Howard J, ***Bekker HL****, McDermott CJ, McNeill A.* ***A survey of service needs to embed Genome Sequencing for Motor Neuron Disease in neurology in the English National Health Service.***

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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 making informed decisions around GS. We undertook an online survey of clinical genomics knowledge and genetic counselling skills in English clinicians who see pwMND. There were 245 respondents to the survey (160 neurology clinicians, 85 genetics 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 genomics knowledge and genetic counselling skills than genetics 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 genomics knowledge and skills in the neurology workforce. This may impede access to GS and precision medicine for pwMND.

Key words

Motor neuron disease (MND), genome sequencing (GS), decision-aid, shared decision making.

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 genetics 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 upon, their genomic test result). In the English NHS, most neurology clinics are based in separate institutions from the genetics 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 (e.g. 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 genomics 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 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 (MIND-IT) 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 Supplementary 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 genomics knowledge and skills, was delivered via *qualtrics,* between January 2023 - 1st May 2023. We followed the consensus-based checklist for reporting of survey studies (CROSS). Full methods are online.

Results

There were 245/ 268 completed surveys, including 160 neurology clinicians (106 consultants, 26 speciality registrars, 28 MND nurses) and 85 clinical genetics clinicians (20 consultants in clinical genetics, 65 genetic counsellors) (Supplementary 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 (Supplementary 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 (Supplementary 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 (Supplementary Table 2). Neurology teams reported multiple, overlapping barriers to GS (Supplementary 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 "fairly" or "very" familiar for each genetic testing guidelines question (Supplementary Table 3). Only a minority of neurology clinicians rating themselves "fairly" or "very" familiar with the genomics test directory, American College of Medical Genetics Criteria or Joint Committee on Genomics in Medicine consent and confidentiality guidance (Supplementary Table 3). A Wilcoxon-signed rank test demonstrated that neurology clinicians scored significantly lower in each item than genetics clinicians (Figure 1, Supplementary Table 4).

Neurology clinicians report low confidence in genetic counselling skills

The majority of consultant clinical geneticists and genetic counsellors rated themselves "fairly" or "very" familiar for each genetic counselling skills question (Supplementary Table 3). Only a relatively small proportion of neurology clinicians were fairly/very confident to explain 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 (Supplementary Table 3). A Wilcoxon-signed rank test demonstrated that neurology clinicians scored significantly lower in each item than genetics clinicians (Figure 2, Supplementary 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, Masters degree programs or a research doctorate. A higher 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 "fairly" or "very" familiar on all genetic testing guidelines questions more frequently than those without (1/13 vs 3/93, chi-squared p=0.4). There were no significant differences for 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 for 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 age under or over 50 years. Suggesting that it is training in genetic counselling skills and not clinical experience which influences genomics knowledge and confidence. Overall, these findings support an influence of training in genetic counselling on confidence in genetic counselling skills among consultant neurologists (Supplementary Figure 5).

Neurology Clinicians lack adequate resources to support MND genetic discussions

We asked neurology clinicians about what resources would best support MND genetics discussions (Supplementary 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 (Supplementary 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 (e.g. Tofersen), noting the need for pretest genetic counselling (usually via a genetic counsellor)[12] [13]. Self-reported genomics knowledge and counselling skills were significantly lower in neurology clinicians than genetics clinicians. Only a minority of neurology clinicians rated themselves "fairly" or "very" familiar/ confident with core genomics knowledge and counselling skills. We found that training in genetics is associated with higher genomics 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 genomics 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 genomics knowledge and skills. Services must ensure that clinicians are trained appropriately. Training curricula for neurology clinicians need revision to include relevant aspects of genomics, educational resources (e.g. 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.

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Competing interests

The authors have no financial or other conflicts of interest to declare

Ethics approval statement

Ethical approval was granted by a UK NHS Research Ethics Committee (22/SW/0047) and the University of Sheffield (050846).

Contributorship statement

JH - designed study, analysed data, wrote paper, approved paper.

HB –designed study, wrote, approved paper.

