

University of Groningen

Changes in empowerment and anxiety of patients and parents during genetic counselling for epilepsy

Vlaskamp, Danique R M; Rump, Patrick; Callenbach, Petra M C; Brilstra, Eva H; Velthuisen, Mary E; Brouwer, Oebele F; Ranchor, Adelita V; van Ravenswaaij-Arts, Conny M A

Published in:
European Journal of Paediatric Neurology

DOI:
[10.1016/j.ejpn.2021.03.015](https://doi.org/10.1016/j.ejpn.2021.03.015)

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
2021

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):

Vlaskamp, D. R. M., Rump, P., Callenbach, P. M. C., Brilstra, E. H., Velthuisen, M. E., Brouwer, O. F., Ranchor, A. V., & van Ravenswaaij-Arts, C. M. A. (2021). Changes in empowerment and anxiety of patients and parents during genetic counselling for epilepsy. *European Journal of Paediatric Neurology*, 32, 128-135. <https://doi.org/10.1016/j.ejpn.2021.03.015>

Copyright

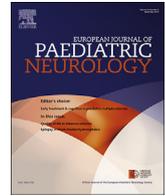
Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license. More information can be found on the University of Groningen website: <https://www.rug.nl/library/open-access/self-archiving-pure/taverne-amendment>.

Take-down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): <http://www.rug.nl/research/portal>. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.



Original article

Changes in empowerment and anxiety of patients and parents during genetic counselling for epilepsy



Daniqne R.M. Vlaskamp ^{a, b}, Patrick Rump ^a, Petra M.C. Callenbach ^b, Eva H. Brilstra ^c, Mary E. Velthuis ^c, Oebele F. Brouwer ^b, Adelita V. Ranchor ^d, Conny M.A. van Ravenswaaij-Arts ^{a, *}

^a University of Groningen, University Medical Centre Groningen, Department of Genetics, Groningen, the Netherlands

^b University of Groningen, University Medical Centre Groningen, Department of Neurology, Groningen, the Netherlands

^c University Medical Centre Utrecht, Department of Genetics, Utrecht, the Netherlands

^d University of Groningen, University Medical Centre Groningen, Department of Health Psychology, the Netherlands

ARTICLE INFO

Article history:

Received 31 August 2020

Received in revised form

26 March 2021

Accepted 28 March 2021

Keywords:

Genetic counselling

Empowerment

Epilepsy

Genetic testing

Outcome

ABSTRACT

Genetic testing and counselling are increasingly important in epilepsy care, aiming at finding a diagnosis, understanding aetiology and improving treatment and outcome. The psychological impact of genetic counselling from patients' or parents' perspectives is, however, unknown. We studied the counselee-reported outcome of genetic counselling before and after genetic testing for epilepsy by evaluating empowerment – a key outcome goal of counselling reflecting cognitive, decisional and behavioural control, emotional regulation and hope – and anxiety. We asked patients or their parents (for those <16 years or intellectually disabled) referred for genetic testing for epilepsy in two university hospitals between June 2014 and 2017 to complete the same two questionnaires at three timepoints: before and after pre-test counselling and after post-test counselling. Empowerment was measured with the Genetic Counselling Outcome Scale (GCOS-18); anxiety with the short State Trait Anxiety Inventory (STAI-6). A total of 63 participants (55 parents with the age of 29–66 years; 8 patients with the age of 21–42 years) were included in our study. Empowerment significantly increased during the genetic counselling trajectory with a medium effect size ($p < 0.001$, $d = 0.57$). A small but significant increase in empowerment was already seen after pre-test counselling ($p = 0.038$, $d = 0.29$). Anxiety did not change significantly during the counselling trajectory ($p = 0.223$, $d = -0.24$). Our study highlights that patients with epilepsy or their parents show a clinically relevant increase in empowerment after genetic counselling. Empowerment was already increased after pre-test counselling, suggesting the importance of counselling before initiating genetic testing for epilepsy. However, individual differences in changes in empowerment and anxiety were seen, suggesting that counselling could be further improved, based on individual needs.

© 2021 The Author(s). Published by Elsevier Ltd on behalf of European Paediatric Neurology Society. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).

1. Introduction

The increasing use of genetic testing in individuals with epilepsy is transforming epilepsy care. Finding a genetic cause for epilepsy, while currently only possible in a minority of patients, precludes unnecessary further diagnostic investigations and leads to a better understanding of the epilepsy aetiology, comorbidities, prognosis

and recurrence risks [1–4]. In a very few cases, finding the genetic variant for epilepsy may even improve treatment and outcome [5,6]. Genetic testing in epilepsy is, therefore, increasingly becoming part of the routine diagnostic care [7–10]. However, little is known about the psychological outcomes of genetic services from the patients' or parents' perspective [11–13].

Previous qualitative studies have shown that patients with epilepsy, or their parents, have a strong hypothetical interest in genetic testing if offered, especially in a scenario where knowing the genetic change would improve medical care [14–16]. The participants mentioned potential benefits, such as better understanding and care in children at risk, more sense of control and less guilt,

* Corresponding author. Department of Genetics CB50, University Medical Centre Groningen, P.O. Box 30.001, 9700 RB, Groningen, the Netherlands.

