Article:
Howard, J. orcid.org/0000-0001-7182-593X, Bekker, H.L., McDermott, C.J. orcid.org/0000-0002-1269-9053 et al. (1 more author) (2024) Survey of service needs to embed genome sequencing for motor neuron disease in neurology in the English National Health Service. Journal of Medical Genetics. ISSN 0022-2593

https://doi.org/10.1136/jmg-2023-109735

OPEN ACCESS

Short report

Survey of service needs to embed genome sequencing for motor neuron disease in neurology in the English National Health Service

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► Additional supplemental material is published online only. To view, please visit the journal online (https://doi.org/10.1136/jmg-2023-109735).

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Received 3 November 2023
Accepted 28 January 2024

To cite: Howard J, Bekker HL, McDermott CJ, *et al*. *J Med Genet* Epub ahead of print: [please include Day Month Year]. doi:10.1136/jmg-2023-109735

ABSTRACT

All people with motor neuron disease (pwMND) in England are eligible for genome sequencing (GS), with panel-based testing. With the advent of genetically targeted MND treatments, and increasing demand for GS, it is important that clinicians have the knowledge and skills to support pwMND in making informed decisions around GS. We undertook an online survey of clinical genomic knowledge and genetic counselling skills in English clinicians who see pwMND. There were 245 respondents to the survey (160 neurology clinicians and 85 genetic clinicians). Neurology clinicians reported multiple, overlapping barriers to offering pwMND GS. Lack of time to discuss GS in clinic and lack of training in genetics were reported. Neurology clinicians scored significantly less well on self-rated genomic knowledge and genetic counselling skills than genetic clinicians. The majority of neurology clinicians reported that they do not have adequate educational or patient information resources to support GS discussions. We identify low levels of genomic knowledge and skills in the neurology workforce. This may impede access to GS and precision medicine for pwMND.

INTRODUCTION

Within the English National Health Service (NHS), all people with motor neuron disease (pwMND) are eligible for genome sequencing (GS),[1] with panel-based reporting. In 20%–30% of apparently sporadic MND, and 60%–70% of familial MND, a potentially causal monogenic variant can be identified.[2 3] As genomic technology advances, more pwMND will be found to have a monogenic cause, leading to an increased demand for testing. GS for MND is delivered by specialist clinical genetics and MND services, who have expertise in supporting people to make decisions about GS for life-limiting conditions with multiple-cause aetiology. In the English NHS, neurology clinics are staffed by consultant neurologists, neurology specialist trainees (postgraduate doctors training to consultant level) and specialist nursing staff. Clinical genetic clinics are staffed by consultants in clinical genetics (a medical doctor trained in clinical and genomic diagnosis of genetic conditions) and genetic counsellors (a non-medical specialist trained to help people understand, and act on, their genomic test result). In the English NHS, most neurology clinics are based in separate institutions from the genetic services.

Key to the NHS 5-year Genomic Medicine strategy is the embedding of GS in mainstream medicine to facilitate the personalisation of care.[4] Currently, there are no clinical patterns to make a judgement about whether a pwMND is likely to have a monogenic cause.[2] The genomic basis of MND, and implications for treatment, is complicated.[3] Variants in more than one gene can contribute to disease in an individual, and there can be variability in age of onset and clinical manifestations (eg, MND or frontotemporal dementia) within a family.[5 6] pwMND will require information about MND genetics, the implications of GS test results for management of MND and the consequences of results for family members.[7] It is unclear what health professionals need to embed GS in current practice and support shared decision making about testing and treatment for pwMND.

We undertook a survey of the genomic knowledge and skills of health professionals in the English NHS who manage pwMND. This study is part of a project to develop a patient decision aid supporting pwMND to make decisions to have GS within neurology services. This project draws on the Medical Research Council (MRC) complex intervention development framework to guide the research studies needed to inform the development of this complex intervention (phase 1). Bekker's Making Informed Decisions Individually and Together framework[8] is used to provide the theoretical scaffolding to developing a decision aid for implementation within healthcare systems that represent the goals, needs and experiences of the different people involved in making GS decisions (see online supplemental figure 1).[9] The research objectives are to (a) describe current practice for GS across England and (b) identify resource needs for health professionals to integrate GS within their service.

MATERIALS AND METHODS

A cross-sectional questionnaire survey, to assess genomic knowledge and skills, was delivered via *qualtrics*, between January 2023 and 1 May 2023. We followed the consensus-based checklist for reporting of survey studies. Full methods are online: supplemental methods.

RESULTS

There were 245/268 completed surveys, including 160 neurology clinicians (106 consultants, 26 specialty registrars and 28 MND nurses) and 85 clinical genetic clinicians (20 consultants in clinical genetics and 65 genetic counsellors) (online supplemental table 1). The qualitative responses from the free text sections were categorised under two themes: (1) current practice and barriers to GS and (2) professional upskilling, patient resources

and service needs for future GS implementation (online supplemental figure 2). The survey's quantitative responses are synthesised under the headings below.

In neurology clinics, most MND genetic testing discussions are undertaken by consultant neurologists

A variable proportion of neurology clinicians reported having been involved in arranging GS for pwMND (63% of consultant neurologists, 83% of neurology trainees and 57% of MND specialist nurses). Of these clinicians, the majority of neurology consultants had both requested GS and discussed results with pwMND, while the majority of MND specialist nurses had only requested testing (online supplemental figure 3). The majority of neurology clinicians would refer to clinical genetics for further discussion of results if requested by pwMND, but only a minority discuss the possibility of predictive testing for unaffected relatives (online supplemental table 2). Neurology teams reported multiple, overlapping barriers to GS (online supplemental figure 4). Lack of time to discuss genomic testing (49%), paperwork (47%) and timescale to get results (37%) were the barriers to offering GS most frequently reported by consultant neurologists.

Neurology clinicians report low levels of familiarity with genetic testing guidelines and criteria

The majority of consultant clinical geneticists and genetic counsellors rated themselves as 'fairly' or 'very' familiar with each genetic testing guidelines question (online supplemental table 3). Only a minority of neurology clinicians rated themselves as

