



# WHO activities for post COVID-19 condition

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**WEDNESDAY 17 AUGUST 2022, 1:30 – 3:30 Central European Time**

# Post COVID-19 Condition (PCC, Long COVID)

## Global Burden of Disease

- IHME estimates that **3.92 billion** individuals were infected with SARS-CoV-2 through the end of 2021 and that **3.7% (144.7 million : 55 – 313)** developed **PCC as defined by the WHO case definition**
  - Three symptom clusters: **fatigue, cognitive problems and shortness of breath.**
  - **Females** and those with more **severe COVID-19** with more episodes.
  - Median duration **4 months** (IQR 3.84-4.20) in community infections and **9 months** (IQR 2.31 – 8.72) in hospitalized patients.
  - **15.1% (21 million)** had persistent symptoms **12 months.**
  - Average disability weight equivalent to severe neck pain, Crohn's disease, and long-term consequences from traumatic brain injury.

# Post COVID-19 condition

## Milestones



**9 February 2021**  
**Webinar 1:**  
Expanding our understanding:  
**Recognition**

**15 June 2021**  
**Webinar 2:**  
Expanding our understanding:  
**Research**

**6 October 2021**  
**Webinar 3:**  
Expanding our understanding:  
**Rehabilitation**

**1 March 2022**  
**Webinar 4:**  
Expanding our understanding:  
**Neurology and mental health**

**17 August 2022**  
**Webinar 5:**  
Expanding our understanding:  
**Children and young people**

**May 2020**  
1st publication with guidance on post COVID-19 condition



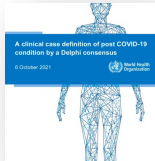
**September 2020**  
ICD published  
**Post COVID-19 condition**



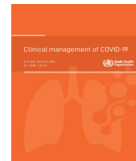
**Feb 2021**  
post COVID-19 CRFs and platform



