EPA-EAN statement on Post-COVID syndrome

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Aim: We aimed to determine the role of the EPA and EAN in the management of Post-COVID condition.

This is a joint statement from the European Association of Neurology (EAN) and the European Psychiatric Association (EPA) on Post-COVID. It is published in the official journals of the two associations, the European Journal of Neurology and European Psychiatry.

INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has rapidly emerged to a pandemic and caused a morbidity and mortality in an inconceivable extend globally [1]. Emergence of different variants resulted in multiple waves of Coronavirus disease 2019 (COVID-19) and have massively affected the world´s health and economy. As of July 2022, 565 million people have been infected with SARS-CoV-2 and 6,3 million died [2]. Acute COVID-19 has rapidly been recognized as multi-organ disease reaching far beyond pulmonary symptoms and signs. These include neurologic, psychiatric, cardiac, and gastrointestinal manifestations among others. Soon, the World Federation of Neurology appealed to national and regional neurological associations to create databases for international neuroepidemiological collaboration [3]. Among others, the European Academy of Neurology (EAN) implemented an international registry to study neurological manifestations and long-term outcome in COVID-19 patients (EAN NEuro-covid ReGistrY, ENERGY*)* [4], and furthermore signed a memorandum of understanding with the American Neurocritical Care Society to enlarge a global network

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[5]. Pre-existing neurological diseases and new onset COVID-19 associated neurological manifestations have now been recognized as risk factors for a more severe disease and poor long term outcome [6, 7]. The European Psychiatric Association (EPA) established its "COVID-19 Resource Centre", an online repository of high-quality COVID-19-related resources for both health professionals and the general public *(https://www.europsy.net/covid-19-resource-centre/).* The EPA and its network also implemented initiatives, such as surveys and events, to better understand the impact of COVID-19 on mental health and on the delivery of care. In addition, EPA supports regional projects such as the interdisciplinary and cross-sectoral care and research network (Post-COVID^{LMU}) at LMU University Hospital in Munich, Germany [8]. Finally, EPA and EAN jointly provide platforms for scientific exchange on COVID-19 and Post-COVID in form of forums and symposia at congresses, conferences and meetings.

Recognition of persistent symptoms and signs after recovery from initial COVID-19 illness have soon been recognized [9], and are currently referred to as "Long-COVID". In fact, "Long-COVID" was created through social media [10], and is a time-based definition of unspecific symptoms and signs persisting beyond 4 weeks. The WHO recently recommended the use of the terminology of "Post-COVID-19 condition", which includes *"individuals with a history of probable or confirmed SARS CoV-2 infection, usually 12 weeks from the onset of COVID-19 with symptoms and that last for at least 2 months and cannot be explained by an alternative diagnosis and has an impact on everyday functioning"* [11]. There is currently a lack of robust evidence on the prevalence of these symptoms due to differences in reporting systems and inconsistency of study designs and definitions of symptoms, signs and diseases related to Post-COVID condition, which renders its global impact speculative. Recent estimates of the Office for National Statistics in Great Britain suggests that 1 in 5 patients with confirmed or suspected exhibits symptoms for a period of 5 weeks or longer and 1 in 10 for 12 weeks or longer [12]. These numbers rapidly change especially as the virus phenotype and infection rate varies. As of January 2022, an estimated 1.5 and 1.1 million people reporting symptoms beyond 4 and 12 weeks, respectively, are living in private household in the UK (2,4% and 1.8% of the population).

Proposed mechanisms of persistent and new onset postinfectious disorders include immune dysregulation with persistent low grade (neuro-)inflammation, immune dysregulation, autoimmunity and viral persistence in various tissues [13]. Each of these hypotheses need confirmation in larger scale studies and build upon direct and indirect neuropathogenic effects of SARS-CoV-2 in the acute phase [14].

Long-term neurologic manifestations include fatigue, neurocognitive symptoms, sleep-wake disorders, dysautonomia, hyposmia, hypogeusia and pain syndromes among others [15].

