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 (e.g., incidence, prevalence, mortality). 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, domestically and abroad, 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. As such, ATSDR had to develop a novel way of identifying ALS cases. Briefly, the Registry uses a two-pronged approach. The first approach identifies ALS cases by a pilot-tested algorithm, a method that is applied to large, national administrative databases including Medicare, Medicaid, and the Veterans Administration. 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 cases are from large, private insurance companies, such as health maintenance organizations (HMOs) and preferred provider organizations (PPOs), that do not share their data with federal agencies like ATSDR. Because of this, ATSDR is using a statistical technique 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 individuals is not practical. For epidemiological studies, capture-recapture has been applied 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?**
   In 2017, the Registry conservatively identified 17,800 adults (lower-bound estimate) who met the Registry definition of ALS, for an age-adjusted prevalence of 5.5 persons with ALS per 100,000 U.S. population. When the capture-recapture methodology was applied, we obtained an upper-bound estimate of 31,843 cases (prevalence of 9.9 per 100,000 U.S. population) with a "mean case count" of 24,821 ALS cases (prevalence of 7.7 per 100,000 U.S. population). The mean case count is the average or midpoint between the low and high estimates and likely represents the most accurate prevalence count/rate.

This is the first-time a method such as capture-recapture has been used to estimate the number of missing ALS cases (more than 14,000) in the United States. Additionally, this is the first Registry report to use ranges (lower, mid-point, and upper-bound estimates) to help estimate the overall effects of ALS disease burden on patients and society. Using this methodology, along with the Registry's established algorithm, will allow the Registry to better describe the epidemiology and demographics of ALS in the United States.

5. **Will capture-recapture be used for future reports?**
The Registry's intends to use capture-recapture for future reports. However, an updated capture-recapture model might be needed if assumptions change. Such changes might include an update to the algorithm or adding 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 anticipate these data agreements will be active and in place soon. These data agreements must also be written and finalized to ensure patient privacy and security.

7. **Why are you just now reporting 2017 results when we are in 2022?** The Registry receives information about ALS cases from the Centers for Medicare and Medicaid Services (CMS), the Veterans Administration (VA), and patients who enroll directly with the Registry at www.cdc.gov/als. The bulk of the case data comes from CMS, which typically takes many months to process and release the data to ATSDR. 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 to form a final dataset. 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. As ATSDR is largely reliant upon other federal agencies to provide source data, the Registry moves as quickly as possible to make annual reports available once 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 receives data from state health departments on most communicable diseases, such as tuberculosis and HIV, and a few non-communicable diseases, such as cancer, but not ALS. Additionally, surveillance systems that cover a state, region, or other large area are not typically able to capture 100% of all cases, even when the disease or condition is notifiable. However, we are taking steps to ensure that the Registry's data are as complete as possible. We hypothesize that many of the missing cases are from private pay insurance companies, such as HMOs and PPOs. ATSDR is contacting insurance companies to determine the feasibility of getting ALS case data. ATSDR is also working with ALS patient organizations, including the ALS Association, Muscular Dystrophy Association, and Les Turner ALS Foundation, to request 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 also cross-referencing its data with the Massachusetts ALS Registry and plans to do so with any other proposed state ALS registries. We are also seeking further governmental approvals to modify the Registry's data collection methods to allow new sources of data to be included for improved case counts.

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, allowing researchers to measure the overall effects of the disease on patients and caregivers, and to identify where health care improvements such as access to care should be made. In addition, this information assists future clinical trials and research studies on the cause(s) and risk factors of ALS. The public can get involved and volunteer in this process by first signing up for the Registry. If you are a patient and wish to find out about how to join, go to www.cdc.gov/als. Adding patients who have not enrolled in the Registry will allow researchers to improve future estimates of ALS prevalence and incidence.