**6 October 2021**  
WHO published Post COVID-19 clinical case definition



**December 2021**  
WHO SC met to discuss update to clinical guidelines



**January 2022**  
1st GDG for rehabilitation guidelines



**May 2022**  
WHO SC for Post COVID-19 case definition for children and young people

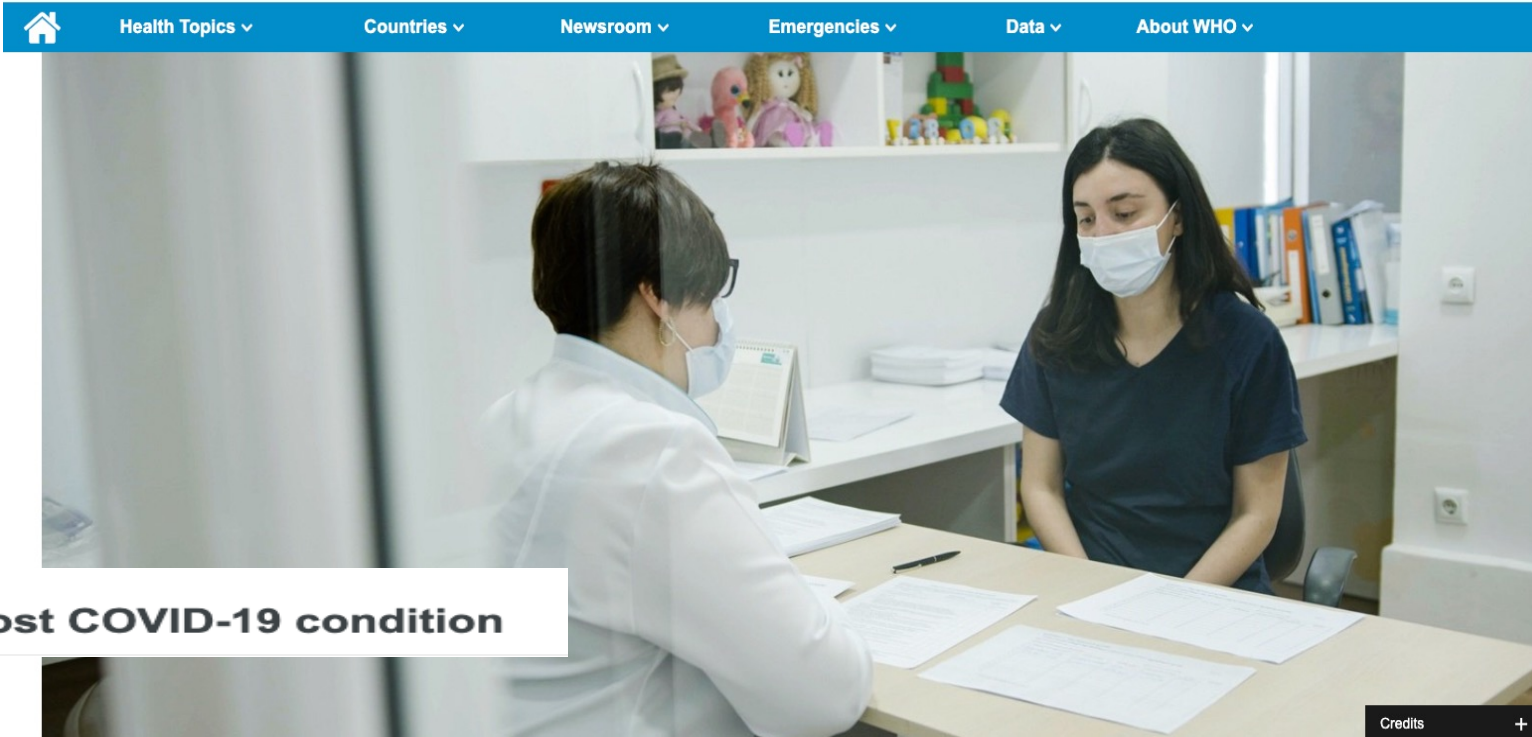


**June 2022**  
Post COVID-19 core outcome set (COS) published

THE LANCET  
Respiratory Medicine

# Post COVID-19 condition

## WHO new updated website



- Post COVID-19 case definition
- Webinar recordings
- Clinical management guidelines & tools
- Research publications
- COVID-19 clinical platform
- Resources for health workers
- Resources for families

<https://www.who.int/teams/health-care-readiness/post-covid-19-condition>

# Post COVID-19 condition

## Clinical management guidelines: care after acute illness (May 2020)

### Clinical management of COVID-19

LIVING GUIDELINE  
23 JUNE 2022



**Stress importance for integration of care into primary care and using an integrated, multidisciplinary care model.**

#### Best Practice Statement

Patients who have had suspected or confirmed COVID-19 (of any disease severity) who have persistent, new, or changing symptoms should have access to follow-up care.

#### Remarks:

##### Recognition

- All patients (and their caregivers) with COVID-19 should be counselled to monitor for resolution of signs and symptoms. If any one or more of these persist, or patient develops new or changing symptom, then to seek medical care according to national (local) care pathways.
- This includes counselling about acute life-threatening complications, such as pulmonary embolism, myocardial infarction, dysrhythmias, myopericarditis and heart failure, stroke, seizures and encephalitis (54,258) for which they should seek emergency care.
- Patients with severe and critical COVID-19 may develop post-intensive care syndrome (PICS), with a range of impairment including (but not limited to) physical deconditioning, cognitive, and mental health symptoms. See Chapter 19. Rehabilitation for patients with COVID-19 for more details on PICS.

##### Management

- National (local), coordinated care pathways should be established that can include primary care providers (i.e. general practitioners), relevant specialists, multidisciplinary rehabilitation professionals, mental health and psychosocial providers, and social care services.
- Management should be tailored according to patient needs and be coordinated.
- Management interventions include addressing promptly life-threatening complications. For non-life-threatening complications, management may entail education, advice on self-management strategies (i.e. breathing techniques, pacing), caregiver support and education, peer-to-peer groups, stress management, stigma mitigation and home modification; prescription of rehabilitation programmes, and/or specialty management.
- See Chapter 19. Rehabilitation for patients with COVID-19 for recommendations regarding screening, assessment and rehabilitation interventions to facilitate onward referrals for inpatient, outpatient, or community-based follow up, to ensure continuity during transitions of care.



