

# Letters

## RESEARCH LETTER

### Use of Genetic Testing in Amyotrophic Lateral Sclerosis by Neurologists

There have been a number of publications describing the important role of genetic counseling in amyotrophic lateral sclerosis (ALS).<sup>1,2</sup> While such attempts at guiding who should undergo genetic testing are welcome, they are put forth in a vacuum because there are no data on where ALS neurologists stand in terms of genetic testing and counseling for the disease, and in terms of what is considered to be familial and sporadic ALS.<sup>3</sup> We attempted to fill this gap by surveying members of the Northeast Amyotrophic Lateral Sclerosis Consortium (NEALS, <http://www.alsconsortium.org>), one of the largest clinical research organizations for ALS.

We sought to understand in which situations genetic testing is used, which genes are tested for, and the attitudes of respondents toward genetic testing and counseling.

**Methods** | The survey was sent via email on June 20, 2016, to 134 principal investigators who are members of NEALS. The deadline for survey completion was July 29, 2016. Data were collated and analyzed using Microsoft Excel (Table). The NIH Office of Human Subjects Research Protection has determined that this type of research falls under exemption for institutional review board approval.

**Results** | We obtained 43 responses, resulting in a response rate of nearly one-third (32.1%). Responses were obtained from centers throughout the United States as well as from Canada, Israel, and Lebanon. The mean annual number of ALS patients seen at each site was 157 (range, 20-500). Forty respondents (93.0%) reported that they screen familial ALS cases for genetic mutations in their routine clinical practice and 13 (30.2%) screen sporadic cases. Genetic testing rates are surprisingly lower in the context of clinical research: only 31 respondents (72.1%) reported that they screen familial ALS cases for genetic mutations in preparation for their enrollment in clinical trials, while only 8 (18.6%) screen sporadic cases in clinical trials.

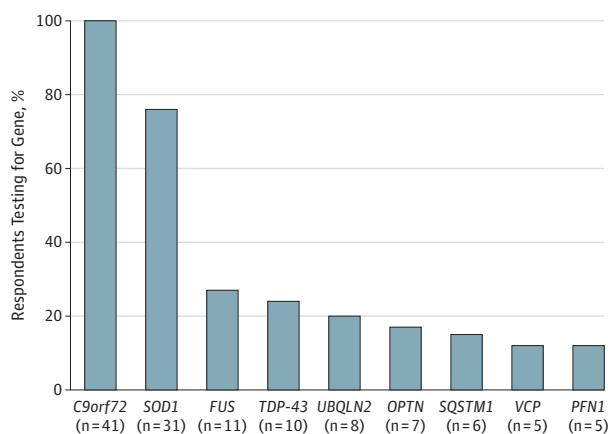
One respondent did not perform genetic testing for clinical trials or everyday clinical practice, and 1 respondent did not specify which genes the site tested for. Of the 41 respondents who specified which genes were tested for, 100% screened for *C9orf72* (Figure). The next most common gene screened for was *SOD1*, with 31 respondents (75.6%). Other genes reported are shown, by prevalence in testing, in the Figure. Of note, 2 respondents reported testing for *Ataxin 2* in addition to other genes.

Just fewer than half of respondents (n = 21; 48.8%) reported using next-generation sequencing techniques at

Table. Survey Questions and Responses of Neurologists Who Study Amyotrophic Lateral Sclerosis (ALS) (N = 43)

Question	Yes	No	No Response
Do you screen familial ALS cases for genetic mutations for clinical trials?	31	11	1
Do you screen sporadic ALS cases for genetic mutations for clinical trials?	8	34	1
Do you screen familial ALS cases for genetic mutations in everyday clinical practice?	40	3	0
Do you screen sporadic ALS cases for genetic mutations in everyday clinical practice?	13	30	0
Do you use next-generation sequencing techniques such as exome sequencing?	21	17	5
Do you use genetic panel testing?	24	17	2
Do you believe panel testing is cost-effective?	18	22	3
Do you provide genetic counseling to patients?	42	1	0
Would your attitude toward genetic testing change if an effective gene therapy became available?	39	4	0

Figure. Results of a Survey Conducted on Genetic Testing Among Members of the Northeast ALS Consortium (n = 41)



Percentage of respondents who reported testing for each gene specified in the survey. The total number of respondents who reported testing for specific ALS genes was 41 (of 43 who responded to the survey).

their sites. More than half of respondents (n = 24; 55.8%) reported using panel testing. Only 14 of the 24 respondents (58.3%) who reported using Sanger sequencing-based panel testing believed it to be cost-effective. Most respondents (n = 42; 97.7%) provide genetic counseling to ALS patients, with only 1 respondent denying the use of genetic counseling. Finally, the overwhelming majority of respondents (n = 39; 90.7%) would change their attitude toward genetic testing if an effective therapy for ALS became available.

**Discussion** | The importance of genetic testing in ALS is shown by the response to the question on whether future gene therapy

trials will influence the practice of genetic testing. Almost uniformly the answer was yes. Our data show that although current efforts at genetic counseling guidelines for ALS patients are important, the pace of discovery in the genetic field means that these guidelines have a relatively short shelf life. Guideline documents need to operate in a dynamic manner with yearly updates, rather than being viewed as dogma.

**Karissa C. Arthur, BS**  
**Carly Doyle, BA**  
**Adriano Chiò, MD**  
**Bryan J. Traynor, MD, PhD**

**Author Affiliations:** Neuromuscular Diseases Research Section, Laboratory of Neurogenetics, National Institute on Aging, National Institutes of Health, Bethesda, Maryland (Arthur, Traynor); The Northeast ALS Consortium, Boston, Massachusetts (Doyle); 'Rita Levi Montalcini' Department of Neuroscience, University of Torino, Turin, Italy (Chiò).

**Corresponding Author:** Bryan J. Traynor, MD, PhD, Neuromuscular Diseases Research Section, Laboratory of Neurogenetics, National Institute on Aging, National Institutes of Health, Bethesda, MD 20892 ([traynorb@mail.nih.gov](mailto:traynorb@mail.nih.gov)).

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*Study concept and design:* Arthur, Chiò, Traynor.

*Acquisition, analysis, or interpretation of data:* Arthur, Doyle, Traynor.

*Drafting of the manuscript:* Arthur, Doyle, Chiò.

*Critical revision of the manuscript for important intellectual content:* Arthur, Chiò, Traynor.

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