TeleNEwCARe: An Italian case-control telegenetics study in patients with Hereditary NEuromuscular and CArdiac diseases

Title: TeleNEwCARe: an Italian case-control Telegenetics study in patients with Hereditary NEuromuscular and CArdiac diseases

Running title: Genetic counselling by Telemedicine

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Abstract.

Telemedicine provides healthcare services remotely and represents a fundamental resource for the management of rare and fragile patients. Tele-health implementation is a main objective of the European Reference Networks (ERNs) mission to accelerate diagnosis for rare diseases.

TeleNewCAre is a pilot case-control project which evaluates the efficacy and satisfaction of telegenetics for neuromuscular and cardiac adult patients, compared to face-to-face genetic counselling. The virtual sessions were co-hosted by a medical geneticist and a neurologist/cardiologist. Specific questionnaires (Clinical Genetics Satisfaction Questionnaire (CGS), Telemedicine Satisfaction Questionnaire (TSQ) and a Satisfaction Questionnaire for medical geneticists) were used to assess the effectiveness and fulfilment of telecounselling, both for patients and health care providers.

Satisfaction expressed for telegenetics did not significantly differ from face-to-face counselling. The virtually enrolled patients declared they had the possibility to relate confidentially with the specialists, to share information and to be informed in an exhaustive way about their disease. Almost all patients declared themselves willing to reuse the telecounselling in the future. The multidisciplinary care was perceived as a significant added value. No overt technical problems were reported although the need for digital skills and tools can limit patients' compliance.

Our experience supports telegenetics as a valid alternative to traditional genetic counselling in cardiac and neuromuscular patients. This innovative approach facilitates multidisciplinary care, grants a periodical follow up, without forcing patients to discomfortable travelling, and allows to maintain expert care. This result meets the ERNs needs to reduce patients' burden to access and monitor their healthcare.

Keywords. Telegenetics, Telemedicine, genetic counselling, hereditary cardiac diseases, hereditary neuromuscular disorders

Introduction

The aim of Telemedicine (the delivery of health care services remotely, through use of information and communication technologies (ICT)) is to provide as many people as possible with health services, to overcome the problem of distance (1-3). The implementation of remote patient care is within the mission of the European Reference Networks (ERNs), a unique example of virtual high-level e-health-based systems, established in 2017 to tackle complex and rare diseases (RDs).

Genetic counselling (GC) is a critical step in the diagnostic process of RDs and genetic testing (GT) should always be provided in a counselling setting. GC is perhaps the most suitable of all medical specialties for telemedicine, being based on an interview with the patient and family members, which does not necessarily require the person's physical presence. Moreover, the increase in knowledge and the acquisition in the diagnostic routine of advanced sequencing technologies have favored a strong increase in the demand for these services, together with big challenges in interpreting genetic data, that require a constant debate among specialists in the context of a growing multidisciplinary care (2-3). In this context, the tendency towards the establishment of highly specialized centers (hubs), whose catchment area is generally regional and even supra-regional, forces patients to travel long distances to referral centers. Furthermore, the need to minimize face-to-face contact due to the worldwide COVID-19 pandemic has forced a sudden increase in telemedicine, including telegenetics (4-8).

Hereditary Neuromuscular (NMDs) and Cardiac Diseases (CDs) are broad groups of genetic conditions with high impact to healthcare systems and families. It has been estimated that NMDs affect 500.000 EU citizens and CDs are a frequent cause of morbidity and a major cause of sudden death in young individuals (9,10). Both NMDs and CDs are characterized by overlapping phenotypes and a huge genetic and allelic heterogeneity, which make GT and its interpretation critical to achieve a genetic diagnosis confirming the clinical suspicion.

Within our role of Health Care Provider of Euro-NMD, ITHACA, and EuroBloodnet ERNs, we provide GC and related GT for many of the diseases in charge of these ERNs (11-12).

The present one-year case-control pilot study aims to assess the feasibility, usability, and fulfillment of telecounselling in the field of neurogenetics and cardiogenetics compared to the face-to-face traditional approach. Enrolled patients participated in the telecounselling performed by the medical geneticists, with the simultaneous presence (physical or via video) of the specialist (neurologist/cardiologist) who requested the GC, giving an added value of a real-time multidisciplinary assessment.