E-mail address: c.m.a.van.ravenswaaij@umcg.nl (C.M.A. van Ravenswaaij-Arts).

blame and anxiety with negative test results. However, they also described potential concerns, including increased blame, guilt, stigma, discrimination, self-imposed limitations on life goals and alterations in fundamental conceptions of 'what epilepsy is' [16]. Individuals with a familial epilepsy for which a genetic cause was identified through research also expressed both positive and negative feelings on receiving a genetic diagnosis [17]. To date, the psychological outcomes of genetic services for epilepsy have not been studied systematically.

In our current clinical practice, genetic testing for epilepsy is both preceded and followed by genetic counselling by a clinical geneticist, as recommended by the International League Against Epilepsy, specifically in children with infantile seizures and in adults with epilepsy and developmental problems [13,18,19]. During pre-test counselling, clinical geneticists first obtain a medical and family history to decide which genetic test would be most suitable. Subsequently, they inform the patients and their families about genetic testing and encourage them to make an informed choice about whether this testing should be done. During post-test counselling, the test results are explained to the patients and families by the same clinical geneticist. The overall aim of genetic counselling is helping people to understand and adapt to the medical, psychological and familial implications of identifying genetic contributions to disease [20]. By this means, genetic counselling can lead to increased knowledge, perceived personal control, positive health behaviour, improved risk perception accuracy and decreased decisional conflict, anxiety and worry [21]. Studying the psychological outcome of genetic services for epilepsy may help counsellors to improve the counselling trajectory in accordance with patients' and their families' needs.

These psychological outcomes can be measured by evaluating the change in 'empowerment' and anxiety. Empowerment is an all-encompassing patient-reported outcome of genetic counselling, defined as the set of beliefs that a person can make important life decisions (decisional control), has sufficient information about the condition (cognitive control), can make effective use of health and social care systems (behavioural control), is able to manage one's feelings about having a genetic condition in the family (emotional regulation) and has hope for a fulfilling family life (hope) [22–24]. We aimed to study the outcome of genetic counselling both before and after genetic testing for epilepsy by evaluating empowerment and anxiety of the counselee (i.e. patient or parent).

2. Methods

2.1. Study cohort and design

Our research was part of a larger genetic counselling outcome study using the Dutch version of the Genetic Counselling Outcome Scale (GCOS) and had the same study design [25,26]. All patients who were referred to a clinical geneticist in the outpatient clinics of the University Medical Centre Groningen (UMCG) or the University Medical Centre Utrecht (UMCU) in the Netherlands were eligible for inclusion in this larger study if they spoke and understood sufficient Dutch to complete the questionnaires. In our follow-up study on epilepsy, patients who were referred for genetic counselling and genetic testing for epilepsy between June 2014 and June 2017 were eligible for inclusion and we studied their change in empowerment and anxiety in more detail. Genetic testing encompassed cytogenetic testing, single gene testing, multiple gene testing (through epilepsy gene panels) and whole exome sequencing.

All patients were asked to complete the same two questionnaires concerning empowerment and anxiety at three timepoints during the genetic counselling trajectory: 1. before pre-test

counselling (T0), 2. around 1–2 weeks after pre-test counselling (T1) and 3. around 1–2 months after genetic testing and post-test counselling (T2, Fig. 1). Pre- and post-test counselling was provided by the same clinical geneticist. If patients were under 16 years of age or intellectually disabled, their parents or caretakers were seen as the counsees. Therefore, one of their parents or caretakers was asked to complete the questionnaires, but from their own perspective as a parent or caretaker. We will use the term 'participants' for those patients or parents who completed the questionnaires. For one patient, a non-parent legal representative completed the questionnaires and was included as a parent. We excluded the participants who declined genetic testing after pre-test counselling or who did not complete all three questionnaires from further analyses. The information letter about this study, the consent form and the questionnaires at T0 were all sent on paper, together with the invitation letter for pre-test counselling. In the T0 questionnaire, participants could indicate whether they wished to receive the follow-up questionnaires at T1 and T2 on paper or electronically.

2.2. Measurement instruments

Empowerment was measured using the validated Dutch version of the genetic counselling outcome scale (GCOS) [25]. This Dutch version includes 18 of the original 24 English questions. We also studied six different subscales of empowerment: hope and coping, knowledge about the condition, knowledge about genetic services, uncertainty about genetic services, negative emotions and uncertainty about heredity (Supplementary Table 1 and 2) [25]. The GCOS-18 shows a satisfactory internal consistency (Cronbach's $\alpha = 0.77$) and excellent test-retest reliability (intraclass correlation coefficient = 0.92) [25]. Anxiety was measured with the short 6-item version of the Spielberger State-Trait Anxiety Inventory (STAI), which is validated for measuring the psychological outcome of genetic counselling [21,27,28]. Questions on baseline characteristics were included in the first questionnaire (demographic characteristics) and extracted from medical records if consent was obtained (information on epilepsy and genetic testing results). The results of genetic testing were categorized into three groups: a disease-associated pathogenic variant, a variant of unknown significance, or normal test results.

2.3. Outcome

Our two primary outcomes were empowerment (GCOS) and anxiety (STAI) scores throughout the genetic counselling trajectory. Secondary outcomes concerned the six abovementioned subscales of empowerment.

