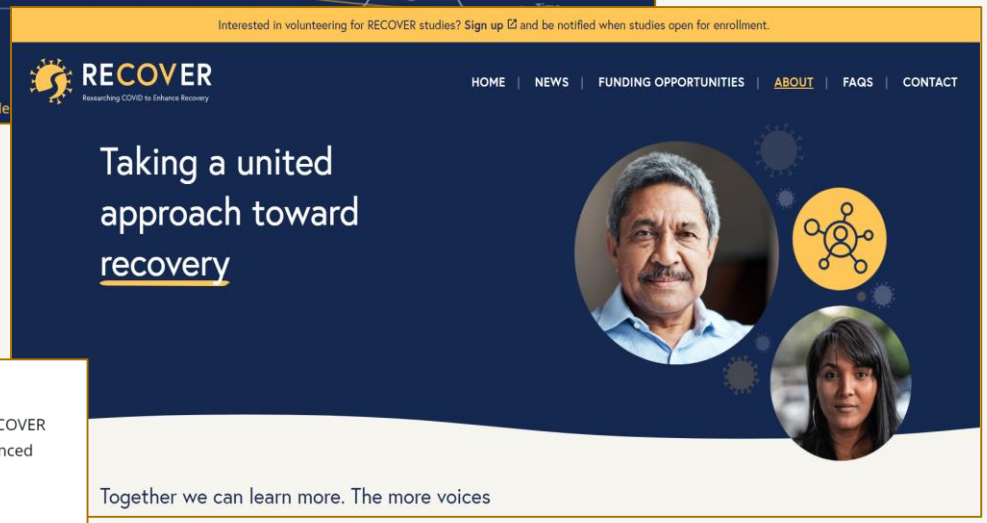
- **PASC is a very challenging and urgent clinical problem. It is a post-viral condition with global impact, highly heterogenous clinical presentation, and no clear pathogenic pathways**
  - Unlike many other post-viral conditions, we know the "culprit"
  - RECOVER designed with scale, scope, and intensity of investigation to leave no stone unturned

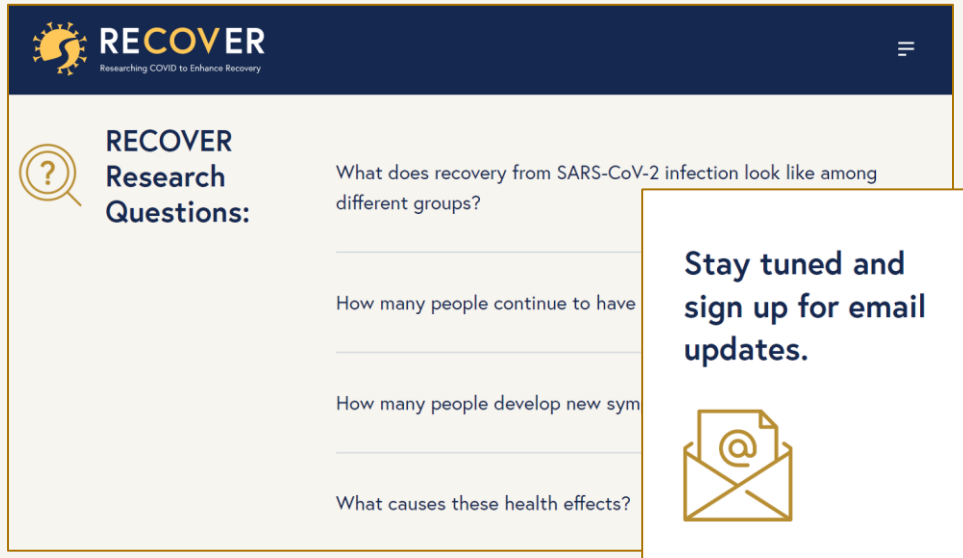
- **PASC Clinical Trials:**
  - **Given the broad range of PASC symptoms, multiple clinical trials are required** to identify safe and effective treatment and preventive strategies for PASC in *both adults and children*
  - Need to be considered on an on-going basis as we learn more about underlying mechanisms of disease that inform identification and prioritization of interventions

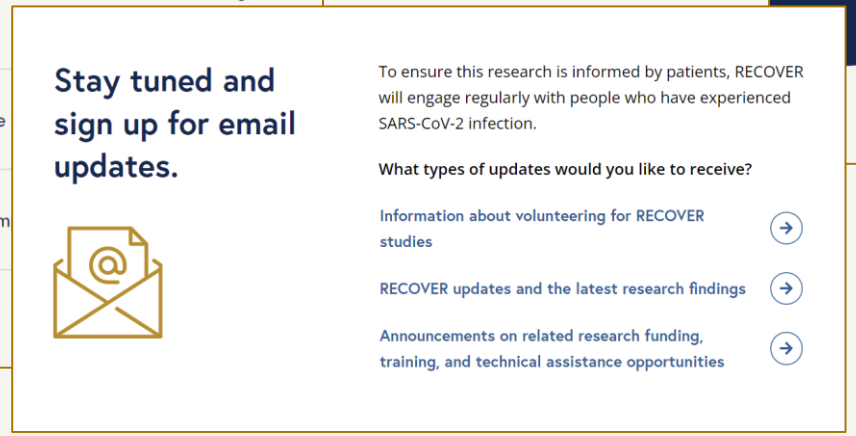
- **Mechanistic studies and ancillary studies are critical to identify and refine biomarkers and diagnostics** and ability to discern and appropriately treat sub-phenotypes

- **Need for longer term follow-up of cohort participants** to be able to detect *and address*:
  - New onset diseases and impact on co-morbidities
  - Longer term impact on disabilities and social determinants of health

- **Need for intensive, sustained, and strategic communications**







RECOVER
Researching COVID to Enhance Recovery

recoverCOVID.org

PATIENT-LED RESEARCH COLLABORATIVE

Value of Patient Engagement in Research

ME/CFS & Long COVID

Michael Sieverts, PLRC

Online EU-US Conference on Long COVID

December 13, 2022

About PLRC

- **45+ Long-COVID** patient-researchers and advocates **across 5 continents**
- Met and formed in April 2020 in Body Politic COVID Support Group
- **Interdisciplinary** team across sciences, technology, policy, media
- IRB from University College London
- Impact:
  - 10 papers in 21 months
  - 800+ research citations
  - Input into policy documents and public health guidelines: US, UK, WHO,...

PATIENT-LED RESEARCH COLLABORATIVE

Patient Engagement: Why and How

Moral/Ethical

- Recognizes patient's right to have input
- Reduces power imbalance

Efficiency

- Increases relevance to patients
- Improves recruitment and retention
- Increases public awareness

