PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (http://bmjopen.bmj.com/site/about/resources/checklist.pdf) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

<table>
<thead>
<tr>
<th>TITLE (PROVISIONAL)</th>
<th>The effect of the COVID-19 pandemic on outpatient care and rehabilitation in neuromuscular clinical practice in Japan: a health insurance claims database analysis</th>
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<tr>
<td>AUTHORS</td>
<td>Saito, Toshio; Matsuo-Tezuka, Yukari; Sugitani, Yasuo; Tajima, Takumi; Fukao-Washino, Junko; Sakai, Sadaoki; Iwagami, Masao</td>
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VERSION 1 – REVIEW

<table>
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<tr>
<th>REVIEWER</th>
<th>Nishio, Nisahide Kobe Gakuin University The Faculty of Rehabilitation, Department of Occupational Therapy</th>
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<td>REVIEW RETURNED</td>
<td>10-Jan-2023</td>
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GENERAL COMMENTS

In this manuscript entitled “The effect of the COVID-19 pandemic on outpatient care and rehabilitation in neuromuscular clinical practice in Japan: a health insurance claims database analysis”, the authors evaluated the impact of the coronavirus disease 2019 (COVID-19) pandemic on outpatient care in Japanese patients with neuromuscular diseases (NMDs), including spinal muscular atrophy (SMA), neuromyelitis optica (NMO), myasthenia gravis (MG), Guillain-Barré syndrome (GBS), myasthenia gravis (MG).

[Summary of the manuscript]
The authors of the manuscript provided an overview of the medical behavior of NMD patients during the COVID-19 pandemic in Japan. According to the authors, across all NMDs assessed, compared with the period before the pandemic, small decreases in outpatient consultation visits and outpatient rehabilitation visits were observed during the 1-year pandemic period.

[Comments to the manuscript- Major issues]
1. According to the Supplemental Figure 1. (Patient selection flow diagram), the authors picked up the patients with a diagnosis of NMD during the inclusion period of January 2018 to February 2019 and pursued them during the follow-up period of March 2019 to February 2021. However, in the Methods section, they described, “All outcomes were calculated for the 1-year period before the COVID-19 pandemic (March 2019 to February 2020) and the 1-year period during the COVID-19 pandemic (March 2020 to February 2021).” Different description of the periods is present in the manuscript.

2. What makes things even more confusing is difficulty of pinpointing the start of the pandemic. The novel virus was first identified in an outbreak in the Chinese city of Wuhan in December 2019. Attempts to contain it there failed, allowing the virus to spread to other areas of Asia and later worldwide. In Japan, the
first case of COVID-19 was found in January 2020. I think it is necessary to precisely determine the study periods in this manuscript.

Related to the comment mentioned above, the authors should state the epidemic situation of COVID-19 in the Introduction section and clearly state the precise study period in the Method section and Supplemental Figure 1. (Patient selection flow diagram).

3. The authors stated that they used the data of 11,940,911 patients identified. In the Supplemental Figure 1. (Patient selection flow diagram), it turned out that the number of 11,940,911 came from the data during the total period of April 2015 to February 2021. I wonder why they showed the patient number identified in the total period of April 2015 to February 2021, though the study period was only a couple of years within the period.

4. I also wonder why they did not pick up a group of patients with non-NMD as a reference group to compare the NMD patients. However, the authors did not use their own data of non-NMD patients to highlight NMD-specific issues which might appear in the COVID-19 pandemic period. I think the authors should discuss NMD-specific issues of the patients with NMD in the COVID-19 pandemic period, compared with the issues of the patients with non-NMD.

5. The authors did not compare the specific issues among patients with different NMDs. According to Figure 1, before and during the COVID-19 pandemic period, there were significant differences in outpatient rehabilitation visit numbers among three groups (SMA group, NMO+MG group, GBS+AIE group). I think the authors should discuss disease-specific issues before and during the COVID-19 pandemic period.

6. The authors said in the Introduction section, “Currently, there are no known curative therapies for NMDs”. This statement was not precise, because not a few drugs for NMDs have already been developed. Actually, the authors also showed curative therapies for NMDs in Supplemental Table 1 (Neurological clinical practice and rehabilitation in the outpatient setting).

