

**Energy and Commerce Subcommittee on Health**  
**Hearing: Barriers to Neurological Disease Research and Development**  
**National Neurological Conditions Surveillance System**  
**Centers for Disease Control and Prevention**  
**July 29, 2021**

**Statement for the Record**

Thank you for providing the Centers for Disease Control and Prevention (CDC) the opportunity to submit a statement for the record for the July 29, 2021 House Energy and Commerce Subcommittee on Health hearing on barriers to neurological disease research and development. We are pleased to update the Subcommittee on the agency's progress in developing the National Neurological Conditions Surveillance (NNCSS).

Millions of people across the United States face substantial and sometimes devastating effects from neurological disorders. For example, CDC has reported higher levels of comorbidity, disability, impaired health-related quality of life, and increased early mortality among people with epilepsy, Alzheimer's disease, and stroke. In 2016, as part of the 21st Century Cures Act (Public Law No. 114-255), Congress authorized the establishment of the National Neurological Conditions Surveillance System (NNCSS), mandating that the CDC, "[e]nhance and expand infrastructure and activities to track the epidemiology of neurological diseases; and...incorporate information...into an integrated surveillance system...designed in a manner that facilitates further research on neurological diseases" [21<sup>st</sup> Century Cures Act, §2061; PHS Act §399S-1(a)-(b)].

CDC has made progress on implementing NNCSS and is near completion of the first stage of this effort—the implementation of demonstration projects for the surveillance of two high consequence

neurological conditions (multiple sclerosis and Parkinson’s disease) for which CDC had not previously collected surveillance data. The findings from these demonstration projects provide CDC, its partners, and other interested parties a stronger foundation to continue to expand surveillance of neurological diseases. These efforts will ultimately help better estimate prevalence, mortality, and incidence of neurological conditions; catalyze research into causes and prevention of neurological conditions; identify gaps in care and opportunities for basic science research; and increase public awareness to help better support impacted patients and their families.

### **How Surveillance can Facilitate Research**

Focused surveillance is essential for expanding understanding of neurological conditions. Surveillance identifies how many people have specific neurological conditions (known as prevalence), how many new cases develop during a certain period (incidence), how long people live with specific neurological conditions (survival time), and how many people die from or with a specific condition (mortality). Surveillance also includes understanding rates of disease or mortality in the context of co-existing health conditions (e.g., cardiovascular disease, obesity, additional neurological conditions), demographic characteristics (e.g., gender, age, race, ethnicity, urban or rural setting, and what region of the country they live in), and indicators of disease burden (e.g., use of healthcare services and long-term care).

These types of surveillance findings can inform research to better understand why certain people are at greater risk of getting or dying from a neurological condition. Such findings can also inform researchers who want to develop strategies for prevention, treatment, treatment compliance, or healthcare access that can be targeted or tailored to those at higher risk. Ultimately, prevalence, incidence, and mortality rates can be compared over time to determine whether new treatments, diagnostics, or prevention strategies are having an impact at a population level—whether nationally, within a state, region, or locality, or within specific population subgroups (e.g., older women and uninsured).

## **CDC's Approach to Surveillance of Neurological Conditions**

When the NNCSS was established in 2016, CDC was conducting surveillance for a handful of neurological conditions (including amyotrophic lateral sclerosis (ALS), autism, cerebral palsy, epilepsy, muscular dystrophy, stroke, Tourette's syndrome, and traumatic brain injury; several other conditions, including Alzheimer's disease, have been added since then). However, there was little to no systematic surveillance of the hundreds of other existing neurological conditions. Fulfilling NNCSS's mandate to enhance and expand surveillance infrastructure and activities therefore included a number of particular challenges: first, how to establish an effective approach to surveillance that could be used for the diverse range of conditions not previously addressed by CDC; and second, how to implement surveillance so that it leveraged CDC's existing efforts to modernize public health data systems and did not result in dozens of new separate, siloed, and resource-intensive surveillance systems.

To address these challenges, CDC established a three-stage approach to NNCSS development, with an initial focus on establishing surveillance for two neurological conditions of high consequence that CDC had not yet addressed: multiple sclerosis and Parkinson's disease. Multiple sclerosis is a disease in which the immune system attacks the protective sheath (myelin) that covers nerve fibers therefore disrupting communication between the central nervous system and the rest of the body. It often starts when people are between the ages of 20 and 40 years, is more common in females, and is a leading cause of disability in young adults. Parkinson's disease is a chronic, progressive disease in which brain cells that make dopamine stop working or die, leading to slowness, stiffness, tremor, and walking and balance problems. It primarily affects people over 60 years old (although younger people can also be affected), is slightly more common in men and causes major disruptions in quality of life.

