Amyotrophic Lateral Sclerosis (ALS) in the United States

Frequently Asked Questions (FAQs)

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 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

   - [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. **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. Such a method is applied to large, national administrative databases including 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.

3. **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 companies, including health maintenance organizations (HMOs) and preferred provider organizations (PPOs), do not share their data with federal agencies such as ATSDR. Because of this, ATSDR is using a modeling method called capture-recapture to estimate missing cases in the Registry. Researchers use the capture-recapture sampling method to estimate an unknown population size when identifying a complete number of affected persons is not practical. For epidemiological studies, ATSDR applies the capture-recapture method to estimate the completeness of existing registries or for disease surveillance using multiple case sources.

4. **What is the Prevalence of Amyotrophic Lateral Sclerosis (ALS) report?**
   The Prevalence of Amyotrophic Lateral Sclerosis report provides the estimated number of people in the United States who are living with ALS. In 2018, the Registry identified 21,655 adults who met the Registry definition of ALS, for an age-adjusted prevalence rate of 6.6 persons with ALS per 100,000 U.S. population. When we applied the capture-recapture methodology, we estimated that 8,159 ALS cases were missing, or about 27.4%, for an adjusted estimate of 29,824 cases (prevalence of 9.1 per 100,000 U.S. population), which is a lower

approximation than the previous year. Such differences might be due to a revision in the algorithm to define a case and a use of different capture-recapture methodology (See question 5). Using this methodology, along with the Registry's established algorithm, allows the Registry to better describe the epidemiology and demographics of ALS in the United States. From the data available and analyzed, there are approximately 30,000 persons living with ALS.

5. **Was the capture-recapture method used for the 2018 prevalence report?**
The Registry previously used a pair-wise capture-recapture method for the 2017 prevalence report. Because of a revision to the algorithm defining Registry-eligible cases for 2018, we used the log-linear modeling method. The log-linear method is better suited for estimating the number of ALS cases from multiple overlapping data sources. The Registry will continue to use these methods to improve case ascertainment in future reporting. However, an updated capture-recapture model might be needed if assumptions change. That might be needed if the Registry adds new sources of data, such as ALS cases from private insurance companies, state health departments, and non-governmental organizations.

6. **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, to get 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. Such 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.

7. **Why are you just now reporting 2018 results when it's 2023?**
Because ALS is a non-notifiable condition in the United States, the Registry receives ALS case data from CMS, VHA and VBA, and patients who enroll directly with the Registry at www.cdc.gov/als. Most of the case data comes from CMS. It takes CMS many months to process and release the data. That typically results in a data lag of several years (e.g., 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. Case data are then merged with Registry self-enrollment case data and duplicate data are removed. The final dataset is sent to the National Death Index to determine who has died so those persons can be removed 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. The COVID-19 pandemic also caused delays in receiving data. 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.

8. **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. We think that many of the missing cases are from private pay insurance companies, such as HMOs and PPOs, for which ATSDR does not have access. ATSDR is contacting some insurance companies to see if they might share future ALS case data.

ATSDR is also 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 are also seeking governmental approvals to modify the Registry's data collection methods to allow new sources of data to be included for improved case counts (See response to Question 6).

9. **How can adding missing cases help researchers and the Registry, and what can the public do to help this process?**
   By knowing how many persons have ALS and adding new cases to the Registry, we will have a more precise estimate of how many people have ALS in the United States. This will also improve overall case counts in the Registry and strengthen our multi-faceted research platform. That will allow researchers to measure the overall effects of the disease on patients and caregivers and to 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 www.cdc.gov/als. Adding patients who had not enrolled in the Registry will allow researchers to improve future estimates of ALS prevalence and incidence.

Disclaimer: The findings and conclusions in this report are those of the author(s) and do not necessarily represent the official position of the Centers for Disease Control and Prevention/Agency for Toxic Substances and Disease Registry.