An Overview of National ALS Registry: Connecting Patients with Researchers

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Patient Registries Summit, Orlando, FL
January 29, 2016
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).
Experience with Registries

Registry experience
- National ALS Registry
- World Trade Center Registry
- Tremolite Asbestos Registry
- National Exposure Registry
- Rapid Response Registry
- Hurricane Katrina Pilot Registry
ALS Background

- ALS (Lou Gehrig’s disease) is a progressive, fatal neurological disease caused by the degeneration of motor neurons
  - Approximately 80% of cases die within 2-5 years of diagnosis
  - 5-10% are familial cases; 90-95% are sporadic cases
  - No known cause for sporadic cases
  - No cure or viable therapeutics

- ALS, like most non-communicable diseases, is a non-notifiable disease

- Lack of reliable incidence, prevalence estimates for U.S. and by geographic area
Notifiable Diseases in US

- Notifiable = diseases reported to CDC from state HDs
- ≈ 100 notifiable diseases in US, most are infectious (e.g. HIV, measles, hepatitis, Ebola, pertussis)
- Only 5 notifiable diseases are non-infectious
  - Cancer
  - Carbon monoxide poisoning
  - Lead blood levels
  - Pesticide-related illnesses
  - Silicosis
- ALS is a non-notifiable disease
- Novel approach was needed to track ALS cases
U.S. ALS Registry Act

- Enacted as Public Law 110-373 (October, 2008)
- Directed CDC/ATSDR to create a population-based ALS registry for the U.S.
- Does not make ALS a notifiable disease
- National ALS Registry launched in Oct, 2010

Registry purposes (as specified by the Act)
- Describe incidence and prevalence of ALS
- Describe the demographics of ALS patients
- Examine risk factors for the disease
National ALS Registry Methodology

National Databases*

Apply Algorithm

Non ALS Patients

Potential ALS Patients

True ALS Patients

Follow-up

National ALS Registry

Web Portal Registration

Validation Questions

True ALS Patients

Non ALS Patients

National ALS Biorepository

Risk Factor Surveys

* Medicare, Medicaid, VHA, VBA
Registry Algorithm

- Pilot tested, validated, and results published
- Algorithm based on:
  - Encounter code for ICD-9
    - 335.20
      - Medicare, Veterans databases
  - Death certificate with ALS as cause of death
  - Visits with neurologist
  - Prescription for Riluzole/Rilutek
The National Amyotrophic Lateral Sclerosis Registry Model

- Published editorial in *JAMA* in 2014
- Used Registry as a model for non-notifiable diseases
  - Parkinson’s
  - MS
- 21 Century Cures Act
  - Possibly establishing surveillance system for other neurological diseases
<table>
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<tr>
<th>Survey (n=17)</th>
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<th>No. Completed</th>
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<td>Occupational history</td>
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<td>Military history</td>
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<td>Smoking and alcohol history</td>
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<td>Physical activity</td>
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<td><strong>Disease progression (ALSFRS)</strong></td>
<td>October, 2010</td>
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<td>Family history of neuro. diseases</td>
<td>October, 2010</td>
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<td>Clinical data (e.g., devices used, body onset)</td>
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<td>Open-ended etiological questions</td>
<td>November, 2013</td>
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<td>Lifetime residential history</td>
<td>May, 2014</td>
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<td>Lifetime occupational history</td>
<td>May, 2014</td>
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<td>Residential pesticide use</td>
<td>May, 2014</td>
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<td>Hobbies with toxicant exposures</td>
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<td>Caffeine consumption</td>
<td>August, 2014</td>
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<td>Reproductive history (women)</td>
<td>August, 2014</td>
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<td>Health insurance status</td>
<td>December, 2014</td>
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<tr>
<td>Head and neck injuries</td>
<td>December, 2014</td>
<td>905</td>
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<tr>
<td><strong>Total (as of 1/25/2016)</strong></td>
<td>---</td>
<td><strong>52,358</strong></td>
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</table>
National ALS Registry Results

