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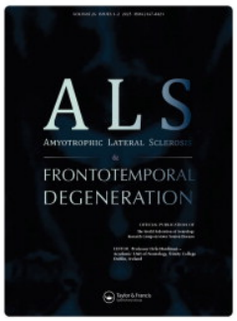

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RESEARCH ARTICLE

Exploring the needs and preferences of people with amyotrophic lateral sclerosis (ALS) when making genomic testing decisions: an interview study

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Abstract

Objective: Whole Genome Sequencing (WGS) for amyotrophic lateral sclerosis (ALS) (also known as motor neuron disease, MND) raises multiple considerations and has a range of implications for individuals and their family. However, it is unclear what needs people with ALS have when making genomic testing decisions. This study explores the experiences, needs and preferences of these individuals when considering WGS and going through the process. *Methods:* A semi-structured interview study was carried out with 14 people with ALS from across the UK who had, or were considering, WGS. Participants were recruited from a local ALS care center and MND Association/MND Scotland channels. Data were analyzed using framework analysis. *Results:* Findings indicate variation in (a) how WGS and access to pretest genetic counseling is provided, (b) the perceived adequacy of information to support decision-making and prepare people with ALS for their test result and its consequences, and (c) preferences for making decisions with family and health professionals that best meets their clinical and life needs along the care pathway. *Conclusions:* There is an urgent need for people with ALS to have relevant, accurate and accessible information that supports proactively their decision-making around WGS, particularly in the context of genetically-targeted treatments and clinical trials. These findings will contribute to the development of a shared decision-making intervention supporting people with ALS to make genomic testing decisions with their family and neurology services.

Keywords: *Genetic testing, genomic testing, whole genome sequencing, motor neuron disease, amyotrophic lateral sclerosis, patient decision aids, shared decision-making*

Introduction

Genomic testing has become an important part of care for people with amyotrophic lateral sclerosis (ALS) (also known as motor neuron disease, MND). In England, all people with ALS (pwALS) are eligible for genomic testing, carried out through Whole Genome Sequencing (WGS), to establish if their condition is linked to an identified genetic variant (1). This service has been embedded in mainstream medicine, as part of the National Health Service (NHS) 5-year Genomic Medicine strategy to facilitate personalization of care through precision medicine (2). The expansion of eligibility criteria, to all pwALS, was due in part to research showing that a proportion of people with no known family history carry an actionable gene variant that would make them eligible for participation in genetically-targeted clinical trials of disease modifying treatments (3). In the USA and parts of Europe, Tofersen is now licensed as a treatment option to slow down

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disease progression in people with SOD1-ALS (4). However, clinicians report a lack of time to introduce genomic testing discussions in neurological care consultations, have difficulty completing the additional testing and referral paperwork, and have low confidence in providing genomic testing information (5, 6). This raises the question of whether pwALS have adequate information and support when making decisions around WGS.

Making decisions about having or not having WGS can be difficult, as it involves uncertainty for the pwALS and their family, and often happens alongside their diagnosis of and adjustment to ALS, and deterioration in health (7). WGS is carried out through a blood test. In ALS it involves screening against the R58 Adult onset neurodegenerative disorder panel (1). Possible results are: negative—no known genetic cause identified; positive—confirmation of one or more known ALS-linked genetic variants, and the potential genetic risk to relatives; uncertain—identification of a variant of uncertain significance (VUS), where the contribution of the genetic variant to the disease is difficult to establish. There is also the possibility of secondary/incidental findings for other unrelated conditions (based on a panel of actionable conditions). In all cases, the implications for pwALS and their family members can be significant.

Historically, genomic testing for ALS was delivered by specialist clinical genetics and ALS services, who have expertise in supporting people to make decisions about genomic testing for life-limiting conditions with multiple-cause etiology. It is unclear what the needs and experiences are of pwALS being offered genetic counseling and WGS within neurology services. Most studies explore genomic testing practices from a service provider perspective (6, 8–11), and reviews of patient records (12). An Australian interview study found pwALS and their family members reported receiving variable information from healthcare professionals about the availability of genomic testing. Some pwALS felt they did not need genetic counseling to have the test, others felt they received little information and did not make an informed decision, and some perceived a lack of post-test support (7).