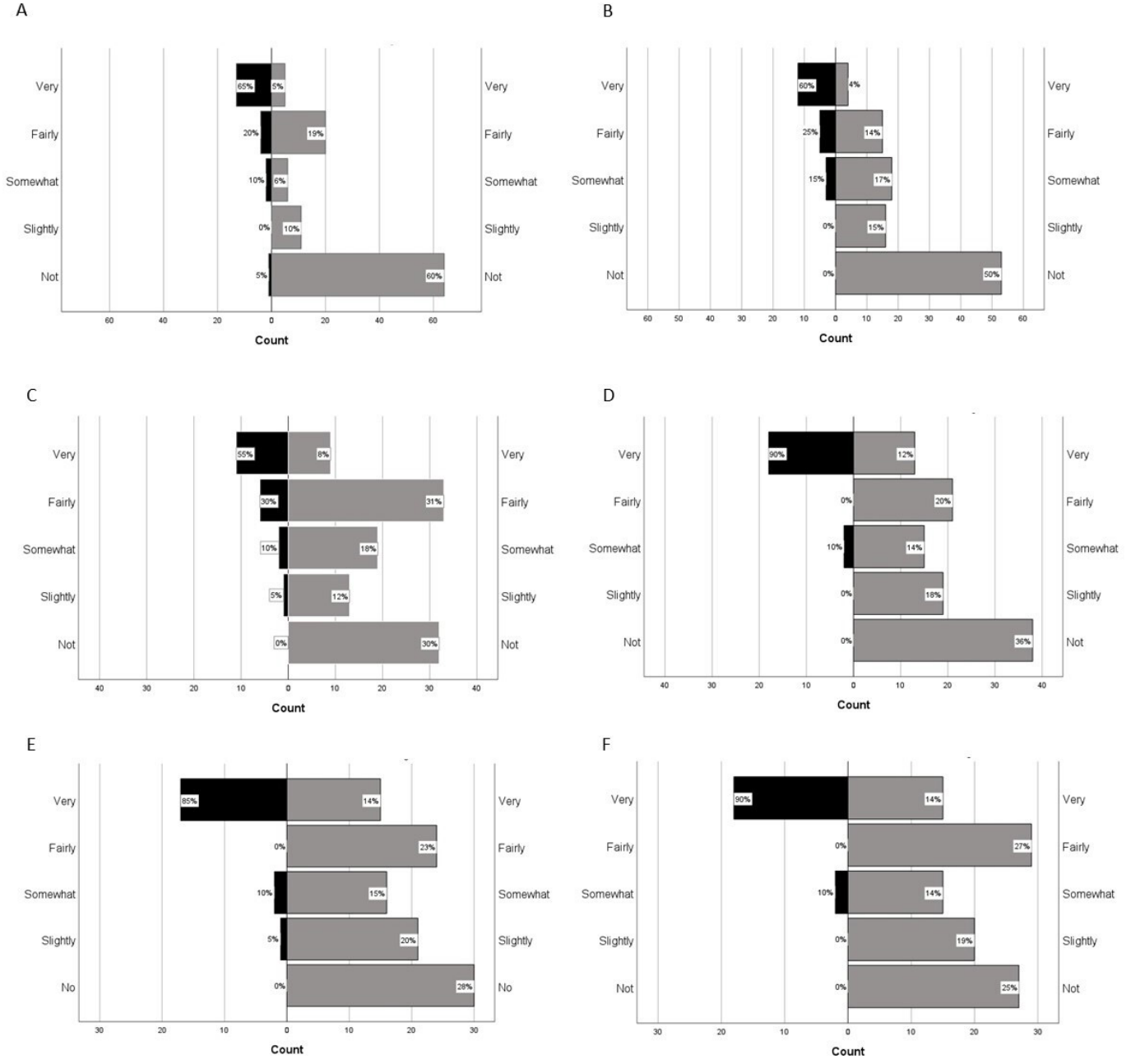

Figure 1 Self-reported genomic knowledge and understanding of predictive testing process for consultant neurologists. Pyramid blots illustrate consultant neurologists' (grey) and consultant geneticists' (black) responses on the 5-point Likert scale. (A) Knowledge of American College of Medical Genetics criteria. (B) Knowledge of Joint Committee on Genomics in Medicine statement on consent and confidentiality. (C) Knowledge of test directory. (D) Understanding of predictive testing process. (E) Understanding of implications of predictive test results. (F) Understanding of reasons for predictive testing.

'fairly' or 'very' familiar with the genomic test directory, American College of Medical Genetics Criteria or Joint Committee on Genomics in Medicine consent and confidentiality guidance (online supplemental table 3). A Wilcoxon-signed rank test demonstrated that neurology clinicians scored significantly lower in each item than genetic clinicians (figure 1, online supplemental table 4).

Neurology clinicians report low confidence in genetic counselling skills

The majority of consultant clinical geneticists and genetic counsellors rated themselves as 'fairly' or 'very' familiar with each genetic counselling skills question (online supplemental table 3). Only a relatively small proportion of neurology clinicians were fairly/very confident in explaining a variant of uncertain significance, oligogenic inheritance or variable clinical expression. In addition, only a small proportion reported being fairly/very confident in undertaking the clinical procedures to request GS of completing the 'Record of Discussion' form, interpreting a genomic laboratory report and communicating results to families (online supplemental table 3). A Wilcoxon-signed rank test demonstrated that neurology clinicians scored significantly lower in each item than genetic clinicians (figure 2, online supplemental table 4).

Genetic counselling training was associated with increased confidence in embedding GS in practice

We sought to understand the effect of genetic counselling training on neurology clinicians' knowledge and skills. We defined genetic counselling training for mainstream clinicians as courses such as continuing professional development courses, Master's degree programmes or a research doctorate. A higher

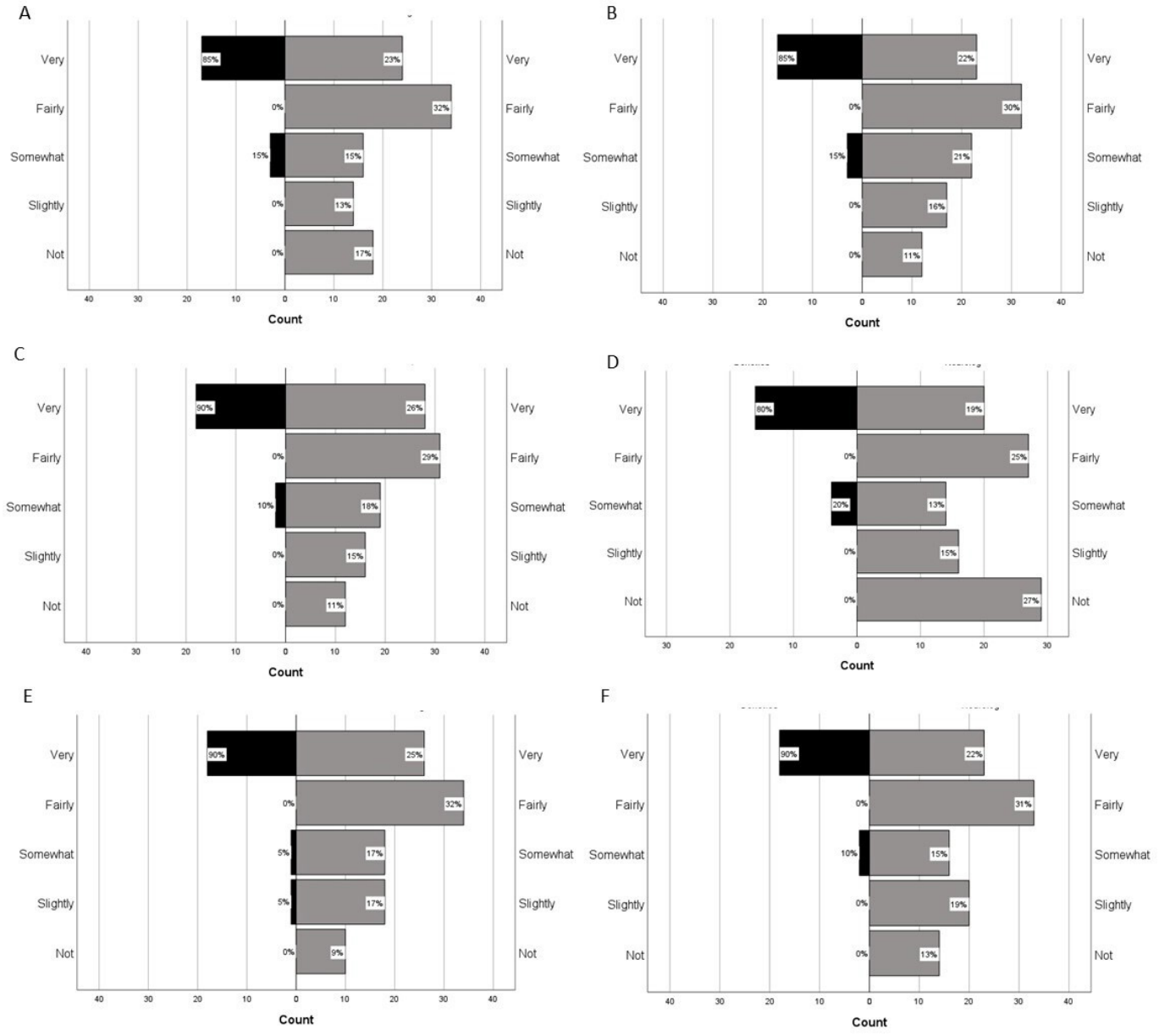

Figure 2 Self-reported confidence in procedures to request genome sequencing and confidence in genetic counselling skills for consultant neurologists. Pyramid blots illustrate consultant neurologists' (grey) and consultant geneticists' (black) responses on the 5-point Likert scale. (A) Completion of record of discussion form. (B) Interpreting a genomic laboratory report. (C) Discussing results with patients. (D) Explaining oligogenic inheritance. (E) Explaining variable expressivity. (F) Explaining a variant of uncertain significance.

