



Long COVID

Dr Gail Carson on behalf of the GloPID R Science Secretariat
gail.carson@ndm.ox.ac.uk

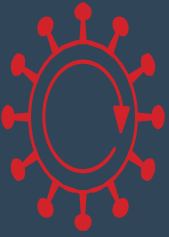
The Secretariat is supported by the European Union's Horizon 2020 Research and Innovation Programme under GloPID-R SEC 2 Grant Agreement no. 874667.

Summary of the Long COVID Forum

Long COVID forum update
9 - 10 December 2020
Dr Gail Carson, GloPID-R &
ISARIC



#LongCovidForum #GLOPIDR #ISARIC
www.glopid-r.org www.ISARIC.org LongCovid.org



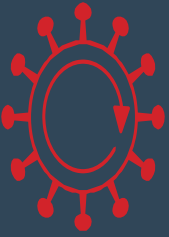
Nothing about us without us

Fantastic to hear from people living with Long COVID, clinicians and researchers from around the world (16 countries, agenda). Co chairs included research funders and the WHO. Joined by almost 900 people (1,400 registered) over the 2 days and over 7,400 views on YouTube so far.

Dr Tedros opened the meeting and used the three R's in relation to Long COVID:

- **Recognition**
- **Research**
- **Rehabilitation**





‘Nothing about us without us’

1) What is causing my illness?

Why me? Why did I get it? Why do others recover quickly?

Is the virus still there? Autoimmunity? What investigations do I need?

2) How do I recover?

Can somebody help me? How do I get my life back? Medications? Rehab? What? Where? How to get? Some people have to pay for their health care or medication. What should I do NOW? Can we be re-infected? What about Vaccination? Shielding?

3) Concern for others

How many others are affected? How to prevent others from getting this? Can early treatment lessen the severity of Long COVID?

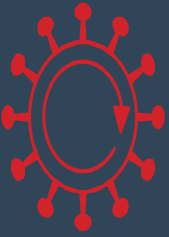
4) How to define Long COVID (case definition and clinical features) count it?

Need a systematic way to define cases - Does the case definition for COVID testing need to be broader?

One/many conditions?

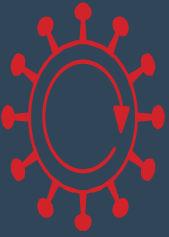
Patterns to predict progression?

Long-term disability and mortality?



‘Nothing about us without us’

- 5) Children and Long COVID does occur but less well recognised
- 6) Long COVID and people living with other conditions, e.g. HIV, TB.
 - Lessons learnt from following up other illnesses such as Ebola, HIV, chikungunya
- 7) Mental health impact possibly direct effect of virus, and consequence of effect on quality of life, loss of earnings, relationship breakdown etc.
- 8) The need for early interventions studies – (e.g. ANTICOV, Principle study)



Whilst so much good work is being done, it is **striking how much we do not know**:

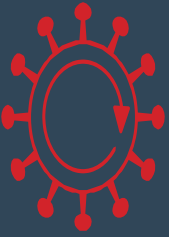
Only **45/5000+** COVID-19 research projects are looking at Long COVID

How many of these are focused only on post-hospitalised patients?