Political/Practical

- Increases transparency and accountability
- Improves public support

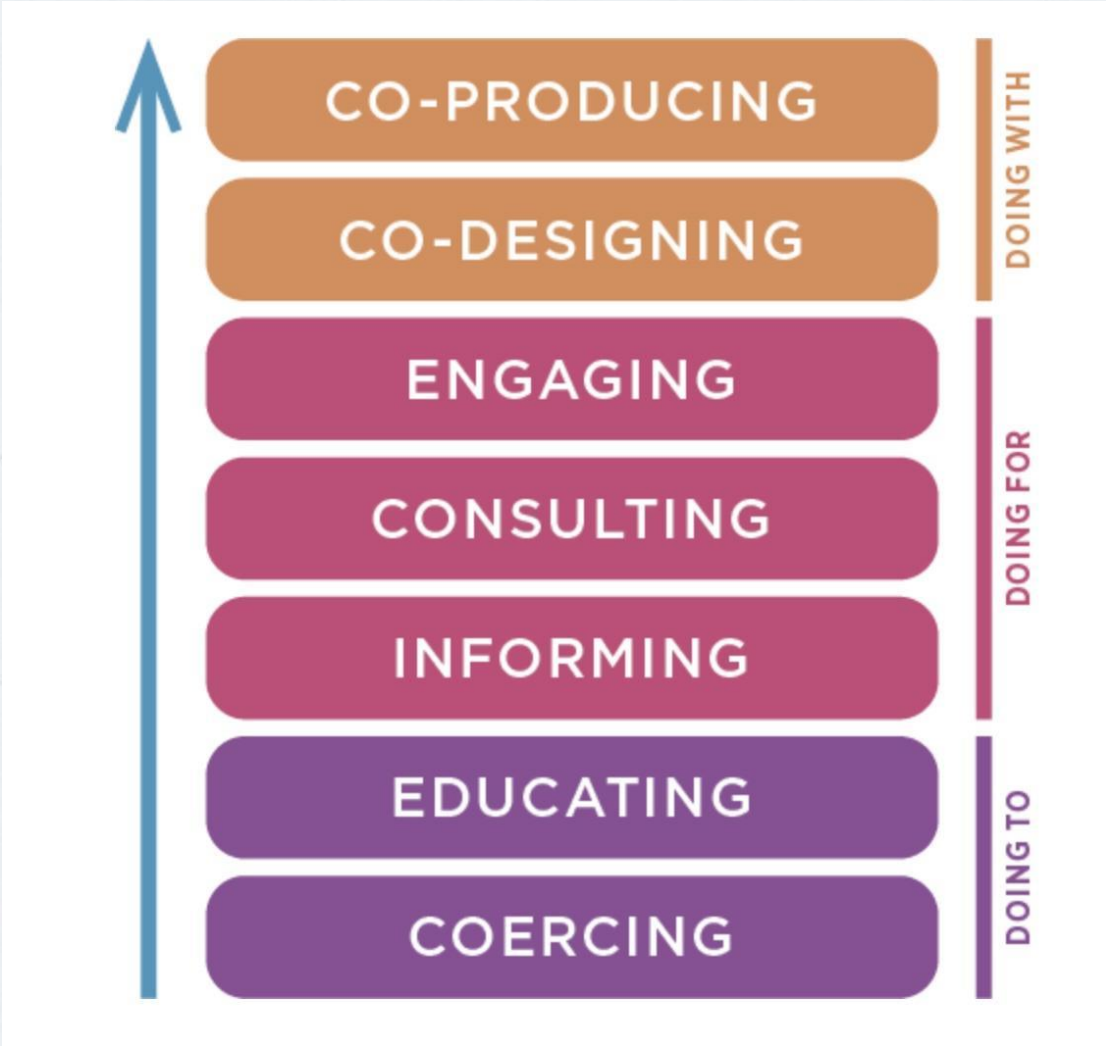


Image Source: The New Economic Foundation, 1998, https://neweconomics.org/uploads/files/e59722efbe227ca37e_4fm6b0lv9.pdf

PATIENT-LED RESEARCH COLLABORATIVE

Key Issues we see in Long COVID research

- Not building off existing research on infection-associated illness.
- Not addressing the relevant symptoms or accounting for post-exertional malaise in study design.
  - Often missing neurological, especially cognitive, PEM, gastro, and reproductive symptoms.
- Not conducting the right tests (see ME/CFS Clinician Coalition).
  - Many standard tests come back normal.
- Using questionnaires re: anxiety and depression that include “palpitations” and “fatigue.”
  - Leads to physical symptoms caused by other factors being attributed to MH issues.

PATIENT-LED RESEARCH COLLABORATIVE

Key Issues we see in Long COVID research

- Need comprehensive selection of patients
  - Most LC patients were not hospitalized; many had “mild” cases.
  - Many didn’t experience respiratory symptoms or were asymptomatic.
  - Many were not PCR positive/antibody positive (must include clinical diagnosis subset).
  - Not enough research on children.
- A control group who never had COVID is nearly impossible. Stop trying!
  - Most COVID cases are unreported + many are asymptomatic.
  - 36% of people with LC, and majority of children, do not seroconvert; and 28% serorevert by 60 days; 60% of mile cases lose antibodies by 6 months.
- EHR data: potential for bias
  - Need representative patient and symptom datasets.
  - ICD 10 Code (U 09.9) is great – **when it's used.**
- Accessibility

PATIENT-LED RESEARCH COLLABORATIVE

Thank you!