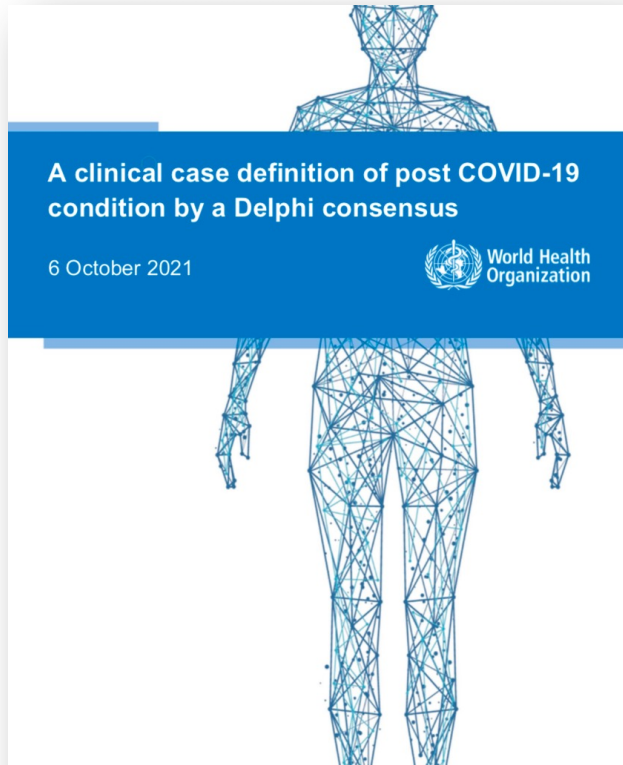
# Post COVID-19 condition

## The case for one clinical case definition

- One name and definition will simplify our global common understanding and communication.
- Allows physicians, patients, epidemiologists, ministers of health, policy-makers, governments to be aligned in their understanding and informed to make policy decisions.
- Enables researchers to aggregate data in a consistent and reliable manner and to conduct interventional studies using common enrolment criteria, case record form and core outcome sets.

# Post COVID-19 condition

## A clinical case definition by a Delphi consensus (October 2021)



Post COVID-19 condition occurs in individuals with a history of **probable** or **confirmed** SARS-CoV-2 infection, usually **3 months** from the onset of COVID-19 with symptoms and that last for at least **2 months** and cannot be explained by an alternative diagnosis.

Common symptoms include **fatigue**, **shortness of breath**, **cognitive dysfunction** but also others and generally have an impact on **everyday functioning**.

Symptoms may be **new onset** following initial recovery from an acute COVID -19 episode or **persist** from the initial illness. Symptoms may also **fluctuate** or **relapse** over time.

\* A separate definition may be applicable to children

## A clinical case definition of post-COVID-19 condition by a Delphi consensus

Joan B Soriano, Srinivas Murthy, John C Marshall, Pryanka Relan, Janet V Diaz, on behalf of the WHO Clinical Case Definition Working Group on Post-COVID-19 Condition

Published in *Lancet Infectious Diseases* 21 December 2021

[https://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(21\)00703-9/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(21)00703-9/fulltext)

Published by WHO 6 October 2021

<https://apps.who.int/iris/bitstream/handle/10665/345824/WHO-2019-nCoV-Post-COVID-19-condition-Clinical-case-definition-2021.1-eng.pdf>

# Post COVID-19 condition

## Priority research questions (February 2022)

- **Natural history**
  - adults, children, pregnant women
  - clinical characteristics (symptom clusters)
  - risk factors
  - variations by regions, variant circulation
  - Impact of treatments for acute disease
- **Pathophysiology**
  - viral persistence
  - immune dysregulation
  - thrombotic
- **Clinical interventions**
  - pharmacologic interventions
  - rehabilitation interventions
- **Impact of COVID-19 vaccination**
- **Mid- & long- term complications**
  - cardiac, metabolic, neurologic, gastrointestinal



24–25 February 2022 13:00–18:00 Central European Time

<https://www.who.int/news-room/events/detail/2022/02/24/default-calendar/covid-19-global-research-and-innovation-forum-an-invitation-to-the-research-community>



# Post COVID-19 condition

## Core outcomes set-what to measure (June 2022)

### A core outcome set for post-COVID-19 condition in adults for use in clinical practice and research: an international Delphi consensus study



Daniel Munblit\*, Timothy Nicholson\*, Athena Akrami, Christian Apfelbacher, Jessica Chen, Wouter De Groote, Janet V Diaz, Sarah L Gorst, Nicola Harman, Alisa Kokorina, Piero Olliaro, Callum Parr, Jacobus Preller, Nicoline Schiess, Jochen Schmitt, Nina Seylanova, Frances Simpson, Allison Tong, Dale M Needham\*, Paula R Williamson,\* and the PC-COS project steering committee†

#### Methods

##### Multi-step study:

1. Reviewed outcomes reported in studies of post COVID-19 condition to develop a list
2. Outcomes were grouped using the COMET taxonomy to present in a consensus process
3. A two-round online international modified Delphi consensus process, 3 stakeholder groups to prioritize outcomes:
  - people with post COVID-19 condition and their carers
  - health care professionals and researchers
  - health care professionals and researchers with post COVID-19 condition
4. International consensus meeting to finalize the core outcome set

#### Results

1535 participants from 71 countries, representing 6 continents were involved in the modified Delphi process (1148 participated in both rounds)