This paper aims to explore the views and experiences of pwALS who have either considered or had WGS in the UK. Given decision-making considerations may be broadly similar across contexts, findings will have relevance for other healthcare systems too. The study is part of a mixed methods needs assessment carried out to inform the development of a complex intervention to support pwALS, and family members, to make informed decisions around genetic/genomic testing. Study findings will inform the content, structure and implementation of a patient decision aid and staff training resources.

Materials and methods

Ethics approval for this research was granted by a UK NHS Research Ethics Committee (22/SW/0047) and the University of Sheffield (050846). The project has been guided throughout by a steering committee. The steering committee includes people with a range of expertise, including individuals with lived experience of ALS and genetic/genomic testing.

This study comprises 14 semi-structured interviews with pwALS from across the UK who had had or considered genomic testing. Participants came from broad geographical areas including England, Scotland and Northern Ireland. Interviews were carried out between July 2023 and February 2024. Participants were recruited through a local ALS center ($n = 6$) and MND Association/MND Scotland channels ($n = 8$). For the former, they were approached by a member of the neurology team and given a recruitment pack including a participant information sheet with details of the study. If the latter, this was sent when they contacted the research team directly. Participants were given the chance to ask questions before consent was taken. Recruitment was stopped when interviews were deemed to hold sufficient information power (13).

The majority of interviews were held virtually via google meet, with two face-to-face interviews in a hospital meeting room at the preference of participants. The interview approach was adapted to support participation of individuals with diverse needs, including the use of communication aids or the presence of a family member/carer to support communication. In some cases, questions were provided in advance to facilitate this, adapted from a topic guide which was used flexibly in line with the semi-structured approach. Interviews were audio recorded for transcription by a professional transcriber. Framework analysis was used to analyze the data (14) facilitated by NVivo. This paper presents three core themes to elucidate participant's needs around WGS.

Pseudonyms have been used throughout and quotations have been lightly edited for readability. Quotations are accompanied by brief information to indicate participant age, gender, and genomic testing status.

Results

Participants included 14 individuals with a variety of genomic testing decisions and outcomes. Participants ranged in age from their 30s to 60s, were both male and female, and all described their

Table 1. Participant characteristics.

Pseudonym	Age	Sex	Genomic testing status
Adrian	60–69	M	Tested (awaiting results)
Bart	60–69	M	Tested negative
Cliff	60–69	M	Not tested
Deana	50–59	F	Not tested
Kat	40–49	F	Tested positive
Leslie	60–69	M	Not tested
Liz	50–59	F	Tested negative
Lorna	60–69	F	Tested positive
Nigel	60–69	M	Not tested
Ralph	60–69	M	Not tested
Rosanna	40–49	F	Tested (awaiting results)
Sean	30–39	M	Tested positive
Victoria	40–49	F	Tested positive
Vince	50–59	M	Tested (Unclear result—awaiting appointment with clinical genetics)

ethnicity as White British. Participant details are included in Table 1.

Decision-making and the genomic testing process

People described mixed experiences of genomic testing. Not everyone recalled being offered genomic testing, but those who had either sought it proactively or were offered it by their clinical team. Some valued the counseling provided by their clinical team, and felt they were given adequate and comprehensive information on genetics in ALS, and implications and considerations around genomic testing before going ahead. Others recalled receiving minimal pretest genetic counseling and described going into it "blind" or having such discussions at a later date (Table 2, Q1–2). A perceived lack of information impacted decision-making (Table 2, Q3). Access to formal genetic counseling was variable. Not everyone remembered consenting to the test or having the blood sample taken, especially where they had many tests in a short space of time or were tested as part of a clinical trial (Table 2, Q4).

