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Was the rate of Long Covid as high as 45%-a scary report with flaw

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Long Covid has worried the public as the COVID-19 pandemic continues. We are interested in the report by O'Mahoney et al. on the systematic review and metaanalysis of the prevalence and long-term health effects of Long Covid among hospitalized and non-hospitalized populations.1 We were surprised that 45% of COVID-19 survivors, regardless of hospitalization status, experienced a range of unresolved symptoms at \sim 4 months. First, these data suggest that a large population worldwide had Long Covid in the past two years up to the end of 2021. The authors collected data from publications until January 2022. Based on the report from World Health Organization (https://www.who.int/ publications/m/item/weekly-epidemiological-update-oncovid-19-31-August-2021), as of December 26, over 278 million cases were reported globally. If 45% of them have the Long Covid, 130 million people worldwide suffer from Long Covid after 4 months of COVID-19. Secondly, these data are significantly different from public perception. According to the December 15, 2022 report from the Centers for Disease Control and Prevention (https://www.cdc.gov/nchs/covid19/pulse/longcovid.htm), the prevalence of Long Covid was less than 20%. Most importantly, it differs from a credible recent publication.² Based on the data of 486,149 nonhospitalized individuals, Subramanian and colleagues found that 5.3% of men and 9.8% of women had Long COVID symptoms 12 weeks after the index date.² As such, we examined the data from the systematic review and found some discrepancies and would like to bring them to public attention.

The authors provide a summary of the data retrieved from 194 studies in supplementary Table 3. Because the result of this review is mainly based on the data collected in this table, we checked the data accuracy to validate the results from the authors' systematic review. Based on supplementary Table 3, we found that there is a considerable discrepancy between the data being published and shown in this table. These inconsistencies and our questions are listed below.

- 1. Authors found that of the 735,006 participants sampled in the 194 studies, on average, at least 45% of COVID-19 survivors, regardless of hospitalization status, went on to experience at least one unresolved symptom (mean follow-up = 126 days). We then calculated the total number of participants and those with symptoms based on the data from each study in this supplementary table. Based on the data in Table 3, only 11% (86,552 out of 735,006) of patients showed the symptoms. Obviously, there is a tremendously difference between 45% and 11%.
- 2. In interpreting their findings, authors reported "Our work shows that 45% of COVID-19 survivors, regardless of hospitalization status, were



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experiencing a range of unresolved symptoms at ~ 4 months." Among the 194 studies, some of the followup days are less than "~ 4 months". We then calculated the 98 studies with follow-up data equal to or more than 111 days. The data showed that only 25% of patients had the symptoms. Thus, 18,800 out of 74,674 patients had symptoms at ~ 4 months after the COVID-19 disease. To explore the possibility that the data was calculated with the percentages regardless of the total number of subjects from each study, we next collected the percentages of every study and then divided the total number by 194. In this way, we obtained a 30.6%. The same calculation for the studies of 4 months received a 30.3%.

3. The above two calculations suggest that the accurate percentage from these data may be close to what has been previously reported,² as less than 10% of the non-hospitalized patients had Long Covid. Such a set of data encouraged us to examine the data in depth. In O'Mahoney et al.'s supplementary Table 3,1 for every study, the authors provided the "Total # of participants" and "Total # with symptom." Therefore, the percentage of the patients showing the symptoms in each study can be obtained by dividing the number by symptoms using the total number of patients. Such a calculation showed that the percentages of patients with the symptoms in these studies are extraordinarily variable, from as less as 3% to as much as 91%. Understandably there are variations among different populations because of race, region, and environmental factors. However, the range of such a difference is unexpected. We further checked the accuracy of data extracted from the original studies in the article of O'Mahoney et al.

We were not able to double-check the data from the majority of the study, as it is difficult to identify the correct corresponding publication based only on the authors' names and the number of patients. However, we are confident that we found the right articles for the three with the least percentages of patients with the symptoms. Therefore, we could compare the data of the original publications of three studies with the data from the table. To our surprise, the data in these three original publications differ from those listed in the article. The first study is by O'Keefe et al.3 In the O'Mahoney et al. publication, 1 patient was listed in the "Total # with symptom" category. However, authors in the original publication reported that among 304 primarily outpatients, patients with persistent symptoms at 30 days were 1% of 209 in the mild initial symptom severity group; at least 9% of 91 in the group of moderate initial symptom severity; 3 out of 4 in the group of non-hospitalised patients with severe initial symptom severity (Table 1). Similar differences were found between the original publications by Venturelli et al.4 and Tessitore.⁵ In contrast, the original publications reported a greater number of patients with symptoms than in the article in O'Mahoney et al.1

Given the fact that the table reported fewer numbers than those in the original studies in these three studies with the least percentages of patients with symptoms of Long Covid, we suspect that the remaining data may be incorrect, especially those with a percentage greater than 70%. However, with limited information on these articles, we could not correctly locate these studies with the data in the systematic review. It is highly appreciated that authors add enough information for readers to track the sources of articles from this review.

| First Authors | Data type | Total # of participants | Total # with symptom | Original publication information |
|---------------|---------------|----------------------------|--|---|
| O'Keefe (A) | Reported | 304 | 1 | BMJ Open. 2021 Mar 5; 11 (3):e044154. https://doi.org/10. 1136/bmjopen-2020-044154. |
| | Original data | 304 | 1% of 209 of in mild initial symptom severity group; at least 9% of 91 in the group of moderate initial symptom severity; 3 out of 4 in the group of non-hospitalized patients with severe initial symptom severity | |
| Venturelli | Reported | 767 | 4 | Epidemiol Infect. 2021 Jan 19; 149:e32. https://doi.org/10. 1017/50950268821000145 |
| | Original data | | 51.4% still complained of symptoms | |
| Tessitore | Reported | 165 | 1 | Swiss Med Wkly. 2021 Dec 13; 151:w30093. https://doi.org/10.4414/smw.2021.w30093. eCollection 2021 Dec 6. |
| | Original data | | One year after discharge, the main complaints were persistent fatigue in 27% (45/165) of patients, neurological problems in 17% (28/165) and dyspnoea in 14% (23/165). Eight percent (14/184) of patients declared being significantly worried 1 month after discharge and 5% (9/184) feeling depressed | |

4. The difference in the Long Covid among different strains of the ARS-CoV-2 has been well known. The data in this meta-analysis¹ were collected from publications until January 2022. During this period of time, new mutations or strains of ARS-CoV-2 have occurred from different countries and regions. It is unclear whether the strain difference caused the significant difference among different reports among these 194 articles.

5. It is also known that vaccines may affect the symptoms, thereafter impacting the prevalence of long-COVID-19. Because the review article by O'Mahoney et al.¹ collected data from 194 articles, it is likely that the disease rates among these populations varied because of different vaccination rates. We hope the authors would have noted this aspect during their data collection.

In summary, the COVID-19 pandemic has caused the deaths of millions and global panic of the public. We believe that the rate of Long Covid is around 20% or below, as previously reported by others. We sincerely hope that all authors in the studies of Long Covid are careful with data collection and analysis. Any inaccurate data about such an important disease may mislead or scare the public.

Contributors

LY, DS, and WG developed the concept and drafted the manuscript. LY, LA, JCG, GW, and WG participated in data analysis and manuscript drafts. All authors interpreted the data and results and edited the manuscript.

Declaration of interests

We declare no competing interests.

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