11/24 outcomes met consensus after the two Delphi rounds and consensus meeting

#### Next steps

Determine which instruments best measure these outcomes

#### Panel: COS for adults with post-COVID-19 condition

##### Physiological or clinical outcomes

- 1 Cardiovascular functioning, symptoms, and conditions
- 2 Fatigue or exhaustion
- 3 Pain
- 4 Nervous system functioning, symptoms, and conditions
- 5 Cognitive functioning, symptoms, and conditions
- 6 Mental functioning, symptoms, and conditions
- 7 Respiratory functioning, symptoms, and conditions
- 8 Post-exertion symptoms

##### Life impact outcomes

- 9 Physical functioning, symptoms, and conditions
- 10 Work or occupational and study changes

##### Survival

- 11 Survival

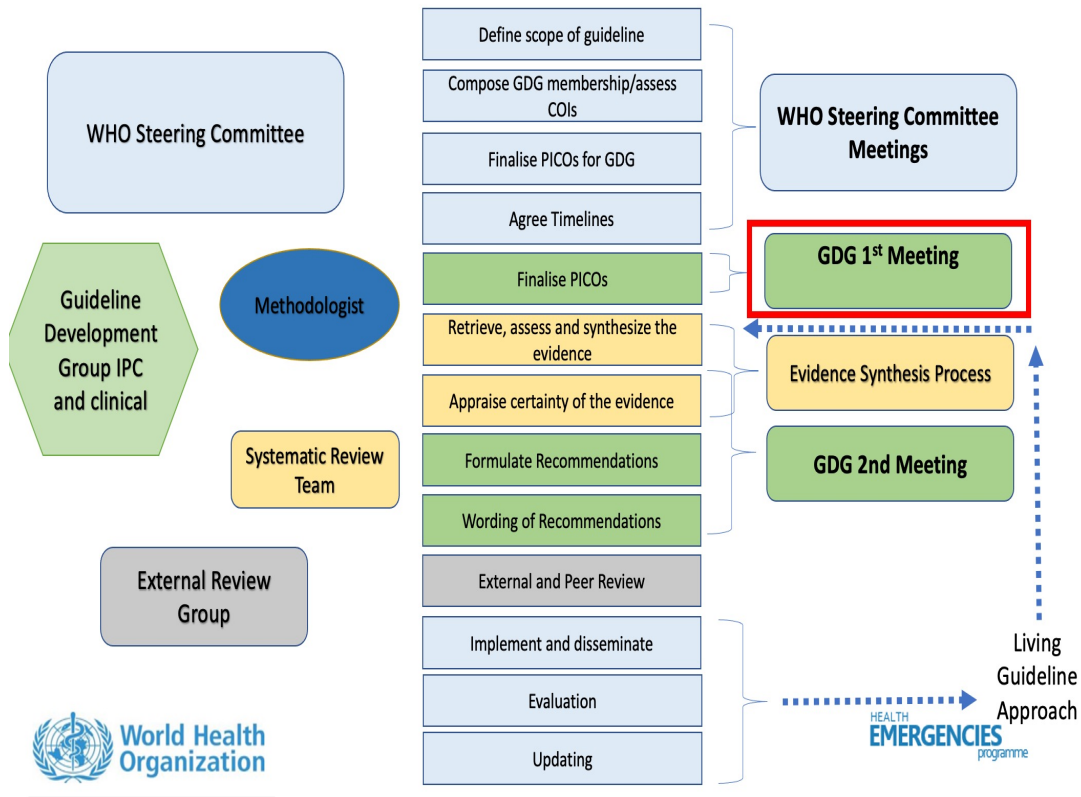
##### Outcome from previous COS

- 12 Recovery\*

COS=core outcome set. \*Outcome was included in a previously published COS for COVID-19<sup>14</sup> and, owing to its relevance to post-COVID-19 condition, was automatically included in this COS.

