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Original article

# Consensus on post COVID in the Spanish national health system: Results of the CIBERPOSTCOVID eDelphi study

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ABSTRACT

*Background:* In 2021, the Spanish Ministry of Health launched the CIBERPOSTCOVID project to establish what post COVID was. The present study reports the level of agreement among stakeholders on post COVID and its clinical and diagnostic characteristics in the Spanish health system.
*Methods:* The agreement on post COVID among clinicians, public health managers, researchers and patients' representatives was explored in a real-time, asynchronous online Delphi. In a two-wave consensus, respondents rated from 1 (total disagreement) to 6 (total agreement) 67 statements related to terminology, duration, etiology, symptoms, impact on quality of life, severity, elements to facilitate diagnosis, applicability in the pediatric population, and risk factors. Consensus was reached when 70 % of ratings for a statement were 5 or 6, with an interquartile range equal or less than 1.
*Findings:* A total of 333 professionals and patients participated in this eDelphi study. There was agreement that post COVID was "a set of multi-organic symptoms that persist or fluctuate after acute COVID-19 infection and are not attributable to other causes" with a minimum duration of 3 months. The highest levels of agreement were found in the most frequent symptoms and its impacts on everyday activities. Aspects related to the diagnostic process and the measurement of its severity reached a lower level of consensus. There was agreement on the need to rule out previous health problems and assess severity using validated functional scales. However, no agreement was reached on the risk factors or specific features in the pediatric population.
*Interpretation:* This policy-based consensus study has allowed the characterization of post COVID generating collective intelligence and has contributed to an operational definition applicable in clinical practice,

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health services management and useful for research purposes in Spain and abroad. Agreements are consistent with existing evidence and reference institutions at European and international level.


## Introduction

SARS-CoV-2 infection can trigger a wide range of multi-organ symptoms that may persist over a long period. Since the emergence of this virus, studies have reported a variety of symptoms associated with the infection lasting beyond the first weeks of the acute episode that may have significant consequences for patients' quality of life and everyday activities [1]. The appearance of new infections and variants such as Omicron over the course of the pandemic, have led to an increase in infected people, with an estimated 10–20 % of these experiencing effects after recovering from acute SARS-CoV-2 infection [2]. In addition, 6.2 % of people who have had symptomatic COVID-19 report at least one persistent symptom three months later [3].

Post COVID is a novel health problem that requires effective and rapid decision-making and service planning; nevertheless, the currently available scientific evidence is scarce or inconclusive. In this context, seeking expert opinion and consensus, such as Delphi techniques, appears to be a valid strategy to formulate recommendations for health policies and clinical practice [4,5]. Moreover, they allow us to assess the level of agreement between stakeholders on complex topics whose management remains a matter of debate and serve to broaden the existing knowledge [6]. Reference institutions such as the World Health Organization (WHO) applied the Delphi methodology to establish an international consensus definition of post COVID [7,8].

Likewise, in the UK, the National Institute for Health and Care Excellence, the Royal College of General Practitioners and the Scottish Intercollegiate Guidelines Network (NICE-RCGP-SIGN) published protocols and guidelines for the management of post COVID patients based on the best available evidence at the time and expert judgment [9,10]. In Spain, the Spanish Society of General Medicine (SEMG, for its acronym in Spanish) and the Catalan Health Service designed guidelines aimed to broaden the understanding of patients with post COVID symptoms, to homogenize the criteria to apply in clinical practice, and to integrate the perspectives of both professionals and the people affected [11,12].

Despite the publication of studies on the subject, in 2021 there was still no clear consensus in Spain on the clinical and etiological characteristics of post COVID (or terms such as "long COVID" or "persistent COVID") to facilitate an accurate diagnosis and, consequently, no way of calculating its prevalence and incidence in a robust manner. In fact, there remains a need for epidemiological studies that include explicit diagnostic criteria, sufficiently large representative samples, and precise incidence and prevalence estimates using a common agreed definition [13,14]. In addition, the evidence of clinical manifestations in children and adolescents is limited [15]. Therefore, there is a compelling need to capture and generate collective knowledge and better understand the impact of COVID-19 beyond the acute infection.

In this context, the Spanish Ministry of Health commissioned the Instituto de Salud Carlos III and CIBER (a consortium of relevant scientific groups of biomedical research in Spain) to carry out the CIBERPOSTCOVID project, aimed to provide new evidence on post COVID and to identify the key features that could aid its characterization and management [16].

The present report, part of the CIBERPOSTCOVID project, describes the level of agreement among key multidisciplinary stakeholders in the Spanish Health System on post COVID and its clinical and diagnostic characteristics.

## Methods

A descriptive quantitative online consensus study (using an online modified Delphi – eDelphi) was carried out between March and May 2022 among key stakeholders.

### *Statements included in the eDelphi study*

A previous qualitative study with key informants and a scoping review of the literature to identify relevant documents including definitions of post COVID and its key features (clinical characteristics, diagnosis, risk factors, severity, impact on daily life, pediatric population) were performed as part of the CIBERPOSTCOVID project [16]. The research team triangulated the information of these substudies and 100 items (statements) were proposed for the eDelphi pilot test (Fig. 1). Forty-seven participants with different professional backgrounds and patient representatives were selected by convenience for the pilot test.