Fatigue was shown in a recent metaanalysis including 36 studies and a total of 9944 participants to be the most common symptom (mean 52.8%; 95% Confidence Interval 19.9 - 84.4) [16]. The large 95% confidence intervals highlight the need for a more strict and homogenous definition of the Post-COVID syndrome and its symptoms. The authors also suggest a better analysis in future studies of the longitudinal course of symtpoms, which appear to strongly fluctuate within the first year post SARS-CoV-2 infection and even during the day.

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Neurocognitive symptoms are commonly associated with impaired performance in neuropsychological testing and are expected sequelae among ICU survivors including those with COVID-19. Of note, early reports of frontotemporal FDG-PET hypometabolism [17] during acute COVID-19 have now been replicated in the subacute phase and associated with memory deficits and executive dysfunction [18]. Despite longitudinal recovery from cognitive deficits [19], the increased risk for neurological and psychiatric diagnoses in the 6 months after infection deserves attention [20]. These data derive from a large retrospective cohort of more than 250.000 survivors of COVID-19 reporting even a higher risk compared to propensity score matched cohorts of influenza patients and those with other respiratory infections [20]. Interestingly, even patients with mild and moderate COVID-19 report poor concentration, lack of intellectual clarity and mental fatigue which is referred to as “brain fog” and is poorly captured by conventional testing including the MOCA test [21]. This and other consequences of COVID-19 lack of specificity and need a more precise definition. In general, neurological manifestations improve over time [22, 23], however, long-term effects and new onset neurological diseases including autoimmune diseases and neurodegenerative diseases need close surveillance through national and international registries.

Non-pharmacological treatment strategies such as those recommended by the National Institute for Health and Excellence (NICE) are available for different symptoms of the Post-COVID syndrome including self management strategies, pacing and multidisciplinary rehabilitation *(COVID-19 rapid guideline: managing the long-term effects of COVID-19 (magicapp.org)).* Pharmacological treatment for Post-COVID neurological disease are based on proposed neuropathogenic mechanisms of SARS-CoV-2 infection including immunomodulation, IVIG/plasma-exchange for antibody/immune/cytokine mediated para- and postinfectious diseases.

Specific guidelines however do not exist for Post-COVID. Randomized controlled trials are needed to provide further treatment recommendations for subpopulation with distinct features. There will not be a single treatment alleviating all Post-COVID symptoms. Researchers and clinicians are asked to link clinical phenotypes with biomarkers and define endpoints that can be used for clinical trials. A summary of ongoing clinical trials targeting several endpoints including neurocognition, anosmia and headache has been recently published [24].

Among psychiatric disorders, anxiety, depression, insomnia, cognitive impairment, and post-traumatic stress disorder (PTSD) are the most common [25]. Relevant studies show a significantly increased incidence of mental disorders immediately following SARS-CoV-2 infection compared to unaffected populations [26]. A large-scale US study (n= 62,354) found an increased 3-month incidence of psychiatric diagnoses (18.1%) and first-episode psychiatric disorders (5.8%) after SARS-CoV-2 infection [27]. In a further study, an increased 6-month incidence of mental disorders (13.7% depression, 17.4% anxiety, 1.4% psychotic disorders, 6.6% addictive disorders, 5.4% insomnia) was observed [28].

The etiology of the psychiatric sequelae of SARS-CoV-2 infection is multifactorial and includes direct effects of viral (CNS) infection, excessive immune response, social isolation, uncertainty about the course of the disease, persistent symptom manifestation, and concern about recurrence of symptom exacerbation a.o. [29, 30, 31]. Studies suggest that immune system

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dysregulation can be associated with depressive symptoms [32] which may explain some of the psychiatric morbidity also following SARS-CoV-2 infection. As a correlate of COVID-19, imaging studies have found changes in the limbic system and related areas (prefrontal, anterior cingulate, and insular cortex). An abnormal functional disconnectivity may also play an important role [33]. These structural brain changes may lead to a link between COVID-19 and its psychopathological consequences in the long-term course of the disease.