The outpatient consultation visits may be closely related with medication (or treatment with drugs). Thus, it should be much more discussed about the possibility of continuation of treatment with such drugs for NMD patients in the COVID-19 pandemic period. I think the discussion about this problem is essential, but the authors did not discuss it.

[Comments to the manuscript- Minor issues]
1. (Methods section) The authors stated that they analyzed the data of NMD patients in the metropolitan, rural-urban and depopulated areas of Japan. However, in the manuscript, the definition or characterization of these areas were not properly described, though the authors cited “Wellness Co., Ltd. Secondary medical area database [in Japanese]. 2011 http://www.wellness.co.jp/siteoperation/msd/”.

2. (Discussion section) The authors said, “Among patients with ≥1 outpatient visit during the 2-year follow-up period, less than half
and greater than half of the patients showed a >30% decrease in the number of outpatient consultation and outpatient rehabilitation visits, respectively, during the COVID-19 pandemic." But I cannot understand what the authors want to say by "less than half and greater than half of the patients".

**REVIEWER**
Masiero, S
Università degli Studi di Padova Scuola di Medicina e Chirurgia, Rehabilitation

**REVIEW RETURNED**
15-Jan-2023

**GENERAL COMMENTS**
The manuscript is interesting. However, there are issues that need to be resolved before it can be published. First of all, in the abstract, I suggest highlighting the size of the sample taken into consideration for the reworking of the data. Furthermore, I suggest to expand the conclusions in the abstract by highlighting what future perspectives are opened up by the observation of this reduction in services. In the introduction I suggest citing World Health Organization Rapid assessment of service delivery for NCDs during the COVID-19 pandemic 29 May 2020. This report investigated the reduction of services in several countries during the first period of the pandemic. The text is written in good English and the materials and methods are clearly explained. However, I suggest updating the current database size (updated to February 2022). It would also be interesting to see data on the possible resumption of activities from 2021 to the present, with another follow-up. The results of the study are well described, also graphically through figures and tables. In the discussion, I suggest adding what the reduction of services implies and what solutions are proposed. In this way, from the data collected the authors can suggest solutions for the future. For example, it is possible to cite Balton S, Vallabhjee AL, Pillay SC. When uncertainty becomes the norm: The Chris Hani Baragwanath Academic Hospital’s Speech Therapy and Audiology Department’s response to the COVID-19 pandemic. S Afr J Commun Disord. 2022;69(2):e1-e11. Published 2022 Aug 8. doi:10.4102/sajcd.v69i2.913; Citarelli G, Garofalo C, Esposito MG, Torre V, Magliano L, Politano L. Impact of the COVID-19 pandemic on rehabilitation setting. Part 1: professionals' views on the changes in routine care provided by a rehabilitation centre for patients with muscle diseases. Acta Myol. 2021;40(3):132-134. Published 2021 Sep 30. doi:10.36185/2532-1900-054; Maccarone MC, Masiero S. The Important Impact of COVID-19 Pandemic on the Reorganization of a Rehabilitation Unit in a National Healthcare System Hospital in Italy: Lessons From Our Experience. Am J Phys Med Rehabil. 2021;100(4):327-330. doi:10.1097/PHM.000000001707; Maccarone MC, Kamioka H, Cheleschi S, Tenti S, Masiero S, Kardes S. Italian and Japanese public attention towards balneotherapy in the COVID-19 era. Environ Sci Pollut Res Int. 2021;28(43):61781-61789. doi:10.1007/s11356-021-15058-z; Wei X, Yuan H, Sun Y, et al. Health Services Utilization in China during

Line 27-28 of the discussion states “however, the reasons for the higher impact are currently unclear and must be investigated in future studies.” It would be interesting if this point were discussed more, probably the greater involvement of European countries and the different management of the pandemic may have influenced hospital and rehabilitation admissions. I suggest expanding these reflections by reporting data in the literature.