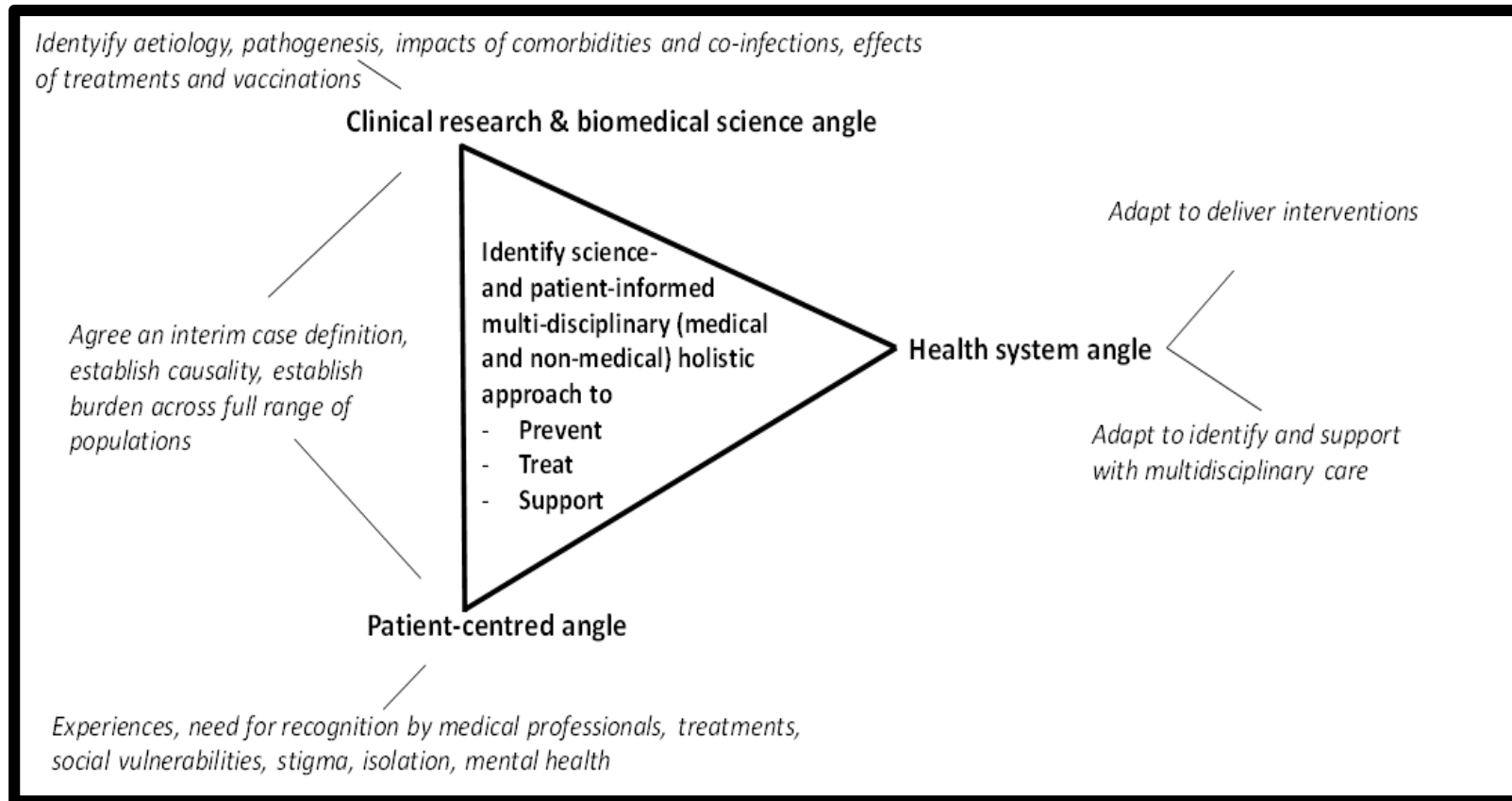
Not a single study into the long-term effects in children!

Results from living systematic review:

- *Need clear **case definition***
- *High quality **case-controlled studies** to establish causal links*
- *Need to **include younger patients and children, data from LMICs and those managed in the community***



Lancet ID Feb 4th 2021 Olliaro et al



Research priorities for Long Covid: refined through an international multi-stakeholder forum

Gail Carson* and Long Covid Forum Group

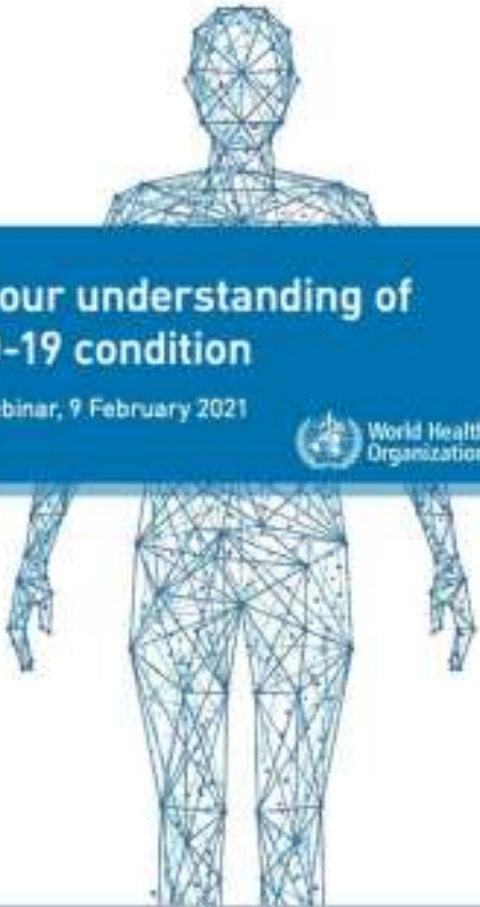
Carson and Long Covid Forum Group *BMC Medicine*
<https://doi.org/10.1186/s12916-021-01947-0>



