Amyotrophic Lateral Sclerosis (ALS) in the United States
Frequently Asked Questions (FAQs)

About the Registry

1. **Why is the National ALS Registry important?**
   The Agency for Toxic Substances and Disease Registry (ATSDR), which is part of the Centers for Disease Control and Prevention (CDC), operates and maintains the only National ALS Registry. This Registry helps to describe the epidemiology of ALS in the United States. It gathers data on the occurrence and prevalence of ALS and associated deaths. However, the Registry does a lot more than just count ALS cases. It is a multi-faceted research platform that includes the following:
   - funds research to better understand the causes and risk factors of ALS;
   - supports patient recruitment for clinical trials and epidemiological studies on behalf of pharmaceutical companies, ALS referral centers, and universities;
   - collects blood and tissue for its National ALS Biorepository to support and conduct research in the areas of genetics analyses, biomarker identification, and disease progression; and
   - provides epidemiological datasets and biospecimens to researchers worldwide for ALS research.

2. **What is Public Law 110-373?**
   This public law was enacted in 2008 by Congress to better understand the ALS disease burden among adult populations in the United States. The Centers for Disease Control and Prevention/Agency for Toxic Substances and Disease Registry was given the authority to organize and develop guidance for ALS surveillance for gathering more information about persons living with ALS. In 2010, the National ALS Registry was created and tasked with collecting data and reporting of the national prevalence and incidence of ALS cases.

Identifying ALS Cases

3. **How are ALS cases identified in the United States?**
   ALS, like most non-communicable diseases, is not a notifiable disease in the United States. This means that state health departments currently do not notify ATSDR of newly diagnosed and existing ALS cases in their jurisdiction. As such, ATSDR had to develop a novel way to identify ALS cases. The Registry uses a two-pronged approach. The first approach uses a pilot-tested algorithm to identify ALS cases. This method is applied to large, national administrative databases including the Centers for Medicare and Medicaid Services (CMS), the Veterans Health Administration (VHA), and the Veterans Benefits Administration (VBA). The algorithm includes elements such as ALS diagnostic and billing codes, frequency of visits to a neurologist, and prescription drug use. The second approach uses a secure web portal to allow persons with ALS to self-register, which helps identify cases not collected through the first approach.

4. **What is deduplication?**
   The National ALS Registry uses a couple of approaches to estimate case counts by gathering information about the persons living with ALS from multiple administrative databases. This includes data from CMS, VHA/VBA, and the Registry web-portal platform. Deduplication occurs during data processing to identify individuals who have records found in more than one source to count them as a single case. This minimizes the duplicity and inaccurate count of ALS cases in the administrative national database.

5. **Are cases missing from the National ALS Registry?**
   ATSDR has determined that some ALS cases are missing in the Registry. Many of these missing cases represent persons with ALS who are covered by large, private insurance companies. Such insurance companies, including health maintenance organizations (HMOs) and preferred provider organizations (PPOs), do not share their data with federal agencies such as ATSDR. Previous publications reporting prevalence rate at the national level have used a modeling method called capture-recapture to estimate missing cases in the Registry. However, this modeling method was not applied to the state-level estimation at the time of analysis. We are currently evaluating the feasibility of using capture-recapture method to better identify the state-level case numbers for our future reports.

6. **Why is the Registry missing so many cases and what is the Registry doing to find these missing cases?**
   ALS, like most non-communicable conditions, is not a notifiable disease that is required to be reported to federal government authorities in the United States. CDC/ATSDR receives data from state health departments on many communicable diseases, such as tuberculosis and HIV, and a few non-communicable diseases, such as cancer, but not ALS. Even when the disease or condition is notifiable, surveillance systems that cover a state, region, or other large area rarely capture 100% of all cases. However, we are taking steps to ensure that the Registry's data are as complete as possible. Missing cases may be from private pay insurance companies, such as HMOs and PPOs, for which ATSDR does not have access.

   ATSDR is working with ALS patient organizations, including the ALS Association, Muscular Dystrophy Association, and Les Turner ALS Foundation, to obtain data on ALS cases they support through their nationwide offices, chapters, and clinics. This information will be cross-referenced with the Registry's data to add any missing cases. The Registry is cross-referencing its data with the Massachusetts ALS Registry and plans to do so with other proposed state ALS registries. We now have the approval to modify the Registry's data collection methods to allow new sources of data to be included for improved case counts.