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<th>REVIEWER</th>
<th>Sukocheva, Olga</th>
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<td>Flinders University, Health Sciences</td>
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| The current manuscript is a retrospective cohort study which assessed data from patients in Japan with neuromuscular diseases (NMDs). The cohort was divided into “before COVID-19” (before March 2020) and “during COVID-19” (after March 2020) which allowed to compare the influence of COVID-19. The study was properly designed and included a large cohort of 11,940,911 patients. The authors assessed patients with spinal muscular atrophy (SMA; n=82), neuromyelitis optica (NMO; n=342), myasthenia gravis (MG; n=1347), Guillain-Barré syndrome (GBS; n=442), or autoimmune encephalitis/encephalopathy (AIE; n=133). Authors demonstrated a small reduction in the proportion of patients with outpatient consultation and outpatient rehabilitation visits for the “before the COVID-19” group. Outcomes were categorized by secondary healthcare areas. The authors concluded that “outpatient consultation” and “rehabilitation visits” during the COVID-19 pandemic were affected in Japanese patients with NMD. Authors did not conduct proper statistical analysis. This is the main problem of this study. The study is interesting and important to publish. However, there are several problems to address.

1. Abstract text should be improved. Authors should use shorter sentences to keep the idea clear (it is recommended by English grammar/academic style). The clear accent should be made on the difference between before and during covid. A “small reduction” should be clarified: was it significant or not? If it is not significant – it should be indicated.
2. How data was compared? What statistical tools were used? What statistical software was used? It is all missing in the Abstract.
3. Conclusions should also indicate how significant were the differences.
4. Strength and Limitations should be presented as plain text: avoid using bullet points.
5. Introduction should site recent (from 2022) large review articles which discussed the long or post COVID conditions/post SARS-CoV-2 syndrome and its association with ME/CFS (potential links were identified for myalgic encephalomyelitis/chronic fatigue syndrome). The authors should clarify whether NMD which was used in this study is similar or includes myalgic encephalomyelitis/and/or chronic fatigue syndrome. This part is essential and should be accented.
6. Methods should indicate which types of statistical analysis and used software. I understand that this study is “exploratory”. However, the large cohort and the amount of data allows the use/application of statistical tests.
7. Table 1: gender bias is possible and should be addressed/discussed. Neuromyelitis optica – females - 71.6 %, while GBS – females – only 38.5% - these dereferences look significant to me; therefore, gender-related bias should be discussed. Possible contribution of steroid hormones may be mentioned.

8. Supplementary material: some graphs present “zero” data (Gastrostomy etc) – why they are included? They can be removed. Statistical analysis (relevant tests for significance) is required (currently it is missing). The authors indicated that this is ‘explanatory’ study. However, the retrospective cohort studies require proper statistical analysis. It should be conducted.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
Comments to the Author:
In this manuscript entitled “The effect of the COVID-19 pandemic on outpatient care and rehabilitation in neuromuscular clinical practice in Japan: a health insurance claims database analysis”, the authors evaluated the impact of the coronavirus disease 2019 (COVID-19) pandemic on outpatient care in Japanese patients with neuromuscular diseases (NMDs), including spinal muscular atrophy (SMA), neuromyelitis optica (NMO), myasthenia gravis (MG), Guillain-Barrés syndrome (GBS), myasthenia gravis (MG).

[Summary of the manuscript]
The authors of the manuscript provided an overview of the medical behavior of NMD patients during the COVID-19 pandemic in Japan. According to the authors, across all NMDs assessed, compared with the period before the pandemic, small decreases in outpatient consultation visits and outpatient rehabilitation visits were observed during the 1-year pandemic period.

Comment 1: According to the Supplemental Figure 1. (Patient selection flow diagram), the authors picked up the patients with a diagnosis of NMD during the inclusion period of January 2018 to February 2019 and pursued them during the follow-up period of March 2019 to February 2021. However, in the Methods section, they described, “All outcomes were calculated for the 1-year period before the COVID-19 pandemic (March 2019 to February 2020) and the 1-year period during the COVID-19 pandemic (March 2020 to February 2021).” Different description of the periods is present in the manuscript.

Response: Thank you for the comment. In the Methods (Study design and data source) section, we described that, “The patient inclusion period was between January 2018 and February 2019, and the follow-up period was between March 2019 and February 2021.” This is in line with Supplemental Figure 1.

The follow-up period (March 2019-February 2021) was further divided into “before the COVID-19 pandemic” (March 2019-February 2020) and “during the COVID-19 pandemic” (March 2020-February 2021) to evaluate changes before and after the COVID-19 pandemic.

