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Systematic review of the prevalence of Long Covid

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Background:

Long Covid occurs in those infected with SARSCoV2 whose symptoms persist or develop beyond the acute phase. We conducted a systematic review to determine the prevalence of persistent symptoms, functional disability or pathological changes in adults or children at least 12 weeks post-infection.

Methods: We searched key registers and databases from 1st January 2020 to 2nd November 2021, limited to publications in English and studies with at least 100 participants. Studies where all participants were critically ill were excluded. Long Covid was extracted as prevalence of at least one symptom or pathology, or prevalence of the most common symptom or pathology, at 12 weeks or later. Heterogeneity was quantified in absolute terms and as a proportion of total variation and explored across pre-defined subgroups (PROSPERO ID CRD42020218351).

Results: 120 studies in 130 publications were included. Length of follow-up varied between 12 weeks - 12 months. Few studies had low risk of bias. All complete and subgroup analyses except one had $I^2 \geq 90\%$, with prevalence of persistent symptoms range of 0% - 93% (pooled estimate (PE) 42.1%, 95% prediction interval (PI): 6.8% to 87.9%). Studies using routine healthcare records tended to report lower prevalence (PE 13.6%, PI: 1.2% to 68%) of persistent symptoms/pathology than self-report (PE 43.9%, PI: 8.2% to 87.2%). However, studies systematically investigating pathology in all participants at follow up tended to report the highest estimates of all three (PE 51.7%, PI: 12.3% to 89.1%). Studies of hospitalised cases had generally higher estimates than community-based studies.

Conclusions: The way in which Long Covid is defined and measured affects prevalence estimation. Given the widespread nature of SARSCoV2 infection globally, the burden of chronic illness is likely to be substantial even using the most conservative estimates.

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Lay summary

Long Covid is the state of not fully recovering for many weeks, months or years after infection with SARSCoV2, the coronavirus that causes COVID-19 disease. It influences the daily lives of many people globally. We conducted a systematic review of 120 published studies to estimate how common (prevalent) Long Covid is. The studies showed a very wide range of estimates of Long Covid prevalence, with between 0% and 93% of infected people still having signs or symptoms after 12 weeks. However, we could see that studies fell into groups according to how Long Covid was defined and measured. Studies analysing routine healthcare records tended to report lower prevalence, whereas studies investigating damage to organs and tissues reported higher prevalence. We concluded that the way in which Long Covid is defined and measured affects prevalence estimation, which is important for designing future research in this area. Given

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the high rates of SARSCoV2 infection globally, the burden of Long Covid is likely to be substantial even using the most conservative estimates.

Key words: Long Covid, Systematic Review, Prevalence, SARSCoV2

INTRODUCTION

Long Covid is the state of not fully recovering for many weeks, months or years after contracting SARSCoV2 infection. The World Health Organization (WHO) defines Post COVID-19 Condition (Long Covid) as the condition occurring in individuals with a history of probable or confirmed SARSCoV2 infection 3 months after the onset with symptoms that last at least 2 months, cannot be explained by an alternative diagnosis and generally impacts everyday functioning(1). These symptoms may be the same as the acute illness or new symptoms developing weeks or months after the acute phase. Clinical guidelines(2, 3) in the UK and the US consider Long Covid as symptoms ongoing for four weeks or more.

Long Covid can occur across the spectrum of severity of initial infection(4). A wide range of symptoms have been reported with exhaustion, breathlessness, muscle aches, cognitive dysfunction, headache, palpitations, dizziness and chest tightness or heaviness amongst the most common(5, 6). Patients are still struggling to access adequate recognition, support, medical assessment and treatment(7, 8).

Studies assessing the prevalence of Long Covid have produced wide-ranging results due to varying settings, case definitions, population denominators and methods of ascertainment. This is exemplified in the UK Office for National Statistics estimates of Long Covid during 2020-21 where three different approaches were used resulting in three different estimates: approach 1 estimated 5.0% prevalence based on respondents reporting any of 12 common symptoms at 12-16 weeks after infection; approach 2 estimated 3.0% prevalence based on respondents reporting any of 12 common continuous symptoms at least 12 weeks after infection; and approach 3 estimated 11.7% prevalence based on respondents describing themselves as having Long Covid(9).

For the purposes of this review, we define Long Covid as persistent (constant, fluctuating or relapsing) symptoms and/or functional disability and/or the development of new pathology following SARSCoV2 infection for equal or more than 12 weeks from onset of symptoms or from time of diagnosis, in people where the infection is self-described, clinically diagnosed, and/or diagnosed through a laboratory test.

We aimed to systematically collate, appraise and synthesise studies that describe the prevalence of Long Covid and to characterise its typology including patient demographics, symptoms/function disability and pathology.

METHODS

Search strategy and selection criteria

Included study designs were cohort, cross-sectional and case control studies with an estimate of the denominator where participants were followed-up/assessed at a minimum of 12 weeks post-infection. Studies were restricted to those published in English between 1st January 2020 and 2nd November 2021, including peer-reviewed articles, online reports, letters, and preprints. Only studies with a sample size of 100 or more participants (at the time of follow-up assessment if longitudinal study) were included (50 or more per subgroup).

Studies of adults and children with a confirmed or probable SARSCoV2 infection in any age group (as defined by each study) were included. The control group in studies that included one is individuals with a confirmed or probable case of SARSCoV2 infection (as defined by the study) who have recovered (duration as defined by study as long as under 12 weeks from symptom onset or confirmation of infection) and have no new pathology attributed to SARSCoV2 infection. Studies that compared population-based prevalence as the control arm were excluded from the control analysis.

Community-based, hospital-based, and mixed studies were all included, apart from studies that only reported outcomes for critically ill patients admitted to intensive care, because this review did not aim to estimate delayed recovery following ICU admission (post-ICU syndrome). Patients who were not hospitalised within two weeks of symptom onset but were subsequently hospitalised were counted as non-hospitalised for the purpose of this review.

A systematic search was conducted using MEDLINE (Ovid), Embase (Ovid), the Cochrane Covid-19 Study register (www.covid-19.cochrane.org; includes Cochrane Central Register of Controlled Trials (CENTRAL), WHO International Clinical Trials Registry Platform (ICTRP), medRxiv, Cochrane CENTRAL, MEDLINE (PubMed), ClinicalTrials.gov, and the WHO Global research on coronavirus disease (COVID-19) database(10). The initial search was run on 13 November 2020 and updated on 2 November 2021, both by VL. An example of the search strategy applied to Medline is provided in the Supplementary material; it was adapted for other databases as needed.

The screening management software Covidence was used to screen for eligibility. All articles were screened independently by two reviewers at each stage (title, abstract, and full text) with any discrepancies resolved by NAA. This review is reported in line with PRISMA guidelines(11). The protocol was published on the international prospective register of international reviews, PROSPERO (CRD42020218351): https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=218351.

Data analysis

Data for each study was extracted independently by two of four reviewers (MW, DCG, CC, NZ). Any discrepancies were resolved by consensus between the two reviewers for each study or by a third reviewer (NAA). Where multiple publications were identified as originating from the same study, all data was extracted but each data point was only used once in the analysis. In addition to excluding duplicate reports, or duplicate results from the same study, a number of general decisions were made to cope with multiple publications from the same study, either focusing on different lengths of follow-up, different timepoints, or different subgroups. These were guided by principles of (1) avoiding double counting individuals, (2) using the most appropriate outcome, for example, general Long Covid definition, in the broadest group such as the widest population, largest sample, most recent update, (3) unless stratifying by length of follow-up, we took the earliest and/or most complete follow-up as the main result.

The primary outcome is Long Covid, defined as non-recovery from COVID-19, according to symptoms, functional ability or pathology. SARSCoV2 infection can be confirmed, probable or suspected with prolonged symptoms (including but not limited to those explicitly defined as 'new onset'), functional disability or pathology for equal to or more than 12 weeks from onset of symptoms or positive test date (as defined by the study). Secondary outcomes included the demographics of people with Long Covid in relation to each study's denominator, prevalence of specific persistent or relapsing symptoms, prevalence of functional disability, and the characterisation of post-COVID-19 pathology.

A Long Covid-specific risk of bias tool was developed, based on the Newcastle-Ottawa scale, but tailored to the relevant sources of bias. The domains used are reported in Supplementary Table 3. Risk of bias was particularly assessed in relation to the denominator, how the symptoms were assessed (active or passive elicitation of the symptoms) and hospital stay. Subgroup analysis by risk of bias was performed. In studies where follow-up was measured post-hospital admission or discharge, symptom onset was estimated to have been 7 or 14 days prior to discharge respectively and estimated as 21 days if follow-up was measured from a post-infection negative test.

The prevalence was extracted as cumulative incidence. In extracting the prevalence of persistent symptoms, we used either prevalence of at least one symptom or pathology, or the prevalence of the most common symptom/pathology, depending on the data reported by the study. Data for each symptom was extracted separately in studies that reported on the prevalence of individual symptoms but did not provide an overall estimate of prevalence of Long Covid. We used the symptom with the highest estimate as our best estimate of overall prevalence, though it is likely to be an underestimate of actual prevalence. In studies with controls, the prevalence of the same symptom was used for comparison. Where length of follow-up varied between study participants, we report a measure of average (e.g. mean or median) length of follow-up, or the midpoint of the reported range.