Reasons for having genomic testing included: access to clinical trials and potential treatments; to support research and contribute to knowledge on the disease; a desire to have all the information available; to support planning and preparation; and to seek information that could be relevant for relatives, in particular establishing the potential risk to children. People sought reassurance that their children would be ok, but also felt knowing could enable relatives to plan and make their own decisions, and facilitate early detection and access to treatments if they were to develop symptoms (Table 2, Q5–6).

Four participants said they had genomic testing as part of the diagnostic process, and described going along with all the tests they were offered to establish the cause of their symptoms. One individual was not sure if her genetic status was determined through her participation in a research project or through a separate test, and had not expected to receive her result (Table 2, Q7). In such cases, results were delivered alongside the diagnosis which could be difficult to take in and "devastating" (Table 2, Q8). At the same time, people recognized the benefits of a quicker diagnosis and clinical trial access.

Although not everyone felt they had made an active choice, there were also those who described weighing the decision, and discussing it with relatives before proceeding. In some cases the decision was a "no-brainer", but for others, it was complicated in part by the possible family implications. People recalled a concern that a positive result could cause upset amongst relatives or affect family dynamics, and questioned how relatives would cope. This was a particularly prominent concern for a participant with children in early adulthood (Table 2, Q9). Whilst certain individuals had concerns about financial implications including insurance impacts, there was a view that discrimination based on genomic testing was not happening currently and trust in the NHS provided reassurance (Table 2, Q10). There was a hope that results would be used for good and several participants described being focused on "breaking codes" (above worrying about such possibilities). Participants were sometimes unsure how their data could be used.

Others had not pursued WGS, because they were not sure the information would be valuable or beneficial due to their personal circumstances or lack of treatment and cure (Table 2, Q11). For parents in particular, there could be a reluctance to know if children could be affected, and one participant questioned her obligation to share the results with her children (Table 2, Q12). Not all participants were eligible for WGS (e.g. when living outside England).

Priorities for information and support around genomic testing

People came to WGS decisions with varying levels of knowledge. Some felt they knew enough and didn't need or want to know more, although they recognized family members may have different needs (Table 3, Q1). Others, however, recalled delayed access to relevant information, unmet needs and unanswered questions, even after genomic testing. Three participants who had not had WGS expressed that they did not understand what it involves (Table 3, Q2–3).

Understanding the genetics of ALS could be difficult for participants, particularly where genetics had not been discussed before they sought or were offered WGS. Participants expressed unanswered questions on pathogenic variants associated with ALS, the link between ALS and other neurological conditions, and the meaning of a negative result

Table 2. Quotations on "decision-making and the genomic testing process".

