Supplemental Online Content

Global Burden of Disease Long COVID Collaborators. Estimated global proportions of individuals with persistent fatigue, cognitive, and respiratory symptom clusters following symptomatic COVID-19 in 2020 and 2021. *JAMA*. Published online October 10, 2022. doi:10.1001/jama.2022.18931

List of abbreviations

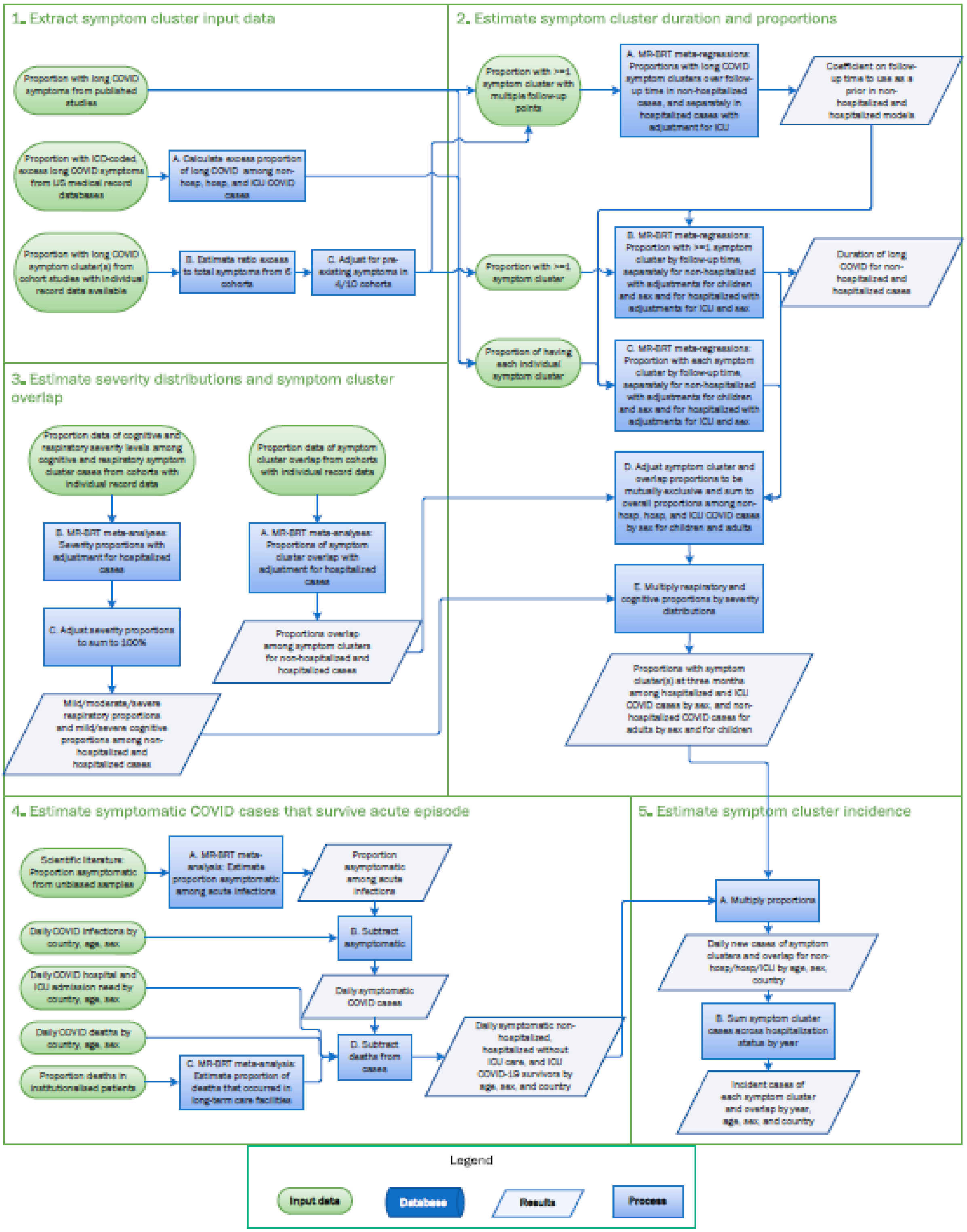
This supplemental material has been provided by the authors to give readers additional information about their work.

List of abbreviations

Abbreviation	Full phrase
ACE-2	angiotensin converting enzyme-2
COVID-19	coronavirus disease 2019
DW	Disability weight
GATHER	Guidelines for Accurate and Transparent Health Estimates Reporting
GBD	Global Burden of Diseases, Injuries, and Risk Factors Study
IDR	infection-detection ratio
IFR	infection-fatality ratio
IHR	infection-hospitalization ratio
MRTool	Meta-Regression Tool
P1	SARS-CoV-2 Gamma variant
PCR	polymerase chain reaction
RT-PCR	reverse transcription-polymerase chain reaction
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2
UI	uncertainty interval
ICU	intensive care unit
WHO	World Health Organization
YLD	Years lived with disability

eSection 1: Extract long COVID symptom cluster input data

eFigure 1. Flowchart of data, analytical processes, and long COVID symptom cluster outcomes.



Case definition
On October 6, 2021, the World Health Organization published a clinical case definition of Post COVID-19 condition developed by Delphi consensus.[1] During the Delphi consensus process, the following items attained the pre-defined threshold for consensus (70% of answers in range of 7-9 on Likert scale:[2]

1. a history of SARS-CoV-19 infection
2. three symptoms: cognitive dysfunction/brain fog, fatigue, and shortness of breath
3. importance of including "persistent" as descriptor of the nature of symptoms in case definition
4. post COVID-19 is to be considered a diagnosis of exclusion determined by a health provider when symptoms cannot be explained by an alternative diagnosis
5. that symptoms have an impact on everyday functioning
6. importance to include a separate case definition for post-COVID-19 condition for children

All other items did not reach the threshold for consensus and should be labelled "partial consensus". In terms of Delphi methodology, therefore, they should not have appeared in the case definition. The authors of the WHO Post COVID-19 clinical case definition state that they also included additional items that "reached borderline significance" without defining the threshold.

In our analysis, we focus on those items listed above that have reached the threshold for consensus:

1. a SARS-CoV-19 infection is our starting point
2. the three symptoms mentioned are the three key symptoms of the three symptom clusters we defined, and our algorithms for the ten cohort studies required mention of impact on everyday functioning (most commonly, a score of 2 or higher on the usual activities question of EQ5D-5L)
4. item 4 above pertains to a clinical case definition, rather than a case definition in a research setting; the equivalence in research would be exclusion of those who reported the same or worse symptoms prior to COVID-19. This has been built into our definition
6. lastly, we found that we could apply the same case definitions to children and adults

With regards to the minimum duration included in the WHO case definition, all of the options from 2 weeks to 6 months were in the range of "partial consensus" with small differences in the proportions mentioning a value between 1 and 3 months. There was no option given to respondents to choose one particular duration only. Similarly, the "minimum period from onset COVID-19 to presence of symptoms" items had answers for all options between 1 and 6 months, as well as "no time period" within the range of "partial consensus". For this paper, we chose to make three months from the acute infection symptom onset the starting point of long COVID.

For the purposes of quantifying all health loss due to COVID-19 in the Global Burden of Disease study, we also quantify the health loss during the acute infection phase and that experienced by cases of long COVID prior to meeting the criterion of a minimum duration of three months after infection.

Data sources
Data sources include published articles identified through systematic literature review, ongoing cohort studies who shared individual-level data with this study, and USA administrative datasets, detailed in eTable 1.

Systematic literature review

Methods
The design and dissemination of findings for this systematic literature review and meta-analysis followed the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) statement (eFigure 2, Checklist in Appendix 4).[3] The study protocol was documented in the International Prospective Register of Systematic Reviews (PROSPERO), Registration Number: CRD42020210101.[4]

Information sources and search
Search terms for the study were initially developed by co-authors at Duke University in consultation with a medical librarian who specializes in systematic literature reviews. Search terms were used to identify articles describing non-fatal, clinical outcomes in patients with confirmed COVID-19. The search strategy was reviewed and refined by the

team and medical librarian before searching the following databases: MEDLINE/PubMed, CINAHL, the Cochrane Library, Embase, Web of Science, EBSCO, Global Health, WHO Regional Indices, ClinicalTrials.gov, COVID-19 Open Research Dataset Challenge, WHO Global COVID-19 research database, WHO International Clinical Trials Registry Platform, preprint servers (bioRxiv, medRxiv, and Social Science Research Network First Look), and the coronavirus resource centers of The Lancet, JAMA, and the New England Journal of Medicine. We conducted the first comprehensive search on July 24, 2020 and an updated search was performed on August 25, 2020. The updated search included the following terms, and captured 1123 articles: [“fatigue” OR “anosmia” OR “ageusia” OR “confusion” OR “memory” OR “concentrat” OR “brain fog” OR “cough” OR “shortness of breath” OR “myocarditis” OR “stroke” OR “ischemic heart” OR “myocardial infarction” OR “depression” OR “anxiety” OR “dialysis” OR “chronic kidney disease” OR “preterm” OR “premature” OR “multisystem inflammatory” OR “thrombosis” OR “arrhythm” OR “smell” OR “taste” OR “pediatr” OR “children” OR “neonat” OR “pregnancy”]. Twelve additional sources were identified in a long COVID living systematic review accessed November 3, 2020 and sent through our long COVID collaboration[5], and 16 additional sources were identified through a PubMed search with 432 hits on September 8, 2021 using search terms [“long covid” OR “post-covid condition”].[6]

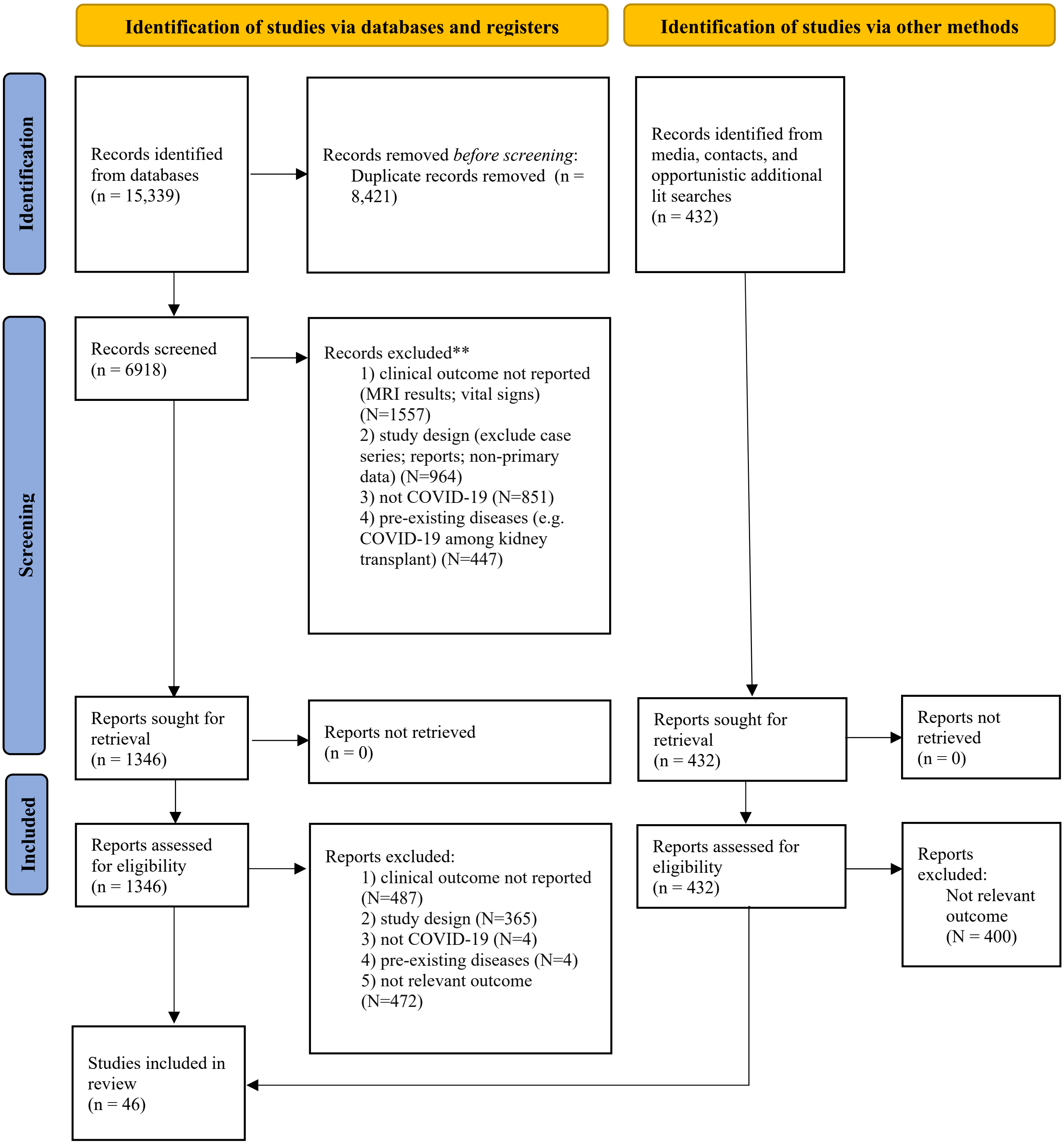
Eligibility criteria

We included studies of people with SARS-CoV-2 confirmed by a RT-PCR test with clinical outcomes caused by COVID-19 and diagnosed by health professionals. We excluded studies among populations with pre-existing conditions and where COVID-19 was self-reported or there were suspected cases. We excluded papers that only reported imaging (i.e., CT images) and/or laboratory tests alone without reporting non-fatal clinical outcomes. We also excluded the following study types: case reports with a sample size of 20 or less, editorials, commentaries, and protocol papers without primary data.

Study selection and data extraction

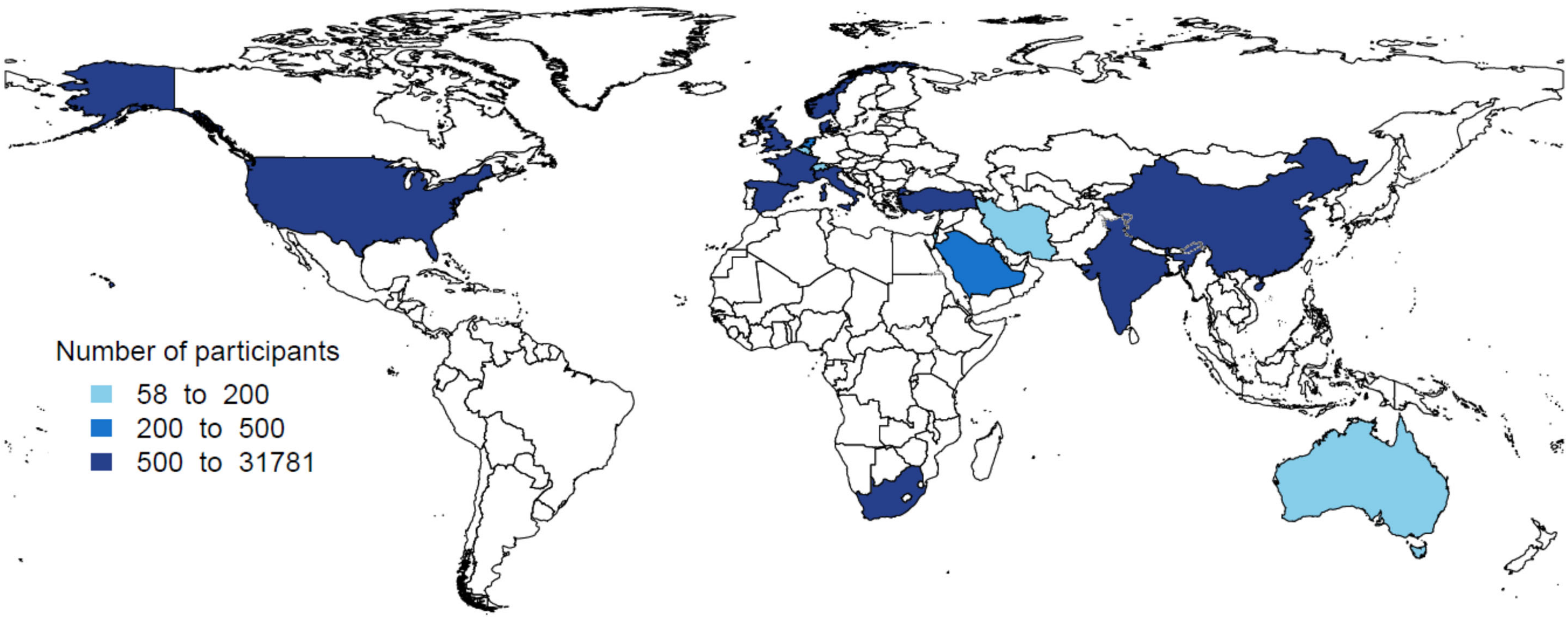
Studies identified in each database were imported into DistillerSR, a systematic review software, and duplicates were removed. Eight reviewers independently screened in pairs at the title/abstract and full-text levels against the inclusion and exclusion criteria. Thirty-six articles published in languages other than English were screened along with those in English; articles in Chinese were screened directly by reviewers who are able to read Chinese, and Google translate was used to help screen the few articles published in other languages. Then six reviewers extracted data independently using an extraction form built by the team in DistillerSR. The extracted variables included geographical location, sample characteristics, COVID case definition, clinical outcomes, and length of follow-up. We extracted the most detailed data reported by age and sex. For clinical outcomes, we extracted proportions and uncertainty values reported by the authors. Published articles included in the analysis are described in eTable 1, and aggregated samples sizes by country are depicted in eFigure 3.

eFigure 2. PRISMA flow diagram of systematic literature review for long COVID.

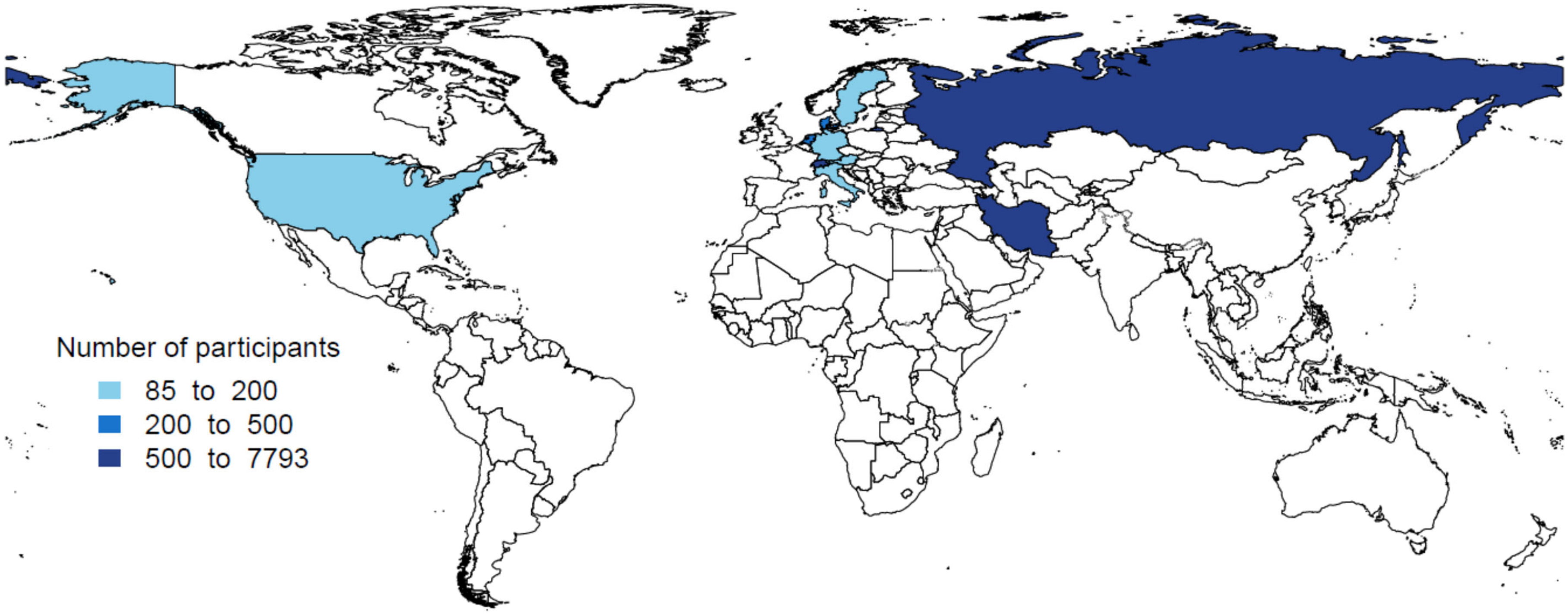


From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71. For more information, visit: http://www.prisma-statement.org/

eFigure 3. Geographic distribution of published input data sources without access to individual-level data, with shading corresponding to total sample size per country.



eFigure 4. Geographic distribution of cohort studies with access to individual-level data, with shading corresponding to total sample size per country.



eTable 1. Follow-up studies of long COVID, age and sex distributions, their inclusion of community and/or hospitalized cases, sample sizes, follow-up period, comparison method, and reported symptoms or symptom clusters.

Follow-up study	Data collection period	Age distribution Mean (SD)	% male	Non-hospitalized sample size	Hospital/ICU sample size	Follow-up since end of acute episode (days)	Comparison group	Outcomes
Cohort studies with individual-level data								
StopCOVID Cohort (Russia)[7,8]	Apr 2020-Dec 2021	Mean 54 (23)	48%		885 children, 6908 adults	171, 247, 351	Self-reported pre-COVID health status	Fatigue cluster, respiratory cluster by severity, cognitive cluster
Isfahan COVID Cohort (Iran)[9]	Mar 2020-Nov 2020	Mean 57 (15)	55%		1938 all ages	120	Self-reported pre-COVID health status	Fatigue cluster, respiratory cluster, cognitive cluster
Zürich SARS-CoV-2 Cohort (Switzerland)[10]	Prosp: Aug 2020-Jan 2022; Retro: Feb 2020-Aug 2021	Prosp: mean 50 (17) Retro: mean 46 (16)	Prosp: 49%; Retro: 51%	Prosp: 888 adults; Retro: 316 adults	Prosp: 40 adults; Retro: 74 adults	7, 23, 83, 173, 263, 353 (comm); 3, 63, 153, 243, 333 (hosp/ICU)	Self-reported pre-COVID health status	Fatigue cluster, respiratory cluster by severity, cognitive by severity cluster
CO-FLOW (Netherlands)[11]	July 2020-Jan 2022	Mean 60 (11)	69%		285 adults	81, 171	Self-reported health status one year prior to survey	Fatigue cluster, respiratory cluster by severity, cognitive cluster
Rome ISARIC (Italy)[12]	Feb 2020-Jan 2021	Mean 25 (19)	48%	82 children, 52 adults		42 (adults); 56 (children)	Self-reported pre-COVID health status	Fatigue cluster, respiratory cluster, cognitive cluster
Helbok et al. (Austria)[13]	Apr 2020-Dec 2020	Mean 56 (14)	61%	17 adults	68 adults	81	Self-reported health status one year prior to survey	Fatigue cluster, cognitive cluster
Faroe Islands[14]	Apr 2020-Dec 2020	Mean 40 (19)	46%	362 all ages	8 all ages	0, 16, 46, 76	None[a]	Fatigue cluster, respiratory cluster, cognitive cluster

Follow-up study	Data collection period	Age distribution Mean (SD)	% male	Non-hospitalized sample size	Hospital/ICU sample size	Follow-up since end of acute episode (days)	Comparison group	Outcomes
US Longitudinal COVID-19 Cohort HAARVI (USA)[15]	Aug 2020-Nov 2020	Mean 48 (15)	44%	160 adults	17 adults	164 (comm); 143 (hosp)	None[a]	Fatigue cluster, respiratory cluster, cognitive cluster
pa-COVID (Germany)[16,17]	May 2020-Feb 2021	Mean 57 (15)	64%	29 adults	145 adults	42, 90, 180, 365	None[a]	Fatigue cluster, respiratory cluster by severity, cognitive cluster
PronMed ICU (Sweden)[18,19]	Mar 2020-June 2021	Mean 60 (9)	72%		158 adults	121, 166, 346	None[a]	Fatigue cluster, respiratory cluster, cognitive cluster
Administrative data sources								
PRA administrative data (USA)[20]	Mar 2020-Mar 2021	Mean 52 (22)	41%	772,611 all ages	237,274 all ages	87 (comm); 73 (hosp); 101 (ICU)	Matched 1:1 to non-COVID controls[b]	ICD codes for fatigue, respiratory, and cognitive symptoms
Veterans Affairs administrative data (USA)[21,22]	Mar 2020-Mar 2021	Median 61 [IQR 48-72] Mean* 60 (17)	88%	73,435 adults	13,654 adults	143 (comm); 123 (hosp); 150 (ICU)	Matched to 4,990,835 non-COVID controls[b]	ICD codes for fatigue, respiratory, and cognitive symptoms
Published articles without access to individual-level data								
Coronavirus Infection Survey (CIS) (UK)[23,24]	April 2020-March 2021	Mean* 41 (16)	48%	3489 children, 21,622 adults		26, 75 (children); 26, 33, 40, 47, 54, 61, 68, 75, 82, 89, 96, 103, 110 (adults)	Matched 1:1 to non-COVID controls	Fatigue, cough
Berg et al. (Denmark)[25]	July 2021-Sept 2021	Median 18 [IQR 17-19] Mean* 18 (2)	42%	5106 children		53, 83, 173, 263, 353	Matched COVID-free control group (either not tested	Fatigue, trouble breathing, trouble concentrating

Follow-up study	Data collection period	Age distribution Mean (SD)	% male	Non-hospitalized sample size	Hospital/ICU sample size	Follow-up since end of acute episode (days)	Comparison group	Outcomes
							or tested negative)	
CLoCk (England)[26]	April 2021-June 2021	Range 11-17 Mean* 14 (1)	37%	3065 children		83	Matched to COVID test-negative controls	Tiredness, shortness of breath, confusion/disorientation/drowsiness, any symptom
Søraas et al. (Norway)[27]	March 2020-Nov 2020	Mean 49 (14)	43%	676 adults		119	COVID test-negative group	Fatigue, dyspnoea, any symptom
Xiong et al. (China)[28]	March 2020-June 2020	Median 52 [IQR 41-62] Mean* 49 (14)	46%		538 adults	81	COVID-free control group (n=184) with similar demographic traits	Fatigue, dyspnoea
Wanga et al. (USA)[29]	April 2021	Median 39 Mean* 40 (13)	52%	417 adults	48 adults	21	COVID test-negative group	Fatigue, dyspnoea, cognitive problems
COVID Symptom Study (CSS) App (UK)[30,31]	April 2020-Sept 2020 Approx.*	Child median 13 [IQR 10-15] Mean* 13 (1) Adult mean 43 (SD 13)	Child: 50%, Adult: 29%	1734 children, 4182 adults		19, 47, 75	None	Fatigue, cough, shortness of breath
Huang et al. (China)[32]	June 2020-Sept 2020	Median 57 [IQR 47-65] Mean* 56 (13)	52%		1655 adults	171 (hosp); 170 (ICU)	None	Fatigue or muscle weakness, dyspnoea
Dryden et al. (South Africa)[33]	Jan 2021-April 2021	Median 51 [IQR 40-61] Mean* 56 (13)	46%		1258 adults	19	None	Fatigue, confusion, dyspnoea
Naik et al. (India)[34]	Oct 2020-Feb 2021	Mean 41 (14)	69%	523 adults	711 adults	63, 84	None	Fatigue, dyspnea

Follow-up study	Data collection period	Age distribution Mean (SD)	% male	Non-hospitalized sample size	Hospital/ICU sample size	Follow-up since end of acute episode (days)	Comparison group	Outcomes
Kayaaslan et al. (Turkey)[35]	Dec 2020-Feb 2021	Mean 45 (16)	54%	591 adults	416 adults	113	None	Fatigue, dyspnoea, concentration or memory problems
Venturelli et al. (Italy)[36]	May 2020-July 2020	Mean 63 (14)	67%		767 adults	72	None	Confusion, dyspnoea
Peghin et al. (Italy)[37]	Sept 2020-Nov 2020	Mean 53 (16)	47%	502 adults	39 adults	182 (comm); 161 (hosp); 191 (ICU)	None	Fatigue, dyspnoea
Chopra V et al. (USA)[38]	May 2020-Sept 2020	Median 62 [IQR 50-72] Mean* 61 (16)	52%		488 adults	51	None	Cough, shortness of breath, chest tightness, wheezing
COMEBAC (France)[39]	July 2020-Sept 2020	Mean 61 (16)	42%		478 adults	104	None	Memory loss, mental slowness, concentration problems, fatigue, dyspnoea, cough
Anastasio et al. (Italy)[40]	June 2020-Oct 2020 Approx.*	Median 56 [IQR 49-63] Mean* 56 (10)	46%		379 adults	135	None	Dyspnoea, memory loss
ANOSVID (France)[41]	Jan 2021-March 2021	Mean 49 (19)	36%	233 adults	121 adults	259	None	Fatigue, dyspnoea, any symptom from their symptom list
Sigfrid et al. (UK)[42]	April 2020-Jan 2021 Approx.*	Median 60 [IQR 52-68] Mean* 60 (12)	59%		327 adults	192	None	Fatigue, shortness of breath, any symptom
COD19 (Italy)[43]	Feb 2021-March 2021	Median 53 [IQR 42-63] Mean* 53 (16)	52%	114 adults	189 adults	366	None	Fatigue, respiratory disorders
Moreno-Pérez et al. (Spain)[44]	March 2020-	Median 56 [IQR 42-68]	53%		277 adults	77	None	Fatigue, dyspnoea, cough, amnesic complaints

Follow-up study	Data collection period	Age distribution Mean (SD)	% male	Non-hospitalized sample size	Hospital/ICU sample size	Follow-up since end of acute episode (days)	Comparison group	Outcomes
	June 2020	Mean* 55 (19)						
Heesakkers et al. (Netherlands)[45]	Up to June 2021	Mean 61 (9)	72%		246 young adults and adults	365	None	Fatigue, cognitive failure, dyspnea
Bellan et al. (Italy)[46]	June 2020-Oct 2020 Approx.*	Median 61 [IQR 50-71] Mean* 61 (16)	60%		238 adults	96	None	Dyspnoea
Cirulli et al. (USA)[47]	Jan 2020-Sept 2020	Median 58 (range 18-89+) Mean* 56 (16)	36%	225 adults	8 adults	28, 58, 88	None	Fatigue, cough, dyspnoea.
Tleyjeh et al. (Saudi Arabia)[48]	June 2020-Jan 2021 Approx.*	Mean 52 (14)	77%		222 adults	122	None	Fatigue, shortness of breath, concentration issues, memory impairment, any persistent symptoms
Mandal S et al. (UK)[49]	Not reported	Mean 60 (16)	62%		217 all ages	45	None	Fatigue, breathlessness, cough
Taboada et al. (Spain)[50]	Sept 2020-Nov 2020 Approx.*	Mean 66 (14)	60%		183 adults	171 (hosp); 170 (ICU)	None	Dyspnoea
Sibila et al. (Spain)[51]	June 2020-July 2020 Approx.*	Mean 56 (20)	57%		172 all ages	81	None	Dyspnoea
García-Abellán et al. (Spain)[52]	Up to Dec 2020	Median 64 [IQR 54-76] Mean* 65 (16)	60%		104 adults (2-month follow-up), 116 adults (6-month follow-up)	51, 171	None	Fatigue, dyspnoea, respiratory symptoms, any symptom from their symptom list

Follow-up study	Data collection period	Age distribution Mean (SD)	% male	Non-hospitalized sample size	Hospital/ICU sample size	Follow-up since end of acute episode (days)	Comparison group	Outcomes
Carvalho-Schneider C et al. (France)[53]	March 2020-June 2020	Mean 49 (15)	44%	116 adults	34 adults	30	None	Dyspnoea
Carfì A et al. (Italy)[54]	April 2020-May 2020	Mean 57 (15)	63%		143 adults	27	None	Fatigue, dyspnoea
Suárez-Robles et al. (Spain)[55]	April 2020-June 2020 Approx.*	Mean 59 (19)	46%		134 all ages	81	None	Fatigue, dyspnoea
Horwitz et al. (USA)[56]	April 2020-Nov 2020 Approx.*	Median 62 [IQR 52-68] Mean* 61 (12)	60%		126 adults	171	None	Fatigue, dyspnoea, cognitive fuzziness/brain fog/difficulty concentrating
Garrigues et al. (France)[57]	June 2020-Sept 2020 Approx.*	Mean 63 (16)	63%		120 all ages	88 (hosp); 81 (ICU)	None	Fatigue, cough, dyspnoea, memory loss
Arnold D et al. (UK)[58]	May 2020-Sept 2020 Approx.*	Median 60 [IQR 46-73] Mean* 60 (20)	56%		110 adults	60 (hosp); 53 (ICU)	None	Fatigue, cough, shortness of breath
Jacobson et al. (USA)[59]	Up to Nov 2020	Mean 43 (14)	53%	96 all ages	22 all ages	112 (comm); 92 (hosp/ICU)	None	Memory problems, fatigue, dyspnoea
Klein et al. (Israel)[60]	April 2020-Oct 2020	Mean 35 (12)	62%	103 adults		171	None	Fatigue, breathing difficulties
Darcis et al. (Belgium)[61]	June 2020-April	Mean 61 (14)	63%		101 adults (3-month follow-up), 78 adults (6-	85, 171	None	Fatigue, exertional dyspnoea, confusion

Follow-up study	Data collection period	Age distribution Mean (SD)	% male	Non-hospitalized sample size	Hospital/ICU sample size	Follow-up since end of acute episode (days)	Comparison group	Outcomes
	2021 Approx.*				month follow-up)			
Halpin S et al. (UK)[62]	May 2020-June 2020	Hosp: median 71 (range 20-93) Mean* 64 (16) ICU: median 59 (range 34-84) Mean* 59 (12)	54%		100 adults	39 (hosp); 38 (ICU)	None	Fatigue, breathlessness, concentration problems, short-term memory problems
Say et al. (Australia)[63]	March 2020-March 2021	Median 3 [IQR 1-8] Mean* 4 (5)	53%	97 children		128	None	Fatigue
Becker et al. (Switzerland)[64]	March 2020-July 2021	Mean 60 (15)	26%		90 adults	90, 365	None	Fatigue, concentration difficulties, shortness of breath, any symptom from their symptom list
Lerum et al. (Norway)[65]	May 2020-June 2020 Approx.*	Median 59 [IQR 49-72] Mean* 60 (17)	52%		69 adults	59 (hosp), 55 (ICU)	None	Dyspnoea
Elkan et al. (Israel)[66]	Aug 2020-April 2021 Approx.*	Median 59 [IQR 50-68] Mean* 59 (14)	44%		66 adults	261	None	Fatigue, dyspnoea, memory/concentration impairment
Asadi-Pooya et al. (Iran)[67]	March 2021	Mean 12 (3)	48%		58 children	246	None	Fatigue, dyspnoea
Chopra N et al. (India)[68]	Not reported	Mean 35 (12)	53%		53 all ages	21	None	Fatigue, exertional dyspnoea

Studies are ordered first by three types of data sources (cohort studies with access to individual record data, administrative databases, and published studies without access to individual record data). Second, the cohort studies and published studies are ordered by whether they had a comparison (either by controls or information on pre-COVID health status). Lastly, studies were ordered by sample size within these categories.

