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ORIGINAL ARTICLE

The European Academy of Neurology NeuroCOVID-19 Task Force: A lesson for the future

Francesco Cavallieri[1] | Johann Sellner[2] | Tamar Akhvlediani[3] | Claudio L. Bassetti[4] | Daniel Bereczki[5] | Alessandra Fanciulli[6] | Saša R. Filipović[7] | Alla Guekht[8,9] | Raimund Helbok[10] | Sonja Hochmeister[11] | Filippo Martinelli Boneschi[12,13] | Tim J. von Oertzen[14] | Serefnur Özturk[15] | Alberto Priori[16,17] | Dauren Ramankulov[18] | Barbara Willekens[19,20] | Martin Rakusa[21] | Elena Moro[22] | on behalf of the NeuroCOVID-19 Task Force of the European Academy of Neurology

Correspondence
Elena Moro, Division of Neurology, Grenoble Alpes University, CHU of Grenoble, 38043 Grenoble, France.
Email: emoro@chu-grenoble.fr

Abstract

Background: The COVID-19 pandemic has made its mark on world history forever causing millions of deaths, and straining health systems, economies, and societies worldwide. The European Academy of Neurology (EAN) reacted promptly. A special NeuroCOVID-19 Task Force was set up at the beginning of the pandemic to promote knowledge, research, international collaborations, and raise awareness about the prevention and treatment of COVID-19-related neurological issues.

Methods: Activities carried out during and after the pandemic by the EAN NeuroCOVID-19 Task Force are described. The main aim was to review all these initiatives in detail as an overarching lesson from the past to improve the present and be better prepared in case of future pandemics.

Results: During the pandemic, the Task Force was engaged in several initiatives: the creation of the EAN NEuro-covid ReGistrY (ENERGY); the launch of several surveys (neurological manifestations of COVID-19 infection; the pandemic's impact on patients with chronic neurological diseases; the pandemic's impact of restrictions for clinical practice, curricular training, and health economics); the publication of position papers regarding the management of patients with neurological diseases during the pandemic, and vaccination hesitancy among people with chronic neurological disorders; and the creation of a dedicated "COVID-19 Breaking News" section in EANpages.

Conclusions: The EAN NeuroCOVID-19 Task Force was immediately engaged in various activities to participate in the fight against COVID-19. The Task Force's concerted strategy may serve as a foundation for upcoming global neurological emergencies.

KEYWORDS
COVID-19, EAN, neurology, pandemic, SARS-Cov-2

For affiliations refer to page 7.

INTRODUCTION

With its 7 million deaths, the COVID-19 pandemic represented the largest pandemic in the last 100 years [1]. Nowhere and no one has been spared the direct and/or indirect consequences of this unprecedented infectious disease [1, 2]. The pandemic caused by SARS-CoV-2 was a worldwide emergency that infected almost a billion people and strained the health systems, economies, and societies of most nations around the world. As a consequence, the COVID-19 pandemic has indirectly influenced, for at least 3 years, the management of patients with acute and chronic neurological conditions worldwide. In addition, during the first waves of the outbreak, many neurologists worked within COVID units when and where additional manpower was needed. Many others had to practice from their homes, and find new ways to manage neurological patients remotely [3, 4]. All these changes occurred very abruptly due to the rapid spread of the pandemic around the world, further emphasizing and highlighting the existence of organizational and economic differences between the health systems of high- and low-income countries.

COVID-19 was initially believed to cause only a respiratory infection [5]. However, with the accumulating clinical observations and knowledge, it was realized that the virus could directly or indirectly affect multiple systems of the human body including the central and peripheral nervous systems [6]. Indeed, besides the common respiratory symptoms, neurological manifestations are quite common, including headache, fatigue, myalgia, anosmia, ageusia, sleep, and autonomic disturbances [7, 8], whereas clinical syndromes include mainly encephalopathy, stroke, seizures, Guillain-Barré syndrome, and other immune-mediated peripheral neuropathies, revealing the need for neurologists in the care of COVID-19 patients [6, 9, 10]. Therefore, as soon as COVID-19 was spreading in Europe and declared to be a pandemic, the European Academy of Neurology (EAN) set up a special NeuroCOVID-19 Task Force (https://www.ean.org/home/organisation/committees-and-working-groups/eancore-covid-19-task-force) to initiate several activities aimed at promoting knowledge, research, and international collaborations against the concurrent outbreak [1, 11–15].

