Experiences of telemedicine in neurological outpatient clinics during the COVID-19 pandemic

Espen Saxhaug Kristoffersen1,2, Else Charlotte Sandset3,4, Bendik Slagsvold Winsvold3,5, Kashif Waqar Faiz1 & Anette Margrethe Storstein6

1Department of Neurology, Akershus University Hospital, Lørenskog, Norway
2Department of General Practice, University of Oslo, Oslo, Norway
3Department of Neurology, Oslo University Hospital, Oslo, Norway
4The Norwegian Air Ambulance Foundation, Oslo, Norway
5Division of Clinical Neuroscience, Department of Research, Innovation and Education, Oslo University Hospital, Oslo, Norway
6Department of Neurology, Haukeland University Hospital, Bergen, Norway

Correspondence
Espen Saxhaug Kristoffersen, Department of Neurology, Akershus University Hospital, PO Box 1000, 1478 Lørenskog, Norway. Tel: +47 22850679; Fax: +47 22 85 06 50; E-mail: e.s.kristoffersen@medisin.uio.no

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Abstract

Objective: The COVID-19 pandemic has led to rapid changes in the delivery of medical care worldwide. The main objective of this survey was to investigate the initial experiences of neurologists with the use of telemedicine for different neurological conditions during the first phase of the COVID-19. Methods: All hospital-based neurologists in Norway (n = 400) were invited to a questionnaire survey by e-mail in April 2020. The study focused on telemedicine and all questions were answered with regard to the first weeks of the pandemic lockdown in Norway. Results: One-hundred and thirty-five neurologists responded. Overall, 87% reported a shift toward more telemedicine, with significantly more use of telephone than video consultations for both new referrals (54% vs. 30%, P < 0.001) and follow-ups (99% vs. 50%, P < 0.001). Respondents deemed it much more professionally satisfactory to conduct follow-up consultations by telephone, than to carry out consultations with new patients by telephone (85% vs. 13%, P < 0.001). Teleconsultations were better suited for headache and epilepsy patients as compared to multiple sclerosis and movement disorder patients. There was no significant difference between residents and senior consultants regarding how they experienced teleconsultations. Female neurologists found telemedicine better and more effective than male neurologists. Interpretation: Telemedicine was rapidly implemented in Norwegian neurological departments during the first weeks of the COVID-19 pandemic. Teleconsultations were better suited for follow-ups than for new referrals, and better for headache and epilepsy patients as compared to multiple sclerosis and movement disorder patients.

Introduction

The coronavirus disease of 2019 (COVID-19) was declared a pandemic by the World Health Organization (WHO) in March 2020 and led to challenges and rapid changes in the delivery of medical care worldwide, including a shift toward eHealth and telemedicine instead of in-person consultations. Telemedicine includes consultations by telephone, video, or other web- or app-based interfaces. The potential for increased use of telephone or video consultations in neurology has been acknowledged for a long time, and feasibility studies have been conducted for conditions such as headache, epilepsy, movement disorders, stroke, and multiple sclerosis. Although some of these studies have shown promising results, there is a long way from feasibility and efficacy studies to a sudden, forced, and rapid full-scale implementation in daily practice, as seen in many countries during the first phase of the pandemic. For many patients, the shift to telemedical follow-up may have ensured continued access to care despite strict infection control measures. For others, lack of a proper clinical
examination and in-person treatment may have resulted in suboptimal quality of care or patient dissatisfaction. Thus, the experiences of telemedical consultations during the pandemic should be evaluated.

The main objective of this “Neurology during a pandemic (NeuroPan)” study was to investigate the initial experiences of neurologists with the use of telemedicine for different neurological conditions during the first phase of the COVID-19 pandemic in Norway.

Methods and Materials
Design and setting
There are 17 hospitals with a Department of Neurology in Norway, varying from smaller district hospitals to larger university hospitals, employing around 400 neurologists (approximately 50% residents and 50% senior consultants). Norwegian hospitals are almost exclusively publicly financed. Patients need a referral from a general practitioner in order to visit the hospital, except in emergencies. Norway has an all-covering national health insurance. Thus, all patients are referred on the same conditions and with the same threshold for further investigations, treatments, and follow-ups.

The study was conducted as an anonymous online survey among Norwegian neurologists about neurological diseases during the primary stage of the COVID-19 pandemic. The survey was distributed by e-mail in April 2020 to hospital-based Norwegian neurologists.