Methods

Study setting and participants

The Medical Genetics Unit of the University Hospital of Ferrara, Italy, is a regional HUB center and a national reference center for Clinical Genetics and Molecular Genetics and it holds regular clinics for outpatients from different Italian territories. The TeleNEwCARe project (Local Ethical Committee Approval, N. 696/2019/Sper/AOUFe) was a single-center one-year case-control study to assess patients' and professionals'

satisfaction for telecounselling in the field of neurogenetics and cardiogenetics. The place of telegenetics' delivery was the Medical Genetics Unit, where medical geneticists remotely connected with neurologists/cardiologists and patients (either at Neurology/Cardiology clinic or at home). The telegenetics service was equipped with a high-resolution full HD video camera, a 24-inch monitor, a standalone microphone and an audio system. For the telecounselling, the Lepida Web Conference videoconferencing system (available at https://videoconferenza.lepida.it) was utilized since it is a free encrypted system available for Public Administration Services in Emilia Romagna region. Platform choice and privacy protocols were defined with the hospital's ICT department, which also provided technical support.

The total number of enrolled subjects was 114 (52 cases and 62 controls). Criteria for inclusion of "cases" in the study were: i) male and female adult patients affected by a NMD or CD (probands) or with a positive family history of a hereditary NMD or CD (relatives); ii) written consent to participate in the study; iii) filling in two questionnaires (CGS and TSQ - **Supplementary File 1**). Exclusion criteria were: i) underage patients (<18yrs); ii) reason for referral different from a hereditary NMD or CD; iii) failure to fill in the questionnaires. "Controls" included male and female adult patients evaluated faceto-face weekly in the same study period at the neurogenetic/cardiogenetic clinics of the Medical Genetics Unit, who completed only the CGS questionnaire. The robustness of our sample allocation (cases and controls) was statistically tested (see Selection bias analyses and **Supplementary Tables 1, 2, 3**).

Telecounselling procedure

Preliminarily to the telecounselling, written informed consent was collected from patients by the specialist requesting the GC. A telecounselling schedule of weekly sessions was

created, with up to six 40-minutes visits in each session. Clinical records were made available to medical geneticists by the specialists through certified email, prior to the connection. Appointment information, login instructions and PIN code to access the "virtual room" were sent to patients and physicians few days before the connection. Questionnaires were sent by email to patients within 24 hours after the online session and collected in an anonymous form.

Genetic counselling satisfaction measurements and data analysis

Genetic counselling satisfaction was measured using a modified seven-item Clinical Genetics Satisfaction (CGS) indicator, with a 1-5 Likert scale response mode where higher scores indicate higher satisfaction (13-14), for both cases and controls. The Telemedicine Satisfaction Questionnaire (TSQ), modified from literature (3,13), was used to measure cases' perceived satisfaction and all items, except for item 20, have a 15 Likert scale response mode. TSQ was adapted with the inclusion of item 21 evaluating the patients' satisfaction with the simultaneous presence of the specialist (neurologist/cardiologist). A specific counsellors' satisfaction questionnaire was completed by medical geneticists after telecounselling sessions (modified from (15)) (**Supplementary File 1**).

We calculated the mean score, the range, and the standard deviation (SD) of numerical variables; the empirical distributions of nominal variables were expressed by percentage values (%). For each item of CGS, TSQ (except item Q15 "I would like to meet the genetic counsellor in person"), and counsellors' questionnaires, we established a cut-off of 3 (neutral value) to assess satisfaction. Single variable means and pairwise comparisons between two variable means were performed by one-sample and two-sample Student's t-tests, respectively. The correlation analysis involving the variable "age" was carried out

by Pearson test. Statistical analyses were performed by R Studio and Excel. Firstly, the mean score for each item of CGS and TSQ was calculated. A univariate analysis by Student's t-test for pairwise comparison between cases and controls, for the mean score of each CGS item, was performed. Subsequently, the total mean for each subject (the so-called individual mean) was calculated, separately across all CGS and TSQ items and a multivariate analysis was carried out to analyse the TSQ questionnaire with respect to the clinical characteristics of patients: sex (males versus females), age (above mean age versus under mean age), disease type (NMD versus CD), outcome of the genetic analysis (positive versus negative, variant of unknown significance (VUS) versus negative, positive versus VUS). For counsellors' questionnaire, the mean score of each item was calculated.