Four years have passed since the creation of this Task Force. In this article, we describe the overarching activities that have been carried out to date, in the hope that this work might serve as a lesson in being better prepared in case of future pandemics.

ACTIVITIES OF THE EAN NEUROCOVID-19 TASK FORCE

The Task Force was initially composed of a core group of neurologists from all over Europe who had already dealt with COVID-19 patients, and who had certified expertise in neuroimmunology, neuroepidemiology, neuroinfectious diseases, or neurocritical care. Since its creation, members of the Task Force have scheduled periodic online meetings initially weekly (for 2 years) and then monthly to discuss, propose, and update all members about the Task Force's activities. Two in-person meetings were also conducted during the EAN Congresses in Vienna (2022) and Budapest (2023). The paragraphs that follow summarize the Task Force's range of activities (Figures 1 and 2).

Facilitating early access to COVID-19-related information

One of the very first activities of the Task Force was producing a dedicated information portal on the ean.org website. Given that the EAN's 45,000 members were all facing the challenge of diagnosing and treating a thus far unknown disease, easy access to the growing pool of information seemed crucial. The EAN coreCOVID-19 website initially included links to external sources providing information on SARS-COV-2 and COVID-19 of clinical and scientific interest (https://www.ean.org/research/eancore-covid-19/external-resources). This information included literature research resources, links regarding clinical advice, statements from international and other bodies, as well as other neurological societies. The developing resources and activities of the Task Force were later added to the website portal.

International EAN survey on neurological symptoms in patients with COVID-19 infection

At the very beginning of the outbreak, Chinese colleagues from Wuhan firstly reported that patients with COVID-19 could manifest neurological symptoms and signs, often in the most severe cases [1, 16]. After this seminal study, several case reports and small case series were published underlying the existence of multiple neurological manifestations of COVID-19 infection, later renamed "Neuro-COVID". However, at that time, the frequency, determinants, and evolution of neurological manifestations associated with the infection remained unknown, because of the limited data that were available, publication bias, and the retrospective nature of most reports [14, 17]. Moreover, only limited clinical data were available from previous coronavirus epidemics [18]. Based on these premises, the NeuroCOVID-19 Task Force promoted an online survey focused on neurological symptoms in patients with COVID-19 infection [19]. The survey was made available on the EAN website and distributed to EAN members and other worldwide physicians starting from the beginning of April 2020 [19]. Data from 2343 responders (mainly neurologists) were collected, confirming a high prevalence of neurological symptoms in COVID-19 such as headache, myalgia, anosmia, ageusia, impaired consciousness, and psychomotor agitation [19]. The most reported syndromes were encephalopathy and acute cerebrovascular disorders [19]. This study was important for two main reasons. First, it confirmed that during the first pandemic wave neurologists were actively involved in the management of COVID-19 patients who were facing several