CM -secured funding, analysed data, wrote paper, approved paper.

AM - secured funding, designed study, analysed data, wrote paper, approved paper.

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Legends

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.

Figure 2. Self-reported confidence in procedures to request GS 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 genomics laboratory report. C. Discussing results with patients. D. Explaining oligogenic inheritance. E. Explaining variable expressivity. F. Explaining a variant of uncertain significance.

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.

Figure 1

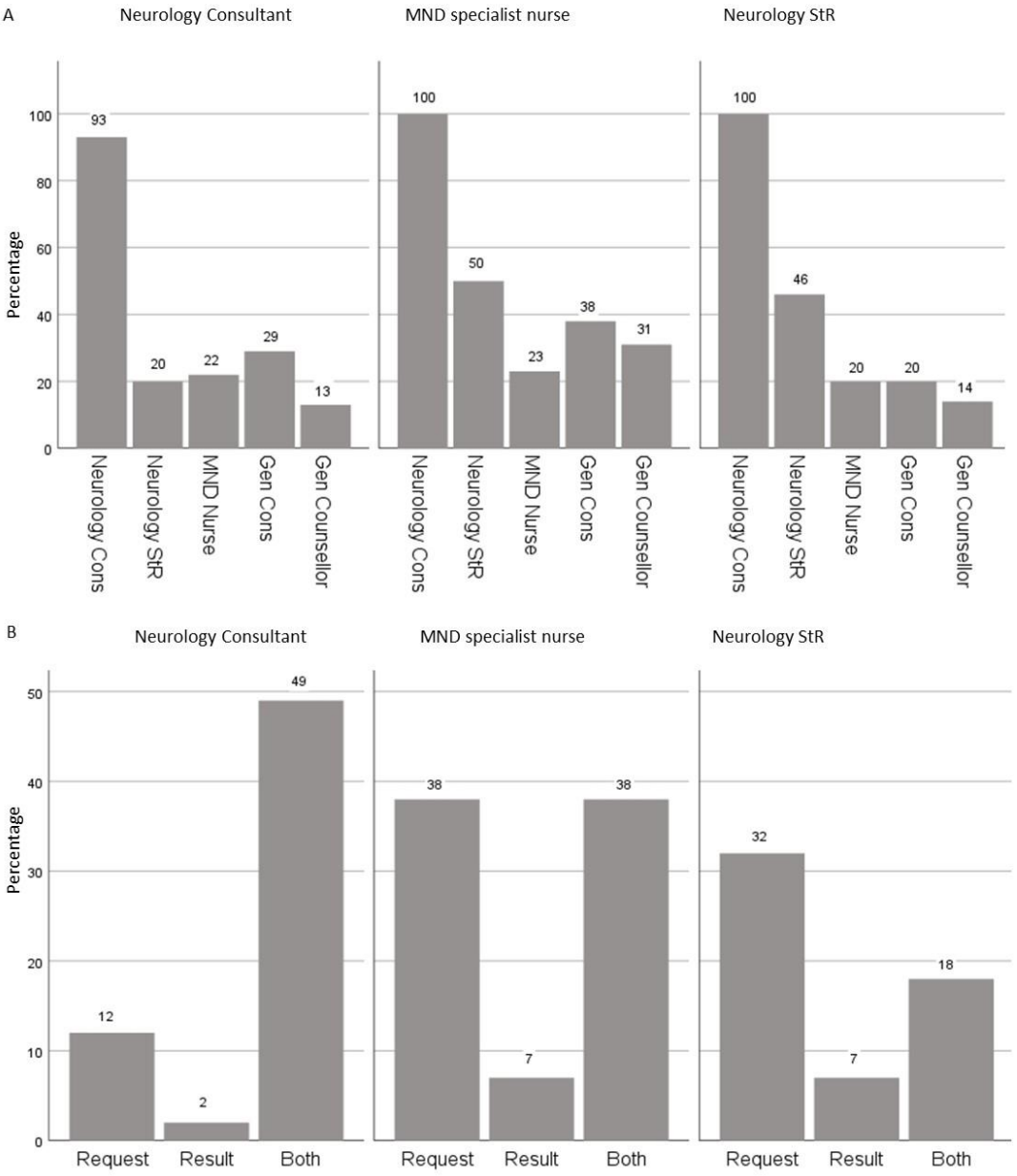
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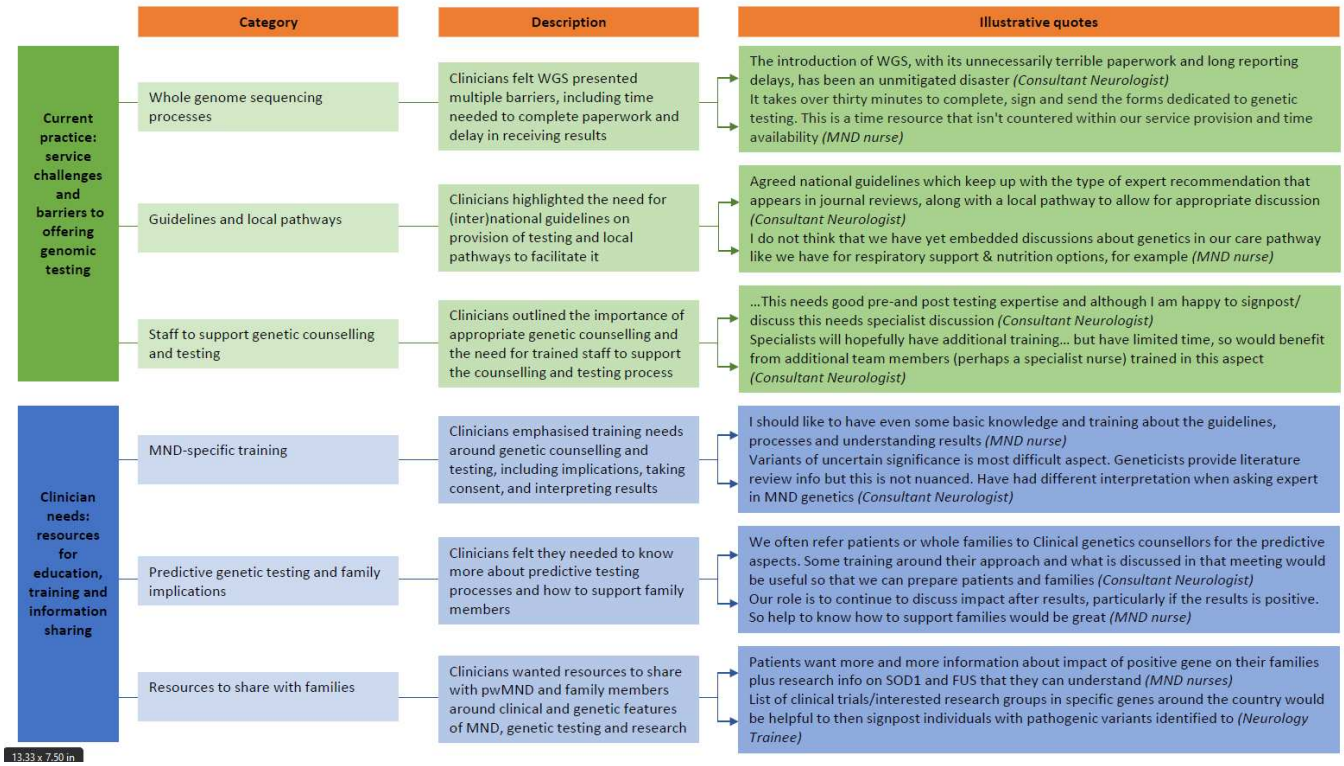
Figure 2