Sixty-seven statements were finally selected for the eDelphi study. They were classified in nine domains: terminology (4 statements), clinical characteristics (duration, etiology, evolution - 12

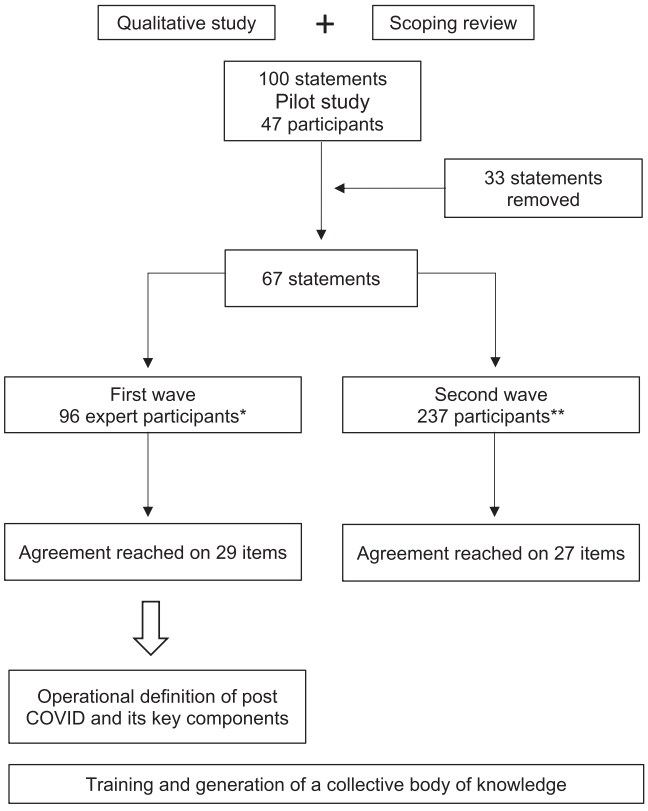


**Fig. 1.** Flow chart of the consensus study. *96 expert participants voted the first statement, in two rounds; 71 voted on all 67 statements. **237 participants voted the first set of statements, in two rounds; 171 voted on all 67 statements.

**Table 1**
Participants' profiles in each wave of consensus in the eDelphi on post COVID.

| | | Participants in the 1st wave; n (%) who | | Participants in the 2nd wave; n (%) who | |
|---|---|---|---|---|---|
| | | voted at least the first statement (n = 96) | voted all statements (n = 71) | voted at least the first statement (n = 237) | voted all statements (n = 171) |
| Gender | Men | 36 (37.5) | 26 (36.6) | 116 (48.9) | 87 (50.9) |
| | Women | 59 (61.5) | 45 (63.4) | 121 (51.1) | 84 (49.1) |
| | Non-binary | 1 (1.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Age (years) | Less than 39 | 18 (18.8) | 15 (21.1) | 54 (22.8) | 36 (21.1) |
| | 40–59 | 58 (60.4) | 39 (54.9) | 142 (59.9) | 103 (60.2) |
| | 60 and over | 20 (20.8) | 17 (23.9) | 41 (17.3) | 32 (18.7) |
| Participant profile | Clinician | 39 (40.6) | 33 (46.5) | 138 (58.2) | 97 (56.7) |
| | Patients' representative | 17 (17.7) | 14 (19.7) | 24 (10.1) | 23 (13.5) |
| | Public health manager | 10 (10.4) | 6 (8.5) | 15 (6.3) | 9 (5.3) |
| | Researcher | 30 (31.3) | 18 (25.4) | 60 (25.3) | 42 (24.6) |
| Previous experience in COVID-19 or post COVID | None | 12 (12.5) | 5 (7.0) | 26 (11.0) | 16 (9.4) |
| | Yes, as a patient | 17 (17.7) | 14 (19.7) | 24 (10.1) | 23 (13.5) |
| | Yes, in research/ teaching | 19 (19.8) | 14 (19.7) | 39 (16.5) | 32 (18.7) |
| | Yes. In clinical management | 8 (8.3) | 7 (9.9) | 12 (5.1) | 6 (3.5) |
| | Yes. In clinical practice | 40 (41.7) | 31 (43.7) | 136 (57.4) | 94 (55.0) |
| Previous COVID-19 | I have had COVID-19 | 53 (55.2) | 41 (57.7) | 118 (49.8) | 93 (54.4) |
| | I have not had COVID-19 | 43 (44.8) | 30 (42.3) | 119 (50.2) | 78 (45.6) |
| Post COVID | With post COVID | 21 (21.9) | 17 (23.9) | 25 (10.5) | 24 (14.0) |
| | Without post COVID | 75 (78.1) | 54 (76.1) | 212 (89.5) | 147 (86.0) |
| Professional practice | Adult population | 55 (57.3) | 39 (54.9) | 185 (78.1) | 134 (78.3) |
| | Geriatric population | 5 (5.2) | 5 (7.0) | 7 (3.0) | 6 (3.5) |
| | Pediatric population | 9 (9.4) | 8 (11.3) | 14 (5.9) | 11 (6.4) |
| | Not applicable | 27 (28.1) | 19 (26.8) | 31 (13.1) | 16 (9.4) |

statements), symptomatology (9), risk factors (12), impact on daily life and quality of life (7), severity profiles (4), diagnostic process (6), specific issues in pediatric populations (8) and future challenges for research (5) (supplementary material file 1).

