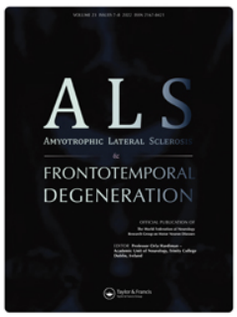

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RESEARCH ARTICLE

Toward genetic counseling practice standards for diagnostic testing in amyotrophic lateral sclerosis and frontotemporal dementia

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Abstract

Objective: Genetic counseling and diagnostic genetic testing are considered part of the multidisciplinary care of individuals with amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD). We aimed to investigate the ideal components of genetic counseling for ALS/FTD diagnostic testing amongst various stakeholders using an online, modified Delphi survey. *Methods:* Experts in genetic counseling and testing for ALS/FTD were purposively then snowball recruited and included genetic health professionals, health professionals outside of genetics and consumer experts (patients, relatives, and staff representatives from ALS/FTD support organizations). First-round items were informed by two systematic literature reviews and qualitative interviews with patients and families who had experienced diagnostic testing. Analysis of each round informed the development of the subsequent round and the final results. *Results:* Forty-six experts participated in the study, 95.65% completed both rounds. After round one, items were updated based on participant responses and were presented again for consensus in round two. After round two, a high level of consensus (≥80% agreement) was achieved on 16 items covering various topics related to genetic counseling service delivery, before and after diagnostic testing is facilitated. *Conclusions:* Genetic counseling for individuals with ALS/FTD and their families should include the provision of client-centered counseling, education and support throughout. The items developed are adaptable to varied healthcare settings and may inform a standard of genetic counseling practice for health professionals who facilitate testing and counseling discussions. This area of work is timely, given demand for testing is likely to increase as more genotype-driven clinical trials become available.

Keywords: *Genetic counseling, genetic testing, amyotrophic lateral sclerosis, frontotemporal dementia, motor neurone disease*

Introduction

As genotype-targeted therapy trials emerge for amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD), availability and interest in genetic testing will likely increase (1). Diagnostic testing is the initial genetic testing performed in families to search for a pathogenic variant (mutation). Diagnostic testing may occur as part of the process of confirming a clinical diagnosis of ALS/FTD in an individual, or later, after a clinical diagnosis is made to confirm whether a familial ALS/FTD pathogenic variant is present. Genetic counseling enables clients to make informed testing decisions while minimizing adverse outcomes and should accompany any genetic testing discussion. However, the amount of counseling required or recommended is unknown (2). We sought input from health professionals (HPs) and consumers to develop practice standards for genetic counseling when offering diagnostic testing for ALS and/or FTD.

Pathogenic variants in several genes associated with ALS, FTD, or both ALS and FTD have been identified (3,4). Approximately 20% of ALS and FTD patients have pathogenic/likely pathogenic variants (5,6), and family history cannot be relied upon to confirm the presence of all pathogenic

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variants (7,8). Consequently, offering diagnostic testing to all individuals with ALS/FTD is increasingly recommended (3,4). In addition to providing the opportunity for certain patients to be involved in emerging genotype-targeted therapy trials (9), detection of a pathogenic variant provides relatives with the option to clarify their risk through predictive/presymptomatic genetic testing or to inform future family planning decisions through reproductive genetic testing. Clinical trials are being developed for presymptomatic carriers (10), and requests for predictive testing are increasing (11).

The decision of whether or not to proceed with testing is informed by personal, familial, and practical factors (2). Genetic counseling is a communication process that accompanies genetic testing and integrates the following four goals:

- Interpretation of family and medical histories to assess the chance of disease occurrence/recurrence (12,13).
- Education about a condition's natural history, inheritance pattern, testing, management, prevention, support resources, and research (12,13).
- Counseling to promote informed choices in view of risk assessment, family goals, ethical and religious values (12–14).
- Support to encourage the best possible adjustment to the disorder and/or the risk of recurrence (13,14).

Genetic counseling and diagnostic testing practice in ALS/FTD may differ depending on the context in which testing is undertaken (2,15). As not all individuals with ALS/FTD have the capacity to consent for diagnostic testing, carers and/or relatives may be required to consent on the patient's behalf (16). The client responsible for discussing diagnostic testing therefore may be the patient, their relative/s and/or carer/s. Thus, the process and outcomes of diagnostic testing may concern the patient and others (17,18).