Quotation number	Quotation
Quotation 1	I found the whole process very straightforward. This was assisted by the comprehensive information shared by [consultant neurologist] on the process and potential outcomes (Adrian, 60–69, M, tested—awaiting results)
Quotation 2	I didn't know what was going on. I wanted to get to the bottom of what was wrong with me, so if a doctor says to you "We're going to do this", nine times out of ten you're going to go "Yeah alright then, you're the doctor" … it was probably such a blur as well because I probably wasn't taking a lot of it in, either … It wasn't until after he identified that I had the gene that I had to deal with that "oh actually you know what I could pass this down to my children" and stuff like that. So I suppose upfront it would be good to know (Victoria, 40–49, F, tested positive)
Quotation 3	I enquired about it … but I struggled to find who to talk to. But the [study] research doctor managed to speak to the neurologist and they offered me a blood test but it was a very short email with no counseling, so I thought that wasn't appropriate for us (Deana, 50–59, F, Not tested)
Quotation 4	It's just been done through the trial. So I've had bloods taken. It was that trial, I had bloods taken constantly, breathing tests, it's just developed through that (Lorna, 60–69, F, tested positive)
Quotation 5	it was a no brainer to be genetically screened … it might show something like the SOD1 gene involvement which could result in treatment that might slow the progression of my MND. From an altruistic perspective, having my genetic data on file for future research may lead to further developments to assist others … My lifetime approach to anything is "knowledge is power" as this allows you to plan (Adrian, 60–69, M, tested—awaiting results)
Quotation 6	As a parent you don't want to harm your kids, do you, so you want to know that there's no malicious, no boogeyman, nothing that's there in their future (Vince, 50–59, M, tested—uncertain result)
Quotation 7	They were taking donors for the 100,000 Genomes Project at that point and they said to me was I willing and I said, "well yeah of course", you know, any old test that's flying past I'll jump in and have a go. But nobody had said, "we are really really really looking at YOUR genetics" … I never, I never got spoken to about testing my genes because from everything everybody was saying to me, it wasn't anything really to worry about (Kat, 40–49, F, tested positive)
Quotation 8	I was given nothing, to be honest. No information, I was just told SOD1, that's it, confirmed. And I literally said to the lady who diagnosed me, "How do I know then if I've got Motor Neuron", and she said, "Well I've just more or less told you" … her saying that to me is always going to be in my head (Sean, 30–39, M, tested positive)
Quotation 9	I was worried about how my kids would deal with it … if it was that I did have a gene, then they've got to make a second decision, haven't they, do they get the test? … say for example not all of them agreed about—then what would we do? Because some would have the result, others wouldn't, how would that affect us all? (Liz, 50–59, F, tested negative)
Quotation 10	Well there is that issue about the insurance … but I don't think we're at that point yet … at the minute the fact that it's just within the NHS, you say well yeah, that's fair enough. It's got patients' interests at its center (Vince, 50–59, M, tested—uncertain result)
Quotation 11	I don't need to know about my genetics. I know what I've got, I know what's coming … I don't have children through choice, so all I think about is myself and what I can do to help anybody else … I know there's nothing that can be done for me now, so is genetic testing for me at this moment in time going to have any impact (Cliff, 60–69, M, Not tested)
Quotation 12	Am I the gatekeeper of such information? Do you have an obligation to share it? (Deana, 50–59, F, not tested)

(which generally cannot rule out an inherited form of the disease) (Table 3, Q4). The identification of less common/VUS results could cause confusion. One participant was referred to clinical genetics for a more detailed explanation of his result but expressed uncertainty about what he would be told whilst waiting for this appointment (Table 3, Q5).

The implications of WGS and of receiving a genetic diagnosis were also areas where education was important. Some did not engage with this until after having the test or receiving the result. In these cases it was either raised by a member of the clinical team or discovered through their own research/online searching—as described by one participant who found out about the risk to her children after being given her result (Table 2, Q2). Post-test support was at times perceived to be inadequate (Table 3, Q6).

Generally, participants felt there was a need for support to find relevant, reliable and in-depth information, as well as access to knowledgeable healthcare professionals to whom they could ask questions. Misinformation and a lack of comprehensive resources could cause additional stress (Table 3, Q7). Whilst some people wanted to find out anything they could, there were also those whose approach was to avoid proactive information seeking before it was strictly necessary. Where people had limited knowledge on WGS, it could be hard to know what questions to ask. This was particularly the case for a participant who had told he could have genomic testing at the point his diagnosis was confirmed, notably only shortly before the interview (Table 3, Q8).

These aspects were reflected in the diverse areas participants felt should be covered in

Table 3. Quotations on "priorities for information and support around genomic testing".