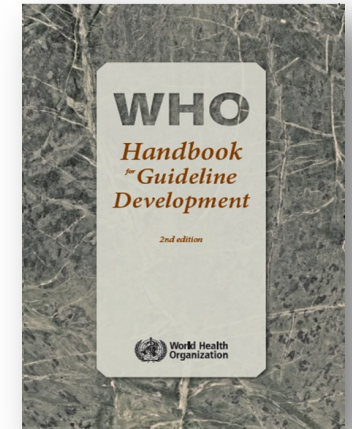
# Post COVID-19 condition

## Ongoing activities



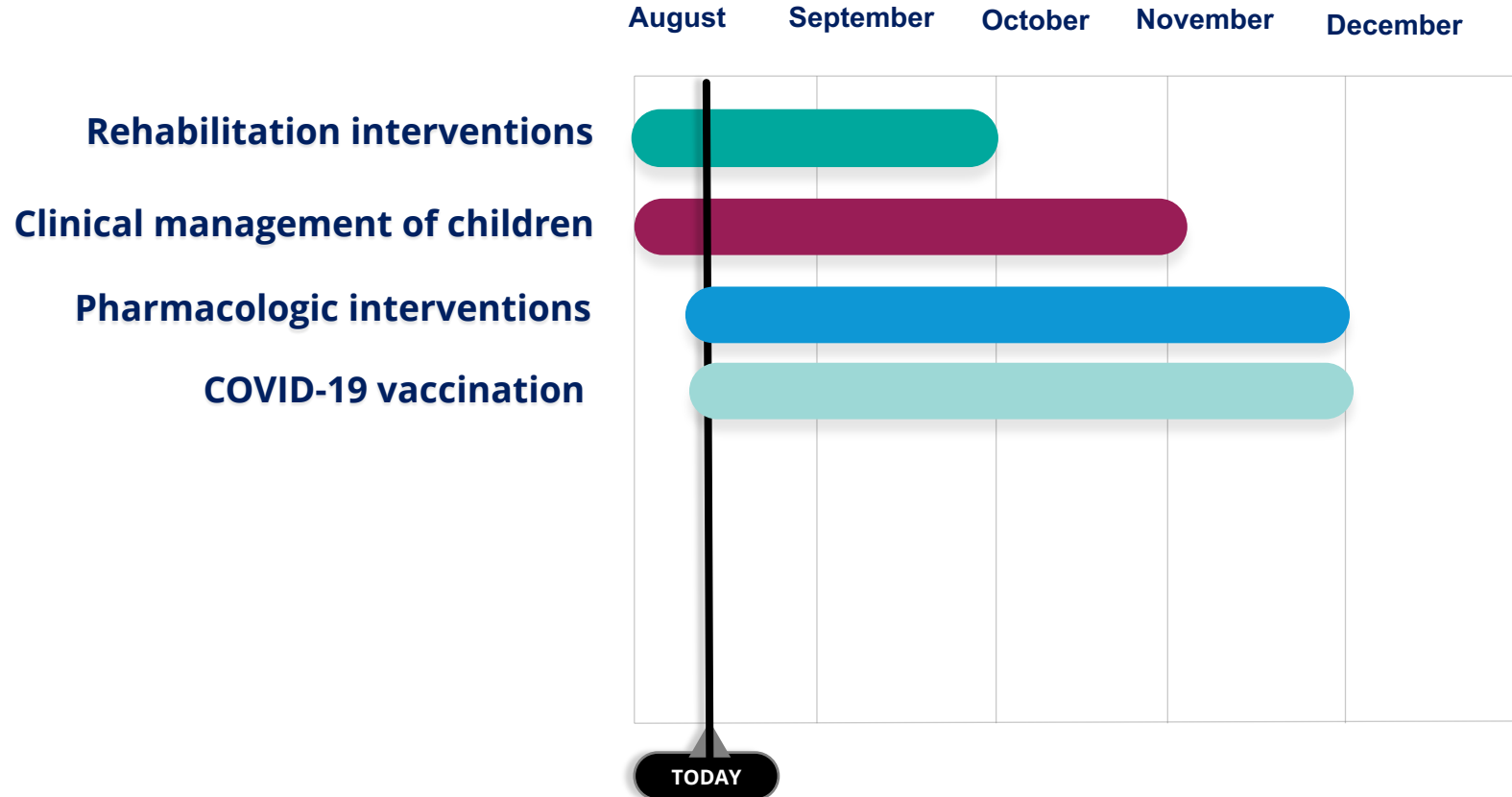
## WHO living guideline on COVID-19 clinical management: GRADE based

- Rehabilitation interventions: under review by GRC
- Systematic reviews to update chapter on post COVID-19 condition:
  - impact of vaccination
  - pharmacologic interventions



# Post COVID-19 condition

## Ongoing WHO activities



### Clinical management of COVID-19

LIVING GUIDELINE  
23 JUNE 2022



**Considerations:**  
Timeline from systematic review to publishing/update of guideline is 8-10 weeks.

# Post COVID-19 condition

## Ongoing activities

### WHO clinical characterization & research working group on post COVID-19 condition meets bi-weekly

- **Core outcomes set for adults:** how to measure (under development, Delphi methodology)
- **Core outcomes set for children: what and how to** (under development, Delphi methodology)
- **Post COVID-19 case definition for children:** under development (meeting September 2022)
  - Systematic review completed: 60 studies (39 cohort, 15 cross-sections, 6 case series)
  - Expert consensus meeting planned for **13 September 2022** with 30 experts and advocates invited from around the world





WHO Global Clinical Platform  
for COVID-19  
*Data for public health response*

# WHO Global Clinical Platform for COVID-19



WHO Global Clinical Platform initiative launched in May 2020.