There is no consensus on how genetic counseling should be facilitated in diagnostic testing for ALS/FTD (2). Guidelines for diagnostic testing of other adult-onset neurodegenerative diseases have been developed (19) but additional challenges may arise in genetic counseling for ALS/FTD due to clinical and genetic heterogeneity, resulting in greater uncertainty for families (2). Neurology followed by clinical genetics teams most commonly facilitates diagnostic testing, but this differs depending on local resources and guidelines (20). Despite the potential benefits of genetic counseling and testing for the patient and family, many HPs who specialize outside genetics do not feel confident engaging in genetic testing and counseling discussions and lack resources to direct them (21). Access to genetic counseling and testing is considered a fundamental right of people living with ALS (22) yet, it is not consistently offered. ALS clinicians have indicated that they would be more likely to offer testing if guidelines were available (23). There is little data on the offer or uptake of testing and counseling in patients with FTD (2,11).

The aim of this study was to investigate the extent of consensus on the ideal components of genetic counseling for ALS/FTD diagnostic genetic testing amongst various stakeholders using an online, modified Delphi survey. We hope that results will inform practice standards for HPs offering genetic counseling for ALS/FTD, generate discussion regarding the implementation of genetic counseling in practice, and better support individuals with ALS/FTD and their families. Although diagnostic testing can also occur in asymptomatic relatives of ALS/FTD patients (for example, when a person with ALS/FTD is unavailable to be tested), these situations have not been considered in detail in this study as they require a modified predictive/presymptomatic testing genetic counseling protocol (24).

Materials and methods

This study was approved by the University of Technology Sydney (UTS) Human Research Ethics Committee (ETH20-5122/ETH21-5883). The Delphi is a structured, iterative, multi-round survey method that aims to (as objectively as possible) facilitate group consensus from a diverse range of experts on a particular topic (25,26). Each round builds on the previous results, allowing participants to reconsider their views based on the input of others (26). As motor neurone disease (MND) is the preferred term for ALS in some locations, all study information included both terms.

Recruitment

We recruited a diverse range of participants from one of three expert subgroups with experience in ALS, FTD, genetic testing and counseling (Table 1). All identified experts were forwarded an invitation email. Those interested were emailed an information sheet and demographic/eligibility survey. The survey gathered relevant demographic data and confirmed consent and availability to participate. If no response was received upon forwarding these emails, potential participants were emailed again once.

Patient and family member participants were required to complete five additional survey questions to ensure informed consent. Participants were eligible for this study if they did not have an enduring medical guardian/power of attorney who made healthcare decisions on their behalf and correctly answered four yes/no questions about the study based on the content of the participant

Table 1. Expert definitions and recruitment.

Expert group category	Genetic HPs	HPs outside genetics	Consumers (patient or family experts)	
Definition	Clinical genetics health professional experts who have experience providing genetic counseling or diagnostic testing for ALS/FTD (e.g., genetic counselors, clinical geneticists, genetic nurses)	Health professional experts specializing in areas outside of clinical genetics who have experience providing genetic counseling or diagnostic testing for ALS/FTD (e.g., neurologists, palliative care physicians, psychologists, psychiatrists)	Staff of ALS/FTD support organizations who are familiar with the diagnostic testing experience of ALS/FTD families	People with ALS/FTD and their family members who have experienced genetic counseling regarding diagnostic testing (regardless of whether they proceeded with testing)
Eligibility requirements*	Worldwide		Australia only	
	>2 years of experience working in the area and >5 genetic testing and/or counseling discussions about ALS/FTD per year or >10 discussions over their career			Personal experience of diagnostic testing genetic counseling for ALS/FTD
Recruitment	Purposive			
	Corresponding authors of papers published on the topic of genetic counseling and/or testing for ALS/FTD (sourced from primary author's systematic literature reviews(2,20)) or key clinical contacts from relevant organizations		Key contacts from recruiting organizations for previous study (unpublished) (e.g., Dementia Australia, MND Australia and state-based associations)	Previous study participants (unpublished) who were eligible and had consented to be contacted about relevant future research projects
	Snowball: All possible participants were asked to share the invitation email with others who may be eligible#			
	Contact details of relevant possible participants were forwarded directly to the primary author to contact			N/A: all possible participants had to contact the primary author directly

N/A: not applicable; HP: health professional; *: constitutes adequate experience for the purpose of the study; #: Although no patients and family members were recruited through snowball sampling, the protocol required that potential participants were screened first by the primary author by telephone or email to confirm their eligibility.

information sheet. This strategy has been used in a recent study on stroke survivors (27) and was used in the qualitative study from which consumers were purposively recruited (unpublished).