Multiple sclerosis and Parkinson's disease were selected due to a number of similarities and a few important differences. Both involve significant morbidity; both place a substantial burden on patients

and their families; and both have engaged patient advocacy organizations and communities who were committed as part of an informal coalition to establish surveillance for multiple sclerosis, Parkinson's disease, and other neurologic conditions. Differences between these two conditions allowed us to learn how to address different challenges, thereby increasing the relevance of the Stage 1 demonstration projects to a broader range of neurological conditions. For example, the differences in age of onset required CDC to carefully compare the relative usefulness of data sources consisting largely of older populations (e.g., identifying cases of a disease by using the diagnostic codes included in de-identified Medicare claims) versus younger populations (e.g., identifying cases through diagnostic codes in de-identified employer-based health insurance claims). Additionally, diagnosis of Parkinson's disease is complicated by a lack of biomarkers and because some symptoms are shared by other neurodegenerative disorders (e.g., multiple system atrophy, progressive supranuclear palsy, Lewy body dementia). Currently, there are no standard diagnostic criteria for Parkinson's disease. In contrast, standard diagnostic criteria do exist for multiple sclerosis. These differences required CDC to look very closely at the impact of diagnostic coding challenges when defining an eligible case.

NNCSS is being developed in three stages, presented below with timelines. CDC is completing Stage 1 and preparing for the initiation of Stage 2.

- **Stage 1 (Demonstration Projects):** Undertake NNCSS Demonstration Projects, using multiple sclerosis and Parkinson's disease, to produce national surveillance estimates and determine the best methodological approaches. [10/2018 – 9/2021]
- **Stage 2 (Build Out):** Build out NNCSS for ongoing surveillance of multiple sclerosis and Parkinson's disease using the proposed approaches; also develop criteria to assist with deciding which neurological conditions could be added to NNCSS in future years. [10/2021 – 9/2022]

- **Stage 3 (Expansion):** Extend NNCSS to additional neurological conditions while maintaining surveillance of multiple sclerosis and Parkinson’s disease. [10/2022 and beyond]

The timelines above have been adjusted to accommodate CDC’s response to the COVID-19 pandemic. NNCSS personnel are among the agency’s top experts in surveillance and as a result many NNCSS personnel deployed to serve CDC’s COVID-19 response, which caused some delays in implementation timelines. However, despite delays, work in modernizing data systems through the COVID-19 response has yielded unexpected benefits. New data sources have recently been made available to NNCSS, and new analytic tools thought to be a decade away are currently being built to collect COVID-19 data and will now be available to NNCSS much earlier.

Below is a detailed description of work to date advancing Stage 1 Demonstration projects.

### **NNCSS Stage 1: Demonstration Projects**

With the three years of appropriations that NNCSS has received to date (\$5M in each of the fiscal years (FY) 2019 - 2021), CDC has made substantial progress in developing the NNCSS and is near the completion of initial demonstration projects for MS and PD (Stage 1). The findings from these efforts will be essential to continued expansion of neurological surveillance capabilities.

Consistent with CDC’s data modernization efforts, CDC is not building stand-alone, one-off surveillance systems for neurological conditions that could become obsolete over time. Instead, NNCSS is part of a connected data ecosystem to harness the power of multiple data sources for better understanding of prevalence of neurological conditions. For example, as part of Stage 1, CDC reviewed existing data sources as well as newly emerging and future data sources and tools that could potentially be useful for surveillance of multiple sclerosis , Parkinson’s disease, and other neurological conditions. Assessing the

usefulness and contributions of each of these sources as well as other sources identified over time will help NNCSS surveillance to remain state-of-the-art and interoperable with other surveillance systems.

CDC's three-stage developmental strategy for NNCSS is using step-by-step, systematic methods to identify and test an effective approach to the surveillance of neurological conditions that will inform the continued growth of these surveillance capabilities for additional neurological conditions. As part of CDC's Public Health Data Modernization Initiative, the agency is dedicated to unlocking the full potential of data for disease detection by using a systems approach that builds upon the best existing data sources; explores new data sources, methods, and tools to ensure that NNCSS methods remain state-of-the-art; and continues to derive actionable and timely information.

Evaluating multiple data sources has also been important because of how complex it is to diagnose many neurological conditions. Diagnostic information is missing from many traditional population-based data sources (e.g., surveys) and many neurological conditions are omitted from household surveys that have unique limitations associated with declining response rates and respondent bias. Newer data sources and tools [e.g., electronic health records (EHR)] can provide detailed diagnostic information and more efficient opportunities for case validation as diagnostic criteria can change over time.

