bijwerkingen centrumlareb

Long COVID-like symptoms following immunization with COVID-19 vaccines

Introduction

To date, the following five COVID-19 vaccines have been authorized for *active immunization against SARS-CoV-2* in The Netherlands: BioNTech/Pfizer (Comirnaty®)(1), Moderna (Spikevax®)(2), AstraZeneca (Vaxzevria®)(3), Janssen (Jcovden®)(4), and Novavax (Nuvaxovid®)(5). BioNTech/Pfizer and Moderna are both mRNA vaccines, AstraZeneca and Janssen are both vector-based vaccines, and Novavax is a protein subunit vaccine containing a saponin based matrix-M immune-stimulating adjuvant (1-5). Since the start of the Dutch mass immunization program against SARS-CoV-2 (January 2021), until the latest Corona dashboard update on October 1st 2023, 12,370,518 persons have received the primary series and 4,187,145 have received a repeat dose during the last round of repeat vaccinations in the fall of 2022 (6, 7). Until August 16th 2023 the Netherlands pharmacovigilance center Lareb received 254,293 reports on COVID-19 vaccines directly from patients and health care professionals. Most reports concerned BioNTech/Pfizer (127,995) followed by Moderna (53,497), AstraZeneca (38,036), Janssen (15,099), and Novavax (60).

The Netherlands Pharmacovigilance Centre Lareb aimed to investigate whether there were specific clinical descriptions that could indicate hitherto unknown, long-lasting, adverse reactions related to COVID-19 vaccination. In total, 2,282 reports were received containing a total of 5,245 long-lasting Adverse Events Following Immunization (AEFI). Long-lasting AEFI were defined as *AEFI with a time to onset of 28 days or less after COVID-19 vaccination and a duration of 6 months or more*. Duration is only reported for recovered AEFI. For not recovered and recovering AEFI, an assumption of the duration was made by subtracting the startdate of AEFI from the date of reporting. Reports that do not adhere to this, were not selected. Also, reports containing long-lasting AEFI with a time to onset within 28 days of COVID-19 infection were not selected to reduce the chance of reported symptoms being related to COVID-19 infection. In addition, reports with (serious) AEFI for which a long time to recovery is to be expected such as Guillain-Barré syndrome (GBS) or various forms of thrombosis were not selected.

Most reported long-lasting AEFI were fatigue (n=531), myalgia (n=399), arthralgia (n=382), headache (n=283), and malaise (n=250). Less, but also remarkably frequent reported long-lasting symptoms are dyspnoea (n=86) and palpitations (n=66). Also other 'Long COVID-like symptoms' like paraesthesia (33), muscular weakness (23) and disturbance in attention (24) were reported. The reports contain diverse combinations of long-lasting AEFI. To get an indication of where to focus on, an exploratory analysis of all selected reports on long- lasting AEFI was performed. Combinations of reported AEFI were investigated to see whether there were clinical clusters in the data. Sets of individual cases were reviewed by clinical assessors for the presence of a clinical description, whether a patient was seen by a healthcare professional, diagnostic procedures were performed and if a diagnosis was made, among other elements of information. Based on this review, in combination with case-descriptions of Long COVID from both scientific literature as well as press-releases it was decided to further focus our analysis on Long COVID-like symptoms (8-11).

Selection of reports

Based on the previously mentioned case-descriptions of Long COVID, we have classified the following symptom-groups that are commonly reported in Long COVID after COVID-19 infection: *peripheral neurological symptoms, cognitive dysfunction symptoms, cardiovascular symptoms including POTS,*

hypotension and hypertension, and dyspnoea symptoms (see Appendix A for included MedDRA terms). We have selected the following reports for further analysis: Reports containing the MedDRA term *post vaccination syndrome*, *post-acute COVID-19 syndrome*, *chronic fatigue syndrome*, *or viral fatigue syndrome*; reports containing symptoms from at least two or more of the above listed *Long COVID symptom-groups*. These reports can also include other long-lasting AEFI such as headache or fatigue. Of these selected reports, the most frequently reported (combinations of) long-lasting AEFI, patient demographics and AEFI characteristics are described. Additionally, we described clinical presentation, diagnostics and course of these 'Long COVID-like' symptoms in more detail.