Questionnaire and outcomes
The questionnaire was based on the authors’ clinical experiences from the first weeks of the pandemic in addition to their general knowledge and experience in neurology and health services research. The questionnaire included background variables including age, sex, training status (resident/senior consultant), and type of hospital. Furthermore, the participants answered various questions regarding their personal considerations and their own handling of patients with neurological disorders during the pandemic. There were both general questions and questions specific for certain neurological conditions. All questions were asked in relation to the first weeks of the pandemic lockdown. The questions are listed in Tables 2 and 4.

Statistical analyses
For descriptive data, proportions, means, and standard deviations (SD) or 95% confidence intervals (CI) are given. The total number of respondents to each question in Tables 2 and 4 varies as all follow-up questions were not relevant for all participants, for example, a neurologist who did not do teleconsultations during the pandemic did not receive further follow-up questions on this topic. Groups were compared using the t-test (continuous data) or the χ² test (categorical data).

Multivariable logistic regression with the dependent variable being either (1) telephone/video consultations are more effective and better than the regular in-person appointment (yes or no) or (2) from a professional perspective, follow-ups by telephone consultation do work satisfactorily (yes or no) was performed. Sex, age, and type of hospital (university vs. nonuniversity) were included as independent variables. Since training status (resident vs. senior consultant) was significantly correlated with age, it was not included in the regression models.

Statistical significance was defined by P < 0.05, using a two-sided test. Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 26.00 (SPSS Inc., Chicago, IL).

Ethics approval
In accordance with the Norwegian law on medical research, the project did not require an approval from the Regional Committee for Medical Research Ethics. Informed consent was obtained from all respondents.

The Data Protection Officer at Akershus University Hospital approved the study. The study (NeuroPan) was registered in the COVID-19 trial registration at the Norwegian Clinical Research Infrastructure Network.

RESULTS
In total, 135 neurologists answered the questionnaire. Of these, 58% (n = 78) were women, mean age was 42 years (SD 10.0, range 27–60), 58% (n = 78) were senior consultants, and 60% (n = 81) worked at a university hospital (Table 1).

Only 8% maintained a regular outpatient clinic with in-person appointments (Table 2).

Overall, 87% reported a shift toward more telemedicine, with significantly more use of telephone than video consultations for both new referrals (54% vs. 30%, P < 0.001) and follow-ups (99% vs. 50%, P < 0.001). Respondents deemed it much more professionally satisfactory to conduct follow-up consultations by telephone, than to carry out consultations with new patients by telephone (85% vs. 13%, P < 0.001). Telephone and video consultations were deemed equally satisfactory from a professional perspective. Typically, less time was spent using telemedicine compared to in-person appointments.
Telemedicine During the COVID-19 Pandemic

Table 1. Description of the sample ($n = 135$).

|                          | Men       | Women     | Residents | Senior consultants | Total     |
|--------------------------|-----------|-----------|-----------|--------------------|-----------|
| Age, mean (SD)           | 44.3 (11.7) | 40.3 (8.2) | 34.2 (4.2) | 47.8 (9.0)         | 42.1 (10.0) |
| Gender, n (%)            |           |           |           |                    |           |
| Men                      | 57 (100)  | 0 (0)     | 25 (44)   | 32 (41)            | 57 (42)   |
| Women                    | 0 (0)     | 78 (100)  | 32 (56)   | 46 (59)            | 78 (58)   |
| Neurologist status, n (%)|           |           |           |                    |           |
| Residents                | 25 (44)   | 32 (41)   | 57 (100)  | 0 (0)              | 57 (42)   |
| Senior consultants       | 32 (56)   | 46 (59)   | 78 (0)    | 78 (100)           | 78 (58)   |
| Type of hospital, n (%)  |           |           |           |                    |           |
| University hospital      | 38 (67)   | 43 (55)   | 40 (70)   | 41 (53)            | 81 (60)   |
| Nonuniversity hospital   | 19 (33)   | 35 (45)   | 17 (30)   | 37 (47)            | 54 (40)   |
| Outpatient treatment of, n (%)| | | | | |
| Epilepsy                 | 38 (67)   | 65 (83)   | 42 (74)   | 61 (78)            | 103 (76)  |
| Headache                 | 31 (54)   | 49 (63)   | 33 (58)   | 47 (60)            | 80 (59)   |
| Multiple sclerosis       | 24 (42)   | 38 (49)   | 25 (44)   | 37 (47)            | 62 (46)   |
| Movement disorders       | 22 (39)   | 31 (40)   | 12 (21)   | 41 (53)            | 53 (39)   |