Selection bias analyses

Considering that the match of cases and controls was performed by general category (neurogenetics and cardiogenetics) rather than by single diseases, thus potentially determining a bias in genetic counselling satisfaction, we performed robustness analyses by discarding patients with diseases appearing only in cases or only in controls (see **Supplementary Table 1**), and then by re-adding the cases whose diseases were not present also in controls (see **Supplementary Table 2**). Statistical results did never differ relevantly.

Moreover, considering a possible selection bias towards the more cooperative cases, since about one-third of the patients invited for teleconsultation did not fill out the questionnaires, a statistical comparison was performed between respondent and nonrespondent patients by sex, NMD/CD, pre/post-test visits and genetic test result

(chisquared tests), and age (t-test). The p-values were never significant, thus showing homogenous characteristics of the two cohorts (data available in **Supplementary Table 3**).

Results

Cases and controls

A total of 82 patients, affected by NMD or CD (probands) or with a positive family history of a hereditary NMD or CD (relatives) were offered telecounselling. 6 patients refused to perform it: 4 for low technology skills, 1 for personal reasons and 1 preferred face-to-face contact. Among the 76 patients who accepted to perform a telecounselling, 24 failed to fill in the questionnaires and were excluded from the cohort. Finally, a total of 52 patients were enrolled as cases in the project from April 2020 to April 2021. During the same period, 62 patients referred to the conventional neurogenetic and cardiogenetic clinics were enrolled as the control group. Gender, age and type of counselling both for cases and controls are summarised in **Table 1**.

	CASES	CONTROLS
Number of patients	n=52	n=62
Sex male/female (n/n)	26/26	38/24
Type of counselling: pre/post test (n/n)	5/47	61/1
Indication: Cardiogenetics/Neurogenetics (n/n)	31/21	43/19

Mean age in years (range) for Cardiogenetics patients	47.3 (20-66)	52 (20-78)
Mean age in years (range) for Neurogenetics patients	38.2 (18-65)	46.8 (22-75)

Table 1: *Characteristics of the patients' groups (cases and controls)*

Both cases and controls originate mostly from Northern Italy, few from Central Italy, only one case was from Southern Italy. Gender distribution and global age were similar between the two groups; patients referred for NMD indication were slightly younger than those referred for CD, both among cases and controls. Post-test GC was largely prevalent for cases (47 out of 52, of which 31 for a cardioGC and 16 for a neuroGC). Only 5 cases, referred for a NMD, were enrolled for a pre-test GC. Differently, 61 out of 62 controls were enrolled for a pre-test GC (of which 42 for a cardioGC and 19 for a neuroGC). Indication for referral was prevalently cardiac in both cases and controls. 31 cases (59.6%) and 43 controls (69.3%) were enrolled for a cardioGC and 21 cases (40.4%) and 19 controls (30.7%) for a neuroGC. The referral clinical indications were heterogeneous in both cases and controls (**Supplementary File 2**).

Patients' experience: CGS and TSQ questionnaires results

Patients' satisfaction for genetic telecounselling compared to the standard approach was assessed by comparing the average score for each CGS item in the two groups. The satisfaction with the GC did not differ significantly between cases and controls, according to the pairwise comparison analysis (**Table 2**).