2.4. Statistical analysis

The total- and subscores on the GCOS and STAI were calculated by adding all item scores after reversing item scores for negatively formulated questions. STAI scores were converted to the 20-item STAI questionnaire to allow comparison with reference values, as was recommended by the manual [27]. Missing items of the GCOS or STAI were imputed using the mean of the other GCOS or STAI item scores for that individual if $\leq 20\%$ of the items were missing. If $>20\%$ items of the GCOS or STAI were missing, the participant was excluded from the analyses on this questionnaire. We compared baseline characteristics between participants who accepted or declined genetic testing and between participants who did or did not complete all follow-up questionnaires using Fisher's exact tests.

We studied the change in empowerment and anxiety scores during the genetic counselling trajectory in the total study group

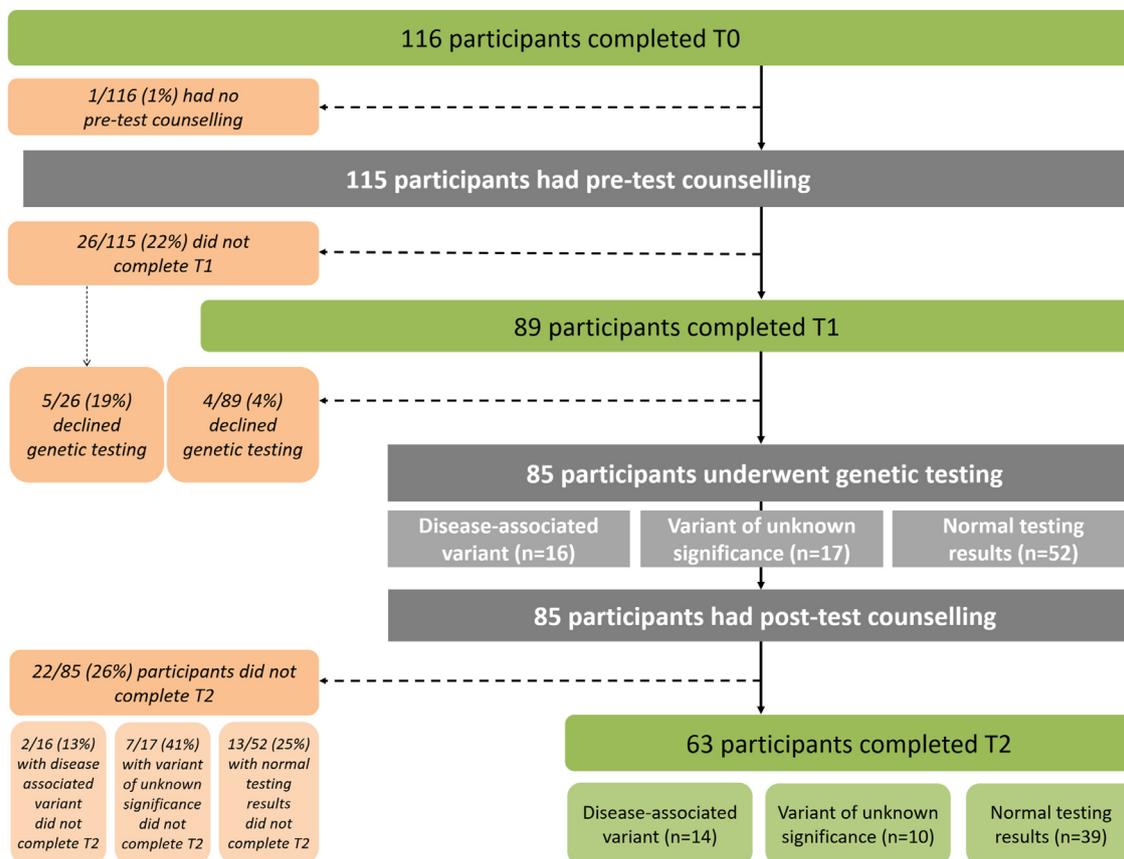


Fig. 1. Inclusion and exclusion of participants in our study cohort.

using repeated measurements ANOVA tests. Indicators for change were statistical significance and effect sizes. Effect sizes reflect the difference between two means divided by the standard deviation (Cohen's *d*). An effect size ≥ 0.2 was considered small, ≥ 0.5 medium and ≥ 0.8 large [29]. An effect size of >0.5 was seen as a minimal clinically important change for our patient-reported outcome measures [30,31]. To evaluate the outcome of genetic counselling on an individual level, we calculated the changes in GCOS and STAI scores between T2 and T0 and their individual effect sizes for each individual. Individual changes with an effect size >0.5 were considered as a clinically relevant increase, changes with an effect size between 0.5 and -0.5 as stable and changes with an effect size < -0.5 as a clinically relevant decrease [30,31].

We studied the influence of demographic characteristics and genetic testing results on GCOS and STAI scores at baseline (ANOVA tests) and over time (T0-T2; full-factorial repeated measures ANOVA tests). We also compared the number of participants with clinically relevant increased, stable, or decreased GCOS and STAI scores over time between subgroups of participants based on these same demographic characteristics and genetic testing results (Fisher's exact tests).