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All analysis was conducted in Stata version 17(12). The distribution, prevalence estimates, numerators, denominators, and assessment time points in different populations was qualitatively summarised. We used random-effects meta-analysis on the logit of the proportions to ensure estimates and confidence limits did not go below 0% or over 100%, transforming back to the original scale for presentation.

The heterogeneity was quantified both in absolute terms (range of individual study estimates) and as a proportion of total variation (I^2), and explored across pre-defined subgroups described below. In a variation to our protocol, we present pooled estimates alongside 95% prediction intervals to evaluate and incorporate uncertainty in the analysis, as recently recommended for prevalence studies, where true between-study heterogeneity is expected(13, 14) . Heterogeneity was explored by stratifying on pre-defined subgroups: outcome type (pathology, symptom, functional status), geographical region (China, Europe, North America, Mixed and other), source of sample (community, healthcare workers, outpatients, hospital inpatients), length of follow-up, study design, confirmed diagnosis, and other risk of bias domains. We also stratified by severity score based on the WHO Clinical Progression Scale [supplemental methods].

Potential small study effects such as publication bias were investigated using contour-enhanced funnel plots and Egger's test of funnel plot asymmetry.

Role of funding source

None

Patient consent statement

This systematic review analysed publicly available data included in published scientific papers. No patient consent or ethical approval were required.

RESULTS

Literature search

The searches found 11,518 studies in total. After deduplication and title and abstract screening, 457 full text studies were assessed for eligibility. Hand-searching sourced an additional 9 studies and in total 130 publications were included, 120 of which were discrete studies (Figure 1). 24 studies were conducted in China (including Hong Kong), 66 in Europe, 14 in North America and 16 in various other countries(9, 15-143). Reasons for exclusion are listed in Supplementary Table 1.

Table 1 summarises the included studies' key characteristics and primary outcome for the first follow-up. Study design was reported as described by each study or designated based on study description if not explicitly stated. Most studies were in adults and included patients who were hospitalised in the acute phase (24 studies with <10% of the sample hospitalised in the acute phase). However, hospitalisation did not always correspond with disease severity, probably due to local diagnostic, treatment, and containment policies. Most studies used PCR testing to identify COVID-19 cases at baseline. However most did not perform COVID-19 diagnostic tests at follow-up and therefore did not consider the impact of reinfection on their results. Out of the included studies, 21 were community-based studies, 17 outpatient settings, 3 social media and 8 healthcare worker-based studies.

Prevalence estimates

The prevalence of Long Covid for studies with more than 12 weeks from infection ranged between 0% to 93% (pooled estimate (PE) 42.1%, 95% prediction interval (PI): 6.8% to 87.9%) (Figure 2). For all complete and subgroup analyses except one, I^2 was >75%. All subgroup analysis results including pooled estimates and prediction intervals can be found in Supplementary Table 4.

73 included studies had a follow up of 12 weeks to 5 months (PE 39.8% (PI: 5.1% to 89.1%), 49 had a follow-up of 6-11 months (PE 44.9% (PI: 8% to 88.4%), and 12 had a follow-up of 12 months or more (PE 48.5% (PI: 12.7% to 86%). Recognising most are not within-study comparisons, longer follow-up times showed higher pooled estimates (Supplementary Figure 1).

Hospitalisation and severity of acute infection were key factors influencing Long Covid prevalence estimates. The prevalence range in analyses where less than 10% of the participants were hospitalised was 0% to 67% (n=24) (PE 26.4%, PI: 2.6% to 82.8%) but in studies where all participants were hospitalised for acute COVID-19 (n=65), the prevalence range was 5% to 93% (PE 47.5%, PI: 8.3% to 90.0%) (Supplementary Figure 2). 31 analyses had 10% or more of their sample admitted to intensive care unit (ICU) during their acute COVID-19 illness with a Long Covid prevalence estimate of 48.8% (PI: 5.7% to 93.7%) compared to PE 34.9% (PI: 5.2% to 84%) in studies with <5% of their sample admitted to ICU (Supplementary Figure 3). Studies including more hospitalised participants or more patients in ICU tended to report higher prevalence estimates (Supplementary Table 4). Likewise using the WHO CPS, studies including those with ambulatory mild disease (n=38) generally reported lower prevalence estimates (PE 23.5%, PI: 1.6 to 85.7%) than those with hospitalised severe disease who needed oxygen by NIV or high flow (n=27) (PE 54.8%, PI: 7.7 to 94.7%) (Supplementary Figure 4).

The prevalence of not returning to full health/fitness after at least 12 weeks from infection ranged between 8% to 70% (PE 34.5%, PI: 4.3% to 85.9%, n=10) (Supplementary Figure 5). The prevalence of lower quality of life after at least 12 weeks was 31% (n=2) (Supplementary Figure 6). With regard to individual symptoms, common symptoms reported included fatigue (pooled estimate 21.6%, PI: 2.5% to 74.7%, n=72) followed by breathing problems (pooled estimate 14.9%, PI: 1.6% to 64.9%, n=78), sleep problems (pooled estimate 13.2%, PI: 1.2% to 64.9%, n=42), tingling or itching (pooled estimate 11.3%, PI: 0.7% to 69.5%, n=14), and joint/muscle aches and pains (pooled estimate 10.6%, PI: 1.0% to 57.5%, n=61) (Figure 5). With regard to pathology, lung pathology was the most common (pooled estimate 38.9%, PI: 3.4% to 91.9%, n=26) followed by heart (pooled estimate 6.0%, PI: 0.1% to 79.3%, n=12) or neurological pathology (pooled estimate 5.3%, PI: 0.5% to 36.5%, n=11) (Figure 5 and Supplementary Figures 7-40). Pathology tended to be reported in only a small number of studies, with the exception of lung pathology which was reported in 26 studies.

There were very few studies with a low risk of bias (Supplementary Table 2). Few studies used a sample that was representative of all COVID-19 cases in the population. Approximately half of the studies indicated that symptoms had not been present prior to infection, while the rest did not report ascertaining this. When stratifying by risk of bias, generally lower prevalence estimates were seen in studies with COVID-19 diagnoses confirmed for all participants, studies scored as having a representative sample, studies with an internal or external non-COVID-19 comparator, studies that assessed all participants in the same way, and studies based on community participants (Supplementary Figure 41-42).

Comorbidities, ethnicity and other demographic data were not reported in all studies. Higher prevalence of Long Covid was observed in studies where study samples had higher proportions of older people (<50yrs pooled estimate 38.5%, PI: 7.9% to 82.1%; 50+yrs PE 47.7%, PI 7.9% to 90.6%), males (<50% female pooled estimate 45.6%, PI 5.5% to 92.4%; 50%+ female PE 38.7%, PI 8.5% to 81.2%), people of non-white ethnicity (<50% white ethnicity pooled estimate 56.3%, PI 22.3% to 85.2%; 50%+ white ethnicity PE 37.6%, PI 1.7% to 95.3%), diabetes (<10% pre-existing diabetes pooled estimate 35.4%, PI 5.7% to 83.2%; 10%+ pre-existing diabetes PE 51.9%, PI 8.3% to 92.8%), hypertension (<30% pre-existing hypertension pooled estimate 37.3%, PI 7.0% to 82.5%; 30%+ pre-existing hypertension PE 58.5%, PI 16.9% to 90.7%), cardiovascular disease (<10% pre-existing CVD pooled estimate 38.2%, PI 5.9% to 85.9%; 10%+ pre-existing CVD PE 54.7%, PI 9.4% to 93.4%), and other comorbidities including obesity, respiratory disease, liver disease, kidney disease and immunological disorder or allergy (Supplementary Figure 43). Prevalence of Long Covid did not differ substantially with smoking status.

When subgrouping by study design, the range was 0% to 93% (PE 41.3%, PI: 6.0% to 88.6%) in cohort studies and 10% to 82% (PE 45.9%, PI 11.2% to 85.1%) in cross sectional studies. (Supplementary Figure 50). Prevalence estimates derived from assessing Long Covid as self-reported symptoms and function (n=93) on the whole tended to report higher prevalence (PE 43.9%, PI: 8.2% to 87.2%) than those that used clinical coding in healthcare records (n=9) (PE 13.6%, PI 1.2% to 68%). However, studies that had dedicated pathology follow-up of COVID-19 patients (for example pulmonary function tests or scans with pathology discovered at follow-up) tended to report the highest prevalence (n=20) (PE 51.7%, PI 12.3% to 89.1%) (Figure 3). Studies that defined Long Covid as at least one of multiple symptom or pathology domains tended to report a slightly higher prevalence than those that assessed a single symptom/pathology domain (Supplementary Figure 44).