7. **How can adding missing cases help researchers and the Registry?**
   By adding new cases to the Registry, we will improve overall case counts and strengthen our multi-faceted research platform allowing us to have a more precise estimate of how many people have ALS in the United States. This enables researchers to measure the overall effects of the disease on patients and caregivers and identify where health care improvements, such as greater access to care, should be made. This information also helps future clinical trials and research studies on the cause(s) and risk factors of ALS. To participate, a person living with ALS simply needs to register and enroll in the Registry portal. If you are a patient and wish to find out about how to join, go to http://www.cdc.gov/als. Adding new patients to the Registry allows researchers to improve future estimates of ALS prevalence and incidence.

8. **What can the public do to help the Registry and researchers find missing cases?**
   To participate, a person living with ALS simply needs to register and enroll in the Registry portal. If you are a patient and wish to find out about how to join, go to http://www.cdc.gov/als. Adding new patients to the Registry allows researchers to improve future estimates of ALS prevalence and incidence.

Prevalence, Incidence, and Age-based Rate Adjustment

9. **What is the *Prevalence of Amyotrophic Lateral Sclerosis (ALS) in all 50 States in the Unites States, Data from the National ALS Registry, 2011-2018* report?**
   The state-level prevalence of amyotrophic lateral sclerosis report provides a descriptive summary of an estimated number of people in all 50 states and the District of Columbia who are living with ALS. Following the guidelines of the Office and Management Budget (OMB), annual prevalence for years 2011 to 2018 was calculated to get an 8-year average prevalence rate for each state. Direct standardization using the 2000 US Standard Population was applied to report age-adjusted rates. The five states with the highest 8-year average count (observed cases) were California, Florida, Texas, New York, and Pennsylvania, but that is to be expected since these states have large populations. When the counts were age-adjusted per 100,000 (to account for population differences), the five states with the highest age-adjusted average prevalence were Vermont, Minnesota, New Hampshire, Massachusetts, and Wisconsin. Five states/territory with the lowest counts were the District of Columbia, Wyoming, Alaska, North Dakota, and Hawaii, while those with the lowest age-adjusted prevalence were Hawaii, Nevada, District of Columbia, Alaska, and Mississippi. Our study does not establish an association between living in states with higher prevalence rate with the likelihood of developing ALS.

10. **What are the definitions of incidence and prevalence?**
    Prevalence refers to the proportion of individuals in a population who have a particular disease in specific timeframe, regardless of when they first developed the disease or condition. It reflects the total burden of disease within a population. It is different from incidence which refers to the number of new cases of a disease within a defined population over a specified period of time.

11. **What does it mean to adjust rates based on age?**
    Age-adjusting rates is a method used to eliminate differences that might solely be explained by one population having residents that are older or younger than another population. The ALS prevalence state report used this method to account for differences in age distribution when comparing rates across states. Adjusting to the 2000 U.S. standard population has become the method of age-adjustments that is most used to account for these differences when reporting official rate data.

12. **Why are the prevalence rates for each year not included in the report?**
    The Registry must adhere to the Terms of Clearance set forth by the Office of Management and Budget (OMB). OMB approves all federal data collection activities. In 2021, the Registry submitted a formal request to OMB to release state level data and meet the repeated requests of the public for more detailed ALS data. OMB approved the Registry's request in the Spring of 2023. One caveat to release these data were to provide a minimum four-year average of the cases. This ensured data stability for states with a small number of ALS cases. For this reason, the Registry chose to publish state prevalence data as an eight-year average.

13. **Can ALS cases in a particular state increase or decrease over time?**
    This is the first time the National ALS Registry has described overall case numbers and prevalence rates at the state-level using the most recent data available (2011-2018). To determine the trends for the number of ALS cases over time in each state, the Registry would need to evaluate future data as it becomes available.