We used SPSS Statistics Version 23.0 (IBM Corporation, NY, USA). Analyses were two-tailed. A *p*-value $<0.05/2$ was considered statistically significant for our two primary outcomes (empowerment and anxiety), and a *p*-value $<0.05/6$ as statistically significant for our two secondary outcomes (subscales of empowerment). In the post-hoc analyses for comparisons between T0-T1, T1-T2 and T0-T2, Bonferroni corrections were applied and *p*-values <0.05 were considered statistically significant.

2.5. Ethical statement

The Institutional Medical Ethical Committee of the University Medical Center Groningen gave permission for this study (M13.139274). All participants gave written consent for participation in the study.

3. Results

3.1. Characteristics of the study cohort

In total, 116 initial participants who were referred for genetic counselling and testing for epilepsy agreed to participate. Of them, 106 (91%) decided to undergo genetic testing and 63/106 (59%) completed all questionnaires and were included in our study (Fig. 1). Of them, 55 were a parent (87%; age 29–66 years) and eight were a patient (13%; age 21–42 years). Table 1 shows the characteristics of all initial participants, those who underwent genetic testing and those included in our study. The majority of these participants were parents (87%). Participants who declined genetic testing had a higher baseline empowerment score ($p = 0.003$), were more often from the UMCU ($p = 0.014$), were more often a patient ($p = 0.001$) and more often lived without children ($p = 0.016$) compared to those who decided to undergo genetic testing. Among the participants who underwent genetic testing, follow-up questionnaires were significantly more often completed by participants who had a higher education ($p = 0.030$). Other demographic characteristics, genetic testing results and baseline empowerment and anxiety scores did not differ between those who did and did not decide to undergo genetic testing and those who did and did not complete the follow-up questionnaires (data not shown).

Table 1
Characteristics of participants.

	All initial participants (n = 116)	Participants who underwent genetic testing (n = 106)	Study cohort (n = 63)
Demographic characteristics			
Hospital^a			
- UMCG (%)	70 (60.3)	68 (64.2)	45 (71.4)
- UMCU (%)	46 (39.7)	38 (35.8)	18 (28.6)
Participants			
- Patient (%)	24 (20.7)	17 (16.0)	8 (12.7)
- Parent (%)	92 (79.3)	89 (84.0)	55 (87.3)
* Mother	76 (65.5)	74 (69.8)	46 (73.0)
* Father	16 (13.8)	15 (14.2)	9 (14.3)
Marital status			
- Living together with children (%)	77/115 (67.0)	74/105 (70.5)	44 (69.8)
- Living together without children (%)	16/115 (13.9)	12/105 (11.4)	6 (9.5)
- Living alone with children (%)	7/115 (6.1)	5/105 (4.8)	4 (6.3)
- Single (%)	5/115 (4.3)	5/105 (4.8)	4 (6.3)
- Different situation ^b (%)	10/115 (8.7)	9/105 (8.6)	5 (7.9)
Employment status			
- Working (%)	64/108 (59.3)	58/98 (59.2)	34/57 (59.6)
- Studying (%)	7/108 (6.5)	6/98 (6.1)	3/57 (5.3)
- Unemployed (%)	25/108 (23.1)	22/98 (22.4)	14/57 (24.6)
- Unable to work (disabled) (%)	9/108 (8.3)	9/98 (9.2)	4/57 (7.0)
- Retired (%)	3/108 (2.8)	3/98 (3.1)	2/57 (3.5)
Education level^{a,c}			
- Low (%)	24/110 (21.8)	21/100 (21.0)	9/58 (15.5)
- Intermediate (%)	56/110 (50.9)	52/100 (52.0)	28/58 (48.3)
- High (%)	30/110 (27.3)	27/100 (27.0)	21/58 (36.2)
Seizures			
- Patient is symptomatic (%)	114 (98.3)	104 (98.1)	61 (96.8)
- Patient is pre-symptomatic ^d (%)	2 (1.7)	2 (1.9)	2 (3.2)
Genetic testing characteristics			
Genetic testing			
- Genetic testing performed between T1 and T2 (%)	106 (91.4)	106 (100)	63 (100)
- Follow-up genetic testing after T2 (%)	16/109 (14.7)	16/105 (15.2)	8/62 (12.7)
Results from genetic testing			
- Disease causing variant (%)	21/106 (19.8)	21 (19.8)	14 (22.2)
- Variant of unknown significance (%)	21/106 (19.8)	21 (19.8)	10 (15.9)
- Normal (%)	64/106 (60.4)	64 (60.4)	39 (61.9)
Baseline empowerment and anxiety			
Empowerment			
- Mean total score on GCOS at T0 (SD, n)	92.3 (12.4, 115)	91.3 (12.0, 105)	91.3 (11.7, 63)
Anxiety			
- Mean total score on STAI at T0 (SD, n)	40.1 (13.0, 113)	40.8 (13.0, 103)	39.6 (11.2, 62)

^a Characteristic differed significantly between the participants who were (n = 63) and were not (n = 57) included in the study cohort (data not shown).

^b Different situation includes living with one of both parents or assisted living.