Data collection

All survey data were collected between January-May 2021 and managed using REDCap (Research Electronic Data Capture) tools hosted at UTS (28,29). Participants' unique survey links allowed them to save and return to it at any time. Each round was open for three weeks, with three weeks allocated between rounds for data analysis and development of the next survey (26). A maximum of three rounds were planned. Non-completers were forwarded email reminders 7, 14, and 21 days after the initial invitation for that round. Those who had not completed the survey 48 hours after closing were not eligible to complete the next round.

The survey components for both rounds are listed in supplementary table 1. Participants were asked to rate the importance of certain items using a five-point Likert scale based on their expertise rather than any possible limits to service access in their region. They were also asked to consider their responses for all client types (patient/family member/carer). Free-text boxes were available to elaborate on responses, add new items or suggest changes to the wording. Participants could choose to select their answer for all situations where diagnostic testing is arranged, or they could respond differently depending on whether an individual was likely to have familial or sporadic disease. Some items in round one also had the option to select one or more discrete-time categories, but this was removed in round two due to several comments suggesting this was difficult to generalize. To ensure that consensus was not forced, all questions had the option to select 'I don't know'. In round two, the survey included a summary of

the results and changes made from round one, including the percentage agreement stratified between the three expert groups. A supporting information document was available in both rounds and included further instructions, key definitions, and a complete list of the items developed (supplementary files 1 and 2).

Twenty items were generated for round one (supplementary table 2), informed by the results of the primary author's systematic and scoping literature reviews (2,20) and the preliminary outcomes of a qualitative study about experiences of diagnostic testing for ALS/FTD amongst patients and their family members (unpublished). Consultation and piloting took place with representatives from the target groups before dissemination to ensure functionality and clarity (26). At round two, no items were removed or added. Instead, four items were merged with others, resulting in 16 updated items for review (supplementary table 2). Updated items were developed in discussion with all coauthors accounting for the lack of consensus to the discrete-time categories, the number of times the suggestion was made, and the relevance to how the suggested change affected the wording/meaning. A planned round three was not required as all items reached consensus. Minor changes to item wording were considered following round two and are detailed in the results and discussion.

Data analysis

Survey responses from each of the three participant groups were assessed and summarized after each round. Quantitative data were reported using descriptive statistics only. Consensus was defined as $\geq$ 75% agreement (30). Discrete variables (differences between time of discussion and case characteristics) were reported as counts and percentages. Continuous variables (the Likert scale) were reported as mean, median, and range scores and percentages. Consensus for the Likert scale questions was considered if $\geq$75% of participants scored the question within the top 2 (strongly agree/agree) or bottom 2 (strongly disagree/disagree). Free text responses were analyzed and used to illustrate conflicts or confusion over the items and inform changes to the item's wording in the subsequent round.

Results

Ninety-one possible participants were purposively identified and directly approached. An additional 30 were approached after snowball sampling. Although 52 expressed interest in the study, only 47 completed the demographics and eligibility survey within the required timeframe. One genetic HP did not fulfill the inclusion criteria and was excluded. In total, 46 participants were eligible to participate in round one (Table 2). No HPs or ALS/FTD association staff (from the consumer group) had personally undergone genetic counseling for ALS/FTD genes.

Outcomes from round one

Forty-six participants (100%) completed round one (supplementary table 2). In total, 16 of the 20 items achieved $\geq$75% consensus agreement that they were important. As there was minimal agreement to the timing question within and between groups, comments about timing were subsequently incorporated into relevant items in round two, and the timing question was removed. Three hundred and seventy unique free-text responses were also provided across the 20 items and in the final comments box (mean 17.62 per item, 8.04 per participant).

Outcomes from round two

Forty-four participants completed round two (95.65% completion rate: 96% Genetics HPs, 100% HPs outside genetics and 90.91% consumers). A consensus agreement of at least 80% was reached for every item across all participant groups (Tables 3 and 4; supplementary table 2). One hundred twenty-seven unique free-text responses were provided across the 16 items and in the final comments box (mean 7.47 per item, 2.89 per participant). A summary of the additional changes to consider is outlined with the final consensus items in Tables 3 and 4. Figure 1 demonstrates how one item evolved throughout the Delphi process.

Unresolved issues raised by participants

In both rounds, the free-text comments included suggestions for changes to the wording or content and further justifications to the quantitative responses provided. Fewer suggestions for changes to wording or content were made in round two, summarized briefly in Tables 3 and 4, and in detail in supplementary table 2.