Member States, health care facilities and research networks were invited to share patient-level anonymized clinical data of people hospitalized with confirmed or suspected COVID19 using standardized data collection tools

## WHO Global Clinical Platform for COVID-19

*Data for public health response*






WHO Global Clinical Platform  
for COVID-19  
Data for public health response

# WHO CALL to ACTION: Post COVID-19 Condition

Member States, health care facilities and research networks were invited to collect anonymized, individual-level clinical data from individuals recovered from acute COVID-19 using a **standardized POST-COVID-19 case report form (CRF) and share data with WHO Global Clinical Platform.**

Platform outputs will inform evidence-based guidance and public health policies and interventions on clinical management of post COVID-19 at the country, regional and global levels

1. Characterize **regional variations** and **temporal trends** in clinical phenotypes, clinical care, therapeutics, outcomes, reinfections, variants, vaccination
2. Derive **risk factors** associated with mortality, severity, and ICU admission globally and by region
3. Characterize clinical phenotypes, clinical care and therapeutics, interventions, risk factors in **subpopulations** (i.e. children, pregnant women, people living with HIV, TB, etc)
4. Describe **mid- and long- term sequelae** of patients discharged from hospitals or managed at home

 World Health Organization

**WHO Global Clinical Platform for COVID-19  
Case Report Form (CRF) for COVID-19 sequelae ("Post COVID-19 CRF")**

The WHO has established a Global Clinical Platform<sup>1</sup> of COVID-19 and invites all Member States and health facilities to report anonymised patient-level clinical information to the WHO platform using standardized Case Report Forms (CRF):

- Core CRF captures clinical information on individuals hospitalized for COVID-19
- Core-P CRF has information on pregnant women hospitalized for COVID-19
- MIS-CRF has information related to multisystem inflammatory syndrome in children and adolescents temporally related to COVID-19
- Post COVID-19 CRF, designed to build upon the Core CRF and assess the medium- and long-term sequelae of COVID-19

The Post COVID-19 CRF includes 3 modules:  
Module 1 includes background, demographic and clinical information related to the acute episode of COVID-19.  
Module 2 includes questions pertaining to the post-acute illness period to help identify patients who require further clinical evaluation  
Module 3 includes medical assessment and results of examinations, tests, or diagnoses made during the follow up visit. Based on results, patients should be referred for clinical care or rehabilitation as per national protocols.

**The Post COVID-19 CRF is intended to serve as:** (i) A clinical tool that can be used by Member States to document the mid- and long-term sequelae of COVID-19. Uniformity in the follow up of patients will ensure that mid- and long-term clinical and rehabilitation needs are identified, and patients are provided the care they need; (ii) WHO is not necessarily recommending the comprehensive testing described in the CRF for all individuals; clinician judgement is required to select the test needed for clinical care. This CRF is a tool for gathering standardized information regarding post COVID-19 sequelae through the WHO Global Clinical Platform. Such data collation and its analysis would improve national and global knowledge of the consequences of COVID-19, inform further public health responses and prepare for large investigational studies.

**Criteria for completion of Post COVID-19 CRF:** Variables' data dictionary available on the WHO website<sup>1</sup> support data entry. The CRF can be administered either as part of routine follow up or at a specific time point to any patient in the post-acute phase of COVID-19, regardless of hospitalization. While it is suggested to prioritize the completion of the CRF for patients who were hospitalized for a severe or critical episode of COVID-19, the CRF should be administered, where possible, also to patients who suffered from COVID-19, including those with mild or moderate illness, and who received care either at home or in a hospital setting.

**Time-points for administration:** The form can be completed any time during follow up after an acute episode of COVID-19. However, to support standardization and data comparability, it should preferably be completed 4 to 8 weeks after hospital discharge from the acute ward or after acute illness, and every 6 months thereafter. However, in case of persistent symptoms/signs at 4-8 weeks after hospital discharge or after acute illness, it is recommended to complete the CRF at 3-month intervals, for as long as needed (see figure below).

**Mode of administration:**  
Module 1-2: face-to-face administration and completion by a health care worker is preferred. However, when this is not possible, the form can be either self-administered, or completed remotely (online or through telephone) by the caregiver. For children, the form should be completed by the primary caregiver (preferred) or by the legal guardian.  
Module 3: face-to-face administration and completion by a health care worker.  
Module 1 needs to be completed only once during the first follow up visit, while Modules 2 and 3 should be completed at every follow up visit.