*Modified eDelphi consensus study*

The consensus study was conducted using the Smart Delphi platform (Onsanity Solutions Inc., Barcelona), which allows asynchronous and real-time voting (supplementary material file 2 includes more information about this eDelphi instrument). Consensus was carried out in two waves. The first included a restricted sample of expert professionals and patients' representatives and their scores were used as reference values, while the second wave involved a broader range of participants.

Each participant was asked to rate their level of agreement of the 67 statements (items) on a score range from 1 (total disagreement) to 6 (total agreement). There were two rounds of voting in each wave. In the first round, participants blindly rated a statement and then visualized the aggregated score given by their peers. If they wished, they could modify their rating during this second round. Descriptive statistics of ratings for each statement in the first wave were used as reference values for participants in the second wave.

*Sampling and participants*

For the first wave of consensus, participants were designated by the referring scientific societies and institutions/organizations. Their selection was based on a stratified and intentional theoretical sampling to obtain a broad, multidisciplinary perspective of professionals (clinicians, public health managers and researchers) and representative patients' groups from Spain's 17 regions (as the Spanish national health system is decentralized, with major health responsibilities being discharged at regional level).

The research team contacted the executive boards and directors of reference institutions, including 23 scientific societies, 17 general directorates of public health and occupational health, 5 biomedical research networks linked to CIBER, — other state research bodies, three patients' associations, asking them to collaborate and propose participants. In the first wave, a sample of 114 key participants were invited to participate, anticipating a response rate of 80 %. In the second wave, these institutions provided their associates with a link to participate directly and anonymously in the eDelphi consensus study.

In order to characterize participants in both waves, their sociodemographic characteristics (age, gender, previous diagnosis of COVID-19 and/or post COVID, and region) and professional profile (clinician, public health manager, researcher or patients' representative) were collected. Although participants could identify themselves with more than one professional profile, they could only check one of the proposed categories and they were asked to choose the one with which they felt most identified.

*Statistical analysis*

The scores of the two consensus waves were analyzed separately. A descriptive analysis of participants' level of agreement with each statement, including the number of participants, mean, standard deviation (SD), median, interquartile range (IQR) and percentage of participants in scores 5–6 was performed. The project's steering group established that a consensus on a particular statement was reached when at least 70 % of participants' ratings were 5 or 6 and IQR 0–1 [4,7]. Moderate agreement was defined when around 70 % of scores and median were 5 and 6, but the IQR was 2 or when a little less than 70 % of scores were 5 or 6 and the IQR was 1. The completion rate of the consensus was calculated by dividing the number of votes for the first statement (item 1) by the number of votes for the last statement (item 67) in both waves.

*Ethical considerations*

The study was approved by the IDIAP Jordi Gol ethics committee (21/244-PCV; 11/09/2021). After obtaining their consent, participants in the first wave received a link by e-mail to participate. Although prospective respondents were addressed by name in this invitation, their participation in the eDelphi voting was completely

anonymous; once they had accessed the digital platform, it was not possible to associate the responses to the participants in either wave. In the second wave, participants voted directly through a published link to the eDelphi and no personal information was recorded.

## Results

### *Participation*

In total, 333 participants voted in at least one of the consensus waves. In the first wave of the CIBERPOSTCOVID eDelphi, the response rate was 84 % (96 of the 114 invited participants agreed to participate, voting on at least one of the first statements) and the overall response rate (i.e., those who voted on all 67 statements included in the consensus) was 62 %. In the second wave, since it was an open call to participate in the consensus exercise, it was not possible to calculate the response rate. In this case, the overall completion rate was 72 % (171 participants rated the 67 statements).

Table 1 shows the characteristics of participants in the first and second waves. In the first wave, the participation of women was higher than of men (62 % vs. 37 %). No differences according to gender were found in the second wave. Most participants were aged from 40 to 59 years (59 % and 60 % in the first and second waves respectively). All of Spain's 17 autonomous communities were represented. The most common profile was "clinician" (40 % and 58 %, respectively). The participation of patients' representatives was higher in the first wave (18%) than in the second (10 %). Around 88 % of participants in both waves reported previous experience in clinical practice or research in either COVID-19 or post COVID. In the two waves, more than half of the participants reported having had COVID-19 at some point, while 22% in the first wave and 14% in the second reported post COVID. Most participants reported experience in managing or treating COVID-19 in adults (first wave 57%, second wave 78%), but few had specifically treated geriatric (5% and 3%) or pediatric populations (9% and 6%).

### *Statements on which agreement was reached*

In the first wave, participants agreed that post COVID is a set of multi-organic clinical symptoms and manifestations that persist or fluctuate for at least three months after an acute episode of COVID-19 infection and are not attributable to other causes (Table 2). They also agreed that its operational definition should include not only symptoms, duration and etiology, but also the impact on patients' quality of life, everyday activities and work. The second wave yielded similar results, but participants did not reach the pre-defined agreement on whether the clinical symptoms or manifestations might fluctuate (72 % of ratings between 5 and 6, IQR 2) or whether post COVID had an impact on patients' work activity (73 % of ratings between 5 and 6, IQR 2).

As for the sets of symptoms that characterize post COVID (Table 2), in both waves, agreement was reached for systemic symptoms (fatigue or lack of energy, among others), neurological, neuromuscular, neurocognitive, psychological, psychiatric, and musculoskeletal symptoms. Agreement regarding respiratory and cardiopulmonary manifestations and symptoms was found to be at the limit of the pre-established consensus threshold (69 % of ratings between 5 and 6, IQR 2 in the first wave; 72 %, IQR 2 in the second).