Quotation number	Quotation
Quotation 1	I was pretty comfortable. I think the non-biologists in my family found it harder. And probably there were things that they didn't understand … if you don't know anything about genetics … you end up asking quite a lot of questions (Bart, 60–69, M, tested negative)
Quotation 2	I don't really know what genetic testing involves … see for me if you're talking about genetics, you think about Frankenstein (Leslie, 60–69, M, not tested)
Quotation 3	To me, genetic testing is a little bit of the dark arts. People take blood, they go away and do whatever they do with it … it's just something that there's not much information out there … a way needs to be found so that people can understand it a little bit easier (Cliff, 60–69, M, Not tested)
Quotation 4	When I first started reading, I just thought it was one gene, however it can be several or a combination, I think. And that is complicated. I don't quite know how you would uncomplicate that tangle. But it would be helpful (Liz, 50–59, F, tested negative)
Quotation 5	So [consultant neurologist] said there were two main genetic forms of MND and I'd tested negative for both of those … so that was the positive side of it, and then she said oh but you also have things which I think I interpreted as being, as I remember she said that they kind of, that they weren't causative … it's all a bit vague, hopefully they'll tell me more when I go to the genomics clinic. But I was just happy with the "OK. you don't have these two forms which we do know about". This other stuff seems to be more kind of, people with blue eyes, or people who whatever, are more likely to … so whether it is that or whether it's more than that I don't know.
Quotation 6	It was devastating, obviously. And I was on my own … so then you're on some waiting list for a 12 week mental health crappy pointless thing and stuff like that, so there just wasn't any of the crash mats that should have been there waiting for me (Kat, 40–49, F, tested positive)
Quotation 7	I've read bits on Google, especially when I was first diagnosed with it and I ended up in tears and not knowing what's true and what's not true, so I try to stay away from it and I rely on the specialists (Leslie, 60–69, M, not tested)
Quotation 8	I'm not aware of anything like that at all regarding genetic testing, what it involves, or anything like that … I don't really know what questions to ask (Ralph, 60–69, M, not tested)
Quotation 9	I think your expectation should be limited, because now after the SOD1 drug breakthrough … I think a lot of people don't realize the variety of genes that can contribute to MND. It's not just SOD1. So I think that should be made, really made clear. Also the psychological effects, because it's a massive decision. Even after I made it, at the time I thought it was the right decision and I still do now … but you can't help questioning while you're waiting (Liz, 50–59, F, tested negative)
Quotation 10	There's a sort of practical side of making sure that someone understands that the gene you've got is dominant and therefore will be passed on … there's a whole set of genetic stuff that people need to know. But then there's another side to it … and that is supporting people in dealing with finding out some pretty uncomfortable stuff about your future … there's a bunch of support that needs then to be in place, both in terms of the genetic counseling and the consequences for families, but also in terms of your personal prognosis and answering the questions that you've got (Bart, 60–69, M, tested negative)
Quotation 11	Being able to provide the individual with an information sheet that might enable them to start a conversation with their family, of almost frequently asked questions type of stuff, just to support having that discussion as a better informed one (Adrian, 60–69, M, tested—awaiting results)
Quotation 12	I think it needs to be open to show all of the pitfalls and the benefits of genetic testing, and to discuss the process … there's no way to wrap this in cotton wool … The package needs to be flexible [so] it's made clear to everybody at the same level, both before and after. Support, information, follow-up, to ensure that the information that has been delivered has not left the incorrect impact or a lasting impact on the sufferer and the family (Nigel, 60–69, M, not tested)
Quotation 13	I don't need any personally, however everyone is different. Some may need counseling or just a friendly chat with others who have been through the same (Rosanna, 40–49, F, tested—awaiting results)

information provided to people considering WGS. Key points included a need for clear and comprehensible information on genetics and inheritance patterns; the WGS process; the "pitfalls and benefits" of each option; and the possible outcomes, including implications for the individual and wider family (psychological, clinical, financial etc.). Interviews suggested a need for clarity on genetically-targeted clinical trials and treatments following a positive result, including clear information on eligibility for Tofersen, and for research participation opportunities generally (Table 3, Q9). There is also a need for support to be available for pwALS and their relatives, as well as resources to support communication around genetics and information sharing within families. People should be offered the opportunity to ask questions following their test result, so they can seek tailored information that meets their personal and clinical needs (Table 3, Q10–12). Genetic counseling was seen as important to support decision-making and reduce inconsistencies in information provision. Access to peer support was also raised, as well as the need for decision support tools (Table 3, Q13).

Preferences for service provision

Participants commented on when they thought genetics in ALS and WGS should be discussed. Early and timely information provision was favored by

Table 4. Quotations on "preferences for service provision".