Table 2. Data on experiences and views on the use of telemedicine at the outpatient clinic.

| Statement                                                        | Yes | No |
|-----------------------------------------------------------------|-----|----|
| My work situation changed compared to normal ($N = 128$)        | 94  | 34 |
| We have maintained the regular outpatient clinic (with in-person appointments as the norm) ($N = 132$) | 10  | 122|
| We have switched to primarily telephone/video consultations ($N = 131$) | 114 | 17 |
| We assess newly referred patients via telephone consultation ($N = 120$) | 65  | 44 |
| We assess newly referred patients via video consultation ($N = 119$) | 36  | 83 |
| We do follow-ups via telephone consultation ($N = 130$)         | 129 | 1  |
| We do follow-ups via video consultation ($N = 123$)             | 62  | 61 |
| Telephone/video consultations are more effective and better than the regular in-person appointment ($N = 109$) | 38  | 71 |
| Do you spend less time on telephone/video consultations than at the regular in-person appointment? ($N = 118$) | 91  | 27 |
| From a professional perspective, are telephone consultations with newly referred patients satisfactorily ($N = 86$) | 11  | 75 |
| From a professional perspective, are video consultations with newly referred patients satisfactorily ($N = 43$) | 8   | 35 |
| From a professional perspective, do follow-ups by telephone consultation work satisfactorily ($N = 115$) | 98  | 17 |
| From a professional perspective, do follow-ups by video consultation work satisfactorily ($N = 57$) | 42  | 15 |

Numbers given as n (%).

There was no significant difference between residents and senior consultants regarding the proportion that experienced telephone and video consultations effective and better than regular in-person appointments (28% vs. 39%, $P = 0.22$). No significant difference was found between residents and senior consultants regarding the statement “from a professional perspective, follow-ups by telephone consultation do work satisfactorily” (87% vs. 84%, $P = 0.62$).

More women than men experienced telephone and video consultations effective and better than regular in-person appointments (44% vs. 22%, $P = 0.02$). This finding was consistent in the multivariable analysis adjusting for age and hospital type (odds ratio 2.61, 95% CI 1.05; 6.49, $P = 0.039$) (Table 3).

There was a significant difference between women (91%) and men (78%, $P = 0.046$) regarding the statement “from a professional perspective, follow-ups by telephone consultation do work satisfactorily”. However, this difference was no longer statistically significant after adjusting for age and hospital type (Table 3).

The proportion of participating neurologists involved in the outpatient treatment of epilepsy, headache, multiple sclerosis, and movement disorders was 76%, 59%, 46%, and 39%, respectively (Table 1). Table 4 shows how Norwegian neurologists answered the questions about telemedicine related to these four neurological conditions.

Sixty-one percent of the neurologists within headache care reported that telephone consultations with new referrals worked satisfactorily, compared to only 6% and 4% in multiple sclerosis and movement disorders, respectively ($P < 0.001$).

There were significant differences between the four neurological conditions regarding whether the neurologist perceived...
The first wave of the COVID-19 pandemic in Norway in March 2020 forced a “real-world” and immediate shift in outpatient care from in-person to telemedicine in Norwegian neurology departments. The use of telemedicine was reported by neurologists as more satisfactory for follow-up of patients than for newly referred patients. Teleconsultations were perceived as better suited for headache and epilepsy patients as compared to multiple sclerosis and movement disorder patients. This immediate implementation of radical changes in practice and care was done without a long period of discussions and preparations. Telemedicine has for a long time been seen as part of the future medical care, to allow remote and widespread management for many patient groups. The delays in this much-awaited paradigm shift toward more telemedicine and eHealth have been based on regulatory barriers, privacy concerns, data protection, lack of investments in the hospitals, and reimbursement obstacles. Further, in some places, physicians have been negative to implementation since telemedicine has been regarded as a way to save time and money for the hospitals instead of being of benefit for the patients. The shift during the COVID-19 pandemic shows that it is possible to implement fast-track changes and to overcome barriers if deemed necessary from a professional point of view perspective. However, the flip side of a forced and rapid implementation is the lack of scientific evaluation, which should follow such large changes in the health-care system.