^c Education level was determined based on the highest educational degree: primary or secondary school or lower vocational education (low), middle vocational education (intermediate) and higher vocational education or university (high).

^d In these participants, a disease causing gene variant for epilepsy that was already known in the family was tested in a pre-symptomatic relative.

Abbreviations: GCOS-18 = genetic counselling outcome scale, STAI = Spielberger State-Trait Anxiety Inventory.

3.2. Empowerment

The mean empowerment score significantly increased during the genetic counselling trajectory ($p < 0.001$; Fig. 2A, Table 2). The overall change in empowerment had a medium effect size ($d = 0.57$), indicating a clinically relevant increase. Empowerment was already increased after pre-test counselling compared to baseline ($p = 0.038$), and a further increase was seen after post-test counselling compared to after pre-test counselling ($p = 0.033$). Both changes had a small effect size ($d = 0.28$ and $d = 0.30$, respectively). On an individual level, 32/63 (50.8%) participants showed a clinically relevant increase in empowerment during the counselling trajectory, whereas 6/63 (9.5%) showed a clinically relevant decrease, and empowerment scores remained stable in the remaining 25/63 (39.6%).

3.3. Anxiety

The mean anxiety score decreased during the genetic counselling trajectory, but the effect size was small ($d = -0.24$) and the differences were not statistically significant ($p = 0.223$; Fig. 2B, Table 2). These results were based on 58/63 participants with <20%

missing STAI items. On an individual level, we observed a clinically relevant decrease in anxiety in 23/58 (39.7%) participants, but a clinically relevant increase in 14/58 (24.1%) participants, and a stable score in the remaining 21/58 (36.2%) participants.

Of the 23 participants with a clinically relevant decreased anxiety score, 15 (65.2%) also had an increased empowerment score, 6 (26.1%) had a stable empowerment score and 2 (8.7%) participants had a decreased empowerment score. Furthermore, of 14 participants with a clinically relevant increased anxiety score, only 2 (14.3%) also had a decreased empowerment score, while 8 (57.1%) had a stable empowerment score and 4 (28.6%) had an increased empowerment score.

3.4. Empowerment subscales

During the genetic counselling trajectory, significant increases in scores were seen in 3/6 subscales of the GCOS-18. These subscales were knowledge about genetic services ($p = 0.008$, $d = 0.44$), uncertainty about genetic services ($p = 0.006$, $d = 0.38$) and uncertainty about heredity ($p < 0.001$, $d = 0.63$) (Table 2). Higher scores indicated more knowledge and less uncertainty. In line with this, more participants had relevant increases in these three