IQR = interquartile range; SD = standard deviation; hosp = hospitalized cases

Mean*: Mean (SD) converted from median and IQR or range using method by Wan et al (2014).[69] Means were weighted by sample size to get the mean values reported for aggregated categories in table 2 in the main paper. Standard deviations were pooled by first computing the coefficient of variation (i.e., SD/mean) for each study, weighting these coefficients of variation by sample size and then multiplying this pooled value by the pooled mean.

Approx.*: Data collection period was approximated by adding follow-up period to the reported COVID diagnosis period if surveys were conducted only at follow-up, and specific follow-up data collection period was not reported in the study.

[a] Data from four studies with individual record data that did not report on the differences in pre-COVID health and health at follow-up were adjusted based on ratios of excess to total reported symptom clusters from six cohorts that did contain this information**.**

[b] The two US administrative databases allowed the identification of controls matched to those with a positive PCR test for COVID-19 based on a range of demographic and comorbid conditions. We took the difference between cases and controls as the proportion of symptoms attributable to COVID-19.

Cohort studies with individual record data
None of the published articles included above provided detailed information on the overlap or severity of symptoms, and the data on single symptoms was insufficient to fully quantify the symptom clusters of interest. To enrich the available published data, study authors of published studies and ongoing COVID-19 follow-up studies that were registered at the ISRCTN registry were contacted.[70] From 23 positive responses of 42 study authors contacted, ten were able to share individual record symptom cluster data in time for inclusion in this study (Table 2, eTable 1, eFigure 4). With researchers from the ten follow-up studies, algorithms were developed to define the three symptom clusters by severity level by choosing symptom questions and measures employed in each study that would most closely match the wording of the lay descriptions that were presented to respondents of the GBD disability weight surveys (Table 1). Details of the algorithms for each of the included studies are below. 203 respondents who were missing responses required to apply the below algorithms were excluded.

Several of these cohort studies relied on self-reported symptoms (yes/no) or a Likert scale of frequency or severity of the symptom(s). In addition, five cohorts incorporated formal assessments in their questionnaires and algorithms for various symptom cluster components:

Fatigue with bodily pain and mood swings

- Daily Fatigue Impact Scale (FIS)[71]
- Multidimensional Fatigue Inventory (MFI)[72]
- Fatigue Assessment Scale (FAS)[73]
- Patient Health Questionnaire (PHQ-9)[74]
- Generalized anxiety disorder (GAD-7)[75]
- 5-level EQ-5D (EQ-5D-5L)[76] pain/discomfort and anxiety/depression dimensions
- Depression Anxiety Stress Scales (DASS-21)[77]

Respiratory problems

- the Modified Medical Research Council (mMRC) dyspnea scale[78,79]

Cognitive problems

- the Montreal Cognitive Assessment (MoCA)[80]

All cohort studies with individual record data are described in eTable 1 in detail, and aggregated sample sizes by country are depicted in eFigure 4.

Case Selection Algorithms

1. **CO-FLOW (Netherlands)**
   Symptom cluster cases at 12 month follow-up were restricted to those who met the criteria for each symptom cluster at the 6 month follow-up point.

- **Fatigue, bodily pain and mood swings**;
  - lay description: "is always tired and easily upset. The person feels pain all over the body and is depressed"
    - **rule 1 (3 and 6 month follow-up cases):** RAND S-36 health worse than 1 year ago (slightly worse or much worse)
      Compared to a year ago, how would you *now* rate your health in general*?*
      - *Much better than a year ago*
      - *Slightly better than a year ago*
      - *About the same as a year ago*
      - *Slightly worse than a year ago*
      - *Much worse than a year ago*
    - **rule 2 (12 month follow-up cases):** met the criteria for this symptom cluster at previous follow-up (3 or 6 months)

        - **rule 3**: Ziektelast Q14 ('how often in past week were you bothered by fatigue?'): 3+ (7-point scale; 3=regularly, 4=very often, 5=most of the time, and 6=always) **plus** either [Q3 or Q4 3+ (how often in last week did you feel anxious and depressed, respectively; same scale as Q14] **or** pain/discomfort from EQ5D-5L 3+
        - **rule 4:** Ziektelast Q14 (fatigue): 2 **plus** (Q3-anxiety or Q4-depressed 3+) **and** pain/discomfort from EQ5D-5L 3+
    - **3 and 6-month follow-up formula:** rule 1 **and (**rule 3 **or** rule 4)
    - **12-month follow-up formula:** rule 2 **and (**rule 3 **or** rule 4)
- **Cognition problems**
    - Mild cognitive problems
        - lay description for mild: "has some trouble remembering recent events, and finds it hard to concentrate and make decisions and plans"
        - **rule 1 (3 and 6 month follow-up cases):** RAND S-36 health worse than 1 year ago (slightly worse or much worse)
        - **rule 2 (12 month follow-up cases):** met the criteria for this symptom cluster at previous follow-up (3 or 6 months)
        - **rule 3:** MoCA 19-25 and EQ5D-5L usual activities 2+
        - **rule 4:** pre-existing dementia = no
    - **Mild 3 and 6-month follow-up formula:** rule 1 **and** rule 3 **and** rule 4
    - **Mild 12-month follow-up formula:** rule 2 **and** rule 3 **and** rule 4
    - Severe cognitive problems
        - lay description for severe: "has memory problems and confusion, feels disoriented, at times hears voices that are not real, and needs help with some daily activities"
        - **rule 1 (3 and 6 month follow-up cases):** RAND S-36 health worse than 1 year ago (slightly worse or much worse)
        - **rule 2 (12 month follow-up cases):** met the criteria for this symptom cluster at previous follow-up (3 or 6 months)
        - **rule 3:** MoCA <=18 and EQ5D-5L usual activities 2+
        - **rule 4:** pre-existing dementia = no
    - **Severe 3 and 6-month follow-up formula:** rule 1 **and** rule 3 **and** rule 4
    - **Severe 12-month follow-up formula:** rule 2 **and** rule 3 **and** rule 4
- **Respiratory problems**
    - Mild respiratory problems
        - lay description for mild respiratory problems: "has cough and shortness of breath after heavy physical activity, but is able to walk long distances and climb stairs"
        - **rule 1 (3 and 6 month follow-up cases):** RAND S-36 health worse than 1 year ago (slightly worse or much worse)
        - **rule 2 (12 month follow-up cases):** met the criteria for this symptom cluster at previous follow-up (3 or 6 months)
        - **rule 3:** Ziektelast Q2 (shortness of breath during exercise) = 3 or cough = 3+ **and** at least two of the following statements are true:
            - Q14 (fatigue) = 0/1 (never or rarely)
            - Q7 ('how much did you feel limited due to breathing problems in past week to carry out strenuous activities?') = 2/3 (little or somewhat limited)
            - Q8, Q9 and Q10 (same as Q7 but asking about moderate activities (walking, housework, shopping), daily activities (washing, shaving) and social activities (talking, interacting with children, visiting friends or relatives)) = 0-2 (not, little or somewhat limited)
        - **rule 4:** Ziektelast Q2 (shortness of breath during exercise) 4+ (very often, most of the time or always) **and** none or only one of the following statements are true:
            - Q5 (cough) = 3+
            - Q14 (fatigue) = 2+
            - Q7 (strenuous activities) = 4+
            - Q8 (light activities) = 3+
    - **Mild 3 and 6-month follow-up formula:** rule 1 **and** (rule 3 **or** rule 4)

- **Mild 12-month follow-up formula:** rule 2 **and** (rule 3 **or** rule 4)
- Moderate respiratory problems
  - lay description for moderate respiratory problems: "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"
  - **rule 1 (3 and 6 month follow-up cases):** RAND S-36 health worse than 1 year ago (slightly worse or much worse)
  - **rule 2 (12 month follow-up cases):** met the criteria for this symptom cluster at previous follow-up (3 or 6 months)
  - **rule 3:** Ziektelast Q2 (shortness of breath during exercise) = 3 (sometimes) or cough = 3+ (regularly or more often) **and** at least two of the following statements are true:
    - Q14 (fatigue) = 2+ (sometimes or more often)
    - Q7 (strenuous activities) = 4+
    - Q8 **or** Q9 **or** Q10 (light activities) = 3+
  - **rule 4:** Ziektelast Q2 (shortness of breath during exercise) 4+ **and** at least two of the following statements are true:
    - Q5 (cough) = 3+
    - Q14 (fatigue) = 2+
    - Q7 (strenuous activities) = 4+
    - Q8 (light activities) = 3+
  - **rule 5:** Ziektelast Q1 (shortness of breath during rest) = 3 (sometimes) **and** none or only one of following statements are true:
    - Q5 (cough) = 3+
    - Q14 (fatigue) = 3+
    - Q8 (light activities) = 4+
- **Moderate 3 and 6-month follow-up formula:** rule 1 **and** (rule 3 **or** rule 4)
- **Moderate 12-month follow-up formula:** rule 2 **and** (rule 3 **or** rule 4)
- Severe respiratory problems
  - lay description for severe respiratory problems: "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"
  - **rule 1 (3 and 6 month follow-up cases):** RAND S-36 health worse than 1 year ago (slightly worse or much worse)
  - **rule 2 (12 month follow-up cases):** met the criteria for this symptom cluster at previous follow-up (3 or 6 months)
  - **rule 3:** Ziektelast Q1 (shortness of breath during rest) = 4+; or
  - **rule 4:** Ziektelast Q1 (shortness of breath during rest) = 3 **and** at least two of following statements is true:
    - Q5 (cough) = 3+
    - Q14 (fatigue) = 3+
    - Q8 (light activities) = 4+
- **Severe 3 and 6-month follow-up formula:** rule 1 **and** (rule 3 **or** rule 4)
- **Severe 12-month follow-up formula:** rule 2 **and** (rule 3 **or** rule 4)

2. Faroe Islands

- For all cases of long COVID: question on asymptomatic infection = no
- Fatigue, bodily pain and mood swings cluster:
  - **Define case** as:
    - fatigue = mod or sev **and** (muscle pain **or** joint pain = mod or sev); **or**
    - [fatigue = mild **and** (muscle pain **or** joint pain = mild)] **and** D-FIS (Daily Fatigue Impact Scale) >8
- Cognitive cluster
  - **Define case of mild** cognitive problems as:
    - Person does not qualify as severe (see below); **and**

    - At least two of the three questions D-FIS 5 (‘make decisions’), D-FIS 6 (‘finish tasks that require thinking’), D-FIS 7 (‘slowed down in thinking’) are scored as ‘moderate’ (2) or worse.
  - **Define case of severe** cognitive problems as:
    - Two out of D-FIS 5, 6 and 7 are scored big (3) or extreme (4) and D-FIS 2 is scored 3 or 4
- Respiratory cluster
  - **Define case of mild** respiratory problems as:
    - (shortness of breath **or** difficulty in breathing = mild and cough = mild/mod/sev) **or** (shortness of breath **or** difficulty in breathing = moderate **and** cough = mild)
  - **Define case of moderate** respiratory problems as:
    - (shortness of breath **or** difficulty in breathing = mod and cough = mod/sev) **or** (shortness of breath **or** difficulty in breathing = severe **and** cough = mild)
  - **Define case of severe** respiratory problems as:
    - (shortness of breath **or** difficulty in breathing = severe and cough = mod/sev)

3. US Longitudinal COVID-19 Cohort HAARVI (Seattle USA)

This study has a lot of free text information making it more difficult to write a comprehensive algorithm. A starting point was to select rule 1 and rule 2:

Rule 1: Did you experience symptoms due to COVID-19 = yes

Rule 2: Are you still experiencing symptoms = yes

However**,** three cases mentioned no on this question but in text fields reported shortness of breath when running a short distance; ‘brain fog’ and being overwhelmed by easiest tasks; and easily fatigues, anxious and difficulty comprehending a lot of info, respectively. These three cases were classified as mild respiratory, severe cognition and fatigue + mild cognitive.

Among those with a lower rating on general health barometer currently compared to before COVID:

- mention of fatigue plus either anxiety/depression or bodily pain defined them as a case of the fatigue cluster
- mention of shortness of breath climbing stairs defined mild respiratory problems
- mention of shortness of breath during light activities (personal grooming/dressing, using toilet/bathing, household chores, managing personal affairs) defined moderate respiratory problems (note no questions about shortness of breath while at rest and hence no one qualified for severe respiratory problems)
- mention of problems remembering, brain fog, lack of concentration in free text field describing reasons for problems with daily activities. The 5 cases selected for cognitive problems were graded into mild and severe based on the severity expressed in the free text field

4. Helbok et al. (Austria)

- **Fatigue, bodily pain and mood swings**;

  Define a case as rule 1 **and** rule 2
  - **rule 1**: select those reporting their health as ‘fair’ or ‘poor’ on SF-36 Q1 and reporting their health as ‘somewhat or much worse’ than a year ago (SF-36 Q2)
  - **rule 2**:
    - yes on self-report fatigue question **or** at least one of SF-36 Qs 9e (full of energy) 4/5 (seldom, never), 9g (fatigued) and 9i (tired) <4 (always, most of the time or sometimes) **and**
    - [(SF-36 Q7 (pain) **or** SF-36 Q8 (pain limiting daily activities) answered as ‘moderate’, ‘severe’, or ‘very severe’) **or**
    - Hospital Anxiety and Depression Scale (HADS-a) > 7 **or** HADS-d > 7 **or**
    - SF-36 Qs 9b (very nervous), 9c (so depressed that nothing can cheer you up) or 9f (despondent and sad) answered as ‘often’, ‘most of the time’ or ‘continuous’)

- cognition problems
    1. define a mild case as rule 1 **and** rule 2; a case of severe cognition problems as rule 1 **and** rule 3
        i. **rule 1**: select those reporting 'fair' or 'poor' on SF-36 Q1 and reporting their health as 'somewhat or much worse' than a year ago (SF-36 Q2)
        ii. **rule 2**: MoCA 19-25
        iii. **rule 3**: MoCA <=18

Note: no questions on respiratory problems

5. Isfahan COVID Cohort (Iran)

- **Fatigue, bodily pain and mood swings cluster:** rule 1 **and** rule 2 **and** rule 3
    - **Rule 1**: Hp19a.6 ('reduced ability for daily functions *prior* to COVID')= no and at least two out of Hp19a.8 ('feeling sad most of them time *prior* to COVID'), Hp19a.9 ('frustration and no hope *prior* to COVID'), and Hp19a.10 ('dissatisfaction and not enjoying life *prior* to COVID')= no;
    - **Rule 2**: MHA1.2 (general weakness) = yes **or** MHA2.5 (fatigue during normal activity) = yes **or** MHA9.2 (muscle weakness) = yes
    - **Rule 3**: MHA9.1 (joint pain) = yes **or** MHA9.4 (muscle pain) = yes **or** MHA11.1 (depression) = yes **or** MHA11.2 (anxiety) = yes

- **Cognition cluster:**
    - MHA 11.3 (memory loss) = 1 **and** Hp19a.4 (reduced concentration and ability for decision making *before* disease) = no **and** Hp19b.4 (reduced concentration and ability for decision making *after* disease) = yes
        - There is not enough information to grade by severity

- **Respiratory cluster:**
    - **mild =** rule 1 **and** rule 2 **and** rule 5
    - **moderate =** rule 1 **and** rule 2 **and** rule 4
    - **severe =** rule 1 **and** rule 2 **and** rule **3**
    - **Rule 1**: mhb25 (history *before* admission of dyspnea) = no **and** mb261= no (no history of use of oxygen *prior* to admission)
    - **Rule 2:** mhb25 = yes (history *before* admission of dyspnea**)** **and** mhb251= 1 (dyspnea 'during climbing' *prior* to covid) **and** dyspnea *post* COVID (mha1021) is 1 (at rest) or 2 (during normal activities))
    - **Rule 3:** MHA10.3 (need for O_2 therapy) = yes **or** MHA10.2.1 =1 (shortness of breath at rest)
    - **Rule 4:** MHA10.2.1 = 2 (shortness of breath during normal activities) and MHA10.3 (need for O_2 therapy) = no
    - **Rule 5:** MHA10.2.1 = 3 (shortness of breath during strenuous activity) and MHA10.3 (need for O_2 therapy) = no

6. pa-COVID (Germany)

1. **Fatigue, bodily pain and mood swings** cluster:
    a. Case defined as: rule 1 **and** (rule 2 **or** rule 3 **or** rule 4 **or** rule 5)
        - **rule 1:** any of the 4 questions on 'Fatigue' in Promis-29 questionnaire (in last week 'I am fatigued', 'I have trouble starting something because I feel tired', 'how drained to you feel generally', and 'how fatigued have you been in general') = often **or** always
        - **rule 2:** any of the 4 questions on 'Anxiety' = sometimes **or** often **or** always
        - **rule 3:** any of the 4 questions on 'Depressivität' = sometimes **or** often **or** always
        - **rule 4:** any of the 4 questions on impairment due to pain ('how much does pain affect your daily activities, house work, social interactions, domestic activities?') = rather **or** a lot
        - **rule 5:** Pain intensity >4

2. Cognitive cluster
    a. **Mild** cases
        - Question in fatigue screen: ongoing complaints: concentration problems = moderate
    b. Moderate cases

- Question in fatigue screen: ongoing complaints: concentration problems = strong

3. Respiratory cluster
   a. **Mild** defined as rule 1 **and** rule 2 **and** rule 3
      - **rule 1**: I get short of breath when climbing stairs = moderate **or** considerable **or** a lot
      - **rule 2:** I am having difficulty breathing = a little or moderately
      - **rule 3**: does not qualify as moderate or severe
   b. **Moderate** defined as rule 1 **and** rule 2 **and** rule 3
      - **rule 1**: I get short of breath walking 10 paces on even ground at normal pace = moderate **or** a lot
      - **rule 2:** I get short of breath when dressing = moderate **or** a lot
      - **rule 3**: does not qualify as severe
   c. **Severe** defined as: (rule 1 **or** rule 2) **and** rule 3
      - **rule 1**: I get short of breath when sitting or lying = moderate **or** a lot
      - **rule 2:** I get short of breath when I speak = moderate **or** a lot
      - **rule 3:** I get out of breath getting out of bed or a chair = moderate **or** a lot

7. PronMed Sweden COVID ICU study

Symptom cluster cases at 12 month follow-up were restricted to those who met the criteria for each symptom cluster at the 6 month follow-up point.

Fatigue, bodily pain and mood swings: rule 1 **and (**rule 2 **or** rule 3)
rule 1: Fatigue (MFI00) > 5
rule 2: Depression (PHQ) > 9 **or** anxiety (GAD) > 9
rule 3: EQ5D-5L pain/discomfort score plus EQ5D-5L anxiety/depression score >= 4 (i.e. at least 'slight problems' on both items or 'moderate problems' on one)

Cognitive problems

- **Mild:** rule 1 **and** rule 2 **and** rule 3
  rule 1: Cognitive dysfunction (MoCA) < 26
  rule 2: at least one of difficulties concentrating, memory problems and problem finding words = yes
  rule 3: EQ5D-5L usual activity score = slight or moderate problems (2 or 3)
- **Moderate:** rule 1 **and** rule 2 **and** rule 3
  rule 1: Cognitive dysfunction (MoCA) < 26
  rule 2: at least one of difficulties concentrating, memory problems and problem finding words = yes
  rule 3: EQ5D-5L usual activity score = severe or extreme problems (4 or 5)

Note: One respondent missing a MoCA score was allowed to be assigned mild cognitive symptom cluster because they met the remaining criteria and one missing value was allowed.

Respiratory problems

- **Mild:** rule 1 **or (**rule 2 **and** rule 3)
  rule 1: (Shortness of breath = 1 **or** cough/sore throat = 1) **and** EQ5D-5L usual activity score = slight
  rule 2: (Shortness of breath = 1 **or** cough/sore throat = 1) **and** EQ5D-5L usual activity score = moderate
  rule 3: Not more than one of the following applies: fatigue (MFI00) > 5, depression (PHQ) > 9, anxiety (GAD) > 9
- **Moderate:** (rule 1 **and** rule 2) **or** (rule 3 **and** rule 4)
  rule 1: (Shortness of breath = 1 **or** cough/sore throat = 1) **and** EQ5D-5L usual activity score = moderate
  rule 2: Not more than one of the following applies: fatigue (MFI00) > 5), depression (PHQ) > 9), anxiety (GAD) > 9
  rule 3: shortness of breath = 1 **or** cough/sore throat = 1) **and** EQ5D-5L usual activity score = severe

rule 4: Not more than one of the following applies: fatigue (MFI00) > 5), depression (PHQ) > 9), anxiety (GAD) > 9

- **Severe:** (rule 1 **and** rule 2) **or** (rule 3 **and** rule 4)
  rule 1: (Shortness of breath = 1 **or** cough/sore throat = 1) **and** EQ5D-5L usual activity score = severe
  rule 2: Two or more of the following applies: fatigue (MFI00) > 5), depression (PHQ) > 9), anxiety (GAD) > 9
  rule 3: shortness of breath = 1 **or** cough/sore throat = 1) **and** EQ5D-5L usual activity score = extreme
  rule 4: At least one of the following applies: fatigue (MFI00) > 5), depression (PHQ) > 9), anxiety (GAD) > 9

8. **Rome ISARIC Pediatrics (Italy)**

Overarching rule for any case is 'fully recovered' <10.

Fatigue, bodily pain and mood swings: rule 1 **and** (rule 2 **or** rule 3 **or** rule 4)

rule 1: fatigue_comp_before = 4 **or** 5 (i.e. worse than before COVID) **or** fatigue_last7d = 1
rule 2: gen_hlth_rating_after < gen_hlth_rating _before
rule 3: emot_comp_before > 2 (i.e. same or worse than before COVID)
rule 4: jointpain = Yes **or** muscle_pain = Yes

Cognition cluster: rule 1 **and** (rule 2 **or** rule 3)
rule 1: Confusion_lack_concentration = yes
rule 2: gen_hlth_rating_after < gen_hlth_rating _before
rule 3: classroom_learn > 2 (same or worse than before COVID)

Respiratory cluster: rule 1 **and** (rule 2 **or** rule 3)
rule 1: difficulty_breath = yes
rule 2: gen_hlth_rating_after < gen_hlth_rating _before
rule 3: pain_breath = Yes **or** chest_pain = Yes **or** persit_cough =Yes

9. **StopCOVID ISARIC Cohort (Russia)**
Symptom cluster cases at 12 month follow-up are restricted to those who met the criteria for each symptom cluster at the 6 month follow-up point.

<u>**Adults**</u>

Fatigue, bodily pain and mood swings

rule 1: (persistent fatigue = yes **or** limb weakness = yes) **and** flw_fatigue = 3+ (on a scale from 0-10)
rule 2: EQ5D5L anxiety/depression (ad) >2 **or** EQ5D5L pain/discomfort (pd) >2
rule 3 (6 month follow-up cases): at least one of EQ5D5L ad, EQ5D5L pd and EQ5D5L ua (usual activities) is scored worse at follow-up compared to the rating giving for health status prior to COVID
rule 4 (12 month follow-up cases): met the criteria for this symptom cluster at previous follow-up (6 months)

- **6-month formula:** rule 1 **and** rule 2 **and** rule 3
- **12-month formula:** rule 1 **and** rule 2 **and** rule 4

Allow one of the defining items (per_fat, flw_limb_weakness, flw_fatigue, flw_eq5d_ad_2, and flw_eq5d_pd_2) to have missing value

Cognition problems

Mild

rule 1: (forgetfulness = yes **or** confusion = yes) **and** remember_today ('do you have difficulty remembering or concentrating?') = yes, some difficulty **and** EQ5D5L ua = moderate or worse problems
rule 2: (forgetfulness = yes **or** confusion = yes) **and** remember_today = yes, a lot of difficulty **and** EQ5D5L ua = some or moderate problems
rule 3 (6 month follow-up cases): remember_today is worse than answer to question on problems remembering or concentrating prior to COVID-19
rule 4 (12 month follow-up cases): met the criteria for this symptom cluster at previous follow-up (6 months)

- **6-month formula:** (rule 1 **or** rule 2) **and** rule 3
- **12-month formula:** (rule 1 **or** rule 2) **and** rule 4

Severe
rule 1: (forgetfulness = yes **or** confusion = yes) **and** remember_today ('do you have difficulty remembering or concentrating?') = yes, a lot of difficulty **and** EQ5D5L ua = worse or extreme problems
rule 2: (forgetfulness = yes **or** confusion = yes) **and** remember_today = 'cannot do' **and** EQ5D5L ua = some or worse problems
rule 3 (6 month follow-up cases): remember_today is worse than answer to question on problems remembering or concentrating prior to COVID-19
rule 4 (12 month follow-up cases): met the criteria for this symptom cluster at previous follow-up (6 months)

- **6-month formula:** (rule 1 **or** rule 2) **and** rule 3
- **12-month formula:** (rule 1 **or** rule 2) **and** rule 4

Respiratory problems

Mild: (rule 1 **or** rule 2 **or** rule 3) **and (**rule 4 **or** rule 5)
rule 1: (breathless_now = 2 **or** persistent cough = yes) **and** EQ5D5L ua =2+ (some or worse problems)
rule 2: breathless_now = 3 ('I walk slower than most people of my age because of breathlessness, or have to stop for breath when walking at own pace') **and** persistent cough = yes **and** EQ5D5L ua =2 (some problems)
rule 3: breathless_now = 3 **and** persistent cough = no **and** EQ5D5L ua =3+ (moderate or worse problems)
rule 4 (6 month follow-up cases): breathlessness now is worse than same question asking about breathlessness prior to COVID
rule 5 (12 month follow-up cases): met the criteria for this symptom cluster at previous follow-up (6 months)

- **6-month formula:** (rule 1 **or** rule 2 **or** rule 3) **and** rule 4
- **12-month formula:** (rule 1 **or** rule 2 **or** rule 3) **and** rule 5

Moderate: (rule 1 **or** rule 2 **or** rule 3) **and (**rule 4 **or** rule 5)
rule 1: (breathless_now = 4 **and** persistent cough = yes) **and** EQ5D5L ua =3+ (moderate or worse problems)
rule 2: breathless_now = 4 ('I stop for breath after walking 100 yards/ 90-100 meters, or after a few minutes on level ground') **and** (EQ5D5L ua =2 (some problems) **or** FAS = 4-6)
rule 3: breathless_now = 5 ('Too breathless to leave the house, or breathless when dressing/undressing') **and** (EQ5D5L ua =2 **or** FAS = 4-6)
rule 4 (6 month follow-up cases): breathless_now is worse than same question asking about breathlessness prior to COVID
rule 5 (12 month follow-up cases): met the criteria for this symptom cluster at previous follow-up (6 months)

- **6-month formula:** (rule 1 **or** rule 2 **or** rule 3) **and** rule 4

- **12-month formula:** (rule 1 **or** rule 2 **or** rule 3) **and** rule 5

Severe: (rule 1 **or** rule 2) **and (**rule 3 **or** rule 4)
rule 1: (breathless_now = 4 **and** (EQ5D5L ua =3+ **or** FAS = 6+ **or** PHQ_stress = 3+ **or** PHQ_worries=3+)
rule 2: breathless_now = 5 **and** (EQ5D5L ua =3+ **or** FAS = 6+)
rule 3 (6 month follow-up cases): breathless_now is worse than same question asking about breathlessness prior to COVID
rule 4 (12 month follow-up cases): met the criteria for this symptom cluster at previous follow-up (6 months)

- **6-month formula:** (rule 1 **or** rule 2) **and** rule 3
- **12-month formula:** (rule 1 **or** rule 2) **and** rule 4

Note: If a patient is classified into two severities within the same symptom cluster (for example, both moderate and severe respiratory symptoms), then the more severe state will be assigned to that patient.