**General guidance:** Please contact [COVID\\_ClinPlatform@who.int](mailto:COVID_ClinPlatform@who.int) if you need assistance with data entry, if you have any query on the CRF, and to let us know that you are using the forms.

**Flowchart:**

For individuals who were hospitalized with suspected or confirmed diagnosis of COVID-19:

From hospital discharge

If symptoms/signs persist: follow up visit at 4-8 weeks, and every 3 months thereafter as long as needed

Post COVID CRF: module 1, 2, 3

4-8 weeks

4-5 months

7-8 months

13-14 months

For individuals who were not hospitalized with suspected or confirmed diagnosis of COVID-19:

From acute illness of COVID-19

If symptoms/signs do not persist: follow up visit at 4-8 weeks, and every 6 months thereafter, if possible

<sup>1</sup> <https://www.who.int/teams/health-care-readiness-clinical-unit/covid-19/data-platform>

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WHO reference number: WHO/2019-cov/Post\_COVID-19\_CRF/2021.2



# Case Report Form (CRF): Post COVID-19 Condition

➤ Eligible populations: people *discharged from hospital* after acute COVID-19 or *managed at home*

**World Health Organization**  
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General guidance: Please contact COVID\_ClinPlatform@who.int if you need assistance with data entry, if you have any query on the CRF, and to let us know that you are using the forms.

**Flowchart:**

- For individuals who were hospitalized with suspected or confirmed diagnosis of COVID-19:
  - From hospital discharge: Post COVID CRF: module 1, 2, 3 (4-8 weeks), Post COVID CRF: module 2, 3 (4-6 months), Post COVID CRF: module 2, 3 (7-8 months), Post COVID CRF: module 2, 3 (13-14 months)
- For individuals who were not hospitalized with suspected or confirmed diagnosis of COVID-19:
  - From acute illness of COVID-19: Post COVID CRF: module 2, 3 (4-8 weeks), Post COVID CRF: module 2, 3 (4-6 months), Post COVID CRF: module 2, 3 (7-8 months), Post COVID CRF: module 2, 3 (13-14 months)

<sup>1</sup> <https://www.who.int/teams/health-care-readiness-clinical-unit/covid-19/data-platform>

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WHO reference number: WHO/2019-nCoV/COVID-19-CRF-2021.1

## MODULE 1 Acute COVID-19 episode

### Retrospective information

- Demographics
- Diagnostic/other tests
- Co-morbidities
- Medications
- Complications/Co-infections
- Clinical Management (therapeutics + supportive care)
- Pregnancy Status upon Admission

## MODULE 2 Follow-up

### Physician Encounter

- Reinfection
- Vaccination status
- Occupation
- Functional status
- Signs and symptoms since acute episode