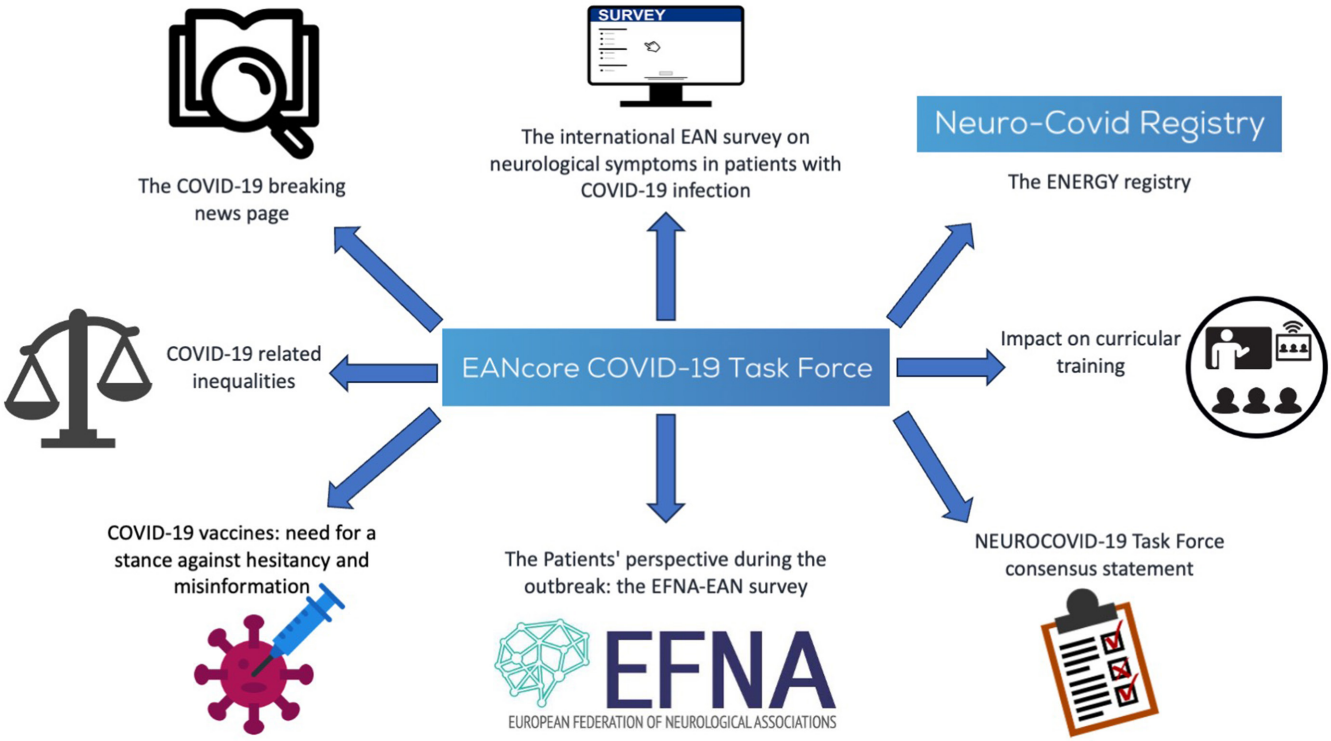

FIGURE 1 Summary of the different activities of the NeuroCOVID-19 Task Force. EAN, European Academy of Neurology.