<u>**Children**</u>

Fatigue, bodily pain and mood swings

rule 1: Persistent fatigue = yes
rule 2: VAS fatigue has worsened (4 or 5 on 5-point scale)
rule 3: Worse fatigue is attributed by patient or parent to COVID-19 infection or to both COVID-19 infection and the overall impact of the COVID-19 pandemic

- **Formula:** rule 1 **and** rule 2 **and** rule 3

Cognition problems

- **Formula:** Confusion = yes

Note: No other relevant variables were available in the pediatric questionnaire for the cognitive symptom cluster.

Respiratory problems

- **Formula:** Troubled breath/tightness in chest = yes

Note: No other relevant variables were available in the pediatric questionnaire for the respiratory symptom cluster.

10. Zurich SARS-CoV-2 Cohort (Switzerland)

Symptom cluster cases at later follow-up times (6 and 12 months in prospective sample, and 12 month in retrospective sample) were restricted to those who met the criteria for each symptom cluster at the previous follow-up point.

- **Fatigue, bodily pain and mood swings**
    - Has symptoms at follow-up:
        1. muscle and/or body pain
        2. joint pain
        3. follow-up EQ5D5L PD>2
        4. follow-up EQ5D5L PD > pre-COVID EQ5D5L PD
        5. tiredness or exhaustion
        6. FAS
            - Prospective sample: FAS score >= 22 at follow-up AND follow-up FAS score > pre-COVID FAS score (#44 in follow-up, #133 in baseline questionnaire)
            - Retrospective sample: FAS score >= 22 at follow-up

7. follow-up EQ5D5L UA > pre-COVID EQ5D5L UA
8. depression or anxiety symptoms
    a) DASS-21 (follow-up depression score >= 7 AND follow-up depression score > pre-COVID depression score) OR (follow-up anxiety score >= 6 anxiety AND follow-up anxiety score > pre-COVID anxiety score) (#45 in follow-up, #134 in baseline questionnaire)
    b) DASS-21 (follow-up depression score >= 7 OR (follow-up anxiety score >= 6 anxiety
9. EQ5D5L AD
    a) Follow-up EQ5D5L AD>2 AND follow-up EQ5D5L AD > pre-COVID EQ5D5L AD
    b) Follow-up EQ5D5L AD>2
10. EQ5D5L UA > 2

Where AD=anxiety/depression, PD=pain/discomfort, UA=usual activities

- **Prospective sample Formula = {[(1 OR 2 OR 3) AND 4] OR (8a OR 9a)} AND [(5 OR 6a) AND 7]**
- **Retrospective sample Formula = [(1 OR 2 OR 3) OR (8b OR 9b)] AND [(5 OR 6b) AND 10]**
- Allow one of the defining items to have missing value

- **Cognition problems**
    - Mild case
        1. Newly diagnosed COVID-19-related brain disorder
        2. EQ5D5L UA
            a) Follow-up EQ5D5L UA = 2-3 AND follow-up EQ5D5L UA > pre-COVID EQ5D5L UA
            b) Follow-up EQ5D5L UA = 2-3
        3. Follow-up FAS concentration score = 5 ("I have trouble concentrating almost daily")
        4. Follow-up FAS concentration score > baseline FAS concentration score
        5. Follow-up FAS clear thinking score = 5 ("I have problems thinking clearly almost daily")
        6. Follow-up FAS clear thinking score > baseline FAS clear thinking score
    - **Prospective sample Formula = [1 OR (3 AND 4) OR (5 AND 6)] AND 2a**
    - **Retrospective sample Formula = (1 OR 3 OR 5) AND 2b**
    - Severe case
        1. Newly diagnosed COVID-19-related brain disorder
        2. EQ5D5L UA
            a. Follow-up EQ5D5L UA = 4-5 AND follow-up EQ5D5L UA > pre-COVID EQ5D5L UA
            b. Follow-up EQ5D5L UA = 4-5
        3. Follow-up FAS concentration score = 5 ("I have trouble concentrating almost daily")
        4. Follow-up FAS concentration score > baseline FAS concentration score
        5. Follow-up FAS clear thinking score = 5 ("I have problems thinking clearly almost daily")
        6. Follow-up FAS clear thinking score > baseline FAS clear thinking score
    - **Prospective sample Formula = [1 OR (3 AND 4) OR (5 AND 6)] AND 2a**
    - **Retrospective sample Formula = (1 OR 3 OR 5) AND 2b**
- **Respiratory problems**
    - Mild case
        1. mMRC-dyspnea scale = 1 at follow-up
        2. mMRC-dyspnea scale follow-up score > pre-COVID score
        3. Cough = yes
        4. Dyspnea/shortness of breath = yes

5. follow-up EQ5D5L UA > pre-COVID EQ5D5L UA
6. follow-up EQ5D5L UA > 2

- **Prospective sample Formula: (1 AND 2) AND (3 OR 4) AND 5**
- **Retrospective sample Formula: 1 AND (3 OR 4) AND 6**
- Moderate case

1. mMRC-dyspnea scale = 2-3 at follow-up
2. mMRC-dyspnea scale follow-up score > pre-COVID score
3. Cough = yes
4. Dyspnea/shortness of breath = yes
5. follow-up EQ5D UA > pre-COVID EQ5D UA
6. follow-up EQ5D5L UA > 2

- **Prospective sample Formula: (1 AND 2) AND (3 OR 4) AND 5**
- **Retrospective sample Formula: 1 AND (3 OR 4) AND 6**
- Severe case

1. mMRC-dyspnea scale = 4 at follow-up
2. mMRC-dyspnea scale follow-up score > pre-COVID score
3. Cough = yes
4. Dyspnea/shortness of breath = yes
5. follow-up EQ5D UA > pre-COVID EQ5D UA
6. follow-up EQ5D5L UA > 2

- **Prospective sample Formula: (1 AND 2) AND (3 OR 4) AND 5**
- **Retrospective sample Formula: 1 AND (3 OR 4) AND 6**

Administrative data

In addition, analyses were received from collaborators at two US administrative databases—Veterans Affairs Health Administration and Pharmaceutical Research Associates (PRA) Health Sciences, a data collection of private health insurance plans—based on the International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) codes for the primary symptoms belonging to the three symptom clusters of interest among cases with COVID-19 compared to non-COVID-19 cases matched on demographic characteristics and pre-existing common health problems (Appendix 2 Data Inputs).[20–22] ICD codes are provided in eTable 2.

Veterans Affairs COVID cases were matched to 4,990,835 controls using the procedure outlined in Al-Aly et al.[21]

PRA Health Services COVID cases were matched 1:1 to 1,009,885 controls by month of diagnosis, 10-year age group, sex, race, and previously diagnosed diabetes, heart failure, cancer, and stroke. COVID patients were included if their initial diagnosis was between March and October 2020 and they also had at least one outpatient or inpatient visit between November 2020 and January 2021. Controls were eligible for matching if they had no COVID diagnosis prior to January 2021, had at least two visits between March and October 2020, and had at least one outpatient or inpatient visit between November 2020 and January 2021.

After matching, the excess rate of symptoms associated with COVID-19 diagnosis was defined as the difference in the reported symptom ICD codes between cases and controls.

eTable 2. ICD-10-CM codes used to extract administrative data for cognitive symptoms, fatigue, and respiratory symptoms.

ICD-10-CM CODE	ICD-10-CM CODE DESCRIPTION	Symptom cluster
'R404'	Transient alteration of awareness	Cognitive
'R410'	Disorientation, unspecified	Cognitive
'R411'	Anterograde amnesia	Cognitive
'R412'	Retrograde amnesia	Cognitive
'R413'	Other amnesia	Cognitive
'R4182'	Altered mental status, unspecified	Cognitive
'R41840'	Attention and concentration deficit	Cognitive
'R41841'	Cognitive communication deficit	Cognitive
'R4189'	Other symptoms and signs involving cognitive functions and awareness	Cognitive
'R419'	Unspecified symptoms and signs involving cognitive functions and awareness	Cognitive
'R531'	Weakness	Fatigue
'R5381'	Other malaise	Fatigue
'R5382'	Chronic fatigue, unspecified	Fatigue
'R5383'	Other fatigue	Fatigue
'J9610'	Chronic respiratory failure, unspecified whether with hypoxia or hypercapnia	Respiratory
'J9611'	Chronic respiratory failure with hypoxia	Respiratory
'J9612'	Chronic respiratory failure with hypercapnia	Respiratory
'J9620'	Acute and chronic respiratory failure, unspecified whether with hypoxia or hypercapnia	Respiratory
'J9621'	Acute and chronic respiratory failure with hypoxia	Respiratory
'J9622'	Acute and chronic respiratory failure with hypercapnia	Respiratory
'J9690'	Respiratory failure, unspecified, unspecified whether with hypoxia or hypercapnia	Respiratory
'J9691'	Respiratory failure, unspecified with hypoxia	Respiratory
'J9692'	Respiratory failure, unspecified with hypercapnia	Respiratory
'J988'	Other specified respiratory disorders	Respiratory

ICD-10-CM CODE	ICD-10-CM CODE DESCRIPTION	Symptom cluster
'J989'	Respiratory disorder, unspecified	Respiratory
'J99'	Respiratory disorders in diseases classified elsewhere	Respiratory
'R05'	Cough	Respiratory
'R0600'	Dyspnea, unspecified	Respiratory
'R0602'	Shortness of breath	Respiratory
'R0603'	Acute respiratory distress	Respiratory
'R0609'	Other forms of dyspnea	Respiratory
'R071'	Chest pain on breathing	Respiratory

Data adjustments

Adjust for underlying rates of symptom clusters

In order to maintain our case definition of symptom clusters due directly to COVID-19, the proportions of patients with each symptom cluster needed to account for pre-existing symptoms. For cohorts with questions about pre-COVID-19 health status (see Algorithms for CO-FLOW, Helbok et al, Isfahan CC, StopCOVID, Rome ISARIC, and Zurich prospective sample), this excess risk of each symptom cluster could be directly calculated. Some cohorts, however, lacked such questions in the survey instruments and thus reported inflated counts of symptoms among COVID-19 patients (Faroe Islands, pa-COVID, PronMed ICU, and HAARVI). We adjusted the proportion data from these latter cohorts using the observed adjustment among cohorts with pre-COVID-19 health status.

First, data were re-extracted from the six cohort studies with individual record data that reported information on pre-COVID health status, with adapted algorithms to exclude the information on pre-COVID health status in order to make these data comparable to the cohort studies that lack this information. The logit differences between data with and without pre-COVID health status for these six cohorts were pooled in a meta-analysis with a study-level random effect, separately by symptom cluster in order to estimate four overall adjustment factors (eTable 3). These coefficients were then applied to corresponding symptom cluster data for the other four cohorts with individual record data (Faroe Islands, pa-COVID, PronMed ICU, and HAARVI) to adjust their data for pre-COVID health status. These adjustments were done using the crosswalk package in R 4.0.5.

eTable 3. Model coefficients for adjustment to account for underlying rates of symptom clusters.

Symptom cluster	Adjustment Beta Coefficient, Logit (SD)
Any long COVID	0.657 (0.266)
Post-acute fatigue syndrome	0.576 (0.336)
Respiratory symptoms	0.626 (0.166)
Cognitive symptoms	0.148 (0.040)

Adjust for reporting individual symptoms and administrative data

We accounted for other sources of bias within the metaregressions described below by including indicator variables for bias characteristics and estimating a correction factor within the models. For data that reported individual symptoms rather than symptom clusters (fatigue, shortness of breath, and single cognitive issues) or reported overall long COVID proportions from a longer symptom list than our 3 symptom clusters, we estimated correction factors within each model (eTable 4, eTable 5, eTable 6, eTable 7, eTable 8, eTable 9). Also, given that administrative data likely under-estimates true disease rates, we adjusted VA and PRA data sources using an indicator variable (eTable 8 and eTable 9).

eSection 2: Estimate symptom cluster duration and proportions

Duration estimates

All symptom cluster models were logit-linear regressions, in order to constrain the outcome proportions between zero and one, and were conducted in MRTool 0.0.1.[81]

We estimated the rate of recovery among COVID patients with long COVID with a logit-linear regression of the logit-transformed prevalence of any symptom cluster on follow-up time of cohort data with multiple follow-up points. Given the scarcity of data (in the hospital model in particular), we assumed the same recovery rate applies to all symptom clusters. These models only included data with multiple follow-up points, regardless of symptom cluster, in order to avoid spurious trends over follow-up time that could be introduced by heterogeneous data with varying single follow-up times. No data were trimmed in these recovery pattern models because all follow-up data points within each study were needed to inform the recovery pattern. Then this shape (the coefficient on follow-up time) was used as "prior" to inform the shape of the subsequent proportion models. A study-level random effect was used to capture unexplained variance between studies.

Separate models were run for symptomatic non-hospitalized cases and for hospital/ICU cases. The non-hospitalized cases model had a fixed effect on sources that used a long symptom list to define patients with at least one long COVID symptom; these data were included despite this different measurement due to the added value of multiple follow-up points, and the fixed effect enabled us to adjust the data points to the level of the other cohort data (eTables 4-5, eFigure 5). For non-hospitalized cases, data from the Swiss and Faroe studies were used and supplemented with data derived from three published studies.[10,14,24,30,31,47] For hospitalized cases, data from the cohort studies in Russia, Sweden, Switzerland and the Netherlands were used and supplemented with data derived from two published studies in Switzerland and Spain, both adjusted as in the non-hospitalized cases recovery model.[7,8,10,11,18,52,64] The longest follow-up from these studies was 12 months in the studies from Russia, Switzerland and the Netherlands.[7,8,10,11] In both models, a logit-linear decline was assumed in the proportion of cases affected by long COVID. The coefficients on the rate of decline in these initial models were then entered as priors into the models that used all available follow-up data, described below in "Overall long COVID" and "Individual symptom clusters".

eTable 4. Model parameters for non-hospitalized long COVID duration.

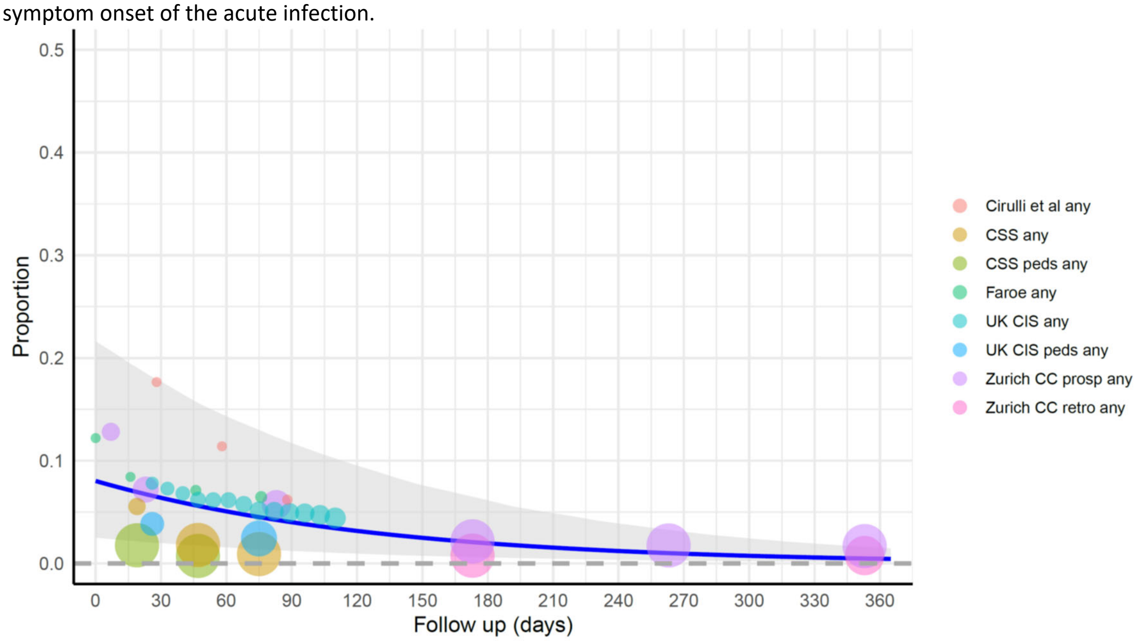
Fixed effect	Beta Coefficient, Logit (SD)
Intercept	-2.44 (0.392)
Follow-up time	-0.00818 (0.000546)
under age 20 (ref: over age 20)	-1.09 (0.563)
Uses publication-specific long list of symptoms to define "any long COVID symptom"	0.960 (0.536)

eTable 5. Model parameters for hospital/ICU long COVID duration.

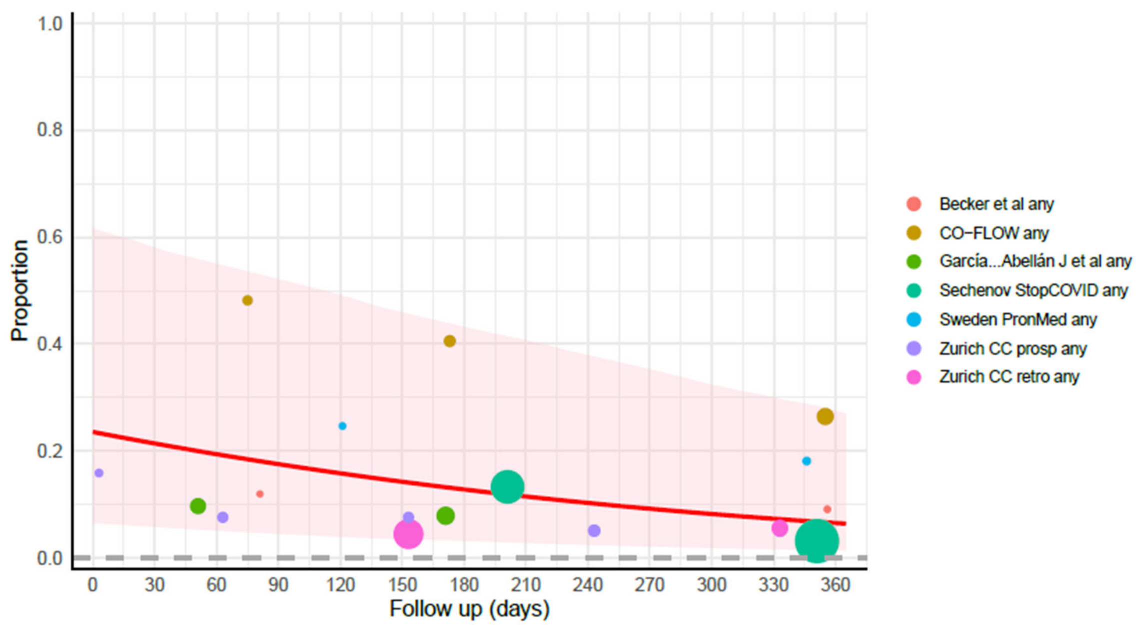
Fixed effect	Beta Coefficient, Logit (SD)
Intercept	-1.18 (0.366)
Follow-up time	-0.00412 (0.00059)
Uses publication-specific long list of symptoms to define "any long COVID symptom"	3.17 (0.928)

eFigure 5. Logit-linear model results of symptom cluster data with multiple follow-up points, used to calculate duration among non-hospitalized COVID cases and hospitalized COVID cases.

eFigure 5a. Non-hospitalized COVID cases; median duration of long COVID 121.5 days from incidence at 3 months after symptom onset of the acute infection.



eFigure 5b. Hospitalized/ICU COVID cases; median duration of long COVID 268.9 days from incidence at 3 months after symptom onset of acute infection.



Note: Follow up day 0 reflects 2 weeks post-infection among non-hospitalized cases, 5 weeks post-infection in cases needing hospitalization, and 6 weeks post-infection in cases needing ICU care. The durations mentioned at top of each graph are the median durations, calculated from incidence at three months after symptom onset of the acute infection. For calculation of prevalence and severity-weighted prevalence of long COVID, we make use of the distribution of values of duration to propagate uncertainty. Size of data points vary according to inverse of standard error (larger studies, bigger circles)

We observed a slower rate of recovery among COVID cases who needed hospitalization/ICU care during their acute infection. We then incorporated the recovery patterns as priors in the proportion models of having at least one symptom cluster, separately for non-hospitalized and hospitalized cases (described below in section "Overall Long COVID"). From those models, we calculated distributions of durations integrating the area below the fitted curve using the following equation.

$$Duration = \frac{\int_{F=0}^{F_{end}} \frac{e^{\beta_0} * e^{\beta_1 * F}}{1 + e^{\beta_0} * e^{\beta_1 * F}} dF}{prop_{start}}$$

where F represents follow-up day, β_0 is the intercept of the model, β_1 is the slope on follow-up day, and F_{end} represents the follow-up day when the proportion of cases with long COVID drops below 0.001, a threshold selected as the end of the recovery curve. F_{end} is calculated as

$$F_{end} = \frac{\log\left(\frac{0.001}{1 - 0.001}\right) - \beta_0}{\beta_1}$$

Evaluating the above integral gives

$$Duration = \frac{\frac{1}{\beta_1} * \log\big(abs\big(1 + e^{\beta_0}\big) * e^{\beta_1 * F_{end}}\big) - \frac{1}{\beta_1} * \log\Big(abs\big(1 + e^{\beta_0}\big)\Big)}{prop_{start}}$$

where $prop_{start}$ is the intercept in normal space as

$$prop_{start} = \frac{e^{\beta_0}}{1 + e^{\beta_0}}$$

We sampled the parameters of each model 1000 times in order to evaluate the above equations 1000 times and to propagate uncertainty into the overall duration estimates that we report with 95% uncertainty intervals.

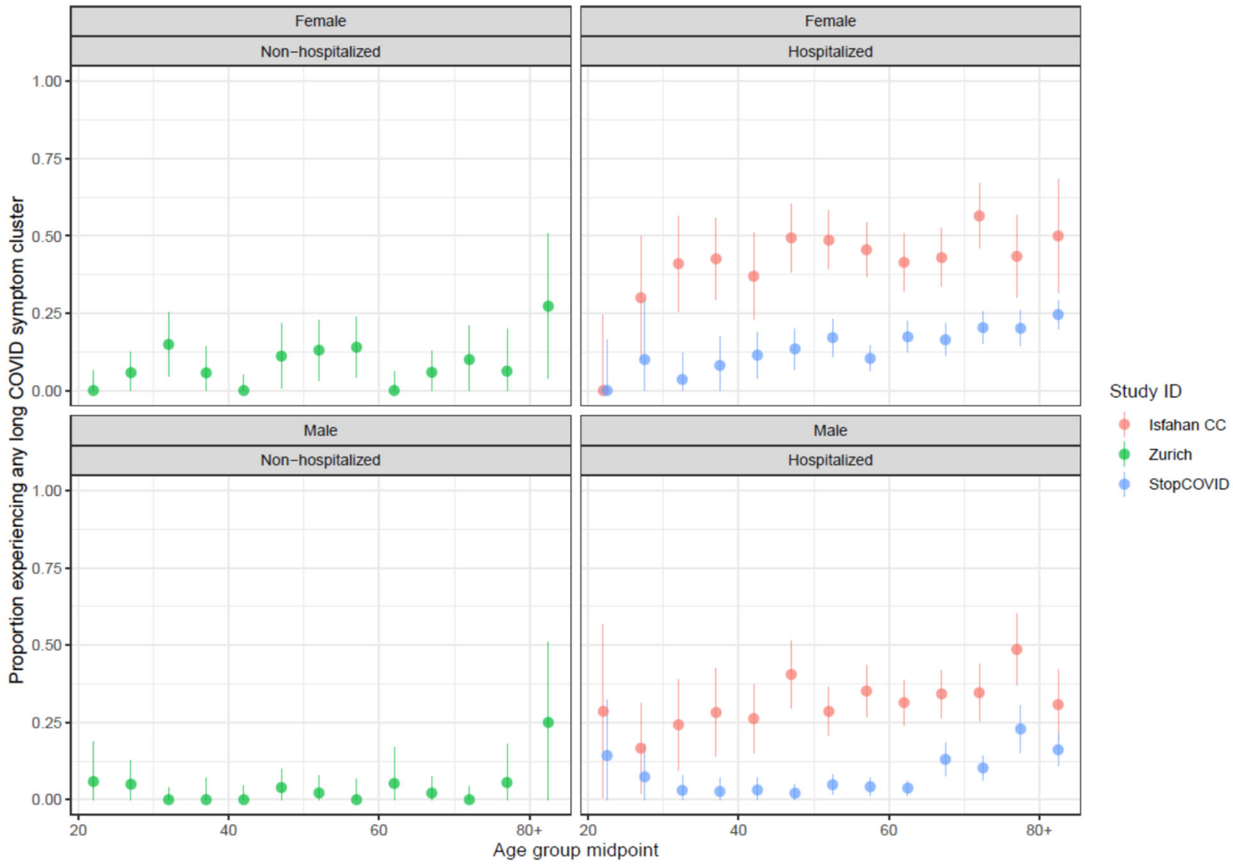
Prevalence estimates

Age pattern

For non-hospitalized cases, we had several studies (CSS, UK CIS, PRA) that collected data on both people under and over 20 with the same survey methods, which enabled us to make separate estimates for those under 20 in all of the following non-hospitalized symptom cluster proportion models. We also explored estimating a full age pattern among adults by examining data from the three cohorts for which we have individual-level age-specific data and sufficient sample sizes in smaller age groups: Zürich SARS-CoV-2 Cohort for non-hospitalized cases, and Isfahan CC and StopCOVID Cohort for hospitalized cases.

eFigure 6 shows these extracted data in 5-year age groups from age 20 onwards, by sex and separately for non-hospitalized and hospitalized. In the StopCOVID cohort, there was an increase in ages 65-95, but a similar increase was not observed in the Isfahan CC. We decided that these sources did not provide sufficient evidence for a trend over age among adults, and we assumed that proportions with symptom cluster(s) were the same across age for adults.

eFigure 6. Age pattern of the proportion of surviving, symptomatic COVID-19 cases with at least one symptom cluster among the three largest cohort studies with individual record data, by sex and hospitalization status. Error bars represent 95% uncertainty intervals.



Overall long COVID

Prevalence of overall long COVID was defined as having at least one of the three symptom clusters when extracted from the individual-level cohort data. First we modelled this prevalence of overall long COVID. Estimates of individual symptom clusters and overlaps between clusters were adjusted to sum to overall long COVID.

For the overall long COVID models among symptomatic non-hospitalized cases and hospital/ICU cases, we included cohort data from which we were able to extract the number of patients with at least one of the three symptom clusters. For symptomatic non-hospitalized cases, the MRTool regression had a random effect on study, and fixed effects on whether the study used a more comprehensive symptom list (as in the recovery pattern model above), whether the data were among females only or males only, whether the data were among individuals <20 years, and on follow-up time (eTable 6, eFigures 7a-c). The hospital/ICU regression also had a random effect on study, and fixed effects on whether the data were among ICU patients, whether the data were among females only or males only, and on follow-up time (eTable 7, eFigures 7d-g). We modeled hospital and ICU data together because there were insufficient data on ICU admissions to support a separate model. To obtain estimates among ICU cases, we simply included the beta coefficient on ICU in the posterior estimates, and we excluded it for estimates among hospital cases.

MRTool trimmed 10% of the data points in order to make the estimates more robust. Trimming observations according to the likelihood is a method from the field of robust statistics.[82,83] We used a Least Trimmed Squares

(LTS) estimator that seeks to fit the specified majority of the most self-coherent data, giving an understanding of the overall relationship in the face of outlying observations as described in Zheng et al.[81]

eTable 6. Model parameters for non-hospitalized overall long COVID.

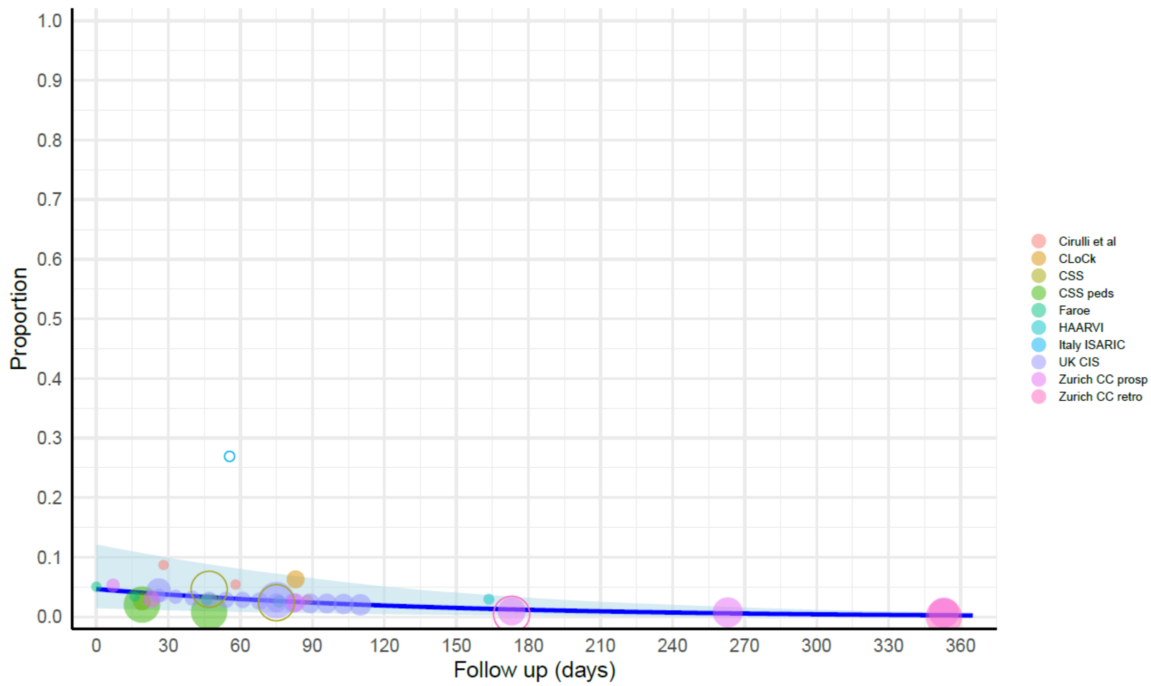
Fixed effect	Prior (SD)	Source of prior	Final estimated Beta Coefficient, Logit (SD)
Female (ref: Both sexes)	0.322 (0.0743)	Simple random effect meta-analysis of only sources with sex-specific and both-sex data	0.375 (0.0674)
Male (ref: Both sexes)	-0.414 (0.0864)	Simple random effect meta-analysis of only sources with sex-specific and both-sex data	-0.495 (0.0764)
Follow-up time	-0.00819 (0.000819)	Non-hospitalized duration model	-0.00752 (0.000455)
Under age 20 (ref: Over age 20)	n/a	n/a	-0.960 (0.0492)
Uses publication-specific long list of symptoms to define "any long COVID symptom"	n/a	n/a	0.825 (0.372)

eTable 7. Model parameters for hospital/ICU overall long COVID.