Comparison to controls

Twenty-four of the 130 publications included comparison to at least one group of controls (Supplementary Figure 45). The majority of studies used test-negative controls (antigen and antibody, with some matching), but others used untested controls. In community-based studies with controls, the relative risk ranged between 1.0 to 51.4 (pooled relative risk 2.7, 95% PI: 0.2 to 39.4) and the absolute risk difference ranged between -1% to 35% (pooled risk difference 10.1%, 95% PI: -12.7% to 32.8%) (Supplementary Figures 46-47). In community-based samples with controls and assessed as having a low risk of bias (n=4), the pooled relative risk of experiencing symptoms/ill health after COVID-19 was 1.33 compared to controls (95% PI: 1.30. 1.36, I^2=28.1%) (Figure 4) and the absolute risk difference between cases and controls ranged between 1% to 9% (Supplementary Figure 48).

There was no evidence of small-study effects such as publication bias (Supplementary Figure 49).

DISCUSSION

This systematic review which included 120 studies assessing Long Covid symptoms, functional status, or pathology published up to November 2021 demonstrates substantial between-study heterogeneity and wide variation in prevalence estimates. This is due to differences sources of study samples (community, outpatient clinic, occupational, hospitalised) and number of assessed symptoms and method of assessment (self-reported individual or collective symptoms, healthcare records, clinical investigations at follow up). The only pooled estimate with low between-study heterogeneity was a 33% (95% PI: 30% to 36%) excess risk of experiencing prolonged symptoms in COVID-19 cases compared to controls in community-based studies with low risk of bias. Although studies that included controls showed, on the whole, lower net prevalence of Long Covid than studies that did not, the evidence from most of these studies is that COVID-19 is associated with a substantially higher risk of being ill 12 weeks after infection than those not infected.

In characterising Long Covid, the review demonstrated higher prevalence estimates in study samples where a substantial proportion of included individuals were hospitalised during the acute phase of the infection and/or had severe acute disease. It is difficult to comment on prevalence difference by ethnicity, deprivation or gender as although we conducted subgroup analyses by proportion of participants by gender or ethnicity in included studies, the difference between the prediction estimates may be related to other confounding factors, such as, for example, studies that included more males may indicate that they also include a high proportion of those who had severe acute illness(144). Many studies did not report ethnicity or deprivation. These factors will be important to include in future studies if a comprehensive understanding of Long Covid and inequity is to be gained.

Long Covid's proposed pathophysiological mechanisms are multiple and potentially overlapping including persisting viral reservoirs, immune dysfunction, micro-clotting and end-organ damage(145). It is concerning that studies that specifically investigated for pathology tend to report higher prevalence estimates than those depending on healthcare records or even self reporting of symptoms. The review found that Long Covid presents a significant burden of functional disability, symptoms and pathology, with a pooled estimate of 34.5% of people not returning to full health/fitness after at least 12 weeks, and estimates of the most common symptoms/pathology including lung pathology (38.9%), fatigue (34.5%), breathing problems (14.9%), sleep problems (13.2%) and tingling or itching (11.3%). The paucity of long-term longitudinal studies following individuals' disease progression means it is difficult to comment on which symptoms are most persistent over time.

The UK's Office for National Statistics (ONS) produces population-level Long Covid prevalence estimates where the denominator is the whole population in the specific reported population group, for example, by age, sex, or occupation(146). These fall out of our inclusion criteria. The ONS also produced prevalence estimates based on following up those with confirmed SARSCoV2 infection and we used the most recent estimate within the review's search period(9). This study used multiple approaches including assessing individual symptoms compared to controls and asking participants if they believe they have Long Covid. The latter approach, in the absence of a standardised method of assessment, may realistically be the best way to assess the presence of Long Covid as most people will take the combination of their symptoms, duration, fluctuation, effect on functional ability and change from pre-COVID19 health to shape their responses.

The lack of consensus on the precise definition of Long Covid plays an important part in the wide differences in prevalence assessments, however we found that specifically the way the question is asked and the source of retrieved clinical information at follow-up are likely to play a crucial role. The ONS study is an example of how different methods of assessment at time of follow-up can produce substantially different Long Covid estimates(9). This was illustrated by our analysis where studies that asked about multiple symptoms/domains tended to report higher prevalence estimates than single domain studies. Our analysis indicated higher prevalence estimates with longer follow-up time, though we recognise these were mostly not within-study comparisons. However, in four of ten longitudinal studies, prevalence was higher at the time of the second follow-up. These results could be explained by several factors e.g. by the episodic nature of Long Covid, whereby in the early stages people may feel they have got over their illness, but with passing time and phases of relapse and remittance, people may be more cautious about reporting they have recovered. People may also be developing new symptoms over time, or perhaps there is more study drop-out by people who feel they have recovered. Overall however, the results indicate that, over time, prevalence does not substantially reduce.

Studies that used questionnaires/surveys to ask participants about their symptoms, health status or quality of life tend to report higher prevalence estimates than those that recorded symptoms from healthcare records' clinical coding. This is manifested in the prevalence from Al-Aly et al(16) studies being on the lower side in our analysis as we only included those with symptoms rather than recorded post-COVID-19 pathology, and such symptoms are expected to be severe enough to prompt seeking medical help and being recorded in medical notes. Studies that had dedicated pathology follow-up and discovery of COVID-19 patients tended to report the highest prevalence. This is possibly because, in addition to pathology that leads to recognisable signs and symptoms, specific medical investigations as part of the research protocol can pick up latent pathology that may not be accompanied by clinical manifestations.

Studies such as Al-Aly et al investigating medical diagnoses in the period following COVID-19, report cardiovascular, neurological, and other system-specific clinical sequelae providing a substantial excess burden in those who survived the acute phase of COVID-19(13). However, there is no agreement yet whether these outcomes are classed as Long Covid. They are generally not recorded by symptom studies and the WHO does not yet specifically include such outcomes within its clinical case definition of Post-COVID-19 Condition (also known as Long Covid) (1). A specific pathology diagnosed after COVID-19 could have been triggered by the infection, but identification as such will depend on the extent of clinical investigations identifying and labelling specific pathology as opposed to differences in the disease manifestation themselves.

Other sources of heterogeneity between studies include study design with some including assessment at one point in time, whereas others were longitudinal where assessment of COVID-19 status was conducted prior to the development of Long Covid. This assessment itself varied in terms of using PCR or antigen testing or self-reporting of history of acute infection.

Ideally, excess absolute risk in comparison to controls is a good measure to estimate the burden of Long Covid. This is likely dependent on the approach to control selection, whether based on self-report of absence of infection history or lab results that are not accurate enough to ascertain the state of previous infection (antigen or antibody), and timing of assessment given the predominant episodic nature of Long Covid.

Few studies had a low risk of bias, which suggests there is a gap in the evidence base for strong studies of Long Covid prevalence. In terms of causal inference, many studies were liable to potential collider bias, which presented as selection bias caused by restricting analyses to people who were hospitalised, self-selected for PCR or lateral flow tests based on symptoms, or simply volunteered their study participation(147). Similarly, our exploration of potential sources of heterogeneity may be prone to table 2 fallacy in the original studies, where these subgroups do not derive from the focal research question, so should be interpreted descriptively rather than causally(148).

The strengths of our review include comprehensive electronic searching for relevant studies and comprehensive assessment of risk of bias, data extraction and checking with each of these processes being done independently by two authors. We also adapted the Newcastle-Ottawa scale (Supplementary Table 3) for this prevalence systematic review which can be used by other researchers for risk assessment and/or to build high quality study designs. The quality assessment criteria and process were discussed within the study team which includes two authors with lived experience of Long Covid.

Our review was limited by the substantial between study heterogeneity. We used the most common reported symptom estimate for studies and did not combine multiple individual symptoms into one overall estimate of prevalence of Long Covid. The symptom with the highest prevalence differed from study to study, so may not be entirely comparable. We did not include more recent studies that assessed the prevalence of Long Covid following infection with different variants of SARSCoV2 and/or in double or triple vaccinated populations. Recent estimates point to a prevalence of 4-5% of reporting Long Covid at 12 to 16 weeks after first confirmed SARSCoV2 infection depending on variant, with no evidence of difference between variants among those who are triple vaccinated when infected(149). In those double vaccinated, the prevalence of persistent symptoms was around 10% compared to 15% of unvaccinated controls(150).

We extracted estimates of "new-onset" Long Covid/symptoms where possible. Where the proportion is of a symptom like fatigue for example, we picked the one quoted as new-onset fatigue if available, or we downgraded quality because it was not possible to ascertain that the symptom is 'new' following infection. Because Long Covid is a novel condition, prevalence of the condition is considered equivalent to cumulative incidence. When comparing with controls, we estimated cumulative incidence from reported absolute risk, when appropriate. When reporting risk ratio, we included incidence rate ratio and hazard ratios, but did not consider the odds ratio an adequate approximation because of the high potential prevalence in some populations.

We know that significant numbers of people experience ill health following SARSCoV2 infection. Long Covid impacts on society, particularly in places with continuing waves of infection. Through reviewing how different research approaches attempted to quantify the population burden of Long Covid, our findings provide insight into how to get more accurate estimates of prevalence and severity. With quantification of prevalence and the associated inequity, we can understand the investment needed for prevention, diagnosis, and treatment as well as the policy decisions needed to resource healthcare and social care services both adequately and equitably, and to mitigate the wider social and economic impact of Long Covid.