Commonly known tools such as the Patient Health Questionaire (PHQ), the State and Trait Anxiety Index (STAI), the PTSD Checklist (PCLC), and the Fatigue Assessment Scale (FAS) are used frequently for symptom classification of Post-COVID. To differentiate a depressive disorder from fatigue, it is recommended to ask about core depressive symptoms according to DSM-5 or ICD-11. Cognitive and memory impairment, attention and executive function can be assessed by using neuropsychological test batteries [34, 35].

The current German S1 guideline for post-COVID/long-COVID primarily recommends multimodal treatment approaches [36]. Recent literature provides evidence for anti-inflammatory and antiviral properties of various antidepressants, particularly selective serotonin reuptake inhibitors (SSRIs) in the acute phase of infection [37]. However, despite the large number of patients affected, there is no report on the efficacy of pharmacological treatment of Post-COVID. Comorbid psychiatric disorders (depression, anxiety disorders, PTSD) should therefore be treated according to the current guidelines. Serotonin and norepinephrine reuptake inhibitors (SNRIs) with pain modulating effects may be considered for additional pain symptomatology. Psychotherapy and cognitive training as well as measures to strengthen protective factors such as social support, and stress coping strategies should be used primarily. Since the cognitive impairments in post-COVID mainly affect planning thinking, concentration, memory, and language skills, targeted cognitive training methods and programs can be attempted [8]. The first specific group psychotherapy programs have been developed, including knowledge transfer of post-COVID, mindfulness exercises, cognitive restructuring, and management of depressive moods, pain, and physical complaints [8]. However, in order to determine treatment success, such therapy programs should first be evaluated, e.g., by neurocognitive pre- and posttests.

CONSEQUENCES

Looking at the literature in detail, it can be stated that the current data on Post-COVID do not yet allow concrete conclusions for clinical care: 1) Due to the lack of specific diagnostics of Post-COVID (missing Post-COVID specific screening measures and biomarkers), differentiation from other diseases associated with similar symptoms, such as fatigue syndrome, intensive care syndrome, or depression due to contact prohibition, remains difficult [35, 38]. 2) Post-COVID may also generate novel complex and subjective symptoms, although it remains unclear to what extent the nature and duration of these symptoms correspond to the signs of other severe infectious diseases and whether established therapeutic approaches are applicable [39]. 3) In addition, causes, course and duration, and predictors of Post-COVID syndrome, particularly in its severe form, have not been adequately specified yet. Further research is needed in this area, especially with regard to the long-term recording of symptoms

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and the frequency of complex Post-COVID cases. 4) Finally, there is a lack of holistic care structures and treatments for this unclear but quite complex illness. The organizational structures, treatment strategies, the human and material resources needed in the long term to adequately treat patients with severe Post-COVID, and the impact of care delivery on disease progression, remain unclear. However, studies on implementation and evaluation of interdisciplinary and multisectoral health and research networks for evidence-based treatment of patients with severe post-COVID syndrome are already underway, which will help us to better understand this complex clinical picture [8, 40].

FUTURE PERSPECTIVE

Post-COVID highlights the link and transition between brain diseases and mental health. Accordingly, the Post-COVID syndrome exemplifies the need for clinical, research and teaching collaborations between neurology, psychiatry, infectious diseases and others. Understanding and managing long-term neurological and psychiatric sequelae after COVID-19 will require additional common research investments and health care resources. Patient-centered services for Post-COVID care requires proper definition of patient tracks from the primary care physician to specialized care. This should be built up on existing infrastructure on a level-based approach. Furthermore, longitudinal follow up with phenotyping (clinical, biomarker, genetics, among others) is needed to better understand the global burden of Post-COVID syndrome on a regional, community and global level. Interdisciplinary longitudinal care needs to be accompanied by research to further understand disease mechanisms, risk factors, and prognosis. Federal funding initiatives designed to support a deeper comprehensive understanding of Post-COVID syndrome are strongly needed. This will help to phenotype acute and Post-COVID for specific treatment trials.

