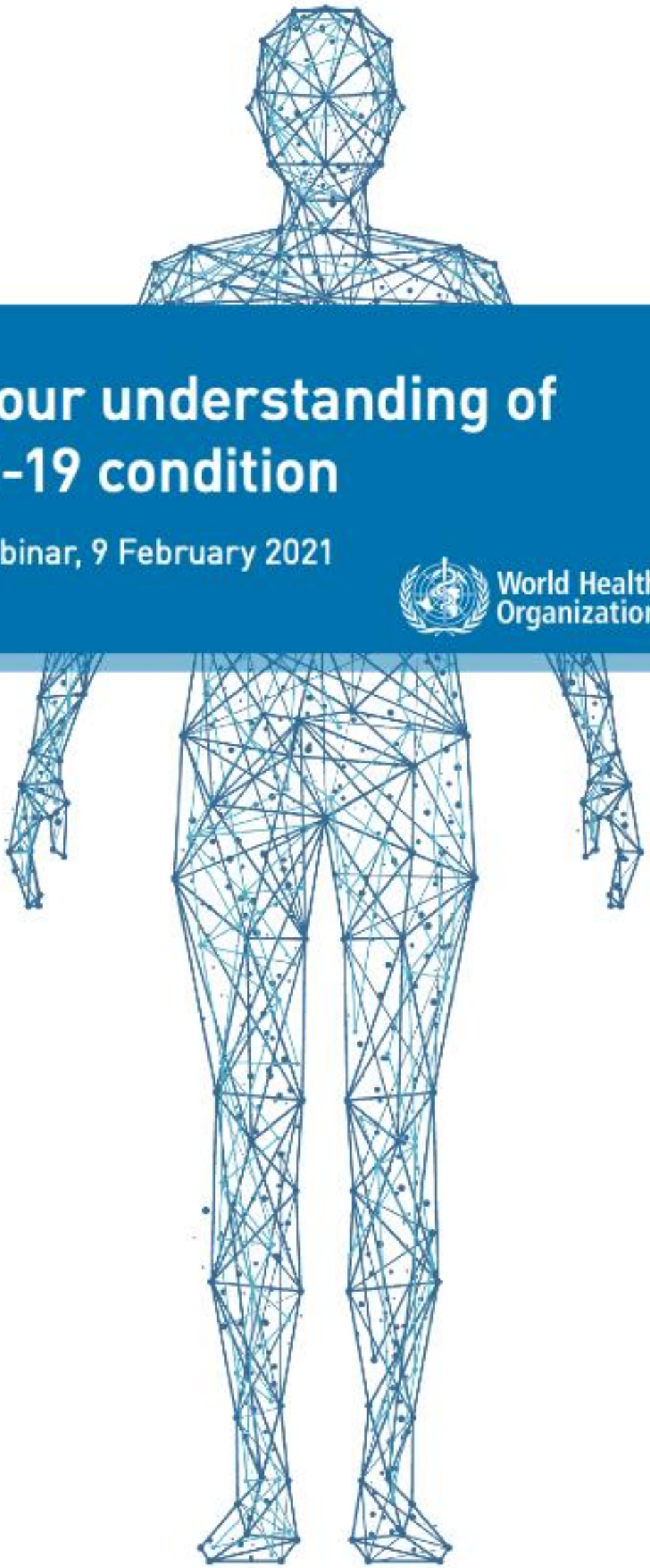

Expanding our understanding of Post COVID-19 condition

Report of a WHO webinar, 9 February 2021

World Health Organization

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Acknowledgements

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Thanks are also due to all the chairs, speakers and, most importantly, the panel members for their outstanding contributions during the meeting. See Annexes 1 and 2 for complete lists of speakers and panel participants.

Abbreviations

ACE-2	angiotensin-converting enzyme 2
AI	artificial intelligence
ARDS	acute respiratory distress syndrome
CAP	community-acquired pneumonia
CFS	chronic fatigue syndrome
COVID-19	coronavirus disease 2019
CRF	case report form
DLCO	diffusing capacity for carbon monoxide
EHR	electronic health records
GI	gastrointestinal
GloPID-R	Global Research Collaboration for Infectious Disease Preparedness
GP	general physician
IASC	Inter-Agency Standing Committee
ICU	intensive care unit
ISARIC	International Severe Acute Respiratory and Emerging Infection Consortium
LMICs	low- and middle-income countries
ME	myalgic encephalomyelitis
NIH/NIAID	National Institutes of Health/National Institute of Allergy and Infectious Diseases
PICS	post-intensive care syndrome
PTSD	post-traumatic stress disorder
RCT	randomized clinical trial
SARS-CoV-2	severe acute respiratory syndrome coronavirus-2
SEID	systemic exertion intolerance disease
WHO	World Health Organization
6-MWT	six-minute walk test

Introduction

During the first wave of the COVID-19 pandemic, investigators already began to assemble longitudinal cohort studies to assess COVID-19 sequelae. By August 2020, WHO met with patients from the LongCovidSOS group and affirmed the need for recognition, research and rehabilitation. By September 2020, WHO had established the ICD-10 code for the Post COVID-19 condition. By January 2021, WHO had published its initial guidance on clinical management of patients after acute illness.