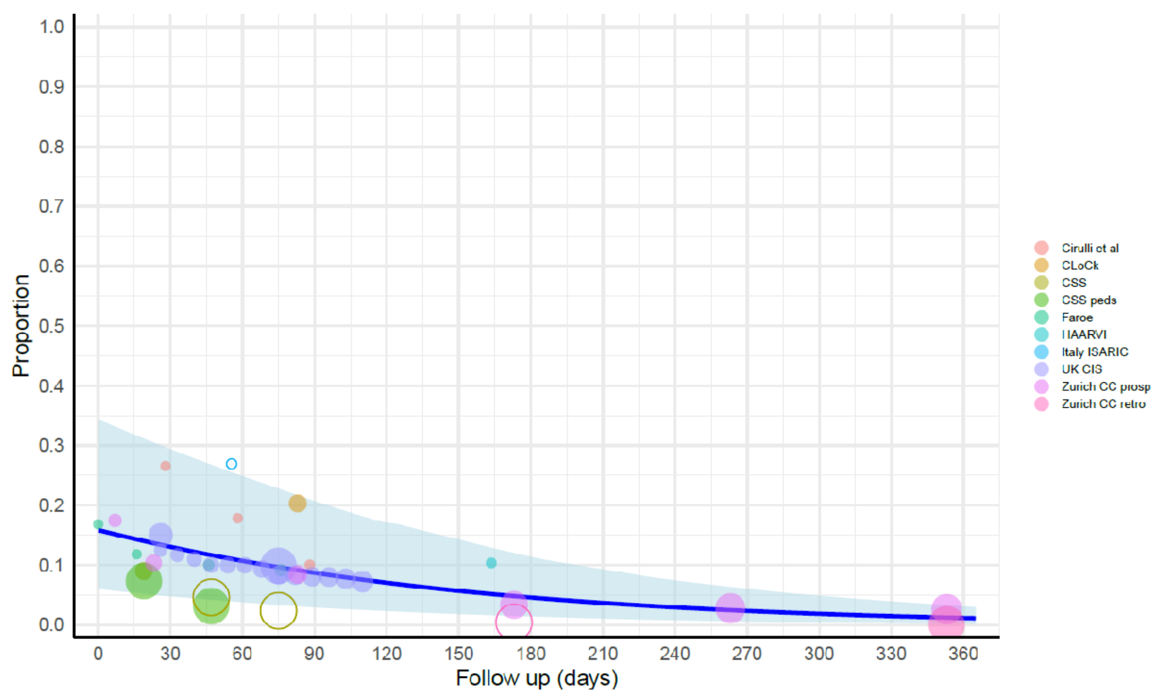
Fixed effect	Prior (SD)	Source of prior	Final estimated Beta Coefficient, Logit (SD)
ICU	0.709 (0.0661)	simple random effect meta-analysis of only VA and PRA hospital and ICU data	0.710 (0.0671)
Female (ref: Both sexes)	0.322 (0.0743)	Simple random effect meta-analysis of only sources with sex-specific and both-sex data	0.274 (0.0642)
Male (ref: Both sexes)	-0.414 (0.0864)	Simple random effect meta-analysis of only sources with sex-specific and both-sex data	-0.379 (0.0746)
Follow-up time	-0.00413 (0.000413)	Non-hospitalized duration model	-0.00421 (0.000352)
Uses publication-specific long list of symptoms to define "any long COVID symptom"	n/a	n/a	1.474 (0.304)

eFigure 7. Model results: Overall long COVID.

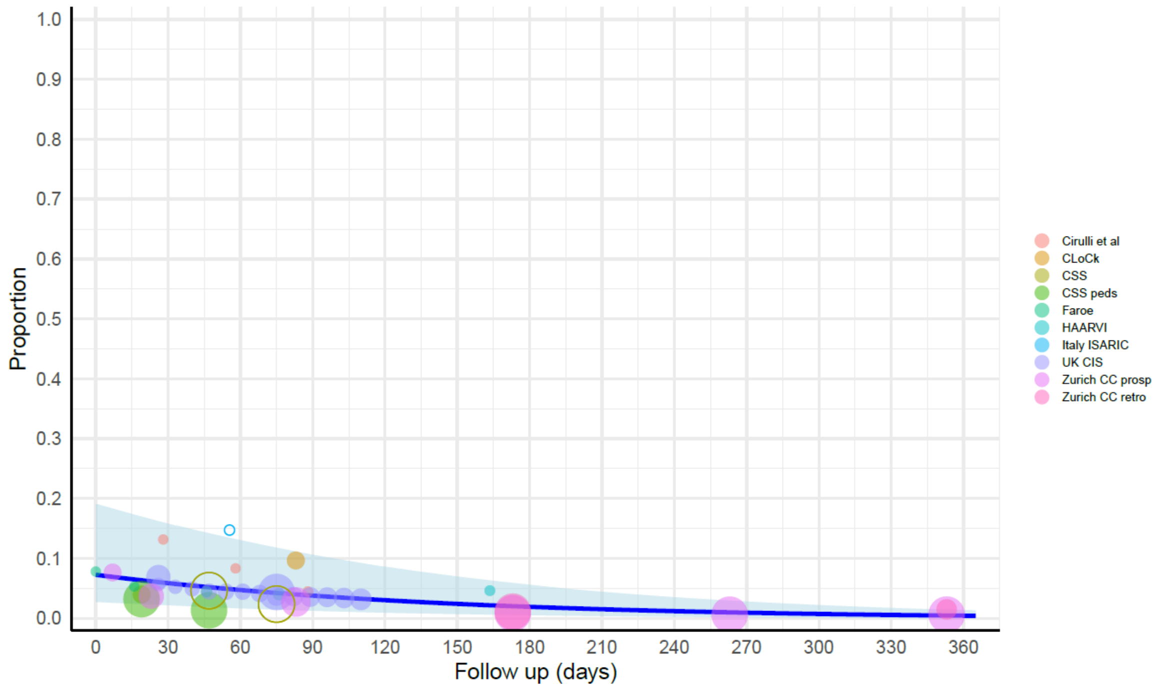
eFigure 7a. At least 1 symptom cluster among those who experienced symptomatic COVID infection not needing hospitalization, both males and females, ages 0-19. Open circles are trimmed data points.



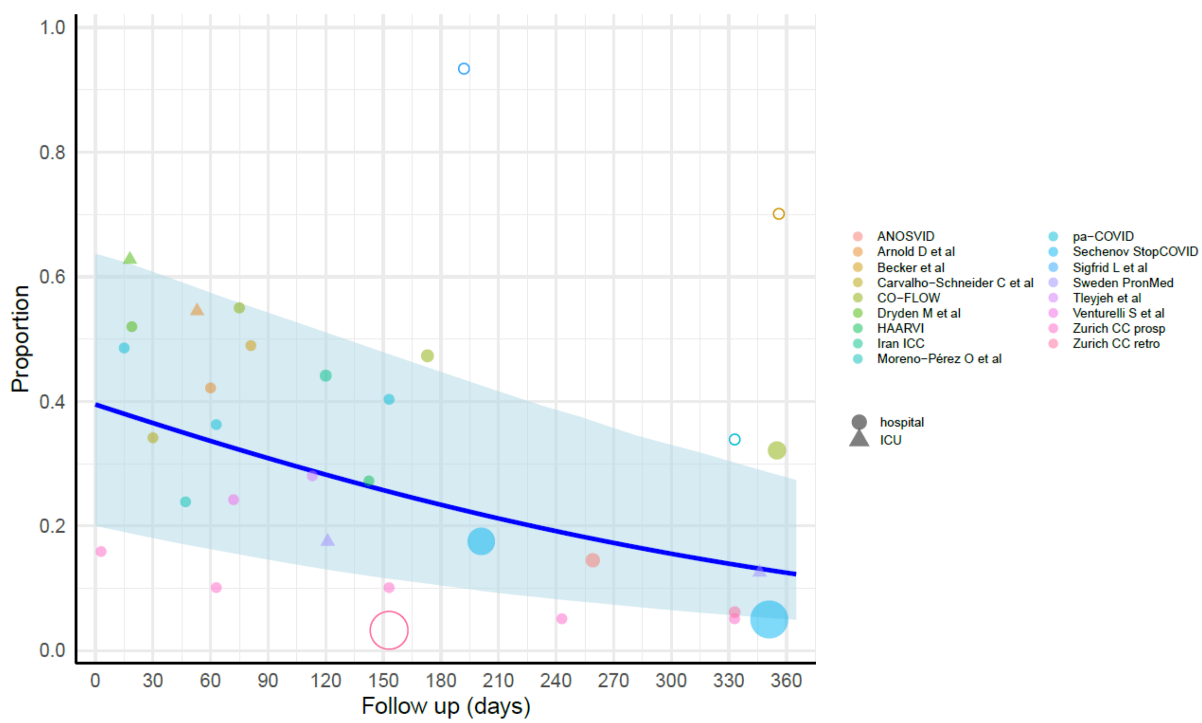
eFigure 7b. At least 1 symptom cluster among those who experienced symptomatic COVID infection not needing hospitalization, females, ages 20+. Open circles are trimmed data points.



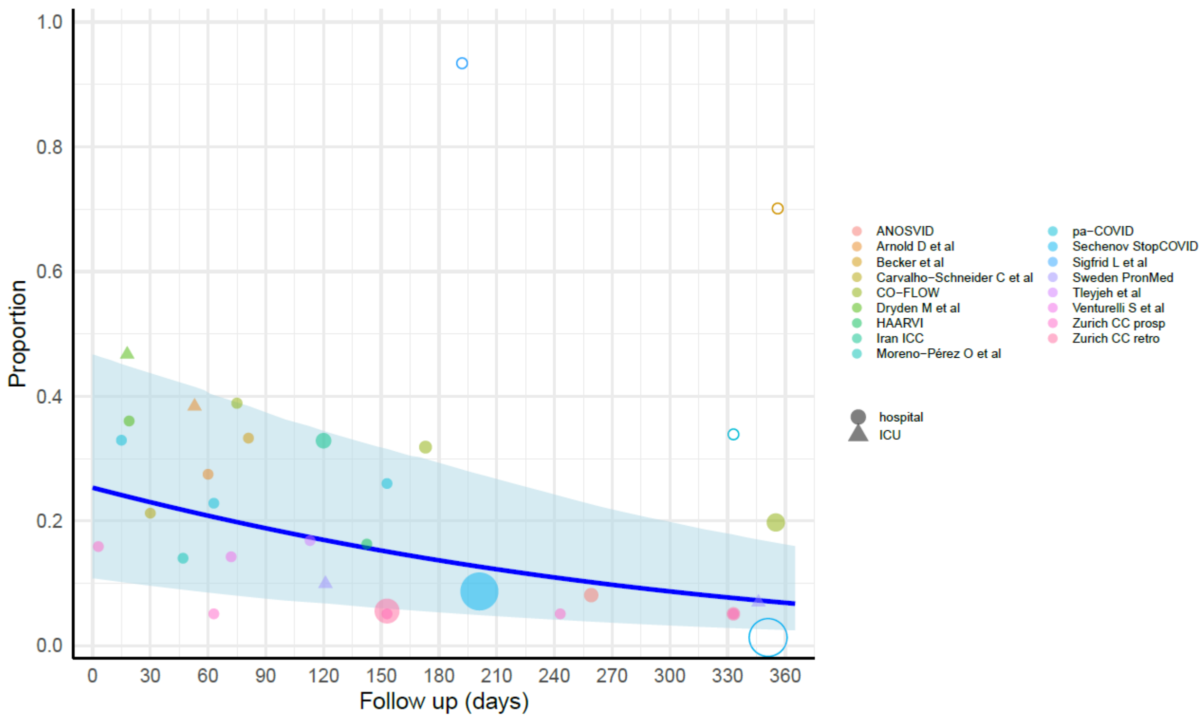
eFigure 7c. At least 1 symptom cluster among those who experienced symptomatic COVID infection not needing hospitalization, males, ages 20+. Open circles are trimmed data points.



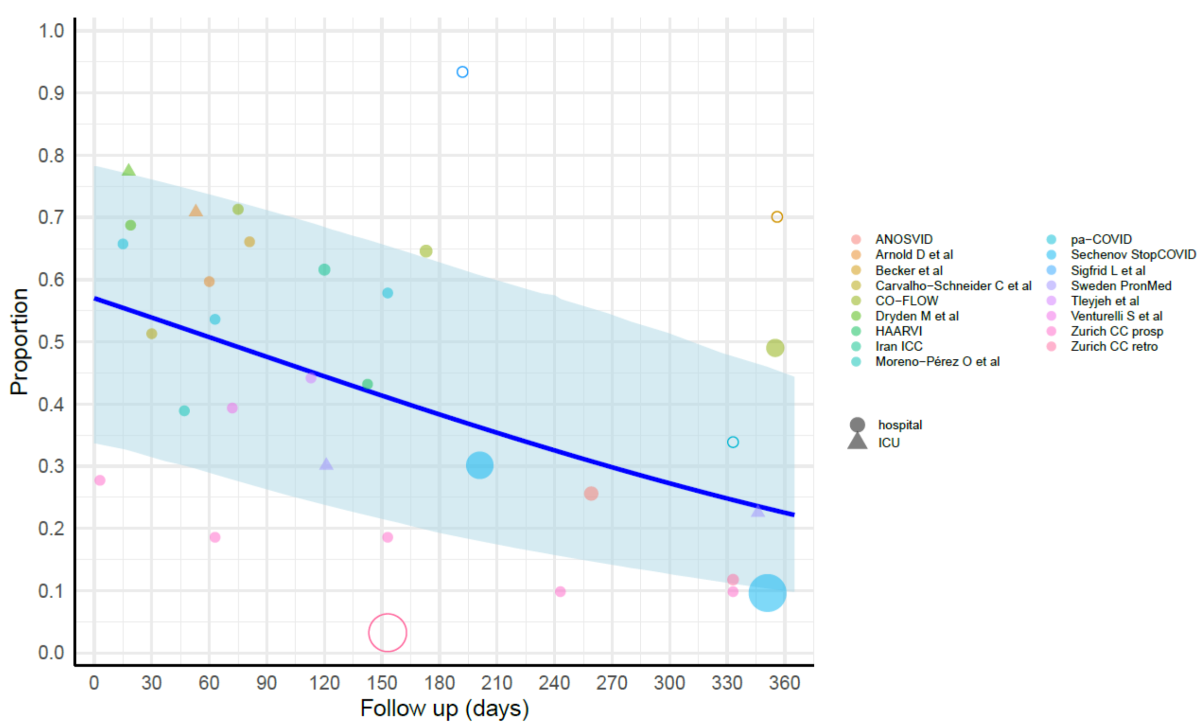
eFigure 7d. At least 1 symptom cluster among those who experienced severe COVID infection needing hospitalization, females, all ages. Open circles are trimmed data points.



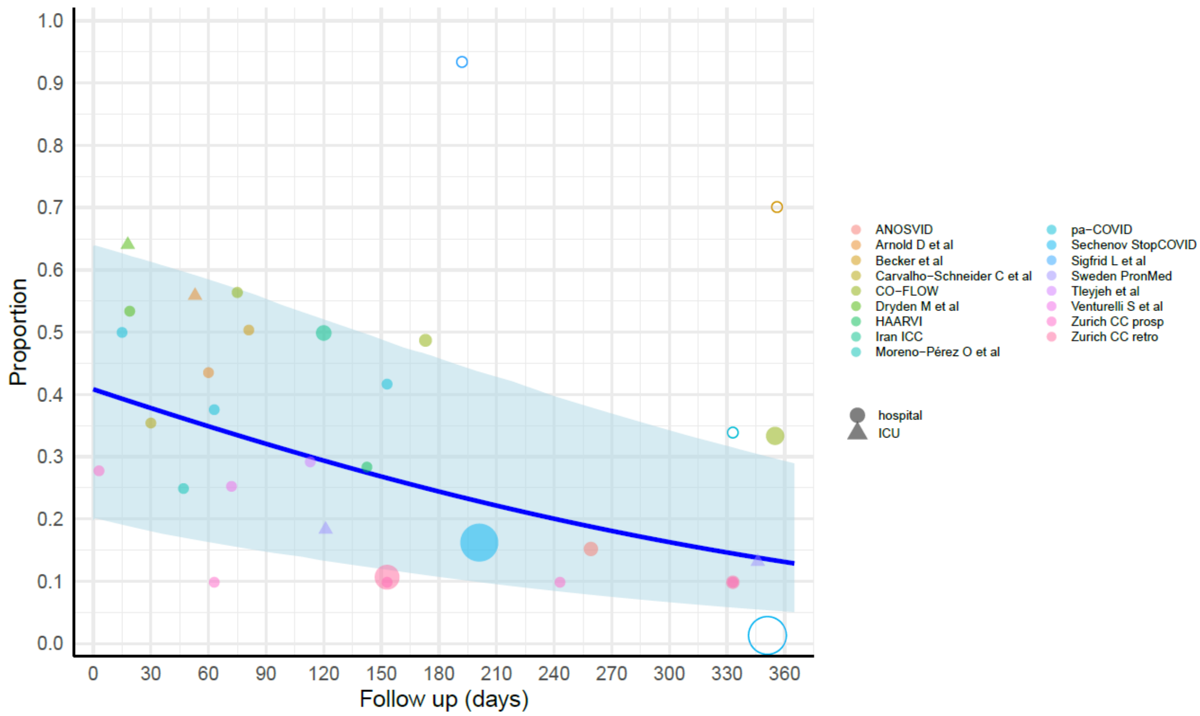
eFigure 7e. At least 1 symptom cluster among those who experienced severe COVID infection needing hospitalization, males, all ages. Open circles are trimmed data points.



eFigure 7f. At least 1 symptom cluster among those who experienced critical COVID infection needing ICU care, females, all ages. Open circles are trimmed data points.



eFigure 7g. At least 1 symptom cluster among those who experienced critical COVID infection needing ICU care, males, all ages. Open circles are trimmed data points.



Note: Follow up day 0 reflects 2 weeks post-infection among non-hospitalized cases, 5 weeks post-infection in cases needing hospitalization, and 6 weeks post-infection in cases needing ICU care. For long COVID at 3 months after symptom onset, we use follow-up days at 3 months minus the length of symptomatic acute episode (for non-hospitalized vs needing hospitalization vs needing ICU care) to obtain the corresponding follow-up days since end of acute episode in all of these models.

Individual symptom clusters

To model individual symptom clusters, we ran MRTool metaregression models on all data of each symptom cluster, including administrative data and published sources that reported symptoms we mapped to symptom clusters, such as cough mapping to respiratory symptoms. MRTool trimmed 10% of the data points in order to make the estimates more robust (eFigures 8-10). There were too few data points to run separate models for ICU-admitted cases; in the hospital models for each symptom cluster, an indicator variable was used for those admitted to ICU in order to predict their proportions, with the coefficient informed by the observed relationship between ICU and general hospital ward data.[20,22] In addition, indicator variables were added for sex, whether the data were from an administrative source, and for individual symptoms reported in the published articles (fatigue, cognitive dysfunction, shortness of breath). eTable 8 and eTable 9 display the fixed effects included in the non-hospitalized and hospital/ICU models, respectively, and each model also had a random effect on study.

eTable 8. Model parameters for each symptom cluster model among non-hospitalized cases. Sources of the priors are the same as in the overall long COVID models.

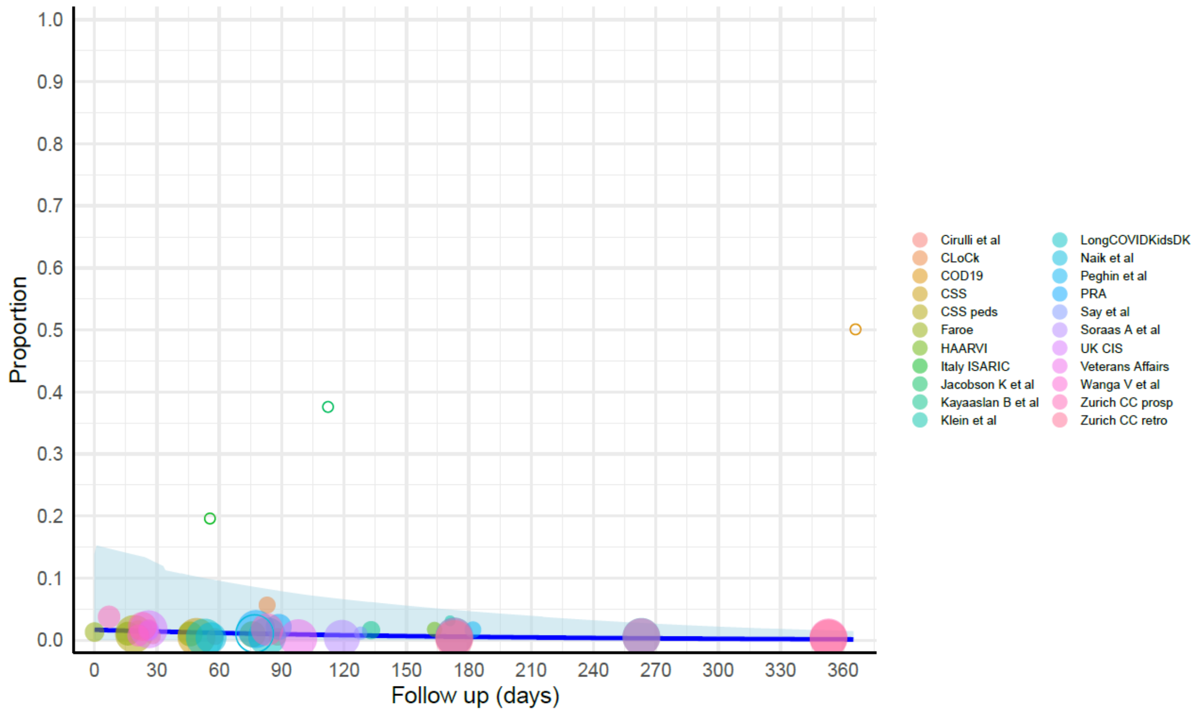
Fixed effect	Fatigue Prior (SD)	Fatigue Beta Coefficient, Logit (SD)	Respiratory Prior (SD)	Respiratory Beta Coefficient, Logit (SD)	Cognitive Prior (SD)	Cognitive Beta Coefficient, Logit (SD)
Administrative data	n/a	-0.644 (0.557)	n/a	0.323 (0.532)	n/a	n/a
Female (ref: Both sexes)	0.345 (0.114)	0.345 (0.116)	0.203 (0.104)	0.187 (0.102)	0.313 (0.106)	0.306 (0.109)
Male (ref: Both sexes)	-0.406 (0.116)	-0.406 (0.112)	-0.273 (0.114)	-0.239 (0.110)	-0.369 (0.126)	-0.341 (0.124)
Follow-up time	-0.00819 (0.000819)	-0.00574 (0.000459)	-0.00819 (0.000819)	-0.00644 (0.000507)	-0.00819 (0.000819)	-0.00400 (0.000570)
Alternative outcome definitions from publications (fatigue, memory problems, cough, shortness of breath)	n/a	Fatigue 1.058 (0.514)	n/a	Shortness of breath 0.229 (0.419)	n/a	Memory problems 0.212 (0.522)
Under age 20 **(ref: Over age 20)**	n/a	-1.134 (0.0841)	n/a	-0.552 (0.149)	n/a	-1.454 (0.136)

eTable 9. Model parameters for each symptom cluster model among hospital/ICU cases. Sources of the priors are the same as in the overall long COVID models.

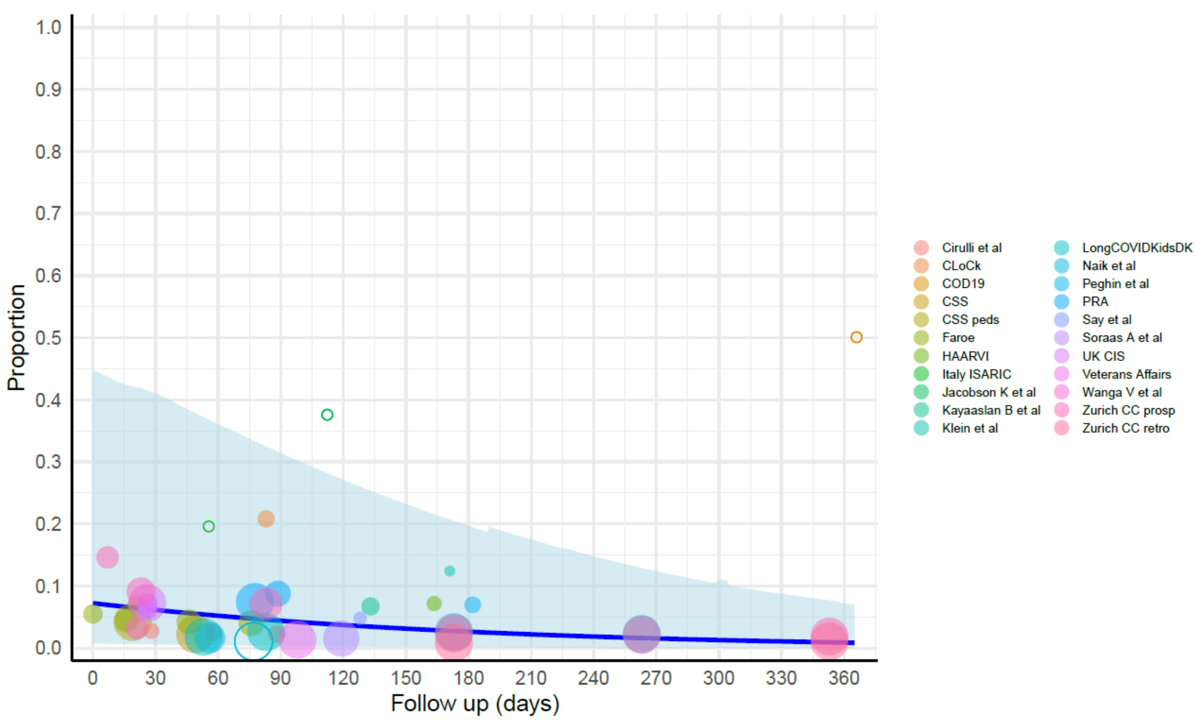
Fixed effect	Fatigue Prior (SD)	Fatigue Beta Coefficient, Logit (SD)	Respiratory Prior (SD)	Respiratory Beta Coefficient, Logit (SD)	Cognitive Prior (SD)	Cognitive Beta Coefficient, Logit (SD)
Administrative data	n/a	-2.067 (0.416)	n/a	n/a	n/a	n/a
ICU	0.709 (0.0661)	0.694 (0.0581)	0.709 (0.0661)	0.733 (0.0608)	0.709 (0.0661)	0.644 (0.0566)
Female (ref: Both sexes)	0.345 (0.114)	0.316 (0.0941)	0.203 (0.104)	0.189 (0.0862)	0.313 (0.106)	0.309 (0.0939)
Male (ref: Both sexes)	-0.406 (0.116)	-0.371 (0.0905)	-0.273 (0.114)	-0.268 (0.0904)	-0.369 (0.126)	-0.377 (0.101)
Follow-up time	-0.00413 (0.000413)	-0.00378 (0.000316)	-0.00413 (0.000413)	-0.00351 (0.000325)	-0.00413 (0.000413)	-0.00418 (0.000356)
Alternative outcome definitions from publications (fatigue, memory problems, cough, shortness of breath)	n/a	Fatigue 1.194 (0.258)	n/a	Shortness of breath 0.523 (0.308)	n/a	Memory problems 0.646 (0.340)

eFigure 8. Individual symptom clusters model results: fatigue.

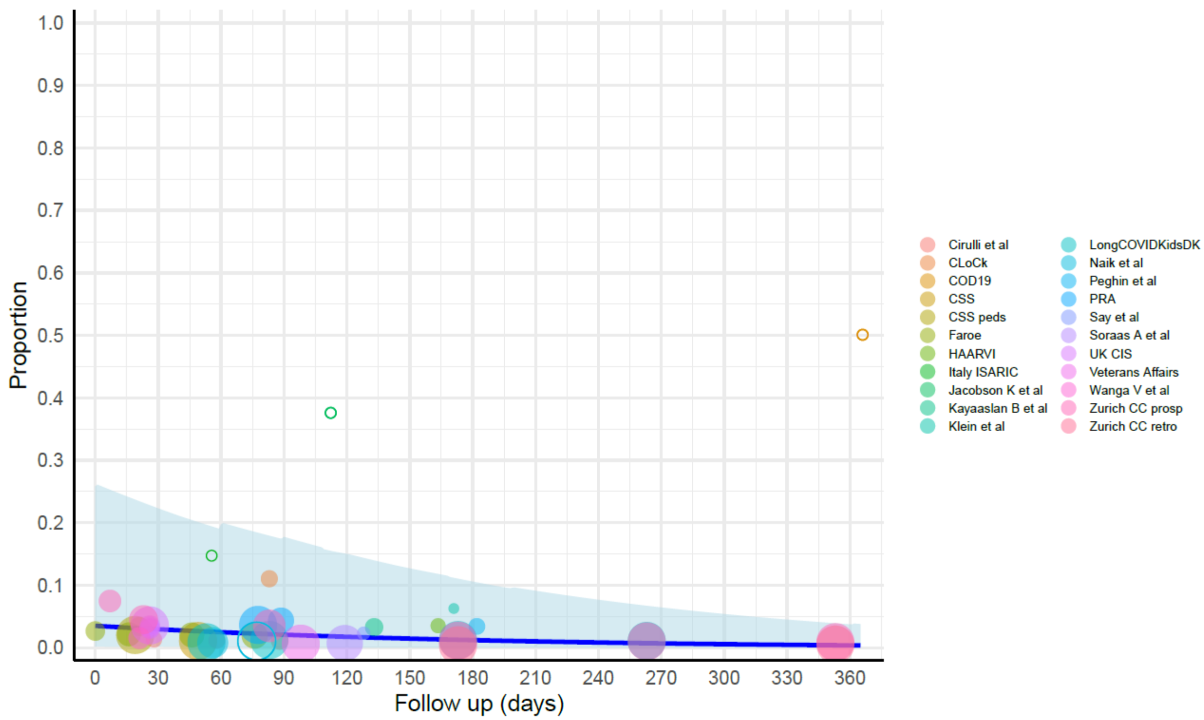
eFigure 8a. Fatigue cluster among those who experienced symptomatic COVID infection not needing hospitalization, both males and females, ages <20. Open circles are trimmed data points.