Common agenda for clinical care and research:

- Research to better underestand the neurobiological and other determinants of Post-COVID syndrome including the impact of the different SARS-CoV2 variants on incidence and phenomenology to identify the risk of an unrestricted ongoing SARS-CoV2 infection for the society.
- Identification of specific phenoytpes and biomarkers of Post-COVID syndrome to improve prediction, prevention, diagnosis and treatment.
- Validation of new technologies (patient app, smartwatches, internet based psychological interventions) for early recognition and care of Post-COVID patients.
- Development of international and multidisciplinary recommendations/guideliens for the diagnosis and treatment of Post-COVID syndrome.
- Cross-sectoral and interdisciplinary care concept for Post-COVID integrating tailored prevention, pharmacotherapies and rehabilitation.
- Regular evaluation of the newly developed care structures, patient pathways, the effects of interdisciplinary treatment strategies on the course of the disease.
- Interdisciplinary clinical and research interactions on a national and international level.

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CONCLUSION

While most people with COVID-19 recover completely, a substantial number of patients experience prolonged symptoms. Addressing the patient´s needs of Post-COVID syndrome requires a significant investment in existing resources and funding. The EAN and EPA join forces by organizing regular meetings of the "Post-COVID working groups". It is planned to combine data from longitudinal cohorts from both organizations to establish predictive data sets to identify individuals at risk for developing Post-COVID syndrome. In addition, clinical trails are underway to develop evidence based treatments of Post-COVID mental and neurological syndromes. A special attention is being paid to cognitive outcome as they form the basis of unfavourable outcome in a substantial proportion of patients with Post-COVID-syndrom.

LITERATURE

1. Dong E, Du H, Gardner L. An interactive web-based dashboard to track COVID-19 in real time. Lancet Infect Dis. 2020 May;20(5):533-534. doi: 10.1016/S1473-3099(20)30120-1. Epub 2020 Feb 19. Erratum in: Lancet Infect Dis. 2020 Sep;20(9):e215. PMID: 32087114; PMCID: PMC7159018.
2. https://covid19.who.int
3. Román GC, Spencer PS, Reis J, Buguet A, Faris MEA, Katrak SM, Láinez M, Medina MT, Meshram C, Mizusawa H, Öztürk S, Wasay M; WFN Environmental Neurology Specialty Group. The neurology of COVID-19 revisited: A proposal from the Environmental Neurology Specialty Group of the World Federation of Neurology to implement international neurological registries. J Neurol Sci. 2020 Jul 15;414:116884. doi: 10.1016/j.jns.2020.116884. Epub 2020 May 7. PMID: 32464367; PMCID:PMC7204734.
4. Beghi E, Helbok R, Crean M, Chou SH, McNett M, Moro E, Bassetti C; EAN Neuro-COVID Task Force. The European Academy of Neurology COVID-19 registry (ENERGY): an international instrument for surveillance of neurological complications in patients with COVID-19. Eur J Neurol. 2021 Oct;28(10):3303-3323. doi: 10.1111/ene.14652. Epub 2021 Jan 3. PMID: 33220127; PMCID:PMC7753513.
5. Helbok R, Chou SH, Beghi E, Mainali S, Frontera J, Robertson C, Fink E, Schober M, Moro E, McNett M, Bassetti CL; GCS-NeuroCOVID consortium; EAN COVID task force. NeuroCOVID: it's time to join forces globally. Lancet Neurol. 2020 Oct;19(10):805-806. doi: 10.1016/S1474-4422(20)30322-7.Epub 2020 Sep 16. PMID: 32949535; PMCID: PMC7494307.
6. Beghi E, Helbok R, Ozturk S, Karadas O, Lisnic V, Grosu O, Kovács T, Dobronyi L, Bereczki D, Cotelli MS, Turla M, Davidescu EI, Popescu BO, Valzania F, Cavallieri F, Ulmer H, Maia LF, Amodt AH, Armon C, Brola W, Victoria G, Riahi A, Krehan I, von Oertzen T, Azab MA, Crean M, Lolich M, Lima MJ, Sellner J, Perneczky J, Jenkins T, Meoni S, Bianchi E, Moro E, Bassetti CLA; ENERGY Study Group. Short- and long-term outcome and predictors in an international cohort of patients with neuro-COVID-19. Eur J Neurol. 2022 Jun;29(6):1663-1684. doi: 10.1111/ene.15293. Epub 2022 Mar 7. PMID: 35194889; PMCID: PMC9111799.
7. Chou SH, Beghi E, Helbok R, Moro E, Sampson J, Altamirano V, Mainali S, Bassetti C, Suarez JI, McNett M; GCS-NeuroCOVID Consortium and ENERGY Consortium. Global Incidence of Neurological Manifestations Among Patients Hospitalized With COVID-19-A Report for the GCS-NeuroCOVID Consortium and the ENERGY Consortium. JAMA Netw Open. 2021 May