- U.S. prevalence rate: 3.9 cases/100,000 population\(^1\)
  - Based on 12,187 cases identified Oct 2010–December 2011
- Persons with ALS (PALS) more likely to be white, male, non-Hispanic, and 50-79 years old\(^1,2,3\)
- Median age at diagnosis = 64 years\(^2\)
- Males develop disease more often than females\(^1\)
  - 1.5 males to females
- Findings largely consistent with European ALS registries and small-scale U.S. epidemiological studies

\(1\) Morbidity and Mortality Weekly Report, 2014
\(2\) State/Metro manuscript in publication
\(3\) Rechtman et al, ALS FTD, 2014
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
* Researchers will ultimately determine eligibility to participation in studies
Simple system and less cumbersome than clinicaltrials.gov

Over 70,000 emails sent to ALS patients since inception

Year by year increase in notifications sent

Recruitment of PALS by researchers:
  - National recruitment is best
  - Currently over 5,000 PALS will receive notifications via email at one time
  - Yields a greater pool of potential recruits
  - Study needs to be geared towards a national study
  - Researchers need to be prepared for volume of inquiries by PALS

Local or geographic specific recruitment can be limiting
Recruitment Criteria

Specific Age Range (e.g. 40-50, 50-60, 60-75):

Specific time period since diagnosis (e.g. 1 year, 2 to 4 years):

Specific Sex (e.g. female only, male only):

City and / or State(s) of residence or region of the United States (e.g. Los Angeles, CA, Dallas, TX, State of Arizona, State of Georgia and Florida):

*Additional variables are available on a subset of the population, such as registrants with a history of military service, smoking / alcohol consumption or specific ALSFRS score. If you wish to use these as eligibility requirements, please contact the ALS Research Notification System Administrator.

☐ I do not want to prescreen for eligibility (e.g. I want to have research materials sent to all participants taking part in the notification process).
Research Notification System Benefits

- **PALS:**
  - Delivers timely and tailored opportunities for research participation

- **Researchers:**
  - Speeds-up study recruitment time
  - Increases study sample size
  - Achieves geographic diversity
  - Efficiently identifies PALS who meet specific recruitment requirements
  - Free service
Benefits for Biotech/Pharma

- Registry is looking to partner with Biotech/Pharma companies

- Benefits for Biotech/Pharma:
  - Already established National ALS Registry
  - Largest recruitment pool
  - National recruitment

- Tremendous interest from patients for any and all possible treatments and therapeutics

- Need help from neurologists, researchers, and ALS organizations to get the message out to Pharma
Feedback from Researchers

- Overall very positive
- Recruitment for studies ranged between <5% to 80%
- All researchers would recommend using Registry mechanism to other researchers

Recommendations for improvement:
- Send out more than one reminder to PALS (consensus)
  - IRB limitation, would need to be revisited
- Advertise or inform PALS about the research studies
  - Link to recruitment materials may be added to website