Table 1 Research priorities identified at the Long Covid Forum. Framework for identifying research needs from the Long COVID Forum

Research priorities (aligned to the WHO mid-term and long-term research priorities: 2019 novel coronavirus [4])	Identified sub-priority for Long Covid	Populations (multi-country studies needed)
Virus: natural history, transmission and diagnosis	<ul style="list-style-type: none"> - Identify pathogenesis - Investigate the impact of chronic and acute co-infections 	Hospitalised patients; non-hospitalised patients; clinical diagnosis only; individuals; children; vulnerable communities; resource-constrained populations
Epidemiological studies	<ul style="list-style-type: none"> - Define the clinical presentations of Long Covid and characterise the burden and spectrum of Long Covid across populations according to clear case definition - Determine any associations between host genetic factors and Long Covid 	
Clinical characterisation and management	<ul style="list-style-type: none"> - Agree case definition and diagnosis - Establish causality - Relationship between acute disease and Long Covid development - Describe underlying mechanisms to identify potential therapeutic targets - Investigate pathogenesis to explain, e.g. thrombotic tendencies, organ impairment - Investigate the impact of chronic and acute co-infections and co-morbidities - Characterise mental health and neurological impacts 	
Candidate therapeutics R&D	<ul style="list-style-type: none"> - Investigate antiviral and anti-inflammatory therapeutics and therapeutic timings to prevent Long Covid - Investigate therapeutics to treat Long Covid symptoms and non-pharmaceutical interventions 	
Candidate vaccines R&D	<ul style="list-style-type: none"> - Investigate the impact of COVID-19 vaccination on people with Long Covid - Investigate whether vaccination prevents Long Covid - Investigate re-infection in people with Long Covid and impact on vaccine priority list 	
Social sciences in the outbreak response	<ul style="list-style-type: none"> - Health systems research on identifying and supporting Long Covid cases (through holistic care) 	

WHO Post COVID-19 Condition: updates on work areas



Expanding our understanding of Post COVID-19 condition

Report of a WHO webinar, 9 February 2021



Next webinar scheduled for 15 June 2021

- Share **Clinical case definition** (preliminary results of Delphi survey).
- Focus on **pathophysiology** and mechanisms.
- Simultaneous **working groups** on mechanisms and care models.

Expanding our understanding of Post COVID-19 condition

Tuesday, 15 June 2021, 13:00 – 16:00 CET WHO EB Room



2nd webinar 4 June 2021

Expanding our understanding of Post COVID-19 condition

2nd webinar

15 June 2021, 13:00-16:00 CET

WHO Executive Board Room, Geneva HQ and Zoom

Meeting background and agenda

Background

As of June 2021, over 170 million confirmed cases of COVID-19 and over 3.5 million deaths have been reported to WHO (<https://covid19.who.int>), although Institute for Health Metrics and Evaluation (IHME) estimates greatly surpass these figures (<https://covid19.healthdata.inglobal.com/>). The estimate of total persons affected with sequelae after experiencing COVID-19 remains unknown, but published reports identify that about 10% or more COVID-19 patients experience lingering symptoms for weeks/months after acute SARS-CoV-2 infection, identified under the umbrella Post COVID-19 condition or related terms. After a successful first WHO webinar held on 9 February 2021 on Post COVID-19 condition, focusing on recognition and burden, WHO conducted a Delhi survey to come to a consensus on the clinical case definition of Post COVID-19 condition.

This second WHO webinar will present the consensus clinical case definition from the global Delhi exercise, and then expand on understanding the mechanisms that may cause Post COVID-19 condition, and the care models to manage it. We all recognize that "without an established mechanism, there will be no COVID-19 new treatments".

