Review of: "Long COVID Syndrome: A Systematic Review of Persistent Symptoms Post-Pandemic"

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Potential competing interests: No potential competing interests to declare.

Dear colleagues

In the introduction, this sentence attracts my attention

“Fatigue is the primary complaint in up to 20% of cases seeking primary care in Germany. Its prevalence increases with age and affects women . Musculoskeletal pain affects mid 13.5% and 47.0% and has risk factors associated with age, sex, lifestyle habits, emotional state, and sleep disturbances . According to the American Thoracic Society, dyspnea constitutes 50% of hospitalizations in the tertiary health system and 25% of ambulatory cases . Anxiety and depression are present in 25% of cases in general clinical practice, often presenting as comorbid symptoms . In 2017, the Global Burden of Disease reported 792 million people with mental disorders, representing a ratio of one in ten people globally (10.7%) . After experiencing crises, as occurred during the COVID-19 pandemic, an increase in these symptoms is common. However, a study conducted in the Netherlands among individuals with and without depression, anxiety, and obsessive-compulsive disorder showed a significant increase in mental disorder symptoms in the general population during the SARS-CoV-2 pandemic .”

I examined the 8 references in detail

3 written by a rheumatologist

4 also a rheumatologist

5 a nurse working in a hospital in pneumology

6 a psychiatrist

7 Ph.D. in psychiatric genetics

8 also a psychiatrist

I can understand that you want to highlight the fact that the symptoms of long COVID are ubiquitous. But taking a specialty for each symptom doesn't guarantee you a coherent view of a problem. Specialists usually work in hospitals, and their views of the reality of patients are biased. There is no shortage of primary care databases, fed by doctors in the field, to show the prevalence of this type of symptom.

May I suggest these types of references

- Kjeldsberg, M., Tschudi-Madsen, H., Mdala, I., Bruusgaard, D., & Natvig, B. (2021). Patients in general practice share a common pattern of symptoms that is partly independent of the diagnosis. *Scandinavian Journal of Primary Health Care*, *39*(2), 184–193. https://doi.org/10.1080/02813432.2021.1913886
- Rosendal, M., Carlsen, A. H., Rask, M. T., & Moth, G. (2015). Symptoms as the main problem in primary care: A cross-sectional study of frequency and characteristics. *Scandinavian Journal of Primary Health Care*, *33*(2), 91–99. https://doi.org/10.3109/02813432.2015.1030166

Following your text

“Considering the occurrence of these symptoms in the general population and their potential association with COVID, this study aims to provide insights into the relationship between the clinical manifestations presented and SARS-CoV-2 viral infection. Understanding the magnitude of the problem is essential for healthcare services, which must address both daily demands and those related to Long COVID.”

I don't think you fully understand Long Covid. It's important to stress that for doctors, it's a set of medically unexplained symptoms (MUS) that don't correspond to any usual pathology. There is no shortage of literature on this subject

- Aamland, A., Malterud, K., & Werner, E. L. (2014). Patients with persistent medically unexplained physical symptoms: a descriptive study from Norwegian general practice. *BMC family practice*, *15*, 1-6.

And when doctors are not at ease with patients' symptoms, patients feel it, communication breaks down, and patients feel abandoned.

- Au, L., Capotescu, C., Eyal, G., & Finestone, G. (2022). Long covid and medical gaslighting: Dismissal, delayed diagnosis, and deferred treatment. *SSM - Qualitative Research in Health*, *2*, 100167. https://doi.org/10.1016/j.ssmqr.2022.100167

But the most important symptom of Long Covid is the profound change in patients' state of health, whatever their state of morbidity before Covid. This change is profound, and patients are generally in mourning for themselves.

It is fascinating to realize that the nearly most accurate definition of Long Covid was written in 1992

“*New onset of persistent or relapsing, debilitating fatigue or easy fatigability in a person who has no previous history of similar symptoms, that does not resolve with bedrest, and that is severe enough to reduce or impair average daily activity below 50% of the patient's premorbid activity level for a period of at least 6 months*”. in ;

- Holmes, G. P., Kaplan, J. E., Gantz, N. M., Komaroff, A. L., Schonberger, L. B., Straus, S. E., Jones, J. F., Dubois, R. E., Cunningham-Rundles, C., & Pahwa, S. (1988). Chronic fatigue syndrome: a working case definition. *Annals of Internal Medicine*, *108*(3), 387–389. https://doi.org/10.7326/0003-4819-108-3-387 available here; https://paradigmchange.me/me/wp-content/uploads/2017/03/Holmes-1988.pdf

Following

I don't really have the time to analyse in detail the immense amount of work you have done and for which you deserve to be congratulated. Few researchers are working intensively on this new disease.

Yet I have to say that I disagree with your conclusion: You write *"The WHO recognizes that knowledge about the Long COVID Syndrome is limited."*

I believe that over the last two years (2023-2024), scientists from all over the world have made giant strides in understanding this new chronic viral disease that affects the entire human body, producing severe encephalitis with the loss of numerous cerebral control systems, as well as autoimmune phenomena that are still not fully understood. Check out the online videos from the latest Unitetofight2024 conference to see the major advances in the field.
https://www.youtube.com/@UniteToFight2024

Attentamente,

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