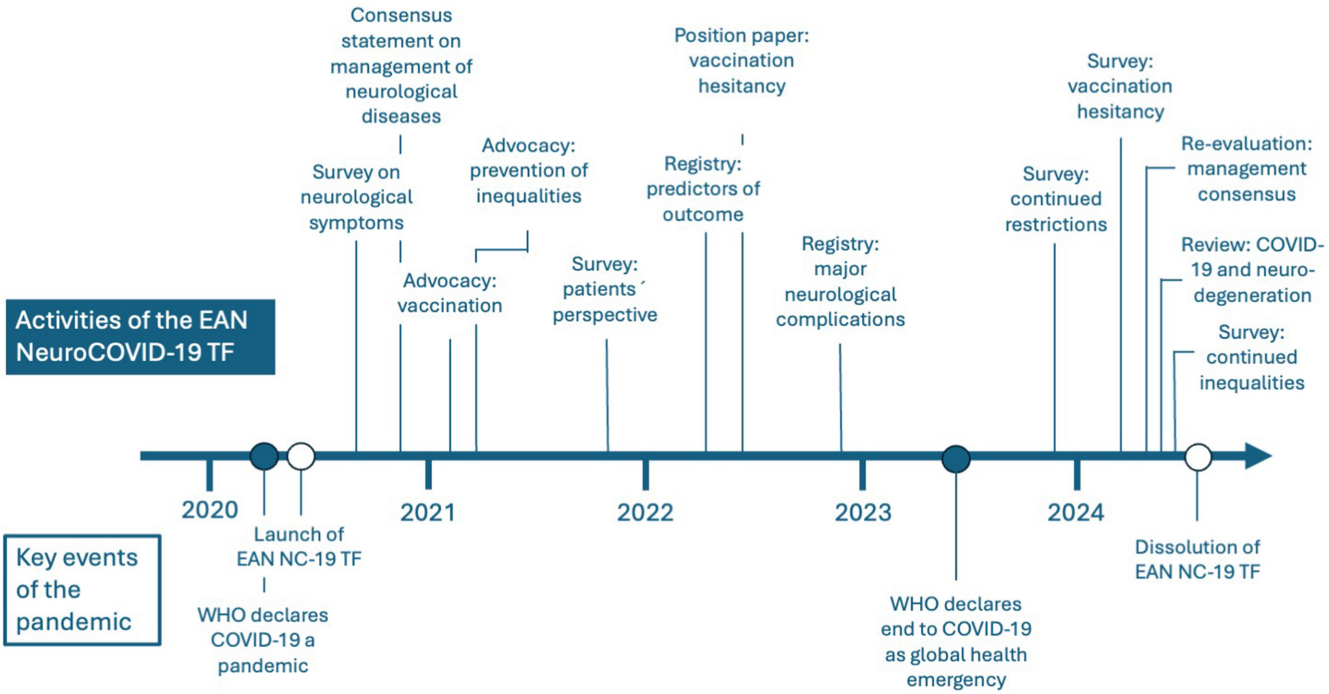

FIGURE 2 Timeline of the activities of the NeuroCOVID-19 Task Force. EAN, European Academy of Neurology; TF, Task Force; WHO, World Health Organization.

neurological complications. Second, it confirmed the need for the creation of prospective registries led by neurologists to capture the prevalence of COVID-19 patients with neurological manifestations, to describe the characteristics of these different neurological manifestations, and to assess the contribution of the neurological manifestations in the definition of the outcome of the infection.

Need for a systematic approach in studying Neuro-COVID: the ENERGY registry

As previously mentioned, during the first months of the outbreak, clinical data about Neuro-COVID were mostly driven by case reports and small case series. Moreover, in published reports the distribution of neurological symptoms and syndromes varied significantly in terms of prevalence, incidence, and phenotypical characteristics. This variability could mostly be explained by the differing sources of cases (hospital- vs. community-based), the accuracy of the diagnostic approach, and the physicians' interpretation of the patients' complaints. It was obvious that in a fast-evolving pandemic, evidence-based studies were lacking. Thus, a standardized approach was needed to provide a clearer outline of the spectrum of neurological disorders of COVID-19 [20]. The EAN NeuroCOVID-19 Task Force developed an international registry to study neurological manifestations and long-term outcomes in COVID-19 patients, the EAN NEuro-covid ReGistrY (ENERGY) [11]. The ENERGY registry was started in May 2020, and included data on neurological signs and symptoms in adult patients with COVID-19 infection seen by neurologists in outpatient services, emergency rooms, and hospital departments in European and non-European countries [11, 21]. In the first study utilizing ENERGY data, the authors found that older age, stupor/coma, stroke, and intensive care unit (ICU) admission were predictors of worse outcome at discharge in Neuro-COVID patients, while older age, cancer, cardiovascular complications, refractory shock, stupor/coma, and ICU admission were associated with death [22]. These results confirmed that Neuro-COVID could develop into a condition with an unfavorable/detrimental outcome, particularly in older subjects and those with comorbidities and acute COVID-19 complications [22]. A second study from the ENERGY registry focused on phenotyping of infected patients with and without specific neurological manifestations of the infection, finding that patients with COVID-19 and neurological manifestations presented distinct phenotypes. Indeed, differences in age, general and neurological comorbidities, and infection severity characterized the various neurological manifestations of COVID-19 [21].