proportion of consultant neurologists who had genetic counselling training had arranged MND genomic testing (12/13 vs 57/93, chi-squared p=0.028). Consultant neurologists with genetic counselling training did not rate themselves as 'fairly' or 'very' familiar on all genetic testing guideline questions more frequently than those without (1/13 vs 3/93, chi-squared p=0.4). There were no significant differences in these individual item scores between consultant neurologists with and without genetic counselling training. More consultant neurologists with training were likely to self-rate 'fairly' or 'very' confident for all genetic counselling (8/13 vs 19/93, p=0.0014), all clinical procedures (10/13 vs 32/93, p=0.003) and all predictive testing (7/13 vs 24/93, p=0.037) items than those without training. There were no statistically significant differences in genetic counselling skills, procedures to request GS or predictive testing individual item scores between trained and untrained consultant neurologists. There was no difference in any of the item scores for neurology consultants aged under or over 50 years. Suggesting that it is training in genetic counselling skills and not clinical experience which influences genomic knowledge and confidence. Overall, these findings support an influence of training in genetic counselling on confidence in genetic counselling skills among consultant neurologists (online supplemental figure 5).

Neurology clinicians lack adequate resources to support MND genetic discussions

We asked neurology clinicians about what resources would best support MND genetic discussions (online supplemental table 5). Only 50% of neurology consultants, 46% of neurology trainees and 19% of MND nurses felt that they currently have adequate resources to support such discussions. The most popular choice of resource was training materials on MND genetics (online supplemental figure 6).

DISCUSSION

We found that, in the English NHS, most GS for pwMND is requested by neurology consultants. A recent survey of English neurology consultants identified variability in offering GS for pwMND; less than 50% would discuss GS with newly diagnosed pwMND.[10] Our findings illustrate a low proportion of neurology clinicians discuss the possibility of predictive genetic testing. A recent global survey of neurologists found that only 48% discuss predictive testing.[11] It is crucial that neurology clinicians address predictive testing, where appropriate, given the potential role for presymptomatic treatments (eg, tofersen), noting the need for pretest genetic counselling (usually via a genetic counsellor).[12 13] Self-reported genomic knowledge and counselling skills were significantly lower in neurology clinicians than genetic clinicians. Only a minority of neurology clinicians rated themselves as 'fairly' or 'very' familiar/confident with core genomic knowledge and counselling skills. We found that training in genetics is associated with higher genomic knowledge and skills in neurology consultants, and greater likelihood of requesting GS for pwMND. Neurology clinicians reported multiple barriers to offering GS including a lack of time to discuss genomic testing in clinics with pwMND, and burdensome paperwork.

Our findings provide a potential explanation for variability in practice for GS and identify needs for changes to innovate genomic testing in neurology clinics. Our findings resonate with recent findings in the UK and globally suggesting these are important ingredients for interventions to integrate genomic testing in the NHS. North American primary care doctors reported low levels of confidence with requesting and interpreting genomic tests, and low understanding of ethical and legal frameworks.[14] A systematic review of barriers to offering GS, found lack of genomic knowledge, time and guidelines, as well as ethical concerns, were consistently identified as barriers.[15]

Our findings have implications for clinical practice and service innovation. Genomic testing for pwMND is being requested by neurology clinicians with low genomic knowledge and skills. Services must ensure that clinicians are trained appropriately. Training curricula for neurology clinicians need revision to include relevant aspects of genomics, and educational resources (eg, the NHS Genomics Education Programme) could be updated to include details on more complex aspects of MND genomic testing and clinician guidelines produced.[16 17] Additionally, neurology clinicians cited a lack of resources to support genomic testing discussions for pwMND, which suggests that pwMND may lack important information and guidance when considering genomic testing options. Resources such as information leaflets, videos or patient decision aids could be developed to fill this gap. In conclusion, we suggest that mainstream genomic testing for pwMND requires increased clinician training, streamlined processes and resources supporting shared decision making.

Acknowledgements We thank all those who participated in the survey.

Contributors JH designed the study, analysed the data and wrote and approved the paper. HLB designed the study and wrote and approved the paper. CJM secured the funding, analysed the data and wrote and approved the paper. AM secured the funding, designed the study, analysed the data and wrote and approved the paper.

Funding This study was supported by a project grant from the Motor Neuron Disease Association (McNeill/Oct21/967-794).

Competing interests None declared.

Patient consent for publication Not applicable.

Ethics approval Ethical approval was granted by a UK NHS Research Ethics Committee (22/SW/0047) and the University of Sheffield (050846). Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

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Supplementary Figure 1.

Supplementary Figure 2. Summary of the framework analysis of free text responses.

Supplementary Figure 3. Current practice of neurology clinicians requesting genomic testing for MND.

A. Bar chart displaying the percentage of each clinician group (neurology consultant, neurology StR, MND nurse, genetics consultant, genetic counsellor) reported to undertake discussion of genomic testing with pwMND in clinic.
B. Bar chart displaying the percentage of each clinician group (neurology consultant, neurology StR, MND nurse) who had either discussed GS with a pwMND (bar labelled request), discussed the results of GS with a pwMND (bar labelled "result") or both aspects (bar labelled "both").

Supplementary Figure 4. Hierarchical cluster analysis of barriers to GS reported by neurology clinicians.

Hierarchical clustering analysis was performed using Clustergrammer, with Euclidean distance. Shaded boxes indicate that the barrier to offering genome sequencing was reported by the participant. The top level of the dendrogram identified 3 clusters. The top cluster reported barriers concerning time and paperwork. The middle cluster reported barriers relating to training and protocols. The bottom cluster reported also ethical barriers. The clinicians found in each cluster (top, middle, bottom cluster) are in supplementary table 8.

Supplementary Figure 5. Hierarchical cluster analysis of survey item scores and genetic counselling training.