https://patientresearchcovid19.com/

@patientled

Michael Sieverts
team@patientledresearch.com

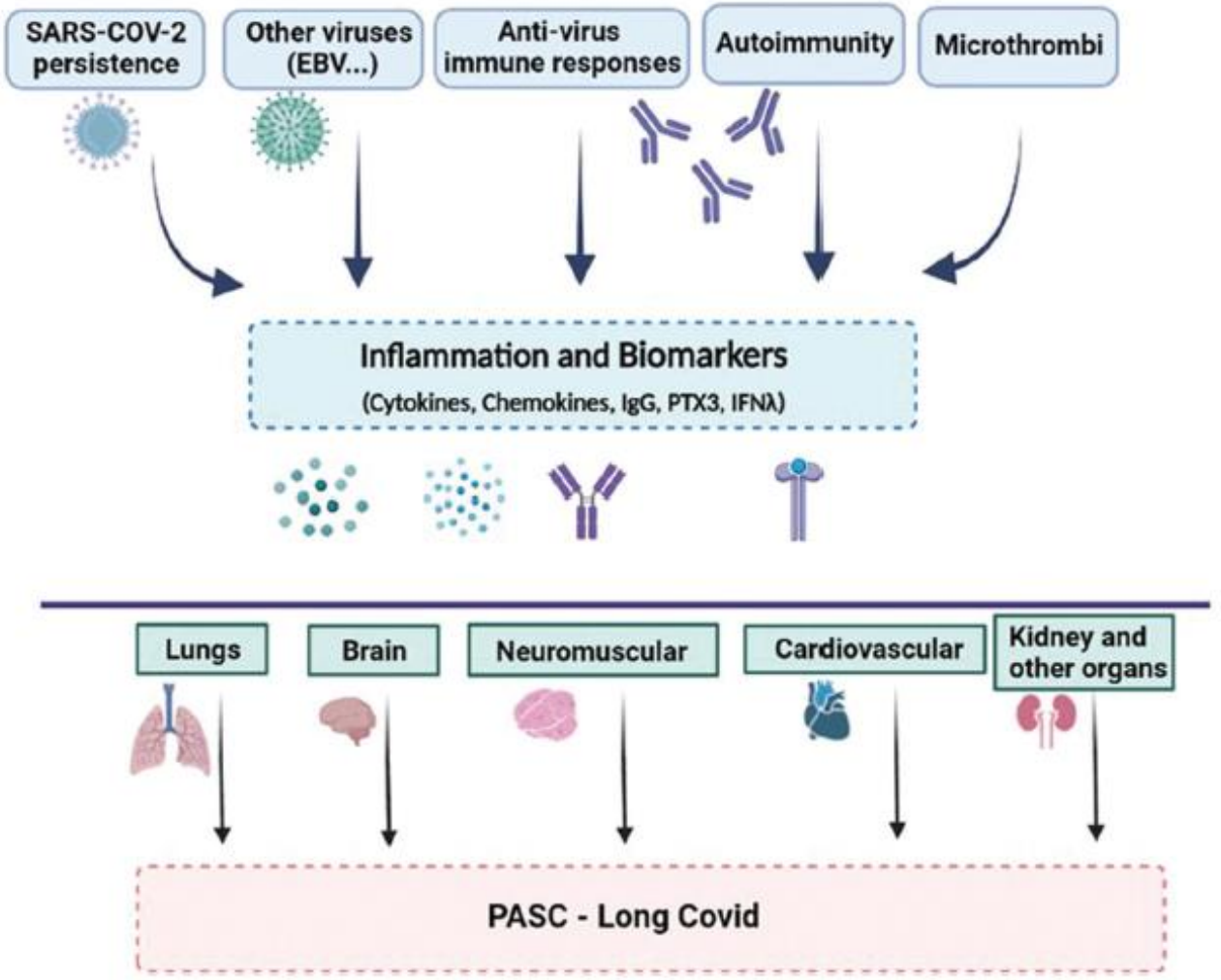
PATIENT-LED RESEARCH COLLABORATIVE

Research Evidence: What we know and do not know in Long COVID

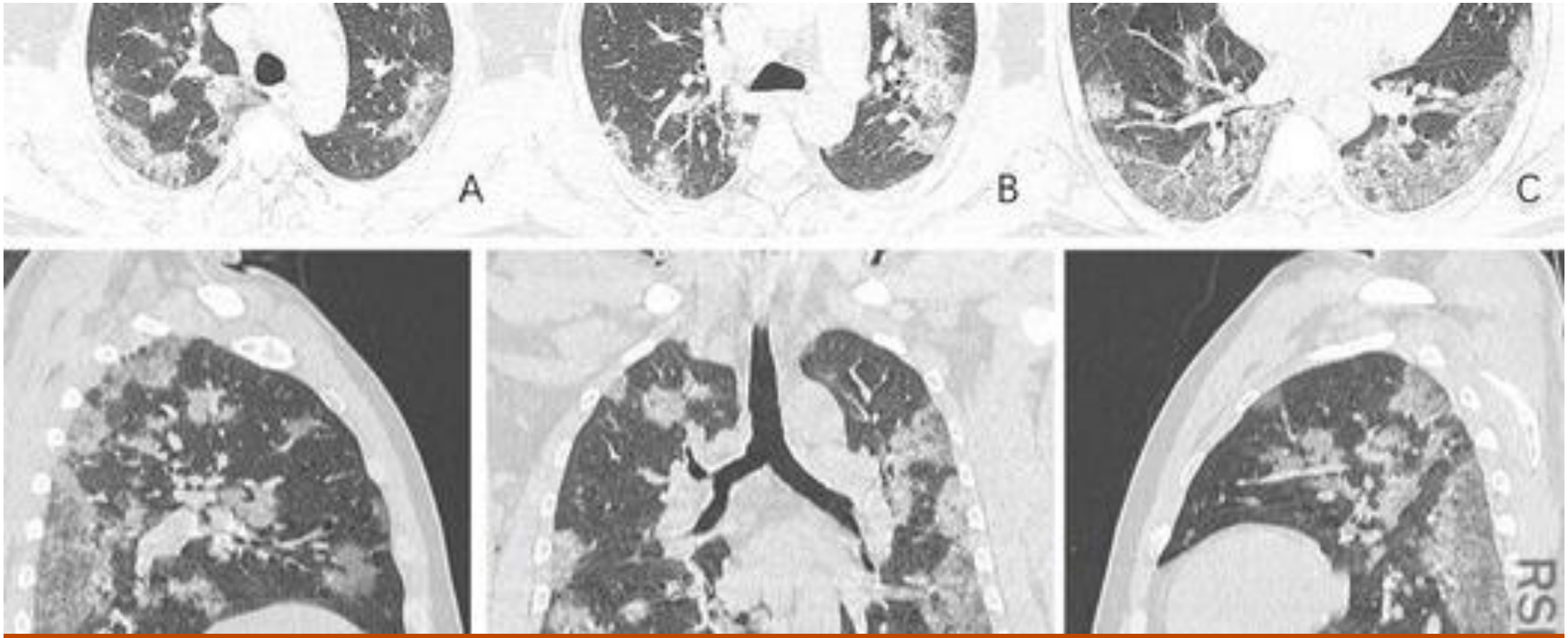
Monica Verduzco-Gutierrez, MD
Professor and Chair
Department of Rehabilitation Medicine
Joe R. & Teresa Lozano Long School of Medicine
UT Health San Antonio
@MVGutierrezMD

UT Health San Antonio

Pathogenesis and Targets of PASC



UT Health San Antonio

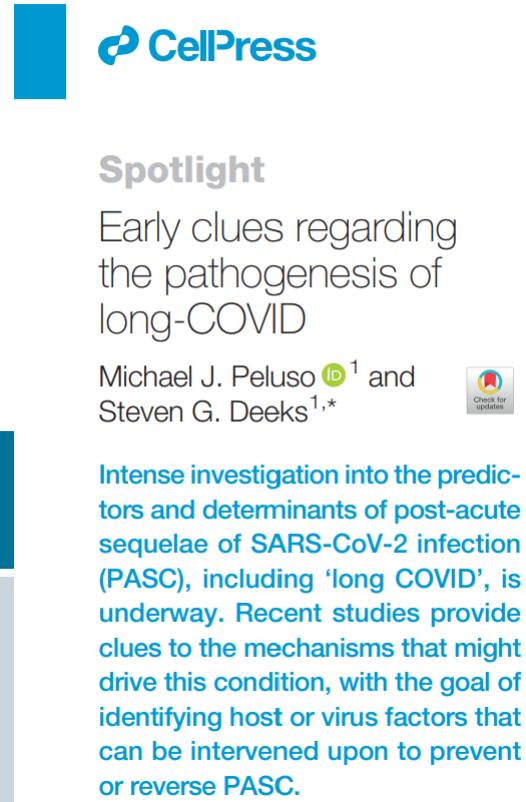


What we know for treatments?

UT Health San Antonio

Long COVID: Mechanisms
Possible therapeutic strategies

Mechanism	Treatment
Acute viral infection with irreversible tissue damage	Prevention Anti-virals Post-acute vaccine Anti-inflammatory drugs Rehabilitation



UT Health San Antonio

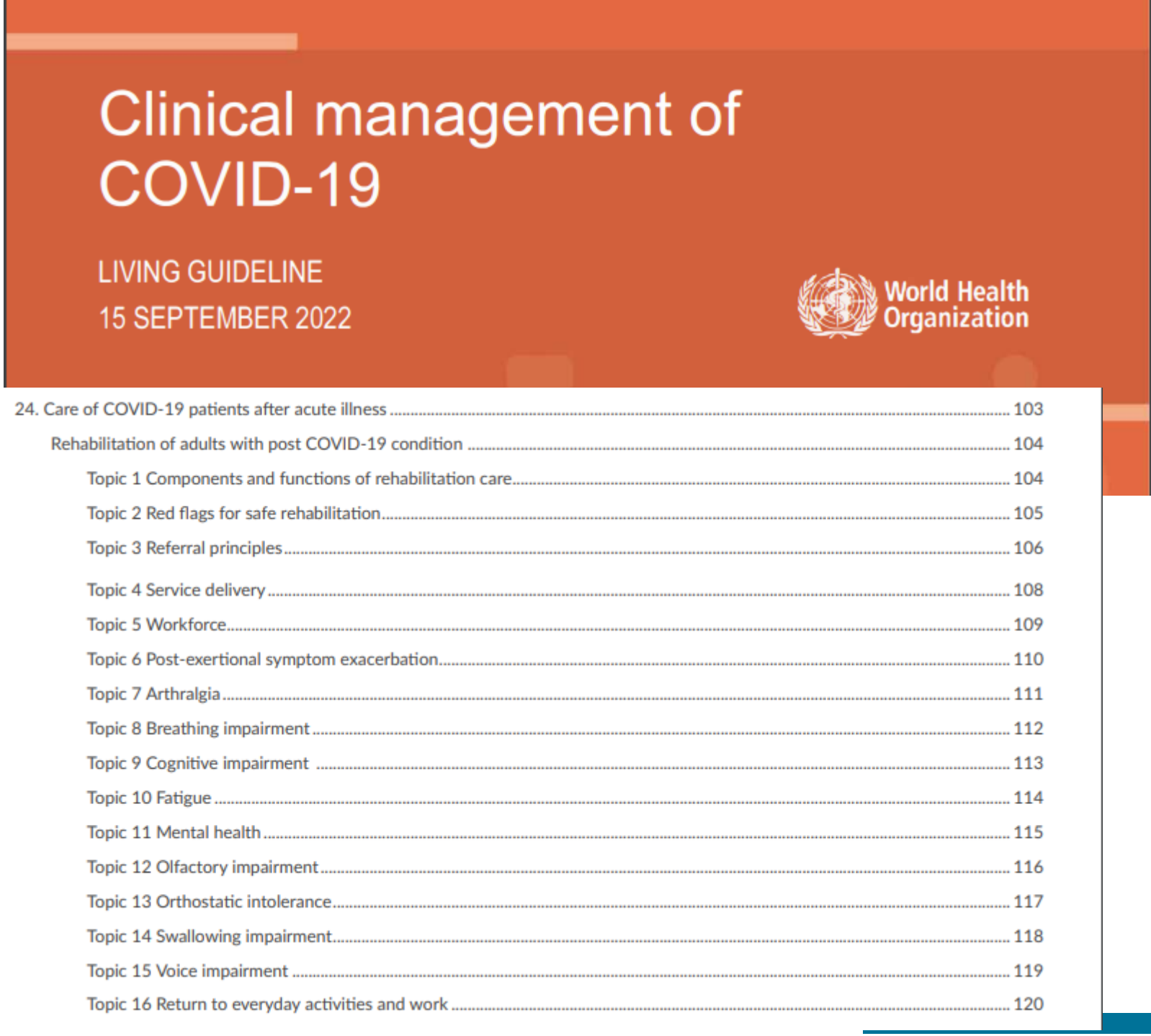
- Components and functions of rehab care
  - Multidisciplinary
  - Continuity & coordination of care
  - People-centered & shared decision-making

