

# How the National ALS Registry can Support your Research

**Paul Mehta, MD**

*Principal Investigator, National ALS Registry*

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National Center for Environmental Health  
Agency for Toxic Substances and Disease Registry



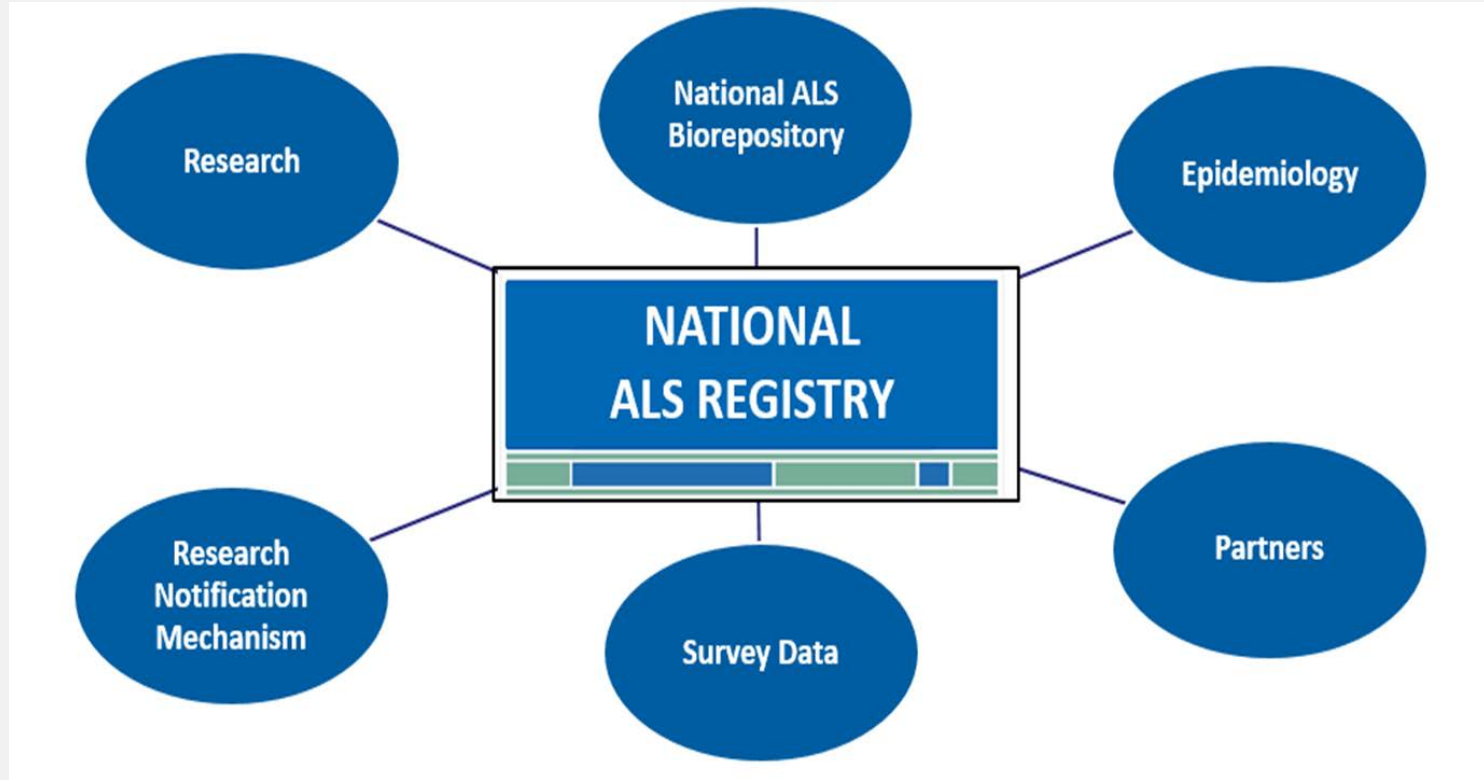
# Disclosures

- 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

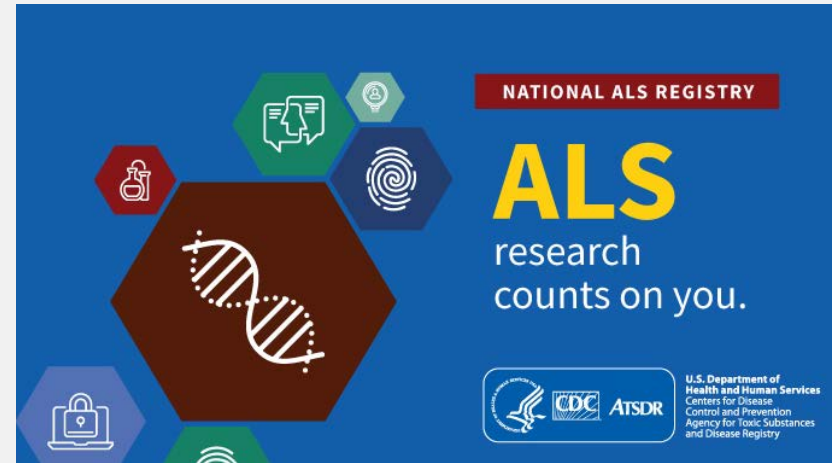


# Risk Factor Surveys-Taken After Registration

Survey (n=17)	Release Date	No. Completed
Demographics	October, 2010	9353
Occupational history	October, 2010	8497
Military history	October, 2010	8322
Smoking and alcohol history	October, 2010	8176
Physical activity	October, 2010	7840
Family history of neuro. diseases	October, 2010	7642
Disease progression (ALSFRS)	October, 2010	7674
Clinical data (e.g., devices used, body onset)	November, 2013	3234
Open-ended etiological questions	November, 2013	2958
Lifetime residential history	May, 2014	3580
Lifetime occupational history	May, 2014	3560
Residential pesticide use	May, 2014	3321
Hobbies with toxicant exposures	August, 2014	3056
Caffeine consumption	August, 2014	2861
Reproductive history (women)	August, 2014	1557
Health insurance status	December, 2014	2561
Head and neck injuries	December, 2014	2523
<b>Total (as of 10/7/2019)</b>	---	<b>86,715</b>

# 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 1<sup>st</sup> 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 (Mitsumoto):
  - 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