The first part of the questionnaire referred to all neurological outpatients and thus represents the view of teleneurology in general. Interestingly, there were no significant differences between telephone and video consultations, suggesting that telephone, which is more widely available, may be as good as video consultations. This may be especially important in health-care systems with less resources than the Norwegian. Our findings from Norway clearly show that telemedicine is seen as better suited for follow-ups than for new referrals. This was reported both in general and for the specific neurological conditions included in the second part of the questionnaire. Many neurological patients have increased risk for severe COVID-19 due to their age, comorbidities, or conditions that require immunosuppressive treatments. For these patients, teleconsultations may provide a safe way to maintain follow-up care. Nevertheless, telemedicine comes with possible disadvantages including changed nature of clinical care, breakdown in the relationship between health-care providers and patient, missing important nonverbal information and communication, discontinuation of personal care, and issues concerning data security, stable updated software, and disclosure of sensitive personal information. Even minor disruptions in audio connection or freezing picture may potentially cause problems in the communication, especially if patients or health-care providers are not sufficiently

### DISCUSSION

The first part of the questionnaire referred to all neurological patients and thus represents the view of teleneurology in general. Interestingly, there were no significant differences between telephone and video consultations, suggesting that telephone, which is more widely available, may be as good as video consultations. This may be especially important in health-care systems with less resources than the Norwegian. Our findings from Norway clearly show that telemedicine is seen as better suited for follow-ups than for new referrals. This was reported both in general and for the specific neurological conditions included in the second part of the questionnaire. Many neurological patients have increased risk for severe COVID-19 due to their age, comorbidities, or conditions that require immunosuppressive treatments. For these patients, teleconsultations may provide a safe way to maintain follow-up care. Nevertheless, telemedicine comes with possible disadvantages including changed nature of clinical care, breakdown in the relationship between health-care providers and patient, missing important nonverbal information and communication, discontinuation of personal care, and issues concerning data security, stable updated software, and disclosure of sensitive personal information. Even minor disruptions in audio connection or freezing picture may potentially cause problems in the communication, especially if patients or health-care providers are not sufficiently

### Table 3. Multivariable logistic regression.

|                          | N  | Odds Ratio | 95% CI      | P-value |
|--------------------------|----|------------|-------------|---------|
| Telephone/video consultations are more effective and better than the regular in-person appointment |    |            |            |         |
| Age                      | 105| 1.00       | 0.97–1.05   | 0.7     |
| Sex                      |    |            |             |         |
| Men                      | 43 | 1.00       |             |         |
| Women                    | 62 | 2.61       | 1.05–6.49   | 0.039   |
| University hospital      |    |            |             |         |
| Yes                      | 60 | 1.00       |             |         |
| No                       | 45 | 1.30       | 0.56–3.02   | 0.54    |
| From a professional perspective, do follow-ups by telephone consultation work satisfactorily? |    |            |             |         |
| Age                      | 111| 0.96       | 0.91–1.01   | 0.10    |
| Sex                      |    |            |             |         |
| Men                      | 47 | 1.00       |             |         |
| Women                    | 64 | 2.30       | 0.68–7.74   | 0.18    |
| University hospital      |    |            |             |         |
| Yes                      | 61 | 1.00       |             |         |
| No                       | 50 | 2.66       | 0.74–9.55   | 0.13    |
Table 4. Data on experiences and views on the use of telemedicine in different neurological disorders.

|                          | Yes    | No |
|--------------------------|--------|----|
| **Epilepsy**             |        |    |
| Follow-up of epilepsy patients are primarily conducted by telephone consultations (N = 96) | 95 (89) | 5 (5) |
| Follow-up of epilepsy patients are primarily conducted by video consultations (N = 73) | 11 (15) | 62 (85) |
| If you have started conducting telephone/video consultations for epilepsy patients during the pandemic, do they function satisfactorily for the patients (N = 75) | 68 (91) | 7 (9) |
| If you have started conducting telephone/video consultations for epilepsy patients during the pandemic, do they function satisfactorily for you (N = 76) | 68 (89) | 8 (11) |
| From a professional perspective, is it satisfactory to make dosage changes for epilepsy patients by the telephone (N = 87) | 80 (92) | 7 (8) |
| From a professional perspective, is it satisfactory to assess frequency and type of seizure by the telephone (N = 88) | 69 (78) | 19 (22) |
| Reduced standard of care has been available to epilepsy patients during the pandemic (N = 91) | 27 (30) | 64 (70) |
| **Headache**             |        |    |
| If you assess newly referred patients by telephone consultation, does it work satisfactorily for the patients (N = 45) | 29 (64) | 16 (36) |
| If you assess newly referred patients by telephone consultation, does it work satisfactorily for you (N = 49) | 30 (61) | 19 (39) |
| If you are conducting follow-up with headache patients by telephone consultation, does it work satisfactorily for the patients (N = 75) | 69 (92) | 6 (8) |
| If you are conducting follow-up with headache patients by telephone consultation, does it work satisfactorily for you (N = 74) | 72 (97) | 2 (3) |
| Reduced standard of care has been available to headache patients during the pandemic (N = 74) | 31 (42) | 43 (58) |
| **Multiple sclerosis**   |        |    |
| From a professional perspective, is it satisfactory to assess newly referred multiple sclerosis patients by telephone consultations (N = 54) | 3 (6) | 51 (94) |
| Follow-ups of patients with multiple sclerosis are primarily conducted by telephone consultations (N = 58) | 54 (93) | 4 (7) |
| Follow-ups of patients with multiple sclerosis are primarily conducted by video consultations (N = 48) | 5 (10) | 43 (90) |
| If you have started conducting telephone/video consultations for multiple sclerosis patients during the pandemic, do they function satisfactorily for the patients (N = 42) | 32 (76) | 10 (24) |
| If you have started conducting telephone/video consultations for multiple sclerosis patients during the pandemic, do they function satisfactorily for you (N = 48) | 32 (53) | 16 (26) |