In both waves, participants agreed that post COVID had an impact on health-related quality of life and on physical and psychological functioning, that it limited daily, family and social activities, and that

**Table 2**
Level of agreement on the statements related to clinical characteristic, symptoms and impacts of post COVID.

| | First wave (expert participants) | | | | | Second wave (larger group of respondents) | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Mean | SD | IQR | Votes 5–6 | Consensus | Mean | SD | IQR | Votes 5–6 | Consensus |
| **Clinical characteristic of post COVID** | | | | | | | | | | |
| Symptoms that persist after acute COVID-19 | 4.9 | 1.1 | 1 | 75 % | Yes | 4.7 | 1.3 | 1 | 71 % | Yes |
| It could include a single symptom | 2.4 | 1.5 | 2 | 12 % | No | 2.6 | 1.5 | 3 | 15 % | No |
| Symptoms are maintained after acute infection | 4.6 | 1.2 | 1 | 66 % | No | 4.5 | 1.3 | 1 | 62 % | No |
| Symptoms fluctuate after acute infection | 5.1 | 0.9 | 1 | 84 % | Yes | 4.8 | 1.1 | 2 | 72 % | Moderate |
| New symptoms not present during COVID-19 | 4.0 | 1.4 | 2 | 43 % | No | 3.5 | 1.3 | 2 | 26 % | No |
| Symptoms are not attributable to other causes | 5.1 | 1.1 | 1 | 85 % | Yes | 4.8 | 1.3 | 1 | 80 % | Yes |
| Duration after acute COVID-19 | | | | | | | | | | |
| - At least 3 months | 5.1 | 1.0 | 1 | 84 % | Yes | 5.0 | 0.9 | 1 | 83 % | Yes |
| - At least 6 months | 3.4 | 1.5 | 3 | 32 % | No | 3.6 | 1.6 | 3 | 37 % | No |
| - At least 12 months | 2.3 | 1.2 | 2 | 10 % | No | 2.5 | 1.5 | 2 | 13 % | No |
| **Its definition should include the impact on** | | | | | | | | | | |
| - Physical and psychological functioning | 5.3 | 0.9 | 1 | 86 % | Yes | 5.2 | 1.0 | 1 | 84 % | Yes |
| - Daily activities | 5.4 | 0.8 | 1 | 87 % | Yes | 5.2 | 0.9 | 1 | 85 % | Yes |
| - Work activities | 5.1 | 1.1 | 1 | 78 % | Yes | 5.0 | 1.1 | 2 | 73 % | Moderate |
| **Specific sets of manifestations and symptoms** | | | | | | | | | | |
| Systemic | 5.3 | 0.8 | 1 | 83 % | Yes | 5.3 | 0.9 | 1 | 91 % | Yes |
| Neurological and neuromuscular | 5.2 | 1.0 | 1 | 83 % | Yes | 5.1 | 0.8 | 1 | 84 % | Yes |
| Neurocognitive | 5.5 | 0.8 | 1 | 94 % | Yes | 5.3 | 1.0 | 1 | 88 % | Yes |
| Psychological and psychiatric | 4.8 | 1.1 | 1 | 76 % | Yes | 5.0 | 1.1 | 1 | 82 % | Yes |
| Respiratory or cardiopulmonary | 4.9 | 1.1 | 2 | 69 % | Moderate | 4.8 | 1.1 | 2 | 72 % | Moderate |
| Musculoskeletal | 5.3 | 0.9 | 1 | 85 % | Yes | 5.1 | 0.9 | 1 | 88 % | Yes |
| Gastrointestinal | 4.6 | 1.2 | 2 | 54 % | No | 4.2 | 1.2 | 1 | 43 % | No |
| Dermatological | 4.6 | 1.1 | 2 | 58 % | No | 4.3 | 1.3 | 1 | 48 % | No |
| Others not specified above | 4.6 | 1.2 | 2 | 55 % | No | 4.3 | 1.2 | 1 | 48 % | No |
| **Impact on quality of life and daily activities** | | | | | | | | | | |
| Health-related quality of life | 5.6 | 0.6 | 1 | 99 % | Yes | 5.6 | 0.5 | 1 | 97 % | Yes |
| Physical function | 5.6 | 0.6 | 1 | 98 % | Yes | 5.4 | 0.8 | 1 | 93 % | Yes |
| Psychological function | 5.4 | 1.0 | 1 | 93 % | Yes | 5.6 | 0.6 | 1 | 96 % | Yes |
| Daily activities | 5.4 | 0.8 | 1 | 90 % | Yes | 5.5 | 0.7 | 1 | 93 % | Yes |
| Family and social activities | 5.3 | 0.9 | 1 | 82 % | Yes | 5.3 | 0.8 | 1 | 87 % | Yes |
| Work activities | 5.4 | 0.8 | 1 | 88 % | Yes | 5.4 | 0.8 | 1 | 91 % | Yes |
| Work, leading to temporary sick leave | 5.5 | 0.9 | 1 | 89 % | Yes | 5.5 | 0.7 | 1 | 93 % | Yes |

SD: standard deviation; IQR: interquartile range. The data collection period for the first wave was from March 31 to April 10, 2022, and for the second wave, from April 11 to April 26, 2022.