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)
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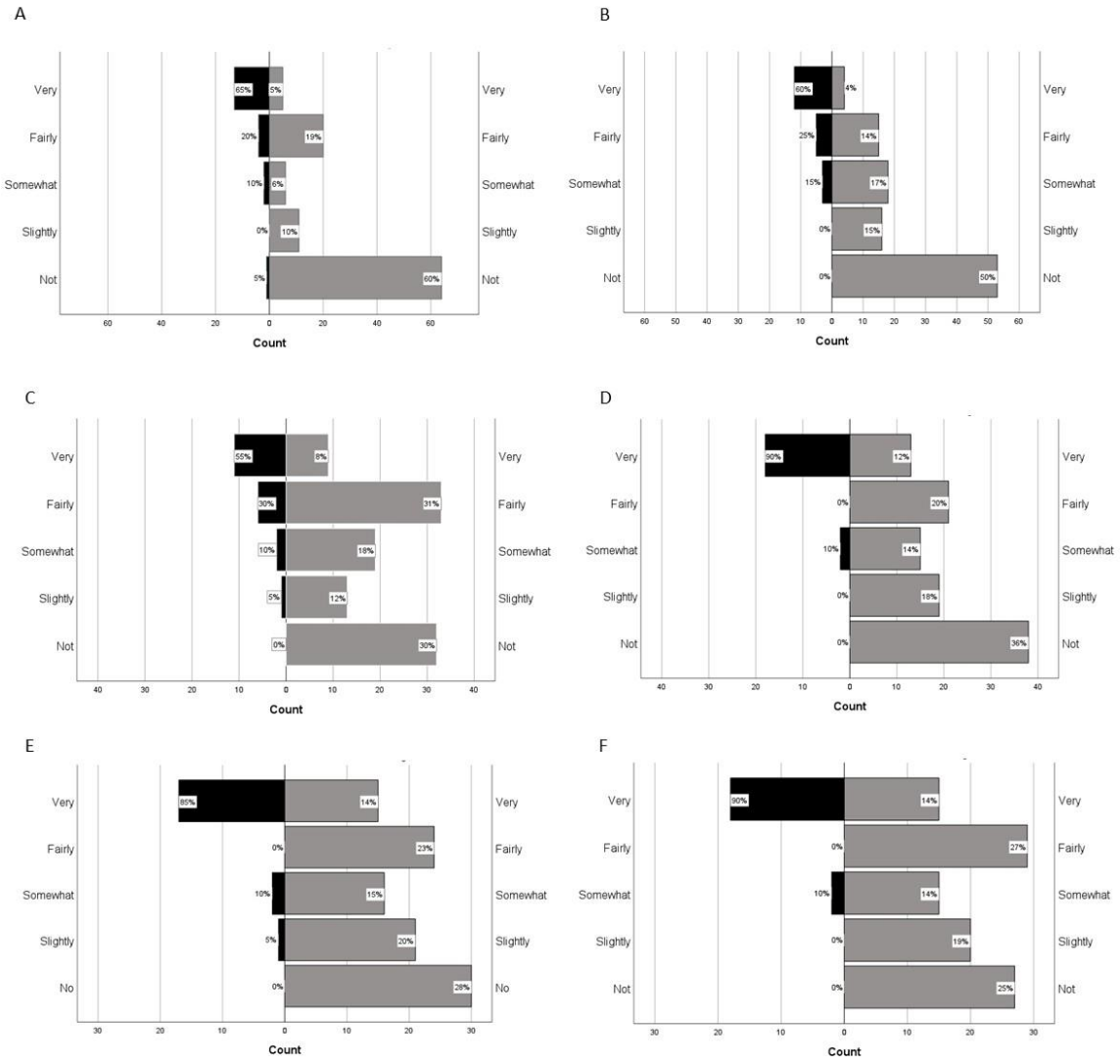