Reports

There were 78 reports selected which contained 425 long-lasting symptoms in total. On average, these reports contained 6 long-lasting symptoms per report. Almost all cases were reported by consumers or other non-health care professionals (n=77; 99%), one case was reported by a physician. The most frequently reported COVID-19 vaccine brand was Pfizer (59%), followed by Moderna (19%), Janssen (12%), and AstraZeneca (10%). Of these cases, 59 concerned females and 19 males with a median age of 47 years. Median time to onset from COVID-19 vaccination to startdate of long-lasting AEFI was 3 days. Median duration was quite long, 248 days, with most AEFI (98.1%) still not (fully) recovered at time of reporting. Of these 425 long-lasting symptoms, 40 (9%) were considered serious according to CIOMS criteria; 1 AEFI was ''life threathening'', 8 AEFI led to ''hospitalisation'', 23 AEFI were ''disabling'', and 11 AEFI were described as ''other medically important condition''. In 39 cases (50%) a previous COVID-19 infection was reported.

Reported symptoms

The most frequently reported symptoms are shown in Table 1.

Table 1. Most frequently reported symptoms.

AEFI	Times reported	% reported
Dyspnoe	41	53
Fatigue	34	44
Malaise	20	26
Chest pain	19	24
Palpitations	19	24
Dizziness	18	23
Headache	17	22
Myalgia	16	21
Arthralgia	15	19
Disturbance in attention	10	13
Post-acute COVID-19 syndrome	10	13
Nausea	9	12
Injection-site pain	8	10
Chest discomfort	7	9
Memory impairment	7	9
Balance disorder	6	8
Chills	6	8
Muscular weakness	5	6
Paraesthesia	5	6
Pyrexia	5	6

Long-lasting AEFI that were co-reported most often were malaise, fatigue, and headache sometimes in combination with myalgia, dyspnoea, arthralgia, disturbance in attention and/or nausea.

Clinical characteristics

Overall, the burden of symptoms on daily life is remarkable in these reports. The number of patients that described to be disabled from work and/or normal daily functionioning was 16 out of 78 (21%). More than half of these patients sought medical care. In 41 cases (53%) medical diagnostics were performed, 22 patients (28%) were referred to a medical specialist, and in 16 cases a diagnosis was made. In 19 cases (21%) treatment focused on physical reconditioning was received in the form of ergotherapy, physiotherapy, specialised physiotherapy for Long COVID, a rehabilitation trajectory or a combination of therapies. Furthermore, for 8 cases (10%) two or more medical specialists were consulted.

Table 2. Overview of clincal characteristics of cases.

Characteristic	Times reported
Effect on daily life	
Disabled from work and/or normal daily functionioning	16
Unknown	62
Previous COVID-19 infection	
Yes	39
Unknown	39
Alternative causes present	
Yes	13
Long COVID*	4
Chronic fatigue syndrome	2
COPD	2
Autism	1
Chronic leukemia	1
Risperidon as concomitant medication	1
Hypertension	1
Interstitial lung disease	1
Rheumatoid arthritis	1
No	0
Unknown	65
Medical diagnostics performed	
Yes	41
Blood laboratory investigations	21
ECG	15
Pulmonary function tests	7
Chest X-ray	6
Bicycle exercise test	6
CT	5
Cardiac ultrasound	5
MRI	4
Coronary angiography	4
Electromyography	2
Memory and psychological evaluation	1
Abdominal ultrasound	1
Colonoscopy	1
Thyroid ultrasound en biopsy	1
Bronchoalveolar lavage	1
No	10
Unknown	27
Referred to a medical specialist	
Yes	22
Cardiologist	14
Pulmonologist	7
Neurologist	6
Internist	4
Reumatologist	1