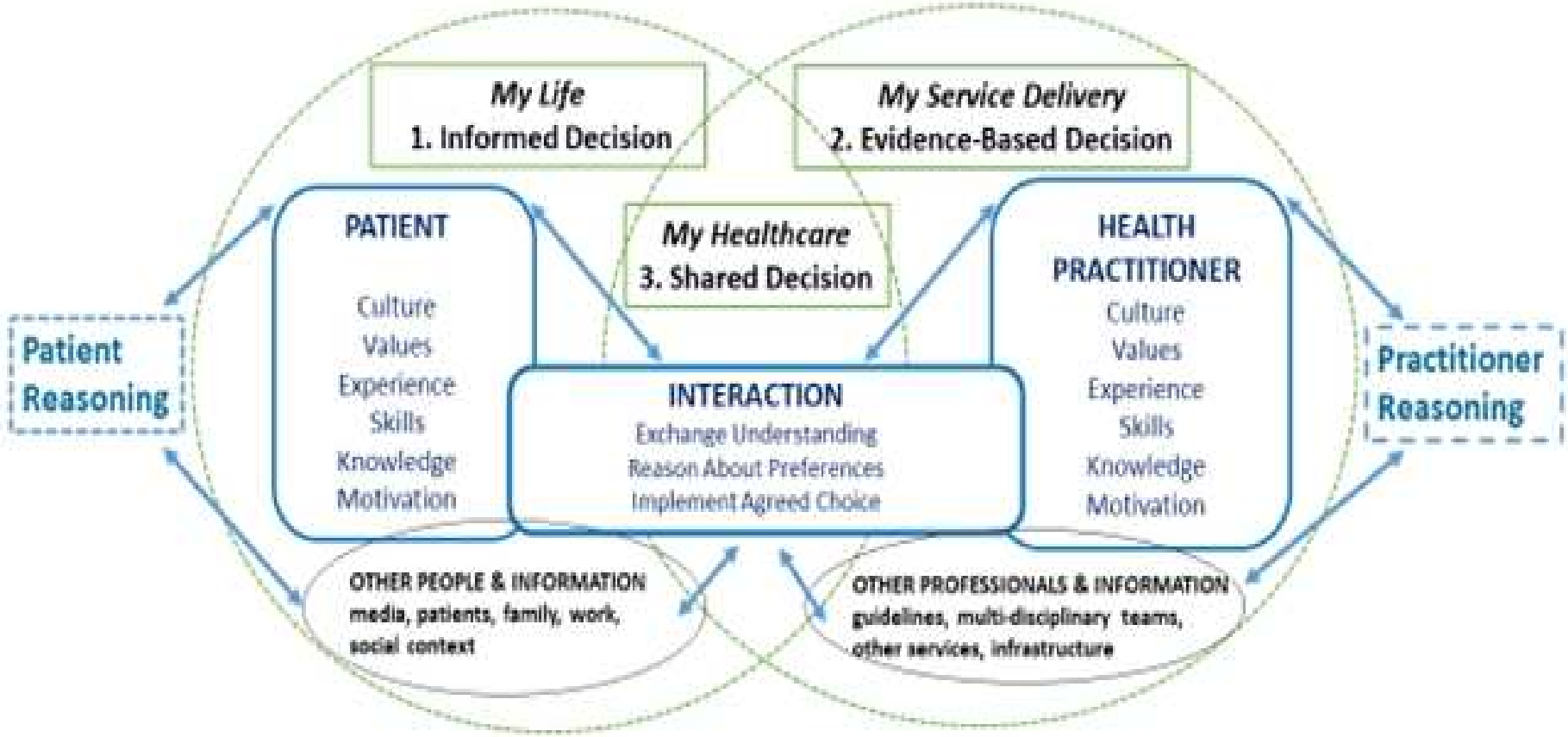
Hierarchical clustering analysis was performed using Clustergrammer, with Euclidean distance. Shaded boxes in columns under each item represent the confidence level reported, with darker shades of red representing increased confidence. The Training column is shaded if the participant reported having training in Genetic Counselling. This demonstrates that clinicians with training tend to have higher survey scores than those

without. The clinicians found in each cluster (top, bottom cluster) are in supplementary table 9.

Supplementary Figure 6. Neurology Clinicians preferred resources to support genomic testing discussions.

The Venn diagram indicates that Neurology Clinicians would value multiple resources to support genomic testing discussions. The most frequent combination of resources (80) desired was a combination of training resources, local protocols, guidelines and a patient decision aid.

Making Informed Decisions Individually and Together (MIND-IT) in Healthcare: Multiple-Stakeholder Decision Makers Intervention Framework (©Bekker, 2022)



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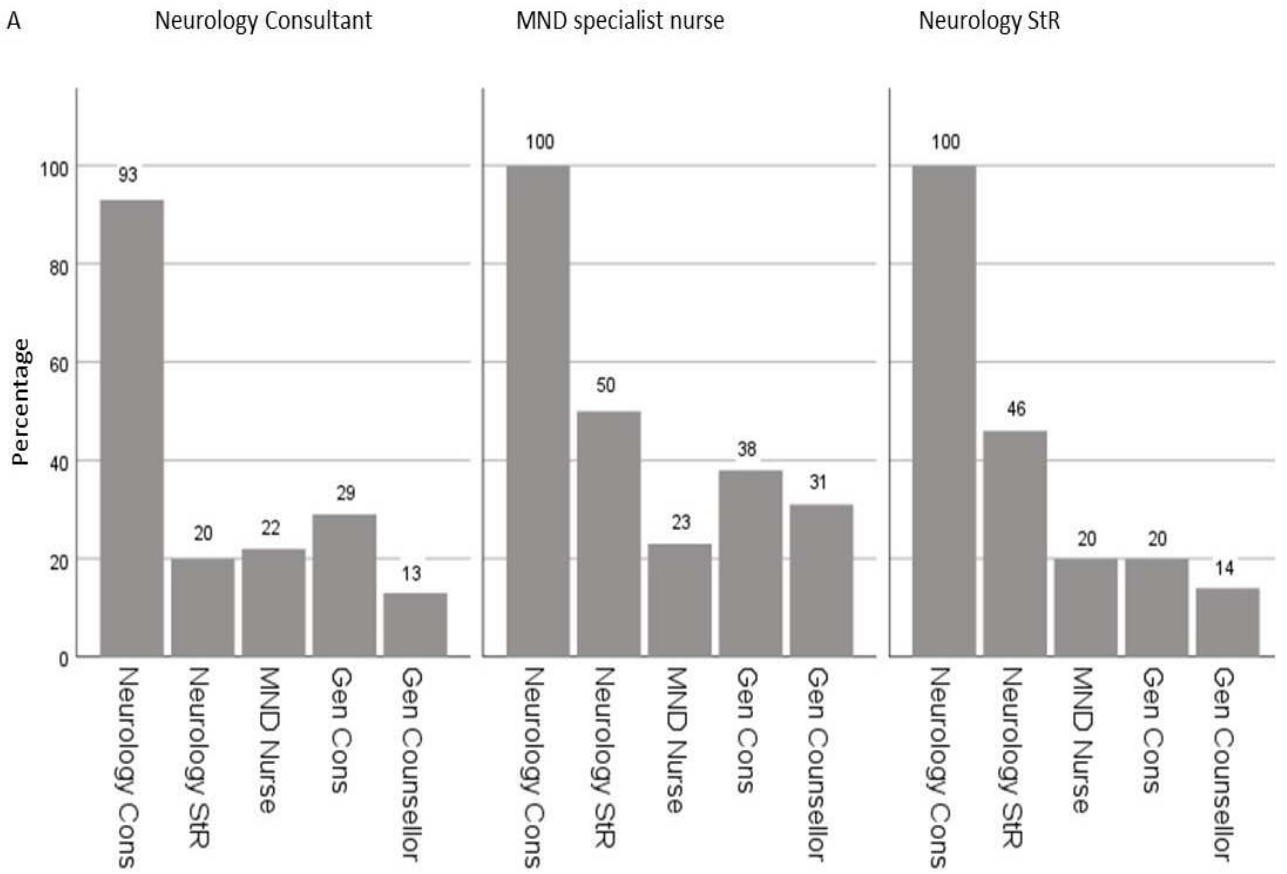
Category
Description
Illustrative quotes
Current practice: service challenges and barriers to offering genomic testing
Whole genome sequencing processes
Clinicians felt WGS presented multiple barriers, including time needed to complete paperwork and delay in receiving results
The introduction of WGS, with its unnecessarily terrible paperwork and long reporting delays, has been an unmitigated disaster (Consultant Neurologist)
It takes over thirty minutes to complete, sign and send the forms dedicated to genetic testing. This is a time resource that isn't countered within our service provision and time availability (MND nurse)
Guidelines and local pathways
Clinicians highlighted the need for (inter)national guidelines on provision of testing and local pathways to facilitate it
Agreed national guidelines which keep up with the type of expert recommendation that appears in journal reviews, along with a local pathway to allow for appropriate discussion (Consultant Neurologist)
I do not think that we have yet embedded discussions about genetics in our care pathway like we have for respiratory support & nutrition options, for example (MND nurse)
Staff to support genetic counselling and testing
Clinicians outlined the importance of appropriate genetic counselling and the need for trained staff to support the counselling and testing process
…This needs good pre-and post testing expertise and although I am happy to signpost/ discuss this needs specialist discussion (Consultant Neurologist)
Specialists will hopefully have additional training… but have limited time, so would benefit from additional team members (perhaps a specialist nurse) trained in this aspect (Consultant Neurologist)
Clinician needs: resources for education, training and information sharing
MND-specific training
Clinicians emphasised training needs around genetic counselling and testing, including implications, taking consent, and interpreting results
I should like to have even some basic knowledge and training about the guidelines, processes and understanding results (MND nurse)
Variants of uncertain significance is most difficult aspect. Geneticists provide literature review info but this is not nuanced. Have had different interpretation when asking expert in MND genetics (Consultant Neurologist)
Predictive genetic testing and family implications
Clinicians felt they needed to know more about predictive testing processes and how to support family members
We often refer patients or whole families to Clinical genetics counsellors for the predictive aspects. Some training around their approach and what is discussed in that meeting would be useful so that we can prepare patients and families (Consultant Neurologist)
Our role is to continue to discuss impact after results, particularly if the results is positive. So help to know how to support families would be great (MND nurse)
Resources to share with families
Clinicians wanted resources to share with pwMND and family members around clinical and genetic features of MND, genetic testing and research
Patients want more and more information about impact of positive gene on their families plus research info on SOD1 and FUS that they can understand (MND nurses)
List of clinical trials/interested research groups in specific genes around the country would be helpful to then signpost individuals with pathogenic variants identified to (Neurology Trainee)