- Red flags for safe rehabilitation
  - Exertional desaturation & cardiac impairment should be ruled out before physical exercise

- Post-exertional symptom exacerbation
  - Assess PESE
  - Pacing/energy conservation
  - Graded exercise should NOT be offered

- Orthostatic intolerance
  - Screen
  - Self-management skills

- Return to everyday activities and work
  - Energy conservation, assist products
  - Prolonged & flexible phased RTW



Long COVID:
Mechanism & Possible Therapeutic Strategies

Pathogenesis	Potential Treatment
Persistent microclots/Microvascular disease/Endothelial dysfunction	Anticoagulants, Thrombolytics, dialysis Rivaroxaban, Triple therapy (clopidogrel, ASA, apixaban) EECP
Inflammation - Direct or Indirect	Anti-inflammatories (steroids, colchicine, mAbs), antihistamines, Viral reactivation & Dysbiosis
Viral reservoir/Persistent viral infection and ongoing tissue harm	Anti-virals (Paxlovid, molnupiravir, remdesivir) Virus monoclonal antibodies (ex. Evusheld) Therapeutic vaccine
Autoimmune/Autoantibodies	IVIg, B cell-directed therapies
Acute viral infection with irreversible tissue damage	Rehabilitation
Mitochondrial dysfunction	AXA1125, mito-directed therapies

Currently 75 Clinical Trials for Long COVID in ClinicalTrials.gov

PHIRI
Population Health Information Research Infrastructure

Long COVID: registries, organisation of care & guidelines

Long COVID Webinar – 13 December 2022

sciensano

Gesundheit Österreich GmbH

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 101018317

Aim

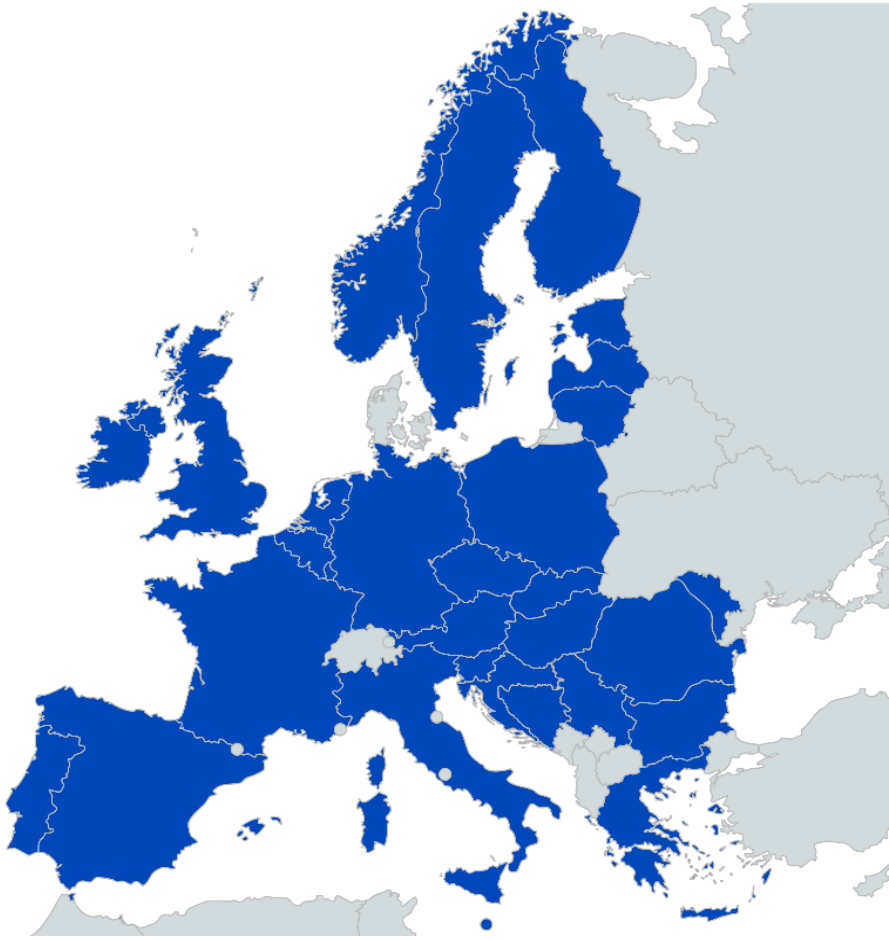
The Population Health Information Research Infrastructure for COVID-19:

- a **European mechanism**, that aims to
- facilitate and support **data-driven population health research**
- and **exchange of best practices**
- to support **decision making**

41 partners

30 countries

3 years



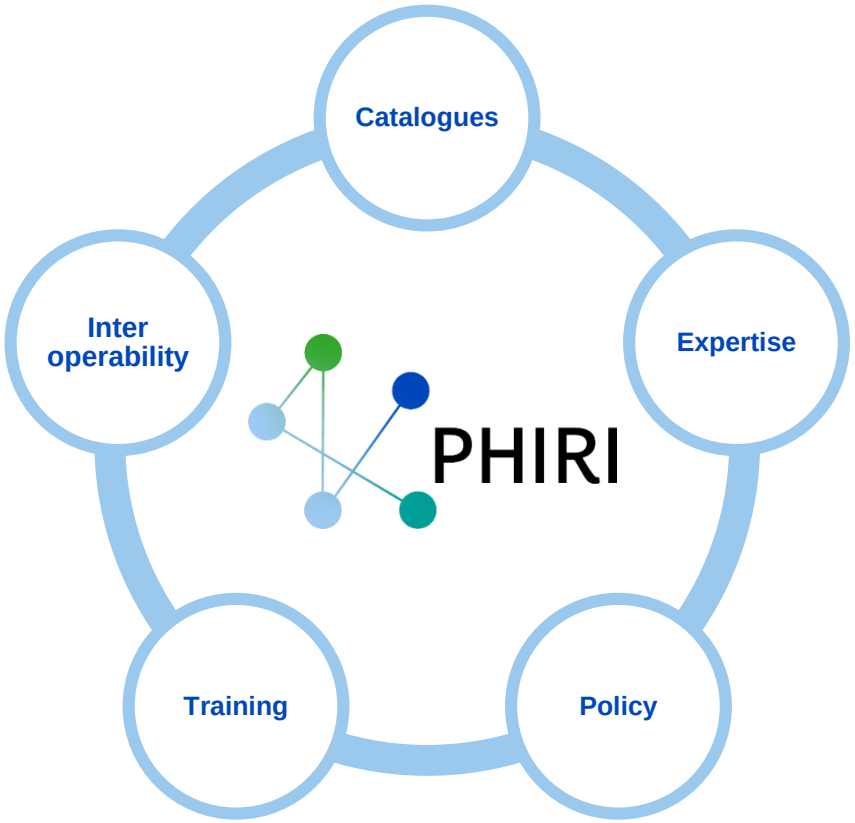
Map of PHIRI Partners

PHIRI
Population Health Information Research Infrastructure

www.phiri.eu

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 101018317

Objectives



1. To provide a **Health Information portal** for COVID-19 with FAIR catalogues. To link different data sources and to use Pan-European data in a GDPR compliant, federated way.