Characteristic	Times reported
≥2 medical specialists	8
No	2
Unknown	54
Long COVID-like symptoms categories	
Cardiovascular symptoms	50
Dyspnoea-related symptoms	43
Peripheral neurological symptoms	28
Cognitive dysfunction-related symptoms	23
Diagnosis was made	
Yes	16
Long COVID*	11
New-onset	7
Exacerbation	4
Chronic fatigue syndrome	3
New-onset	1
Exacerbation	2
Hyperthyreoidism	2
Pericarditis	1
Neuropathy	1
Bronchial hyperreactivity	1
Cardiac arrhythmia	1
Mitral valve disorder	1
No	7
Unknown	55
Received treatment	
Yes	19
Ergotherapy	5
Physiotherapy	9
Pulmonary Physiotherapy	1
Specialised physiotherapy for Long COVID	1
Rehabilitation trajectory	2
Amitryptillin	2
Celecoxib and paracetamol	1
Anticoagulant and antihypertensives	1
Ibuprofen and colchicine	1
Inhalation corticosteroids	1
No	2
Unknown	57

*For most reports with a medical history and/or with a diagnosis of Long COVID (exacerbation) it is unknown if this diagnosis was confirmed by a medical specialist.

Although there was a great diversity of symptoms overall, it was possible to identify some commonality in the cases. Fatigue with cognitive impairment, sometimes described as brainfog, was mentioned in some of the reports. Sometimes in combination with physical deconditioning. In some cases there were also cardiovascular, neurological or dyspnoea-related symptoms. Commonly reported descriptions of symptoms include difficulty thinking, concentration ability impaired, word finding problems, not being able to deal with stimuli, memory loss, shortness of breath, headache, myalgia, dizziness, and chest pain. Several reporters describe to be unable to function, are incapacitated and feel there is no hope for improvement. Some patients report a possible diagnosis of Long COVID in the absence of a (confirmed) COVID-19 infection as medical specialists found their symptoms comparable.

Literature and other sources

A medical case definition for Long COVID following COVID-19 infection was developed by the World Health Organization (WHO), there are however no strict diagnostic criteria yet (12). Long COVID is defined as the continuation or development of new symptoms 3 months after the initial SARS-CoV-2

infection, with these symptoms lasting for at least 2 months with no other explanation. The most commonly reported symptoms of Long COVID include fatigue, dyspnoea and cognitive dysfunction but there are more than 200 symptoms that have been reported for this syndrome that can have an impact on everyday functioning (13, 14). Recently, a study has been published in JAMA which provides a framework for identifying Long COVID cases based on symptoms that were present more often in COVID-19 infected participants at 6 months or more after infection compared with uninfected participants (13). Symptoms seen more often in COVID-19 infected participants included post-exertional malaise, fatigue, brain fog, dizziness, gastrointestinal symptoms, palpitations, changes in sexual desire or capacity, loss of or change in smell or taste, thirst, chronic cough, chest pain, and abnormal movements.

Chronic fatigue syndrome (CFS) and Long COVID share similar symptoms and biological abnormalities and are both related to infections (15, 16). Researchers have raised the question if these two syndromes actually represent two examples of a broader illness in which symptoms are generated by a carefully orchestrated, stereotyped, multi-system response to infection and injury. A distinctive symptom of both Long COVID and CSF is post-exertional malaise, which is associated with a worsening of fatigue- and pain-related symptoms after acute mental or physical exercise (17, 18).