https://doi.org/10.1192/j.eurpsy.2022.2317 Published online by Cambridge University Press

3;4(5):e2112131. doi: 10.1001/jamanetworkopen.2021.12131. PMID: 33974053; PMCID:PMC8114143.

8. Adorjan K, Heindl B, Stubbe HC. Post-COVID[LMU]: Post-COVID[LMU]: implementation and evaluation of an interdisciplinary and cross-sectoral healthcare and research network for evidence-based treatment of patients with severe post-COVID syndrome]. Nervenarzt. 2022 Jun 13:1–7. German. doi: 10.1007/s00115-022-01322-1. Epub ahead of print. PMID: 35695907; PMCID: PMC9190193.
9. Jiang DH, Roy DJ, Gu BJ, Hassett LC, McCoy RG. Postacute Sequelae of Severe Acute Respiratory Syndrome Coronavirus 2 Infection: A State-of-the-Art Review. JACC Basic Transl Sci. 2021 Sep-Oct;6(9):796-811. doi: 10.1016/j.jacbts.2021.07.002. Epub 2021 Sep 15. PMID: 34541421; PMCID:PMC8442719.
10. https://doi.org/10.1016/j.socscimed.2020.113426
11. Soriano JB, Murthy S, Marshall JC, Relan P, Diaz JV; WHO Clinical Case Definition Working Group on Post-COVID-19 Condition. A clinical case definition of post-COVID-19 condition by a Delphi consensus. Lancet Infect Dis. 2022 Apr;22(4):e102-e107. doi: 10.1016/S1473-3099(21)00703-9. Epub 2021 Dec 21. PMID: 34951953; PMCID: PMC8691845.
12. https://www.ons.gov.uk
13. Balcom EF, Nath A, Power C. Acute and chronic neurological disorders in COVID-19: potential mechanisms of disease. Brain. 2021 Dec 31;144(12):3576-3588. doi: 10.1093/brain/awab302. PMID: 34398188; PMCID: PMC8719840.
14. Spudich S, Nath A. Nervous system consequences of COVID-19. Science. 2022 Jan21;375(6578):267-269. doi: 10.1126/science.abm2052. Epub 2022 Jan 20. PMID: 35050660.
15. Balcom EF, Nath A, Power C. Acute and chronic neurological disorders in COVID-19: potential mechanisms of disease. Brain. 2021 Dec 31;144(12):3576-3588. doi:10.1093/brain/awab302.PMID: 34398188; PMCID: PMC8719840.
16. Pinzon RT, Wijaya VO, Jody AA, Nunsio PN, Buana RB. Persistent neurological manifestations in long COVID-19 syndrome: A systematic review and meta-analysis. J Infect Public Health. 2022 Jun 23;15(8):856-869. doi: 10.1016/j.jiph.2022.06.013. Epub ahead of print. PMID: 35785594; PMCID: PMC9221935.
17. Helms J, Kremer S, Merdji H, Clere-Jehl R, Schenck M, Kummerlen C, Collange O, Boulay C, Fafi-Kremer S, Ohana M, Anheim M, Meziani F. Neurologic Features in Severe SARS-CoV-2 Infection. N Engl J Med. 2020 Jun 4;382(23):2268-2270. doi: 10.1056/NEJMc2008597. Epub 2020 Apr 15. PMID:32294339; PMCID: PMC7179967.
18. Hosp JA, Dressing A, Blazhenets G, Bormann T, Rau A, Schwabenland M, Thurow J, Wagner D, Waller C, Niesen WD, Frings L, Urbach H, Prinz M, Weiller C, Schroeter N, Meyer PT. Cognitive impairment and altered cerebral glucose metabolism in the subacute stage of COVID-19. Brain. 2021 May 7;144(4):1263-1276. doi: 10.1093/brain/awab009. PMID: 33822001; PMCID:PMC8083602.
19. Blazhenets G, Schroeter N, Bormann T, Thurow J, Wagner D, Frings L, Weiller C, Meyer PT, Dressing A, Hosp JA. Slow but Evident Recovery from Neocortical Dysfunction and Cognitive Impairment in a Series of Chronic COVID-19 Patients. J Nucl Med. 2021 Jul 1;62(7):910-915. doi:10.2967/jnumed.121.262128. Epub 2021 Mar 31. PMID: 33789937; PMCID: PMC8882885.
20. Taquet M, Dercon Q, Luciano S, Geddes JR, Husain M, Harrison PJ. Incidence, co-occurrence, and evolution of long-COVID features: A 6-month retrospective cohort study of 273,618 survivors of COVID-19. PLoS Med. 2021 Sep 28;18(9):e1003773. doi: 10.1371/journal.pmed.1003773. PMID:34582441; PMCID: PMC8478214.
21. Graham EL, Clark JR, Orban ZS, Lim PH, Szymanski AL, Taylor C, DiBiase RM, Jia DT, Balabanov R, Ho SU, Batra A, Liotta EM, Koralnik IJ. Persistent neurologic symptoms and cognitive dysfunction in non-hospitalized Covid-19 "long haulers". Ann Clin Transl Neurol. 2021 May;8(5):1073-1085. doi:10.1002/acn3.51350. Epub 2021 Mar 30. PMID: 33755344; PMCID: PMC8108421.

https://doi.org/10.1192/j.eurpsy.2022.2317 Published online by Cambridge University Press