There are at least seven mechanisms to be considered: inflammation/hyperinflammatory state; immune dysregulation/autoimmune; coagulation/hemostasis; direct viral toxicity/viral persistence/long-term infection; autonomic dysfunction/neurologic; endocrine/metabolic; and maladaptation of the ACE2 pathway. Likely, many interact synergistically. Thus, this global meeting brings together stakeholders to advance the field in solidarity.

Objectives of the meeting

The objectives of this second WHO webinar are to:

1. Present the WHO clinical case definition of Post COVID-19 condition and other global activities to advance our understanding of Post COVID-19 condition.
2. Present up-to-date research on Post COVID-19 condition with a special focus on pathophysiology and care models, and other large observational studies, with presentations

from public health and clinical researchers, patient representatives and key partner organizations.

3. Convene parallel panel sessions to further explore bringing pathophysiology into our clinical understanding of Post COVID-19 condition and on care models, to develop research priorities.

Methods

An inclusive and participatory manner is being adopted in this series of seminars. Participants have been invited via clinical networks, research networks and collaborating centres, and speakers selected to present findings from clinical and laboratory experience, and population studies from systematic literature searches and through our partners. Working groups will be assembled with multidisciplinary panels to delve into pre-specified questions, led by two chairs (one external and one WHO). We are suggesting a listing of independent preferences identified and considered together, for any cross-fertilization during joint working group discussions. Similar to the first WHO webinar in this series, the outcomes of the plenary sessions and working groups will be published as a meeting report and other deliverables. WHO has collected, evaluated and managed conflicts of interest for all speakers and working group panelists.

Agenda

Time (CET)	Topic	Speakers
Plenary session		
13:00-13:15	Welcome remarks	Dr Tedros Adhanom Ghebreyesus Director-General, WHO
Part 1: Post COVID-19 condition: scene setting and lessons learned on mechanisms		
13:15-13:30	WHO updates: clinical case definition and monitor Post COVID-19 condition	Dr Janet Diaz Health Care Readiness, WHO
13:30-13:38	Ten things we can learn from Long Covid	Dr Nilsen Alvan Southampton, United Kingdom
13:38-13:46	Immunology and mechanisms (I): children	Professor Petter Brodin Karolinska Institutet, Sweden
13:46-13:56	30-day persistent symptoms and new complications in SARS-CoV-2 infected children: the global PERM COVID-19 prospective cohort study	Anna L. Funk, PhD Calgary, Alberta, Canada
13:56-14:06	Higher level and combinations of COVID-19 mechanisms	Professor Maximilian Ackermann Wuppertal, Germany
14:06-14:16	Published cohorts from Bangladesh	Dr Reza Mahmud Dhaka, Bangladesh

14:16-14:20	Published cohorts from South Africa	Dr Murray Dryden Johannesburg, South Africa
14:20-14:30	Immunology and mechanisms (II): infection	Professor Akiko Iwasaki Yale University, New Haven, United States of America
14:30-14:40	Funding opportunities	Professor Charu Kaushic McMaster University, Hamilton, Canada
14:40-14:45	Summary of Part 1 and Q&A	Professor Joan B Soriano Health Care Readiness, WHO
14:45-14:50	Break	

Part 2: Two parallel sessions: small group panels and discussion sessions

14:50-15:45	Group I: Pathophysiology Chaired by: Dr Manu Shankar-Hari (United Kingdom) Dr Soumya Sureshbabhan (WHO)	Questions: - Are we able to describe the natural history of COVID-19, the recovery period and when it inserts into the Post COVID-19 condition? - Are we any closer to understanding the etiology and pathophysiology of Post COVID-19? - Have we identified any pathophysiological steps where interventions may be focused on? Research priorities Open forum for questions and answers.
14:50-15:45	Group II: Care models Chaired by: Dr Colin Brown (United Kingdom) Dr Antony Duffine (PAHO)	Questions: - Care Models in Primary (with/without Hospital care)? - How to succeed in integrated care? - Advance secondary or tertiary care needs - Case studies for success Research priorities Open forum for questions and answers.
Part 3: Wrapping up and Closing remarks		
15:45-15:55	Wrapping up, instructions, calendar	All working group chairs
15:55-16:00	Closing remarks	Dr Michael J Ryan Health Emergencies Programme, WHO

[2021 NIH-Wide COVID-19 Strategic Plan](#) (PDF | 13 MB) outlines our plans to address the most recent challenges of COVID-19, such as Post-Acute Sequelae of SARS-CoV-2 Infection (PASC), or Long COVID, and SARS-CoV-2 variants.