2. To provide structured exchange between countries on COVID-19 **best practices and expertise**.

3. To promote **interoperability** and tackle health information inequalities. PHIRI support COVID-19 research queries and provides **capacity building**.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 101018317

PHIRI's services

HEALTH INFORMATION PORTAL

- Health information sources
- Publications and reports
- International guidelines, initiatives and projects
- Training material and courses
- Ethical and legal tools
- Experts on health topics

FEDERATED RESEARCH

Use cases

- Vulnerable populations
- Perinatal health
- Delayed cancer care
- Mental health

Federated platform for queries

HEALTH INFORMATION SUPPORT

- Rapid exchange forum
- Research methodologies to assess the impact of Covid19
- Foresight: modelling and scenarios
- COVID-19 Health information system assesments

TRAINING

European School on Health Information

- Foresight
- Infodemic management Data hubs developer training
- Health Information System assessments
- Digital tools
- Research methodologies

PHIRI
Population Health Information Research Infrastructure

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Population Health Information Research Infrastructure

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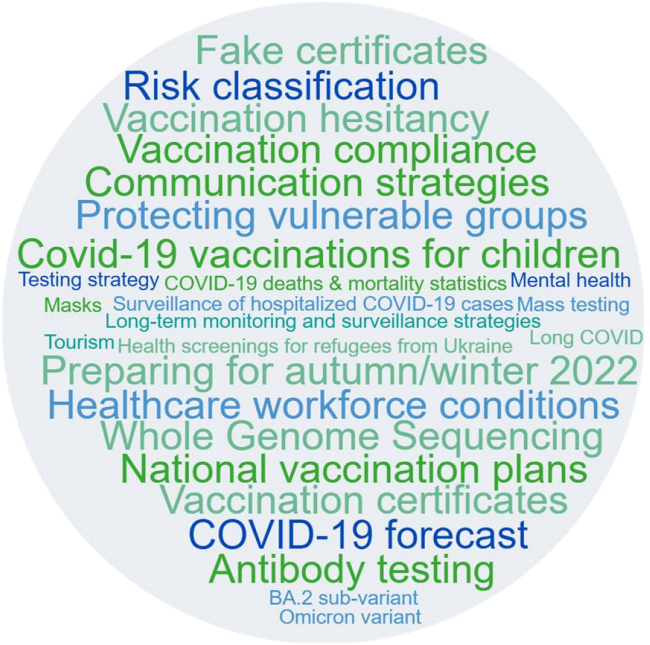
Rapid Exchange Forum

The **Rapid Exchange Forum** is a **structured platform for regular exchange of fellow countries, policy advisors, commission services and researchers** in the joint efforts to manage the COVID-19 pandemic, and increasingly addresses topics beyond COVID-19

Examples of topics addressed:

- Which **indicators and thresholds** are used in order to change the risk level for stricter restriction measures? Dec/Jan 2021
- What are the main measures that MS are putting in place to address **mental health COVID-19 cases**? March 2021
- How does your country organise the treatment/management of **long COVID patients**? April 2021, June 2021, Jan 2022



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How does your country organise the treatment/management of long COVID patients?

April 2021

- Is your country collecting data or conducting studies on long COVID?
- Which guidelines or recommendations are your country following considering the definition, diagnosis and treatment of long COVID?

June 2021

Are there specialised organisations being developed?

- Which professional groups and disciplines are involved?
- How can individuals access the clinics?
- Are the clinics stand-alone entities or part of larger institutions

Jan 2022

Processes for coordinated management of care?

- tools for (differential) diagnosis / symptom screening for clinicians?
- standardised treatment pathways for long COVID patients?
- patient information material about long COVID?
- registries of long COVID patients?

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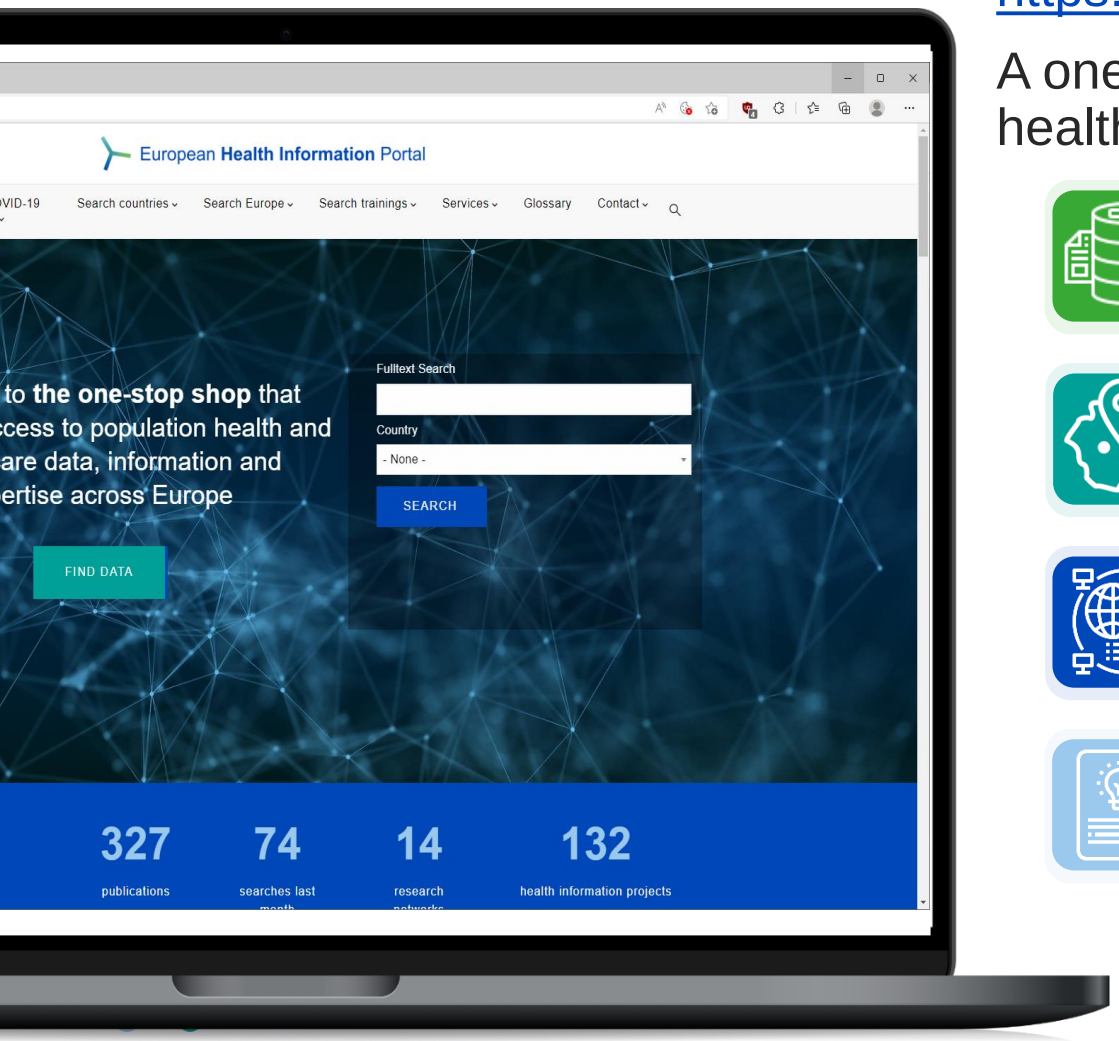
The European Health Information Portal



https://www.healthinformationportal.eu/rapid-exchange-forum

A one-stop shop that facilitates access to population health and health care data, information and expertise across Europe.

- **Health information (data) sources**
- **Publications**
- **Countries and national nodes**
- **Trainings in all areas of population health**
- **Research infrastructures, Research networks**
- **COVID-19 Policy measures**
- **Health information projects**
- **COVID-19 Rapid Exchange Forum**

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Update on Long COVID management - 05-Dec-2022

- Have there been any major changes in your country following your possible original response in early 2022 (29 REF) when it comes to existing or planned processes for coordinated management of care for long COVID patients in your country?
- Specifically, do these processes also relate to tools for (differential) diagnosis / symptom screening for clinicians, and standardised treatment pathways for long COVID patients?
- In addition, could you briefly describe how your country organises the treatment/management of long COVID patients? Specifically, are there specialised clinics/departments/centres and are these clinics stand-alone entities or part of larger institutions such as hospitals or primary care centres?
- Does your country have a registry of Long COVID patients?