Contributors: NAA, DCG, RT, AA, VL, MW conceptualised and designed the study. MW drafted the protocol and search strategy with input from all co-authors. VL conducted the search. All authors contributed to screening the articles. MW, DCG, NZ, RT, CC extracted and quality-assessed the data. NAA, MW, DCG, NZ, CC contributed to the process of checking and verifying the extracted data. DCG planned and conducted the statistical analyses and produced the forest plots. MW, DCG, NZ, NAA interpreted the data and drafted the manuscript. All authors reviewed the final manuscript. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Potential conflicts of interest: The authors declare no competing interests.

Data sharing: All data used in this review is available in the published included studies. Data extractions and analytic code is available from the authors on reasonable request.

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	Author	**Country**	**Study design (as described by study, * if not stated)**	**Denominator[2]**	**Controls** N, type	**Setting**	**Age (years)** Mean/SD Median (IQR)	**% female**	**COVID-19 diagnostic method**	**Severity**	**Follow-up time[3]** Days	**Finding**: % with at least one symptom or pathology remaining at follow-up
1.	Abdelrahman, M et al(15)	Egypt	Prospective cohort	172	-	Hospitalised patients and non-	41.8/17.6	65.7	'Tested positive'	12.8% hospitalised (including 4% ICU)	240-300 (range) following 'improvem	61.0%

[1] Different denominators specific to each outcome have been used in cases where data are incomplete or where individual symptoms have different denominators. 2 a – mean no. of days post-symptom onset or positive test; b - median no. of days post-symptom onset or positive test; c – mean no. of days post-hospital admission; d - median no. of days post-hospital admission; e – mean no. of days post-hospital discharge; f – median no. of days post-hospital discharge; g – mean no. of days post-negative test following infection; h - median no. of days post-negative test following infection.
Papers coded variously with the following symbols are different publications from the same study data: Ω, ▪, ◊, ¥, †, ∞, π

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						hospitalised					ent of acute COVID-19'	
2.	Al-Aly, Z et al(16)	USA	Cohort with controls	60255	4526737 without COVID-19	Non-hospitalised	61 (4872)	12.1	'Positive test'	-	126[b]	2.9%

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					and not hospitalised							
2 a.	Al-Aly, Z et al (16)	USA	Cohort with controls	11800	11868 hospitalised with seasonal influenza	Hospitalised patients	70 (61-76)	5.8	PCR confirmed	26.3% ICU	150[b]	9.2%
3.	Aminian, A et al (18)	USA	Retrospective	2839	-	Hospitalised patients	52.7/20.1	52.3	PCR confirmed	ICU excluded	243[b]	44.2%
4.	Arnold, D et al(151)	UK	Prospective cohort	110	-	Hospitalised patients	60 (46-73)	44.0	PCR confirmed or clinico-radiological	Mixed	90[b]	73.6%
5.	Augustin, M et al(20)	Germany	Longitudinal prospective cohort	442	-	Non-hospitalised patients	43 (31-54)	52.3	PCR confirmed	97.5% mild	131[b]	27.8%
6.	Ayoubkhani, D et al(21)	UK	Observational retrospective matched cohort (with controls)	47780	47780 matched for age, sex	Hospitalised patients	64.5/19.2	45.1	Laboratory confirmed or clinical diagnosis	9.9% ICU	140[e]	21.5

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7.	Baricich, A et al(22)	Italy	Cross-sectional	204	-	Hospitalised patients	57.9/12.8	40.0	'Confirmed diagnosis'	13% ICU	124.7[e]	32.4%
8.	Becker, J et al(23)	USA	Cross-sectional	740	-	Hospitalised patients, outpatients and ER attendees	49 (38-59)	63.0	Tested positive or antibody positive	-	228[a]	24.1%
9.	Bellan, M et al(24)	Italy	Prospective cohort	238	-	Hospitalised patients	61 (50-71)	40.3	PCR confirmed bronchial swab, serological testing, or suggestive CT	27.7% did not require oxygen 11.8% ICU	91-121[e]	53.8%
10.	Blanco, J et al(25)	Spain	Prospective	100	-	Hospitalised patients	54.9/10.3	36.0	PCR confirmed	47% severe	104[b]	52.0%
11.	Bliddal, S et al(26)	Denmark	Cohort	129	-	Non-hospitalised patients	44.8 (13.6)	70.0	PCR confirmed	Non-hospitalised	90[a]	40.3%

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12.	Blomberg, B et al(17)	Norway	Prospective cohort with controls	312	60 seronegative household contacts	Hospitalised patients and non-hospitalised	46 (30-58)	51.0	'Tested positive'	2% asymptomatic, 78% symptomatic in community, 21% hospitalised	152-213 (range) after illness	60.6%
13.	Boscolo-Rizzo, P et al(27)	Italy	Prospective	304	-	Community	47 (n/a)	60.9	PCR confirmed	Mild-to-moderate (home-isolated)	365[a]	53.0%
14.	Carrillo-Garcia, P et al(28)	Spain	Longitudinal observational	165	-	Hospitalised older adult patients	88.5/6.7	69.1	PCR confirmed and suspected cases (clinical, imaging and laboratory results)	-	3m post-hospital discharge	66.2%
15.	Caruso, D et al(29)	Italy	Prospective	118	-	Hospitalised patients with	65/12	53.0	PCR confirmed	Moderate to severe	6m post-hospital admission	77.1%

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						interstitial pneumonia						
16.	Caspersen, I et al(30)	Norway	Matched cohort	774	72953	Community (MoBa: population-based pregnancy cohort study)	25+	58.0	PCR confirmed	-	334-365 (range) after infection	16.5%
17.	Castro, V et al(31)	USA	Retrospective cohort	5571	30193 hospitalised COVID-19 negative patients	Hospitalised patients	63 (50-76)	47.0	PCR confirmed	13% ICU	91-150 days post-hospital admission	10.9%
18.	Chai, C et al(32)	China	Multi-centre ambidirectional cohort	546	-***	Hospitalised cancer and non-cancer patients	65 (59-70)	51.0	PCR confirmed	24% severe	370[d]	28.6%
19.	Cirulli, E et al(33)	USA	Prospective longitudinal	357	-	Community	-	-	PCR confirmed	-	90[a]	14.8%

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20.	Clavario, P et al(34)	Italy	Prospective cohort	200	-	Hospitalised patients	58.8 (51.6-66.0)	43.0	PCR confirmed	89% required at least oxygen support	107[f]	80.0%
21.	Cristillo, V et al(35)	Italy	Cohort*	101	-	Hospitalised patients	63.6/12.9	27.7	'Hospitalised for COVID-19'	hospitalized for mild to moderate COVID	6m post-hospital discharge	49.5%
22.	Diaz-Fuentes, G et al(36)	USA	Retrospective cohort	111	-	Hospitalised patients and non-hospitalised	60/13.9	53.1	Positive nasal swab	Mixed	12 weeks post-infection	79.3%
23.	Domenech-Montoliu, S et al(37)	Spain	Prospective cohort	483	-	Community	37.2/17.1	62.1	Laboratory confirmed	11.2% asymptomatic	7m post-infection	53.4%
24.	Erol, N et al(38)	Turkey	Cohort	121	95 randomly selected from non-COVID patients attending the ward	Hospitalised and non-hospitalised children	9.2 (10.9-17.9)	46.2	'Tested positive'	22.3% hospitalised	5.6m post-infection	37.2%

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25.	Evans R, et al (PHOSP-COVID study) (39) **(¥)**	UK	Prospective longitudinal cohort	804	-	Hospitalised patients	58.0/12.6	39.0	PCR confirmed or clinician diagnosed	Mixed	365[f]	48.8%
26.	Evans, R et al (PHOSP-COVID study)(40) **(¥)**	UK	Prospective longitudinal cohort	1077	-	Hospitalised patients	57.9/13	35.7	Confirmed or clinician-diagnosed	Mixed	176[f]	92.6%
27.	Fernandez-de-Las-Penas, C et al(43) **(∞)**	Spain	Multi-centre observational	1142	-	Hospitalised patients	61/17	47.5	PCR confirmed	7% ICU	210[e]	81.4%
28.	Fernandez-de-Las-Penas, C et al(41) **(∞)**	Spain	Multicentre observational	1142	-	Hospitalised patients	61/17	47.4	PCR confirmed	7% ICU	210[e]	49.6%
29.	Fernandez-de-Las-Penas, C et al(42) **(∞)**	Spain	Multi-centre cohort	1950	-	Hospitalised patients	61/16	46.9	PCR confirmed	6.6% ICU	340[e]	81.2%

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30.	Frija-Masson, J et al(44)	France	Retrospective	137	-	Not stated	59 (50-68)	49.0	PCR confirmed	90.5% required respiratory support	3m post-symptom onset	75.2%
31.	Froidure, A et al(45)	Belgium	Single-centre cohort	107	-	Hospitalised patients	60 (53-68)	41.0	PCR confirmed	Severe and critical	103[b]	68.2%
32.	Fu, L et al(46)	China	Cross-sectional	199	-	Hospitalised patients	18+	53.3	Not stated	2.5% ICU	6m post-hospital discharge	10.1%
33.	Gaber, T et al(47)	UK	Cross-sectional	138	-	98% non-hospitalised health care workers	-	92.0	83% PCR confirmed 17% no laboratory confirmation	2% hospitalised	4m post-infection	44.2%
34.	Garcia-Abellan, J et al(48)	Spain	Prospective longitudinal	116	-	Hospitalised patients	64 (54-76)	39.7	PCR confirmed	14% ICU	180[a]	24.1%
35.	Garratt, A et al(49) (•)	Norway	Cross-sectional survey of a geographical cohort	447	Norwegian general population norms	Community	49.5/15.3	56.0	PCR confirmed	Non-hospitalised	117.5[b]	35.3%