Caring for neurological patients with COVID-19 infection: the NeuroCOVID-19 Task Force consensus statement

The management of patients living with neurological diseases and then affected by COVID-19 represented another important challenge that neurologists faced in the first year of the outbreak, particularly regarding the administration of immunosuppressive treatments. To provide guidance in caring for neurological patients with COVID-19, in 2020 the NeuroCOVID-19 Task Force developed a consensus statement for the management of patients with neurological diseases during the pandemic [23]. The involvement of all scientific panels, representing the many different subspecialities in neurology, enabled comprehensive expert input from several hundred specialists using a revised Delphi process [23]. This represented the first published structured consensus statement on good clinical practice in patients with neurological disease during the COVID-19 pandemic, allowing the provision of immediate guidance for neurologists [23]. Currently, the Task Force is working on an updated version of the EAN consensus statement that will include both a revision of the previous statement and 'new' statements related to vaccination and long-COVID (article in preparation).

"COVID-19 Breaking News" page: a free resource enabling neurologists to keep up to date on the pandemic

As already mentioned, at the beginning of the pandemic neurologists were faced with the management of both neurological complications in patients with COVID-19 and COVID-19 infection in patients living with neurological diseases. However, at that time it was very difficult for neurologists to stay up to date with the mounting scientific knowledge about the pathophysiology, clinical manifestations, and treatment of COVID-19 infection. In addition, very often neurologists were on the front line working full time in COVID-19 units. These issues made necessary the rapid dissemination of COVID-19-related news and scientific updates within the European and global neurological communities. In response to this need, since April 2020 the EAN NeuroCOVID Task Force developed the "COVID-19 Breaking News" page on the EAN website. As a result, the Task Force members began a monthly review of all the scientific literature produced on COVID-19 and selected the articles of greatest interest and relevance. This allowed readers of the webpage to be updated on the latest COVID-19-related news quickly. In addition, the "COVID-19 Breaking News" page was structured from the beginning by subdividing the articles based on the type of study (randomized controlled trials [RCTs], prospective cohort studies, cross-sectional studies, retrospective studies, case series, case reports, metanalysis, systematic reviews, narrative reviews, and basic science) with the aim of facilitating the consultation of the webpage and the selection of articles of interest. In 4 years, as many as 900 articles have been screened and published on the "Breaking News" page, now renamed "COVID-19 Distillery", allowing readers to stay up to date with the latest news and findings related to the neurological, pathophysiological, epidemiological, and clinical studies on COVID-19.

Patients' perspective during the outbreak: the EFNA-EAN survey

To investigate the impact of the first wave of the pandemic on individuals living with neurological diseases, as well as the hopes

and fears of these patients about the post-pandemic phase, the NeuroCOVID-19 Task Force joined forces with the European Federation of Neurological Associations (EFNA) to promote an online survey that was directed at any person living with a neurological disorder in Europe [24]. This survey raised several patients' issues related to the pandemic: the unsatisfactory overall care of their neurological diseases during the outbreak due to significant delays in accessing medical care; the insufficient amount of reliable information received about the potential impact of COVID-19 on their neurological disease; and the substantial lack of involvement in their disease management decisions [24]. Obviously, participants were aware of the great sacrifices and efforts that were being expended in dealing with the pandemic by healthcare systems across Europe; however, they felt that they had been left behind [24]. In addition, the participants were also concerned about the possible delays in the rescheduling of visits in a post-pandemic setting, the social isolation, and the possible delays in clinical trials with disinvestment in neuroscience research [24]. In a future pandemic situation these issues must be considered in order to better organize the care of patients with neurological diseases.