Subsequently, there has been an increase in the number and scope of Post COVID-19 condition research activities by public health agencies, academics, patient-led research groups and other stakeholders. However, a lack of consensus on the clinical case definition and limited understanding of the clinical characterization during the recovery period and associated pathophysiology have limited progress in diagnosis, treatment and management.

With the goal of advancing this field by bringing together stakeholders from around the world, WHO has organized a series of webinars with the following specific objectives:

- action priorities on recognition, research and rehabilitation;
- present up-to-date scientific knowledge on Post COVID-19 condition;
- enrich the discussion through working groups with expert panels.

On 9 February 2021, a first webinar entitled “Expanding our understanding of Post COVID-19 condition” was held under the auspices of WHO and in consultation with the International Severe Acute Respiratory and Emerging Infection Consortium (ISARIC), Global Research Collaboration for Infectious Disease Preparedness (GloPID-R), National Institutes of Health/National Institute of Allergy and Infectious Diseases (NIH/NIAID), LongCovidSOS and patient representatives. The meeting took place over a 5-hour period divided into the following three sessions:

- Session 1: Post COVID-19 condition: scene setting and lessons learned
- Session 2: Observations on Post COVID-19 condition: what we know
- Session 3: Working groups to develop clinical case definition and research gaps/methods.

For this initial webinar, participants were invited through various clinical networks, research networks and collaborating centres. Over 700 participants attended. Speakers were selected to present findings from large, published cohort studies that were found in systematic literature searches and through other relevant sources. Declarations of conflicts of interest were collected, assessed and managed by the responsible technical unit according to standard WHO procedures for all the speakers. All speakers were assessed as having no financial conflicts of interest.

The working groups were constituted with multidisciplinary panels to delve into pre-specified questions. The WHO steering committee was responsible for setting the agenda, the selection of speakers and formulating the working group questions. The outcomes from each working group are now being used to inform a Delphi process that will be used to draft a clinical case description for Post COVID-19 condition.

Session 1. Post COVID-19 condition: scene setting and lessons learned

This session had six speakers who were chosen to present information to set the scene. High-level summaries will follow, but for complete presentations please refer to our website *(1).*

An historical perspective

The first two presentations focused on learnings from other diseases: “Learning from previous viral infections, influenza, SARS, MERS, Zika” and “Learning from previous critical illness: post-intensive care syndrome”.

Dr Carlos A Pardo described the various infectious disease outbreaks of the past two centuries, such as the influenza pandemics of 1918 (H1N1), 1957 (H2N2), 1968 (H3N2), 2009 (H1N1), as well as other viral outbreaks of emerging viruses such as Ebola Virus Disease (2014), Chikungunya (2013–2015), Zika virus (2015–2016), SARS (2002–2004) and MERS (2012); all in the run-up to this current pandemic of SARS-CoV-2 (2019). Neurologic complications have been well described. Dr Pardo cited an article in the *Lancet* published in 1891 reporting on the influenza pandemic describing various neurologic manifestations (i.e. neuralgia, nerve exhaustion, inertia) and the exceptionally “low tone of human vitality”*(2)*, this was then followed by reports of neurologic effects of the influenza pandemic of 1918, and then more recently the neurologic complications associated with Zika virus (i.e. Guillain–Barré syndrome, encephalitis and optic neuritis, etc.) and with Chikungunya virus (i.e. disability at discharge) *(3).* He concluded that COVID-19 clearly had systemic and neurologic manifestations during the acute phase and that it also may last into the convalescent and recovery phases, leading to Post COVID-19 condition.

Professor Dale Needham presented on the post-intensive care syndrome (PICS), a syndrome developed by the Society of Critical Care Medicine to raise awareness about long-lasting symptoms and functional impairments experienced by survivors of critical illness *(4)*. PICS is described as new or worsening impairments in one or more of the three main domains: physical, cognitive *(5)* and mental *(6)* health, arising after intensive care unit (ICU) treatment and persisting beyond acute care hospitalization. Notably, this term can be applied to either a survivor or family member. Over time, other symptoms have also been observed, including fatigue *(7)* and impairments that affect quality of life *(8, 9)* and employment *(10, 11).* Professor Needham described the work on the PICS core outcome set, which is sponsored and funded by the United States National Institutes of Health (NIH) and aims to improve long-term outcomes research for acute respiratory failure for every study of ICU survivorship *(12-14).* This core outcome set is being created via an international modified Delphi consensus process with panel members from more than 16 countries across six continents, including approximately 25% patient or family representatives *(15).* This same methodology can be used to develop a core outcome set for Post COVID-19 condition.

Learnings from global forums on Post COVID-19 condition

The next two presentations focused on learnings from the two most recent global meetings on this topic