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36.	Gonzalez-Hermosillo, J et al(50)	Mexico	Prospective longitudinal	130	-	Hospitalised patients	51/14	34.6	PCR confirmed	Moderate to severe	3m post-hospital discharge	91.5%
37.	Han, X et al(51)	China	Prospective longitudinal	114	-	Hospitalised patients	54/12	30.0	PCR confirmed	Severe	175[a]	62.3%
38.	Havervall, S et al(52)	Sweden	Cohort with controls	323	1072 seronegative	Health care workers	43 (33-52)	83.0	Seropositive	mild/moderate (severe excluded)	122[a]	21.4%
39.	Huang, C et al(53) **(Ω)**	China	Ambidirectional cohort	1655	-	Hospitalised patients	57 (47-65)	48.0	Laboratory confirmed	68% required oxygen therapy 4% ICU	186[b]	76.4%
40.	Huang, L et al(54) **(Ω)**	China	Ambidirectional cohort with controls	1227	3383 community dwelling without SARS-CoV-2 infection, 1164 matched pairs	Hospitalised patients	59 (49-67)	47.0	Laboratory confirmed	4% ICU	185[b]	68.0%
41.	Jacobson, K et al(55)	USA	Cohort*	118	-	Hospitalised patients	43.3/14.4	46.6	PCR confirmed	18.6% hospitalised 9.3% ICU	119.3[b]	66.9%

	Author	Country	Study design (as described by study, * if not stated)	Denominator[2]	Controls N, type	Setting	Age (years) Mean/SD Median (IQR)	% female	COVID-19 diagnostic method	Severity	Follow-up time[3] Days	Finding: % with at least one symptom or pathology remaining at follow-up
						and non-hospitalised						
42.	Kashif, A et al(56)	Pakistan	Cohort*	242	-	Hospitalised patients and non-hospitalised	18-65	30.6	PCR confirmed	Mild	3m post-hospital discharge or visit	41.7%
43.	Kim, Y et al(57)	S Korea	Cohort*	900	-	Hospitalised patients and non-hospitalised	31 (24-47)	69.7	PCR confirmed	12% moderate or severe	195[b]	65.7%
44.	Lemhofer, C et al(58)	Germany	Cross-sectional	365	-	Community	49.8/16.9	59.2	'Positively tested'	Mild and moderate	93.7% - more than 3months post-infection	61.9%
45.	Li, X et al(59)	China	Cohort	289	-	Hospitalised patients	43.6/17.4	48.8	PCR confirmed	19.4% severe/critical	90-150 (range) post-	59.9%

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											symptom onset	
46.	Liao, T et al(60)	China	Cohort*	303	-	Hospitalised healthcare workers	39 (33-48)	80.5	'Infected with COVID-19'	62.7% critical/severe	395[f]	37.3%
47.	Liao, X et al(61)	China	Longitudinal cohort	142	-	Hospitalised patients	47.5 (36-57)	48.8	PCR confirmed	21.1% severe	90[f]	85.9%
48.	Liu, Y-H et al(62)	China	Cross-sectional	1301	466 uninfected spouses who lived together	Hospitalised patients, elderly	68 (66-74)	53.3	'Diagnosis of COVID-19'	1.8% ICU	6m post-hospital discharge	28.7%
49.	Liyanage-Don, A et al(63)	USA	Cohort*	153	-	Hospitalised patients	54.5/16.7	39.9	'Hospitalised for COVID-19'	5.9% ICU	111[b]	64.7%
50.	Logue, J et al(64)	USA	Longitudinal prospective cohort (cross sectional for controls*)	177	21, 'healthy controls recruited via email and flyer advertisements'	Hospitalised and outpatients	48 / 15.2	57.1	laboratory-confirmed	6.2% asymptomatic, 84.7% mild illness, 9.0% moderate or severe disease	169[b]	30.0%

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51.	Lucidi, T et al(65)	Italy	Observational retrospective	110	-	Not stated	41.4/12.3	63.6	'COVID-19 positive patients'	-	6.1 +/- 1.1 months post-infection	36.4%
52.	Lui, D et al(66)	China (HK)	Prospective	204	-	Hospitalised patients	55 (44-63)	53.4	PCR confirmed	3.9% severe	89[d]	20.1%
53.	Maestre-Muniz, M et al(67)	Spain	Cross-sectional	543	-	Hospitalised patients and ER attendees	65.1/17.5	49.3	Laboratory confirmed	Mixed	12m post-hospital discharge	56.9%
54.	Martinez, A et al(68)	Switzerland	Retrospective cohort	260	-	Healthcare workers	Mean range 30-39	75.4	'Positive test'	1.2% hospitalised	168[b]	26.5%
55.	Matteudi, T et al(69)	France	Prospective cohort	137	-	Hospitalised patients and outpatients, paediatric	9.3 (n/a)	-	PCR confirmed	27% asymptomatic	180[a]	16.8%
56.	Mazza, M et al(70)	Italy	Prospective cohort	226	-	Hospitalised	58.5/12.8	34.1	PCR confirmed	78% hospitalised	90.1[e]	35.8%

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						patients and ER attendees						
57.	Mechi, A et al(71)	Iraq	Single-centre cross-sectional	112	-	Hospitalised patients and non-hospitalised	50.6/13.4	34.0	Laboratory confirmed	46.4% hospitalised	9m after acute infection	82.1%
58.	Mei, Q et al(72) **(†)**	China	Cohort*	4328	1500, random sample of general population	Hospitalised patients	59 (47-68)	54.1	Met relevant clinical criteria	Not defined	144[f]	14.2%
59.	Mei, Q et al(73) **(†)**	China	Prospective cohort	3677	-	Hospitalised patients	59 (47-68)	55.5	PCR confirmed	33.7% severe, 2.6% critical	144[f]	26.5%
60.	Menges, D et al(74)	Switzerland	Population-based prospective cohort	431	-	Community	47 (33-58)	49.7	PCR confirmed	10.7% asymptomatic, 38.1% severe/very severe	220[b]	24.6%

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	Author	Country	Study design (as described by study, * if not stated)	Denominator[2]	Controls N, type	Setting	Age (years) Mean/SD Median (IQR)	% female	COVID-19 diagnostic method	Severity	Follow-up time[3] Days	Finding: % with at least one symptom or pathology remaining at follow-up
61.	Milanese, M et al(75)	Italy	Prospective cohort	135	-	Hospitalised patients	59/11	33.0	Not stated	Moderate and severe	182[e]	47.4%
62.	Millet, C et al(76)	USA	Prospective cohort	173	-	Hospitalised patients and outpatients	51.5/n/a	50.6	PCR confirmed	-	12m post-diagnosis	48.0%
63.	Mohiuddin Chowdhury, A et al(77)	Bangladesh	Prospective multi-centre cross-sectional	313	-	Hospitalised patients and outpatients	37.7/13.7	19.8	PCR confirmed	Not critically ill (ICU/HDU)	140[g]	21.4%
64.	Munblit, D et al(78)	Russia	Longitudinal cohort	2649	-	Hospitalised patients	56 (46-66)	51.1	PCR confirmed and clinically diagnosed	2.6% severe	218[f]	57.9%
65.	Nabahati, M et al(79)	Iran	Prospective cross-sectional	173	-	Hospitalised patients	53.6/13.7	67.1	PCR confirmed	54% severe	90[e]	52.0%
66.	Nehme, M, et al(80)	Switzerland	Prospective cohort	410	-	Outpatients	42.7/12.9	67.1	PCR confirmed	Mild and moderate	7-9m post-diagnosis	39.0%

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	Author	Country	Study design (as described by study, * if not stated)	Denominator[2]	Controls N, type	Setting	Age (years) Mean/SD Median (IQR)	% female	COVID-19 diagnostic method	Severity	Follow-up time[3] Days	Finding: % with at least one symptom or pathology remaining at follow-up
67.	Nguyen, N et al(81)	France	Cohort*	125	-	Hospitalised	36 (27-48))	55.0	PCR confirmed	Non-severe	210[a]	24.0%
68.	Nunez-Fernandez, M et al(82)	Spain	Prospective cohort	200	-	Hospitalised patients	62 (n/a)	40.5	PCR confirmed	15.5% ICU	84[e]	29.0%
69.	O'Keefe, J et al(83)	USA	Cross-sectional	198	-	Outpatients	45/14	74.2	PCR confirmed	29.7% moderate, 1.1% severe	119[b]	39.9%
70.	Office for National Statistics(9)	UK	Prospective cohort w	21374	-	Community	2+	52.3	PCR confirmed	-	12 weeks post-infection	11.7%
71.	Ong, S et al(84)	Singapore	Prospective longitudinal multi-centre cohort	175	-	Hospitalised patients	44 (33-56)	24.6	PCR confirmed	30.1% severe	90[e]	7.4%
72.	Orru, G et al(85)	Italy	retrospective	152	-	Community via social media	-	-	Self-report	-	At least 3m post-infection	74.3%
73.	Osmanov, I et al(86)	Russia	Prospective cohort	518	-	Hospitalised children	10.4 (3.0-15.2)	52.1	PCR confirmed	2.7% severe (NIV/IV or PICU)	256[f]	24.3%
74.	Peghin M, et al(87)	Italy	Bidirectional prospective cohort	599	-	Hospitalised patients	53/15.8	53.4	NAAT for confirmed cases;	Mixed	191[b]	40.2%