Mitsubishi Tanabe Pharma America

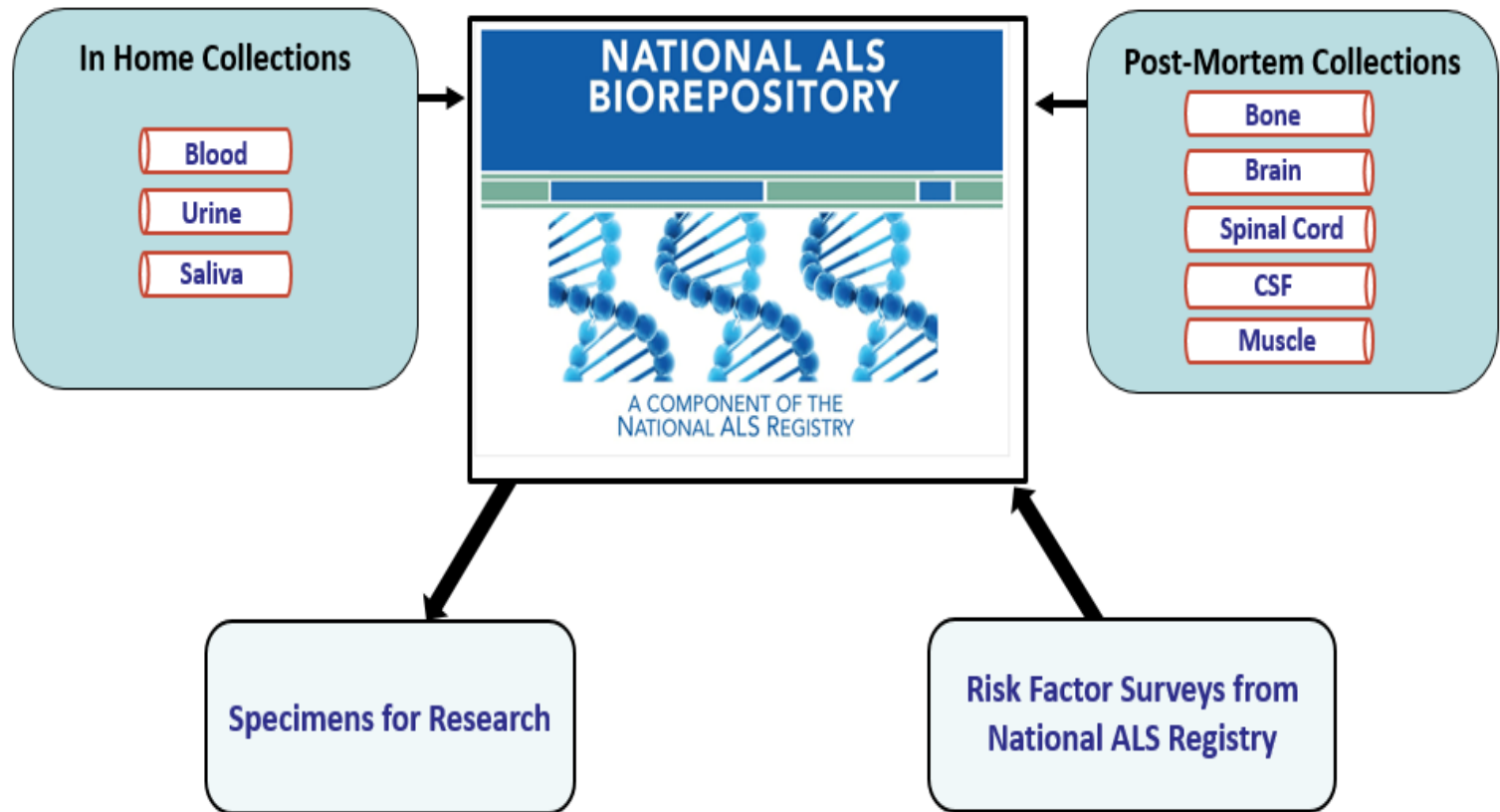


Dartmouth-Hitchcock  
MEDICAL CENTER

# 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



# National ALS Biorepository Samples

In-home Sample Types Participants (N =1,153)	
DNA (2µg)	1,061
RNA (2µg)	933
Plasma (.5ml)	971
Serum (.5 ml)	956
Whole Blood – metals free (1.8 ml)	948
Red Blood Cells (1.0 ml)	957
Buffy Coat (1.0 ml)	269
PBMCs <sup>1</sup>	44
Urine (1.8 ml)	982
Urine with Hg preservative (4.5 ml)	607
Hair	157
Nails	268

Postmortem Sample Types Participants (N=41)	
Brain	41
Spinal Cord	40
CSF <sup>2</sup>	41
Bone	41
Muscle	42
Fibroblasts	24

<sup>1</sup> PBMCs – Peripheral blood mononuclear cells

<sup>2</sup> CSF – Cerebrospinal fluid

\* Updated as of 06/30/19

**Samples  
matched with  
demographic  
data**

# Studies Using Samples from the Biorepository

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

# Registry Funds Research

- **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](mailto:als@cdc.gov) or [pum4@cdc.gov](mailto:pum4@cdc.gov)**

# CMEs for Providers (1.5 contact Hours)

Amyotrophic Lateral Sclerosis (ALS) Continuing Education Module



Training Overview

Part I: Clinical  
Overview of ALS

Part II: Clinical  
Diagnosis,  
Treatment, and  
Management of  
ALS Patient

Part III: The ALS  
Registry

Continuing  
Education

Acknowledgements

## 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).



# Comments/Questions

[www.cdc.gov/als](http://www.cdc.gov/als)



## The National ALS Registry: Get The Facts

The National Amyotrophic Lateral Sclerosis (ALS) Registry enables persons with ALS to fight back and help defeat ALS (Lou Gehrig's Disease). By signing up, being counted, and answering brief questions about your disease, you can help researchers find answers to critical questions.

Learn more at [www.cdc.gov/als](http://www.cdc.gov/als) or (800) 232-4636



### Who can sign-up?

Anyone with ALS

### What do I need?

- A computer with an internet connection
- An email address



### What if I need help?

Caregivers and others can help you in person or even over the phone



### Will my information be private?

- YES! Only approved registry scientists can see it. NOT employers or insurers
- You CANNOT be looked up in the registry by name

### What kind of information is collected?

- Basic demographics (e.g. age, sex, height, weight)
- Military history
- Physical activity
- Family history

### Do I need to update my information?

YES! Every six months – you'll get an email reminder

**YOU JOINING**

More information for research

A better understanding of ALS

The chance to help create a better future for persons with ALS

For more information, contact NCEH/ATSDR  
1-800-CDC-INFO (232-4636)

TTY: 1-888-232-6348      [www.atsdr.cdc.gov](http://www.atsdr.cdc.gov)      [www.cdc.gov](http://www.cdc.gov)  
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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.

