How the National ALS Registry can Support your Research

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Disclosures

- None
- The findings from this presentation are of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention/Agency for Toxic Substances and Disease Registry (CDC/ATSDR).
Outline of Presentation

- Registry does more than count ALS cases
- Surveys
- Notification Mechanism (Connecting PALS & Researchers)
- National ALS Biorepository
- Funding research
- Registry Review Committee/CME Module
- Conclusions/Questions
Registry Does More than Just Count ALS Cases
<table>
<thead>
<tr>
<th>Survey (n=17)</th>
<th>Release Date</th>
<th>No. Completed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographics</td>
<td>October, 2010</td>
<td>9353</td>
</tr>
<tr>
<td>Occupational history</td>
<td>October, 2010</td>
<td>8497</td>
</tr>
<tr>
<td>Military history</td>
<td>October, 2010</td>
<td>8322</td>
</tr>
<tr>
<td>Smoking and alcohol history</td>
<td>October, 2010</td>
<td>8176</td>
</tr>
<tr>
<td>Physical activity</td>
<td>October, 2010</td>
<td>7840</td>
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<tr>
<td>Family history of neuro. diseases</td>
<td>October, 2010</td>
<td>7642</td>
</tr>
<tr>
<td>Disease progression (ALSFRS)</td>
<td>October, 2010</td>
<td>7674</td>
</tr>
<tr>
<td>Clinical data (e.g., devices used, body onset)</td>
<td>November, 2013</td>
<td>3234</td>
</tr>
<tr>
<td>Open-ended etiological questions</td>
<td>November, 2013</td>
<td>2958</td>
</tr>
<tr>
<td>Lifetime residential history</td>
<td>May, 2014</td>
<td>3580</td>
</tr>
<tr>
<td>Lifetime occupational history</td>
<td>May, 2014</td>
<td>3560</td>
</tr>
<tr>
<td>Residential pesticide use</td>
<td>May, 2014</td>
<td>3321</td>
</tr>
<tr>
<td>Hobbies with toxicant exposures</td>
<td>August, 2014</td>
<td>3056</td>
</tr>
<tr>
<td>Caffeine consumption</td>
<td>August, 2014</td>
<td>2861</td>
</tr>
<tr>
<td>Reproductive history (women)</td>
<td>August, 2014</td>
<td>1557</td>
</tr>
<tr>
<td>Health insurance status</td>
<td>December, 2014</td>
<td>2561</td>
</tr>
<tr>
<td>Head and neck injuries</td>
<td>December, 2014</td>
<td>2523</td>
</tr>
<tr>
<td><strong>Total (as of 10/7/2019)</strong></td>
<td><strong>---</strong></td>
<td><strong>86,715</strong></td>
</tr>
</tbody>
</table>
Research Notification System

- Patient recruitment for research can be difficult
- Approx. 95% of Registry PALS want to participate in research
- Registry links PALS with scientists who are recruiting for research (e.g., clinical trials, studies)
- Domestic and international researchers are using the tool for recruitment purposes
- 45 institutions have used it...
User Friendly for Researchers

- CDC IRB approval
  - Not needed, 38 approved institutions to date

- IRB approval by applicant’s institution

- Search criteria
  - Age, sex, time since diagnosis
  - State, region, and national

- For multi-site clinical trials, single IRB approval is satisfactory
  - Protocol(s) are not necessary

- Less than 4 weeks for review/approval
Highlighted Notifications Using the Registry

- **Notable Multi-site Clinical Trials:**
  - **Brainstorm Cell Therapeutics (Berry):**
    - Repeated dosing of NurOwn® (mesenchymal stem cells/MSC) derived from patient’s bone marrow
    - Contacted by over 100 patients on 1st notification, second notification June 2019
  - **Orphazyme (Benatar):**
    - Arimoclomol, extends independent breathing, improves survival, functional health and safety
  - **Orion Pharma (Cudkowicz):**
    - Levosimedam, ODM-109, improves respiratory function
  - **Amylyx Pharmaceuticals (Paganoni):**
    - AMX0035, slows disease progression and improves muscle strength
Highlighted Notifications Using the Registry