COVID-19 vaccines: the need for a stance against hesitancy and misinformation

Throughout the 2020s, the main worldwide efforts of pharmaceutical and scientific research were focused on the development of an effective vaccine against COVID-19 in order to limit the spread of the pandemic that was causing millions of deaths. In late 2020, the first RCTs were published demonstrating the efficacy of mRNA vaccines in reducing the risk of being infected and lowering the risk for an unfavorable outcome.

On 21 December 2020, the European Medicines Agency recommended granting a conditional marketing authorization for the vaccine tozinameran (Comirnaty®), an RNA vaccine, to prevent COVID-19 in people aged 16 years or over [25, 26]. Applications for further vaccines were approved during 2021 with the release of mRNA-1273 (Spikevax®) [27], Ad26.COV2.S (Janssen/Johnson & Johnson®) [28], and ChAdOx1-S (Vaxzevria®) [29, 30]. Despite the excellent short-term initial results, subsequent studies showed that the protection against the infection wanes over time, particularly in the elderly population and in patients treated with immunosuppressive drugs [31]. To overcome this limit, regular vaccine boosters were recommended in order to maintain the efficacy of protection against the virus [32]. However, a high vaccine hesitancy was seen during the first months of the vaccination campaigns around the world, even though at that time the pandemic was at its peak, representing an important worldwide health problem [33]. Several factors influenced the refusal of the vaccine including primarily: being against vaccines in general; concerns about safety/thinking that a vaccine produced in a rush was too dangerous; considering the vaccine useless because of the assumed harmless nature of COVID-19, general lack of trust, doubts about the efficiency of the vaccine; belief about already being immunized, and doubts about the provenience of vaccine [33].

In this setting, the EAN NeuroCOVID-19 Task Force published a statement at the end of 2020 strongly supporting a primary prevention strategy based on vaccination and encouraged neurologists to support its implementation. In addition, a plea was made for giving high priority for early access to vaccination to patients with chronic neurological disorders and for ensuring global and equitable allocation of vaccine batches [26].

However, during the following 2 years, even with the proven benefits of vaccination in terms of prevention of symptomatic, severe, and fatal COVID-19, the willingness to get vaccinated and to receive booster shots remained subpar among people with neurological disorders [31]. In a 2022 position paper, the Task Force summarized the potential barriers to vaccination coverage, and formulated strategies to overcome vaccination hesitancy [31]. In addition, a survey among Task Force members about vaccination hesitancy in people with neurological disease was also performed, highlighting that people with multiple sclerosis and other autoimmune neurological disorders were most skeptical of SARS-CoV-2 vaccination, mainly due to the fear of possible worsening of their pre-existing neurological condition, vaccination-related adverse events, and drug interaction [31]. This position paper underlined the key role of neurologists as advocates of COVID-19 vaccination and primary source of up-to-date scientific information for the individuals living with chronic neurological diseases under their care [31]. The Task Force is currently working on an updated version of the survey on vaccine hesitancy with the aim of reassessing the 2023 attitude of patients with neurological diseases towards the SARS-CoV-2 vaccination (article in preparation).

Impact of the pandemic on the inequalities of societies and healthcare systems, curricular training, and financial burden

Another important consequence of the COVID-19 outbreak was the increase in the inequalities of societies, healthcare systems, and educational offers [34, 35], with a disproportionate impact on already vulnerable communities, particularly in low-income countries [36]. Lessons from previous epidemics and the COVID-19 pandemic reinforced the need to implement mitigation measures. In a review published in 2021, the EAN NeuroCOVID-19 Task Force raised awareness of the potential impact of COVID-19 on inequalities in healthcare systems, and called for action to prevent disparity at individual, national, and supranational levels [36].