	CASES mean scores	CONTROLS mean scores	PAIRWISE COMPARISON p value (CI 95%)
Q1 – I have received all the information from the genetic counsellor	4.94 (0.03)	4.92 (0.03)	0.631 (-0.071–0.118)
Q2- The genetic counsellor answered all questions	4.98 (0.02)	4.95 (0.04)	0.475 (-0.051–0.110)
Q3 – The counselor listened carefully to what I said	5.00 (0.00)	4.98 (0.02)	0.321 (-0.016–0.048)
Q4 – The genetic counsellor explained things in a way that is easy to understand	4.94 (0.03)	4.97 (0.02)	0.523 (-0.104–0.053)
Q5 – I was able to share all the necessary information with the genetic counsellor	4.85 (0.06)	4.94 (0.03)	0.212 (-0.231–0.052)
Q6 – The genetic counsellor has given me enough time	4.98 (0.02)	4.98 (0.02)	0.902 (-0.052–0.047)
Q7 – The genetic counsellor helped me to feel part of the diagnostic process on my condition	4.87 (0.06)	4.92 (0.04)	0.470 (-0.202–0.094)

Table 2: *CGS questionnaire data analysis*

The mean score was slightly lower in cases versus controls for items Q5 and Q7. The absolute score was equal to or greater than 3 for all CGS items for all patients in both groups (**Figure 1**).

The satisfaction of the telecounselling was assessed cumulatively based on the average score per item obtained in the TSQ questionnaires administered to the 52 cases. The mean score was largely greater than the established cut-off of 3 for all TSQ items. Q15 had the lowest mean score, demonstrating that online patients in general did not feel the need to physically meet the counsellor. The degree of satisfaction with the simultaneous presence of the referring clinician was high, as assessed by the average score obtained in item 21 (4.94) (**Figure 2**). Excluding item Q15, which expresses greater effectiveness for telecounselling when the score is lower, the absolute score was 3 or greater for most of

TSQ items. Exceptions were item Q8 (one patient attributed score 1), item Q10 (one patient attributed score 1), items Q13 and Q16 (one patient attributed score 2 and one score 1), and item Q19 (one patient attributed score 1). Among these six "negative" comments, three belong to the same patient: a 52-year-old woman performing a pre-test genetic neuromuscular counselling for a focal dystonia gave "1" to Q8, Q16 and Q19 and declared in Q20 that she prefers "face-to-face contact and audio did not work well". A multivariate analysis of TSQ was carried out with respect to the clinical characteristics of the patients: sex, age, type of pathology, outcome of the genetic analysis. Data show that neither sex nor age nor type of disease influenced the reply to the questionnaire (**Table 3**).

		SEX	
	MALES (n 26)	**FEMALES (n 26)**	**Pairwise comparison: p value (IC 95%)**
Mean of the individual means in the TSQ (Q8-Q14; Q16-19)	4.83	4.78	0.568 (-0.141–0.253)
Absolute mean in Q21 of TSQ	4.96	4.92	0.561 (-0.094–0.171)
		AGE	
	> 45 YEARS (n 22)	**≤ 45 YEARS (n 30)**	**Pairwise comparison: p value (IC 95%)**
Mean of the individual means in the TSQ (Q8-Q14; Q16-19)	4.77	4.85	0.411 (-0.254–0.106)
Absolute mean in Q21 of TSQ	4.97	4.91	0.424 (-0.087–0.203)
		DISEASE	
	CARDIAC (n 31)	**NEUROMUSCULAR (n 21)**	**Pairwise comparison: p value (IC 95%)**

Mean of the individual means in the TSQ (Q8-Q14; Q16-19)	4.86	4.72	0.234 (-0.094–0.366)
Absolute mean in Q21 of TSQ	4.90	5.00	0.083 (-0.207–0.013)

Table 3: *TSQ questionnaire multivariate analysis with respect to age, sex and disease*

Interestingly, a statistically significant difference was detected in the cases' satisfaction when considering the dependence on the outcome of the genetic analysis (positive, negative, VUS results). 47 cases performed a post-test GC and 8 had negative results (NEG), 29 had positive results (POS) and 10 had doubtful results due to one or more VUS. The pairwise analysis showed that patients with VUS results present higher individual mean score compared to both POS and NEG patients in all items of the TSQ questionnaire, with a statistical significance in the VUS versus POS comparison (except for item Q21). The individual mean score of Q15 in VUS patients was also higher than in POS and NEG patients, with a statistical significance in the VUS versus POS comparison. In other comparisons, differences were not statistically relevant (**Table 4**).