There are few pharmacovigilance centers or medicines regulatory authorities worldwide that have published results on reported long-lasting symptoms following COVID-19 vaccination in their country. The Paul-Ehrlich-Institute, the German Federal Institute for Vaccines and Biomedicines, issued a statement on ''Post-Vac-syndrome'' on May 19th 2023 stating that ''Post-Vac-syndrome'' is not a term that refers to a medically-defined disease and is not subject to a clear case definition for reporting a suspected adverse event following immunization (19). The institute analysed reports received by the European Medicines Agency (EMA) till May 19th 2023 containing the following medDRA Prefered Terms: chronic fatigue syndrome, post vaccination syndrome, postural orthostatic tachycardia syndrome (POTS), and post-acute COVID-19 syndrome. Their data-set, which contained a total of 2,817 reports registered worldwide, suggests that the term ''Post-Vac-syndome'' describes a variety of long-lasting symptoms that are comparable to Long COVID. Most reports contained an above-average number of symptoms and often lacked further diagnostic information. Interestingly, more than 50% of suspected cases registered worldwide were reported in Germany, implicating an affect of the amount of media attention that ''Post-Vac-syndrome'' received in this country. The Paul-Ehrlich-Institute concluded that no medically plausible indication of a direct causal relationship between the Long COVID-like symptoms and COVID-19 vaccination was found and therefore no safety signal was issued.

Swissmedic, the Swiss Medicines Regulatory Authority, studied reports of long-lasting AEFI with COVID-19 vaccines received by their institution (20). AEFI with a duration of at least 180 days and outcome ''not recovered'' were considered long-lasting. They found 556 reports that met these inclusion criteria with a total of 1,787 AEFI. The most frequently reported AEFI were urticaria (174 times), pruritus (97 times), fatigue (93 times), headache (70 times), arthralgia (34 times), paraesthesia (33 times), dizziness (32 times), dyspnoea (31 times), myalgia (29 times), and rash (29 times). They conclude that AEFI that were previously known to have a short duration should be further investigated. On their website they have issued a statement regarding ''post-vaccine syndrome'' describing that long-lasting symptoms with a temporal relationship to COVID-19 vaccination are often highly heterogeneous, cover a broad spectrum, and show overlap with Long COVID and chronic fatique syndrome (21). They further underline that there is no recognised standard definition of this syndrome or how it can be distinguished from Long COVID.

In literature, case reports have been published on long-lasting AEFI with COVID-19 vaccines describing a broad spectrum of symptoms (22, 23). A news-item published in January 2022 in the scientific journal Science, describes online communities with thousands of participants with complex, variable, lingering symptoms following COVID-19 vaccination which are difficult to diagnose or even categorize (10). These symptoms include fatigue, severe headaches, nerve pain, blood pressure swings, heart rate fluctuations, muscle weakness, and short-term memory problems. This newsitem also describes a brief study of 34 of these patients. Patients underwent neurological, cardiac, and other tests including lumbar punctures and skin biopsies. The researchers found a temporal relationship but could not draw any conclusions on a causal relationship with COVID-19 vaccination. To date, their case-series has not been published. Schieffer, a German cardiologist who initiated an outpatient clinic for the evaluation of patients with long-lasting symptoms following COVID-19 vaccination, published a perspective paper in which he describes a pattern of symptoms comparable to those of Long COVID but without a preceding symptomatic COVID-19 infection (11). Symptoms may consist of a combination of fatigue, myalgia, chest-pain, dyspnoea, and neurological symptoms like brainfog and concentration impairment. In addition, some patients suffered from dermatological and gastro-intestinal disorders like diarrhoea, skin rush, and burning skin. Schieffer hypothesises a hyperallergic or hyperinflammatory pathophysiology resulting from an imbalanced Renin-Angiotensin-System (RAS). His paper, however, does not contain any further data on these patients or their symptoms. The Yale Listen study at Yale University has included 241 participants with self-reported ''post-vaccination syndrome'' who were recruited from an online patient community (24). The purpose of this study was to understand Long Covid, post-vaccine adverse events and the corresponding immune responses by collecting information about symptoms and medical history from participants. Preliminary results of this study have appeared online but have not yet been certified by peer-review. In a newsarticle published by Science, the immunology department at Yale University has stated that further investigatations will be conducted with the aim to correlate symptoms with immune cell patterns in blood samples of some of these patients (25). Long-lasting AEFI that are further pointed out in this newsarticle are POTS and small fiber neuropathy on which several case reports have been published.