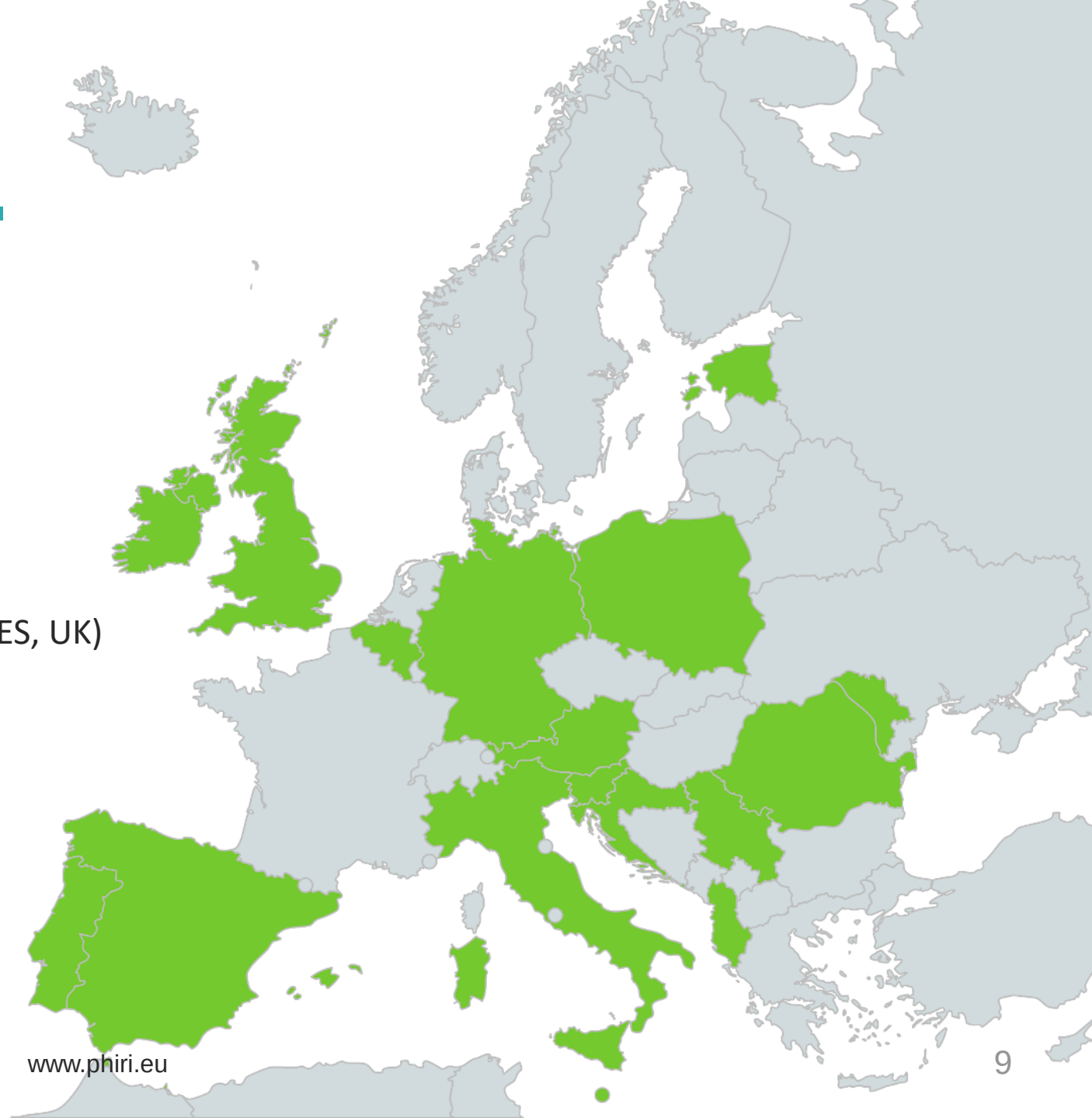
This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 101018317

Responses

17 Country responses

Registries of Long COVID patients?

- Yes (IT)
- No (AL, AT, BE, HR, EW, DE, MD, PL, RO, SI, ES, UK)



Registry long COVID

- IT: The National Center for Disease Prevention and Control (CCM) of the Italian Ministry of Health has a project aims to define a national surveillance system.
  - The data collection form was defined and
  - the clinical centers involved in surveillance were identified.
  - The clinical centers were identified both within the operative units joining in the project and through centers providing assistance for Long CoVID.
  - The data collection form for surveillance has been approved by the ethics committee and is being implemented in its electronic version.
- DE: the BMBF-funded Network University Medicine (NUM) is working on the establishment of a multicenter research registry on Long COVID in children and adolescents.
- Surveys

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 101018317

Organisation of care

- Entry point is General Practitioner
- No specialized centres part of usual hospital activities (BE, EE, MD, RO, RS, UK)
- AT: Entry primary care and “health supply pathway”
- BE: Primary care convention to cover costs primary care. Care coordinator appointed. “post-COVID Care Journey”
- HR: New facilities in September, but no standalone: outpatient facilities and specific clinics.
- DE: specialized post-COVID clinics
- PL: special rehabilitation program for long- and post-COVID patients, referrals until April 2022

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 101018317

Tools for diagnosis / symptom screening and treatment pathways for long COVID patients

- No tool: BE, HR, MD
- No standardized treatment pathway: HR, DE, MD
- The case definition of a post COVID-19 condition presented by the World Health Organization in October 2021 also has a provisional character here and is also only applicable to adults
- AT: Long COVID guideline information and decisions for medical doctors
- EE: Guidelines for primary care
- DE: national guideline for an interdisciplinary, coordinated and structured health care for persons with Long COVID by end 2023 (G-BA)
- DE: National guideline for diagnosis and treatment from medical associations.
- IT: report management principles, symptoms, definition, diagnosis, and treatment published by the Istituto Superiore di Sanità. Also report on good clinical practice
- PL: recommendation on monitoring the health of patients after COVID-19

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Remarks

- An international exchange on "best practice" models for a systematic registration of patients with Long COVID in medical care would be essential.
- Epidemiological and clinical studies as well as basic research will continue to be important to better understand the underlying disease mechanisms and clinical manifestations of Long COVID and to better help patients

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PHIRI

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Thank you for your attention!

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IHME

Long COVID: IHME estimates of three common symptom clusters

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Professor Health Metrics Sciences

December 13, 2022

UNIVERSITY of WASHINGTON

Institute for Health Metrics and Evaluation

Long COVID

WHO clinical case definition:

Newly onset or persisting symptoms **3 months** after an acute episode of COVID-19 which **impact daily functioning** and were **not preexisting** symptoms before SARS-CoV-2 infection.

We chose 3 common symptom clusters:

1. Respiratory symptoms
2. Fatigue with bodily pain and mood swings
3. Cognitive symptoms

Research

JAMA | Original Investigation

Estimated Global Proportions of Individuals With Persistent Fatigue, Cognitive, and Respiratory Symptom Clusters Following Symptomatic COVID-19 in 2020 and 2021

Global Burden of Disease Long COVID Collaborators

Supplemental content

IMPORTANCE Some individuals experience persistent symptoms after initial symptomatic SARS-CoV-2 infection (often referred to as Long COVID).

OBJECTIVE To estimate the proportion of males and females with COVID-19, younger or older than 20 years of age, who had Long COVID symptoms in 2020 and 2021 and assess their symptom severity and expected Long COVID symptom duration.

DESIGN, SETTING, AND PARTICIPANTS Bayesian meta-regression and pooling of 54 studies and 2 medical record databases with data for 1.2 million individuals (from 22 countries) who had symptomatic SARS-CoV-2 infection. Of the 54 studies, 44 were published and 10 were collaborating cohorts (conducted in Austria, the Faroe Islands, Germany, Iran, Italy, the Netherlands, Russia, Sweden, Switzerland, and the US). The participant data were derived from the 44 published studies (10 501 hospitalized individuals and 42 891 nonhospitalized individuals), the 10 collaborating cohort studies (10 526 and 1906), and the 2 US electronic medical record databases (250 928 and 846 046). Data collection spanned March 2020 to January 2022.

EXPOSURES Symptomatic SARS-CoV-2 infection.

MAIN OUTCOMES AND MEASURES Proportion of individuals with at least 1 of the 3 self-reported Long COVID symptom clusters (persistent fatigue with bodily pain or mood swings; cognitive problems; or ongoing respiratory problems) 3 months after SARS-CoV-2 infection in 2020 and 2021, estimated separately for hospitalized and nonhospitalized individuals aged 20 years or older by sex and for both sexes of nonhospitalized individuals younger than 20 years of age.