For these reasons, CDC identified and evaluated more than 25 population-based data sources. All of these data sources meet relevant quality, privacy, safety, and security standards; and the data available to CDC has been de-identified (i.e., there is no personally identifying information). Additionally, CDC adheres to all relevant health privacy laws when evaluating the data sources and using the data for surveillance purposes. CDC maximized speed and efficiency by first assessing in-house data sources, while simultaneously developing mechanisms to secure access to the additional sources. Traditional data sources included administrative data (such as claims from Medicare, Medicaid, and commercial entities, as well as hospital discharge data), surveys (from the National Center for Health Statistics and

elsewhere), and vital records (such as death certificates). Newer data sources included EHR data available through data science organizations that compile EHR data from multiple vendors, and EHR data available through individual EHR vendors (with the latter facilitated by COVID-19 work). Modern analytic methods and tools have included linking EHR and pharmaceutical claims data, exploring the value of machine learning for increasing efficiencies in predicting and diagnosing PD, and assessing opportunities for collaboration with clinical networks.

CDC continues to explore the use of electronic case reporting (eCR). This state-of-the-art capability automatically identifies cases of reportable or notifiable diseases in EHRs within health care settings, triggers case reports to be automatically generated from the EHRs, and transmits the case reports seamlessly, quickly, and securely to local and state health departments for review and action. This reduces the reporting burden on health care providers and enables a cost-effective, bidirectional exchange of information between health care and public health.

Electronic case reporting holds great promise for national surveillance and catalyzing research around neurological conditions. In recent years, Parkinson's disease has become a reportable disease in a handful of states. Receipt of de-identified data from a sufficient number of state registries could secure accurate national surveillance data for Parkinson's disease. Additionally, eCR could make substantial contributions to research by enabling state registries to serve as a source for patient recruitment into clinical trials and other research studies that preserve data quality, privacy, and security, as well as for catalyzing data sharing for research.

From 2018 to early 2020, CDC engaged with health department staff in California, Nebraska, and Utah; stakeholder organizations; and scientists to discuss strengthening of eCR processes within state registries and ultimate sharing of data with NNCSS. During the COVID-19 response all states halted efforts around eCR for Parkinson's disease to focus on building capacity for reporting COVID-19. CDC is

now receiving electronic case reports for COVID-19 from more than 8,800 facilities across the nation; this is up from zero in March of 2020. Through investments made in data modernization, what would have taken a decade or more for reliable eCR data for Parkinson's disease will now be possible within a few years.

Establishing useful and accurate algorithms (i.e., criteria) to identify cases is a critical component of developing all surveillance systems and was a key element of NNCSS Stage 1 efforts. CDC assessed the state of the science used to estimate multiple sclerosis and Parkinson's disease prevalence, incidence, and mortality—a critical step in a population-based approach. CDC conducted systematic reviews of the published literature and other materials to identify all case algorithms that had been used in population-based data sources for surveillance and related purposes. Then CDC carefully examined studies assessing the use and accuracy of these algorithms. This was particularly challenging for Parkinson's disease for which 120 different algorithms have been used to identify Parkinson's disease cases in population-based data sources. CDC also consulted with neurologists who specialize in multiple sclerosis, Parkinson's disease, and related conditions, and with medical coders and other subject matter experts who could provide information about medications, current diagnostic standards and practices, and other clinical aspects. These reviews helped us select the best algorithms to identify multiple sclerosis and Parkinson's disease cases in our available data sources.

CDC has proactively engaged federal partners and interested parties throughout Stage 1. CDC consulted with the National Institutes of Health's National Institute of Neurological Disorders and Stroke (NINDS) to understand the full scope of existing neurological conditions and how NNCSS surveillance findings might be useful to their intramural and extramural research and programs. NINDS has provided individual consultation and participated in meetings of the CDC working group established to provide input into NNCSS methods and findings. NINDS also participated alongside CDC scientists in the pilot



study evaluating the usefulness of machine learning for increasing the efficiency of predicting and diagnosing Parkinson's diseases.

Despite growing neurological burden (e.g., epilepsy) and neuroinfectious disease outbreaks (e.g., Zika), CDC had access to only one full-time neurologist at the start of NNCSS. To better support and enhance NNCSS, CDC has established fellowship mechanisms with Emory University and the Atlanta VA Medical Center to increase capacity for mid-level clinical neurologists specializing in multiple sclerosis and Parkinson's disease to support NNCSS. To continue work in NNCSS and potentially expand to other neurological conditions, CDC will need to acquire additional subject matter expertise in neurology. CDC has also consulted with Morehouse University, NINDS, and others about extending such fellowships in future years to secure specialist expertise for other neurological conditions.