In the Netherlands, C-support, a government appointed organisation, is responsible for the support of people with Long COVID and also offers support for people with long-lasting (> 3 months) symptoms following COVID-19 vaccination since November 2021 (26). Over a time period of 18 months, more than 750 persons have contacted C-support because of long-lasting symptoms following COVID-19 vaccination (27). Of these persons, more than 50% experience any previous symptoms of COVID-19 infection. The most commonly reported symptoms were fatigue (77%), concentration or memory impairment (63%; 54%), vertigo (53%), dyspnoea (52%), difficulty in processing sensory stimuli (52%), and headache (49%). These symptoms are highly similar to those experienced by patients diagnosed with Long COVID. On average, these persons suffered from 10 different symptoms, some persons, however, experienced only one or several very specific symptoms.

Mechanism

Work is ongoing to unravel the underlying pathophysiology of Long COVID after SARS-CoV-2 infection. There are hypotheses explaining exercise tolerance and post-exertional malaise in Long COVID by various pathways such as mitochondrial dysfunction, amyloid-containing deposit

accumulation in blood vessels causing local hypoxia, systemic and local inflammation, disturbed immunological responses, hormonal imbalance, and viral persistence (28-35).
A recent longitudinal case-control study provided new insights into the pathophysiology of post-exertional malaise in patients with Long COVID (17). This study showed that skeletal muscle structure is associated with a lower exercise capacity in patients, and local and systemic metabolic disturbances, severe exercise-induced myopathy and tissue infiltration of amyloid-containing deposits in skeletal muscles of patients with Long COVID worsen after induction of post-exertional malaise. A mechanism for Long COVID-like symptoms after COVID-19 vaccination is unknown. An immune overreaction to SARS-CoV-2 spike protein has been speculatively mentioned as a potential cause, but more research is needed (25).

Discussion

This report was preceded by an extensive exploratory analysis of long-lasting AEFI after COVID-19 vaccination. For this analysis we used strict selection criteria; AEFI had to be present for at least 6 months to be sure of the long-lasting character of the adverse events, the AEFI had to have a time to onset within a month after vaccination and restrictions were made on cases where patients had a recent SARS-CoV-2 infection. Due to the use of these strict criteria, there are probably more cases that also describe 'Long COVID-like' symptoms but were not included in the analysed dataset because they did not adhere to the inclusion criteria. The goal of our current report, however, was not to give a complete description of all (potential) cases, but to demonstrate that there are cases of long-lasting symptoms which are alike to Long COVID after SARS-CoV-2 infection.
The choice for the case selection for this report was based on analysis of (co-)reported AEFI and available clinical information in the previously described 2,282 reports of long-lasting AEFI, in combination with case descriptions in literature, including grey literature, press-releases and discussions with field-experts. Because fatigue was the most commonly mentioned AEFI and present in a large part of the reports (n=531), and thereby, would not attribute to selection, we did not use fatigue as a selection criterium for 'Long COVID-like' symptoms. Long-lasting fatigue was present in 34 out of the 78 selected cases with 'Long COVID-like' symptoms.
Although the reported combinations of 'Long COVID-like' symptoms in 78 reports share some resemblance with Long COVID and a temporal relationship with COVID-19 vaccination is present, establishing a causal relationship is not possible. In 47% of the reports no medical diagnostics were performed, or these were not reported. So it is not known whether there are other causes. In 9% of cases an alternative diagnosis was made explaining, at least part of, the reported symptoms. But in the remaing 44% no explanation was found for the complaints.
Considering the resemblance with Long COVID, the most important consideration in the evaluation of causality between COVID-19 vaccination and these long-lasting symptoms is the possiblity of undiagnosed Long COVID after COVID-19 infection previous to or within a smal time window of COVID-19 vaccination, as an alternative explanation. Reports with a time to onset of 28 days or less between COVID-19 infection and startdate of symptoms were not selected for this analysis. It is, however, still possible that patients in the selected reports have had undiagnosed Long COVID after COVID-19 infection for the following reasons: time to onset of symptoms could be longer than 28 days after COVID-19 infection; patients did not report their COVID-19 infection; patients had an undiagnosed COVID-19 infection because of either mild/asymptomatic course of infection or infection occured in the time period when testing was not yet publicly available. Long COVID is described to occur also frequently after mild and, to a lesser extent, asymptomatic COVID-19 infection (36). For most patients (85%) symptoms started between January and September 2021. This