Comment 2: What makes things even more confusing is difficulty of pinpointing the start of the pandemic. The novel virus was first identified in an outbreak in the Chinese city of Wuhan in December 2019. Attempts to contain it there failed, allowing the virus to spread to other areas of Asia and later worldwide. In Japan, the first case of COVID-19 was found in January 2020. I think it is necessary to precisely determine the study periods in this manuscript.
Related to the comment mentioned above, the authors should state the epidemic situation of COVID-19 in the Introduction section and clearly state the precise study period in the Methods section and Supplemental Figure 1. (Patient selection flow diagram).

Response: Thank you for the comment. As suggested, we have added the following clarification in the Introduction section to address the concern (Page 5; Paragraph 1; Lines 4-6):

“The evaluation period was categorized into before March 2020 and after March 2020 when the impact of the COVID-19 pandemic became apparent and the government task force was established in Japan.”

Comment 3: The authors stated that they used the data of 11,940,911 patients identified. In the Supplemental Figure 1. (Patient selection flow diagram), it turned out that the number of 11,940,911 came from the data during the total period of April 2015 to February 2021. I wonder why they showed the patient number identified in the total period of April 2015 to February 2021, though the study period was only a couple of years within the period.

Response: Thank you for the comment. We set the total period of April 2015 to February 2021 to evaluate the past treatment history in a study that was conducted simultaneously, but as you pointed out, the total period of January 2018 to February 2021 is appropriate in this study. As suggested, we have updated the figure with the correct “total data period” and its associated N number as follows in the abstract, text (Page 8; Paragraph 1; Lines 1-2), and Supplementary Figure 1.

April 2015 to February 2021 (total data period) N=11,940,911
Revised to
January 2018 to February 2021 (total data period) N=10,655,557

Comment 4: I also wonder why they did not pick up a group of patients with non-NMD as a reference group to compare the NMD patients. However, the authors did not use their own data of non-NMD patients to highlight NMD-specific issues which might appear in the COVID-19 pandemic period. I think the authors should discuss NMD-specific issues of the patients with NMD in the COVID-19 pandemic period, compared with the issues of the patients with non-NMD.

Response: Thank you for the comment. We did not consider the comparison with acute-phase diseases appropriate because they are subject to change in a short span or time/duration of follow-up. Moreover, chronic diseases, such as renal failure, are not appropriate for comparison because they are not considered candidates for rehabilitation. Although the trend of receiving medical treatment for chronic diseases such as respiratory failure and heart failure may show the same tendency as that of chronic NMD, there is a possibility that the number of patients may be considerably larger in the group of heterozygous diseases. Putting emphasis on such heterozygous disease would not be in line with the objective of this study. Therefore, in this study, no control group was set, and we focused on the changes in outpatient care and rehabilitation before and during the COVID-19 pandemic, targeting neuromuscular diseases that are chronic and require long-term medical care.

Comment 5: The authors did not compare the specific issues among patients with different NMDs. According to Figure 1, before and during the COV-19 pandemic period, there were significant differences in outpatient rehabilitation visit numbers among three groups (SMA group, NMO+MG group, GBS+AIE group). I think the authors should discuss disease-specific issues before and during the COVID-19 pandemic period.

Response: Thank you for pointing this out. However, we found it difficult to discuss each disease. For example, patients undergoing rehabilitation have decreased motor function in any diseases, but the number of outpatient rehabilitation visits was decreased due to the COVID-19 pandemic. This may be due to a variety of factors. Therefore, we have now added the following clarification to the Discussion section to address the concern (Page 11; Paragraph 2; Lines 6-12):
“Nevertheless, the proportion of patients demonstrating a decrease in outpatient consultation visits was smaller than that for outpatient rehabilitation visits, suggesting that the pandemic had a greater impact on outpatient rehabilitation than on outpatient consultation. Patients who undergo rehabilitation basically have decreased motor function regardless of the disease, but there is a possibility that they refrained from outpatient rehabilitation due to a variety of factors (circumstances at the medical institutions and rehabilitation facilities or the patient’s request [such as due to fear of infection]).”

Comment 6a: The authors said in the Introduction section, “Currently, there are no known curative therapies for NMDs”. This statement was not precise, because not a few drugs for NMDs have already been developed. Actually, the authors also showed curative therapies for NMDs in Supplemental Table 1 (Neurological clinical practice and rehabilitation in the outpatient setting).
Response: Thank you for pointing this out. We have now modified the statement as follows to address the concern (Page 4; Paragraph 2; Lines 1-2):

“NMDs are chronic and require long-term medical care.”