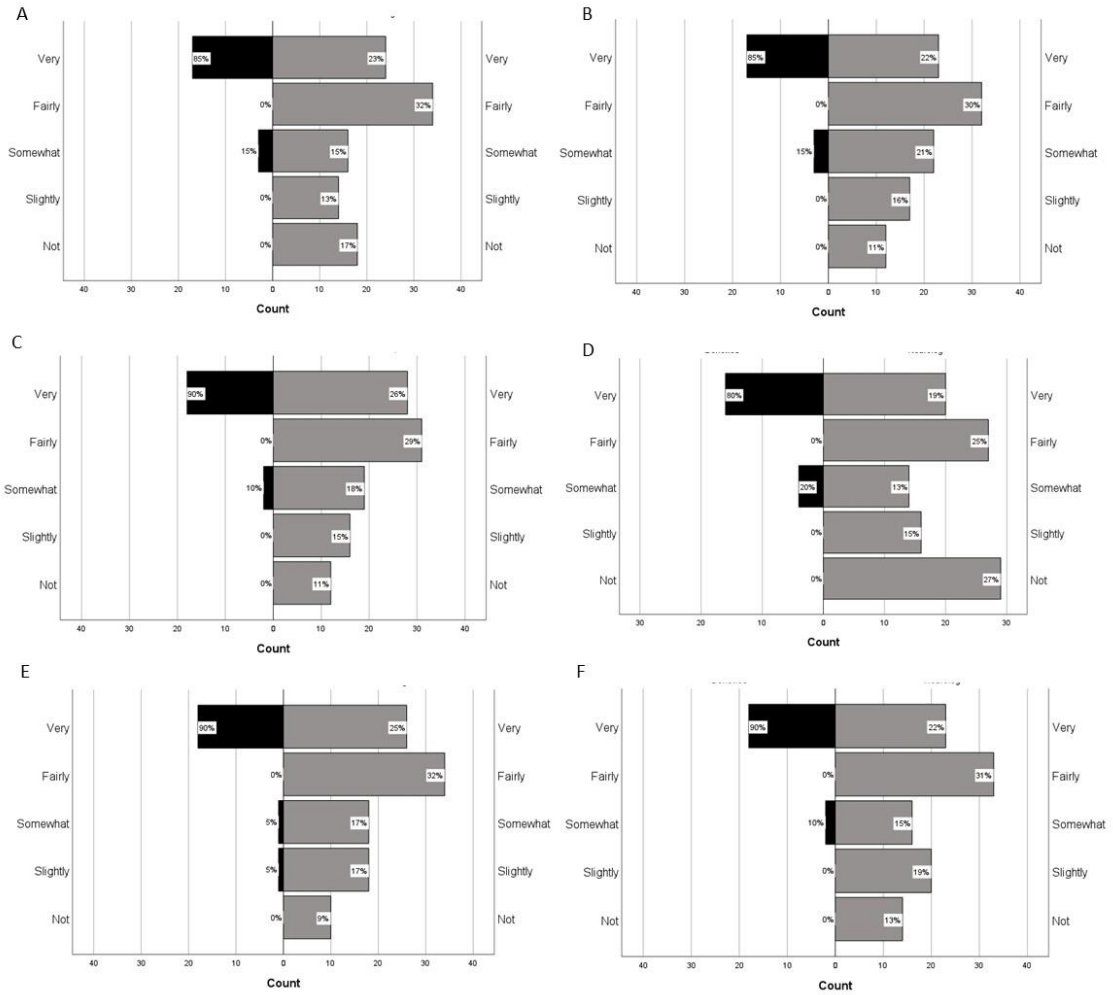
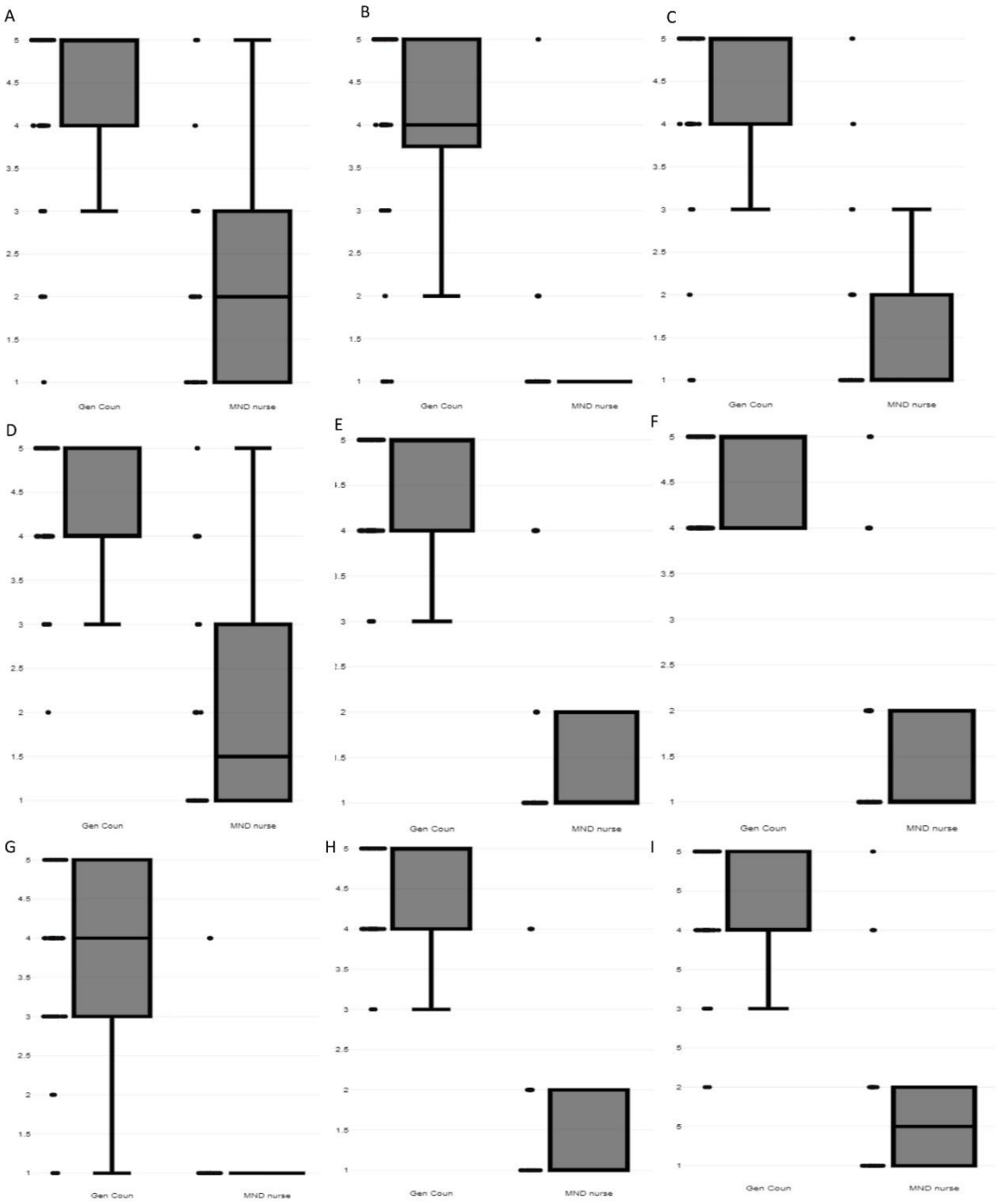
Supplementary Figure 2



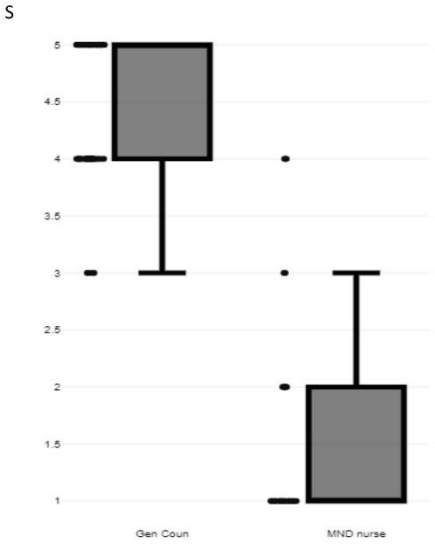
Supplementary Figure 3



Supplementary Figure 4



Supplementary Figure 5



Supplementary Figure 6