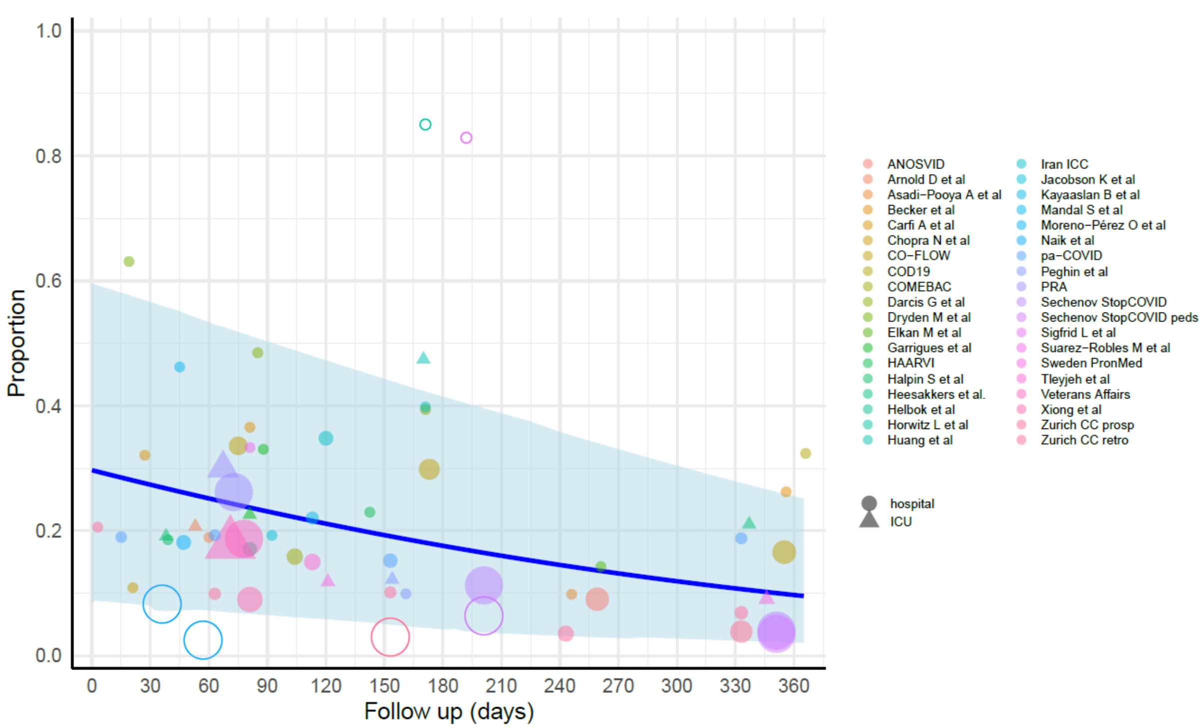
eFigure 8b. Fatigue cluster among those who experienced symptomatic COVID infection not needing hospitalization, females, ages 20+. Open circles are trimmed data points.



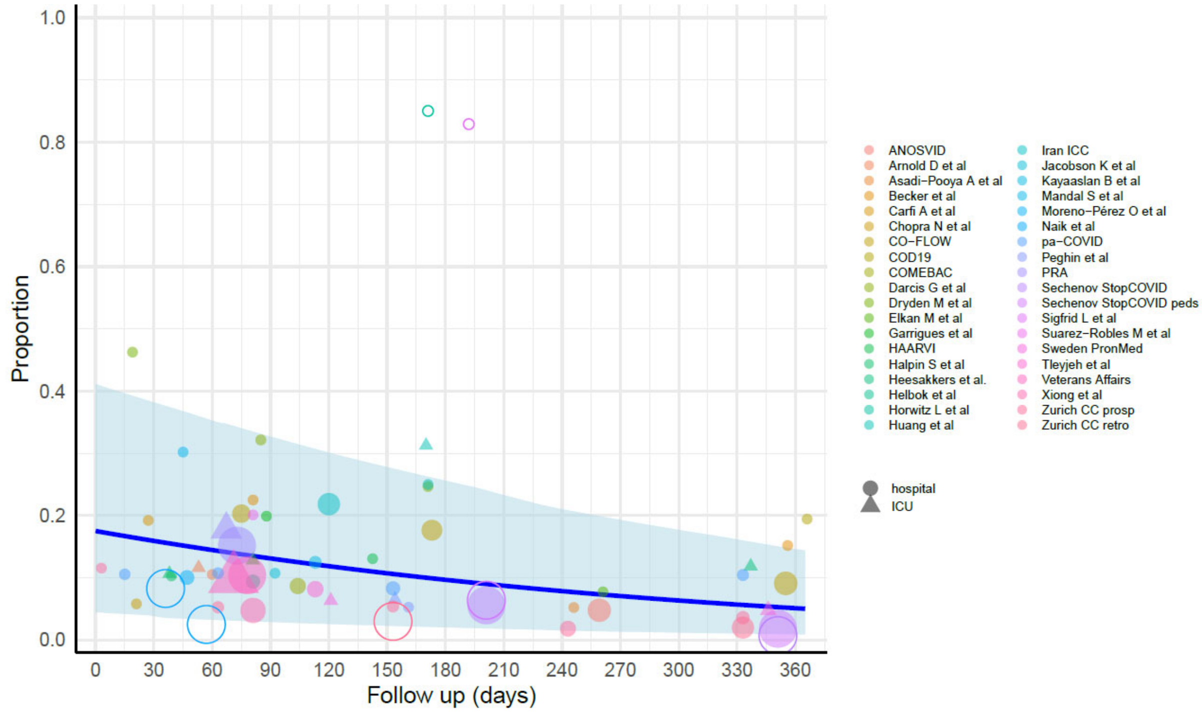
eFigure 8c. Fatigue cluster among those who experienced symptomatic COVID infection not needing hospitalization, males, ages 20+. Open circles are trimmed data points.



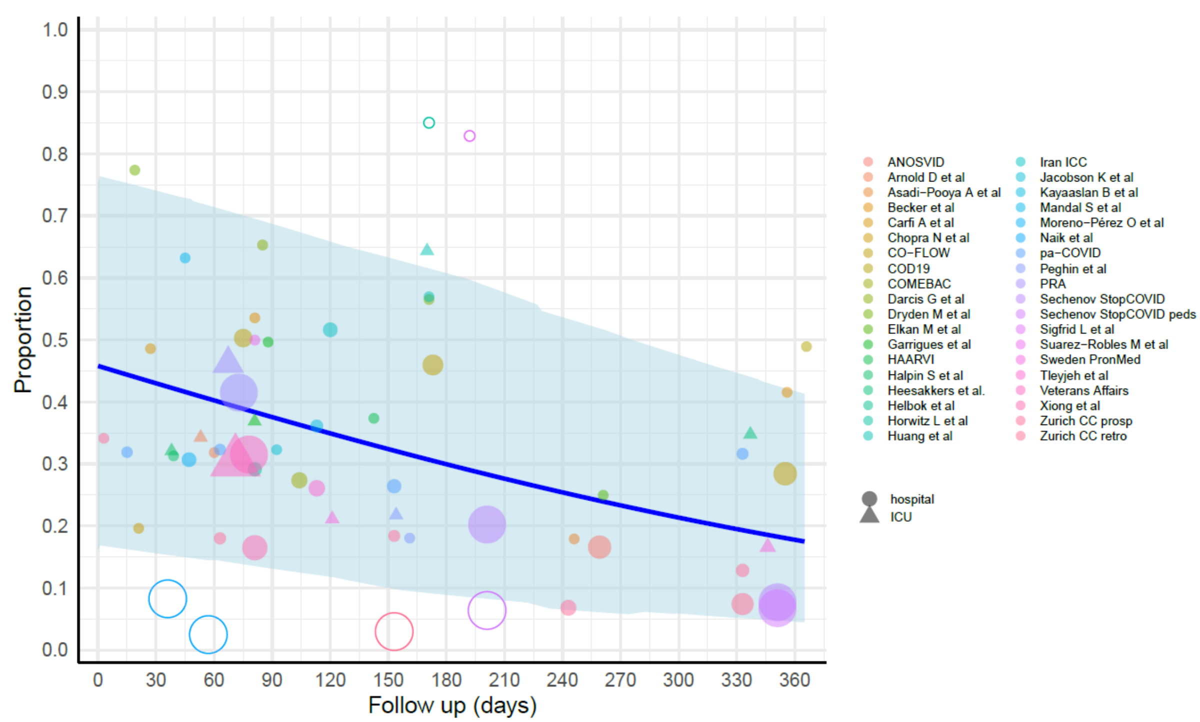
eFigure 8d. Fatigue cluster among those hospitalized for COVID infection, females, all ages. Open circles are trimmed data points.



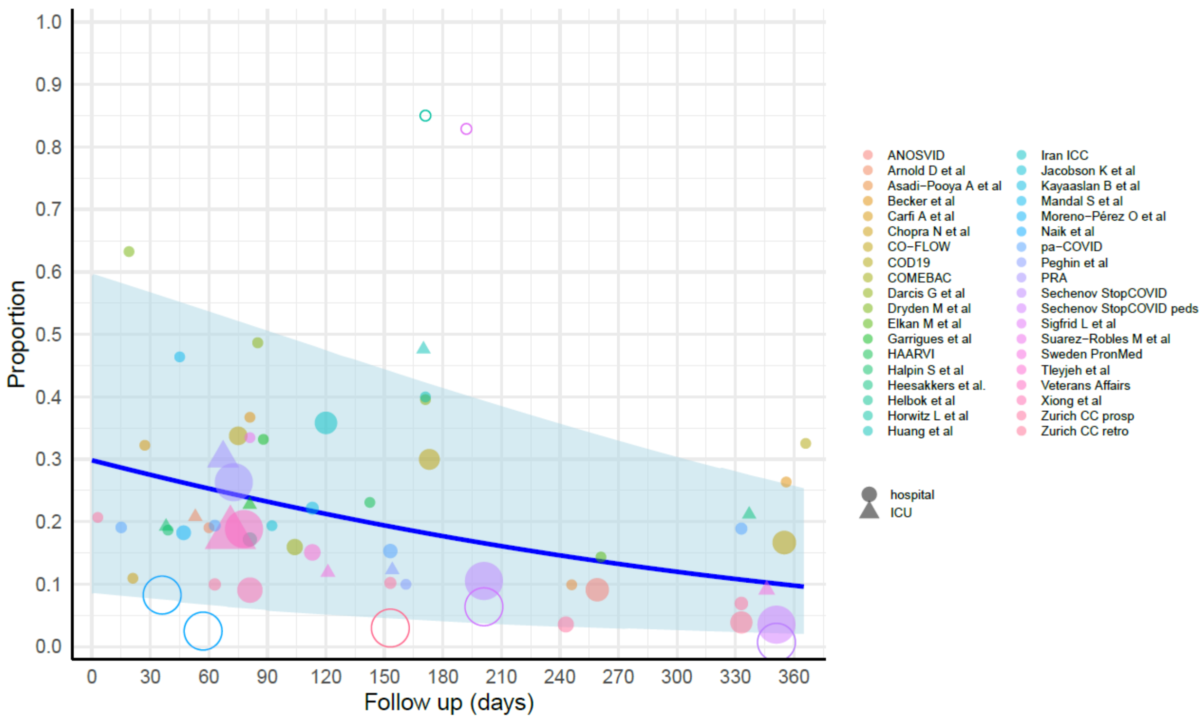
eFigure 8e. Fatigue cluster among those hospitalized for COVID infection, males, all ages. Open circles are trimmed data points.



eFigure 8f. Fatigue cluster among those admitted to ICU for COVID infection, females, all ages. Open circles are trimmed data points.

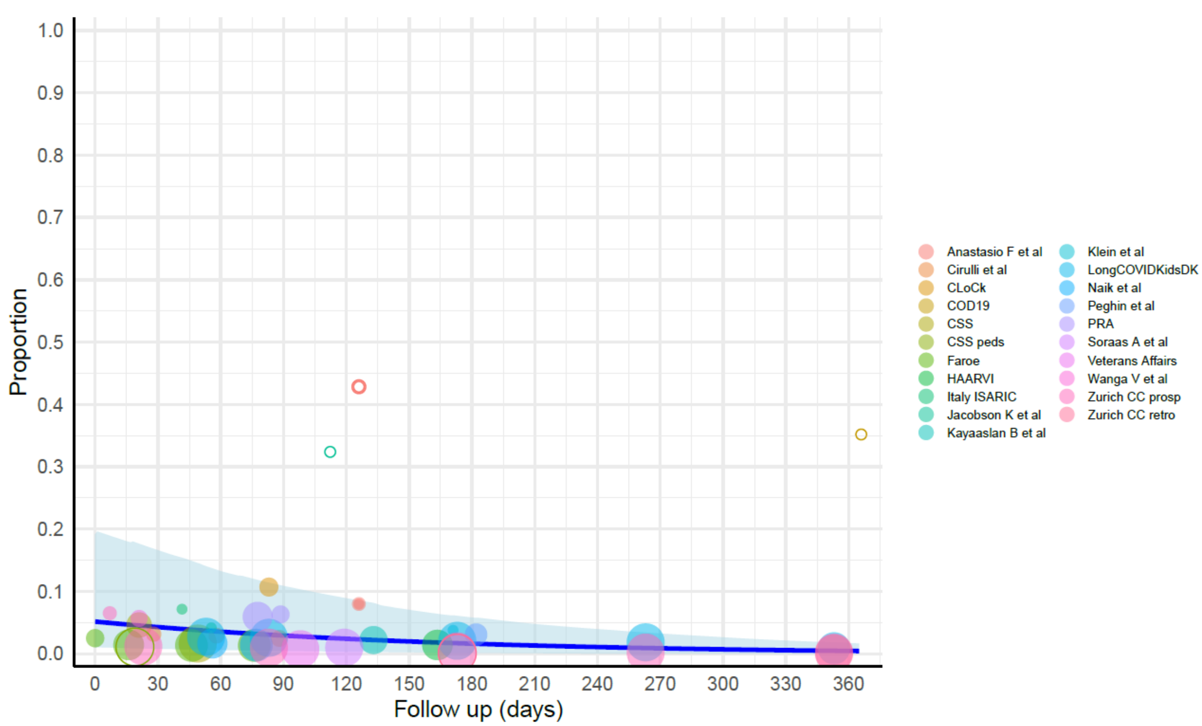


eFigure 8g. Fatigue cluster among those admitted to ICU for COVID infection, males, all ages. Open circles are trimmed data points.

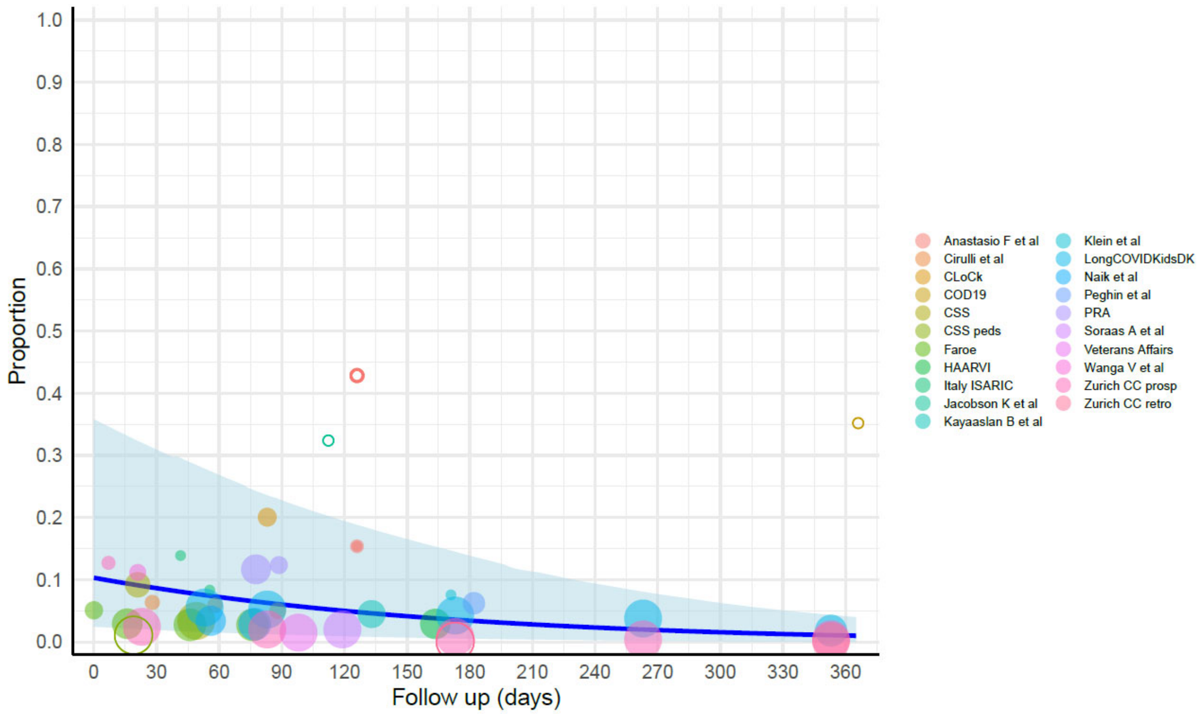


eFigure 9. Individual symptom clusters model results: respiratory.

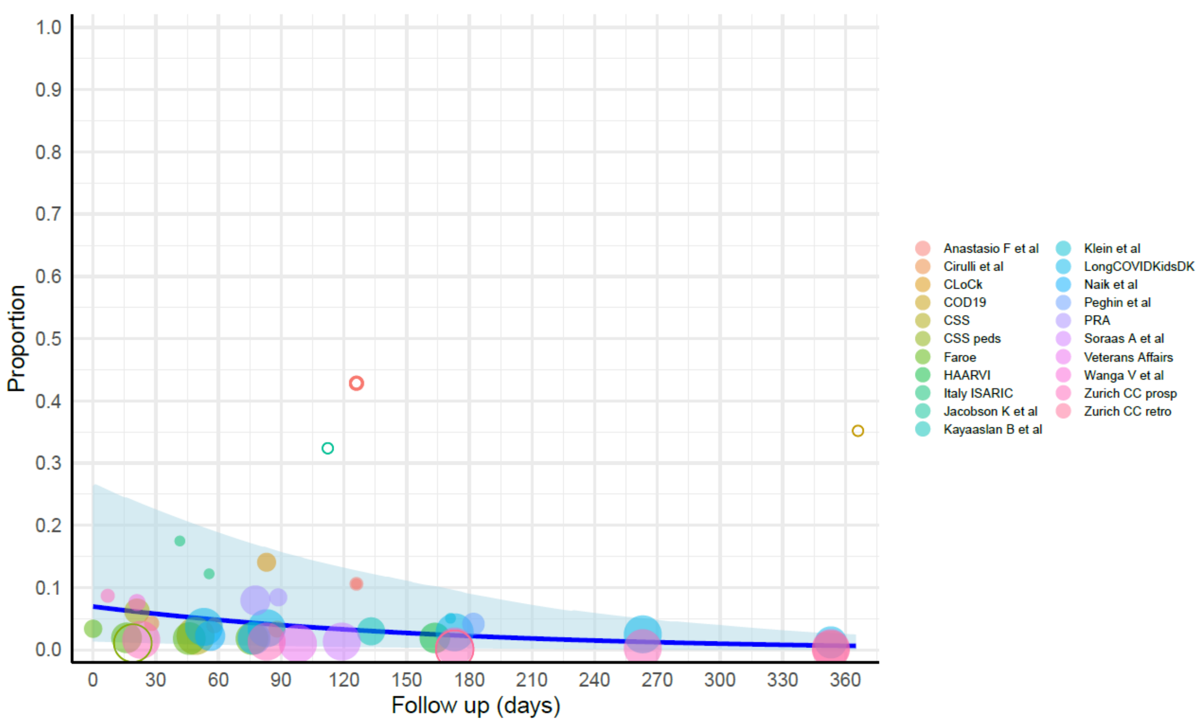
eFigure 9a. Respiratory cluster among those who experienced symptomatic COVID infection not needing hospitalization, both males and females, ages <20. Open circles are trimmed data points.



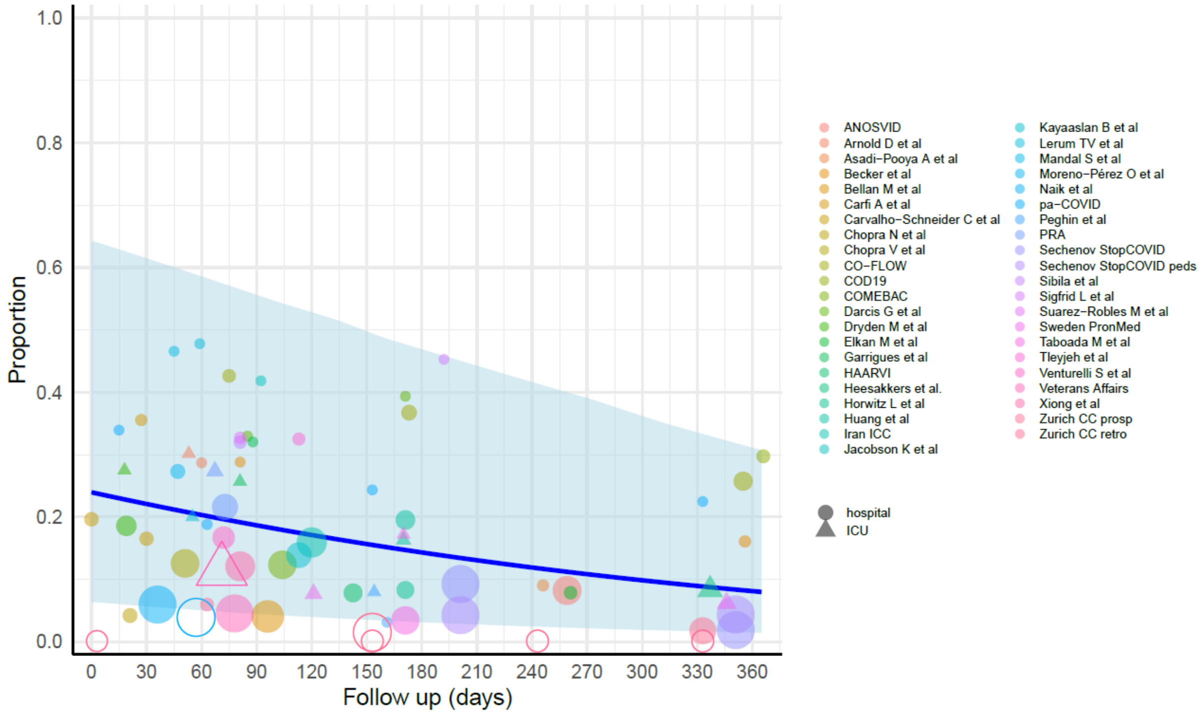
eFigure 9b. Respiratory cluster among those who experienced symptomatic COVID infection not needing hospitalization, females, ages 20+. Open circles are trimmed data points.



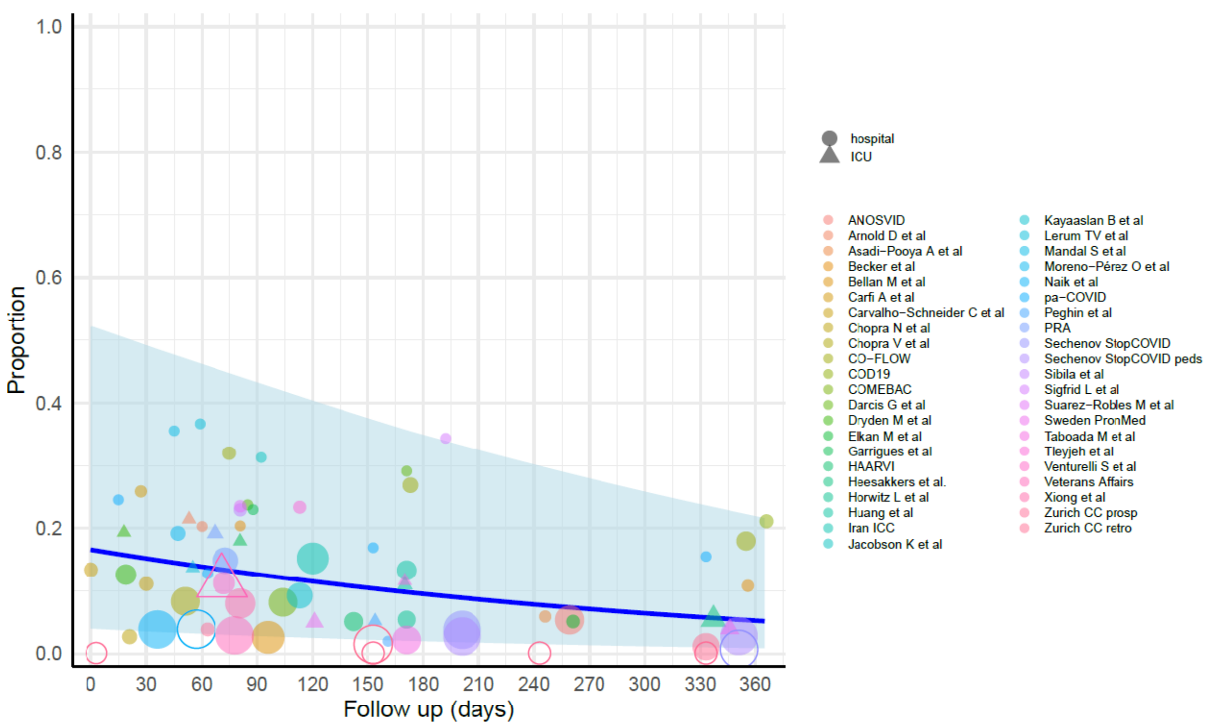
eFigure 9c. Respiratory cluster among those who experienced symptomatic COVID infection not needing hospitalization, males, ages 20+. Open circles are trimmed data points.



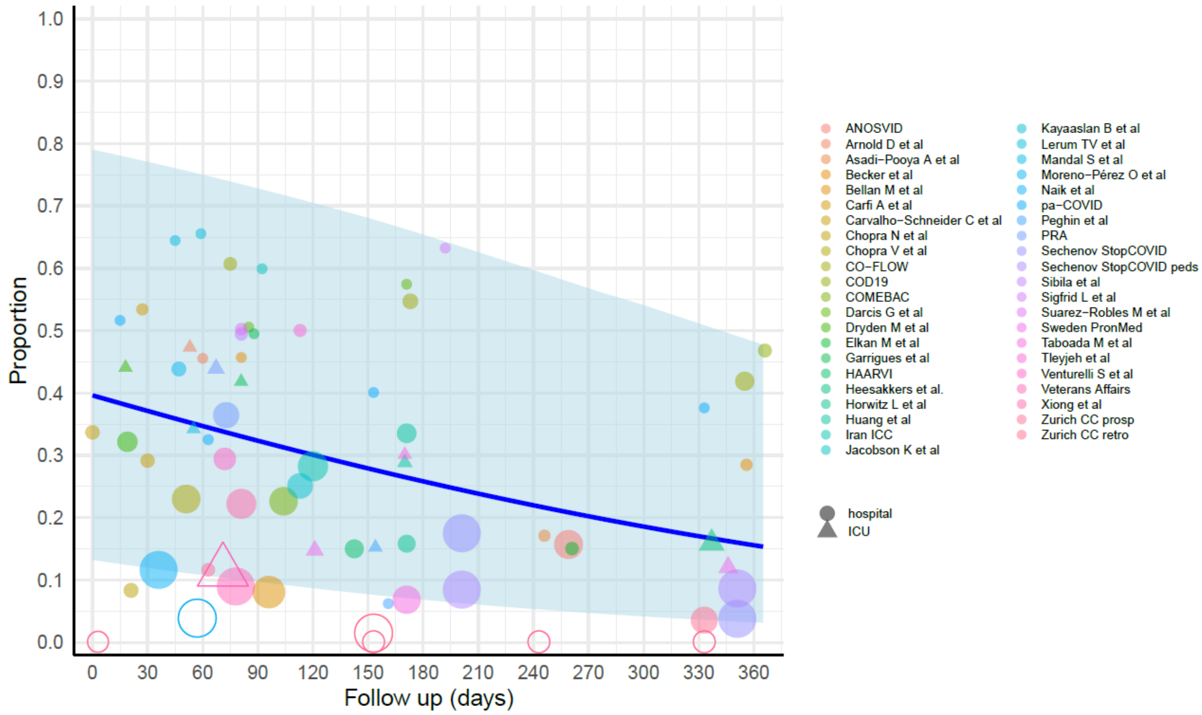
eFigure 9d. Respiratory cluster among those hospitalized for COVID infection, females, all ages. Open circles are trimmed data points.



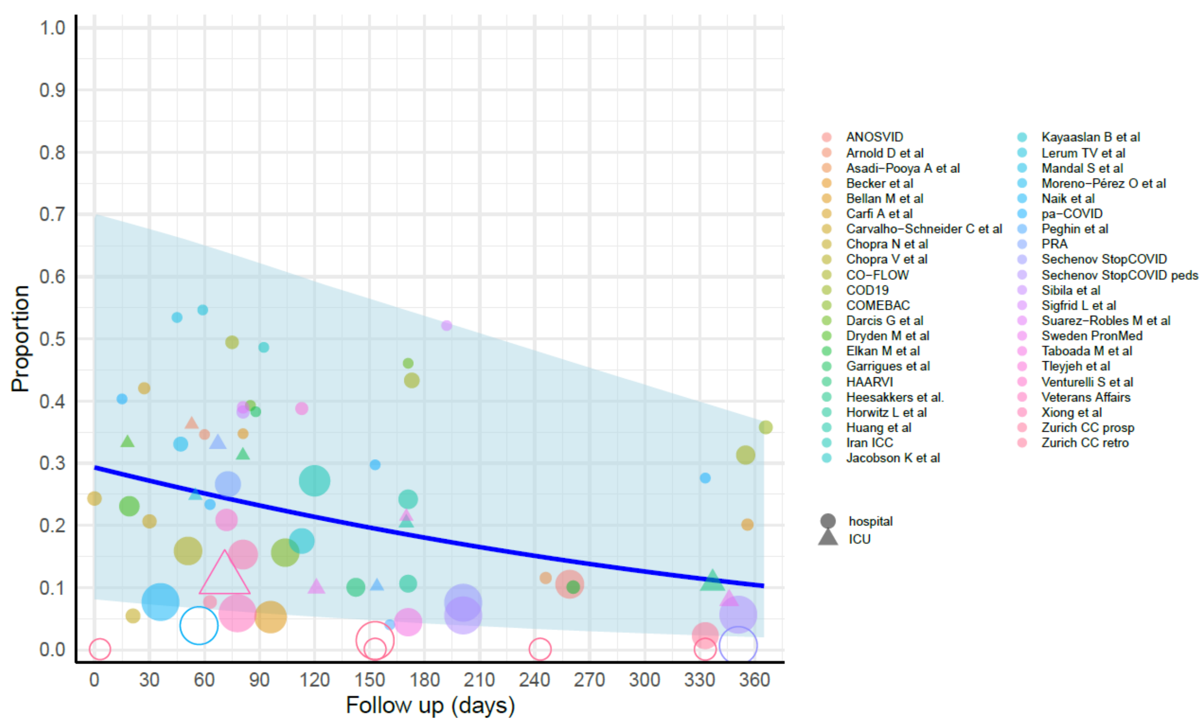
eFigure 9e. Respiratory cluster among those hospitalized for COVID infection, males, all ages. Open circles are trimmed data points.



eFigure 9f. Respiratory cluster among those admitted to ICU for COVID infection, females, all ages. Open circles are trimmed data points.