Quotation number	Quotation
Quotation 1	The first thing that anybody does when they get out of a medical consultation is open their phone and start tapping things into it … it's actually much better that they're told by someone who knows … it's really important to get the information given right at the beginning, so people don't then end up going down rabbit holes (Bart, 60–69, M, tested negative)
Quotation 2	The first two to three weeks, my world fell apart, and I found it difficult to take much in … So some people, if they're told, "You've got MND, would you like genetic testing", I think it would be too much in the same day … Some will be OK straight away, some need longer. Maybe see how the patient and family take the news of the diagnosis … Don't want to leave it too long as it takes a long time until you get results (Rosanna, 40–49, F, tested—awaiting results)
Quotation 3	That's obviously very subjective because there are so many different approaches … I think at an early stage, once the initial shock of the diagnosis—call it shock—has been overcome, then as soon as possible … Some people whose life expectancy is very short with MND probably would want to be engaged at an earlier stage, but then again you get the approach that others would not. They'd look at it with horror, so it's difficult (Nigel, 60–69, M, not tested)
Quotation 4	You need to revisit it often as well … because life is dynamic and your kids have babies (Deana, 50–59, F, not tested)
Quotation 5	I would have preferred to have had that discussion with my MND nurse because I've got a much better rapport with her. I talk about normal things more with her, she seems more interested in everything about my life, not just where I am on the ALS-FRS scale … My consultant I had before that … he didn't have a very good bedside manner … I think it summed it up when I asked if I could have the test, and he just went "oh yeah", as if it wasn't a big deal … It wasn't until I had the conversation with my new consultant neurologist that I had a bit of a grilling and he really questioned my family's motivations and kind of emphasized what a big deal it all was. I didn't really know him, it was the first time I had spoken to him, and I appreciated that he took the time to have that conversation. I think I would have felt more comfortable having that with someone that I had more of a rapport with (Liz, 50–59, F, tested negative)
Quotation 6	I like dealing with the consultant, because you're hearing it from the horse's mouth. I feel I've got a good relationship with him and what he says to me goes … you get a different nurse all the time, you're not seeing the same person, you don't have that same relationship with them (Sean, 30–39, M, tested positive).
Quotation 7	They can be offered it, whether they go forward with it is a different question (Ralph, 60–69, M, not tested)
Quotation 8	I think it's a good thing if someone's got that diagnosis and then gets offered it because then—I'm on Tofersen, which is specifically for SOD1, so therefore that opens that door up to me because I know I've got that gene. If I've got a different gene, C9orf or whatever it is, it may open another door for another trial or medication that's been on the market (Victoria, 40–49, F, tested positive)

some, due to the potentially rapid disease course, likelihood of deterioration in communication and other symptoms, long timescales for receiving results, possibility for clinical trial access, and suggestion that people would look it up online anyway. Others emphasized the need for time to process the diagnosis—with one participant suggesting a flexible approach responsive to each person's reaction to diagnosis. Indeed, the variation in preferences made optimal timing a challenge to determine (Table 4, Q1–3). Another participant felt genetics and WGS should be an ongoing narrative in consultations given the life and family transitions that may impact decision-making (Table 4, Q4).

Participants felt genetics in ALS and WGS should be discussed and carried out by a knowledgeable healthcare professional, with whom they have an ongoing and trusting relationship, and who can communicate with empathy, understanding and in plain language. Some felt ALS specialist nurses would be best equipped to do this, as they may have a more holistic understanding of the individual. Others would favor a consultant neurologist given their technical expertise (Table 4, Q5–6). Another view was that the important part was not the role of the healthcare professional but their skills and knowledge to provide relevant information.

People were generally positive about every person with ALS being offered WGS and having the opportunity to make their own decision, especially given opportunities for clinical trial participation (Table 4, Q7–8). However, it was suggested that this should be conditional on there being guidance and support in place. Some questioned if this would be relevant or beneficial for those without a family history, as well as cost implications. One participant emphasized that WGS should be offered rather than people having to ask.