POST-TEST TELECONSELLING (47 CASES) NEG n=8, POS n=29, VUS n=10	**Pairwise comparison: p-value (IC 95%)**
Mean of the individual means in the TSQ (Q8-Q14; Q16-19)	POS vs NEG Mean 4.83 vs 4.80 0.762 (-0.218–0.289)
	VUS vs NEG Mean 4.95 vs 4.80 0.197 (-0.097–0.397)
	POS vs VUS Mean 4.83 vs 4.95 **0.026** (-0.215 – -0.014)
Absolute mean in Q21 of TSQ	POS vs NEG Mean 4.97 vs 4.88 0.505 (-0.208–0.389)
	VUS vs NEG Mean 4.90 vs 4.88 0.878 (-0.318–0.368)

	POS vs VUS Mean 4.97 vs 4.90 0.548 (-0.167–0.298)
Absolute mean in Q15 of TSQ	POS vs NEG Mean 3.21 vs 3.13 0.905 (-1.376–1.540)
	VUS vs NEG Mean 4.40 vs 3.13
	0.083 (-0.197–2.747)
	POS vs VUS Mean 3.21 vs 4.40 **0.019** (-2.171 – -0.214)

Table 4: *TSQ questionnaire multivariate analysis with respect to the genetic test result*

Counsellors' experience

Four medical geneticists were involved in telecounselling sessions. Their satisfaction and concerns with telecounselling were assessed, based on the average score per item obtained in the counsellors' questionnaires collected after the 52 online counselling sessions. The mean scores were greater than the established cut-off of 3 for all items. The absolute scores also were 3 or higher for all items in all consultations, except for item Q3, which explores the counsellors' perception of a patient discomfort: despite an "impersonal" virtual method of interpersonal connection, patients did not show discomfort or concern during the communication (**Figure 3**).

Discussion

Several reports in the literature have reviewed the feasibility, effectiveness, usability, and diffusion of telegenetics (1,16-21). Telegenetics represents a widespread practice in the United States, especially in cancer genetics (22), while in Europe the diffusion is much more limited and there are fewer studies (2-3, 23-24). A single Italian study reports on the

experience in telegenetics, forced by the spreading of the SARS-CoV-2 infection, by a Medical Genetics department (5).

NMDs and CDs are high-impact pathologies both for families and health systems worldwide, and the possibility to provide remote counselling is of great importance for families facing these disorders, especially in the case of mobility problems.

Telecounselling applied to cardiac genetics has been reported in a study, in which 17 presymptomatic patients with history of cardiomyopathy and long QT syndrome were enrolled for pre- or post-test counselling (3) and, recently, in another study during COVID-19 pandemic (25). A recent study firstly assessed the experience and satisfaction with remote GC of 52 adult patients affected by neurological disorders (6): they declared a high satisfaction for remote counselling (by telephone and video) and in general they felt their psychological concerns to be alleviated after telecounselling, despite receiving genetic diagnosis without a currently available cure.

The TeleNEwCARe study aimed at providing evidence of feasibility, usability, noninferiority and satisfaction of telegenetics compared to the conventional face-to-face genetic counselling when offered to patients affected by or with a family history of inherited neuromuscular or cardiac diseases. We also aimed to assess whether the simultaneous presence of specialists (medical geneticist and neurologist/cardiologist) represents an added value for patients to improve the diagnostic assistance process. In TeleNEwCAre, we have enrolled 52 adult patients for a genetic telecounselling (21 with NMDs and 31 with CDs). 62 controls, matched by age and clinical indication, seen face-to-face in conventional clinics, were enrolled. Specific questionnaires to assess satisfaction were administered to cases and controls.

PROS of Telegenetics: efficacy, fulfillment, and multidisciplinary approach

Benefit and limitation of telegenetics have been recently reviewed by Gorrie A et al. (26), who collected data from 21 published studies conducted between 2001 and 2018, mostly in USA and Australia and mainly focused on cancer genetics. In general, there is agreement in affirming that remote counselling is very useful and well accepted by the patients, who appreciate the possibility of using excellent services by limiting travel.