## MODULE 3 Follow-up

### Clinical examinations, laboratory tests and diagnosis

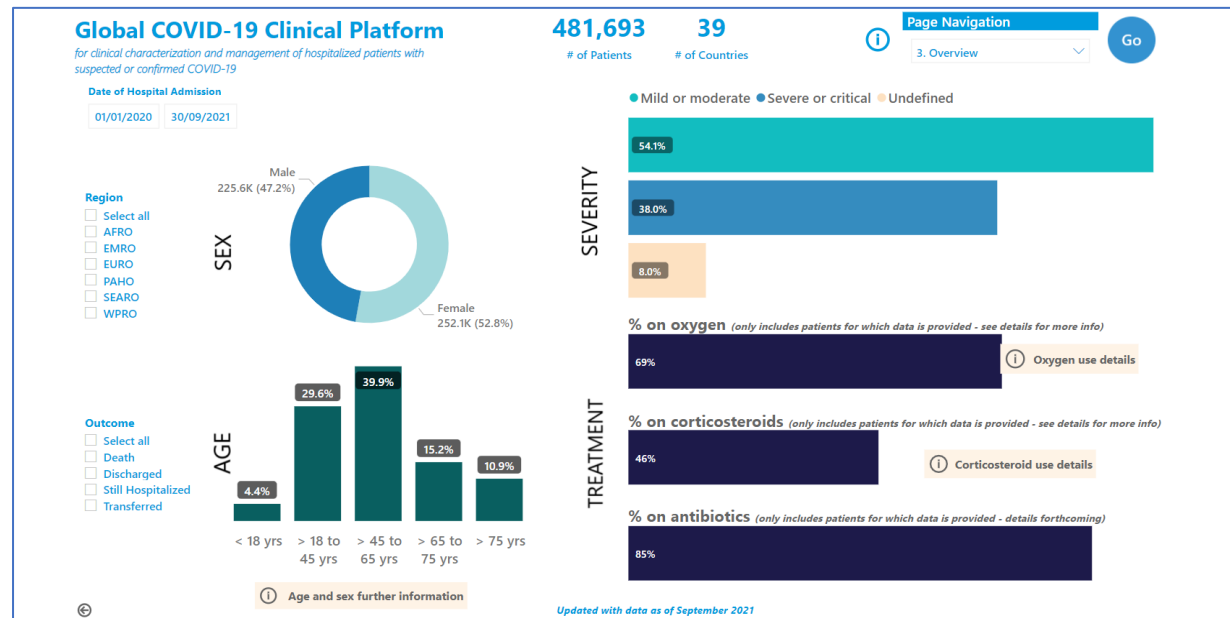
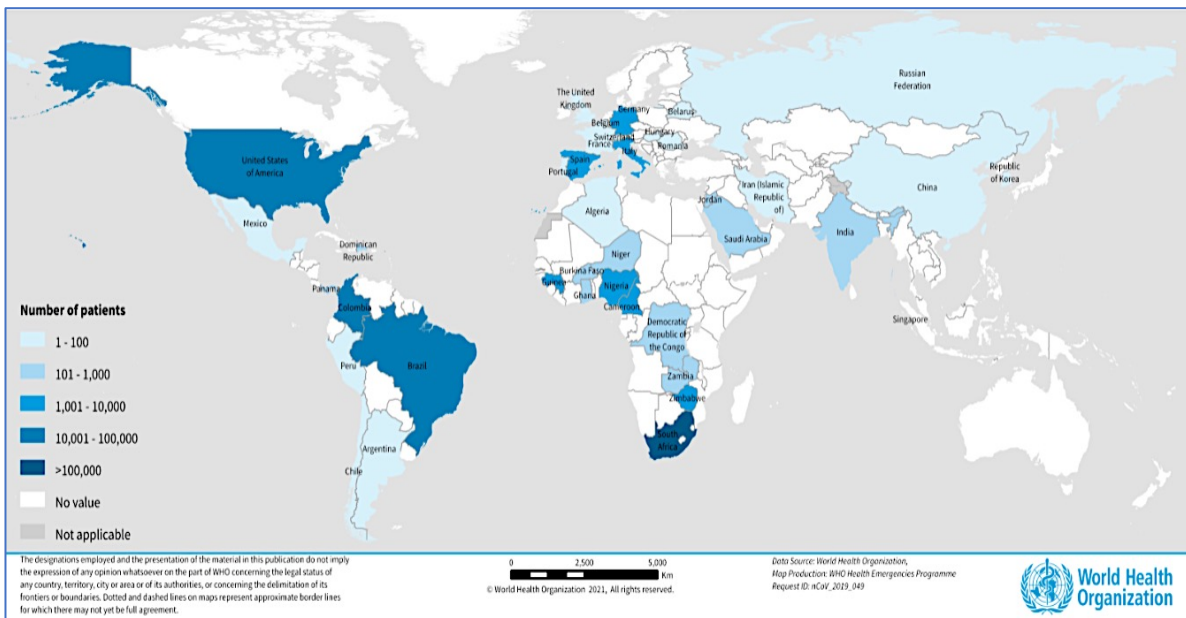
- Neurological exam
- Radiographic exam
- Blood tests
- Other clinical tests and scales
- New diagnosis of illness/complication received





# WHO Global Clinical Platform for COVID-19

## 629 729 hospitalized cases from 50 countries (June, 2022)





# Conclusion

## Opportunities to increase recognition, research and care

Increase uptake of standardized tools for clinical care and research (case definition, COS, CRFs).

Increase recognition in all care settings and multi-disciplinary care delivery models rooted in primary care.

Better understand pathophysiology to identify possible treatments and test those treatments in robust clinical trials.

Ensure all populations are represented along the way;

- Children
- Pregnant women
- Immunosuppressed
- Patients from Low Middle-Income Countries (LMIC)

# Acknowledgements

## WHO Clinical Management Case Definition Working Group, Post COVID-19 Steering Committee, with special thanks to:

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John Appiah  
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Archana Seahwag  
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Khaled Shamseldin

+ Numerous other WHO  
employees and staff,  
patients and patient partners  
and global experts

### For more information:

+ WHO COVID-19 Clinical Platform:  
[COVID\\_ClinPlatform@who.int](mailto:COVID_ClinPlatform@who.int)

+ Post COVID-19 condition & CRF:  
[kuppallik@who.int](mailto:kuppallik@who.int)

# Thank you

For more information please visit our  
Post COVID-19 condition website

<https://www.who.int/teams/health-care-readiness/post-covid-19-condition>