Comment 6b: The outpatient consultation visits may be closely related with medication (or treatment with drugs). Thus, it should be much more discussed about the possibility of continuation of treatment with such drugs for NMD patients in the COVID-19 pandemic period. I think the discussion about this problem is essential, but the authors did not discuss it.
Response: Thank you for the insight. Taking into consideration the comments of Reviewer 2, we would like to add the following to the Discussion section to address the concern (Page 12; Paragraph 2; Lines 11-26):

“Taken together, the results from these two European studies suggest that the impact of the COVID-19 pandemic on patients with NMDs was higher in Europe than in Japan; however, the reasons for the higher impact are currently unclear and must be investigated in future studies. One of the factors may be that Japan did not implement a mandatory lockdown similar to that in Europe. In China, the degree of strict lockdown has been reported to have had an impact on healthcare reductions.[28] Our study did not show any major changes in the treatment approach of NMDs during vs before the COVID-19 pandemic. Furthermore, online medical practice did not increase during this study. This suggested that patients requiring continuous medication or treatment did not interrupt outpatient consultations. In particular, patients with chronic NMDs may have preferred face-to-face treatment with specialists to control their symptoms, even during the pandemic. In addition, immediately after the pandemic, we did not have an environment where we could provide online medical care. On the other hand, the American Academy of Neurology recommends postponing hospital visits and introducing telemedicine.[29] Maccarone et al. also describe a reorganization of rehabilitation during the pandemic.[30] In future, various forms of treatment may be considered while reducing patient risk.”

[Comments to the manuscript- Minor issues]
Comment 1. (Methods section) The authors stated that they analyzed the data of NMD patients in the metropolitan, rural-urban and depopulated areas of Japan. However, in the manuscript, the definition or characterization of these areas were not properly described, though the authors cited “Wellness Co., Ltd. Secondary medical area database [in Japanese]. 2011 http://www.wellness.co.jp/site operation/msd/”.
Response: Thank you for the comment. As suggested, the following definitions have now been included to address the concern (Page 7; Paragraph 2; Lines 7-11):

“Metropolitan areas were defined as secondary healthcare areas with a population of at least 1 million or a population density of at least 2,000/km2. Rural-urban areas were defined as secondary healthcare areas with a population of at least 200,000 or at least 100,000 and a population density of
at least 200/km2, other than the conditions of metropolitan areas. Depopulated areas were defined as secondary healthcare areas other than the conditions of metropolitan and rural-urban areas.”

Comment 2: (Discussion section) The authors said, “Among patients with ≥1 outpatient visit during the 2-year follow-up period, less than half and greater than half of the patients showed a >30% decrease in the number of outpatient consultation and outpatient rehabilitation visits, respectively, during the COVID-19 pandemic.” But I cannot understand what the authors want to say by “less than half and greater than half of the patients”.

Response: Thank you for the observation. We have now included the following modification to address the concern (Page 11; Paragraph 1; Lines 5-10):

“Among patients with ≥1 outpatient visit during the 2-year follow-up, 30.4%, 27.8%, 28.7%, 49.4%, and 50.0% had a >30% decrease in the number of outpatient consultation visits, whereas 58.6%, 75.0%, 50.0%, 76.3%, and 84.6% had a >30% decrease in the number of outpatient rehabilitation visits for SMA, NMO, MG, GBS, and AIE, respectively, during the COVID-19 pandemic.”

Reviewer: 2
Dr. S Masiero, Universita degli Studi di Padova Scuola di Medicina e Chirurgia
Comments to the Author:
The manuscript is interesting. However, there are issues that need to be resolved before it can be published.
Comment 1: First of all, in the abstract, I suggest highlighting the size of the sample taken into consideration for the reworking of the data. Furthermore, I suggest to expand the conclusions in the abstract by highlighting what future perspectives are opened up by the observation of this reduction in services.
Response: Thank you for pointing this out. We have now added the following clarification to the Abstract:
“Patients were required to have ≥1 month of data available, a diagnosis of NMD during the enrollment period, and be available for follow-up.”

Abstract conclusion:
Outpatient consultation and rehabilitation visits during the COVID-19 pandemic were affected in Japanese patients with NMDs. Longer-term evaluations are required to understand if these reductions in outpatient care would affect patient prognosis.