Participants across all expert groups also flagged challenges related to the items being applied in clinical practice. Some cited financial cost as a barrier; others reported difficulties accessing adequate clinicians or time due to resource limitations. Participants also commented about difficulties generalizing these items to all clients as their needs could vary due to patient and family circumstances, disease progression (i.e., the patient's cognitive capacity and concurrent medical needs), the pretest likelihood that a pathogenic variant will be detected (i.e., those with likely sporadic vs likely familial disease), and the subsequent genetic testing results (i.e., whether a pathogenic variant was detected and the resulting residual likelihood of familial disease). Some participants

Table 2. Study participant demographics.

Expert group category	Genetic HPs	HPs outside genetics	Consumers: association staff	Consumers: patients/ family members
TOTAL	**25**	**10**	**5**	**6**
Participant type				
Genetic Counselor	21	–	–	–
Clinical Geneticist	4	–	–	–
Neurologist	–	8	–	–
Psychologist	–	1	–	–
Geriatrician/Care of the Elderly Physician	–	1	–	–
ALS/FTD association staff	–	–	5	–
ALS Patient	–	–	–	1
Relatives with ALS	–	–	–	2
Relatives with FTD	–	–	–	1
Relatives with ALS and FTD	–	–	–	2
Age range				
20-29	1	0	0	3
30-39	5	2	1	2
40-49	10	2	1	0
50-59	6	3	2	1
60-69	2	3	1	0
70+	1	0	0	0
Gender				
Male	0	4	1	2
Female	25	6	4	4
Country				
Australia	8	2	5	6
USA	11	2	–	–
Canada	2	2	–	–
The Netherlands	2	1	–	–
Scotland	1	0	–	–
New Zealand	1	0	–	–
Ireland	0	1	–	–
Italy	0	1	–	–
France	0	1	–	–
Years of experience	**ALS** **FTD**	**ALS** **FTD**	**ALS/FTD**	
None	0 2	1 1	0	–
<2 years	3 4	0 0	2	–
2-5 years	5 6	2 2	2	–
6-9 years	8 5	0 0	0	–
10-19 years	5 4	3 6	1	–
20+ years	4 4	4 1	0	–
Years of experience	**Clinical Research**	**Clinical Research**		
None	0 2	0 1	–	–
<2 years	1 4	0 0	–	–
2-5 years	2 8	1 1	–	–
6-9 years	5 4	1 2	–	–
10-19 years	10 4	3 2	–	–
20+ years	7 3	5 4	–	–
Patients/families seen per year	**ALS** **FTD**	**ALS** **FTD**	**ALS** **FTD**	
None	0 2	1 1	0 1	–
1-5	5 4	2 1	1 3	–
6-10	1 5	0 3	0 1	–
11-20	8 8	0 2	1 0	–
21-49	4 2	0 3	1 0	–
50+	7 4	7 0	2 0	–
Genetic counseling/testing discussions per year				–
1-5	2	2	2	–
6-10	3	1	1	–
11-20	8	2	1	–
21-49	4	1	1	–
50+	8	4	0	–
Personal experience of genetic counseling for another condition				
Yes	13	1	0	2
No	12	9	5	4
Relative has experienced genetic counseling for another condition				
Yes	15	1	2	2
No	10	9	3	4

HP: health professional.

Table 3. Approaches to practice items presented for review in round two, subsequent results and considerations.

Item short form	Item	Minimum level of consensus achieved* (%)	Further changes to consider after round 2#
Approaches to practice			
• Genetic counseling for all	**Anyone with ALS/MND/FTD is offered the option of genetic counseling to discuss diagnostic genetic testing or DNA storage.**	Total: 84.09 Genetic HPs: 83.33 HPs outside genetics: 80 Consumers: 90	• Clarify that different types of health professionals can provide 'genetic counseling'
• Consistent health provider	**Ideally, the health professional who meets the client to discuss diagnostic genetic testing should be the same person to deliver the results. If unavailable or another health professional is preferred, the health professional providing the results should ideally be aware of pretest discussions.**	Total: 90.91 Genetic HPs: 87.5 HPs outside genetics: 100 Consumers: 90	• Add in the statement 'so long as they are equipped with adequate skills and knowledge for this discussion'
• Information in several formats	**Provide information in a variety of formats** during the genetic counseling discussion. This includes a verbal discussion, a written summary and/or the use of visual aids, in response to the client's needs. *NB: Visual aids include presentations, images or videos. At minimum, a written summary should be provided after genetic counseling and/or testing is completed, and may include providing a copy of the test results.*	Total: 95.45 Genetic HPs: 100 HPs outside genetics: 80 Consumers: 100	• Emphasise 'in response to the client's needs'
• Support or information resources	**Provide support or information resources** throughout the genetic counseling and/or testing process in response to the client's needs. Contact details of the clinical team should always be provided. Additional support or information resources may include: • Online information • Details of support resources, including support groups • Referrals to relevant organizations. *NB: Resources are a source of further information and support after the genetic counseling discussion. Resources are expected to help clients at the time of testing and as required in the future.*	Total: 97.73 Genetic HPs: 100 HPs outside genetics: 90 Consumers: 100	• Clarify that contact details could be a generic rather than direct email or phone number (i.e., this is just a means to contact the team)
• Flexible, family-centred approach	**Provide a flexible, family-centered approach to diagnostic genetic testing** by adapting the discussion to the client and family's needs (where possible). This may include: • Adjustments to the type and amount of information, counseling and support provided • Adjustments to the appointment format (e.g., providing genetic counseling at the same time as a regular clinical care appointment, or by telephone or telehealth) • The involvement of a family member/carer or support person in the testing process, although this should not be mandatory.	Total: 100 Genetic HPs: 100 HPs outside genetics: 100 Consumers: 100	• Update phrase to 'family-centered approach to genetic counseling and diagnostic genetic testing' • More clearly state that a support person is recommended but not mandatory