Patients report as the main benefits: saving time and money, improved access to good quality centers and positive psychological impact in terms of reduced anxiety related to hospital setting. Cost-analysis studies also support a benefit for services, especially for those providing outreach clinics, who do not have to face costs for health professionals' travels (1,27).

Our experience further supports telegenetics as a fully applicable model in daily clinical practice, both for cardiac and neuromuscular patients. Overall, and regardless of the reason for the request for genetic advice, the expressed opinion about the efficacy of GC, explored with CGS questionnaire, did not differ statistically between remote and face-toface patients.

Patients were highly satisfied with telecounselling and declared they were able to communicate effectively with the medical geneticist, to understand the information received and to establish a confidential relationship, to the point that they did not feel the need to meet the doctor in person. Furthermore, the majority of patients did not highlight any technical problems in the connection.

Neither sex nor age nor type of disease influenced the reply to the questionnaires, while it emerged that patients with an uncertain genetic result show a high satisfaction for telecounselling. This observation highlights how the patient's emotional state, related to

the GT result, could influence the patient perception of the communication efficacy and emphasizes the relevance of GC in providing a correct and comprehensive interpretation especially in case of uncertain GT results. Interestingly, patients presenting with VUS have demonstrated a greater interest for a face-to-face evaluation with the medical geneticist, showing the need of these patients to be followed-up for the interpretation of their VUS variants, whose pathogenic significance can change over time. Instead, patients with a clear test result have generally already discussed the related implications with their clinicians.

Particularly appreciated by the patients was the simultaneous presence, during the counselling, of the trusted specialist, neurologist/cardiologist, with the medical geneticist. Even the physicians involved in the counselling highly appreciated the possibility to share information with colleagues. This aspect of multidisciplinary care, hardly achievable in face-to-face activities, represents a significant added value of telecounselling, not previously explored and deserving implementation.

CONS of Telegenetics: need for digital literacy, communication difficulties and collection of biological samples

Technical issues associated to remote counselling have not been reported commonly by patients and, overall, have not been considered as a significant problem. Few studies identified as a weak point the patient's need to have adequate equipment for telecounselling and the familiarity with connection systems, which cannot be taken for granted in older population. Furthermore, from the point of view of the counsellor/medical geneticist, the impossibility of interacting in-person was sometimes experienced as a limit (28). A European survey conducted by Otten et al. has highlighted

how, although telegenetics is in general appreciated and with an excellent potential for expansion, some organizational/technical problems preclude a more extensive application (2). It is noteworthy that in our study 4 (4.9%) patients refused telecounselling due to poor digital skills. This suggests that telegenetics could not completely replace the traditional GC, not until the digital literacy will be universal (29). However, considering that in the Dutch study of Otten et al. (3), only 35% of the patients (contacted between 2011 and 2012) accepted a telecounselling, our study demonstrates how digital technology is rapidly becoming widely accessible.

Only two items from the CGS questionnaire received a slightly lower mean score in cases than controls (Q5 and Q7), although the difference did not reach statistical significance. These items investigate the efficiency in the exchange of information between the patient and the professional and the degree to which the patient feels involved in the diagnostic process: these communicative and emotional aspects are probably intrinsically penalized by video interaction compared to a face-to-face interview and deserve improvement, as already pointed out in the literature (26,29).

The main limitation of the present study is the non-random representation of type of counselling among cases and controls, with post-test counselling largely prevalent among cases. Indeed, a pre-test counselling, which includes the blood sampling, is much more difficult to organize as a remote visit. This could be overcome by the collaboration of a local physician involved in sample collection and shipment, but the absence of physical contact still represents the most impassable limit to the application of Telemedicine in first visits. Another important limitation of the present study is the match of cases and controls by general category (neurogenetics and cardiogenetics) rather than by single diseases, but the low prevalence of rare genetic diseases in a one-year-study has not

allowed a stricter pairing and the robustness analyses did not differ relevantly after discarding patients not matched by disease.