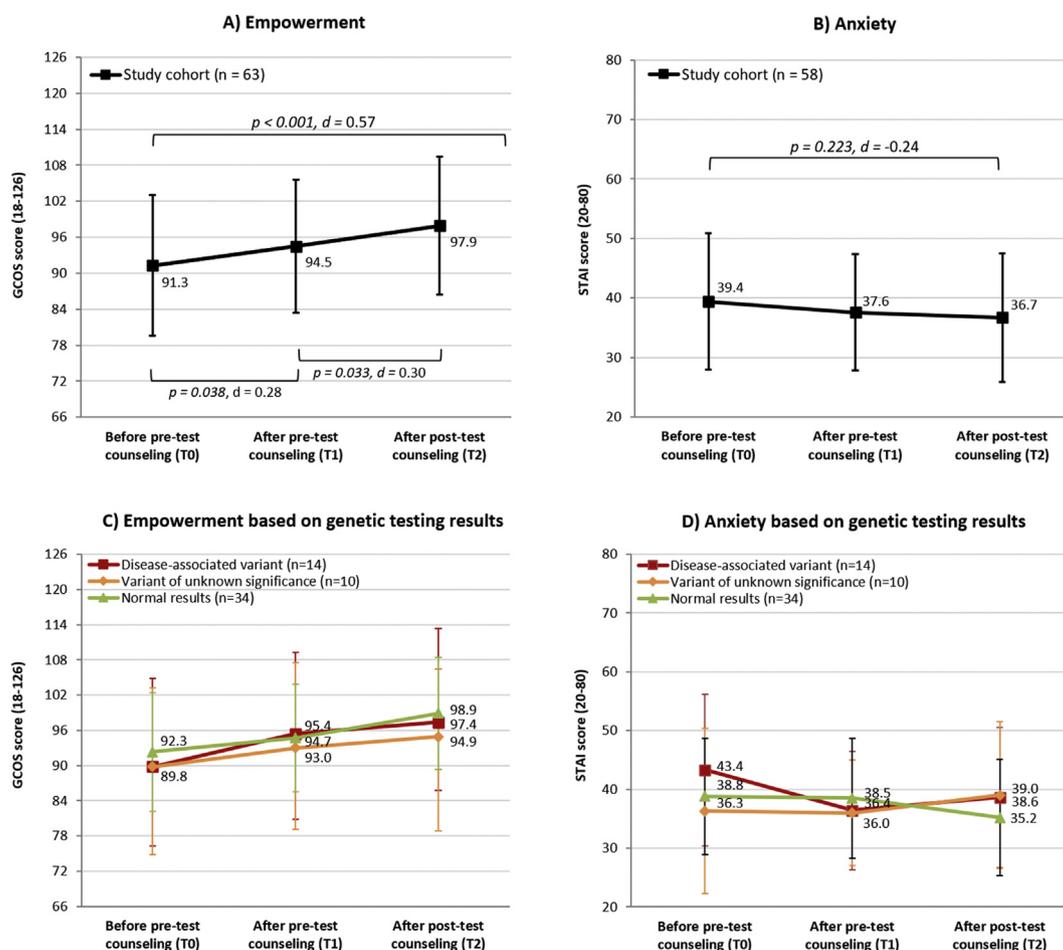


Fig. 2. Empowerment and anxiety during the genetic counselling trajectory in the study cohort (Figure A and B) and in three subgroups based on genetic testing results (Figure C and D). The mean ± SD scores for empowerment and anxiety are presented. Empowerment significantly increased in the study cohort between T0, T1 and T2 (Figure A). Anxiety scores did not decrease significantly in the study cohort (Figure B). The results of genetic testing did not seem to significantly influence the course of empowerment and anxiety during the genetic counselling trajectory (Figure C and D).

subscales compared to other subscales on an individual level (Table 2).

3.5. Empowerment and anxiety in subgroups of participants

At baseline, empowerment and anxiety scores did not differ between subgroups of participants based on demographic and genetic testing characteristics (see Table 1 for tested characteristics, data not shown), except that baseline anxiety scores were significantly higher in participants with a low (48.3, SD 15.0) versus an intermediate (37.2, SD 9.5) or a high (37.6, SD 9.1) education level ($p = 0.020$).

The changes in empowerment and anxiety scores during the genetic counselling trajectory were not significantly influenced by the genetic testing results (Fig. 2C and D) or other demographic or genetic testing characteristics (data not shown). Also, the number of participants with relevant increased, decreased or stable empowerment and anxiety scores did not differ significantly between participants with different demographic and genetic testing characteristics (data not shown).

4. Discussion

With the increasing use of genetic testing for epilepsy, there is a need to study the outcome of genetic services from the perspective

of patients or their parents. We found that our counselees (patients or their parents) show a clinically relevant increase in empowerment after genetic counselling before and after genetic testing for epilepsy, while feelings of anxiety did not change significantly, independent of the genetic testing result. Part of the increase in empowerment was already seen after pre-test counselling, suggesting the importance of pre-test counselling as part of the genetic counselling trajectory. These results were similar to those observed in the larger Dutch genetic counselling outcome study, but in our follow-up study on epilepsy, we studied empowerment in more detail using the six subscales.

4.1. Empowerment

Empowerment is a validated overarching construct that represents many specific outcomes of genetic counselling [24,25]. We found a clinically relevant increase in empowerment, especially in three of six subscales: knowledge about the genetic services, uncertainty about the genetic services and uncertainty about heredity. Higher scores indicate more empowerment and less uncertainty. Translating these subscales into theoretical concepts of empowerment, our results indicate that during the genetic counselling trajectory, participants especially gained in behavioural control (making effective use of health and social care systems) and in some aspects of cognitive control (knowledge about genetic

Table 2
Effects of genetic testing and counselling on empowerment and anxiety in the study cohort.

Questionnaires scores (minimum - maximum possible score)	N	Mean total scores (SD)		P-value for differences between T0, T1 and T2	Effect sizes between T0 and T2		Number of participants with clinically relevant increase (%)	Number of participants with clinically relevant decrease (%)
		Baseline (T0)	After pre-test counselling (T1)		After post-test counselling (T2)	Group level		
Total GCOS score (18–126)	63	91.3 (11.7)	94.6 (11.1)	<0.001*	0.57***	32 (50.8)	6 (9.5)	
Total STAI score (20–80)	58	39.4 (11.4)	37.6 (9.8)	0.180	-0.24	14 (24.1)	23 (39.7)	
GCOS score on subscales^a								
- Hope and coping (4–28)	63	22.6 (4.0)	23.2 (3.2)	0.222	0.21	25 (39.7)	12 (19.0)	
- Knowledge condition (3–21)	63	17.7 (2.8)	17.4 (3.1)	0.321	0.12	17 (27.0)	16 (25.4)	
- Knowledge genetic services (3–21)	63	18.2 (2.5)	18.9 (2.2)	0.008**	0.44	23 (36.5)	6 (9.5)	
- Uncertainty genetic services (3–21)	63	13.1 (4.0)	14.2 (3.4)	0.006**	0.38	26 (41.3)	9 (14.3)	
- Negative emotions (3–21)	63	13.4 (4.2)	13.5 (3.7)	0.092	0.19	20 (31.7)	6 (9.5)	
- Uncertainty heredity (2–14)	63	6.4 (3.7)	7.4 (3.6)	<0.001**	0.63***	33 (52.4)	12 (19.0)	

^a A higher score means more empowerment for the six subscales, more hope and coping, more knowledge about genetic services, less uncertainty about genetic services, less negative emotions and less uncertainty about heredity. * P-value is < 0.05/2, ** P-value is < 0.05/6, *** Medium effect size (d > 0.5). Abbreviations: GCOS = genetic counselling outcome scale (scale for empowerment), STAI = Spielberger State-Trait Anxiety Inventory (scale for anxiety).

services) and emotional regulation (managing feelings of uncertainty). Decisional control was increased in those who declined genetic testing after pre-test counselling. Knowledge about the disorder (another aspect of cognitive control) did not increase significantly, possibly because the participants had already received a lot of information about epilepsy from the referring clinicians. In addition, negative emotions and hope and coping (other aspects of emotional regulation) did not change significantly after counselling.