RESULTS A total of 1.2 million individuals who had symptomatic SARS-CoV-2 infection were included (mean age, 4-66 years; males, 26%-88%). In the modeled estimates, 6.2% (95% uncertainty interval [UI], 2.4%-13.3%) of individuals who had symptomatic SARS-CoV-2 infection experienced at least 1 of the 3 Long COVID symptom clusters in 2020 and 2021, including 3.2% (95% UI, 0.6%-10.0%) for persistent fatigue with bodily pain or mood swings, 3.7% (95% UI, 0.9%-9.6%) for ongoing respiratory problems, and 2.2% (95% UI, 0.3%-7.6%) for cognitive problems after adjusting for health status before COVID-19, comprising an estimated 51.0% (95% UI, 16.9%-92.4%), 60.4% (95% UI, 18.9%-89.1%), and 35.4% (95% UI, 9.4%-75.1%), respectively, of Long COVID cases. The Long COVID symptom clusters were more common in women aged 20 years or older (10.6% [95% UI, 4.3%-22.2%]) 3 months after symptomatic SARS-CoV-2 infection than in men aged 20 years or older (5.4% [95% UI, 2.2%-11.7%]). Both sexes younger than 20 years of age were estimated to be affected in 2.8% (95% UI, 0.9%-7.0%) of symptomatic SARS-CoV-2 infections. The estimated mean Long COVID symptom cluster duration was 9.0 months (95% UI, 7.0-12.0 months) among hospitalized individuals and 4.0 months (95% UI, 3.6-4.6 months) among nonhospitalized individuals. Among individuals with Long COVID symptoms 3 months after symptomatic SARS-CoV-2 infection, an estimated 15.1% (95% UI, 10.3%-21.1%) continued to experience symptoms at 12 months.

CONCLUSIONS AND RELEVANCE This study presents modeled estimates of the proportion of individuals with at least 1 of 3 self-reported Long COVID symptom clusters (persistent fatigue with bodily pain or mood swings; cognitive problems; or ongoing respiratory problems) 3 months after symptomatic SARS-CoV-2 infection.

JAMA. 2022;328(16):1604-1615. doi:10.1001/jama.2022.18931
Published online October 10, 2022.

Authors/Group Information: The authors of the Global Burden of Disease Long COVID study appear at the end of the article.

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jama.com

Long COVID: input data

- Systematic literature review (low yield)
  - 46 published articles from 44 cohort studies
  - Limitations: Single symptoms reported, lack of data on co-occurrence of symptoms
- Administrative data
  - 2 sources: PRA Health Services, Veterans Affairs
  - Advantages: large numbers and ability to define age-sex-race/ethn-comorbid controls
  - Limitations: symptoms based on ICD-10 codes
- Collaborating cohorts with individual record data available
  - 10 ongoing cohort studies (RUS, IRN, USA, ITA, NED, SWE, CHE, AUT, DEU, Faroe Isl)
  - Able to quantify frequency and overlap of disabling symptom clusters
  - 4 of these explicitly asking about general health status/symptoms prior to COVID-19

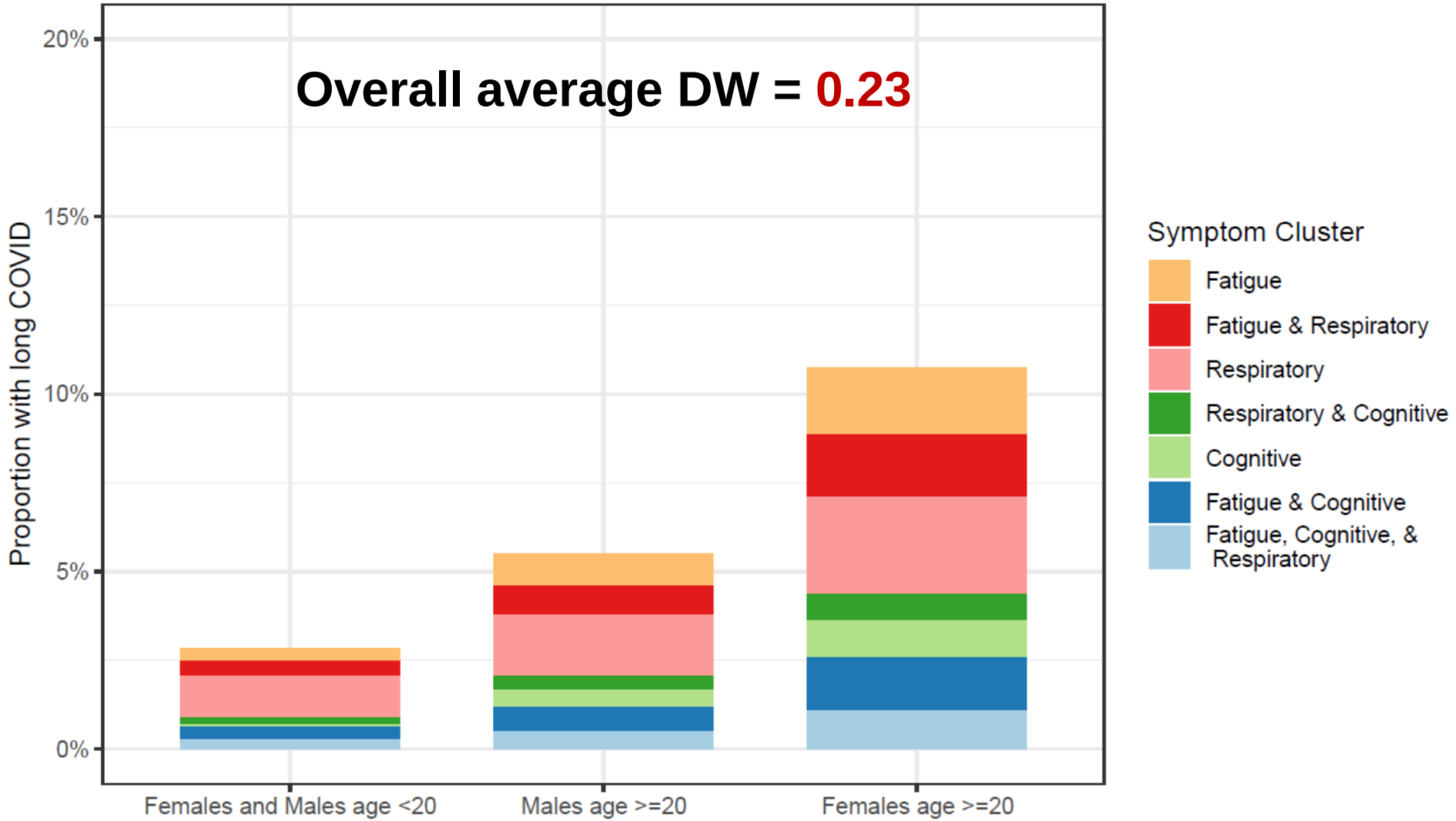
Symptom cluster health states

Outcome	Lay description	DW* (95% UI)
Mild respiratory symptoms	has cough and shortness of breath after heavy physical activity but is able to walk long distances and climb stairs.	0.019 (0.011 – 0.039)
Moderate respiratory symptoms	has cough, wheezing and shortness of breath, even after light physical activity. The person feels tired and can walk only short distances or climb only a few stairs.	0.225 (0.153 – 0.310)
Severe respiratory symptoms	has cough, wheezing and shortness of breath all the time. The person has great difficulty walking even short distances or climbing any stairs, feels tired when at rest, and is anxious.	0.408 (0.273 – 0.556)
Mild cognitive symptoms	has some trouble remembering recent events and finds it hard to concentrate and make decisions and plans.	0.069 (0.046 – 0.099)
Severe cognitive symptoms	has memory problems and confusion, feels disoriented, and needs help with some daily activities.	0.377 (0.252 – 0.508)
Fatigue syndrome	is always tired and easily upset. The person feels pain all over the body and is depressed.	0.219 (0.148 – 0.308)

* Disability weights (DWs) quantify health loss as a fraction of time lived within a health state (1 is full health; 0 is complete loss of health). For severe cognitive symptoms of long COVID we use the health state of moderate cognitive problems that is also used in GBD for moderate dementia.