**Table 3**
Level of agreement on the statements related to severity profiles, diagnostic process and risk factors of post COVID.

| | First wave (expert participants) | | | | | Second wave (larger group of respondents) | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Mean | SD | IQR | Votes 5–6 | Consensus | Mean | SD | IQR | Votes 5–6 | Consensus |
| **Severity of post COVID** | | | | | | | | | | |
| Is unrelated to the severity during acute phase | 4.5 | 1.4 | 2 | 65 % | No | 4.7 | 1.4 | 2 | 68 % | No |
| Severity profiles should be | | | | | | | | | | |
| - Based on functional alteration after the acute phase | 4.7 | 1.1 | 1 | 68 % | Moderate | 4.6 | 1.2 | 1 | 65 % | No |
| - Based on the set of symptoms after the acute phase | 4.8 | 1.1 | 1 | 71 % | Yes | 4.8 | 1.0 | 1 | 69 % | Moderate |
| - Measured using validated functionality scales | 5.4 | 0.8 | 1 | 93 % | Yes | 5.2 | 1.0 | 1 | 87 % | Yes |
| **To diagnose post COVID it is necessary** | | | | | | | | | | |
| - A probable SARS-Cov-2 infection in medical history | 4.6 | 1.4 | 2 | 66 % | No | 4.8 | 1.5 | 2 | 70 % | No |
| - A previous confirmed SARS-Cov-2 infection | 4.2 | 1.8 | 3 | 56 % | No | 4.6 | 1.6 | 2 | 61 % | No |
| - To rule out other health problems | 5.5 | 0.8 | 1 | 90 % | Yes | 5.5 | 0.9 | 1 | 93 % | Yes |
| - Information on previous health problems | 5.2 | 1.3 | 1 | 80% | Yes | 5.4 | 1.0 | 1 | 89 % | Yes |
| The sequelae produced by the infection | | | | | | | | | | |
| - Must be distinguished from post COVID symptoms | 5.4 | 1.2 | 1 | 88 % | Yes | 5.3 | 1.1 | 1 | 86 % | Yes |
| - Are part of the manifestations of post COVID | 3.0 | 1.7 | 4 | 31 % | No | 3.7 | 1.7 | 3 | 38 % | No |
| **Factors that may increase post COVID predisposition** | | | | | | | | | | |
| Female sex | 4.8 | 1.3 | 2 | 67 % | No | 4.6 | 1.2 | 1 | 60 % | No |
| Middle age | 4.3 | 1.4 | 2 | 50 % | No | 4.5 | 1.2 | 1 | 60 % | No |
| Infection during the first wave (2020) | 4.5 | 1.4 | 1 | 60 % | No | 4.3 | 1.3 | 1 | 52 % | No |
| Greater burden of symptoms during the acute phase | 4.2 | 1.4 | 2 | 46 % | No | 3.7 | 1.4 | 2 | 35 % | No |
| Acute infection with hospital admission | 3.6 | 1.5 | 2 | 34 % | No | 3.7 | 1.4 | 2 | 35 % | No |
| Acute infection with ICU admission | 3.7 | 1.6 | 3 | 42 % | No | 3.8 | 1.5 | 2 | 43 % | No |
| Alterations in the immune system | 3.8 | 1.3 | 2 | 38 % | No | 4.0 | 1.3 | 2 | 41 % | No |
| Previous respiratory comorbidities | 3.4 | 1.3 | 2 | 25 % | No | 3.8 | 1.3 | 2 | 33 % | No |
| Previous neurological comorbidities | 3.2 | 1.2 | 2 | 14 % | No | 3.5 | 1.2 | 1 | 18 % | No |
| Previous psychological or psychiatric comorbidities | 3.5 | 1.5 | 1 | 23 % | No | 4.0 | 1.5 | 2 | 42 % | No |
| Other previous comorbidities (not mentioned above) | 3.1 | 1.2 | 2 | 13 % | No | 3.4 | 1.2 | 1 | 21 % | No |
| Lack of sufficient scientific evidence | 4.8 | 1.6 | 2 | 75 % | Moderate | 5.2 | 1.1 | 1 | 86 % | Yes |

SD: standard deviation; IQR: interquartile range: ICU: intensive care unit. The data collection period for the first wave was from March 31 to April 10, 2022, and for the second wave, from April 11 to April 26, 2022.

it may oblige people to take days off sick from work. This group of statements presented the highest level of agreement in this eDelphi (Table 2).

In the first wave, it was agreed that post COVID severity profiles should be established based on the set of symptoms after the acute phase of infection. In the second wave, however, agreement on this statement was just below the pre-established threshold (69 % of ratings between 5 and 6, IQR 1). In both waves, there was a consensus that the severity of post COVID, understood as a functional alteration, should be measured using validated functional scales (Table 3).

In both waves, participants agreed that for the diagnosis of post COVID, other health problems to which their symptoms might be attributed should be ruled out, information on previous health problems should be available, and the existence of possible sequelae of the infection itself or interventions during the acute phase of COVID-19 should be considered (Table 3).

Fig. 2 graphically summarizes the statements related to the clinical characteristics, impacts and diagnostic processof post COVID for which there was agreement (especially in the first wave of key informants).