To conclude, the present study further supports the efficacy of genetic telecounselling and non-inferiority compared to the conventional modality of face-to-face clinics. The possibility of a remote care takes on particular value for patients with RDs whose care needs to be centralized in institutions of excellence. Furthermore, for these patients the possibility of a joint evaluation by different specialists, made possible by the remote modality, assumes a critical value. Pending issues related to the quality of the communication via video and related emotional impact need to be further addressed and ameliorated through an increasing use and familiarization by health professionals.

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Figures and Tables titles and legends

Figure 1: Graphical description of the distribution of absolute scores of the CGS questionnaire among the 52 cases (telecounselling) and 62 controls (face-to-face genetic counselling). Mean values for each item in the two groups of patients are also reported.

Figure 2: Graphical description of the distribution of absolute scores of the TSQ questionnaire among the 52 cases (telecounselling). Mean values for each item are also reported.

Figure 3: Graphical description of the distribution of absolute scores of the counsellors' questionnaire collected from four medical geneticists after the 52 telecounselling sessions. Mean values for each item are also reported.

Table 1: Characteristics of the patients' groups (cases and controls)

Table 2: CGS questionnaire data analysis

Table 3: TSQ questionnaire multivariate analysis with respect to age, sex and disease

Table 4: TSQ questionnaire multivariate analysis with respect to the genetic test result

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Supplemental data.

Supplementary File 1: Questionnaires used in the TeleNEwCARe study: Clinical Genetics Satisfaction indicator, Telemedicine Satisfaction Questionnaire and Counsellors' questionnaire.

Supplementary File 2: Referral indication for genetic counselling in patients' groups.

Data Availability Statement. The data that support the findings of this study are available from the corresponding author upon request.

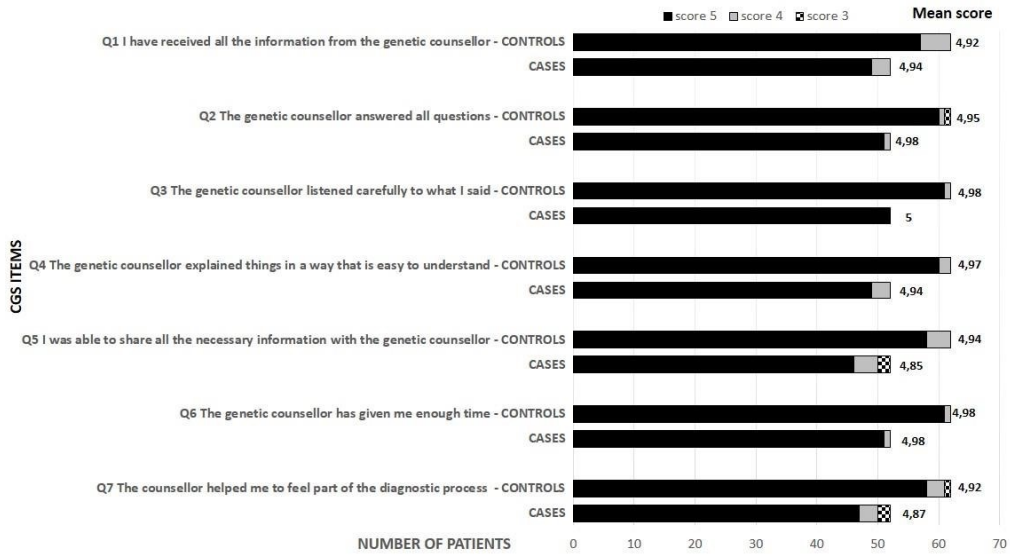

Figure 1: Graphical description of the distribution of absolute scores of the CGS questionnaire among the 52 cases (telecounselling) and 62 controls (face-to-face genetic counselling). Mean values for each item in the two groups of patients are also reported.