14. **When will the Registry add additional data from other sources?**
    The Registry is working with our partner organizations, including the ALS Association, Muscular Dystrophy Association, and Les Turner ALS Foundation, for additional case data. Before we can receive new data, however, necessary governmental approvals and data-sharing agreements must be in place. We expect these data agreements will be active and in place soon. The data agreements must also be written and finalized to ensure patient privacy and security. The federal Office of Management and Budget (OMB) recently approved the Registry's request to amend its protocols to add new data sources. These sources include patient-centric care-giver organizations such as the ALS Association, state-based registries, and private insurance carriers. Originally, only the administrative data sources (CMS and VHA/VBA) were approved for surveillance. Now, with the new amendment, the Registry can receive data from external institutions to better capture ALS cases for a more accurate estimation.

15. **Why are you just now reporting 2018 results when it's 2024?**
    Because ALS is a not a notifiable or reportable disease in the United States, the Registry receives ALS case data from CMS, VHA and VBA, and patients who enroll directly with the Registry at http://www.cdc.gov/als. Most of the case data comes from CMS. It takes CMS time to process and release the data. That typically results in a data lag of several years. For example, ATSDR didn't receive the 2018 CMS data until 2022.

    After the Registry receives the CMS and VA data, epidemiologists and statisticians use various methods to process the data, check for errors, and identify cases. This information is then merged with Registry self-enrollment case data and all case duplication is removed. The final dataset is sent to the National Death Index to determine and remove people who have died from the case count. From the time the Registry receives data from CMS and VA, it typically takes up to 24 months to remove duplicate information from the datasets and finalize the number of ALS cases. While ATSDR largely relies on other federal agencies to provide source data, the Registry moves as quickly as possible to make annual reports available after the data are compiled.

16. **Why are the national ALS prevalence estimates in the state-paper different from the national ALS prevalence estimates in the last annual report?**
    The previous annual report (Prevalence of amyotrophic lateral sclerosis in the United States, 2018) uses the capture-recapture (CRC) sampling method to account for the missing ALS cases at the national level, resulting in the adjusted prevalence rate of 9.1 per 100,000, higher than the observed rate. Current paper did not use the CRC method to adjust for the missingness for each state, as it was not available to apply the modeling method at the state level. This resulted in a lower observed national prevalence of 4.4 per 100,000 population. We do not know the difference of missingness in each state. The Registry continued to use the data obtained from the web portal and the other national administrative databases (CMS, VBA, VHA).

Living in States with Higher ALS Prevalence versus States with Lower Prevalence

17. **What can I do if I live in a state with higher ALS prevalence? Are individuals living in those states at an increased risk? Are there precautions I can take to protect myself or my family?**
    ALS is a non-communicable, non-infectious disease, so there is not a risk of spreading from person to person. However, certain genetic and environmental factors have been associated with increased risk of developing ALS. These may involve having a family history of mutation in high-risk ALS genes (e.g. *C9ORF72, SOD1, FUS, TARDBP*), having a history of serving in the military, and having been exposed to certain environmental conditions (e.g., vigorous leisure time physical activity, pesticide exposure, agricultural chemicals, persistent organic pollutants, ambient air toxins, cyanobacterial fungal algal blooms), However, there is no clear cause of ALS . If a person is concerned about developing ALS, they may benefit by becoming familiar with early symptoms of the disease and consult with a primary care physician..

18. **Why are the prevalence rates higher in some states?**
    Currently, there is no clear relationship between those who have ALS and a residency in a specific state or region. The difference in the estimates may be due to the variable demographic characteristics of persons living with ALS between the states or the presence of multidisciplinary clinics and ALS care centers drawing those who were previously diagnosed to the area. As an underlying environmental cause of ALS remains largely unknown, development of disease could be multi-factorial.

19. **Would moving to a state with lower prevalence decrease a person's chances of developing the disease?**
    Our study does not establish an association between living in states with higher prevalence rate with the likelihood of developing ALS.

20. **What is the International Classification of Diseases (ICD) system and what is the code for ALS, specifically?**
    Centers for Medicare & Medicaid Services lists ICD diagnostic codes for motor neuron diseases and other diseases. The National ALS Registry uses the published ICD-10-CM codes applicable to the year of data analysis. More information can be found here.