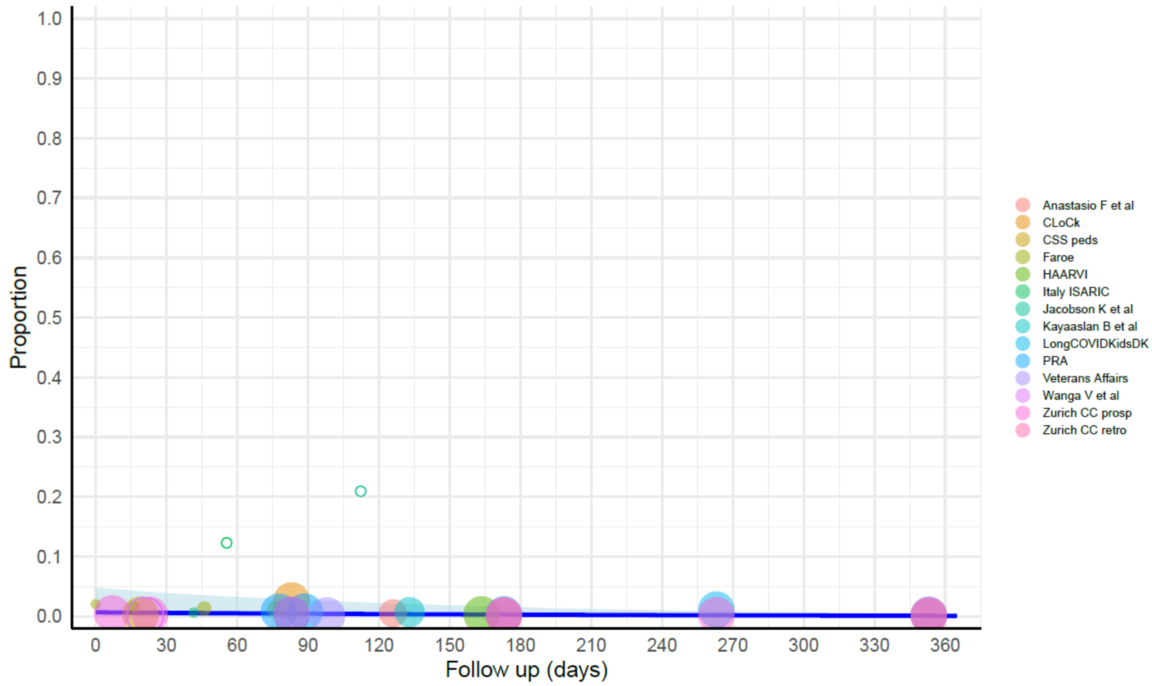


eFigure 9g. Respiratory cluster among those admitted to ICU for COVID infection, males, all ages. Open circles are trimmed data points.

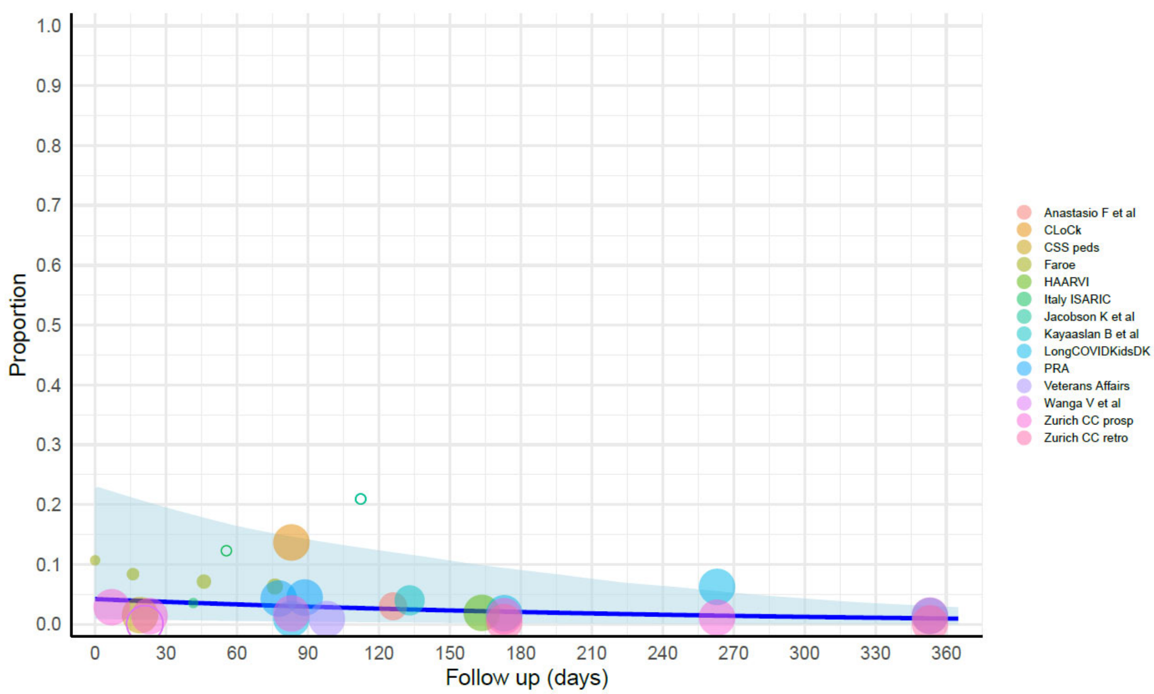


eFigure 10. Individual symptom clusters model results: cognitive.

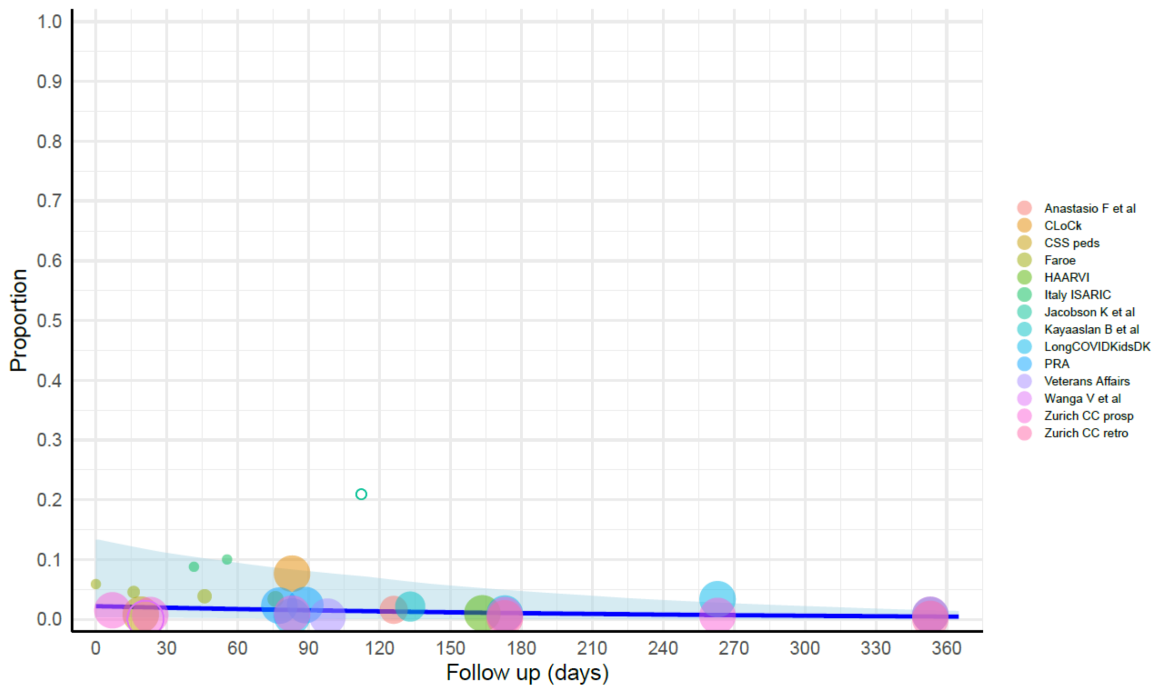
eFigure 10a. Cognitive cluster among those who experienced symptomatic COVID infection not needing hospitalization, both males and females, ages <20. Open circles are trimmed data points.



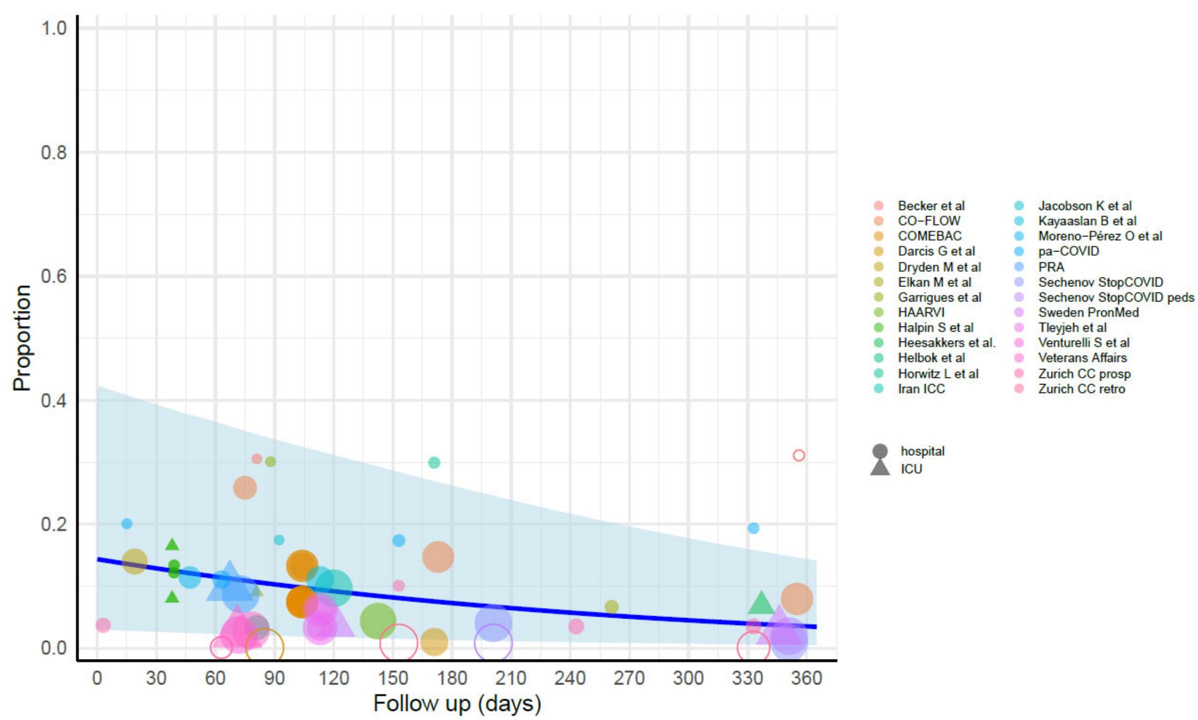
eFigure 10b. Cognitive cluster among those who experienced symptomatic COVID infection not needing hospitalization, females, ages 20+. Open circles are trimmed data points.



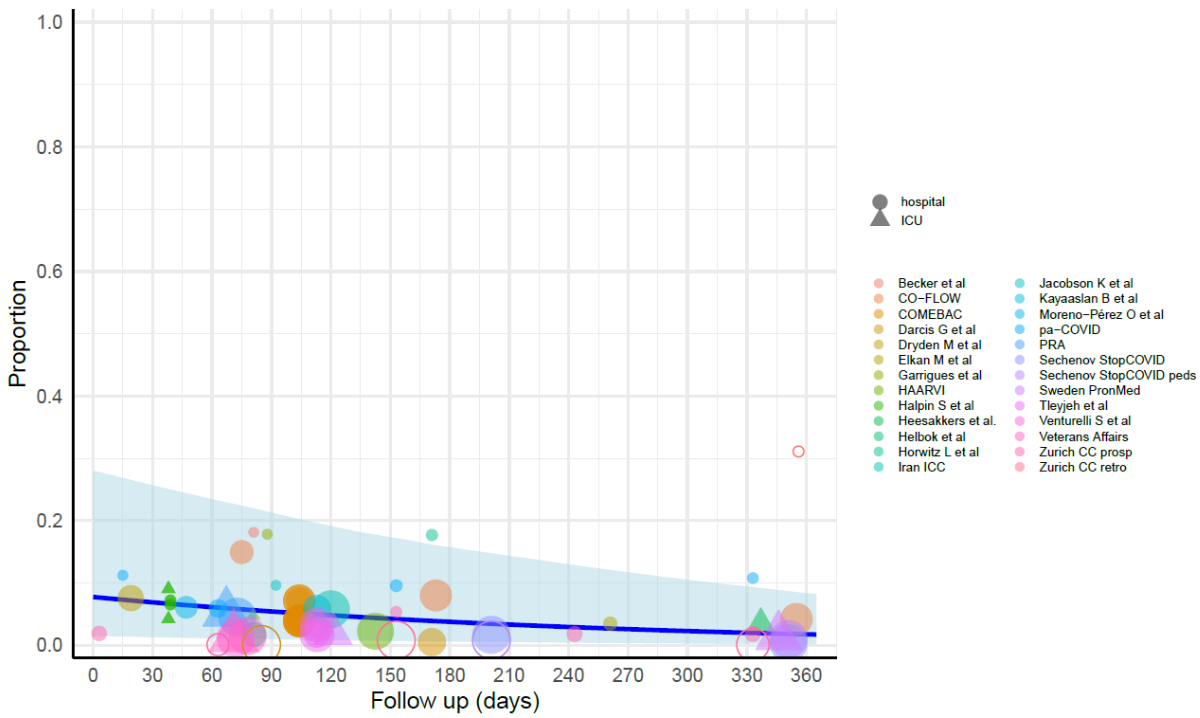
eFigure 10c. Cognitive cluster among those who experienced symptomatic COVID infection not needing hospitalization, males, ages 20+. Open circles are trimmed data points.



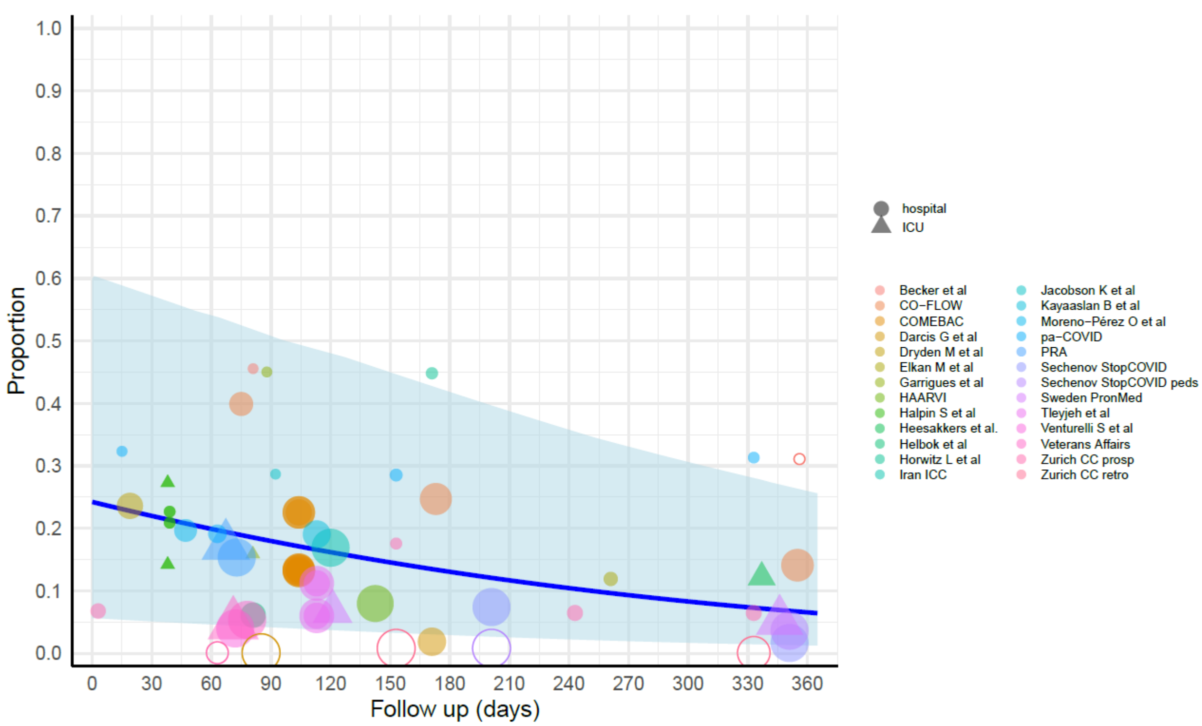
eFigure 10d. Cognitive cluster among those hospitalized for COVID infection, females, all ages. Open circles are trimmed data points.



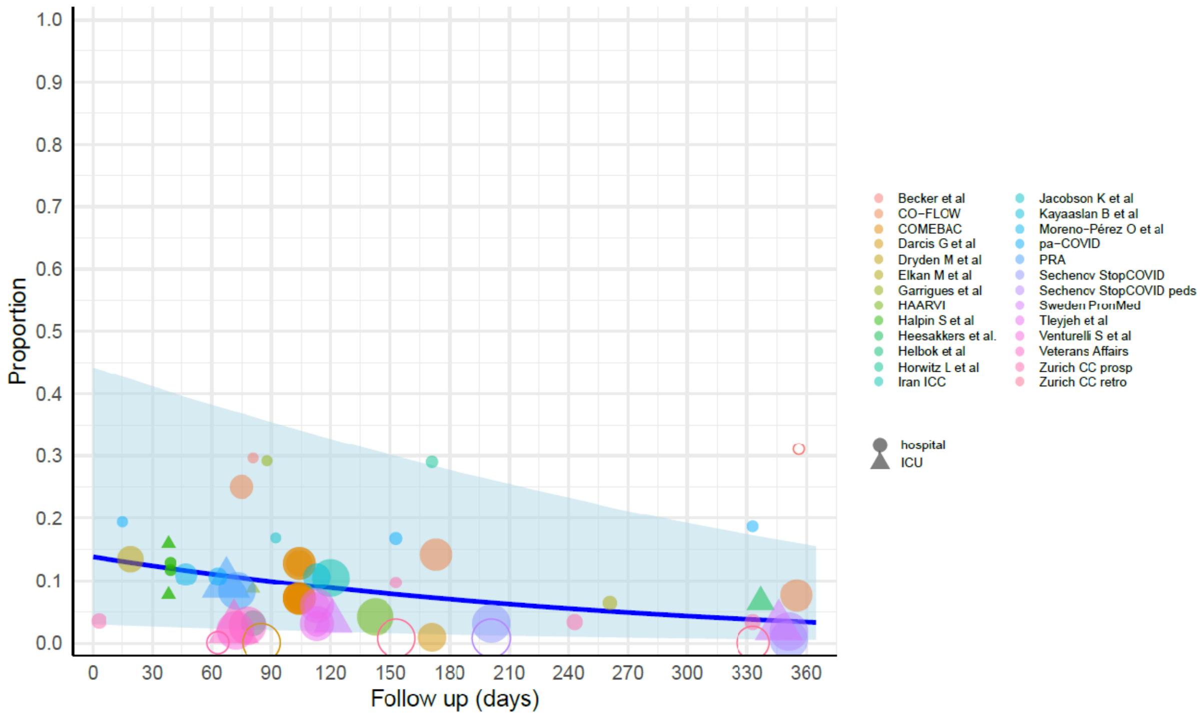
eFigure 10e. Cognitive cluster among those hospitalized for COVID infection, males, all ages. Open circles are trimmed data points.



eFigure 10f. Cognitive cluster among those admitted to ICU for COVID infection, females, all ages. Open circles are trimmed data points.



eFigure 10g. Cognitive cluster among those admitted to ICU for COVID infection, males, all ages. Open circles are trimmed data points.



eSection 3: Estimate symptom cluster overlap and severity distributions

Overlap of symptom clusters

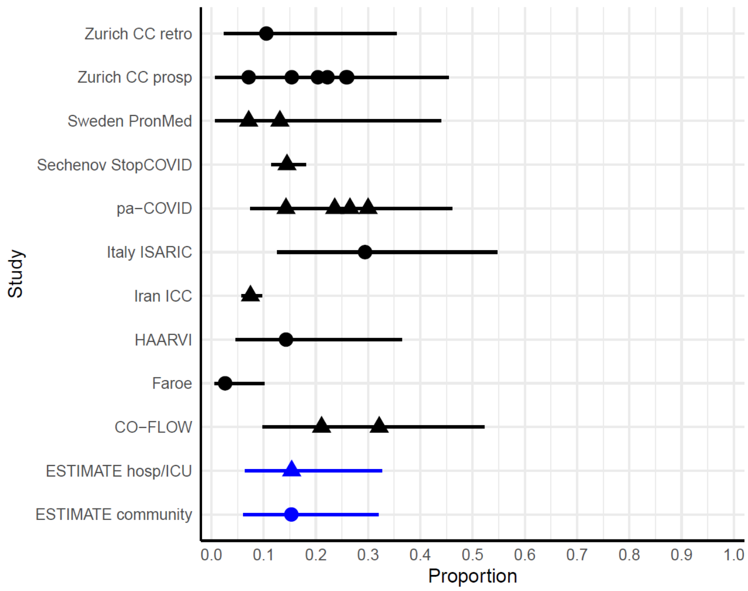
To model the overlap of symptom clusters, we ran MRTool meta-analysis models on available cohort data of each overlap of symptom clusters among long COVID patients, rather than among all COVID patients above, because the proportions are small. eTable 10 displays the fixed effects included in the models, and each model also had a random effect on study. Also due to sparse data, we modeled non-hospitalized data and hospitalized data together with a fixed effect on the latter, and no data were trimmed (eFigure 11).

eTable 10. Model parameters for each overlap of symptom clusters model among long COVID cases.

Fixed effect	Fatigue and Respiratory Beta Coefficient, Logit (SD)	Fatigue and Cognitive Beta Coefficient, Logit (SD)	Respiratory and Cognitive Beta Coefficient, Logit (SD)	Fatigue, Respiratory, and Cognitive Beta Coefficient, Logit (SD)
Hospital/ICU	0.00462 (0.422)	-0.670 (0.356)	0.392 (0.632)	-0.00881 (0.650)

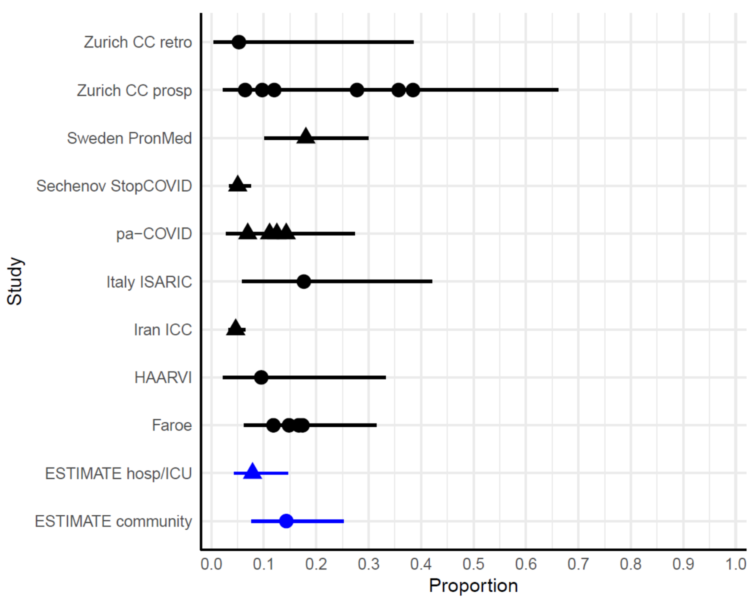
eFigure 11. Model results: Overlap of symptom clusters among long COVID patients.

eFigure 11a. Fatigue and respiratory.



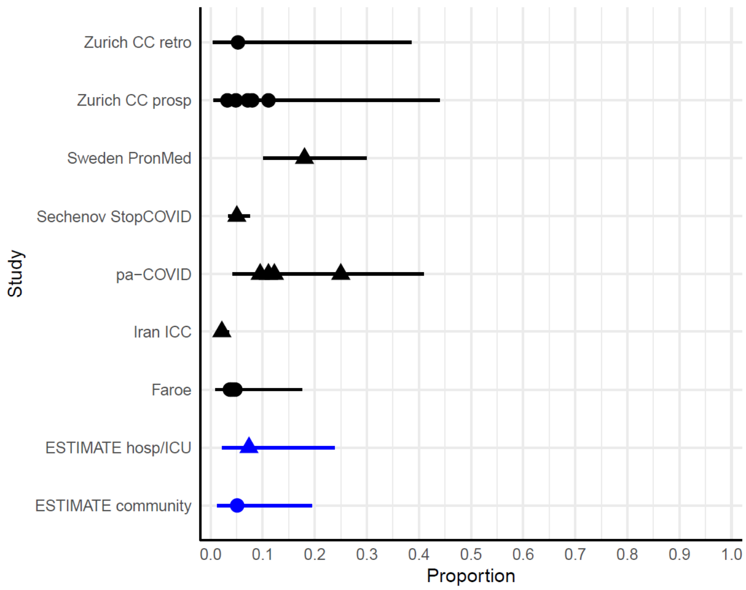
Circles = non-hospitalized cases, triangles = hospitalized/ICU cases

eFigure 11b. Fatigue and cognitive.



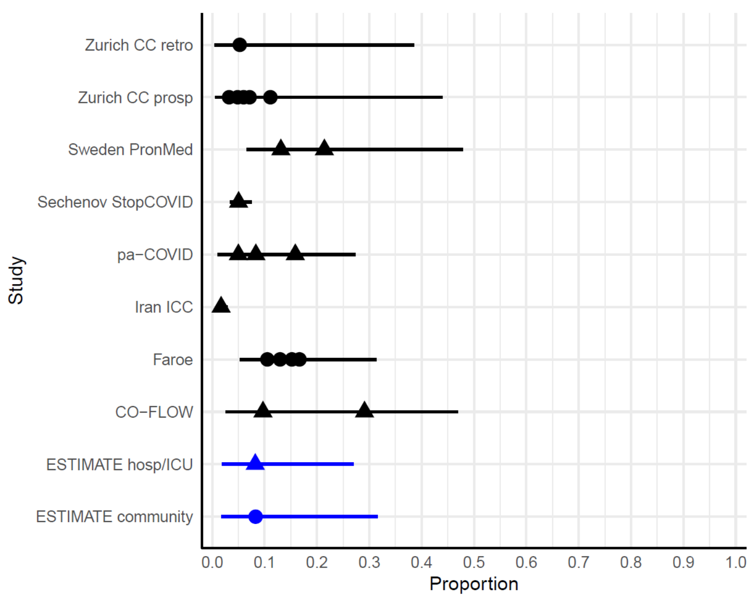
Circles = non-hospitalized cases, triangles = hospitalized/ICU cases

eFigure 11c. Respiratory and cognitive.



Circles = non-hospitalized cases, triangles = hospitalized/ICU cases

eFigure 11d. Fatigue, respiratory, and cognitive.



Circles = non-hospitalized cases, triangles = hospitalized/ICU cases

Severity distributions

We also modeled severity distributions of cognitive and respiratory symptoms using MRTool with available cohort data of each severity among all cognitive or respiratory cases. Each severity-specific model had a random effect on study and a fixed effect on whether the data were among hospitalized patients (eTable 11 and eTable 12). There was insufficient severity-specific data to model these proportions by follow-up time, and no data were trimmed (eFigures 12, 13).

eTable 11. Model parameters for severity-specific cognitive symptom models.

Fixed effect	Mild cognitive Beta Coefficient, Logit (SD)	Severe cognitive Beta Coefficient, Logit (SD)
Hospital/ICU	-0.856 (0.579)	0.337 (0.819)

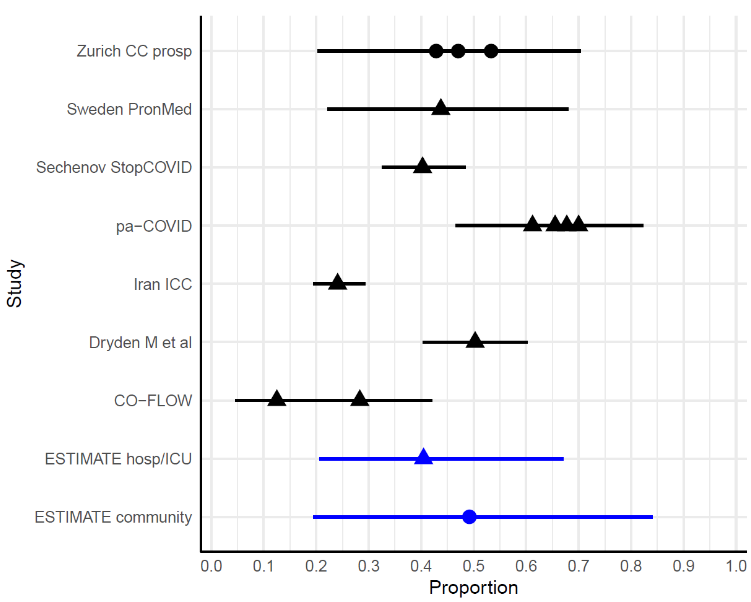
eTable 12. Model parameters for severity-specific respiratory symptom models.

Fixed effect	Mild respiratory Beta Coefficient, Logit (SD)	Moderate respiratory Beta Coefficient, Logit (SD)	Severe respiratory Beta Coefficient, Logit (SD)
Hospital/ICU	-0.354 (0.688)	-0.578 (0.973)	1.572 (1.107)

Severity-specific estimates were adjusted to sum to 100% before being used to split the overall cognitive and respiratory results by severity.

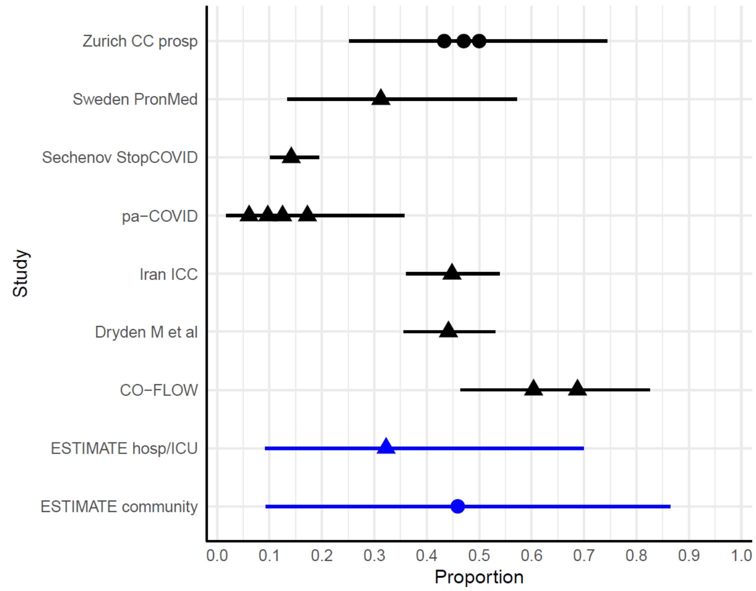
eFigure 12. Model results: Respiratory severity distributions.

eFigure 12a. Respiratory (mild).



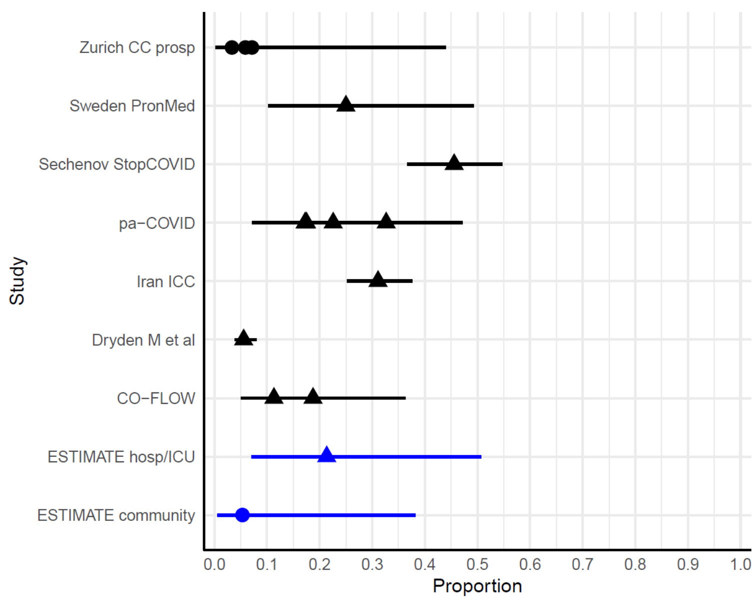
Circles = non-hospitalized cases, triangles = hospitalized/ICU cases

eFigure 12b. Respiratory (moderate).