Input from researchers is INVALUABLE!
<table>
<thead>
<tr>
<th>Study Name (n=21)</th>
<th>Institution</th>
<th>Investigator</th>
</tr>
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<tbody>
<tr>
<td>Risk Factor Analysis in ALS</td>
<td>Medical University of SC</td>
<td>David Stickler, MD</td>
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<tr>
<td><strong>Phase II/III Trial of Arimoclomol in SOD1+ Familial ALS</strong></td>
<td>University of Miami</td>
<td>Michael Benatar, MD, PhD</td>
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<tr>
<td>Mindfulness, psychological well-being, and physical degeneration in people with ALS</td>
<td>Harvard University</td>
<td>Ellen Langer, PhD</td>
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<tr>
<td>Spatial Analysis of ALS in Florida, Ohio, New Hampshire, and Vermont</td>
<td>Dartmouth-Hitchcock Medical Center</td>
<td>Elijah Stommel, MD, PhD</td>
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<tr>
<td><strong>Mexiletine treatment of muscle cramps in ALS</strong></td>
<td>University of California, Davis</td>
<td>Björn Oskarsson, MD</td>
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<tr>
<td>Epidemiologic Risk Factors &amp;Genetics of ALS</td>
<td>University of Michigan</td>
<td>Eva Feldman, MD, PhD</td>
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<td><strong>Exp. Treatment of Bulbar Dysfunction in ALS</strong></td>
<td>Center for Neurologic Study</td>
<td>Richard Smith, MD</td>
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<tr>
<td>The Natural History and Biomarkers of C9ORF72 ALS and Frontotemporal Dementia (FTD)</td>
<td>National Institutes of Health/NINDS</td>
<td>Mary Kay Floeter, MD, PhD</td>
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<tr>
<td>Developing a Satellite ALS Center at a Remote Site Incorporating Regional Resources &amp;Telemedicine</td>
<td>University of Kentucky</td>
<td>Edward Kasarskis, MD, PhD</td>
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<tr>
<td><strong>Evaluating Ibudilast MN 166 in subjects with ALS</strong></td>
<td>Carolinas Neuromuscular AL Center</td>
<td>Benjamin Rix Brooks, MD</td>
</tr>
<tr>
<td>Study Name (n=21)</td>
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<td>Investigator</td>
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<tr>
<td>Prospective Epi. Study in a Large National ALS Registry Cohort to Identify ALS Risk Factors</td>
<td>Columbia University Medical Center</td>
<td>Hiroshi Mitsumoto, MD, DSc</td>
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<tr>
<td>VA Biorepository Brain Bank ALS Study</td>
<td>VA Boston Healthcare System</td>
<td>Neil W. Kowall, MD</td>
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<tr>
<td>Questionnaire of cramps and pain in ALS</td>
<td>University of California, Davis</td>
<td>Björn Oskarsson, MD</td>
</tr>
<tr>
<td>Assessing pain in ALS</td>
<td>Penn State Hershey Medical Center</td>
<td>Zachary Simmons, MD</td>
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<tr>
<td>NeuRx® Diaphragm Pacing System™ (DPS) study</td>
<td>Barrow Neurological Institute</td>
<td>Jeremy M. Shefner, MD, PhD</td>
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<tr>
<td>An online questionnaire for research into ALS</td>
<td>University of Sydney</td>
<td>Roger Pamphlett, MD, MB</td>
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<tr>
<td>ALS and Genetic Testing: A Perspective from the ALS Community</td>
<td>The Ohio State University</td>
<td>Jennifer Roggenbuck, MS</td>
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<tr>
<td>Speech Motor Impairments</td>
<td>MGH Institute of Health Professions</td>
<td>Jordan Green, PhD</td>
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<tr>
<td>RDCRN Contact Registry for the CReATe Consortium</td>
<td>University of Miami</td>
<td>Michael Benatar, MD, PhD</td>
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<tr>
<td>Study to Evaluate the Sensitivity, Specificity, and Overall Accuracy of an ALS Diagnostic Test</td>
<td>Iron Horse Diagnostics, Inc.</td>
<td>Andreas Jeromin, PhD</td>
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<tr>
<td>Phase 2 Pharmacodynamic Study of Ezogabine on Neuronal Excitability in ALS</td>
<td>Massachusetts General Hospital</td>
<td>Brian J. Wainger, MD, PhD</td>
</tr>
</tbody>
</table>

>70,000 email notifications sent to date
Biosamples (e.g., blood, tissue) are important in ALS research
- Biomarkers, genotyping, etc

ATSDR just completed 4 year biorepository pilot study

Pre/post mortem samples collected from ≈ 330 Registry enrollees via pilot
- Blood, hair, nails, saliva, urine
- Brain, bone, spinal cord, CSF, muscle, skin (n=18 PALS)
National ALS Biorepository (con’t)

- ATSDR and an external panel of experts determined that a biorepository linked to the National ALS Registry is feasible

- Launching Fall of 2016

- This biorepository will significantly differ from others by:
  - linking extensive risk factor survey data with biosamples
  - being nationally representative (e.g., beyond referral centers)
  - being 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)
  - containing pre/post mortem samples in one central biorepository
Research Funding