HP: health professional; *: some items had different responses depending on the population group studied (e.g., likely familial and likely sporadic ALS/FTD). The minimum level of consensus achieved is provided in this table; #: further detail is available in supplementary table 2.

Table 4. Discussion and exploration items presented for review in round two, subsequent results and considerations.

Item short form	Item	Minimum level of consensus achieved* (%)	Further changes to consider after round 2#
Provide information (and explore) • Implications for person with ALS/MND/FTD	**Provide information and explore the possible practical, clinical and emotional implications of genetic testing for the person with ALS/MND/FTD**. This may include providing information and engaging in a conversation with the client about their thoughts and feelings related to: • Confirming a diagnosis of ALS/MND/FTD (if not already diagnosed clinically) • Being eligible for research studies or clinical trials if a pathogenic variant (mutation) is confirmed (where available) • Any changes to management if a pathogenic variant is confirmed • Emotional responses to confirming inherited disease and/or associated risks to other family members • Emotional responses to a negative or uncertain result. This can support informed decision-making pretesting and inform the management of the person with ALS/MND/FTD during and after testing.	Total: 95.45 Genetic HPs: 95.8 HPs outside genetics: 100 Consumers: 90	• Add more categories of possible implications (e.g., insurance, financial, psychosocial implications)
• Implications for others	**Provide information and explore the possible practical, clinical and emotional implications of genetic testing for others, including at-risk relatives and carers**. This may include providing information and engaging in a conversation with the client about their thoughts and feelings related to: • Genetic risks for relatives • The option of predictive and reproductive genetic testing for at-risk relatives only if a pathogenic variant (mutation) is identified • Emotional responses to genetic testing identifying inherited disease and/or associated risks • Emotional responses to a negative or uncertain result. Where relevant to the needs of the client and the family, this can support informed decision-making pretesting and inform management during and after testing.	Total: 97.73 Genetic HPs: 95.83 HPs outside genetics: 100 Consumers: 100	• Add a comma between at-risk relatives and carers to clarify carers aren't always at risk
• The condition being investigated	**Before arranging genetic testing, provide information about the condition(s) being investigated**. This should include: • How the condition is inherited (e.g., autosomal dominant)	Total: 93.18 Genetic HPs: 91.67 HPs outside genetics: 100 Consumers: 90	• Add a comment that the level of information provided may differ depending on the client's needs • Clarify that the second dot point relates to uncertainties regarding

(*Continued*)

Table 4. (*Continued*).