Circles = non-hospitalized cases, triangles = hospitalized/ICU cases

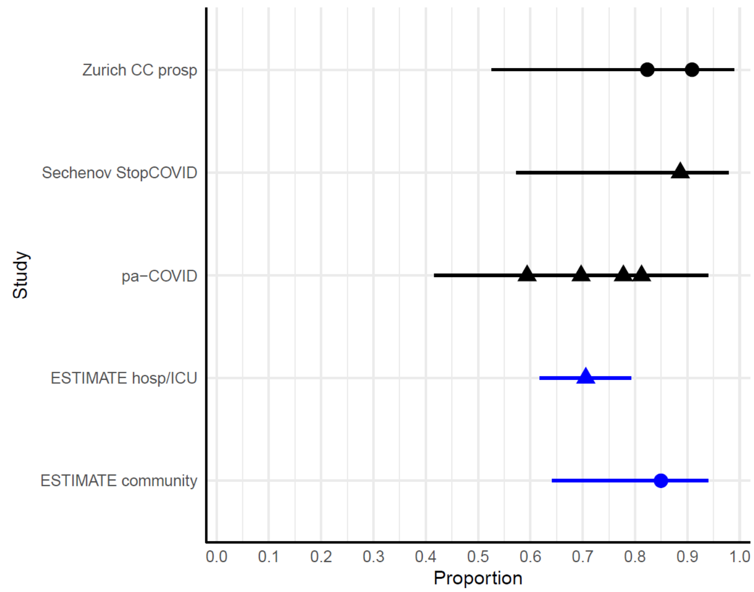
eFigure 12c. Respiratory (severe).



Circles = non-hospitalized cases, triangles = hospitalized/ICU cases

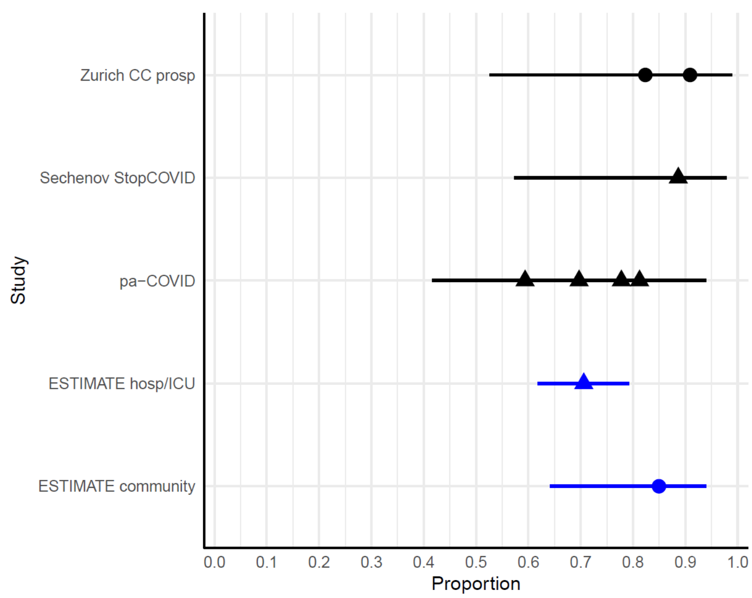
eFigure 13. Model results: Cognitive severity distributions.

eFigure 13a. Cognitive (mild).



Circles = non-hospitalized cases, triangles = hospitalized/ICU cases

eFigure 13b. Cognitive (moderate).



Circles = non-hospitalized cases, triangles = hospitalized/ICU cases

eSection 4: Estimate symptomatic COVID cases that survive acute episode

Asymptomatic cases

Case definition

An asymptomatic case is defined as a person infected with detectable viral load of SARS-CoV-2 but without symptoms.

Data

Data sources were obtained from a published systematic literature review which contains the proportion of confirmed positive COVID cases through antibody testing that were asymptomatic, from studies across the world.[84]

We have two primary inclusion criteria: 1) antibody screening studies; and 2) randomly selected sample to ensure representativeness. Of the 18 antibody screening studies included in the review, 6 met our inclusion criteria (eTable 13).

eTable 13. Input data of proportion asymptomatic among COVID infections.

Author	Location	Sample
Ward et al.[85]	China	17 576
Pollán et al.[86]	Hubei	3 053
Da Silva et al.[87]	Shandong	1 167
Feehan et al.[88]	Bahrain	311
Hippich et al.[89]	Hubei	47
Mahajan et al.[90]	Guangdong	23

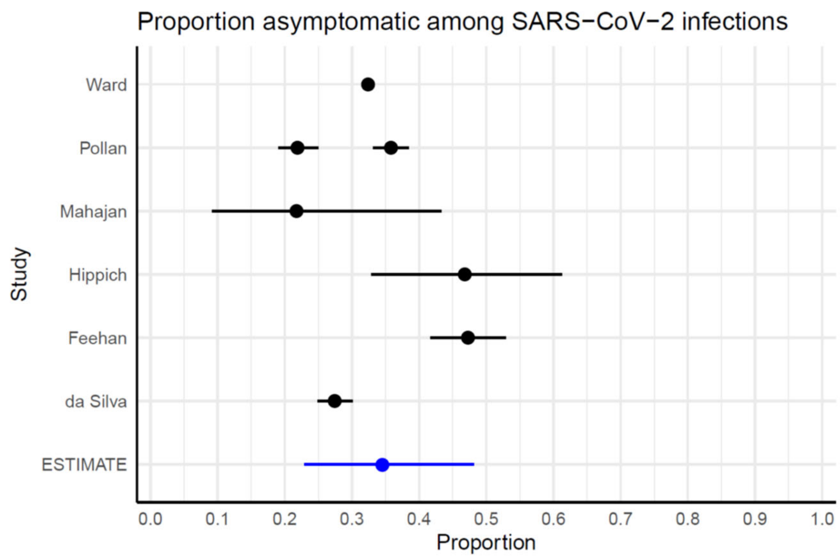
The standard error of each data point was calculated using the following equation for a binomial distribution.

$$Standard\ error = \sqrt{\frac{proportion_{asymp} * (1 - proportion_{asymp})}{sample\ size}}$$

Methods

First we pooled the studies using a meta-analysis in logit space to constrain the estimate between 0 and 1, with a study-level random effect (eFigure 14**Error! Reference source not found.**). The delta method was used to convert the standard error into logit space for the meta-analysis.

eFigure 14. Pooled estimate of proportion asymptomatic among SARS-CoV-2 infections.



The data are high quality but heterogeneous in the observed proportions asymptomatic, ranging from 22% to 47% asymptomatic. This could be due to differential rather than consistent antibody testing capture of SARS-CoV-2 infections in different settings, true variation in the proportion asymptomatic due to different underlying risk factors in the study populations, or differential symptom recall by the patients in these studies.

Cases at risk for long COVID

Asymptomatic cases were assumed to not be at risk for long COVID, due to lack of data. Five cohorts included asymptomatic cases: the UW Coronavirus Cohort (HAARVI), Faroe Islands, Zurich SARS-CoV-2 Cohort, Rome ISARIC pediatrics, and Rome ISARIC adults cohorts, with 9, 22, 182, 27, and 26 cases, respectively, that were asymptomatic during the acute COVID episode. Long COVID according to our definition was not identified among asymptomatic cases that were followed in HAARVI and Rome ISARIC cohorts. In the Faroe Islands cohort, 3 patients who did not report any symptoms during the acute phase developed long COVID symptoms, and in the Zurich SARS-CoV-2 Cohort of 182 asymptomatic infections, 5 developed at least one long COVID symptom cluster at 1 or 3 or 6 months follow-up. The two cohorts did not explicitly measure a difference in symptoms compared to before COVID infection. From the available information we cannot preclude that there is some risk of long COVID among asymptomatic cases, but the number of cases in the available studies is very small, and we prefer to be cautious and exclude them from our calculations until stronger evidence is available.

Non-hospitalized cases

Case definition

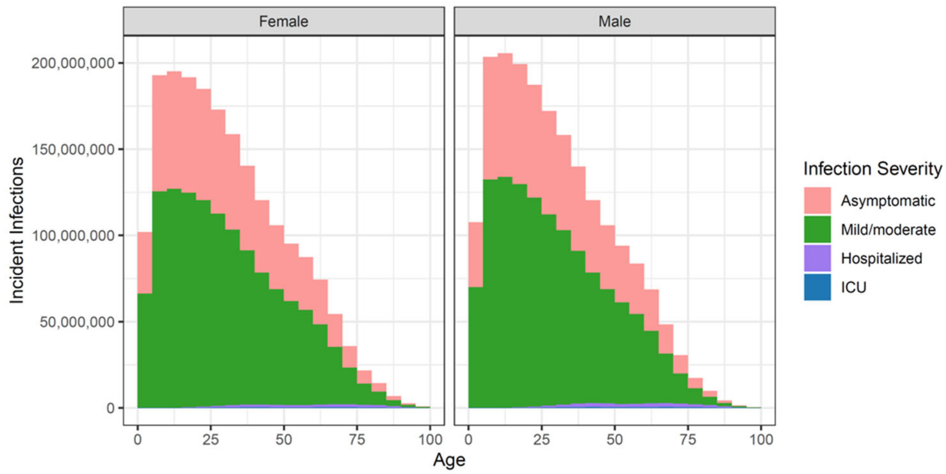
Non-hospitalized cases of COVID-19 are defined as symptomaticcases of COVID-19 not needing hospitalization.

$$inc_{comm} = infections * (1 - prop\ asymp) - hosp\ admissions$$

where $hosp\ admissions$ represents the hospital admissions corresponding to infections from 12 days prior, a lag defined in the IHME COVID model from which we derive cases and hospitalizations.

Estimates of new asymptomatic, non-hospitalized symptomatic, hospitalized, and ICU cases are shown in eFigure 15, with case severity increasing with age for both males and females.

eFigure 15. Age distribution of asymptomatic SARS-CoV-2 infections, non-hospitalized cases, cases needing hospitalization, and cases needing ICU care, by sex.



Note: "Mild/moderate" in this figure refers to non-hospitalized, symptomatic COVID-19 cases

Proportion of deaths in long-term care

Case definition

Non-hospitalized deaths are defined as deaths due to COVID-19 that occurred outside the hospital in long-term care facilities (LTC).

Data

Data sources were obtained from online reports in the Netherlands, Belgium, France, and all USA states which contain the proportion of COVID-19 deaths which occurred in long-term care facilities.[91–94] Total sample size across all reports was 667,928 deaths.

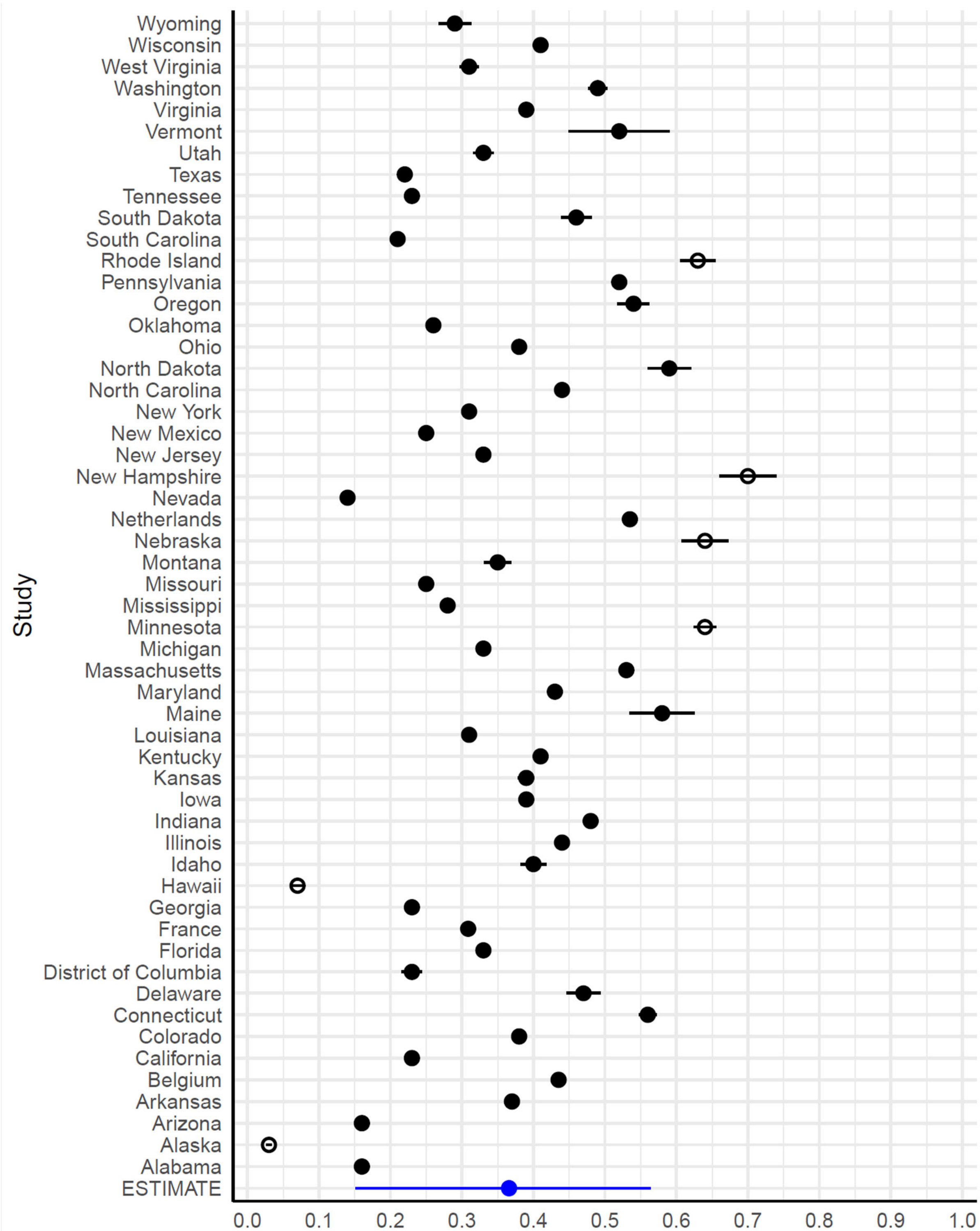
The standard error of each data point was calculated using the following equation for a binomial distribution.

$$Standard\ error = \sqrt{\frac{proportion_{LTC} * (1 - proportion_{LTC})}{sample\ size}}$$

Methods

We pooled the studies using a meta-analysis in logit space to constrain the estimate between 0 and 1, trimming 10% of the data points using MRTool, with a random effect on location (eFigure 16).

eFigure 16. Pooled estimate of proportion of COVID-19 deaths that occurred in long-term care facilities.



Note: Open circles denote data points that were trimmed within the likelihood function.

The resulting estimated proportion of deaths that occurred in long-term care facilities was 36.2% (95% UI 14.4-57.0). We accounted for all estimated deaths from the COVID SEIR model by multiplying this proportion by deaths to obtain non-hospitalized deaths, multiplying hospitalized non-ICU and ICU admissions by age-specific case-fatality ratios (described below in "Proportion deaths among hospitalized and ICU cases") to obtain hospitalized and ICU deaths, and proportionally scaled these three counts of deaths to the total number of deaths by age/sex/location/day.

This analysis assumed that among COVID-19 cases who die, their probability of dying in long-term care facilities did not differ by age. There is currently insufficient available data to evaluate the validity of this assumption.

Hospitalized cases

Case definition

Hospitalized cases of COVID-19 were defined as cases of COVID-19 needing hospitalization but not ICU care, regardless of access or utilization of care. These cases were calculated from hospital admissions by subtracting corresponding ICU admissions from 3 days later, the lag assumed in the overall COVID model, as well as severe cases who died outside a hospital in long-term care facilities.

Proportion deaths among hospitalized and ICU cases

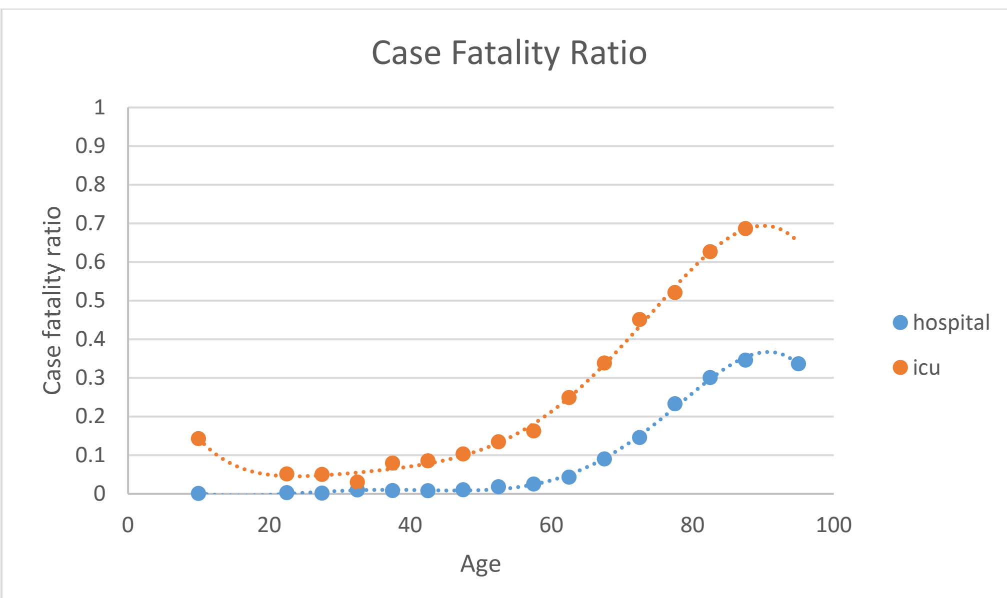
Data

Age-specific data on COVID deaths among hospitalized and/or ICU patients proved extremely difficult to find, and we found only one comprehensive source with this level of detail from the Netherlands COVID-19 ICU online dashboard.[95]

Methods

Case fatality among hospitalized and ICU patients was extracted and fit with a 6th order polynomial to most closely follow the curves of the data so that case fatality estimates could be extracted for every 5-year age group (eFigure 17). The value for case fatality for age group 5-9 was extrapolated back to age 0 due to lack of data at the very young ages.

eFigure 17. Case fatality ratios among hospitalized and ICU COVID-19 patients by age.



ICU cases

Case definition

ICU cases of COVID-19 were defined as cases of COVID-19 needing ICU care due to critical acute symptoms, regardless of access or utilization of care.

eSection 5: Estimate symptom cluster incidence

Incidence estimates

Incidence of long COVID symptom clusters and overlaps was calculated by multiplying surviving symptomatic COVID cases (non-hospitalized, hospitalized, and ICU cases who recovered from the acute infection) by the proportions of symptom clusters that were adjusted to sum to the overall long COVID estimate (eTable 14). All calculations were conducted using 1000 draws of each quantity to propagate uncertainty through each analytical step. The distribution of symptom clusters and their overlap from the final results is shown in eTable 15, and global and country estimates of new long COVID cases are in eTable 16 and eTable 17.

eTable 14. Estimated risk of long COVID among symptomatic community, hospitalized, and ICU COVID-19 cases by symptom cluster, sex and age group 3 months after symptom onset.

	Post-acute fatigue syndrome	Respiratory symptoms	Cognitive symptoms	Any long COVID symptom cluster
Both males and females				
Long COVID risk among community cases (age < 20)*	1·26% (0·0818–4·70)	1·91% (0·299–4·97)	0·784% (0·0352–3·27)	2·73% (0·808–6·65)
Males				
Long COVID risk among community cases (age >= 20)	2·38% (0·194–7·74)	2·85% (0·368–7·87)	1·67% (0·113–5·97)	4·76% (1·53–11·3)
Long COVID risk among hospitalized cases	11·8% (2·48–28·3)	11·9% (2·48–27·6)	6·53% (0·886–19·2)	21·6% (8·90–40·3)
Long COVID risk among ICU cases	19·1% (4·93–41·7)	19·2% (5·20–42·1)	10·6% (1·86–28·3)	35·8% (17·1–58·1)
Females				
Long COVID risk among community cases (age >= 20)	5·51% (0·608–16·7)	5·57% (0·886–14·9)	3·81% (0·301–12·7)	9·88% (3·38–21·2)
Long COVID risk among hospitalized cases	20·0% (5·38–41·2)	17·5% (4·26–39·3)	10·9% (1·87–28·4)	34·8% (16·5–57·3)
Long COVID risk among ICU cases	28·3% (10·1–53·0)	25·0% (7·90–51·2)	16·0% (3·89–37·1)	51·9% (29·7–73·6)

**Note: There were insufficient data to stratify estimates by sex for community cases younger than age 20.*

eTable 15. Distribution of symptom clusters and their overlap among long COVID cases at 3 months after symptom onset. (proportions are mutually exclusive).

Symptom cluster(s)	Proportion (95% UI)
One symptom cluster	
Fatigue with bodily pain/mood swings	18.1% (0.0-70.0)
Respiratory symptoms	33.4% (0.4-75.5)
Cognitive symptoms	10.1% (0.0-49.9)
Two symptom clusters	
Fatigue with bodily pain/mood swings, Respiratory symptoms	13.1% (2.1-37.1)
Fatigue with bodily pain/mood swings, Cognitive symptoms	11.3% (1.9-30.8)
Respiratory symptoms, Cognitive symptoms	5.5% (0.7-21.5)
Three symptom clusters	
Fatigue with bodily pain/mood swings, Respiratory symptoms, and Cognitive symptoms	8.5% (0.8-33.6)

eTable 16. Global new cases of long COVID symptom clusters by sex and severity of initial infection in 2020-2021, in millions.

	Both males and females	Males	Females
Fatigue with bodily pain/mood swings	78.9 (14.4–242)	26.8 (4.51–84.4)	52.1 (9.60–157)
Respiratory symptoms	89.3 (21.1–222)	33.5 (8.04–84.0)	55.8 (12.7–139)
Cognitive symptoms	55.2 (7.40–180)	18.6 (2.49–61.6)	36.6 (4.93–121)
Any long COVID symptom cluster	145 (55.0–312)	52.2 (19.7–115)	92.4 (34.9–199)
among non-hospitalized cases	130 (42.1–301)	45.8 (14.0–109)	84.3 (27.8–190)
among cases needing hospitalization	11.5 (4.91–20.5)	4.99 (1.97–9.35)	6.47 (2.92–10.8)
among cases needing ICU care	3.03 (0.892–7.48)	1.39 (0.381–3.54)	1.64 (0.517–3.96)

UI = Uncertainty interval. Uncertainty intervals are presented in parentheses. Uncertainty intervals are wide due to the heterogeneity in the data sources. The interval is asymmetric because of Bayesian, rather than parametric, estimation methods and the fact that proportions are bounded by zero and one.

eTable 17. Symptomatic infections and new cases of long COVID by country, 2020 and 2021.[a]

Location	Pandemic start	Symptomatic infections during 2020-2021[b] (UI)	New cases of Long COVID during 2020 (UI)	New cases of Long COVID during 2021 (UI)
GLOBAL	December 2019	2,550,000,000 (2,030,000,000–3,020,000,000)	40,500,000 (15,500,000–88,200,000)	104,000,000 (39,400,000–225,000,000)
Central Europe, Eastern Europe, and Central Asia	February 2020	228,000,000 (181,000,000–274,000,000)	2,400,000 (973,000–5,120,000)	10,400,000 (4,270,000–22,000,000)
Central Asia	February 2020	46,200,000 (33,300,000–60,000,000)	727,000 (271,000–1,660,000)	1,790,000 (678,000–4,060,000)
Armenia	February 2020	1,970,000 (1,210,000–2,600,000)	31,200 (11,200–72,100)	82,900 (29,700–182,000)
Azerbaijan	February 2020	6,570,000 (3,380,000–9,170,000)	42,200 (14,300–100,000)	310,000 (95,300–738,000)
Georgia	February 2020	2,380,000 (1,110,000–3,280,000)	2,960 (737–6,860)	124,000 (33,100–293,000)
Kazakhstan	February 2020	7,930,000 (3,420,000–13,900,000)	107,000 (27,100–278,000)	363,000 (97,700–930,000)
Kyrgyzstan	February 2020	3,750,000 (2,410,000–5,500,000)	87,200 (30,500–192,000)	130,000 (43,900–307,000)
Mongolia	February 2020	1,490,000 (968,000–1,870,000)	276 (40–917)	61,200 (21,800–141,000)
Tajikistan	February 2020	5,200,000 (3,010,000–7,030,000)	54,700 (18,200–120,000)	195,000 (66,700–431,000)
Turkmenistan	February 2020	2,800,000 (1,670,000–3,850,000)	30,700 (10,700–68,900)	108,000 (37,500–243,000)
Uzbekistan	February 2020	14,100,000 (4,960,000–22,400,000)	371,000 (99,200–888,000)	415,000 (111,000–1,040,000)
Central Europe	February 2020	54,200,000 (42,900,000–65,500,000)	281,000 (118,000–584,000)	2,700,000 (1,130,000–5,710,000)
Albania	February 2020	1,890,000 (1,280,000–2,370,000)	22,200 (7,820–48,400)	94,100 (35,200–204,000)
Bosnia and Herzegovina	February 2020	2,000,000 (1,330,000–2,660,000)	17,600 (6,640–38,900)	103,000 (41,100–227,000)
Bulgaria	February 2020	4,110,000 (2,230,000–5,790,000)	15,900 (6,030–34,100)	219,000 (72,200–500,000)
Croatia	February 2020	1,900,000 (1,410,000–2,560,000)	6,530 (2,630–14,700)	90,700 (37,900–197,000)
Czechia	February 2020	5,800,000 (3,870,000–7,530,000)	25,000 (9,750–54,000)	317,000 (129,000–684,000)
Hungary	February 2020	4,260,000 (2,810,000–5,680,000)	13,400 (5,230–28,900)	211,000 (81,900–456,000)
Montenegro	February 2020	465,000 (362,000–562,000)	3,040 (1,200–6,460)	24,500 (9,810–51,800)
North Macedonia	February 2020	1,440,000 (970,000–1,820,000)	14,000 (5,480–31,300)	76,300 (29,200–167,000)
Poland	February 2020	16,200,000 (12,400,000–19,900,000)	60,200 (25,400–129,000)	794,000 (322,000–1,750,000)
Romania	February 2020	8,960,000 (5,430,000–12,800,000)	79,500 (32,000–177,000)	415,000 (158,000–931,000)
Serbia	February 2020	4,410,000 (2,870,000–5,960,000)	18,800 (6,810–42,800)	222,000 (83,500–478,000)
Slovakia	February 2020	2,140,000 (1,510,000–3,220,000)	3,190 (1,050–8,080)	103,000 (37,200–228,000)
Slovenia	February 2020	686,000 (418,000–1,160,000)	1,400 (425–3,810)	34,100 (11,600–79,400)
Eastern Europe	February 2020	128,000,000 (101,000,000–157,000,000)	1,390,000 (577,000–2,930,000)	5,870,000 (2,410,000–12,300,000)
Belarus	February 2020	4,340,000 (1,740,000–7,460,000)	58,500 (14,800–155,000)	194,000 (51,100–498,000)
Estonia	February 2020	290,000 (207,000–411,000)	661 (236–1,680)	14,700 (5,740–34,500)
Latvia	February 2020	747,000 (368,000–1,330,000)	1,030 (295–2,530)	35,400 (11,000–88,000)
Lithuania	February 2020	1,340,000 (738,000–2,040,000)	1,870 (584–4,360)	74,400 (23,900–182,000)
Republic of Moldova	February 2020	2,060,000 (1,140,000–3,000,000)	34,800 (10,500–79,100)	92,700 (29,400–215,000)
Russian Federation	February 2020	96,200,000 (74,600,000–116,000,000)	1,130,000 (461,000–2,380,000)	4,450,000 (1,790,000–9,230,000)
Ukraine	February 2020	23,000,000 (12,600,000–36,100,000)	161,000 (50,000–390,000)	1,010,000 (336,000–2,300,000)
High-income	January 2020	171,000,000 (136,000,000–203,000,000)	2,180,000 (899,000–4,500,000)	7,720,000 (3,170,000–15,900,000)
Australasia	February 2020	268,000 (213,000–323,000)	3,620 (1,360–7,800)	6,400 (2,720–13,100)
Australia	February 2020	253,000 (202,000–306,000)	3,490 (1,310–7,540)	6,280 (2,670–12,900)
New Zealand	March 2020	15,000 (11,400–18,800)	125 (50–272)	126 (52–256)
High-income Asia Pacific	January 2020	5,570,000 (4,430,000–6,750,000)	40,300 (17,000–82,600)	319,000 (137,000–651,000)
Brunei Darussalam	February 2020	24,600 (17,600–35,900)	74 (24–176)	894 (318–2,120)
Japan	February 2020	4,200,000 (3,350,000–5,030,000)	29,700 (12,900–60,100)	284,000 (122,000–576,000)
Republic of Korea	January 2020	1,050,000 (689,000–1,710,000)	4,570 (1,580–10,900)	31,000 (12,300–67,900)
Singapore	January 2020	293,000 (224,000–377,000)	5,920 (2,200–13,700)	3,470 (1,460–7,250)
High-income North America	December 2019	80,900,000 (64,500,000–95,900,000)	1,050,000 (436,000–2,210,000)	3,780,000 (1,550,000–7,830,000)
Canada	January 2020	3,120,000 (2,340,000–4,050,000)	27,900 (10,700–58,300)	167,000 (66,800–345,000)
Greenland	February 2020	17,500 (5,350–39,500)	7 (2–16)	62 (22–139)