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	Author	Country	Study design (as described by study, * if not stated)	Denominator[2]	Controls N, type	Setting	Age (years) Mean/SD Median (IQR)	% female	COVID-19 diagnostic method	Severity	Follow-up time[3] Days	Finding: % with at least one symptom or pathology remaining at follow-up
						and outpatients			laboratory, imaging or serology for suspected cases			
75.	Peluso, M et al(88)	USA	Cohort	143	-	Hospitalised patients and non-hospitalised	48 (37-57)	44.0	RNA-confirmed	Mixed	4m post-test or first symptoms	62.2%
76.	Petersen, M et al(89)	Faroe Islands	Longitudinal	180	-	96% non-hospitalised patients	39.9/19.4	54.4	PCR confirmed	4.4% asymptomatic	125[a]	52.8%
77.	Qin, W et al(90)	China	Prospective cohort	647	-	Hospitalised patients	58/15	56.0	PCR confirmed	38% severe	3m post-hospital discharge	13.4%
78.	Qu, G et al(91)	China	Multicentre follow-up	540	-	Hospitalised patients	47.5 (37-57)	50.0	PCR confirmed	9.4% severe	3m post-hospital discharge	32.6%
79.	Radtke, T et al(92)	Switzerland	Longitudinal cohort	109	1246 seronegative	Community, children and	6-16	53.0	Antibody positive	No hospitalisation	84[a]	3.7%

	Author	Country	Study design (as described by study, * if not stated)	Denominator[2]	Controls N, type	Setting	Age (years) Mean/SD Median (IQR)	% female	COVID-19 diagnostic method	Severity	Follow-up time[3] Days	Finding: % with at least one symptom or pathology remaining at follow-up
						adolescents						
80.	Rass, V et al(93)	Austria	Prospective observational cohort	135	-	Hospitalised and outpatients	56 (48-68)	39.0	PCR confirmed	23% severe (ICU), 53% moderate (hospitalised)	90[a]	60.7%
81.	Riestra-Ayora, J et al(94)	Spain	Prospective case–control	195	125 healthcare workers with negative PCR	Hospitalised and non-hospitalised healthcare workers	41.6/n/a	80.0	PCR confirmed	4.4% hospitalised	6m post-positive test	26.7%
82.	Righi, E et al(95)	Italy	Prospective cohort	421	-	Hospitalised patients and outpatients	56 (45-66)	45.1	PCR confirmed	52% hospitalised, 20% ICU	84[a]	19.7%
83.	Roessler, M et al(96) *Split cohort (Adults)*	Germany	Matched cohort	145184	-	Community	-	60.2	‘Laboratory confirmed’	5.8% hospitalised, 2.1% intensive care or ventilation	>90[a]	9.2%

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	Author	Country	Study design (as described by study, * if not stated)	Denominator[2]	Controls N, type	Setting	Age (years) Mean/SD Median (IQR)	% female	COVID-19 diagnostic method	Severity	Follow-up time[3] Days	Finding: % with at least one symptom or pathology remaining at follow-up
83 a.	Roessler, M et al(96) *Split cohort (Children)*	Germany	Matched cohort	11950	-	Community, children	-	48.1	Laboratory confirmed	1% hospitalised, 0.4% ICU	>90[a]	6.1%
84.	Romero-Duarte, A et al(97)	Spain	Retrospective longitudinal observational follow-up	797	-	Hospitalised patients	63/14.4	46.3	PCR confirmed	10.8% ICU	6m post-hospital discharge	63.9%
85.	Sathyamurthy, P et al(98)	India	Single-centre prospective cohort	279	-	Hospitalised older adult patients	71.0/5.6	36.2	PCR confirmed	41.6% severe to critical	90[e]	23.7%
86.	Seeβle, J et al(99)	Germany	Prospective cohort	146	-	Hospitalised and outpatients	57 (50-63)	57.0	PCR confirmed	15.6% mild, 55.2% moderate, 25.0% severe, 4.2% critical	140-154 (range) following symptom onset	73.3%
87.	Shang, Y et al(100)	China	Cohort	796	-	Hospitalised patients	62 (51-69)	49.2	PCR confirmed	90.8% severe, 9.2% critical	6m post-hospital discharge	55.4%
88.	Sibila, O et al(101)	Spain	Prospective cohort	172	-	Hospitalised patients	56.1/19.8	43.0	Not stated	moderate and severe 43% ICU	101.5[e]	57.0%

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	Author	Country	Study design (as described by study, * if not stated)	Denominator[2]	Controls N, type	Setting	Age (years) Mean/SD Median (IQR)	% female	COVID-19 diagnostic method	Severity	Follow-up time[3] Days	Finding: % with at least one symptom or pathology remaining at follow-up
89.	Sigfrid, L et al(102)	UK	Prospective cohort	327	-	Hospitalised patients	59.7 (51.7-67.7)	41.3	PCR confirmed or 'clinically diagnosed highly suspected'	20.8% no O2, 36.1% supplemental O2, 15.0% non-invasive O2, 28.1% mechanical ventilation	222[b]	93.3%
90.	Simani, L et al(103)	Iran	Cohort*	120	-	Hospitalised patients	54.6/16.9	33.3	Spiral chest CT scan or PCR confirmed	7.5% ICU	183[e]	10.0%
91.	Skala, M et al(104)	Czech Republic	Prospective cohort	102	-	Hospitalised patients and outpatients	46.7/n/a	53.9	PCR confirmed	14.7% hospitalised	3m after testing positive	54.9%
92.	Skjorten, I et al(105)	Norway	Multi-centre prospective cohort	126	-	Hospitalised patients	56.2/12.7	38.5	'Discharge diagnosis of COVID-19'	20% ICU	104[f]	46.8%
93.	Sonnweber, T et al(106)	Austria	Prospective observational	145	-	Hospitalised and	57/14	43.0	PCR confirmed	22% ICU	103[a]	54.9%

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	Author	Country	Study design (as described by study, * if not stated)	Denominator[2]	Controls N, type	Setting	Age (years) Mean/SD Median (IQR)	% female	COVID-19 diagnostic method	Severity	Follow-up time[3] Days	Finding: % with at least one symptom or pathology remaining at follow-up
						outpatients						
94.	Soraas, A et al(107) **(π)**	Norway	Cohort	651	5712 SARS-CoV-2–negative + 3342 randomly selected untested	Community	48.6/13.6	57	PCR confirmed	Non-hospitalised, mild	258[a]	51.9%
95.	Soraas, A et al(108) **(π)**	Norway	Prospective cohort	672	6006 SARS-COV2-negative patients	Community	48.5/13.5	56.8	PCR confirmed	Non-hospitalised	126[a]	56.2%
96.	Stavem, K et al(109) **(▪)**	Norway	Cross-sectional	451	-	Community survey	49.7/15.2	56.0	PCR confirmed	-	117[b]	41.0%
97.	Stavem, K et al(110) **(▪)**	Norway	Cross-sectional mixed-mode	458	-	Community	49.5/15.3	56.0	PCR confirmed	-	117.5[b]	46.0%
98.	Stephenson, T et al(111)	UK	Matched cohort	3065	3739 who tested negative	Community, adolescents	11-17	63.5	PCR confirmed	35.4% symptomatic	104[b]	66.5%

	Author	Country	Study design (as described by study, * if not stated)	Denominator[2]	Controls N, type	Setting	Age (years) Mean/SD Median (IQR)	% female	COVID-19 diagnostic method	Severity	Follow-up time[3] Days	Finding: % with at least one symptom or pathology remaining at follow-up
99.	Sudre, C et al(112)	UK, USA and Sweden	Prospective observational cohort	4182	4,182, matched PCR negative***	Community	46.0/15.8	57.0	PCR confirmed	13.9% visited hospital	84[a]	2.6%
100.	Sykes, D et al(113)	UK	Cohort*	127	-	Hospitalised patients	59.6/14	34.3	PCR confirmed	87% required oxygen and/or respiratory support, 20% ICU	113[f]	59.1%
101.	Taboada, M et al(114)	Spain	Cross-sectional observational	183	-	Hospitalised patients	6.9/14.1	40.5	PCR confirmed	18.2% ICU	6 months post-hospitalisation	47.5%
102.	Taquet, M et al(116) **(◊)**	Primarily USA	Retrospective cohort with matching	236,379	105,579 diagnosed with flu, 236,038 with any other RTI including flu	healthcare organisations including hospitals, primary care, and specialist providers	46/19.7	55.6	"confirmed diagnosis"	Mixed	180[a]	12.8%