In addition, in order to assess the pandemic's impact on clinical service, curricular training, and financial burden during the lockdown, and the assumed recovery by 2023, the EAN NeuroCOVID-19 Task Force also promoted an online survey among the EAN community [37]. The results of the survey underlined that the pandemic affected multiple neurological subspecialties to differing extents. Most affected were dementia, neuromuscular, and

movement disorders clinical practice [37]. The need during the outbreak to reorganize the student and residency rotations and congresses, trying to take as much advantage as possible of virtual formats, was also underlined, together with the affordability of neurological care and the problem of medication shortages [37]. As of Spring 2023, it appeared that neurological services have not yet fully recovered following the COVID-19 pandemic outbreak. The Task Force interpreted such continued limitations in neurological healthcare provision as a major threat for brain health of European people, demanding a call for action at a European level [37].

What is boiling in the pot now? Ongoing and next activities of the Task Force and lessons learned to prepare for the future

Currently, the Task Force's activities are still focused on several issues related to COVID-19. First, the assessment of possible disparities related to access to healthcare services among major neurological conditions in the time of the pandemic by means of an online survey shared with 600 participants across 84 different countries (article in preparation). Several in vitro and animal models have highlighted a possible interaction between SARS-CoV-2 virus and key proteins implicated in neurodegenerative diseases such as alpha-synuclein, tau protein, and beta-amyloid [38–43]. In addition, the virus may also lead to microglia activation and neuroinflammation, which has an important role in the pathogenesis of neurodegenerative diseases [44, 45]. This has led to the hypothesis that COVID-19 could represent a factor favoring the long-term development of neurodegenerative diseases. Based on these premises, the Task Force is currently working on a review article that focuses on the potential increase in neurodegenerative diseases after the COVID-19 outbreak, supporting the need for awareness and justification for surveillance of long-term post-COVID neurodegenerative disorders (article in preparation). In this context, the ENERGY registry represents a crucial tool for monitoring the incidence of neurodegenerative diseases in patients who presented neurological manifestations during COVID-19 infection. In fact, the registry provides a 5-year follow-up from the first COVID-19 infection that may allow analysis of the possible role of SARS-CoV-2 as a favoring factor for the development of neurodegenerative diseases in the long term after infection.

The creation of the aforementioned ENERGY registry, which was the first international registry supported and promoted by the EAN, demonstrates that the EAN can coordinate European and non-European data collections and pathology-specific registries. The implementation of registries set up based on the ENERGY registry may thus represent a valuable future tool to be used not only in the context of future pandemics, but also for studying different neurological diseases including rare ones.

Through the web portal and the "Breaking News" page, the EAN NeuroCOVID-19 Task Force has made it possible to keep all neurologists associated with the EAN up to date on COVID-19-related scientific and therapeutic news. The use of the "Breaking News" page has been, and can continue to be, a valuable tool for future pandemics by allowing neurologists to stay up to date without the need for a constant, highly time-consuming, review of the literature.

In addition, this experience has demonstrated that a dedicated Task Force can convene the various EAN expert groups, which are organized into 29 scientific panels covering almost all neurological specialty areas. This was demonstrated by the previously mentioned consensus statement for the management of patients with neurological diseases during the COVID-19 pandemic, which was published early on and proved to be a very useful tool in the management of these patients during the pandemic [23]. Most importantly, the experiences gained underline the importance of collaborating with patients' associations to promptly develop common projects that strengthen the alliance between neurologists and patients during emergency situations such as a pandemic and are ultimately meaningful to European individuals living with neurological diseases.

CONCLUSIONS

We have here summarized the main activities of the EAN NeuroCOVID-19 Task Force from its creation during the first wave of the pandemic until the present day. EAN has demonstrated its ability to react promptly to an unpredictable event by creating a Task Force which immediately engaged in various activities in the fight against COVID-19. Should a new infectious disease appear, scientific societies will be ready to support patients, clinicians, and researchers worldwide.