A
Neurology Consultant
MND specialist nurse
Neurology StR
Percentage
0
20
40
60
80
100
93
20
22
29
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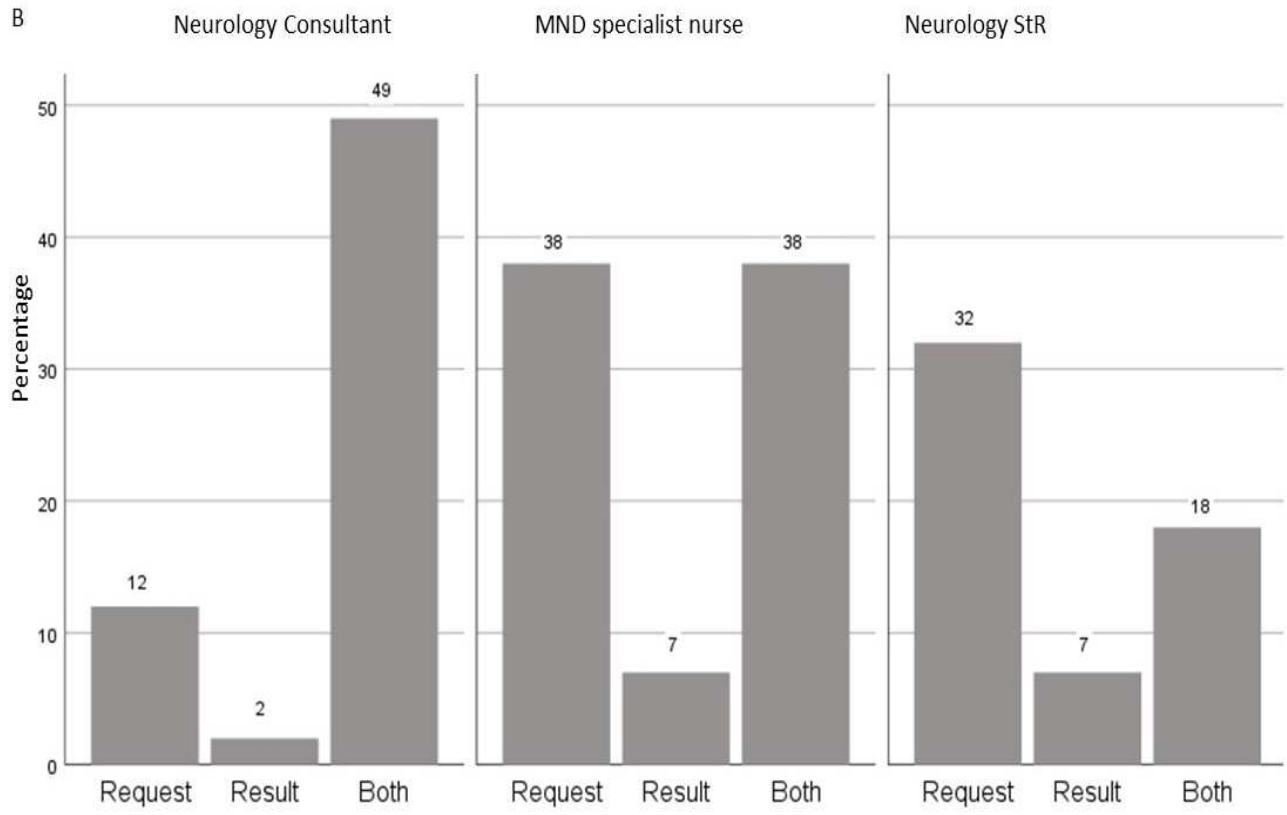
20
14
Neurology Cons
Neurology StR
MND Nurse
Gen Cons
Gen Counsellor