- Epidemiological/Risk Factor Studies
  - **The ALS Association *(Thakur)*:**
    - Patient and caregivers focused care services and preferences
    - Assisting in a future survey for the Association, ALS Focus later in 2019
  - **Columbia University *(Mitumoto)*:**
    - Examine the relationship between oxidative stress (OS) and ALS
    - Helped to recruit about a 100 patients
Upcoming Notifications Using the Registry

- **Studies**
  - **Mitsubishi Tanabe Pharma (Apple/Agnesse):**
    - Biomarker study
    - National, multiple sites
  - **Dartmouth Hitchcock Medical Center (Stommel/Bradley/Cox):**
    - L-Serine clinical trial
    - Pending application
National ALS Biorepository

**Biorepository background:**
- Linking extensive risk factor survey data with biosamples
- Nationally representative (e.g., beyond referral centers)
- User-friendly to PALS (e.g., use in-home phlebotomists to collect samples)
- Collecting specimens specifically for biorepository (i.e., not use leftover study samples to constitute biorepository)
- Pre/post mortem samples in one central biorepository

**Largest collection of pristine ALS samples for research, e.g., genetics, biomarkers, disease progression.**

**No charge for patients and caregivers – user friendly**
National ALS Biorepository Overview

In Home Collections
- Blood
- Urine
- Saliva

Post-Mortem Collections
- Bone
- Brain
- Spinal Cord
- CSF
- Muscle

Specimens for Research

Risk Factor Surveys from National ALS Registry
### National ALS Biorepository Samples

#### In-home Sample Types Participants (N = 1,153)

<table>
<thead>
<tr>
<th>Sample Type</th>
<th>Participants</th>
</tr>
</thead>
<tbody>
<tr>
<td>DNA (2µg)</td>
<td>1,061</td>
</tr>
<tr>
<td>RNA (2µg)</td>
<td>933</td>
</tr>
<tr>
<td>Plasma (.5ml)</td>
<td>971</td>
</tr>
<tr>
<td>Serum (.5 ml)</td>
<td>956</td>
</tr>
<tr>
<td>Whole Blood – metals free (1.8 ml)</td>
<td>948</td>
</tr>
<tr>
<td>Red Blood Cells (1.0 ml)</td>
<td>957</td>
</tr>
<tr>
<td>Buffy Coat (1.0 ml)</td>
<td>259</td>
</tr>
<tr>
<td>PBMCs(^1)</td>
<td>44</td>
</tr>
<tr>
<td>Urine (1.8 ml)</td>
<td>982</td>
</tr>
<tr>
<td>Urine with Hg preservative (4.5 ml)</td>
<td>607</td>
</tr>
<tr>
<td>Hair</td>
<td>157</td>
</tr>
<tr>
<td>Nails</td>
<td>268</td>
</tr>
</tbody>
</table>

#### Postmortem Sample Types Participants (N=41)

<table>
<thead>
<tr>
<th>Sample Type</th>
<th>Participants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brain</td>
<td>41</td>
</tr>
<tr>
<td>Spinal Cord</td>
<td>40</td>
</tr>
<tr>
<td>CSF(^2)</td>
<td>41</td>
</tr>
<tr>
<td>Bone</td>
<td>41</td>
</tr>
<tr>
<td>Muscle</td>
<td>42</td>
</tr>
<tr>
<td>Fibroblasts</td>
<td>24</td>
</tr>
</tbody>
</table>