means, most of these symptoms were reported in the period that the Alpha and Delta COVID-19 variants were prevalent. COVID-19 variants changed over time with the first Omicron variant arising in December 2021. Studies on Long COVID after COVID-19 infection show lower rates of Long COVID after Omicron variants compared to Alpha and Delta variants (37).

Conclusion

Reports were identified with combinations of 'Long COVID-like' symptoms that share resemblance with Long COVID. A causal relationship with COVID-19 vaccination cannot be established since potential alternative causes could not be excluded. Further epidemiological, clinical and immunological research is needed.

References

1. European Public Assessment Report – Product information of COVID-19 vaccine BioNTech/Pfizer (Comirnaty®). (version date 6-5-2022) [Available from: https://www.ema.europa.eu/en/documents/product-information/comirnaty-epar-product-information_en.pdf.
2. European Public Assessment Report – Product information of COVID-19 vaccine Moderna (Spikevax®). (Last updated: 10-5-2022) [Available from: https://www.ema.europa.eu/en/documents/product-information/spikevax-previously-covid-19-vaccine-moderna-epar-product-information_en.pdf.
3. European Public Assessment Report – Product information of COVID-19 vaccine AstraZeneca (Vaxzevria®). (Last updated: 25-5-2022). [Available from: https://www.ema.europa.eu/en/documents/product-information/vaxzevria-previously-covid-19-vaccine-astrazeneca-epar-product-information_en.pdf.
4. European Public Assessment Report – Product information of COVID-19 vaccine Janssen (Jcovden®) (Last updated: 29-4-2022). [Available from: https://www.ema.europa.eu/en/documents/product-information/jcovden-previously-covid-19-vaccine-janssen-epar-product-information_en.pdf.
5. European Public Assessment Report – Product information of COVID-19 vaccine Novavax (Nuvaxovid®). (Last updated: 21-3-2022). [Available from: https://www.ema.europa.eu/en/documents/product-information/nuvaxovid-epar-product-information_en.pdf.
6. Coronadashboard Rijksoverheid. [Available from: https://coronadashboard.rijksoverheid.nl/landelijk/vaccinaties.
7. RIVM. Cijfers COVID-19 vaccinatieprogramma. [Available from: https://www.rivm.nl/covid-19-vaccinatie/cijfers-vaccinatieprogramma.
8. Vrieze Jd. It is not in your head – some people develop long covid like symptoms after their shot. De Groene Amsterdammer, february 2, 2023.
9. NPO radio 1. Nieuws. Deze Duitse arts runt een speciale polikliniek voor mensen met langdurige klachten na vaccinatie. 2022 [Available from: https://www.nporadio1.nl/nieuws/null/3f08427c-a552-436c-b601-463180bba7e2/deze-duitse-arts-runt-een-speciale-polikliniek-voor-mensen-met-langdurige-klachten-na-vaccinatie.
10. JENNIFER COUZIN-FRANKEL GV. In rare cases, coronavirus vaccines may cause Long Covid–like symptoms: Brain fog, headaches, blood pressure swings are being probed by NIH and other researchers Science, News 20 Jan 2022 [Available from: https://www.science.org/content/article/rare-cases-coronavirus-vaccines-may-cause-long-covid-symptoms.