Proportions of surviving, symptomatic COVID-19 cases with long COVID symptom cluster(s) at 3 months after infection in 2020-2021

Children: 1/40
Men: 1/20
Women: 1/10



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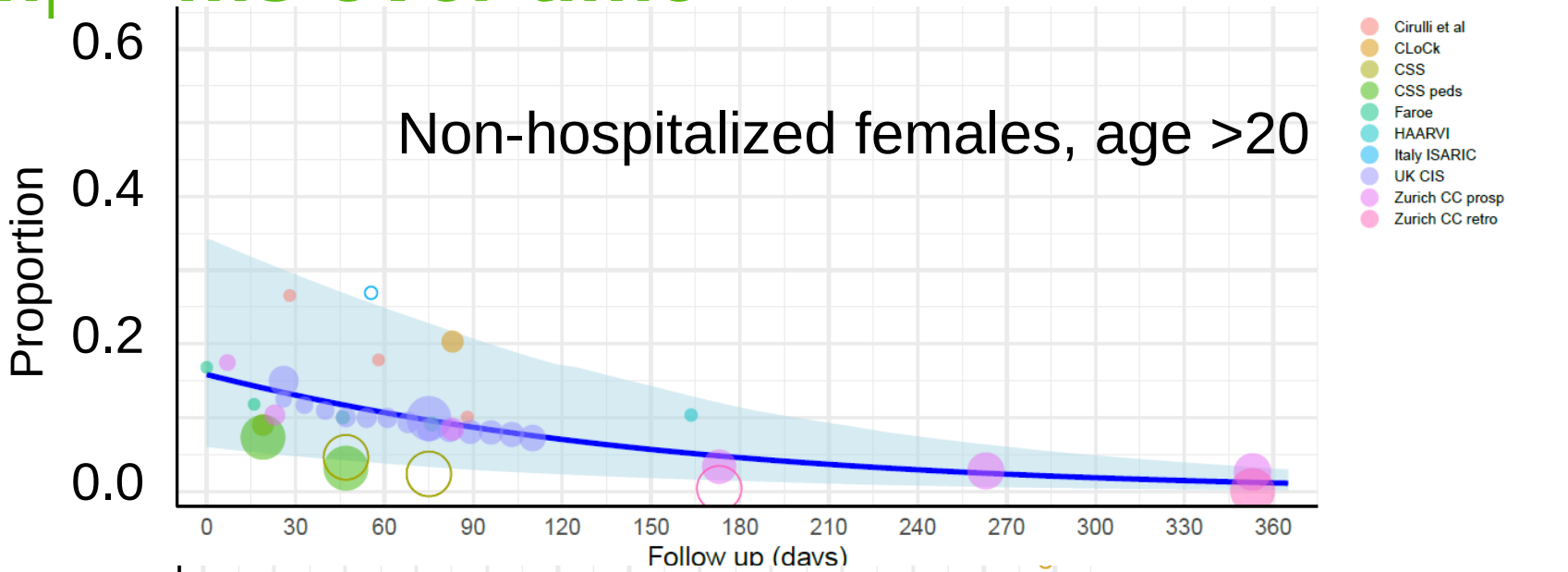
Fatigue = persistent fatigue with bodily pain/mood swings; Respiratory = respiratory problems; Cognitive = cognitive problems

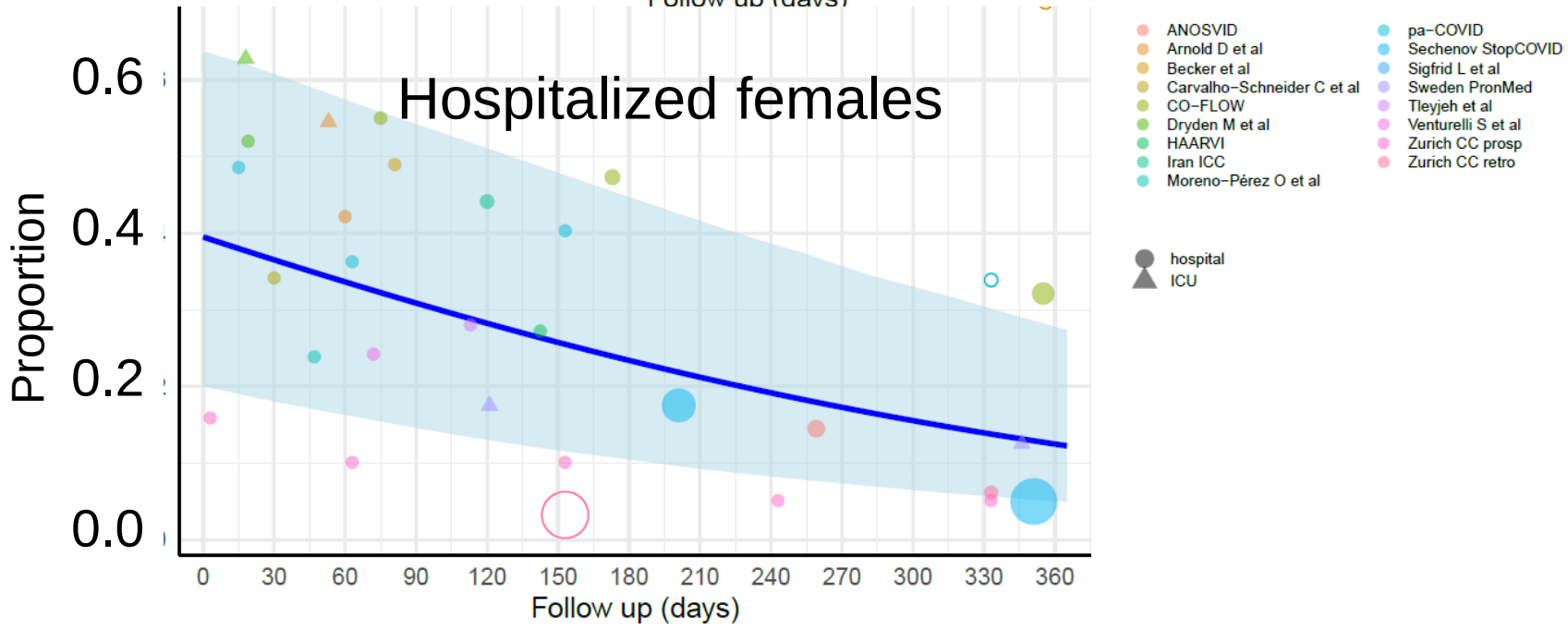
Long COVID: symptoms over time

15% of those who develop long COVID still have symptom cluster(s) at **12 months**

→How many become chronic?

→Need data with longer follow-up





Long COVID: 2020-2021 results

145 million (95% UI 55-312M) new cases of Long COVID **globally** in **2020-2021**

- **90%** from non-hospitalized cases of COVID-19 (130 million)
- **64%** females (92 million)
- 41M in 2020, 94M in 2021

5.6 million (2.2 – 11.0) new cases of Long COVID in **EU countries** in **2020-2021**

(we have estimates by age, sex and year for all countries)

Long COVID: 2022 results (preliminary)

Omicron variant and effect of vaccination (based on single study from UK so far)

- Lower risk of Long COVID: ~1/3 the risk of previous variants (~1/4 if recently vaccinated)

94 million (95% UI 36-182M) new cases of Long COVID in **2022** globally, compared to 104 million in 2021

In EU countries in 2022 we expect 8.0 million (3.2 – 15.9) new cases of Long COVID

In progress: data seeking for more follow-up of omicron cases and impact of vaccination and immunity from (re)infection

Limitations

- Sparse, heterogeneous data → wide uncertainty
- Incomplete follow-up to determine ‘tail’ of duration, particularly in hospitalized cases; so far, three cohorts with 12-month follow-up
- Does not include increased risk of other diseases
- Have not included all symptoms of long COVID but detailed analysis of largest and most complete cohort suggests we have captured almost all more severely affected cases
- Relatively few studies from low/middle-income countries
  - But long COVID is present where studied (e.g. published studies from India, Brazil, Bangladesh, South Africa)

Implications

- Considerable risk of on-going symptoms after acute SARS-COV2 infection
- Highest risk in females
- Majority of cases in people of working age
- Recovery for the majority of long COVID cases within a year
- … but around 15% of those qualifying for long COVID at 3 months are still a case at 12 months
- Considerable support (rehab, income) required as well as help to transition back into the workforce (or education) when symptoms start to wane
- Trigger to better understand the mechanisms leading to long COVID: genetic, auto-immune, persistent virus ……
- A better understanding will hopefully lead to interventions that are more than ‘supportive’ ….and may also be beneficial to other post-infection syndromes and chronic fatigue