AUTHOR CONTRIBUTIONS

Francesco Cavallieri: Conceptualization; data curation; methodology; writing – original draft; writing – review and editing. **Johann Sellner:** Conceptualization; methodology; data curation; writing – original draft; writing – review and editing. **Tamar Akhvlediani:** Writing – review and editing; data curation; methodology. **Claudio L. Bassetti:** Data curation; writing – review and editing; methodology. **Daniel Bereczki:** Data curation; writing – review and editing; methodology. **Alessandra Fanciulli:** Data curation; writing – review and editing; methodology. **Saša R. Filipović:** Data curation; writing – review and editing; methodology. **Alla Guekht:** Data curation; writing – review and editing; methodology. **Raimund Helbok:** Data curation; writing – review and editing; methodology. **Sonja Hochmeister:** Data curation; writing – review and editing; methodology. **Filippo Martinelli Boneschi:** Data curation; writing – review and editing; methodology. **Tim J. von Oertzen:** Data curation; writing – review and editing; methodology. **Serefnur Özturk:** Methodology; data curation; writing – review and editing. **Alberto Priori:** Methodology; data curation; writing – review and editing. **Dauren Ramankulov:** Methodology; data curation; writing – review and editing. **Barbara Willekens:** Methodology; data curation;

writing – review and editing. **Martin Rakusa:** Methodology; data curation; writing – review and editing. **Elena Moro:** Conceptualization; methodology; data curation; writing – original draft; writing – review and editing; supervision.

AFFILIATIONS

[1]Neurology Unit, Neuromotor and Rehabilitation Department, Azienda USL-IRCCS di Reggio Emilia, Reggio Emilia, Italy
[2]Department of Neurology, Landesklinikum Mistelbach-Gänserndorf, Mistelbach, Austria
[3]Neolab Clinic, Tbilisi, Georgia
[4]Department of Neurology, University Hospital and University of Bern, Bern, Switzerland
[5]Department of Neurology, Semmelweis University, Budapest, Hungary
[6]Department of Neurology, Medical University of Innsbruck, Innsbruck, Austria
[7]Institute for Medical Research, University of Belgrade, Belgrade, Serbia
[8]Research and Clinical Center for Neuropsychiatry, Moscow, Russia
[9]Pirogov Russian National Research Medical University, Moscow, Russia
[10]Department of Neurology, Kepler University Hospital, Johannes Kepler University Linz, Linz, Austria
[11]Department of Neurology, Medical University of Graz, Graz, Austria
[12]Neurology Unit, ASST Santi Paolo e Carlo, Milan, Italy
[13]Department of Health Sciences, University of Milan, Milan, Italy
[14]Medical Directorate, University Hospital Würzburg, Würzburg, Germany
[15]Department of Neurology, Faculty of Medicine, Selcuk University, Konya, Turkey
[16]Aldo Ravelli Center for Neurotechnology and Experimental Brain Therapeutics, Department of Health Sciences, University of Milan, Milan, Italy
[17]Clinical Neurology Unit, Azienda Socio-Sanitaria Territoriale Santi Paolo e Carlo and Department of Health Sciences, University of Milan, Milan, Italy
[18]European Academy of Neurology, Vienna, Austria
[19]Department of Neurology, Antwerp University Hospital, Edegem, Belgium
[20]Translational Neurosciences Research Group, University of Antwerp, Wilrijk, Belgium
[21]Division of Neurology, University Medical Centre Maribor, Maribor, Slovenia
[22]Grenoble Alpes University, CHU of Grenoble, Division of Neurology, Grenoble, France

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

Data sharing not applicable to this article as no datasets were generated or analyzed during the current study.

ORCID

Francesco Cavallieri https://orcid.org/0000-0001-5836-1982
Johann Sellner https://orcid.org/0000-0001-8749-5533
Claudio L. Bassetti https://orcid.org/0000-0002-4535-0245
Daniel Bereczki https://orcid.org/0000-0002-8374-0500
Alessandra Fanciulli https://orcid.org/0000-0002-2854-4179
Saša R. Filipović https://orcid.org/0000-0001-8508-3367
Tim J. von Oertzen https://orcid.org/0000-0003-2164-7842
Alberto Priori https://orcid.org/0000-0002-1549-3851
Martin Rakusa https://orcid.org/0000-0003-4433-3985

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