Since empowerment was measured with the relatively new GCOS-18 questionnaire, no ‘normal’ baseline empowerment scores or minimum clinically relevant difference in scores have been established. If we compare the empowerment scores in our participants referred for epilepsy with those of the large Dutch genetic counselling outcome cohort (n = 1479), referred for a wide variety of disorders, comparable baseline (91.3 and 91.4, respectively) and increases in empowerment (d = 0.57 and d = 0.51, respectively) were seen [26]. Baseline and changes in empowerment scores were also similar in our cohort of mainly parents (87%) compared to the subcohort of parents of referred children in the large Dutch genetic counselling outcome cohort (n = 179/1479): baseline empowerment scores were 91.3 and 89.2, respectively, and changes were similar (d = 0.57 in both cohorts) [26]. A comparison with GCOS scores in other genetic counselling cohorts for any reason [32], psychiatric diseases [33–37], cancer [38], cardiovascular disease [39], or suspected inherited retinal dystrophy [40] was not equitable, since their genetic counselling trajectories did not necessarily include genetic testing and their empowerment scores were calculated using the GCOS-24 instead of the GCOS-18. We therefore considered change in empowerment as clinically relevant based on statistics, with an effect size >0.5 indicating minimal clinically important change [30,31]. Recently, a change of 10.3 points in the empowerment score based on the GCOS-24 was considered as a minimum clinically important difference that was meaningful for patients [41]. The mean change of 6.6 points in our cohort is lower than this minimum difference, also after converting the minimum change to a GCOS-18 questionnaire (7.7). However, the participants in our cohort who showed improved empowerment reached this norm with a median change of 9.9 (T0-T2).

4.2. Anxiety

Anxiety was not significantly changed during the genetic counselling trajectory. Remarkably, the subscales of empowerment without significant change mostly reflected emotional outcome (negative emotions and hope and coping). Possibly, our counselees gained less in emotional outcomes, such as emotional regulation and anxiety. This is an important finding, given that our counselees had borderline anxiety levels at baseline. Their mean baseline anxiety score (39.4) was higher compared to that of the normal adult population (30–35) [42–44], and at the proposed cut-off point for clinically significant anxiety symptoms (39–40) [45]. Further comparison of our results with those in the literature (available for females only) shows that the mean baseline anxiety score in the females in our cohort (39.6) was slightly higher than in females making non-invasive health care decisions such as whether genetic testing should be performed (36–39), but far below scores in females making invasive health care or difficult treatment decisions (50–62) [46].

The anxiety scores in our cohort were similar to those in the larger Dutch genetic counselling effect cohort at baseline (39.4 and 38.8 (STAI-6 scores multiplied by 20/6), respectively) [26]. Also, similar decreases in anxiety during the counselling trajectory were seen (d = -0.24 and d = -0.23, respectively), but the anxiety scores only changed significantly in the large Dutch cohort,

probably due to the higher number of participants included [26].

Anxiety was not well captured in the concept of empowerment. A third of the participants with decreased anxiety did not feel more empowerment, while 85% of participants with increased anxiety did not experience less empowerment. Previous studies also found contrary correlations between anxiety and empowerment [23,25]. We therefore recommend taking anxiety into account in evaluating the outcome of genetic counselling for epilepsy.

4.3. The importance of pre-test counselling

The results of our study indicate that genetic counselling before initiating genetic testing for epilepsy is important. First, about half of the increase in empowerment was already seen after pre-test counselling aiming at informed decision making, as was also observed in the larger Dutch genetic counselling effect study [25,26]. Second, our participants were not getting more anxious towards genetic testing, while clinically significant mean anxiety scores were observed both before (47) and after (50) genetic testing in a previously published cohort without genetic counselling [47]. We therefore emphasize the importance of counselling together with genetic testing. Third, and last, 9/115 (8%) of the eligible participants who had pre-test counselling decided not to do genetic testing after pre-test counselling, while they initially agreed with referral to the genetic outpatient clinic. Notably, these participants had higher baseline empowerment scores compared to those who did not decline genetic testing. Possibly, participants with higher baseline empowerment scores feel that their psychological well-being would benefit less from genetic testing or are better equipped to refrain from testing after counselling. It would be interesting to further study which aspect of pre-test counselling (e.g. duration, style, structure or content) is associated with the highest increase in empowerment to further improve these counselling sessions.

4.4. Influence of genetic testing results on empowerment and anxiety

Empowerment was not significantly influenced by the genetic testing results. Clinicians might be worried about decreasing the participants' empowerment by reporting a variant of unknown significance (VUS), but all ten participants with a VUS in our cohort showed increased empowerment after genetic counselling. However, we did observe a trend towards more anxiety in participants with a VUS or disease-associated variant. Further studies are warranted to confirm whether there is a difference in anxiety between participants with different genetic testing results, since we had relatively small subgroups and large variation in anxiety scores within these subgroups.