Item short form	Item	Minimum level of consensus achieved* (%)	Further changes to consider after round 2#
	• How age of onset, severity and progression may vary between different family members. Depending on the client's knowledge of ALS/FTD, this may also include information about: • Main clinical symptoms • How the disease progresses. The above may need to be reviewed and reiterated after testing, depending on the client and family's needs and the genetic testing result.		disease clinical symptoms, progression and penetrance
• The genetic testing available	**Before testing, provide information about the genetic testing available**. This includes: • The process • Possible results • Timeframes • Costs (where relevant) • Limitations • Possible uncertainties. After testing, the limitations and uncertainties of testing may need to be reiterated, depending on the client's needs and the genetic testing result.	Total: 100 Genetic HPs: 100 HPs outside genetics: 100 Consumers: 100	N/A
• Use, privacy and storage of results	**Before arranging genetic testing, provide information about, and gain consent for the use, privacy and storage of results now and in the future.** This includes a discussion about whether results: • Form part of the medical record • Can be shared if the client passes away • Can be shared with family members and/or health professionals to provide accurate genetic counseling to other family members. Consent should be clearly recorded. After results disclosure, the above can be confirmed and clarified with the client.	Total: 100 Genetic HPs: 100 HPs outside genetics: 100 Consumers: 100	N/A
Explore • Access to support	**Throughout the client's care, explore and assess their access to social, community and/or individual support**, both within and outside the family.	Total: 95.45 Genetic HPs: 95.83 HPs outside genetics: 100 Consumers: 90	• Add note that this may be facilitated separately to genetic counseling and testing discussions
• Family communication	**Explore and address family communication**, including: • Family dynamics • Whether the client plans to communicate with other family members about the genetic testing and/or the results • The possible risks and benefits of communicating to family members that a pathogenic variant (mutation) has been identified	Total: 95.45 Genetic HPs: 100 HPs outside genetics: 80 Consumers: 100	N/A

(*Continued*)

Table 4. (*Continued*).

Item short form	Item	Minimum level of consensus achieved* (%)	Further changes to consider after round 2#
	• Offering support to help further family discussion. Depending on the client's needs, this may include a brief discussion before testing, and a more detailed discussion after testing, as informed by the genetic testing results.		
• Patient and family history	**Gather and interpret patient and family history** to provide information about: • The likelihood that a pathogenic variant (mutation) will be identified • The likelihood of familial and sporadic disease • Whether other genes or conditions should be evaluated • How genetic test results should be interpreted.	Total: 100 Genetic HPs: 100 HPs outside genetics: 100 Consumers: 100	• Change final dot point to 'the meaning of the result in the context of the patient's personal and family history' • Replace 'sporadic' with 'apparently sporadic' • Add 'NB: family history is not a perfect tool for risk assessment'
Ensure • Informed/considered decision made	**Ensure that an informed and considered decision has been made about genetic testing**. This includes checking: • The client understands all potential consequences, advantages and disadvantages of testing • Misconceptions and expectations are identified and clarified • The timing of testing, the client's psychosocial readiness and ability to cope has been considered • Information is provided in a non-directive manner.	Total: 100 Genetic HPs: 100 HPs outside genetics: 100 Consumers: 100	• Replace 'non-directive' with 'unbiased' and/or 'assess' with 'ensure'
• Genetic testing is voluntary	**Before arranging genetic testing, and before results disclosure, provide information about the voluntary nature of having genetic testing**. This may include: • the right to opt-out at any time (even if testing is already underway) • Alternative options (e.g., DNA banking or storage, deferring testing, having testing but not receiving the results, having testing but an elected person receives the result instead). *NB: there are risks of inadvertent disclosure should the client elect to have testing but not receive results or elect for another person to receive results instead. This possibility should be discussed and clarified to ensure an informed decision is made.*	Total: 100 Genetic HPs: 100 HPs outside genetics: 100 Consumers: 100	• Remove 'may'
• Counseling and/or support provided	**Provide client and family-centered counseling and/or psychological support throughout including the option of additional appointments** (with the same, or	Total: 95.45 Genetic HPs: 95.83 HPs outside genetics: 100 Consumers: 90	N/A

(*Continued*)

Table 4. (*Continued*).

Item short form	Item	Minimum level of consensus achieved* (%)	Further changes to consider after round 2#
	a different health professional). The goal of this is to: • Provide space to raise questions, doubts and concerns • Express and explore their response to the information provided and result given (regardless of the result received) • Facilitate adjustment and help integrate results into their daily life.		

N/A: not applicable; HP: health professional; *: some items had different responses depending on the population group studied (e.g., likely familial and likely sporadic ALS/FTD). The minimum level of consensus achieved is provided in this table; #: further detail is available in supplementary table 2.

were also unsure that exploring and assessing the client's access to support was a role for the genetic counseling provider but agreed it was a necessary part of ALS/FTD care.