CDC has actively collaborated with patient advocacy and research organizations including the National Multiple Sclerosis Society (NMSS), the Michael J. Fox Foundation for Parkinson's Research (MJFF) and the Parkinson's Foundation (PF). In March 2019, CDC coordinated an initial stakeholder meeting in Washington, DC. During this event, CDC, NINDS, VA, NMSS, MJFF, PF, and other interested parties representing multiple sclerosis and Parkinson's disease discussed NNCSS science, policy, and communication. Participants exchanged information, learned about CDC's approach to standing up surveillance, and discussed NNCSS's logic model. In November 2019, CDC collaborated with the Association of State and Territorial Health Officials to bring together CDC programs related to neurological conditions, NINDS and VA colleagues, and representatives from 34 patient advocacy organizations supporting a broad range of neurological conditions. More than 70 participants discussed research and surveillance needs, NNCSS progress, criteria for choosing future neurological conditions for surveillance, the interests and priorities of stakeholder organizations, and opportunities for collaboration.

CDC has recently initiated a collaborative effort with the Council of State and Territorial Epidemiologists (CSTE) and other interested parties to catalogue existing registries and other data collection efforts within states, tribes, and territories for multiple sclerosis, Parkinson's disease, and other specified neurological conditions. This work aims to identify which of these states, tribes, and territories might (1) have data or information to contribute to NNCSS; (2) conduct research, participate in research, or serve as a source of cases for research based on NNCSS surveillance findings and identified evidence gaps; and (3) inform or participate in public health action based on NNCSS surveillance findings.

### **Next Steps**

Throughout the NNCSS Stage 1 demonstration projects, CDC documented what worked and captured lessons learned. CDC is now combining this information with its scientific findings so that it can propose robust, efficient, replicable, and sustainable approaches that can be scaled up and rolled out for

- NNCSS Stage 2: Building Out the NNCSS—to maintain and refine multiple sclerosis and Parkinson's disease surveillance [FY 2022].
- NNCSS Stage 3: Extending the NNCSS—to add surveillance for other neurological conditions while maintaining surveillance for multiple sclerosis and Parkinson's disease [FY 2023].

Work is also underway to utilize the scientific descriptions of NNCSS's proposed approaches to inform documentation of staffing, budget, and other resource requirements. This includes current estimates of the cost per neurological condition of initiating and maintaining surveillance. These experience-based cost estimates may provide helpful information to supplement the Congressional Budget Office's (CBO) July cost estimate for the Advancing Research for Neurological Diseases Act of 2016 (S. 849; [cbo.gov](https://www.cbo.gov)). In 2016, CBO estimated that it would cost \$4M per year for a total of three years for CDC to complete feasibility studies to determine the appropriate surveillance methods for a neurological condition for

which it was not already collecting surveillance information. These calculations assumed CDC would simultaneously conduct feasibility studies for two of the most prevalent neurological conditions. CBO further estimated that once these feasibility studies were complete, ongoing surveillance would cost about \$5M per year per condition. CBO also provided separate cost estimates for enhancing surveillance work on eight neurological conditions for which CDC was undertaking surveillance in 2016 (amyotrophic lateral sclerosis (ALS), autism, cerebral palsy, epilepsy, muscular dystrophy, stroke, Tourette's syndrome, and traumatic brain injury), estimating \$27M per year of additional cost over and above the \$16M already being spent on surveillance at that time. Also of note are other neurological conditions for which CDC is now collecting data (e.g., Alzheimer's disease, Creutzfeldt-Jakob Disease) as well as recent infectious diseases that have considerable neurological components (e.g., Zika, COVID-19).

CDC is also documenting research gaps identified during Stage 1 so that they may be addressed in future work. These include gaps identified through our systematic reviews of the existing evidence on population-based surveillance, our methodological and analytic work, and our surveillance findings. Prior to finalizing national estimates of multiple sclerosis and Parkinson's disease surveillance and publicly sharing information about our case algorithms, data sources, and surveillance estimates, CDC is sharing the findings with clinician scientist academics specializing in multiple sclerosis and Parkinson's disease, NIH, and professional advocacy organizations for these conditions. The findings will then be shared via publications, the NNCSS website, and other communication materials.

Data from initial stages of NNCSS will help to inform estimates of scope required to robustly monitor each of the two test conditions and to inform requirements for expanding NNCSS to additional conditions. In the coming months, CDC looks forward to engaging with partners and interested parties to inform, participate in, support, and catalyze research to fill priority research gaps. CDC appreciates

the support of Congress and commitment to understanding prevalence of neurological diseases to better inform research and treatment.