Our work continues to be guided by five strategic priorities.



Priority 1: Improve Fundamental Knowledge

of SARS-CoV-2 and COVID-19 disease progression, outcomes, and recovery



Priority 2: Advance Research to Improve Detection

by developing and validating new assays and retooling existing diagnostic platforms



Priority 3: Support Research to Advance Treatment

by evaluating new or repurposing existing treatments and defining implementation strategies



Priority 4: Accelerate Research to Improve Prevention

by developing vaccines, other methods to prevent transmission, and implementation models



Priority 5: Prevent and Redress Poor COVID-19 Outcomes

in health disparity and vulnerable populations



2021 NIH-Wide Strategic Plan for COVID-19 Research

NIH has made incredible progress toward understanding, diagnosing, treating, and preventing SARS-CoV-2 infection and COVID-19.

[READ THE PLAN](#) >

[Back to top](#)

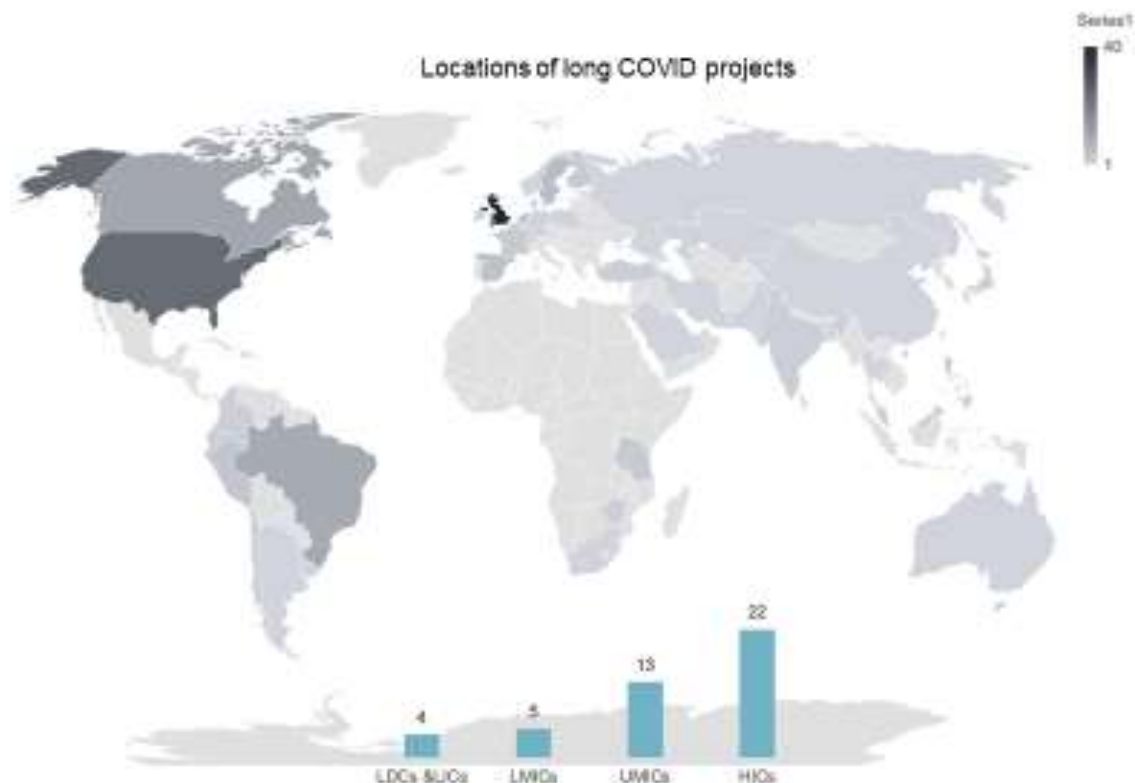


Long COVID projects
June, 2021

Introduction

- Total projects as of 15th April, 2021:
 - 10,608 projects
 - Research involved 142 countries
 - Funding investment of at least \$4.7bn
 - 201 funders

- Long COVID projects:
 - 121 long COVID projects
 - Funding investment of at least: \$205.1m
 - Research involved 44 countries
 - 42 funders