Discussion

This study aimed to investigate the extent of consensus amongst HP and consumer experts on the ideal components of genetic counseling for diagnostic genetic testing in ALS and FTD. Over two Delphi survey rounds, items were developed that covered the genetic counseling goals of interpretation, education, counseling and support (12–14). At least 80% consensus was reached within and between expert groups on each of the 16 items presented in round two, demonstrating high endorsement that these 16 items are important for genetic counseling as part of the diagnostic testing process. Participants across all expert groups emphasized the need to tailor all genetic counseling and testing discussions to the client's current circumstances, highlighting the need to be flexible and client-centered. This message was incorporated in several of the final consensus items, highlighting areas where what is specifically said or provided (and when) could be flexible (e.g., exploring and addressing family communication) and where more rigidity was required (e.g., discussing the voluntary nature of proceeding with testing). Some items were not unique to genetic counseling practice (e.g., exploring access to support) and were important for general ALS/FTD care and management. These consensus items could form a practice standard or core set of principles for HPs providing genetic counseling regarding ALS/FTD diagnostic genetic testing, both before testing, during the decision to undergo testing, when discussing results and facilitating family communication. In saying this, although experts were instructed to respond based on their opinion regarding best practice, several commented that operationalizing these items in routine clinical practice would be difficult. Therefore, the items developed and the issues raised have implications for both clinical practice and research.

Delivery of information in a collaborative, compassionate and client-centered manner is an important genetic counseling outcome (31). This sentiment is echoed in the Huntington's disease diagnostic testing and counseling approach (19), where a flexible practice tailored to the client's unique circumstances is recommended. In the context of diagnostic testing for ALS/FTD, clients will likely receive genetic counseling at the same time as other disease-related stressors such as a new diagnosis or coping with the symptoms associated with these progressive conditions. Therefore, genetic counseling regarding diagnostic testing may not be experienced in isolation from other aspects of healthcare. Exploring and assessing the client's access to support is considered an important part of care, regardless of whether this is part of the genetic counseling consultation or another aspect of multidisciplinary care (32,33).

Many participants noted that the way genetic counseling is provided is difficult to standardize, and a one size fits all approach to both clients and health systems is unlikely to work. Alternative ways to deliver genetic counseling must be considered to improve efficiency and overcome resource barriers, allowing more clients to benefit from genetic counseling (34). The global shortage of genetics HPs, as well as the increased availability of testing, means that HPs from outside disciplines provide some or all aspects of genetic counseling (20,35). Several HP participants commented that neurology and clinical genetics team members work together to provide genetic counseling in their practice. One form of this is 'mainstreaming',