Location	Pandemic start	Symptomatic infections during 2020-2021[b] (UI)	New cases of Long COVID during 2020 (UI)	New cases of Long COVID during 2021 (UI)
United States of America	January 2020	77,800,000 (62,000,000–92,300,000)	1,020,000 (425,000–2,160,000)	3,620,000 (1,480,000–7,490,000)
Southern Latin America	February 2020	11,600,000 (8,220,000–16,000,000)	183,000 (70,600–393,000)	533,000 (202,000–1,180,000)
Argentina	February 2020	8,290,000 (5,440,000–12,400,000)	130,000 (48,900–286,000)	388,000 (140,000–861,000)
Chile	February 2020	2,790,000 (2,040,000–3,640,000)	52,100 (19,500–114,000)	112,000 (42,200–243,000)
Uruguay	February 2020	520,000 (387,000–669,000)	450 (142–1,060)	33,100 (13,300–71,300)
Western Europe	December 2019	72,700,000 (58,100,000–87,400,000)	898,000 (371,000–1,840,000)	3,080,000 (1,280,000–6,310,000)
Andorra	February 2020	34,400 (23,800–45,700)	564 (206–1,220)	1,210 (457–2,860)
Austria	February 2020	1,530,000 (1,150,000–2,050,000)	7,590 (3,030–16,600)	67,000 (24,900–143,000)
Belgium	February 2020	3,050,000 (2,270,000–3,930,000)	40,700 (16,400–88,800)	108,000 (43,300–228,000)
Cyprus	February 2020	153,000 (117,000–202,000)	292 (107–683)	7,640 (3,110–16,000)
Denmark	February 2020	659,000 (500,000–859,000)	6,140 (2,260–13,000)	23,800 (9,610–48,800)
Finland	December 2019	420,000 (300,000–589,000)	3,730 (1,500–7,900)	13,600 (5,530–28,700)
France	February 2020	12,500,000 (8,970,000–17,800,000)	175,000 (65,000–378,000)	513,000 (203,000–1,090,000)
Germany	January 2020	10,900,000 (8,560,000–13,400,000)	55,800 (23,200–114,000)	424,000 (173,000–874,000)
Greece	February 2020	1,190,000 (918,000–1,460,000)	3,110 (1,120–7,100)	56,700 (22,700–120,000)
Iceland	February 2020	21,900 (16,800–27,800)	292 (115–621)	627 (256–1,310)
Ireland	February 2020	847,000 (597,000–1,250,000)	9,480 (3,300–21,300)	30,000 (11,300–65,800)
Israel	February 2020	1,540,000 (1,200,000–1,910,000)	25,700 (10,400–53,800)	67,200 (26,800–146,000)
Italy	January 2020	8,540,000 (6,620,000–10,800,000)	107,000 (44,800–219,000)	433,000 (180,000–907,000)
Luxembourg	February 2020	117,000 (89,000–148,000)	1,180 (455–2,540)	5,210 (2,070–11,000)
Malta	February 2020	47,800 (36,800–59,300)	349 (149–743)	2,720 (1,150–5,620)
Monaco	February 2020	6,150 (4,570–8,090)	29 (13–62)	268 (118–541)
Netherlands	February 2020	3,790,000 (2,860,000–5,330,000)	42,000 (16,100–92,100)	145,000 (57,400–302,000)
Norway	February 2020	486,000 (348,000–678,000)	4,150 (1,570–9,260)	16,300 (6,670–34,500)
Portugal	February 2020	1,670,000 (1,210,000–2,270,000)	13,800 (5,230–30,700)	94,100 (38,000–198,000)
San Marino	February 2020	11,800 (8,670–15,000)	183 (73–390)	460 (188–976)
Spain	February 2020	8,240,000 (6,260,000–10,600,000)	168,000 (73,200–348,000)	373,000 (153,000–797,000)
Sweden	February 2020	1,610,000 (1,240,000–2,040,000)	30,400 (12,000–64,500)	73,700 (31,100–154,000)
Switzerland	February 2020	1,540,000 (1,160,000–2,000,000)	9,810 (3,930–21,400)	63,000 (25,400–133,000)
United Kingdom	January 2020	13,800,000 (10,900,000–16,400,000)	191,000 (78,600–398,000)	560,000 (233,000–1,160,000)
Latin America and Caribbean	January 2020	248,000,000 (196,000,000–296,000,000)	5,200,000 (1,990,000–11,200,000)	10,100,000 (3,870,000–22,000,000)
Andean Latin America	February 2020	33,700,000 (24,900,000–42,500,000)	906,000 (340,000–1,960,000)	1,090,000 (409,000–2,480,000)
Bolivia (Plurinational State of)	February 2020	8,390,000 (5,660,000–10,700,000)	223,000 (79,100–485,000)	257,000 (85,500–590,000)
Ecuador	February 2020	9,450,000 (6,340,000–12,400,000)	218,000 (77,800–469,000)	332,000 (116,000–742,000)
Peru	February 2020	15,900,000 (10,600,000–21,600,000)	466,000 (166,000–1,050,000)	498,000 (177,000–1,130,000)
Caribbean	February 2020	9,060,000 (5,480,000–13,000,000)	147,000 (48,300–342,000)	325,000 (121,000–747,000)
Antigua and Barbuda	March 2020	11,300 (6,770–17,400)	49 (16–131)	622 (209–1,400)
Bahamas	February 2020	81,300 (37,900–132,000)	1,220 (387–2,850)	3,460 (1,110–8,020)
Barbados	February 2020	39,100 (25,000–59,500)	78 (29–172)	964 (390–2,110)
Belize	March 2020	119,000 (51,400–201,000)	683 (190–1,720)	4,490 (1,110–10,900)
Bermuda	March 2020	6,740 (5,080–9,620)	38 (14–84)	409 (168–847)
Cuba	February 2020	1,340,000 (906,000–1,980,000)	1,670 (581–3,970)	88,000 (33,400–197,000)
Dominica	March 2020	11,300 (7,100–17,000)	12 (2–35)	419 (138–1,020)
Dominican Republic	February 2020	2,450,000 (999,000–3,870,000)	68,200 (18,500–170,000)	75,300 (20,600–185,000)
Grenada	March 2020	16,600 (7,370–27,900)	9 (2–25)	999 (297–2,530)
Guyana	February 2020	241,000 (95,200–410,000)	2,400 (632–5,950)	10,300 (2,590–26,600)
Haiti	February 2020	3,110,000 (606,000–6,050,000)	56,900 (10,800–151,000)	69,800 (10,800–190,000)
Jamaica	February 2020	395,000 (193,000–639,000)	2,830 (938–6,710)	19,400 (5,860–45,900)
Puerto Rico	February 2020	296,000 (202,000–406,000)	4,420 (1,680–10,200)	16,400 (6,470–35,800)
Saint Kitts and Nevis	March 2020	5,060 (2,980–8,520)	14 (2–48)	242 (83–601)

Location	Pandemic start	Symptomatic infections during 2020-2021[b] (UI)	New cases of Long COVID during 2020 (UI)	New cases of Long COVID during 2021 (UI)
Saint Lucia	March 2020	30,400 (15,400–48,100)	18 (4–45)	1,790 (581–4,000)
Saint Vincent and the Grenadines	March 2020	14,500 (8,430–21,800)	30 (8–75)	606 (218–1,470)
Suriname	February 2020	217,000 (102,000–326,000)	1,870 (537–4,370)	10,100 (2,880–23,900)
Trinidad and Tobago	February 2020	350,000 (158,000–546,000)	1,430 (452–3,530)	9,680 (2,810–22,500)
United States Virgin Islands	February 2020	19,200 (10,500–38,800)	314 (106–781)	796 (274–1,990)
Central Latin America	February 2020	108,000,000 (84,500,000–130,000,000)	2,110,000 (798,000–4,480,000)	4,460,000 (1,690,000–9,520,000)
Colombia	February 2020	15,100,000 (10,400,000–20,000,000)	252,000 (94,000–563,000)	714,000 (258,000–1,590,000)
Costa Rica	February 2020	1,490,000 (889,000–2,160,000)	18,300 (6,130–41,500)	76,100 (25,400–170,000)
El Salvador	February 2020	1,590,000 (932,000–2,270,000)	24,100 (8,460–53,200)	64,600 (21,300–146,000)
Guatemala	February 2020	8,180,000 (5,000,000–11,600,000)	149,000 (51,800–348,000)	316,000 (99,600–754,000)
Honduras	February 2020	6,160,000 (4,150,000–8,210,000)	99,700 (35,900–231,000)	254,000 (92,000–588,000)
Mexico	February 2020	61,100,000 (48,600,000–72,800,000)	1,290,000 (496,000–2,750,000)	2,430,000 (927,000–5,240,000)
Nicaragua	February 2020	2,560,000 (1,850,000–3,250,000)	44,300 (16,800–98,700)	104,000 (39,800–230,000)
Panama	February 2020	1,140,000 (812,000–1,540,000)	28,300 (10,300–61,900)	41,900 (15,500–91,500)
Venezuela (Bolivarian Republic of)	February 2020	11,000,000 (7,870,000–13,900,000)	199,000 (75,600–434,000)	463,000 (172,000–1,010,000)
Tropical Latin America	January 2020	97,300,000 (76,700,000–117,000,000)	2,040,000 (779,000–4,430,000)	4,270,000 (1,620,000–9,450,000)
Brazil	January 2020	94,100,000 (73,800,000–113,000,000)	2,020,000 (769,000–4,390,000)	4,110,000 (1,550,000–9,050,000)
Paraguay	February 2020	3,200,000 (2,070,000–4,460,000)	22,700 (8,390–50,100)	165,000 (57,300–378,000)
North Africa and Middle East	January 2020	264,000,000 (196,000,000–329,000,000)	4,830,000 (1,800,000–10,900,000)	9,410,000 (3,630,000–21,000,000)
Afghanistan	February 2020	25,900,000 (15,400,000–33,800,000)	428,000 (118,000–996,000)	881,000 (276,000–2,180,000)
Algeria	February 2020	5,730,000 (3,020,000–10,100,000)	118,000 (37,800–297,000)	194,000 (56,900–485,000)
Bahrain	February 2020	569,000 (343,000–803,000)	9,170 (3,280–20,400)	24,300 (8,270–55,000)
Egypt	January 2020	53,600,000 (11,000,000–83,000,000)	1,240,000 (182,000–3,160,000)	1,330,000 (193,000–3,380,000)
Iran (Islamic Republic of)	January 2020	38,000,000 (29,400,000–46,400,000)	552,000 (214,000–1,200,000)	1,750,000 (673,000–3,730,000)
Iraq	February 2020	27,800,000 (17,000,000–36,300,000)	657,000 (194,000–1,460,000)	946,000 (324,000–2,120,000)
Jordan	February 2020	6,280,000 (4,070,000–8,270,000)	8,450 (2,880–19,200)	282,000 (95,500–636,000)
Kuwait	February 2020	1,290,000 (677,000–2,290,000)	27,400 (7,120–67,900)	57,400 (16,900–129,000)
Lebanon	January 2020	2,640,000 (1,650,000–3,540,000)	20,800 (7,050–57,600)	137,000 (48,700–320,000)
Libya	March 2020	4,600,000 (2,910,000–5,930,000)	45,500 (17,300–100,000)	211,000 (76,000–472,000)
Morocco	February 2020	18,400,000 (8,760,000–27,100,000)	224,000 (74,300–506,000)	933,000 (273,000–2,240,000)
Oman	February 2020	1,350,000 (770,000–2,200,000)	25,800 (8,840–62,900)	49,600 (15,800–119,000)
Palestine	February 2020	3,160,000 (1,830,000–4,210,000)	21,700 (7,380–50,700)	142,000 (47,900–325,000)
Qatar	February 2020	1,280,000 (727,000–1,720,000)	37,500 (12,600–86,600)	33,000 (10,700–77,900)
Saudi Arabia	February 2020	5,410,000 (2,950,000–9,230,000)	226,000 (70,300–542,000)	104,000 (29,900–274,000)
Sudan	February 2020	18,400,000 (6,440,000–28,200,000)	415,000 (78,100–1,080,000)	306,000 (75,600–767,000)
Syrian Arab Republic	March 2020	2,110,000 (867,000–3,850,000)	12,900 (3,640–33,900)	79,900 (19,800–231,000)
Tunisia	February 2020	6,970,000 (3,850,000–9,530,000)	22,700 (6,880–54,200)	437,000 (144,000–1,030,000)
Turkey	February 2020	30,500,000 (16,900,000–48,800,000)	475,000 (105,000–1,360,000)	1,240,000 (426,000–2,820,000)
United Arab Emirates	January 2020	1,630,000 (826,000–2,640,000)	22,900 (7,150–53,000)	74,300 (22,800–173,000)
Yemen	March 2020	8,250,000 (2,880,000–16,500,000)	231,000 (28,100–574,000)	179,000 (31,400–584,000)
South Asia	January 2020	880,000,000 (676,000,000–1,060,000,000)	15,700,000 (5,810,000–34,000,000)	36,700,000 (13,500,000–79,300,000)
Bangladesh	February 2020	89,100,000 (56,800,000–127,000,000)	1,550,000 (508,000–3,700,000)	3,850,000 (1,390,000–8,660,000)
Bhutan	February 2020	13,900 (9,390–20,000)	145 (30–401)	664 (245–1,540)

Location	Pandemic start	Symptomatic infections during 2020-2021[b] (UI)	New cases of Long COVID during 2020 (UI)	New cases of Long COVID during 2021 (UI)
India	January 2020	659,000,000 (507,000,000–800,000,000)	11,900,000 (4,500,000–25,800,000)	27,900,000 (10,400,000–59,600,000)
Nepal	February 2020	16,600,000 (12,200,000–24,900,000)	138,000 (51,900–307,000)	840,000 (305,000–1,900,000)
Pakistan	February 2020	115,000,000 (81,700,000–147,000,000)	2,100,000 (726,000–4,800,000)	4,150,000 (1,410,000–9,360,000)
Southeast Asia, East Asia, and Oceania	December 2019	188,000,000 (148,000,000–227,000,000)	1,340,000 (519,000–2,890,000)	8,860,000 (3,360,000–19,100,000)
East Asia	December 2019	1,730,000 (1,330,000–2,120,000)	106,000 (42,300–225,000)	9,780 (3,860–21,300)
China	December 2019	1,610,000 (1,240,000–1,990,000)	104,000 (41,800–223,000)	3,690 (1,490–7,850)
Democratic People's Republic of Korea	January 2020	50,300 (31,600–81,000)	1,060 (308–2,700)	2,060 (767–4,740)
Taiwan (Province of China)	January 2020	67,000 (38,800–122,000)	506 (82–1,830)	4,040 (1,460–9,480)
Oceania	February 2020	3,260,000 (1,680,000–5,110,000)	4,270 (1,310–11,200)	105,000 (32,900–262,000)
American Samoa	December 2020	34,800 (27,400–41,200)	4 (0–15)	6 (0–24)
Cook Islands	March 2020	2,090 (1,280–2,870)	21 (8–47)	71 (25–165)
Fiji	February 2020	200,000 (94,000–293,000)	83 (22–242)	11,000 (3,400–26,100)
Guam	February 2020	55,900 (34,400–84,200)	803 (293–1,890)	2,020 (699–4,660)
Kiribati	April 2021	407 (47–894)	0 (0–0)	22 (2–66)
Marshall Islands	October 2020	351 (70–808)	0 (0–0)	18 (3–54)
Micronesia (Federated States of)	December 2021	10 (4–16)	0 (0–0)	0 (0–1)
Nauru	March 2020	1,220 (749–1,690)	10 (4–24)	35 (12–80)
Niue	--	0 (0–0)	0 (0–0)	0 (0–0)
Northern Mariana Islands	March 2020	33,800 (25,300–44,200)	44 (16–99)	32 (12–75)
Palau	September 2021	18 (10–32)	0 (0–0)	1 (0–2)
Papua New Guinea	March 2020	2,770,000 (1,270,000–4,490,000)	3,090 (782–8,910)	86,300 (25,300–219,000)
Samoa	October 2020	259 (53–590)	0 (0–0)	14 (2–42)
Solomon Islands	September 2020	1,630 (223–5,250)	0 (0–2)	86 (9–330)
Tokelau	--	0 (0–0)	0 (0–0)	0 (0–0)
Tonga	October 2021	449 (23–1,030)	0 (0–0)	0 (0–0)
Tuvalu	March 2020	1,350 (847–1,850)	12 (4–28)	40 (14–91)
Vanuatu	November 2020	1,900 (659–4,630)	0 (0–0)	95 (19–299)
Southeast Asia	December 2019	183,000,000 (145,000,000–221,000,000)	1,230,000 (472,000–2,670,000)	8,750,000 (3,310,000–18,800,000)
Cambodia	January 2020	2,470,000 (1,030,000–3,910,000)	261 (39–899)	127,000 (39,800–318,000)
Indonesia	February 2020	104,000,000 (80,400,000–129,000,000)	770,000 (300,000–1,680,000)	5,370,000 (2,010,000–11,700,000)
Lao People's Democratic Republic	March 2020	1,600,000 (628,000–2,730,000)	121 (10–439)	12,800 (3,180–38,100)
Malaysia	February 2020	6,940,000 (4,550,000–9,590,000)	4,710 (1,370–12,100)	343,000 (124,000–783,000)
Maldives	February 2020	125,000 (85,200–222,000)	1,290 (372–3,550)	5,200 (1,820–12,100)
Mauritius	February 2020	163,000 (97,100–246,000)	227 (59–614)	2,140 (819–4,870)
Myanmar	March 2020	11,800,000 (6,310,000–17,100,000)	53,900 (17,800–127,000)	585,000 (177,000–1,360,000)
Philippines	February 2020	38,400,000 (30,300,000–46,700,000)	389,000 (144,000–833,000)	1,610,000 (605,000–3,470,000)
Seychelles	February 2020	36,300 (27,000–45,000)	28 (8–68)	1,950 (742–4,290)
Sri Lanka	January 2020	2,410,000 (1,670,000–3,300,000)	2,030 (302–6,590)	123,000 (45,800–267,000)
Thailand	December 2019	5,590,000 (2,960,000–9,500,000)	2,700 (360–9,020)	284,000 (94,700–693,000)
Timor-Leste	March 2020	269,000 (133,000–426,000)	41 (5–130)	13,900 (4,170–36,200)
Viet Nam	January 2020	8,420,000 (4,440,000–16,500,000)	1,370 (426–3,590)	249,000 (81,600–578,000)
Sub-Saharan Africa	January 2020	571,000,000 (452,000,000–675,000,000)	8,840,000 (3,240,000–19,200,000)	21,000,000 (7,610,000–46,400,000)
Central Sub-Saharan Africa	February 2020	77,400,000 (53,300,000–98,600,000)	1,350,000 (465,000–2,980,000)	2,690,000 (958,000–6,060,000)
Angola	March 2020	19,900,000 (10,900,000–26,500,000)	189,000 (61,000–439,000)	817,000 (266,000–1,820,000)
Central African Republic	February 2020	2,410,000 (1,510,000–3,570,000)	75,300 (23,800–187,000)	55,500 (17,800–146,000)
Congo	February 2020	2,850,000 (1,910,000–3,810,000)	51,000 (17,400–121,000)	70,100 (24,400–162,000)

Location	Pandemic start	Symptomatic infections during 2020-2021[b] (UI)	New cases of Long COVID during 2020 (UI)	New cases of Long COVID during 2021 (UI)
Democratic Republic of the Congo	February 2020	50,700,000 (28,900,000–65,800,000)	987,000 (319,000–2,260,000)	1,710,000 (565,000–3,870,000)
Equatorial Guinea	February 2020	765,000 (470,000–1,070,000)	25,000 (8,450–58,100)	11,900 (3,240–29,500)
Gabon	February 2020	869,000 (397,000–1,310,000)	17,700 (4,990–42,200)	25,300 (6,330–62,900)
Eastern Sub-Saharan Africa	February 2020	228,000,000 (179,000,000–271,000,000)	2,410,000 (858,000–5,180,000)	9,470,000 (3,410,000–20,700,000)
Burundi	March 2020	1,230,000 (819,000–1,690,000)	8,620 (2,890–19,600)	55,800 (18,300–133,000)
Comoros	April 2020	313,000 (217,000–418,000)	2,260 (404–7,530)	16,200 (5,980–36,200)
Djibouti	February 2020	513,000 (271,000–845,000)	11,200 (3,670–26,100)	17,200 (5,450–41,900)
Eritrea	March 2020	1,610,000 (1,100,000–2,180,000)	2,860 (164–10,200)	57,400 (19,300–126,000)
Ethiopia	February 2020	69,400,000 (53,700,000–84,900,000)	845,000 (308,000–1,860,000)	2,700,000 (981,000–5,970,000)
Kenya	February 2020	33,100,000 (26,200,000–39,100,000)	375,000 (134,000–826,000)	1,430,000 (518,000–3,140,000)
Madagascar	February 2020	16,400,000 (11,700,000–21,000,000)	325,000 (113,000–755,000)	510,000 (168,000–1,180,000)
Malawi	March 2020	11,300,000 (7,300,000–14,000,000)	64,000 (18,000–154,000)	539,000 (184,000–1,220,000)
Mozambique	March 2020	19,700,000 (13,100,000–24,400,000)	82,700 (25,000–200,000)	967,000 (337,000–2,170,000)
Rwanda	February 2020	3,920,000 (2,140,000–5,980,000)	9,690 (2,910–23,400)	212,000 (62,900–506,000)
Somalia	March 2020	12,900,000 (9,320,000–16,800,000)	137,000 (35,900–341,000)	478,000 (154,000–1,120,000)
South Sudan	March 2020	3,800,000 (2,120,000–6,800,000)	88,300 (26,200–230,000)	107,000 (30,200–276,000)
Uganda	March 2020	14,900,000 (9,770,000–20,900,000)	59,500 (20,200–133,000)	714,000 (231,000–1,630,000)
United Republic of Tanzania	April 2020	26,800,000 (20,300,000–32,800,000)	282,000 (102,000–606,000)	1,150,000 (417,000–2,530,000)
Zambia	February 2020	11,600,000 (7,700,000–14,700,000)	119,000 (38,100–283,000)	511,000 (179,000–1,190,000)
Southern Sub-Saharan Africa	February 2020	40,100,000 (31,100,000–48,300,000)	492,000 (184,000–1,070,000)	1,820,000 (664,000–4,000,000)
Botswana	March 2020	1,040,000 (467,000–1,640,000)	1,140 (414–2,510)	61,000 (16,100–150,000)
Eswatini	February 2020	584,000 (296,000–921,000)	6,200 (2,180–14,300)	26,100 (6,570–68,600)
Lesotho	April 2020	919,000 (397,000–1,510,000)	7,060 (2,420–16,300)	46,500 (11,000–112,000)
Namibia	February 2020	1,120,000 (589,000–1,720,000)	6,490 (2,280–14,700)	59,000 (17,900–138,000)
South Africa	February 2020	26,800,000 (20,900,000–32,200,000)	419,000 (157,000–898,000)	1,170,000 (437,000–2,520,000)
Zimbabwe	February 2020	9,600,000 (4,550,000–12,400,000)	51,700 (16,400–125,000)	460,000 (134,000–1,100,000)
Western Sub-Saharan Africa	January 2020	226,000,000 (178,000,000–273,000,000)	4,580,000 (1,680,000–9,970,000)	6,970,000 (2,520,000–15,600,000)
Benin	February 2020	2,790,000 (1,510,000–4,670,000)	36,700 (10,300–102,000)	112,000 (32,100–261,000)
Burkina Faso	February 2020	12,600,000 (7,990,000–17,100,000)	136,000 (42,300–350,000)	378,000 (134,000–860,000)
Cabo Verde	February 2020	240,000 (124,000–352,000)	4,690 (1,450–11,800)	10,400 (3,550–24,800)
Cameroon	February 2020	13,500,000 (1,340,000–22,100,000)	189,000 (19,400–462,000)	465,000 (29,900–1,320,000)
Chad	March 2020	6,960,000 (3,330,000–12,000,000)	153,000 (38,500–412,000)	145,000 (38,800–356,000)
Côte d'Ivoire	January 2020	13,100,000 (8,320,000–17,700,000)	280,000 (81,300–671,000)	424,000 (138,000–977,000)
Gambia	February 2020	1,310,000 (773,000–1,820,000)	27,800 (9,190–62,700)	44,300 (13,400–106,000)
Ghana	February 2020	15,000,000 (8,550,000–21,300,000)	273,000 (94,600–624,000)	541,000 (186,000–1,320,000)
Guinea	February 2020	7,550,000 (4,730,000–10,500,000)	143,000 (45,200–351,000)	266,000 (76,900–628,000)
Guinea-Bissau	March 2020	919,000 (510,000–1,570,000)	27,900 (9,000–67,700)	18,900 (3,130–57,100)
Liberia	February 2020	2,170,000 (1,260,000–3,260,000)	49,200 (15,700–114,000)	68,500 (21,500–178,000)
Mali	March 2020	12,500,000 (7,720,000–17,200,000)	195,000 (52,500–478,000)	369,000 (125,000–886,000)
Mauritania	February 2020	2,040,000 (1,140,000–3,070,000)	27,100 (9,170–66,000)	75,400 (23,300–180,000)
Niger	March 2020	8,890,000 (4,180,000–18,000,000)	115,000 (27,200–295,000)	233,000 (76,000–530,000)

Location	Pandemic start	Symptomatic infections during 2020-2021[b] (UI)	New cases of Long COVID during 2020 (UI)	New cases of Long COVID during 2021 (UI)
Nigeria	February 2020	111,000,000 (87,800,000–134,000,000)	2,700,000 (992,000–5,980,000)	3,240,000 (1,160,000–7,100,000)
Sao Tome and Principe	March 2020	71,400 (50,300–98,200)	2,120 (670–5,430)	1,950 (396–5,380)
Senegal	February 2020	9,020,000 (6,530,000–11,600,000)	110,000 (40,100–253,000)	394,000 (144,000–891,000)
Sierra Leone	March 2020	2,290,000 (1,370,000–3,430,000)	87,300 (28,700–211,000)	39,600 (13,900–94,400)
Togo	February 2020	3,130,000 (1,950,000–4,640,000)	27,900 (9,290–65,400)	145,000 (49,700–331,000)

UI = 95% uncertainty interval. Uncertainty Intervals reflect the reliability of the underlying data for each country and are presented in parentheses. Uncertainty intervals are wide due to the heterogeneity in the data sources. The interval is asymmetric because of Bayesian, rather than parametric, estimation methods and the fact that proportions are bounded by zero and one. Countries are sorted alphabetically within regions and super regions.

[a] Long COVID is defined as having at least one of the three symptom clusters—fatigue with bodily pain/mood swings, respiratory symptoms, and/or cognitive symptoms—at 3 months after symptom onset of COVID-19. New cases of long COVID are projected by applying the proportions with long COVID from this analysis to the estimates of symptomatic infections derived from the IHME COVID model and the estimated proportion asymptomatic described in eSection 4.

[b] Estimates of symptomatic infections are calculated by subtracting the proportion asymptomatic from the estimated number of infections from the IHME COVID model.[96]

Detailed analysis of StopCOVID Cohort

The StopCOVID cohort, lends itself best to an additional analysis of what we may have missed as more serious disability by restricting our analysis to three symptom clusters. This cohort has the advantage of a) being large; b) having explicit questions for each symptom about the difference before and after COVID-19; c) and a general health status measure (EQ5D-5L) which was administered to reflect the health status at follow-up interview as well as a recall of the health status prior to COVID-19. We examined all cases in the Russian cohort who i) did not qualify for any of the three symptoms clusters; ii) reported not having recovered from COVID-19 (answering 'strongly disagree', 'disagree' or 'somewhat disagree' to the question 'Do you feel fully recovered from COVID-19?'); iii) had a worse EQ5D-5L summary score at interview compared to the recall of health status prior to COVID-19 by at least 0.1 point; iv) had a EQ5D-5L summary score of 0.9 or less at the time of interview; v) had a positive PCR test, rather than a clinical diagnosis only; and vi) had valid answers to these qualifying items. We deemed these respondents to be 'at risk' of having substantial ongoing health problems due to COVID-19 that were not captured in the three symptom clusters we quantified.

Of the 1309 PCR confirmed cases of COVID-19, 136 qualified for our definitions of the three symptom clusters of long COVID. An additional 62 qualified for the criteria above of substantial ongoing health problems (eTable 18). Of these 62, 48 had one or more of the symptoms of the three clusters we quantified but in all these cases respondents reported either a score of 1 or 2 on the usual activities item of EQ5D-5L (no or slight problems) or reported similar or better scores on the usual activities item compared on the recall EQ5D-5L prior to COVID-19. Because the low severity of the score on usual activities of EQ5D-5L and an or equal or better score compared to health status as reported before COVID-19, all of these cases did not get picked up by our algorithm. Of the remaining 14 cases, 5 did not report any symptoms, 4 reported symptoms of anxiety or depression, 1 reported weight loss, 1 swollen ankles, 1 bleeding gums and 1 worsening of pre-existing neurological condition.

From this analysis we believe that we have captured the majority of disabling outcomes of long COVID.

eTable 18. Symptoms reported by respondents of the StopCOVID ISARIC Cohort in Russia who did not qualify for any of our long COVID symptoms clusters but reported not having recovered and worse health status than before COVID-19.

Symptom (number of cases)	Detail	Reason why not included in symptom clusters
Fatigue (29)	Fatigue scale (0-10) >4: 17	Reported either no or only some problems with usual activities or reported same or worse on usual activities pre-COVID 19
Joint/muscle pain (9)		
Breathless (12)		
cough, chest pain or pain breathing (17)		
forgetfulness or lack of concentration or confusion (12)		
Anxiety or depressive symptoms (24)	7 reporting moderate problems on the EQ5D anxiety/depression item; 1 severe problems and 2 extreme problems	Separate GBD estimates of increased anxiety/depression in general population due to pandemic would include those with anxiety or depression directly related to COVID-19
Remaining symptoms: **Problems with vision (15)** **Sleep problems (11)** **Hair loss (10)** **Palpitations (9)** **Weight loss/reduced appetite (7)** **Ear problems (6)** **Balance problems (6)**		

Symptom (number of cases)	Detail	Reason why not included in symptom clusters
Digestive symptoms, including nausea, stomach pain, vomiting, diarrhoea (6) **Headache (4)** **Loss of taste/smell (4)** **Problems passing urine (2)** **Tremor (2)** **Double vision (1)** **Difficulty swallowing (1)** **Skin rash (0)**		

Sensitivity analysis of recovery pattern prior

In order to determine the effect of incorporating a prior on the relationship between proportions with symptom cluster(s) and follow-up time, based on the estimated relationship using only studies with multiple follow-up points, we conducted an analysis whererin we removed the prior on follow-up time in the proportion models of having at least one symptom cluster and therefore used all data to estimate duration rather than limiting the duration model to studies with multiple follow-up points. The final proportions show minimal changes, and estimated duration increases for both hospitalized and non-hospitalized cases, from median 9.0 (UI 7.0-12.0) to 9.1 (UI 6.9-12.1) months and from 4.0 (UI 3.6-4.6) to 4.7 (UI 4.0-5.4) months, respectively (eTable 19). By including only studies with multiple follow-up points in our recovery models to inform the relationship with follow-up time, the current analysis better isolates the true recovery pattern by preventing heterogeneous data with single follow-up points from leading to spurious rates of recovery, and leads to slightly tighter uncertainty.

eTable 19. Sensitivity analysis comparing current method with an alternative method which uses all available data to estimate the duration.

	Current analysis	All data used in duration models
Duration, mean (95% UI)		
Non-hospitalized	4.0 (3.6-4.6)	4.7 (4.0-5.4)
Hospitalized	9.0 (7.0-12.0)	9.1 (6.9-12.1)
Proportion with symptom cluster(s), mean (95% UI)		
Non-hospitalized		
Female and Male < 20 y	2.7% (0.8-6.7)	2.7% (0.7-6.6)
Male ≥ 20 y	4.8% (1.5-11.3)	4.7% (1.4-11.2)
Female ≥ 20 y	9.9% (3.4-21.2)	9.7% (3.0-21.2)
Cases needing hospitalization		
Male, all ages	21.6% (8.9-40.3)	21.9% (7.8-43.6)
Female, all ages	34.8% (16.5-57.3)	35.8% (14.8-60.8)
Cases needing ICU care		
Male, all ages	35.8% (17.1-58.1)	36.0% (15.0-61.4)
Female, all ages	51.9% (29.7-73.6)	52.7% (26.5-76.4)

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