Finally, regarding future challenges for research or clinical management (Table 4), agreement was reported on the proposal that the definition of post COVID should be reviewed and refined as new evidence emerges, and that the predisposing risk factors at clinical, biological and sociodemographic characteristics have to be studied in robust cohorts of patients. Participants agreed that t post COVID should be recognized by the health system and by social and labor support systems, and that patients should be involved in the diagnostic process.

*Statements for which agreement was not reached*

In neither wave of consensus did participants agree on the most appropriate term for referring to this health problem in Spain. “Persistent COVID” (or post COVID in English) was the most voted term (53 % of ratings between 5 and 6, IQR 2 % and 56 %, IQR 2, in the first and second wave respectively) compared with other terms such as long COVID or post-COVID condition that appear in the English-language literature (Table 5).

Respondents disagreed that the persistence of a single symptom after the acute infection should be considered as post COVID, and that symptoms might appear even if they were not present during the acute phase. There was no agreement on whether to consider six or 12 months as the minimum duration for the condition to be considered post COVID. Regarding the specific sets of manifestations and symptoms that could appear under post COVID, there was no agreement on gastrointestinal or dermatological symptoms in either wave (Table 2).

No agreement was found on the factors that might predispose to presenting post COVID in either wave or on how severity should be classified (Table 3). When asked about aspects related to the identification and diagnosis, no consensus was reached on whether a previous probable SARS-Cov-2 infection recorded in the medical history or confirmed by laboratory tests was necessary (Table 3).

Finally, in relation to the need for a specific definition of post COVID for the pediatric population, there was a certain agreement that it would be desirable (72% of ratings between 5 and 6, IQR 2 , and 85 %, IQR 1, in the first and second wave respectively) (Table 6). However, no agreement was reached as to how the operational definition should differ with regard to the adult definition, or what specific elements should be included.

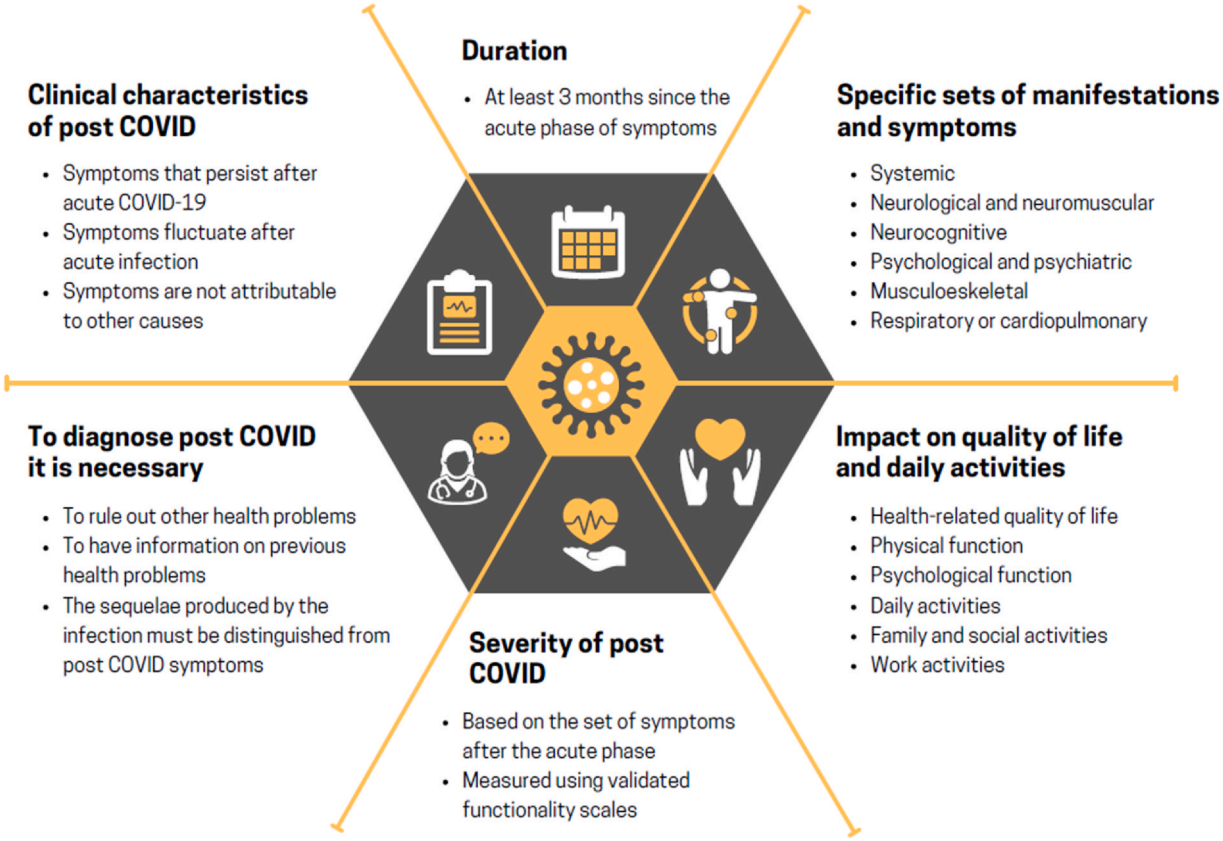


**Fig. 2.** Agreements on clinical characteristics, impacts and diagnostic process of post COVID in the CIBERPOSTCOVID eDelphi.