22. Rass V, Beer R, Schiefecker AJ, Lindner A, Kofler M, Ianosi BA, Mahlknecht P, Heim B, Peball M, Carbone F, Limmert V, Kindl P, Putnina L, Fava E, Sahanic S, Sonnweber T, Löscher WN, Wanschitz JV, Zamarian L, Djamshidian A, Tancevski I, Weiss G, Bellmann-Weiler R, Kiechl S, Seppi K, Loeffler-Ragg J, Pfausler B, Helbok R. Neurological outcomes 1 year after COVID-19 diagnosis: A prospective longitudinal cohort study. Eur J Neurol. 2022 Jun;29(6):1685-1696. doi: 10.1111/ene.15307. Epub2022 Mar 23. PMID: 35239247; PMCID: PMC9111823.
23. Beghi E, Helbok R, Ozturk S, Karadas O, Lisnic V, Grosu O, Kovács T, Dobronyi L, Bereczki D, Cotelli MS, Turla M, Davidescu EI, Popescu BO, Valzania F, Cavallieri F, Ulmer H, Maia LF, Amodt AH, Armon C, Brola W, Victoria G, Riahi A, Krehan I, von Oertzen T, Azab MA, Crean M, Lolich M, Lima MJ, Sellner J, Perneczky J, Jenkins T, Meoni S, Bianchi E, Moro E, Bassetti CLA; ENERGY Study Group. Short- and long-term outcome and predictors in an international cohort of patients with neuro-COVID-19. Eur J Neurol. 2022 Jun;29(6):1663-1684. doi: 10.1111/ene.15293. Epub 2022 Mar 7.PMID: 35194889; PMCID: PMC9111799.
24. Ceban F, Leber A, Jawad MY, Yu M, Lui LMW, Subramaniapillai M, Di Vincenzo JD, Gill H, Rodrigues NB, Cao B, Lee Y, Lin K, Mansur RB, Ho R, Burke MJ, Rosenblat JD, McIntyre RS. Registered clinical trials investigating treatment of long COVID: a scoping review and recommendations for research. Infect Dis (Lond). 2022 Jul;54(7):467-477. doi: 10.1080/23744235.2022.2043560. Epub 2022 Mar 14. PMID: 35282780; PMCID: PMC8935463.
25. Mazza MG, De Lorenzo R, Conte C, Poletti S, Vai B, Bollettini I, Melloni EMT, Furlan R, Ciceri F, Rovere-Querini P; COVID-19 BioB Outpatient Clinic Study group, Benedetti F. Anxiety and depression in COVID-19 survivors: Role of inflammatory and clinical predictors. Brain Behav Immun. 2020 Oct;89:594-600. doi: 10.1016/j.bbi.2020.07.037. Epub 2020 Jul 30. PMID: 32738287;PMCID: PMC7390748.