B
Neurology Consultant
MND specialist nurse
Neurology StR
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2
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38
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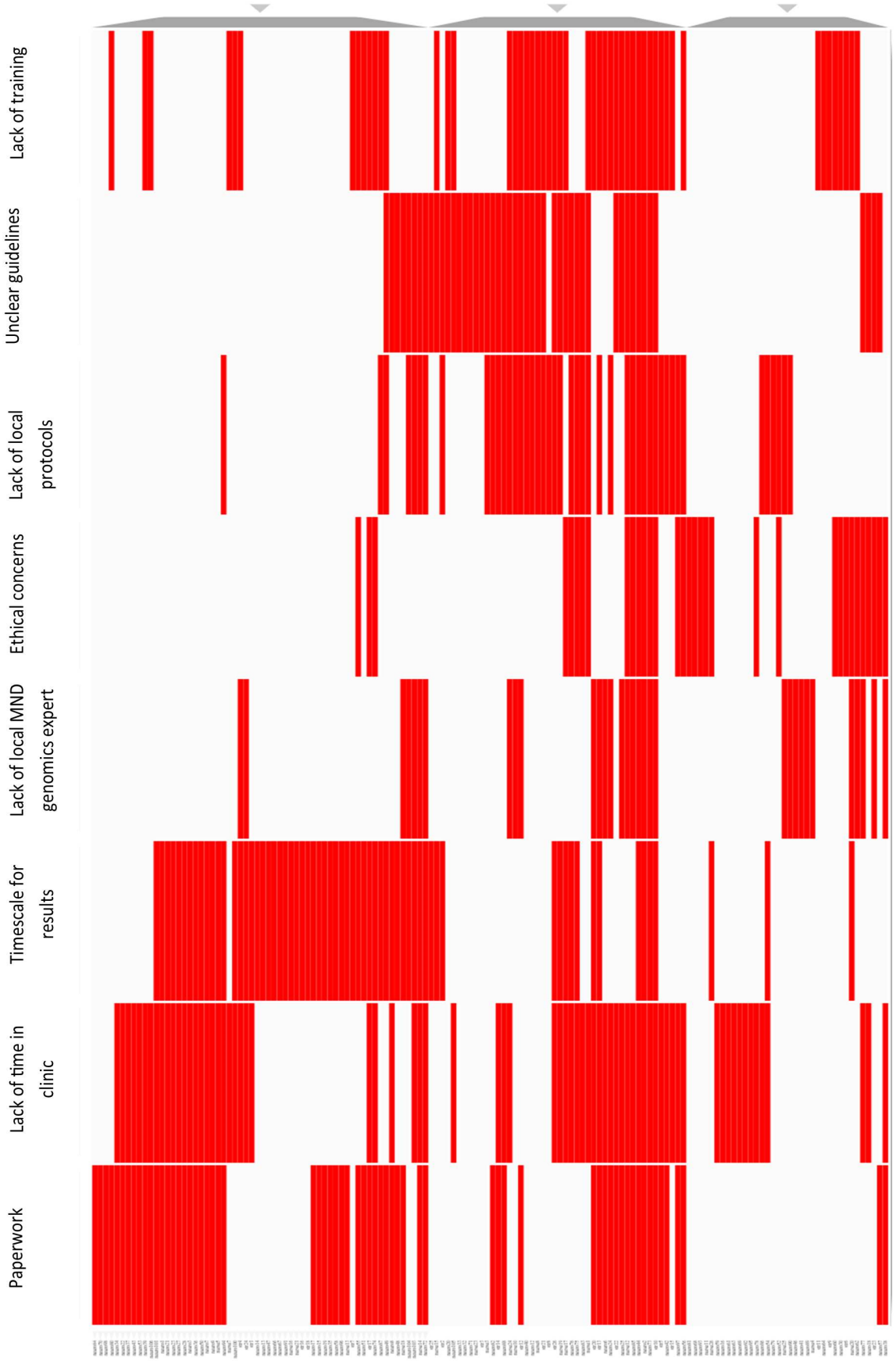
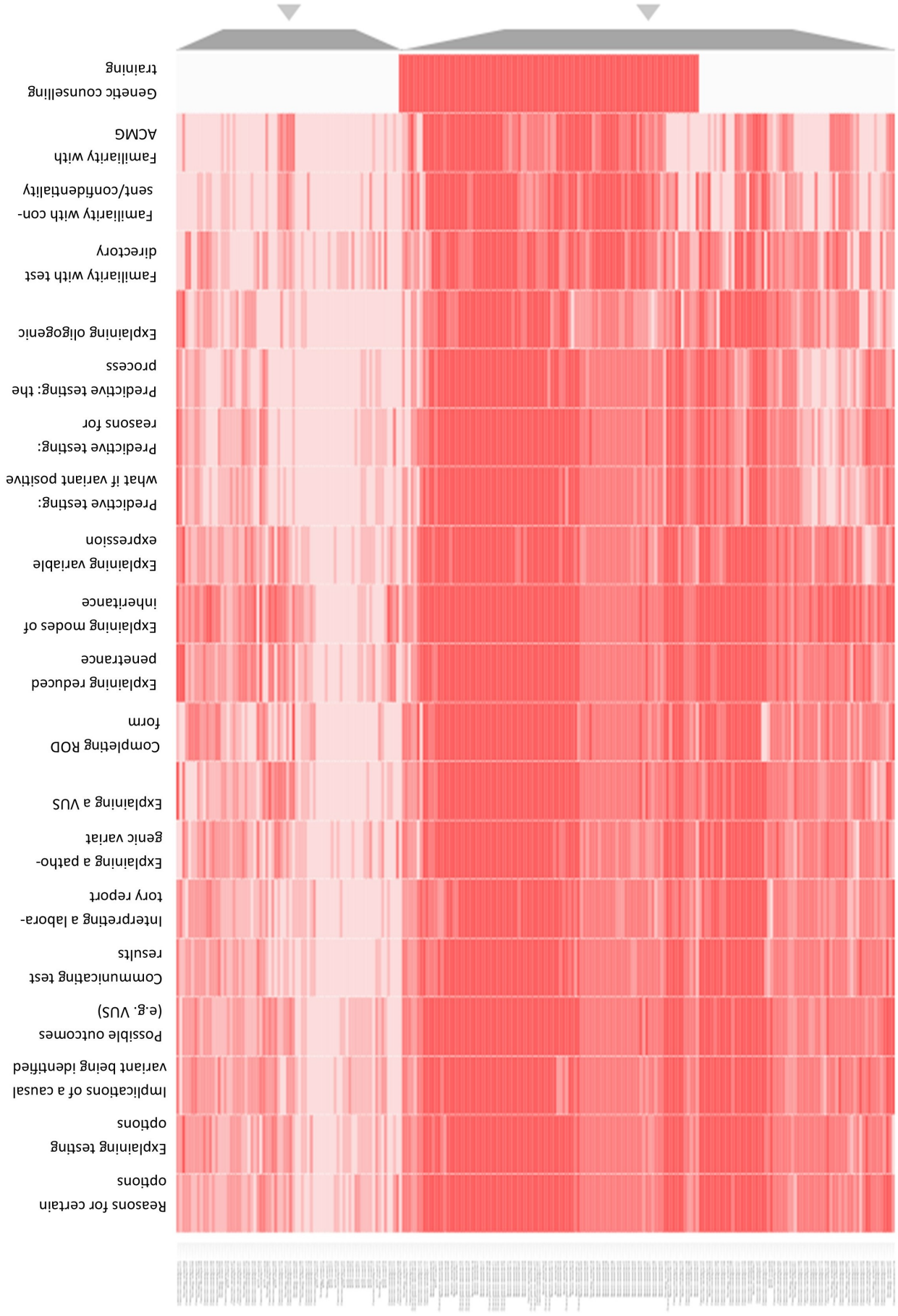
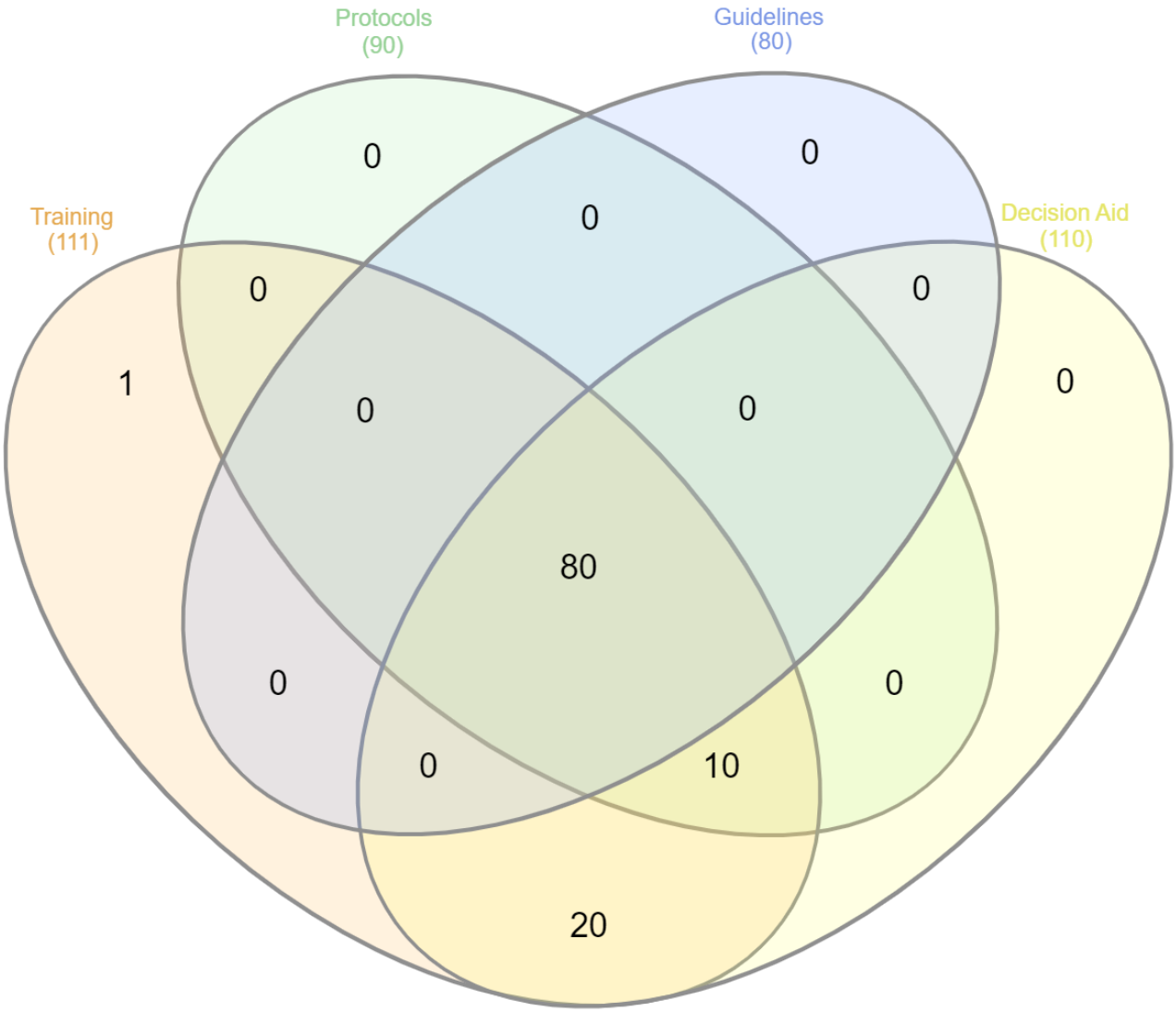
7
18
Request
Result
Both