## Discussion

A government-commissioned eDelphi study consulting multidisciplinary stakeholders was carried out to explore the level of consensus on post COVID in the Spanish health system. The high response rate to the invitations sent in the first wave, reflects the concern with this topic among health professionals and patient associations in our country and in society in general. The results obtained support current knowledge on this new health problem adding to collective knowledge, and identify gaps for future research. More importantly, the agreements shown allow us to propose key elements to include in an applicable definition of post COVID for further research.

Based on the statements for which consensus was reached in the first wave of the exercise and supported by scientific literature, post COVID is agreed to be a set of varied multi-organ symptoms not attributable to other causes, which persist or fluctuate for at least 3 months after the acute phase of the infection of Sars-Cov-2. It affects quality of life, daily activity and job performance. In general, this definition is in line with those presented in previous publications, both at international level (e.g., by the WHO and NICE-RCGP-SIGN [7,9]) and in Spain [11,12].

### *Terminological issues, symptoms and impacts*

Although no agreement was reached on how this health problem should be named, and although many international publications speak of "post-COVID condition" or "long COVID" [7,9,11,13], the Spanish term that received the most votes was "persistent COVID". For this reason, this was the term chosen to refer to this health problem in the CIBERPOSTCOVID study. In this English version, we use the term "post COVID".

Regarding its duration and the most frequent set of symptoms, the agreements were in line with existing evidence and consensus [7,9,11]. The item "respiratory or cardiopulmonary symptoms" only just reached the stipulated level but, since its presence is supported

**Table 4**
Level of agreement on the statements related to post COVID future challenges.

| | First wave (expert participants) | | | | | Second wave (larger group of respondents) | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Mean | SD | IQR | Votes 5–6 | Consensus | Mean | SD | IQR | Votes 5–6 | Consensus |
| To address post COVID it would be necessary | | | | | | | | | | |
| - To review its definition as new evidence becomes available | 5.7 | 0.7 | 0 | 96 % | Yes | 5.8 | 0.4 | 0 | 100 % | Yes |
| - To study clinical, biological and demographic characteristics of groups of patients | 5.8 | 0.5 | 0 | 99 % | Yes | 5.7 | 0.7 | 0 | 94 % | Yes |
| - Recognition by the health system and social and work-related support | 5.5 | 0.8 | 1 | 93 % | Yes | 5.4 | 1.1 | 1 | 88 % | Yes |
| - Specialized multidisciplinary units staffed by trained professionals | 5.0 | 1.4 | 1 | 78 % | Yes | 5.0 | 1.5 | 2 | 75 % | Moderate |
| - To involve patients and family members in its diagnostic process | 5.1 | 1.1 | 1 | 80 % | Yes | 5.1 | 1.3 | 1 | 77 % | Yes |

SD: standard deviation; IQR: interquartile range. The data collection period for the first wave was from March 31 to April 10, 2022, and for the second wave, from April 11 to April 26, 2022.

**Table 5**
Level of agreement on the statements related to **terminology** for post COVID (in Spanish).

| | First wave (expert participants) | | | | | Second wave (larger group of respondents) | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Mean | SD | IQR | Votes 5–6 | Consensus | Mean | SD | IQR | Votes 5–6 | Consensus |
| "Persistent COVID" | 4.4 | 1.5 | 2 | 53 % | No | 4.2 | 1.6 | 2 | 56 % | No |
| "Long COVID" | 3.6 | 1.7 | 3 | 34 % | No | 2.9 | 1.6 | 2 | 20 % | No |
| "Post COVID syndrome" | 3.5 | 1.8 | 3 | 38 % | No | 4.0 | 1.5 | 2 | 45 % | No |
| "Post COVID symptoms" | 2.9 | 1.6 | 2 | 21 % | No | 3.3 | 1.6 | 3 | 30 % | No |

SD: standard deviation; IQR: interquartile range. The data collection period for the first wave was from March 31 to April 10, 2022, and for the second wave, from April 11 to April 26, 2022.

**Table 6**
Level of agreement on the statements related to pediatric of post COVID.

| | First wave (expert participants) | | | | | Second wave (larger group of respondents) | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Mean | SD | IQR | Votes 5–6 | Consensus | Mean | SD | IQR | Votes 5–6 | Consensus |
| A pediatric definition is needed | 5.0 | 1.2 | 2 | 72 % | Moderate | 5.2 | 1.2 | 1 | 85 % | Yes |
| Pediatric symptoms | | | | | | | | | | |
| - Differ with adult populations symptoms | 4.6 | 1.1 | 1 | 65 % | No | 4.7 | 1.0 | 1 | 66 % | No |
| - Are less severe than in adults | 3.4 | 1.5 | 3 | 33 % | No | 3.7 | 1.3 | 2 | 28 % | No |
| - Cognitive functionality is the most frequent symptom | 3.7 | 1.0 | 1 | 20 % | No | 3.6 | 0.9 | 1 | 15 % | No |
| In pediatric populations there is a greater predisposition | | | | | | | | | | |
| - With allergic health problems | 3.1 | 0.9 | 1 | 2 % | No | 3.4 | 1.0 | 1 | 12 % | No |
| - With previous respiratory problems | 3.2 | 1.1 | 1 | 10 % | No | 3.5 | 1.0 | 1 | 16 % | No |
| - In girls than in boys | 3.3 | 1.2 | 1 | 16 % | No | 3.4 | 1.0 | 1 | 12 % | No |
| - In adolescents than in children | 3.4 | 1.2 | 1 | 14 % | No | 3.6 | 1.0 | 1 | 19 % | No |