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	Author	Country	Study design (as described by study, * if not stated)	Denominator[2]	Controls N, type	Setting	Age (years) Mean/SD Median (IQR)	% female	COVID-19 diagnostic method	Severity	Follow-up time[3] Days	Finding: % with at least one symptom or pathology remaining at follow-up
103.	Taquet,. M et al(115) **(◊)**	USA	Retrospective cohort	273618	106,578 matched cohort with influenza and without a diagnosis of COVID-19 or positive test	Hospitalised patients and non-hospitalised	46.3/19.8	55.6	'Confirmed diagnosis', ICD-10 code	Mixed	90[a]	36.5%
104.	Tarsitani, L et al(117)	Italy	Cohort follow-up	115	-	Hospitalised patients	57 (48-66)	46.0	'Confirmed COVID-19'	23% ICU	3m post-hospital discharge	29.6%
105.	Tawfik, H et al(118)	Egypt	Retrospective cohort	120	-	Hospitalised and non-hospitalised healthcare workers	33.7/7.29	58.0	PCR confirmed	28.3% moderate, 10.0% severe	At least 3m post-positive test	33.3%
106.	Taylor, R et al(119)	UK	Cohort*	545	-	Hospitalised patients	58.6/15.3	38.2	'Presumed and confirmed'	-	16weeks post-hospital discharge	47.9%

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	Author	Country	Study design (as described by study, * if not stated)	Denominator[2]	Controls N, type	Setting	Age (years) Mean/SD Median (IQR)	% female	COVID-19 diagnostic method	Severity	Follow-up time[3] Days	Finding: % with at least one symptom or pathology remaining at follow-up
107.	Tempany, M et al(120)	Republic of Ireland	Cross-sectional*	217	-	Healthcare workers	20-69	80.0	PCR confirmed or antibody positive	-	At least 12 weeks post- +ve test	53.5%
108.	The Writing Committee for the COMEBAC Study Group(121)	France	Prospective uncontrolled cohort	478	-	Hospitalised patients	60.9/16.1	42.1	PCR confirmed or by CT scan	29.7% ICU, remainder hospitalised	113[f]	51.0%
109.	Tholin, B et al(122) **(•)**	Norway	Multicentre prospective cohort	683	-	Hospitalised patients and non-hospitalised	52.9/15.5	51.0	PCR confirmed, or discharge diagnosis of 'confirmed or unconfirmed COVID-19'	Mixed	3m after discharge (hospitalised), 4m post-symptom onset (non-hospitalised)	1.8%
110.	Tleyjeh, I et al(123)	Saudi Arabia	Prospective cohort	222	-	Hospitalised patients	52.5/14.0	23.0	PCR confirmed	Mixed 30.2% ICU	122[f]	56.3%

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	Author	Country	Study design (as described by study, * if not stated)	Denominator[2]	Controls N, type	Setting	Age (years) Mean/SD Median (IQR)	% female	COVID-19 diagnostic method	Severity	Follow-up time[3] Days	Finding: % with at least one symptom or pathology remaining at follow-up
111.	Todt, B et al(124)	Brazil	Single-centre cohort	239	-	Hospitalised patients	53.6/14.9	40.2	PCR confirmed	69.7% severe	3m post-hospital discharge	40.2%
112.	Tohamy, D et al(125)	Egypt	Retrospective comparative study with controls	100	100 randomly recruited from hospital registration system without COVID-19	Hospitalised and outpatients	55.5/6.2	43.0	PCR confirmed	25% moderate, 45% severe	3m post-hospital discharge	5.0%
113.	Townsend, L et al(126)	Republic of Ireland	Cross-sectional*	128	-	Hospitalised and non-hospitalised	49.5/15	53.9	PCR confirmed	55.5% hospitalised	72[f]	57.8%
114.	Trunfio, M et al(127)	Italy	Cross-sectional	168	-	Hospitalised patients and outpatients	56 (43-69)	42.0	PCR confirmed	63.7% hospitalised	194[b]	24.4%

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	Author	Country	Study design (as described by study, * if not stated)	Denominator[2]	Controls N, type	Setting	Age (years) Mean/SD Median (IQR)	% female	COVID-19 diagnostic method	Severity	Follow-up time[3] Days	Finding: % with at least one symptom or pathology remaining at follow-up
115.	Ursini, F et al(128)	Italy	Cross-sectional	616	-	Community via social media	45/12	77.4	Positive nasopharyngeal swab	10.7% hospitalised, 1.6% ICU	6 ± 3m post-positive test	43.8%
116.	Venturelli, S et al(129)	Italy	Cohort*	767	-	Emergency Department and hospitalised patients	63/13.6	32.9	PCR confirmed	88.4% admitted 8.6% ICU	105[b]	51.4%
117.	Walle-Hansen, M et al(130)	Norway	Cohort	106	-	Hospitalised older adult patients	74.3/n/a	43.0	PCR confirmed	26% severe	186[f]	53.8%
118.	Weng, J et al(131)	China	Retrospective	117	-	Hospitalised patients	-	44.4	PCR confirmed	28.2% severely ill	89.5[e]	44.4%
119.	Whitaker, M et al(132)	UK	Random community-based survey (REACT-2)	76,155	-	Community	-18+	57.3	Self-reported	0.8% admitted to hospital	84[a]	37.7%

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	Author	Country	Study design (as described by study, * if not stated)	Denominator[2]	Controls N, type	Setting	Age (years) Mean/SD Median (IQR)	% female	COVID-19 diagnostic method	Severity	Follow-up time[3] Days	Finding: % with at least one symptom or pathology remaining at follow-up
120.	Xiong, L et al(133)	China	Ambidirectional cohort	162	-	Hospitalised healthcare workers	36 (31-43)	77.0	'Infected with COVID-19'	100% severe, 5% ICU	153[f]	70.4%
121.	Xiong, Q et al(134)	China	Longitudinal with controls	538	184, volunteers	Hospitalised patients	52 (41-62)	54.5	"confirmed"	5% critical, 33.5% severe	97[f]	49.6%
122.	Yan, B et al(135)	China	Prospective observational	125	-	Mobile cabin hospital, adult males	35 (30-49)	0.0	'Diagnosed with COVID-19'	asymptomatic / mild symptoms	84[e]	0.0%
123.	Yan, X et al(136)	China	Cohort	119	-	Hospitalised patients	53.0/12.2	59.0	PCR confirmed	24% severe	365[e]	39.5%
124.	Yin, X et al(137)	China	Retrospective analysis	337	-	Hospitalised patients	53.5/14.8	49.5	PCR confirmed	12.8% severe, 3.6% ICU	203[a]	55.8%
125.	Zayet, S et al(138)	France	Retrospective cohort	354	-	Hospitalised patients and outpatients	49.6/18.7	63.0	PCR confirmed	34.2% hospitalised, 5% ICU	289[a]	35.9%

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	Author	Country	Study design (as described by study, * if not stated)	Denominator[2]	Controls N, type	Setting	Age (years) Mean/SD Median (IQR)	% female	COVID-19 diagnostic method	Severity	Follow-up time[3] Days	Finding: % with at least one symptom or pathology remaining at follow-up
126.	Zhan, Y et al(139)	China	Prospective cohort	121	-	Hospitalised patients	49 (40-57)	58.7	PCR confirmed	15.7% severe	348[b]	29.8%
127.	Zhang, D et al(140)	China	Retrospective comparative	122	-	Hospitalised patients	51 (31.8-61.0)	50.3	PCR confirmed	mild cases excluded, only patients with pulmonary sequelae at discharge included	92[f]	54.9%
128.	Zhang, J et al(141)	China	Cohort*	245	-	Hospitalised patients	43 (33-54)	43.8	Nucleic acid testing	9.3% severe/critical	90[e]	72.7%
129.	Zhang, X et al(142)	China	Retrospective multi-centre cohort	2433	-	Hospitalised patients	60 (49-68)	50.5	Laboratory confirmed	27.9% severe	364[f]	45.0%
130.	Zhou, M et al(143)	China	Prospective cohort with controls	164	42 healthy controls – negative nucleic acid and antibody tests	Hospitalised patients	-	56.9	PCR and antibody test	54.6% severe	129[b] (severe cases) 125[b] (mild)	69.5%