Discussion

This study provides novel findings about the information and engagement with services needed by pwALS to make informed decisions around WGS.

The decision to undergo WGS was motivated by a range of personal and family considerations, including a desire to access genetically-targeted clinical trials, reinforcing suggestions that such developments could impact interest and uptake in genomic testing (12). The decision not to have WGS was equally multifaceted, based on the perceived utility

of results for the individual, their clinical care, or the potential implications for relatives. Across interviews, parents were particularly aware of the implications—viewed as potentially positive or negative—for their (adult) children. Awareness of these varied factors can help clinicians better support pwALS when discussing WGS.

Notably, the decision to undergo WGS was not always perceived as an *informed* decision by pwALS, a finding that has elsewhere been reported (7). This was particularly the case where genomic testing was carried out to establish a diagnosis, which goes against recommendations that diagnosis should be based on clinical tests and not genomic test results. Receiving genomic testing results alongside the ALS diagnosis was distressing for participants and at times had a lasting negative impact, underscoring the rationale for post-diagnosis testing.

Access to pretest genetic counseling (led by neurology or genetics clinicians) was inconsistent amongst participants. A review of UK patient records between 2012–2016, found pwALS/FTD averaged two genetic counseling appointments before testing (12)—higher than individuals in our study who described delayed access to relevant information, a lack of discussion around possible implications of WGS, and unanswered questions and unmet needs. Our recent survey amongst England-based clinicians highlights multiple barriers to WGS; lack of time, paperwork, low confidence in genomic testing and genetic counseling skills, and a lack of resources to support patients (6) may be impacting ability and willingness of neurology clinicians to discuss and counsel pwALS around WGS. This reinforces research that suggests clinician discomfort in discussing WGS and differences in confidence and may be behind variation in practice (9). Training in genetic counseling skills can increase confidence in discussing genomic testing (6). The need for genetic counseling to be offered to pwALS is included in proposed consensus guidelines for ALS genomic testing (15).

In this study, participants expressed varied preferences for the timing of discussions around genetics and information sharing by clinicians, with suggestions for flexibility and responsiveness to each person's circumstances and approach. Determining the optimal timing of information in ALS care generally has been identified as a challenge by clinicians, who at the same time recognized this as crucial to the ability of patients to make decisions (16). Some participants expressed preferences for who should discuss WGS, though perceived suitability was linked to having the key skills, rapport, and availability. This suggests with appropriate training and pathways in place, WGS could be discussed by a variety of clinicians. As in our study, existing literature suggests that pwALS are supportive of genomic testing being routinely discussed (17) though caution was suggested where cognitive symptoms affect capacity and where there are limited clinical benefits (7). It seems there may be a gap between the views of pwALS and clinicians, who may be more hesitant to offer genomic testing to individuals without a known family history, due to the complex genetic landscape, and possibility of incomplete penetrance and VUS, which can compound challenges of communicating results (9).

Inconsistencies in information provision highlight a key area for intervention, as inadequate information and support can affect decision-making and access to WGS, and with that access to clinical trials and potential treatments. Further, this research has underscored the need for support at various stages of the testing process, including following a positive result. Indeed, a lack of post-test support negatively impacted some participants who described feelings of isolation, confusion and devastation in the period following the delivery of their genomic test result.

Future research should include people from more diverse backgrounds to ensure such interventions meet the needs of as many people as possible. The inclusion of health professionals along the care pathway is also key, to ensure people can be engaged in shared decision-making with clinical teams in a timely and relevant way.

Conclusion

This study highlights variation in practice around ALS genomic testing, suggesting clinician training is needed to ensure all who are interested in WGS are given the relevant information. Even where people had considered or had WGS, they reported delayed access to information or unmet support needs, and some did not feel they made an informed decision. Thus, this study emphasizes an urgent need for information resources and support for pwALS when considering WGS and throughout the process. This is part of a wider mixed-methods study which will result in the development of patient decision aids to support pwALS and their relatives to make informed choices around genetic/genomic testing.

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Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

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