\(^1\) PBMCs – Peripheral blood mononuclear cells  
\(^2\) CSF – Cerebrospinal fluid  
* Updated as of 06/30/19
<table>
<thead>
<tr>
<th>Study Name</th>
<th>Institution</th>
<th>Sample Type</th>
<th>Investigator</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Novel extracellular vesicle and molecular biomarkers of environmental exposure and disease progression in ALS</td>
<td>Columbia University Medical Center</td>
<td>Brain tissue</td>
<td>Neil Shneider, MD, PhD</td>
<td>Ongoing</td>
</tr>
<tr>
<td>Metals analysis</td>
<td>Centers for Disease Control and Prevention (CDC)</td>
<td>Whole blood, serum, urine</td>
<td>National ALS Registry</td>
<td>Ongoing</td>
</tr>
<tr>
<td>Mitochondrial DNA and Micro RNAs in Amyotrophic Lateral Sclerosis</td>
<td>Columbia School of Public Health</td>
<td>Whole blood, plasma, brain and spinal cord</td>
<td>Pam Factor-Litvak, PhD</td>
<td>Ongoing</td>
</tr>
<tr>
<td>Role of FUS protein in inflammation and neurodegeneration, as potentially applied to understanding the development of ALS</td>
<td>Icahn School of Medicine at Mount Sinai/</td>
<td>Human primary cells</td>
<td>Ivan Marazzi, PhD</td>
<td>Ongoing</td>
</tr>
<tr>
<td>ALS risk, exposure sources, and effects on the unfolded protein response pathway</td>
<td>Dartmouth College</td>
<td>Fingernails</td>
<td>Elijah Stommel, MD PhD</td>
<td>Ongoing</td>
</tr>
<tr>
<td>Identification and characterization of potential environmental risk factors for ALS using the ATSDR ALS Registry cases and a control population.</td>
<td>University of Pittsburgh</td>
<td>Blood</td>
<td>Evelyn Talbott, DrPH</td>
<td>Ongoing</td>
</tr>
<tr>
<td>Targeting Ataxin-2 in Amyotrophic lateral sclerosis (ALS)</td>
<td>University of Utah</td>
<td>Human primary cells</td>
<td>Stefan M. Pulst, MD</td>
<td>Ongoing</td>
</tr>
<tr>
<td>Genotyping of Samples for the National ALS Biorepository</td>
<td>National Institutes of Health</td>
<td>DNA</td>
<td>Bryan Traynor, MD, PhD</td>
<td>Ongoing</td>
</tr>
</tbody>
</table>
ATSDR is funding extramural research to learn more about ALS etiology and risk factors.

17 research studies have been funded to date.

Info gleaned also will help ATSDR prioritize topics for future risk factor surveys.

FY2019, whole-genome sequencing via the NIH, Genotyping done.

Future funding is subject to availability.
3 Newly Funded Grants (R01s)

- Dartmouth Hitchcock Medical Center (*Stommel*):
  - Environmental risk factors for ALS: critical time periods and genetic interactions
- University of Michigan (*Feldman*):
  - Metabolomic Signatures Linking ALS to Persistent Organic Pollutant Exposures
- Columbia University (*Shneider*):
  - Novel extracellular vesicle and molecular biomarkers of environmental exposure and disease progression in ALS
New Funded Grants in FY20

- **TS20-001: Identify, Analyze, and Evaluate Potential Risk Factors for Amyotrophic Lateral Sclerosis (ALS)**
  - Objective of the RFA: identify potential risk factors for ALS in humans that are potentially associated with or contribute to the etiology, progression, and pathophysiology of ALS in humans:
    - environmental and occupational
    - military service
    - infectious agents and viruses
    - nutritional intake
    - physical and sports activities
    - pharmaceutical use, and
    - traumatic (brain) injuries

- **Funding 1-4 awards, $400,000 per year, 3 years (subject to funds)**
Registry Review Committee Members

- Need researchers to review applications for:
  - Notification system and Biorepository
  - STEM background preferred
- Open to persons with ALS, researchers, and Neurologists
- 1-3 applications per year
- 1-2 hours at the most per application
- Contact: als@cdc.gov or pum4@cdc.gov
Welcome to the

Amyotrophic Lateral Sclerosis (ALS)

Continuing Education Module

This training was developed by the Agency for Toxic Substances and Disease Registry’s (ATSDR) Division of Toxicology and Human Health Sciences. Participants must take and submit the post-test for this training in order to receive free continuing education (CE).
The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention and the Agency for Toxic Substances and Disease Registry.