Lack of training
Unclear guidelines
Lack of local protocols
Ethical concerns
Lack of local MND genomics expert
Timescale for results
Lack of time in clinic
Paperwork


Reasons for certain options
Explaining testing options
Implications of a causal variant being identified
Possible outcomes (e.g. VUS)
Communicating test results
Interpreting a laboratory report
Explaining a pathogenic variat
Explaining a VUS
Completing ROD form
Explaining reduced penetrance
Explaining modes of inheritance
Explaining variable expression
Predictive testing: what if variant positive
Predictive testing: reasons for
Predictive testing: the process
Explaining oligogenic
Familiarity with test directory
Familiarity with consent/confidentiality
Familiarity with ACMG
Genetic counselling training


Protocols
(90)
Guidelines
(80)
Training
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Decision Aid
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Supplementary Table 1: Characteristics of survey participants by specialism, number (%) *

	Consultant neurologists *n=106*	**Neurology trainees *n=26***	**Clinical genetics consultants *n=20***	**Genetic counsellors *n=65***	**MND nurses *n=28***
Age					
< 30	0 (0)	1 (4)	0 (0)	8 (12)	1 (4)
30 - 39	8 (8)	22 (85)	2 (10)	19 (29)	6 (21)
40 - 49	48 (45)	83 (12)	11 (55)	25 (38)	9 (32)
50 - 59	40 (38)	0 (0)	5 (25)	12 (18)	10 (36)
60 - 69	10 (9)	0 (0)	2 (10)	1 (2)	2 (7)
70 +	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Gender					
Male	64 (61)	20 (77)	9 (45)	3 (5)	4 (14)
Female	40 (38)	6 (23)	11 (55)	61 (94)	24 (86)
Non-binary	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)
Prefer not to say	1 (1)	0 (0)	0 (0)	0 (0)	0 (0)
Years in substantive role					
< 5	20 (19)	18 (69)	3 (15)	16 (25)	13 (46)
5 - 9	22 (21)	8 (31)	7 (35)	10 (15)	5 (18)
10 - 14	21 (20)	0 (0)	3 (15)	19 (29)	4 (14)
15 - 19	21 (20)	0 (0)	4 (20)	7 (11)	3 (11)
20 - 24	13 (12)	0 (0)	1 (5)	5 (8)	3 (11)

25 +	9 (8)	0 (0)	2 (10)	8 (12)	0 (0)
Training in genetic counselling					
Yes	14 (13)	3 (12)	20 (100)	63 (97)	1 (4)
No	92 (87)	23 (88)	0 (0)	2 (3)	27 (96)
Special interest in MND					
Yes	34 (32)	7 (27)	8 (40)	22 (34)	28 (100)
No	72 (68)	19 (73)	12 (60)	43 (66)	0 (0)

**Percentages may not add up to 100 due to rounding*

Supplementary Table 2. Neurology clinicians practice for pwMND who have a causal genetic variant.

		Discuss inheritance risk if variant identified?	Discuss predictive testing options available to relatives?	Refer to clinical genetics?
Consultant neurologist	Yes	80%	58%	82%
	Sometimes	17%	18%	16%
Neurology trainee	Yes	73%	34%	86%
	Sometimes	4%	13%	13%
MND specialist nurse	Yes	31%	25%	56%
	Sometimes	18%	25%	12%

Supplementary Table 3. Percentage of respondents self reporting as "fairly" or "very" familiar/confident per survey item.

Item	Genetic counsellors	Genetic Consultants	Neurology Consultants	Neurology Trainees	MND Specialist Nurses
Genomic testing regulations and criteria					
The National Genomic Test Directory guidance for genetic testing in MND	67%	85%	38%*	19%*	11%*
The American College of Medical Genetics criteria	75%	85%	23%*	23%*	3%*
Joint Committee on Genomics in Medicine report on Consent and Confidentiality in Genomic Medicine	91%	85%	18%*	7%*	7%*
Genetic counselling skills					
Explaining pathogenic MND gene variants	83%	95%	50%*	42%*	21%*
Explaining a	90%	90%	52%*	46%*	21%*

variant of uncertain significance					
Explaining modes of inheritance	100%	90%	78%	65%*	18%*
Explaining oligogenic inheritance	66%	85%	44%*	20%*	10%*
Explaining reduced penetrance	85%	90%	66%*	50%*	15%*
Explaining variable clinical expression	97%	90%	56%*	38%*	15%*
Explaining Genetic testing options (e.g. whole genome sequencing)	86%	90%	59%*	50%*	21%*
Reasons why people might choose these options	91%	90%	59%*	30%*	18%*
Discussing possible outcomes of testing	94%	90%	57%*	30%*	21%*

Discussing implications of a pathogenic variant being identified	98%	85%	55%*	42%*	21%*
Clinical procedures to request WGS					
Completing the 'Record of Discussion' form	94%	85%	52%*	46%*	17%*
Interpreting a genetic laboratory report	83%	85%	50%*	28%*	7%*
Communicating genetic test results to people with MND	94%	90%	55%*	35%*	7%*
Predictive testing process					
Explaining the predictive testing process	98%	85%	31%*	14%*	7%*
Explaining reasons why people might choose predictive testing or not	98%	90%	41%*	28%*	10%*

Explaining Implications of a pathogenic gene variant being identified	94%	85%	33%*	21%*	7%*

*= p<0.05 on chi-squared test. Neurology consultants and trainees compared to genetics consultants. MND specialist nurses compared to genetic counsellors.

Supplementary Table 4. Median scores on Likert-scale for each survey item for each clinician group.