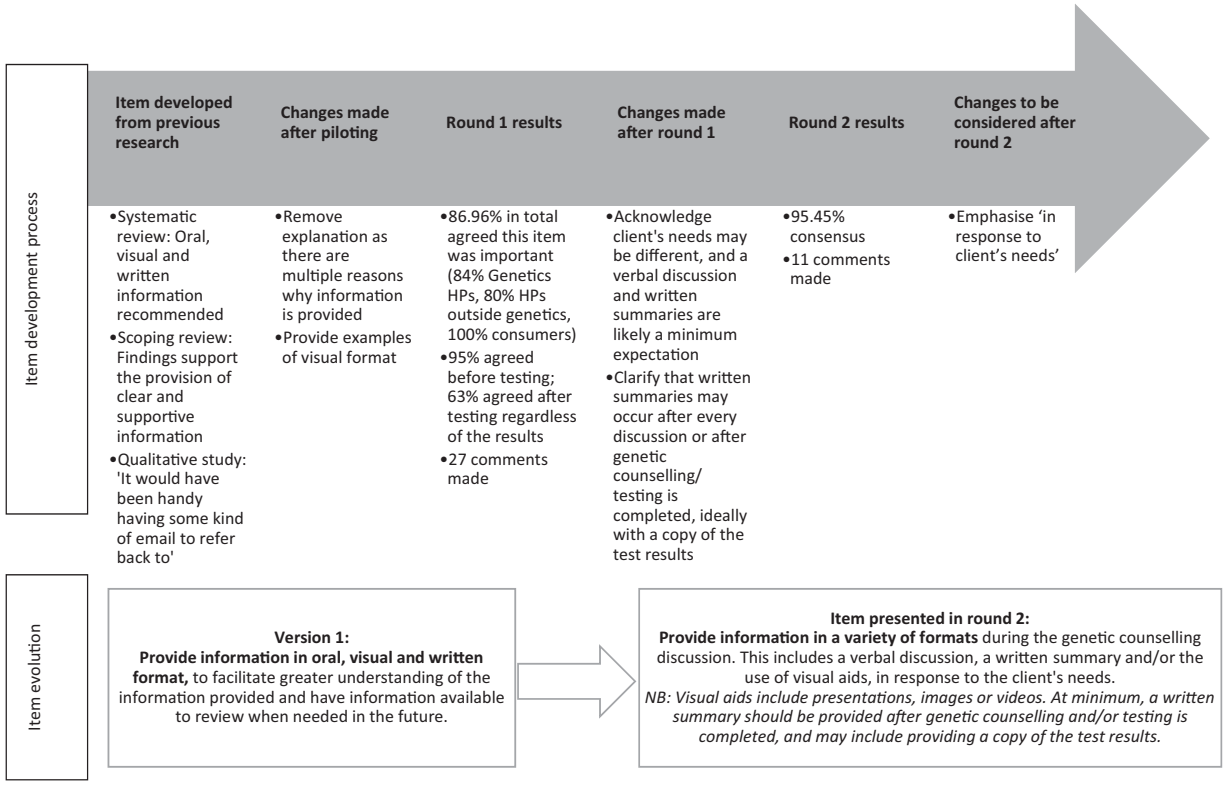

Figure 1. Visual outline demonstrating the development of one of the consensus items.

where HPs specializing outside of genetics initiate genetics discussions, and genetics HPs become involved in interpreting and discussing results and implications if required. Mainstreaming can result in more efficient access to results and their implications, such as targeted treatments or predictive testing (21). Another means to access genetic counseling is through private testing laboratories that have genetic counseling as an included service. However, this could result in a conflict of interest, given genetic testing doesn't always align with the client and health provider's needs (36). Additional innovative ways to increase efficiency include utilizing technology or creating standardized support or information resources to automate parts of the genetic counseling process, allowing more time to focus on client-specific issues and questions (2,20,34,37). The development of resources may also benefit clients who wish to seek information or support but not actively engage in a formal genetic counseling discussion (2). Geographical barriers could also be addressed through telephone or telehealth consultations (20,38,39). Regardless of how genetic counseling is provided, and by whom, the results demonstrate that all HPs who provide genetic counseling regarding diagnostic testing should be equipped with adequate knowledge about genetic testing and its implications, the communication skills to discuss and explore the issues that may arise, and the time to provide care that is client-centered. Genetic counselors are HPs who can provide this as part of multidisciplinary care in some countries (40).

The items developed reached a high level of consensus amongst HP and consumer experts. They could be considered a standard of practice for the various HPs who provide some or all aspects of genetic counseling regarding ALS/FTD diagnostic testing. The items developed are adaptable to all kinds of diagnostic testing provided in ALS/FTD, such as single-gene testing, multigene panel testing, whole exome or genome testing, and in varied clinical and research testing settings where results are returned to the client and their family. Once implemented in practice, these standards would need to be formally evaluated by HPs and consumers. Additional issues in the genetic counseling and testing process that were not the focus of the study were mentioned by participants and present as an area of future research interest (e.g., the best approach to testing, the terminology used for sporadic/simplex/singleton cases, reanalysis and variant interpretation) (2,41).

Strengths and limitations

A strength of this study was the high response rate and engagement from expert participants, with multiple comments made in each round and only two participants not proceeding with round two. The Delphi consensus approach allowed us to involve all relevant and interested participants from several different expert groups (42). Unfortunately, more varied participant perspectives

may have been missing for two reasons. Firstly, recruitment occurred when the COVID-19 pandemic was affecting health systems differently. We speculate that there may have been greater HP expert involvement from some parts of the world (e.g., the United Kingdom) should recruitment have occurred at a different time. Secondly, the consumer group was not representative of all genetic counseling consumers as only one patient and five family members were recruited. In addition, consumers were recruited from Australia only and had greater experience with ALS than FTD and familial compared with sporadic disease. The consumer group was combined to include both representatives of support associations and patients and family members. There may have been benefits of splitting the groups, but the sample size was not large enough. The study was set up to rate item importance but not prioritize them. Prioritizing may have been helpful to guide a minimum standard and may be another area of future research.

Conclusion

A high level of consensus was demonstrated amongst HP and consumer experts regarding the ideal components of genetic counseling regarding diagnostic testing in ALS/FTD. Genetic counseling should include the provision of counseling, education and support in a client-centered way to support individuals with ALS/FTD and their families throughout the diagnostic testing process. Given various health systems and resource limitations, innovative and tailored approaches may be beneficial in implementing genetic counseling as part of routine care. These consensus items are adaptable to varied clinical situations and may inform a standard of genetic counseling practice for the various health professionals who facilitate diagnostic genetic testing and counseling discussions in ALS/FTD. This area of work is timely, given the demand for genetic testing is likely to increase as more genotype-driven clinical trials become available in ALS and FTD.

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Declaration of interest

The authors have no competing interests to declare.

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