26. Vindegaard N, Benros ME. COVID-19 pandemic and mental health consequences: Systematic review of the current evidence. Brain Behav Immun. 2020 Oct;89:531-542.doi:10.1016/j.bbi.2020.05.048. Epub 2020 May 30. PMID: 32485289; PMCID: PMC7260522.
27. Taquet M, Luciano S, Geddes JR, Harrison PJ. Bidirectional associations between COVID-19 and psychiatric disorder: retrospective cohort studies of 62 354 COVID-19 cases in the USA. Lancet Psychiatry. 2021 Feb;8(2):130-140. doi: 10.1016/S2215-0366(20)30462-4. Epub 2020 Nov 9.Erratum in: Lancet Psychiatry. 2021 Jan;8(1):e1. PMID: 33181098; PMCID: PMC7820108.
28. Taquet M, Geddes JR, Husain M, Luciano S, Harrison PJ. 6-month neurological and psychiatric outcomes in 236 379 survivors of COVID-19: a retrospective cohort study using electronic health records. Lancet Psychiatry. 2021 May;8(5):416-427. doi: 10.1016/S2215-0366(21)00084-5. Epub2021 Apr 6. PMID: 33836148; PMCID: PMC8023694.
29. Rogers JP, Chesney E, Oliver D, Pollak TA, McGuire P, Fusar-Poli P, Zandi MS, Lewis G, David AS. Psychiatric and neuropsychiatric presentations associated with severe coronavirus infections: a systematic review and meta-analysis with comparison to the COVID-19 pandemic. Lancet Psychiatry. 2020 Jul;7(7):611-627. doi: 10.1016/S2215-0366(20)30203-0. Epub 2020 May 18.PMID: 32437679; PMCID: PMC7234781.
30. Mehta P, McAuley DF, Brown M, Sanchez E, Tattersall RS, Manson JJ; HLH Across Speciality Collaboration, UK. COVID-19: consider cytokine storm syndromes and immunosuppression. Lancet. 2020 Mar 28;395(10229):1033-1034. doi: 10.1016/S0140-6736(20)30628-0. Epub2020Mar 16. PMID: 32192578; PMCID: PMC7270045.
31. Mazza MG, De Lorenzo R, Conte C, Poletti S, Vai B, Bollettini I, Melloni EMT, Furlan R, Ciceri F, Rovere-Querini P; COVID-19 BioB Outpatient Clinic Study group, Benedetti F. Anxiety and depression in COVID-19 survivors: Role of inflammatory and clinical predictors. Brain Behav Immun. 2020 Oct;89:594-600. doi: 10.1016/j.bbi.2020.07.037. Epub 2020 Jul 30. PMID: 32738287;PMCID: PMC7390748.