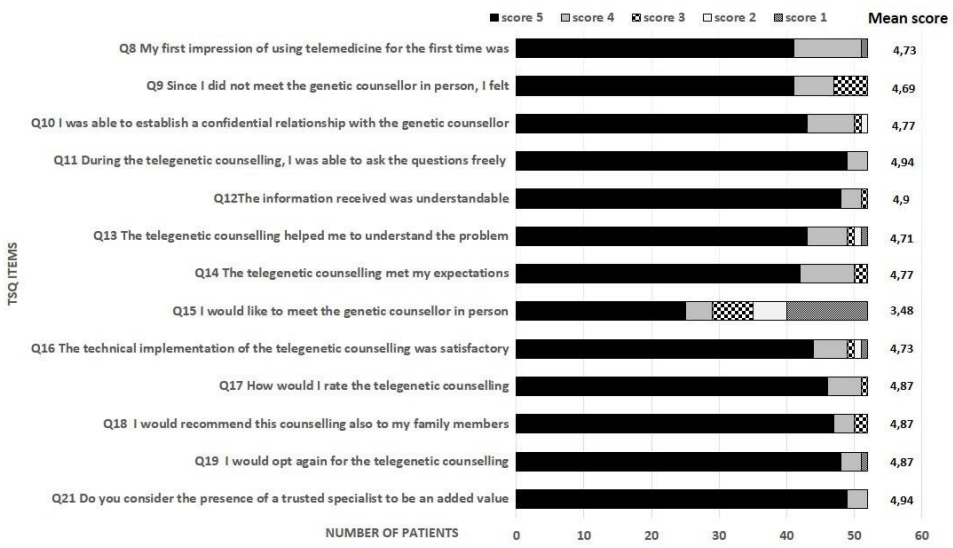

Figure 2: Graphical description of the distribution of absolute scores of the TSQ questionnaire among the 52 cases (telecounselling). Mean values for each item are also reported.

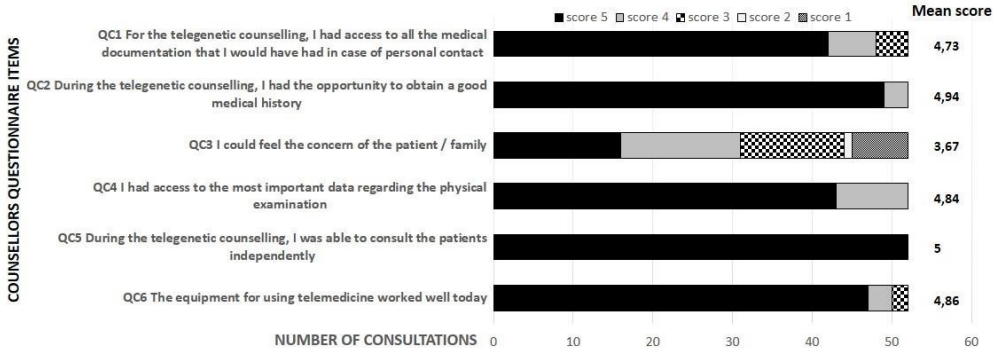

Figure 3: Graphical description of the distribution of absolute scores of the counsellors' questionnaire collected from four medical geneticists after the 52 telecounselling sessions. Mean values for each item are also reported.

Author Contribution Statement. Marianna Farnè: investigation (genetic counselling), formal analysis (data collection and analysis), writing of the manuscript. Francesca Gualandi: project conceptualization and supervision, investigation (genetic counselling), formal analysis, writing of the manuscript. Alessandra Ferlini: project supervision, writing – review & editing. Fernanda Fortunato, Marcella Neri: investigation (genetic counselling, data collection). Annarita Armaroli: ethical submission, project idealization. Matteo Farnè: statistical analysis, writing – review & editing. Cristina Balla, Emilio Albamonte, Andrea Barp, Enrica Perugini, Valeria Carinci, Valeria A Sansone, Valeria Tugnoli, Elisabetta Sette, Mariachiara Sensi, Sofia Straudi, Matteo Bertini: investigation (clinical evaluation and telecounselling). Marco Facchini, Luca Chiarini: ICT support. Teresinha Evangelista: writing – review & editing and Euro-NMD support. All authors have contributed to the work and to the final revision of the manuscript.