11. Schieffer E, Schieffer B. The rationale for the treatment of long-Covid symptoms - A cardiologist's view. Front Cardiovasc Med. 2022;9:992686.
12. WHO case-definition Long COVID [updated December 7, 2022. Available from: https://www.who.int/europe/news-room/fact-sheets/item/post-covid-19-condition.
13. Thaweethai T, Jolley SE, Karlson EW, Levitan EB, Levy B, McComsey GA, et al. Development of a Definition of Postacute Sequelae of SARS-CoV-2 Infection. JAMA. 2023;329(22):1934-46.
14. Li J, Zhou Y, Ma J, Zhang Q, Shao J, Liang S, et al. The long-term health outcomes, pathophysiological mechanisms and multidisciplinary management of long COVID. Signal Transduct Target Ther. 2023;8(1):416.
15. Appel S, Chapman J, Shoenfeld Y. Infection and vaccination in chronic fatigue syndrome: myth or reality? Autoimmunity. 2007;40(1):48-53.
16. Komaroff AL, Lipkin WI. ME/CFS and Long COVID share similar symptoms and biological abnormalities: road map to the literature. Front Med (Lausanne). 2023;10:1187163.
17. Appelman B, Charlton BT, Goulding RP, Kerkhoff TJ, Breedveld EA, Noort W, et al. Muscle abnormalities worsen after post-exertional malaise in long COVID. Nat Commun. 2024;15(1):17.
18. Vernon SD, Hartle M, Sullivan K, Bell J, Abbaszadeh S, Unutmaz D, et al. Post-exertional malaise among people with long COVID compared to myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). Work. 2023;74(4):1179-86.
19. State-ment from the Paul-Ehrlich-In-sti-tut on "Post-Vac Syn-drome" af-ter COVID-19 Vac-ci-na-tion [updated May 19 2023. Available from: https://www.pei.de/EN/newsroom/positions/covid-19-vaccines/statement-postvac.html.
20. 22nd ISoP Annual Meeting "Putting Patients First in Pharmacovigilance: International Perspectives from Global South" 6-9 November 2023 Bali, Indonesia. Drug Saf. 2023;46(11):1173-295.
21. Reports of suspected adverse reactions to COVID-19 vaccines in Switzerland – update 29 [Available from: https://www.swissmedic.ch/swissmedic/en/home/news/coronavirus-covid-19/covid-19-vaccines-safety-update-19.html.
22. Finsterer J. A Case Report: Long Post-COVID Vaccination Syndrome During the Eleven Months After the Third Moderna Dose. Cureus. 2022;14(12):e32433.
23. Finterer J, Scorza FA. A retrospective analysis of clinically confirmed long post-COVID vaccination syndrome. J Clin Transl Res. 2022;8(6):506-8.
24. The Yale LISTEN study [Available from: https://medicine.yale.edu/ycci/listen-study/.
25. Rare link between coronavirus vaccines and Long Covid–like illness starts to gain acceptance [Available from: https://www.science.org/content/article/rare-link-between-coronavirus-vaccines-and-long-covid-illness-starts-gain-acceptance.
26. C-support. Nazorg COVID-19. [Available from: https://www.c-support.nu/langdurige-klachten-na-vaccinatie/.
27. C-support. Feiten en cijfers - klachten na vaccinatie [Available from: https://www.c-support.nu/feiten-en-cijfers-klachten-na-vaccinatie/
28. Klein J, Wood J, Jaycox JR, Dhodapkar RM, Lu P, Gehlhausen JR, et al. Distinguishing features of long COVID identified through immune profiling. Nature. 2023;623(7985):139-48.
29. Hejbol EK, Harbo T, Agergaard J, Madsen LB, Pedersen TH, Ostergaard LJ, et al. Myopathy as a cause of fatigue in long-term post-COVID-19 symptoms: Evidence of skeletal muscle histopathology. Eur J Neurol. 2022;29(9):2832-41.
30. Pretorius E, Vlok M, Venter C, Bezuidenhout JA, Laubscher GJ, Steenkamp J, et al. Persistent clotting protein pathology in Long COVID/Post-Acute Sequelae of COVID-19 (PASC) is accompanied by increased levels of antiplasmin. Cardiovasc Diabetol. 2021;20(1):172.
31. Muri J, Cecchinato V, Cavalli A, Shanbhag AA, Matkovic M, Biggiogero M, et al. Autoantibodies against chemokines post-SARS-CoV-2 infection correlate with disease course. Nat Immunol. 2023;24(4):604-11.