(Continued)

Table 4. Continued.

|                          | Yes    | No |
|--------------------------|--------|----|
| I spend less time on telephone consultations with multiple sclerosis patients than at the usual in-person appointments (N = 54) | 43 (80) | 11 (20) |
| Reduced standard of care has been available to multiple sclerosis patients during the pandemic (N = 55) | 39 (71) | 16 (29) |
| **Movement disorder**    |        |    |
| Some newly referred movement disorder patients are assessed by telephone consultations (N = 48) | 11 (23) | 37 (77) |
| From a professional perspective, is it satisfactory to assess newly referred movement disorder patients by telephone consultations (N = 47) | 2 (4) | 45 (96) |
| Follow-ups of patients with movement disorders are primarily conducted by telephone consultations (N = 48) | 39 (81) | 9 (19) |
| Follow-ups of patients with movement disorders are primarily conducted by video consultations (N = 43) | 6 (14) | 37 (86) |
| If you have started conducting telephone consultations for movement disorder patients during the pandemic, do they function satisfactorily for the patients (N = 46) | 20 (43) | 26 (57) |
| If you have started conducting telephone consultations for movement disorder patients during the pandemic, do they function satisfactorily for you (N = 47) | 20 (43) | 27 (57) |
| Are you more likely to postpone altering dosages after a telephone consultation than a face-to-face meeting (N = 47) | 29 (62) | 18 (38) |
| Reduced standard of care has been available to movement disorder patients during the pandemic (N = 53) | 39 (74) | 14 (26) |

Numbers given as n (%).
where telemedicine has been most thoroughly evaluated also prior to the pandemic.\textsuperscript{5,9,17,18} The findings in the present study confirm the results from previous studies reporting that primary headache disorders may be well suited for telemedicine. It should also be emphasized that patient-reported headache outcomes using telemedicine in previous studies have not been inferior to standard care.\textsuperscript{5,9,17,18}

Also epilepsy has been investigated as a disorder of interest in telemedicine.\textsuperscript{19,20} Telemedicine in epilepsy has been suggested to be noninferior to standard care with regard to seizure control, medication use, medication adherence, and hospitalizations.\textsuperscript{19} In line with our findings, a recent study of epilepsy care comparing China, France, and Italy showed a shift toward more telemedicine, and overall 83% of the neurologists in these countries reported the use of telemedicine from February to July 2020.\textsuperscript{21} In a Spanish study of 255 epilepsy patients, 49% of the patients considered telemedicine very satisfactory and 35% quite satisfactory during the COVID-19 pandemic.\textsuperscript{22} For future follow-up consultations, 38% considered it useful to conduct teleconsultations, while 37% would prefer face-to-face visits as their next consultation.\textsuperscript{22}

A recent comparison of telemedicine versus in-person visits for patients with multiple sclerosis found virtual house calls feasible and cost-effective.\textsuperscript{7} However, this study included 36 patients from a selected university multiple sclerosis clinic, and more studies are needed before telemedicine can be regarded as evidence-based in multiple sclerosis. Only half of the neurologists in the present study reported that telemedicine worked satisfactorily in the follow-up of patients with multiple sclerosis.