https://doi.org/10.1192/j.eurpsy.2022.2317 Published online by Cambridge University Press

32. Wohleb ES, Franklin T, Iwata M, Duman RS. Integrating neuroimmune systems in the neurobiology of depression. Nat Rev Neurosci. 2016 Aug;17(8):497-511. doi: 10.1038/nrn.2016.69. Epub 2016Jun 9. PMID: 27277867.
33. Benedetti F, Palladini M, Paolini M, Melloni E, Vai B, De Lorenzo R, Furlan R, Rovere-Querini P, Falini A, Mazza MG. Brain correlates of depression, post-traumatic distress, and inflammatory biomarkers in COVID-19 survivors: A multimodal magnetic resonance imaging study. Brain Behav Immun Health. 2021 Dec;18:100387. doi: 10.1016/j.bbih.2021.100387. Epub 2021 Nov 2. PMID:34746876; PMCID: PMC8562046.
34. Hellwig S, Domschke K. Post-COVID-Syndrom – Fokus Fatigue [Post-COVID syndrome-Focus fatigue]. Nervenarzt. 2022 May 23:1–7. German. doi: 10.1007/s00115-022-01306-1. Epub ahead of print. PMID: 35606656; PMCID: PMC9126432.
35. Wong TL, Weitzer DJ. Long COVID and Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS)-A Systemic Review and Comparison of Clinical Presentation and Symptomatology. Medicina (Kaunas). 2021 Apr 26;57(5):418. doi: 10.3390/medicina57050418. PMID: 33925784;PMCID: PMC8145228.
36. https://www.awmf.org/uploads/tx_szleitlinien/020-027l_S1_Post_COVID_Long_COVID_2021-07.pdf
37. Lenze EJ, Mattar C, Zorumski CF, Stevens A, Schweiger J, Nicol GE, Miller JP, Yang L, Yingling M, Avidan MS, Reiersen AM. Fluvoxamine vs Placebo and Clinical Deterioration in Outpatients With Symptomatic COVID-19: A Randomized Clinical Trial. JAMA. 2020 Dec 8;324(22):2292-2300.doi:10.1001/jama.2020.22760. PMID: 33180097; PMCID: PMC7662481.
38. Mandal S, Barnett J, Brill SE, Brown JS, Denneny EK, Hare SS, Heightman M, Hillman TE, Jacob J, Jarvis HC, Lipman MCI, Naidu SB, Nair A, Porter JC, Tomlinson GS, Hurst JR; ARC Study Group. 'Long-COVID': a cross-sectional study of persisting symptoms, biomarker and imaging abnormalities following hospitalisation for COVID-19. Thorax. 2021 Apr;76(4):396-398. doi: 10.1136/thoraxjnl2020-215818. Epub 2020 Nov 10. PMID: 33172844; PMCID: PMC7661378.
39. Myall KJ, Mukherjee B, Castanheira AM, Lam JL, Benedetti G, Mak SM, Preston R, Thillai M, Dewar A, Molyneaux PL, West AG. Persistent Post-COVID-19 Interstitial Lung Disease. An Observational Study of Corticosteroid Treatment. Ann Am Thorac Soc. 2021 May;18(5):799-806. doi:10.1513/AnnalsATS.202008-1002OC. PMID: 33433263; PMCID: PMC8086530.
40. Cellai M, O'Keefe JB. Characterization of Prolonged COVID-19 Symptoms in an Outpatient Telemedicine Clinic. Open Forum Infect Dis. 2020 Sep 12;7(10):ofaa420. doi: 10.1093/ofid/ofaa420. PMID: 33117851; PMCID: PMC7543492.

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