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Figure 1: Study selection

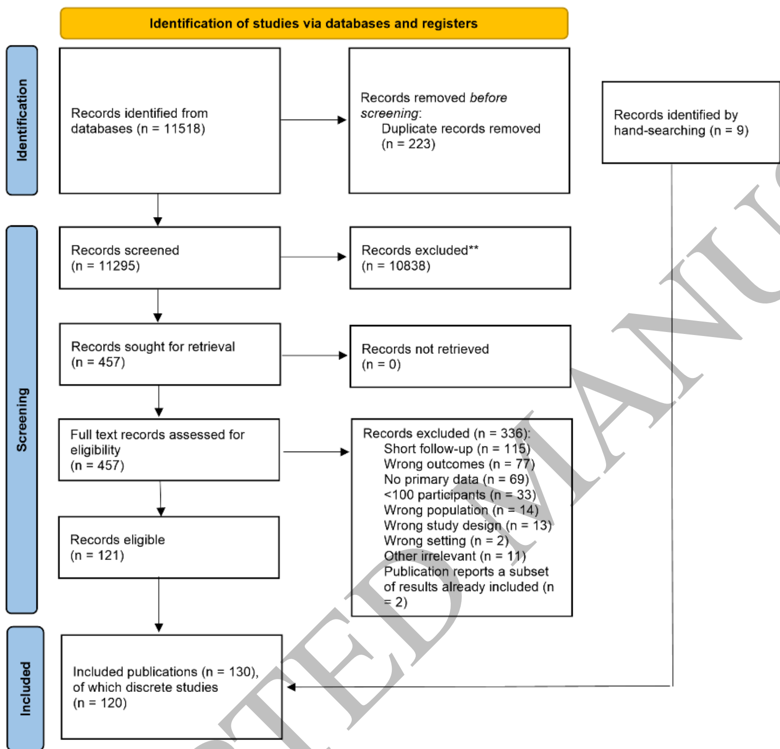

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Figure 2: Forest plot of prevalence of Long Covid in the included studies, with 95% prediction intervals

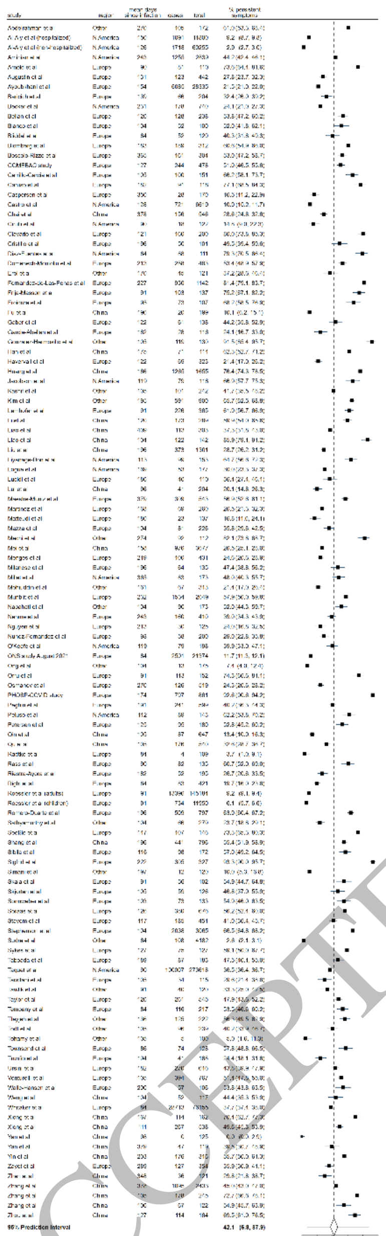

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Figure 3: Forest plot of prevalence of Long Covid in the included studies by method of outcome assessment, with 95% prediction intervals

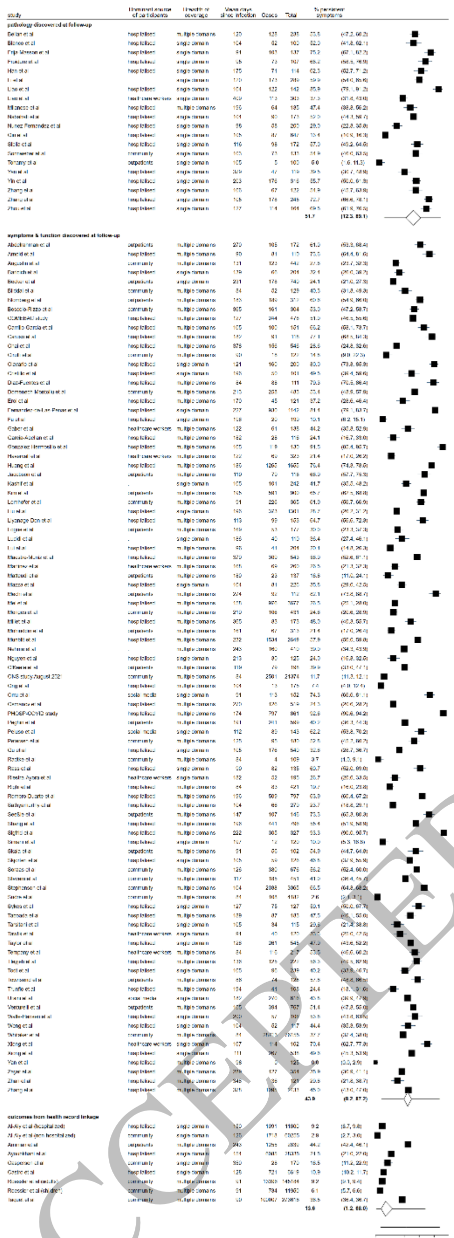

Figure 4: Forest plot of risk of Long Covid in included studies with community-based samples and controls assessed as having low risk of bias, with 95% prediction intervals

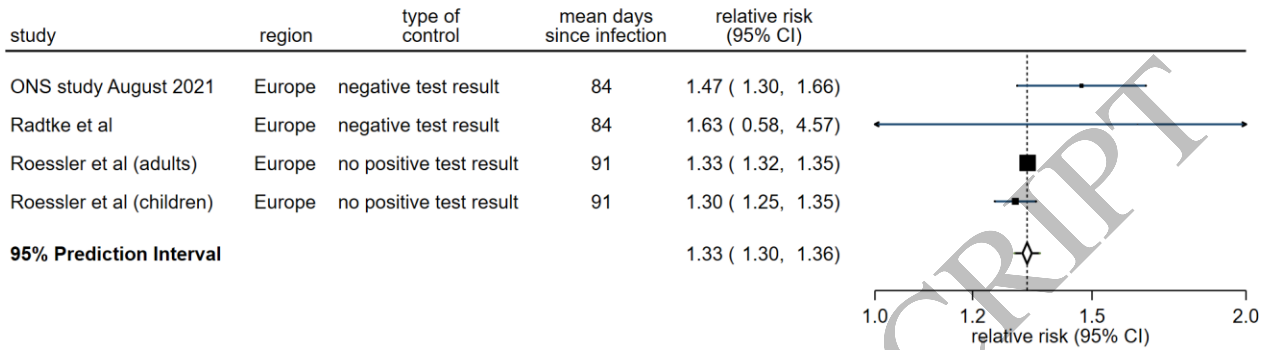

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Figure 5: Forest plot of individual symptoms, pathology and functional disability identified in the included studies, with 95% prediction intervals

persistent problem	% problem	number of studies	I^2
Pathology			
Lung Pathology	38.9 (3.4 to 91.9)	26	99.7%
Heart Pathology	6.0 (0.1 to 79.3)	12	99.9%
Neurological pathology	5.3 (0.5 to 36.5)	11	99.7%
Hypertension	1.5 (1.3 to 1.8)	4	0%
Pancreas Pathology	1.4 (0.0 to 95.9)	3	94.7%
Vascular Problems	0.8 (0.0 to 33.6)	5	99.6%
Kidney Pathology	0.7 (0.0 to 54.7)	6	99.7%
Liver Pathology	0.6 (0.0 to 100.0)	3	98.8%
Symptom			
Fatigue	21.6 (2.5 to 74.7)	72	99.6%
Breathing Problems	14.9 (1.6 to 64.9)	78	99.7%
Sleep Problems	13.2 (1.2 to 64.9)	42	99.0%
Tingling or Itching	11.3 (0.7 to 69.5)	14	98.2%
Aches or Pains In Joints or Muscles	10.6 (1.0 to 57.5)	61	99.7%
Weakness	10.2 (0.5 to 72.2)	21	98.8%
Cognition or Memory Problems	10.1 (0.8 to 60.2)	49	99.4%
Eye Problems	10.0 (0.0 to 96.5)	4	97.3%
Problems with Taste or Smell	9.6 (1.2 to 48.7)	60	98.6%
PTSD	9.3 (0.5 to 65.5)	12	99.2%
Anxiety, Depression or Mood Change	7.7 (0.0 to 94.9)	5	99.1%
Cough	7.4 (1.3 to 33.5)	52	95.8%
Dizziness	7.4 (0.8 to 45.4)	26	97.7%
Alopecia	7.2 (0.5 to 56.7)	17	99.1%
Chest Pain	6.7 (0.9 to 35.8)	43	98.0%
Headache	6.5 (0.6 to 45.6)	51	99.1%
Palpitations	5.8 (1.2 to 24.5)	26	94.9%
Speech or Language Problems	4.3 (0.0 to 88.5)	6	99.0%
Nausea or Vomitting	3.9 (0.4 to 28.8)	49	99.6%
Ear Problems	3.8 (0.2 to 45.0)	11	98.2%
Abdominal Pain	3.7 (0.1 to 63.8)	15	99.2%
Sore Throat	3.5 (0.6 to 17.1)	22	97.1%
Psychological Distress	2.9 (0.0 to 100.0)	3	98.0%
Skin Problems	2.5 (0.0 to 56.2)	6	97.6%
Fever	1.9 (0.1 to 34.7)	24	97.9%
Chills	1.0 (0.0 to 98.8)	4	93.6%
Functional status			
Not Returned to Full Health/Fitness	34.5 (4.3 to 85.9)	10	99.4%