There was an interesting, but not unsurprising, finding that conditions where medical history guided treatment decisions (epilepsy and headache) were reported as better suited than conditions where the neurological examination is more important for decision-making (multiple sclerosis and movement disorders). While it is impossible to conduct direct physical examinations by video, a limited examination or observation can sometimes be undertaken. However, conducting physical examinations or observation by video is not a straightforward replacement of in-person examination. The challenges will depend on the clinical condition, the patient’s knowledge of their symptoms, and the ability to collaborate effectively.

Overall, there were no differences between to what degree the neurologists deemed telemedicine satisfactorily for either the patients or themselves.

We expected that telemedicine would be experienced as a better tool by the younger residents than the older senior consultants since they may be more familiar with novel technology and web-based applications, both privately and at work. Interestingly, there was no difference between the two groups in the present study. Patients with epilepsy, headache, and multiple sclerosis were all seen by a similar proportion of residents and senior consultants. The one condition in the present study that is probably most dependent on clinical examination is movement disorders. More senior consultants than residents were handling movement disorders, still this condition was deemed as unsatisfactory for both new referrals and follow-ups. Further, neurologists were more likely to postpone medication changes for movement disorders during a teleconsultation than in-person consultation. Telemedicine has not yet been implemented as standard care in movement disorders. Some pre-pandemic publications support telemedicine for movement disorders, but there are no publicly available virtual management of device-aided therapies.\textsuperscript{8} As the worldwide use of telemedicine increased also for movement disorders, the Movement Disorders Society Telemedicine Study Group has created a guidance for telemedicine during the pandemic.\textsuperscript{12,23}

Women were more comfortable with telemedicine, and found it better and more effective than men did. This finding should be investigated in more depth in future studies both among neurologists and other physicians.

Many of the telemedicine changes resulting from the COVID-19 may be irreversible. Telemedicine seems to be suited for certain conditions, but hands-on clinical examination and face-to-face meetings should not be underestimated.

Telemedicine requires the technology, but also specific skills that must be trained. As for all communication skills, the health-care planners must secure time for caregivers to train the necessary skills to get the most out of this new technology. Telemedicine should not be used uncritically to save time and money. Using telemedicine during the pandemic has forced governments, care providers, and patients into a new normal. However, institutions, workflow, and staff functions need to adapt to find the right balance in the future. As this new normal becomes the normal, there is an urgent and unmet need for more research on the patients’ perspective and whether their outcomes and prognosis change. Further, institutional strategies for neurological patients and telemedicine are warranted.

Based on our findings, it is probably clinically inappropriate and unsafe to use telemedicine for newly referred, poorly defined, and less predictable conditions. Telemedicine have many advantages but may lead to misdiagnosis or missing the correct diagnosis, overuse of advanced imaging investigations, and, thus, over/under treatment.

Respondents represented all neurological departments in Norway and should ensure good representativeness.

There are approximately 400 neurologists in Norway, but not all have been on duty during this period due to
research or education terms, rotation to other wards, or being in quarantine or on sick leave. Furthermore, neurologists who does not have outpatient clinic are less likely to have answered questions about telemedicine. Thus, a 34% responder rate is a conservative estimate. We regard this as satisfactory, especially since all data were collected during three hectic and uncertain weeks when many changes were implemented for neurologists at the hospitals. Further, based on the age and gender diversity of the sample, there is no reason to suspect such bias. Questionnaire studies such as this may introduce recall bias; however, we do not consider a reason to suspect systematic bias.

CONCLUSION

Telemedicine was rapidly implemented in Norwegian neurological departments during the first weeks of the COVID-19 pandemic. Only 8% of the departments maintained a regular outpatient clinic with in-person appointments. Neurologists deemed it much more professionally satisfactory to conduct follow-up consultations by telephone, than to carry out consultations with new patients by telephone. Teleconsultations were seen as better suited for patients with headache and epilepsy as compared to multiple sclerosis and movement disorders. There was no significant difference between residents and senior consultants regarding how they experienced teleconsultations. Female neurologists were more comfortable using telemedicine, and found it better and more effective than male neurologists did. Overall, more research on the patients’ perspective and institutional strategies for neurological patients and telemedicine is warranted.

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Conflict of Interests

BWS has received speaking fees from Novartis, unrelated to the present work. ECS has received speaking fees from Bayer and Novartis, unrelated to the present work. AMS, ESK, and KWF report no conflict of interest.

Data Availability Statement

The data that support the findings of this study are available on reasonable request from the corresponding author.

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