Comment 2: In the introduction I suggest citing World Health Organization Rapid assessment of service delivery for NCDs during the COVID-19 pandemic 29 May 2020. This report investigated the reduction of services in several countries during the first period of the pandemic.
Response: Thank you for your suggestion. Although, we had cited the WHO report as reference number 7 in the Introduction, we have now added the following statement to the Introduction section to address the concern (Pages 4-5; Paragraph 5; Lines 3-4):
“A definitive reduction in healthcare services in several countries was observed during the first period of the pandemic.[7]”

Comment 3: The text is written in good English and the materials and methods are clearly explained. However, I suggest updating the current database size (updated to February 2022). It would also be interesting to see data on the possible resumption of activities from 2021 to the present, with another follow-up.
Response: Thank you for your suggestion. The current database size is already mentioned in the Methods section as follows (Page 6; Paragraph 1; Lines 4-5):
“The cumulative population size is approximately 14 million individuals (as of February 2022).[20]”
However, we would like to draw your attention to the fact that we have now updated the total data period and associated N number based on the comment of Reviewer 1 as follows (Page 8; Paragraph 1; Lines 1-3; supplemental figure 1):

“A total of 10,655,557 patients with ≥1 month of data available for the total data period (January 2018-February 2021) were identified in the JMDC database, 3160 of whom had a diagnosis of an NMD of interest.”

Comment 3: The results of the study are well described, also graphically through figures and tables. Response: Thank you for the encouraging comment.


Line 27-28 of the discussion states “however, the reasons for the higher impact are currently unclear and must be investigated in future studies.” It would be interesting if this point were discussed more, probably the greater involvement of European countries and the different management of the pandemic may have influenced hospital and rehabilitation admissions. I suggest expanding these reflections by reporting data in the literature.

Response: Thank you for your suggestion. As suggested, we have now cited some of these articles, as follows, to address the concern (Page 12; Paragraph 2; Lines 14-26):

“One of the factors may be that Japan did not implement a mandatory lockdown similar to that in Europe. In China, the degree of strict lockdown has been reported to have had an impact on healthcare reductions.[28] Our study did not show any major changes in the treatment approach of NMDs during vs before the COVID-19 pandemic. Furthermore, online medical practice did not increase during this study. This suggested that patients requiring continuous medication or treatment did not interrupt outpatient consultations. In particular, patients with chronic NMDs may have preferred face-to-face treatment with specialists to control their symptoms, even during the pandemic. In addition, immediately after the pandemic, we did not have an environment where we could provide online medical care. On the other hand, the American Academy of Neurology recommends postponing hospital visits and introducing telemedicine.[29] Maccarone et al. also describe a reorganization of rehabilitation during the pandemic.[30] In future, various forms of treatment may be considered while reducing patient risk.”
Reviewer: 3
Dr. Olga Sukocheva, Flinders University, Royal Adelaide Hospital