Item	**Genetic counsellors**	**Genetic Consultants**	**Neurology Consultants**	**Neurology Trainees**	**Specialist Nurses**
Genomic testing regulations and criteria					
The National Genomic Test Directory guidance for genetic testing in MND	5 (4-5)	5 (4-5)	3 (1-4)*	3 (1-3)*	2 (1-3)**
The American College of Medical Genetics criteria	4 (3.5-5)	5 (4-5)	1 (1-3)*	2 (1-3)*	1 (1-1)**

Joint Committee on Genomics in Medicine report on Consent and Confidentiality in Genomic Medicine	5 (4-5)	5 (4-5)	1.5 (1-3)*	2 (1-3)*	1 (1-2)**
Genetic counselling skills					
Explaining pathogenic MND gene variants	4 (4-5)	5 (5-5)	3.5 (2-4)*	3 (2-4)*	1.5 (1-3)**
Explaining a variant of uncertain significance	5 (4-5)	5 (5-5)	4 (2-4)*	3 (2-4)*	1 (1-2)**
Explaining modes of inheritance	5 (4-5)	5 (5-5)	4 (4-5)*	4 (3-5)*	1 (1-2)**
Explaining oligogenic inheritance	4 (3-5)	5 (5-5)	3 (1-4)*	2 (1-3)*	1 (1-1)**
Explaining reduced penetrance	5 (4-5)	5 (5-5)	4 (3-5)*	3.5 (2-4)*	1 (1-2)**
Explaining variable clinical expression	4 (4-5)	5 (5-5)	4 (2-4.25)*	3 (2-4)*	1.5 (1-2)**
Explaining Genetic	4 (4-5)	5 (5-5)	4 (3-5))*	3.5 (2-4)*	2 (1-3)**

testing options (e.g. whole genome sequencing)					
Reasons why people might choose these options	5 (4-5)	5 (5-5)	4 (3-5)*	3 (2-4)*	2 (1-3)**
Discussing possible outcomes of testing	5 (4-5)	5 (5-5)	4 (2.75-5)*	3 (2-4)*	2 (1-3)**
Discussing implications of a pathogenic variant being identified	4 (4-5)	5 (5-5)	4 (3-5)*	3 (2-4)*	2 (2-3)**
Clinical procedures to request WGS					
Completing the 'Record of Discussion' form	5 (4-5)	5 (5-5)	4 (2-4)*	4 (1.75-4)*	2 (2-3)**
Interpreting a genetic laboratory report	4 (4-5)	5 (5-5)	4 (2-4)*	3 (2-4)*	1 (1-1.75)**
Communicating genetic test results	4 (4-5)	5 (5-5)	4 (2-5)*	3 (2-4)*	1 (1-2)**

to people with MND					
Predictive testing process					
Explaining the predictive testing process	5 (4-5)	5 (5-5)	2 (1-4)*	2 (1-3)*	1 (1-2)**
Explaining reasons why people might choose predictive testing or not	5 (4-5)	5 (5-5)	3 (1-4)*	2 (2-4)*	1 (1-2)**
Explaining Implications of a pathogenic gene variant identified	5 (4-5)	5 (5-5)	3 (1-4)*	2 (1.75-3.25)*	1 (1-2)**

*p<0.05 on Wilcoxon-signed rank test. Genetics consultants compared to neurology consultants or neurology trainees.

**p<0.05 on Wilcoxon-signed rank test. MND specialist nurses compared to genetic counsellors.

Supplementary Table 5. Preferred resources to support genomic testing for pwMND.

	Training resources	Local Protocols	Guidelines	Decision Aid	None of above
Neurology Consultant	65 (61%)	54 (51%)	48 (45%)	69 (65%)	6 (5%)
Neurology StR	20 (77%)	17 (66%)	18 (69%)	20 (77%)	
Specialist Nurse	26 (93%)	19 (67%)	14 (50%)	21 (75%)	

Supplementary material

Methods

Survey

A cross-sectional questionnaire survey was delivered on-line via *qualtrics,* between January 2023 - 1st May 2023. We followed the consensus-based checklist for reporting of survey studies (CROSS). Ethical approval was granted by a UK NHS Research Ethics Committee (22/SW/0047) and the University of Sheffield (050846). The study questionnaire was developed by the authors to capture current practice for MND WGS. Items were informed by the Medical Student Undergraduate curriculum from the British Society of Genomic Medicine, prior research, and current policy. In the UK, guidance on consent and confidentiality in relation to genomic medicine is given by the Joint Committee on Genomics in Medicine document *Consent and Confidentiality* in Genomic Medicine (2019). Genomic variant interpretation follows the American College of Medical Genetics criteria (sequence variants v3.0). Criteria for which patients can access genome sequencing are defined in the National Genomic Test directory. To request genome sequencing clinicians must complete a record of discussion form (in conjunction with the patient or consultee) and then a test order form to activate the genome sequencing test with the laboratory.

Consultant clinical geneticists, and genetic counsellors, were invited via the UK Predictive Genetic Testing Consortium email list, and contact with Lead Clinicians at each Regional Genetics Clinic. Consultant neurologists with a special interest in MND, and MND specialist nursing staff, were recruited via the MND UK Clinical Studies Group (CSG), and email contact with Lead Clinicians at each of the UK MND Care centres. Consultant neurologists and neurology trainees without a special interest in MND were recruited by email contact with Lead Clinicians in Neurology departments without an MND care centre.

The questionnaire was pilot tested with 2 Consultant Neurologists, 2 Consultant Clinical Geneticists and a Genetic Counsellor for content validity and item clarity.

Items assessed: Perceived awareness of UK genomic testing guidelines and criteria (3 questions), Self rated confidence in genetic counselling skills (10 question). Knowledge on predictive testing (3 questions). Self-rated confidence in clinical procedures to deliver WGS (3 questions). Responses were recorded using a 5-point Likert scale. Resources needed to support services offering MND genetic testing were enquired about using free text.

Statistical analyses

Scores on individual survey items were compared using a Wilcoxon-signed rank test. Proportions were compared using a chi-squared test. Significance was taken at the 5% level. All statistical analyses were performed in SPSS. Likert responses were compared between groups using a Wilcoxon-signed rank test. Hierarchical clustering was performed using

Clustergrammer (https://maayanlab.cloud/clustergrammer/). Free text responses were analysed using a framework analysis approach.

Framework analysis of free text survey responses

The analysis of the free text comments was based on a framework analysis approach. This was selected as it is a pattern-based approach to thematic analysis through which the data are presented in a framework. Themes and subthemes are presented in columns whilst cases are presented in the rows, which allows for comparison between and within cases, whilst maintaining a focus on the data.

The framework analysis involved a 5-stage process, starting with familiarisation through repeated reading of and immersion in the data, gaining an overview of the content and recording initial ideas and topics of interest. At this stage, the data were read as part of each survey response to maintain the context of each extract. Early notes and ideas on topics were then refined and expanded as the data were re-read to construct an initial thematic framework of themes and sub-themes. In the next phase, the data were indexed and sorted into this coding framework. Here, data were extracted into NVivo for ease of coding. This was carried out in conjunction with the fourth stage, where extracts were reviewed, and the framework was refined. This was an iterative and comparative process which involved looking at the data coded within and between each theme, re-coding, collapsing, subsuming, and renaming codes where appropriate. The fifth stage involved summarising and displaying the data, with the thematic framework used to develop the framework representing the key themes and subthemes in the data. Given the focus of the study, this was not developed into a more conceptual analysis. An analytic log was kept throughout this process with reflections, decisions, thoughts and ideas.

Given the large sample size of the survey and the significant number of participants who did not submit free text comments, clinician groups have been used as the cases displayed in the rows of the framework, as opposed to each participant individually. This was aligned with the comparative focus of the survey analysis which looks at patterns between clinician groups. The framework presented displays prominent themes but does not include all comments for relevance. Data are presented as submitted.

Data Availability

Anonymised data is available from the authors on reasonable request.