- ATSDR is funding external research to learn more about ALS etiology and risk factors
- Info gleaned also will help ATSDR prioritize topics for future risk factor surveys
## ALS Research Funded by ATSDR

<table>
<thead>
<tr>
<th>Study Name (n=10)</th>
<th>Institution</th>
<th>Investigator</th>
</tr>
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<tbody>
<tr>
<td>Epidemiology of ALS</td>
<td>Harvard University</td>
<td>Marc Weisskopf, PhD, ScD</td>
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<tr>
<td>Large-scale genome-wide association study of ALS</td>
<td>National Institutes of Health</td>
<td>Bryan Traynor, MD, PhD</td>
</tr>
<tr>
<td>Gene-environment interactions in ALS</td>
<td>Northwestern University</td>
<td>Teepu Siddique, MD</td>
</tr>
<tr>
<td>A Prospective Comprehensive Epidemiologic Study in a Large Cohort in The National ALS Registry: A Step to Identify ALS Risk Factors</td>
<td>Columbia University Medical Center</td>
<td>Hiroshi Mitsumoto, MD, DSc</td>
</tr>
<tr>
<td>Identification and Validation of ALS Environmental Risk Factors</td>
<td>University of Michigan</td>
<td>Eva Feldman, MD, PhD</td>
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<tr>
<td>Ecologic Study to Evaluate Spatial Relationships between ALS and Potential Environmental Risk Factors</td>
<td>Dartmouth College</td>
<td>Elijah W. Stommel, MD, PhD</td>
</tr>
<tr>
<td>Cognition, Behavior, and Caregiver Burden in ALS</td>
<td>Boston VA Research Institute, Inc.</td>
<td>Kit Brady, PhD</td>
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<tr>
<td>Prospective study of biomarkers and risk factors for ALS incidence and progression</td>
<td>Harvard School of Public Health</td>
<td>Alberto Ascherio, MD, DrPH</td>
</tr>
<tr>
<td>Case-Control Studies Nested in National ALS Registry to Evaluate Environmental Risks</td>
<td>Columbia University Medical Center</td>
<td>Hiroshi Mitsumoto, MD, DSc</td>
</tr>
<tr>
<td>Antecedent Medical Conditions and Medications: Associations with the Risk and Prognosis ALS</td>
<td>Stanford University</td>
<td>Lorene Nelson, PhD</td>
</tr>
</tbody>
</table>

*Future awards are possible pending funding availability*
Access to Registry Data

- Received numerous requests from researchers and public
- Registry seeks to develop two datasets (non-identifiable), public and researcher use
  - Public: web based, public will be able query ALS prevalence, mortality, and certain risk factor surveys
  - Researcher use: web based application, will be reviewed internally, consists of data not currently published or released
    - Surveys will be matched with Biorepository specimens
- Release timeframe is 2016
Registry Challenges

- Raising awareness without violating IRB
- Adequately communicating with patients
  - Enrolling
  - Taking surveys
  - Being engaged
- Registry leverages:
  - Working closely with stakeholders, ASL Association, MDA, Les Turner
  - Using social media, Twitter and Facebook
  - Attending patient symposiums
  - Have patients involved in Registry meetings
Summary

The National ALS Registry is:

- First and only population-based ALS registry for the U.S.
- Fulfilling Congressional mandate
  - incidence,
  - prevalence,
  - demographics,
  - risk-factors
- Being used as a recruitment tool for ALS research
  (e.g., clinical trials, epidemiological studies)
- Providing funds for external research
- Integrating a full-scale biorepository
- Building the evidence to describe the ALS experience in the U.S.
Comments/Questions?

www.cdc.gov/als

For more information please contact Agency for Toxic Substances and Disease Registry

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Telephone: 1-800-CDC-INFO (232-4636)/TTY: 1-888-232-6348
E-mail: cdcinfo@cdc.gov Web: www.atsdrcdc.gov

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.