32. Wang EY, Mao T, Klein J, Dai Y, Huck JD, Jaycox JR, et al. Diverse functional autoantibodies in patients with COVID-19. Nature. 2021;595(7866):283-8.
33. Kruger A, Vlok M, Turner S, Venter C, Laubscher GJ, Kell DB, et al. Proteomics of fibrin amyloid microclots in long COVID/post-acute sequelae of COVID-19 (PASC) shows many entrapped pro-inflammatory molecules that may also contribute to a failed fibrinolytic system. Cardiovasc Diabetol. 2022;21(1):190.
34. Guo L, Appelman B, Mooij-Kalverda K, Houtkooper RH, van Weeghel M, Vaz FM, et al. Prolonged indoleamine 2,3-dioxygenase-2 activity and associated cellular stress in post-acute sequelae of SARS-CoV-2 infection. EBioMedicine. 2023;94:104729.
35. Soares MN, Eggelbusch M, Naddaf E, Gerrits KHL, van der Schaaf M, van den Borst B, et al. Skeletal muscle alterations in patients with acute Covid-19 and post-acute sequelae of Covid-19. J Cachexia Sarcopenia Muscle. 2022;13(1):11-22.
36. Adler L, Gazit S, Pinto Y, Perez G, Mizrahi Reuveni M, Yehoshua I, et al. Long-COVID in patients with a history of mild or asymptomatic SARS-CoV-2 infection: a Nationwide Cohort Study. Scand J Prim Health Care. 2022;40(3):342-9.
37. Antonelli M, Pujol JC, Spector TD, Ourselin S, Steves CJ. Risk of long COVID associated with delta versus omicron variants of SARS-CoV-2. Lancet. 2022;399(10343):2263-4.

This signal has been raised on January 17, 2024. It is possible that in the meantime other information became available. For the latest information, including the official SmPC's, please refer to website of the MEB www.cbg-meb.nl

Appendix A. Long COVID-like symptoms

Peripheral neurological symptoms

Paraesthesia
Muscular weakness
Muscle spasms
Hypoaesthesia
Neuralgia
Paraesthesia oral
Neuropathy peripheral
Balance disorder
Electric shock sensation
Hypoaesthesia oral
Lumbosacral radiculoplexus neuropathy
Monoparesis
Muscle contractions involuntary
Myoclonus
Neuritis
Nervous system disorder
Pharyngeal paraesthesia
Polyneuropathy
Pseudoradicular syndrome
Gait disturbance
Small fibre neuropathy
Peripheral coldness
Paresis
Allodynia
Hyperaesthesia
Peripheral sensory neuropathy

Cognitive dysfunction-related symptoms

Disturbance in attention
Memory impairment
Confusional state
Amnesia
Cognitive disorder
Brainfog
Burnout syndrome
Hyperresponsive to stimuli
Lethargie
Mental impairment
Feeling abnormal
Hypersomnia
Oversensing
Sensory overload
Sensory processing sensitivity
Somnolence

Cardiovascular symptoms

Palpitations
Chest pain
Arrhythmia
Chest discomfort
Extrasystoles
Heart rate increased
Ventricular extrasystoles
Tachycardia
Cardiac discomfort
Postural orthostatic tachycardia syndrome (POTS)
Hypotension
Hypertension
Blood pressure diastolic increased
Autonomic nervous system imbalance
Heart rate decreased
Heart rate irregular
Sinus tachycardia
Ventricular tachycardia
Angina pectoris
Atrial fibrillation
Atrial flutter
Bundle branch block left
Cardiac fibrillation

Dyspnoea-related symptoms

Dyspnoea
Dyspnoea exertional
Bronchial hyperreactivity
Dyspnoea at rest

AEFI reported as one of the following

Post vaccination syndrome
Post-acute COVID-19 syndrome
Chronic fatigue syndrome
Post viral fatigue syndrome