Comments to the Author:
The current manuscript is a retrospective cohort study which assessed data from patients in Japan with neuromuscular diseases (NMDs). The cohort was divided into “before COVID-19” (before March 2020) and “during COVID-19” (after March 2020) which allowed to compare the influence of COVID-19. The study was properly designed and included a large cohort of 11,940,911 patients. The authors assessed patients with spinal muscular atrophy (SMA; n=82), neuromyelitis optica (NMO; n=342), myasthenia gravis (MG; n=1347), Guillain-Barré syndrome (GBS; n=442), or autoimmune encephalitis/encephalopathy (AIE; n=133). Authors demonstrated a small reduction in the proportion of patients with outpatient consultation and outpatient rehabilitation visits for the “before the COVID-19” group. Outcomes were categorized by secondary healthcare areas. The authors concluded that “outpatient consultation” and “rehabilitation visits” during the COVID-19 pandemic were affected in Japanese patients with NMD. Authors did not conduct proper statistical analysis. This is the main problem of this study.
The study is interesting and important to publish. However, there are several problems to address.
Comment 1: Abstract text should be improved. Authors should use shorter sentences to keep the idea clear (it is recommended by English grammar/academic style). The clear accent should be made on the difference between before and during covid. A “small reduction” should be clarified: was it significant or not? If it is not significant – it should be indicated.
Response: Thank you for pointing this out. We have reduced the size of the sentences in the Abstract, as suggested.
Regarding statistical significance, per protocol, we did not assume hypotheses prospectively, and did not estimate P value of statistical hypothesis testing based on the statement by the American Statistical Association (Wasserstein RL, Lazar NA. Editorial: The ASA’s statement on p-values: Context, process, and purpose. The American Statistician 2016; 70: 129 -133.). However, the results of statistical hypothesis testing were shown below for reference purpose only.
The results confirmed a small reduction in the number of outpatient consultation and rehabilitation visits before vs during the COVID-19 pandemic.
All patients:
Evaluation of difference in the number of patients for outpatient consultation visits (P value: SMA 0.6781; NMO, 0.1647; MG, <.0001; GBS, <.0001; AIE, 0.0833) before vs during the COVID-19 pandemic using Chi-squared test was significant for MG and GBS.
Evaluation of difference in the number of patients for outpatient rehabilitation visits (P value: SMA 0.3990; NMO, 0.0430; MG, 0.6685; GBS, 0.4000; AIE, 0.0508) before vs during the COVID-19 pandemic using Chi-squared test was significant for NMO and GBS.
Evaluation of difference in the number of outpatient consultation visits (P value: SMA 0.2526; NMO, <.0001; MG, <.0001; GBS, <.0001; AIE, 0.0008) before vs during the COVID-19 pandemic using paired t-test was significant for NMO, MG, GBS, and AIE.
Evaluation of difference in the outpatient rehabilitation visits (P value: SMA 0.0686; NMO, 0.0020; MG, 0.8102; GBS, 0.0010; AIE, 0.0293) before vs during the COVID-19 pandemic using paired t-test was significant for NMO, GBS, and AIE.
In the presence/absence of neurology specialists:
Evaluation of difference in the number of patients with > 30% decrease in outpatient consultation visits (P value: SMA 0.4505; NMO, 0.0653; MG, 0.0083; GBS, 0.2428; AIE, 0.8705) in the presence vs absence of neurology specialists using Chi squared test was significant for patients with MG.
Evaluation of difference in the number of patients with > 30% decrease in outpatient rehabilitation visits (P value: SMA 0.1915; NMO, 0.3711; MG, 0.5770; GBS, 0.2138; AIE, 0.4602) in the presence vs absence of neurology specialists using Chi squared test was not significant for any patient category.
Categorized by secondary healthcare areas:
Evaluation of difference in the number of patients with > 30% decrease in outpatient consultation visits (P value: SMA 0.0261; NMO, 0.658; MG, 0.1462; GBS, 0.0321; AIE, 0.3734) for metropolitan vs rural-urban area using Chi squared test was significant for patients with SMA and GBS.

Evaluation of difference in the number of patients with > 30% decrease in outpatient rehabilitation visits (P value: SMA 0.8221; NMO, 0.6115; MG, 0.577; GBS, 0.8708; AIE, 0.2733) for metropolitan vs rural-urban area using Chi squared test was not significant for any patient category.

Evaluation of difference in the number of patients with > 30% decrease in outpatient consultation visits (P value: SMA 0.6356; NMO, 0.8804; MG, 0.7102; GBS, 0.2325; AIE, 0.4762) for metropolitan vs depopulated area using Chi squared test was not significant for any patient category.

Evaluation of difference in the number of patients with > 30% decrease in outpatient rehabilitation visits (P value: SMA 0.2918; NMO, -not evaluable-; MG, -not evaluable-; GBS, 0.0852; AIE, -Not evaluable-) for metropolitan vs depopulated area using Chi squared test was not significant for any patient category.

Comment 2. How data was compared? What statistical tools were used? What statistical software was used? It is all missing in the Abstract.
Response: Thank you for the comment. After much deliberation and given the word count limitation of the abstract, we would not like to add further to the abstract as no statistical hypothesis was tested. Having said that, we have included the statistical tools and software in the Statistical analysis section of the Methods section in the manuscript. In addition, the comparison of changes in outpatient practices before and during the COVID-19 pandemic is included under Primary and secondary outcome measures in the abstract. We hope that our clarification is sufficient to address the concern.

Comment 3. Conclusions should also indicate how significant were the differences.
Response: Thank you for the comment. Regarding statistical significance, per protocol, we did not assume hypotheses prospectively, and did not estimate P value of statistical hypothesis testing based on the statement by the American Statistical Association (Wasserstein RL, Lazar NA. Editorial: The ASA’s statement on p-values: Context, process, and purpose. The American Statistician 2016; 70: 129 -133.). However, the results of statistical hypothesis testing are shown above for reference purpose only.