SD: standard deviation; IQR: interquartile range. The data collection period for the first wave was from March 31 to April 10, 2022, and for the second wave, from April 11 to April 26, 2022.

by the available scientific evidence [1,3,17], it was also included. In fact, a very recent study involving a large panel of experts chose it as one of the basic core outcomes for post COVID research [18]. In this eDelphi no consensus was reached regarding the appearance of new symptoms not present during the acute infection as a clinical feature of post COVID or the fluctuation of the symptoms, in contrast to the WHO international agreements [7]. The need to measure the impact of post COVID manifestations on physical and psychological functioning and on daily activities reached a high agreement in this eDelphi, but not in the WHO consensus study [7].

### *Risk factors and elements in the diagnostic process*

Participants did not reach consensus on the potential risk factors for developing post COVID, probably due to the lack of available scientific evidence and epidemiological data, or perhaps to a divergence of opinions. Relatedly, agreement was reached on the statement that not enough robust scientific evidence available on the risk factors. Variables such as the greater burden of symptoms during the acute phase of COVID-19, female gender, middle age, admission to hospital or to intensive care, previous comorbidities or alterations in the immune system have been mentioned and explored in previous research [11,19–21] However, the available evidence was limited or inconclusive [19–24]. As new evidence emerges, these potential risk factors should be addressed in depth to identify risk patterns for use in planning in clinical care.

In the diagnostic process, a comprehensive medical history was considered necessary in order to rule out previous pathologies or to take into consideration possible sequelae produced by the infection itself (or by subsequent interventions and treatments in the acute phase) that might explain the current symptoms. In line with the WHO consensus study and the SEMG guidelines [7,11], there was no agreement on the need for a confirmed diagnosis of COVID-19 by laboratory tests, as it would exclude a significant number of patients infected during the first months of the pandemic, when tests were not available.

### *The pediatric population*

The statements used in the study focused on adult population. However, in view of the recommendations of the WHO study, a specific definition for the pediatric population was considered necessary. The available evidence regarding specific considerations or risk patterns in the pediatric population was limited, with very few reviews or action protocols in our country [25,26]. In this study, no clear agreement was reached on the proposed statements, probably due to the lack of evidence in this population and the limited presence of specialists in this field among our respondents. However, recent studies focusing on the pediatric population have established a consensus definition for children and adolescents and emphasized the impact of post COVID on daily activity and cognitive dimension in this population [27].

### *Strengths and limitations*

The eDelphi methodology used presents advantages over the conventional Delphi [28]. First, it can incorporate several waves and rounds of consensus, allowing participants to reconsider their votes instantaneously in response to votes made by other participants. This feature permits a larger number of experts participate than in the conventional Delphi, and a substantive number of votes can be collected in a short time. In this sense, a large number of professionals and patients' representatives with a wide range of profiles have been able to participate, providing a broad, inclusive and multidisciplinary view. Thus, it can be considered as a learning process that allows the generation of collective knowledge around a topic.

This study also has limitations. First, the results of study underwent descriptive and global analysis, but they were not stratified according to sociodemographic or professional backgrounds. Therefore, the differences between the positions of different participant profiles could not be explored. In some cases, the same participant might have several profiles at the same time (e.g., clinician and researcher), and the sample sizes of the subgroups did not allow

a disaggregated analysis. Nevertheless, it should be stressed that the objective was to provide an overall description of aspects on which agreement or disagreement was shown. Second, the lack of robust evidence, especially regarding predisposing factors and elements of the diagnostic process available at the time the statements were formulated, may have introduced a bias in favor of the issues most cited in scientific publications. In this regard, the opinion of experts from different disciplines is particularly important: it sheds light on a little-known topic, constitutes a starting point in the absence of robust evidence, and gives a real value to the results of the consensus study.

*Conclusion*

In conclusion, the results of this study have served to broaden our understanding of post COVID in the Spanish national health system. In line with European and international studies, the study highlights key features of this multidimensional health problem, setting an initial framework that enables more structured approaches to clinical diagnosis, identification of health care and related needs and development of policy and public health strategies. A fuller understanding of post COVID and its impacts will also allow adequate coding of patients in information systems for improved management and monitoring, not only in health centers but also at national level for strategic management of currently unmet needs in patients. New independent studies are needed to ensure further advances in the understanding of post COVID and, especially, of its risk factors as well as long-term consequences.

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## CRediT authorship contribution statement

MT, VSS, ASB, AT and MEC contributed to the conceptualization of the research. FBI, MP, ASB, VSS contributed to the funding acquisition and provided the resources to carry out the research. All coauthors participated in the proposal and revision of statements included in the consensus. All coauthors contributed to the recruitment of participants/institutions. JMM, AT provided the software used in the study. MT, VSS, AT and JMM were involved in the data curation and its formal analysis. All coauthors participated on the discussion of results. MEC, ASB, FIB and MP supervised the study. MT and VSS wrote the original draft. All coauthors reviewed the original draft and contributed to the final version.

## Declaration of Competing Interest

All co-authors declare they do not have conflicts of interest.

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## Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.jiph.2023.08.022.

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