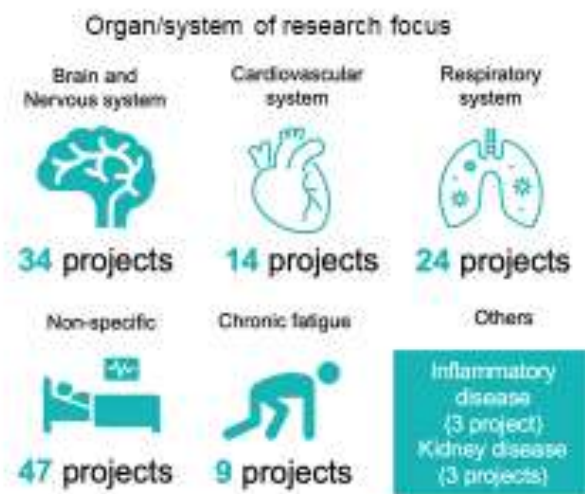


Research focus and study populations

- Most projects investigate the spectrum of long COVID symptoms
- No projects assess impact of vaccination on long COVID
- 6 projects involve on paediatric populations
- 90% of projects in human subjects (in confirmed positive cases)

Human populations	
community cases	26 projects
Hospitalised patients	31 projects
<u>Non-specific</u>	<u>63 projects</u>

Some projects fall under more than one area



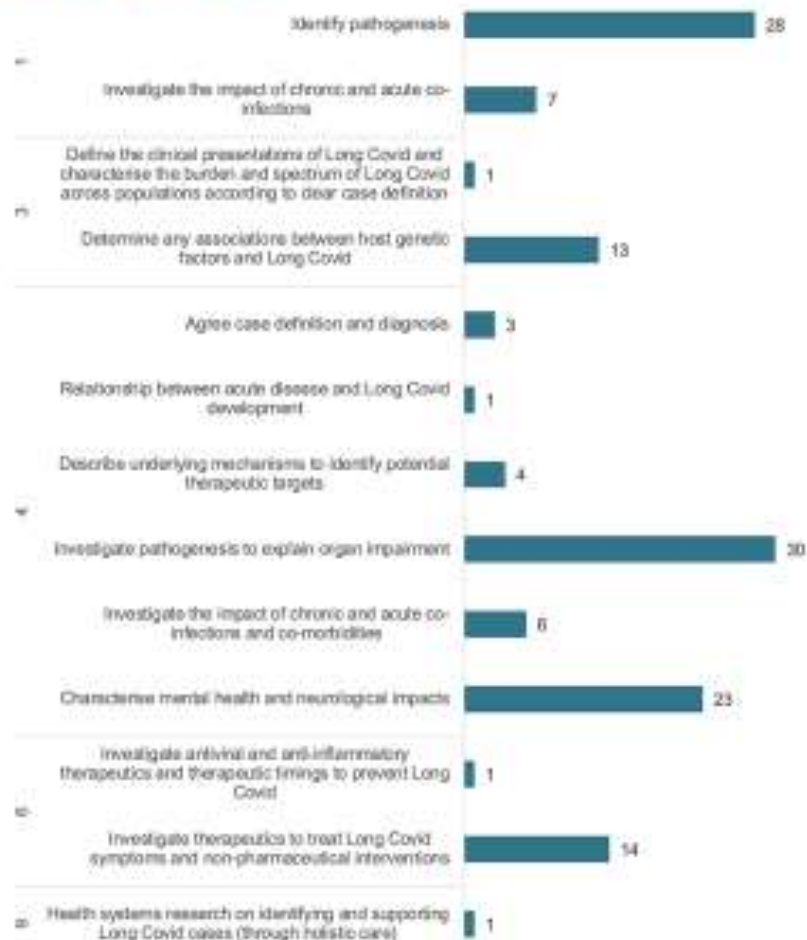
Some projects fall under more than one area

Research focus	Number of projects
Spectrum of long-term symptoms	47
Management	28
Pathogenesis	35
Risk factors	29
Prevalence	15
Prevention	2
Diagnosis	7

Some projects fall under more than one area



Projects mapped to the long COVID research priorities





**“Act before disease becomes persistent through long
delays”**

OVID

Roman poet, a long time ago