Comment 4. Strength and Limitations should be presented as plain text: avoid using bullet points.
****note from the editor: the section Strengths and Limitations directly after the abstract should be a bulleted list - no revisions necessary****
Response: Thank you for the comment

Comment 5: Introduction should site recent (from 2022) large review articles which discussed the long or post COVID conditions/post SARS-CoV-2 syndrome and its association with ME/CFS (potential links were identified for myalgic encephalomyelitis/chronic fatigue syndrome). The authors should clarify whether NMD which was used in this study is similar or includes myalgic encephalomyelitis/ and/or chronic fatigue syndrome. This part is essential and should be accentuated.
Response: Thank you for the insight. As you pointed out, we confirm that several recent reviews (Nature Reviews Microbiology volume 21, pages133–146 [2023]; Advanced Research Volume 40, September 2022, Pages 179-196) have discussed a possible link between long or post COVID-19 conditions and myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS).

However, the disease covered in this study is not related to myalgic encephalomyelitis and/or chronic fatigue syndrome (ME/CFS). In addition, per protocol, the inclusion criteria in this study were patients diagnosed prior to the COVID-19 pandemic (January 2018 to February 2019) and not related to the long-term or post COVID-19 conditions. Therefore, to avoid deviating from the protocol, we did not mention it.
Comment 6: Methods should indicate which types of statistical analysis and used software. I understand that this study is “exploratory”. However, the large cohort and the amount of data allows the use/application of statistical tests.
Response: Thank you for the comment. Regarding statistical significance, per protocol, we did not assume hypotheses prospectively, and did not estimate P value of statistical hypothesis testing based on the statement by the American Statistical Association (Wasserstein RL, Lazar NA. Editorial: The ASA’s statement on p-values: Context, process, and purpose. The American Statistician 2016; 70: 129-133.). However, the results of statistical hypothesis testing were shown above for reference purpose only.
Having said that, we have included the statistical tools and software in the Statistical analysis section of the Methods section in the manuscript. We hope that our clarification is sufficient to address the concern.

Comment 7: Table 1: gender bias is possible and should be addressed/discussed. Neuromyelitis optica – females - 71.6 %, while GBS – females – only 38.5% - these dereferences look significant to me; therefore, gender-related bias should be discussed. Possible contribution of steroid hormones may be mentioned.
Response: Thank you for the comment. As you pointed out, patients with NMO had a higher proportion of women and those with GBS had a higher proportion of men. However, these findings are consistent with previous epidemiological studies. That is, gender differences exist in the incidence of each disease.
Examples from the literature
1) The number of MS patients has been rapidly increasing for the past 30 years. The demographic features of the present series were compared with those of the three past nationwide surveys. The ratio of female to male patients has increased from 1.3 to 2.9. (Kira J. [Epidemiology of multiple sclerosis in Japanese: with special reference to opticopsinal multiple sclerosis]. Rinsho Shinkeigaku. 2006 Nov;46(11):859-62. Japanese. PMID: 17432201.)
2) GBS incidence increased by 20% for every 10-year increase in age; the risk of GBS was higher for males than for females (Sejvar JJ, Baughman AL, Wise M, Morgan OW. Population incidence of Guillain-Barré syndrome: a systematic review and meta-analysis. Neuroepidemiology. 2011;36(2):123-33. doi: 10.1159/000324710. Epub 2011 Mar 21. PMID: 21422765; PMCID: PMC5703046.)
3) MS is more common in women, with a male-to-female ratio of 1:2-3. Website: https://www.nanbyou.or.jp/entry/3806

Comment 8: Supplementary material: some graphs present “zero” data (Gastrostomy etc) – why they are included? They can be removed. Statistical analysis (relevant tests for significance) is required (currently it is missing). The authors indicated that this is “exploratory” study. However, the retrospective cohort studies require proper statistical analysis. It should be conducted.
Response: Thank you for the comment. As you pointed out, there is indeed a lot of “zero” data that can be difficult to read. However, we did investigate it as an item of interest, and would appreciate if we could leave it as it is.
In addition, the Statistical analysis section has been updated as mentioned in comment 1. We hope our responses are sufficient to address the concern.