Two previous studies have reported the outcome of genetic services in parents of children, albeit with developmental problems of whom only a minority had epilepsy. One study reported a higher quality of life in mothers of children with a diagnostic result from microarray versus those with inconclusive array results [48]. Another study identified that the experiences of parents of children with epilepsy with genetic testing vary and are associated with the genetic testing results and the presence of parental depression and anxiety after receiving these results [49].

We found individual differences in the changes in (the subscales of) empowerment and anxiety during the genetic counselling trajectory, with a minority of individuals showing a decrease in empowerment or increase in anxiety. As we could not explain these individual differences based on demographic or genetic testing variables, the reason for these differences remains unknown. It is possible that the severity of epilepsy and the presence of comorbidities might play a role. However, in our small cohort, we could

not reliably determine the influence of all these disease-related variables on the change in empowerment and anxiety during the genetic counselling trajectory. Moreover, personal factors such as personality or coping style might affect the change in empowerment and anxiety. Gaining insight into the inter-individual differences may help counsellors to adapt counselling sessions to the specific individual's needs.

4.5. Limitation

We have to address two important limitations of this study. First, in our single cohort study, we had no control group with participants who had genetic testing without counselling, but this would also be unethical to do. Therefore, we cannot exclude the effect of other individual factors (such as life events) apart from the genetic counselling itself on the empowerment of participants during the genetic counselling trajectory. Still, empowerment was measured with the GCOS-18, which has shown to be very stable over time if no counselling occurs, with an excellent test-retest reliability [20]. The changes in empowerment over time, therefore, likely reflect the effect of counselling (possibly together with other factors) and not of time itself. Further randomized controlled trials with different forms of counselling in different groups may help to identify which parts of counselling are most effective in terms of gaining empowerment.

Second, although we had an average responder rate of 58% ($n = 70/120$) in the UMCG and an unknown responder rate in the UMCU [50], a significant proportion of the responders did not complete the follow-up questionnaires and were thus excluded. This drop out seemed partially explained by education level, since participants with a higher level of education were more likely to complete the questionnaires, but not by any other demographic or genetic testing variable or by baseline empowerment and anxiety scores. The mode of delivery of follow-up questionnaires (on paper vs electronically) was chosen by each participant, indicating that this did not influence the rate of response. Participants more often completed the last questionnaires if they had a disease-associated variant (87%) or normal test result (75%) compared to having a VUS (56%). Although these differences were not statistically significant, the genetic test results may have influenced the willingness of participants to complete the last questionnaire. In addition, parents mentioned that filling out the questionnaires was time-consuming, possibly contributing to a lower response rate. As a result of this drop out, the size of our remaining study cohort may have been too small to detect significant differences in the effect of genetic services on empowerment and anxiety between patient subgroups based on demographic characteristics and genetic testing results.

4.6. Conclusion and future research directions

Our study gives insight into the outcomes of genetic counselling before and after genetic testing for epilepsy, which may help genetic counsellors of patients with epilepsy. Patients with epilepsy or their parents show increased empowerment after genetic counselling both before and after genetic testing, especially in the domains knowledge about genetic services, uncertainty about genetic services and uncertainty about heredity, independent from the results of genetic testing. Anxiety remained stable during the genetic counselling trajectory. On an individual level, half of the participants showed a clinically relevant increased empowerment. Further research is warranted to identify the individual differences in the outcome of genetic services and which aspects of counselling are most effective in terms of gaining empowerment. Such studies may help to further improve the genetic counselling trajectory

personalized to the participants' needs.

Declaration of competing interest

None of the authors have any conflicts of interest to disclose.

Acknowledgements

We thank all patients and their parents for their participation in our study. We are thankful for the help of all research assistants, especially Rianne Lieben, Denise Blom, Elise Boersma and Sumalai Sompitak, for data collection and input. We thank Kate Mc Intyre/Jackie Senior for editing our manuscript.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ejpn.2021.03.015>.

References

- [1] I.E. Scheffer, Epilepsy genetics revolutionizes clinical practice, *Neuropediatrics* 45L (2014) 70–74.
- [2] S.F. Berkovic, Genetics of epilepsy in clinical practice, *Epilepsy Current* 15 (2015) 192–196.
- [3] D. Mei, E. Parrini, C. Marini, R. Guerrini, The impact of next-generation sequencing on the diagnosis and treatment of epilepsy in paediatric patients, *Mol. Diagn. Ther.* 21 (2017) 357–373.
- [4] C.A. Ellis, S. Petrovski, S.F. Berkovic, Epilepsy genetics: clinical impacts and biological insights, *Lancet Neurol.* 19 (2020) 93–100.
- [5] S. Balestrini, S.M. Sisodiya, Pharmacogenomics in epilepsy, *Neurosci. Lett.* 667 (2018) 27–39.
- [6] R.S. Møller, T.B. Hammer, G. Rubboli, et al., From next-generation sequencing to targeted treatment of non-acquired epilepsies, *Expert Rev. Mol. Diagn.* 19 (3) (2019) 217–228.
- [7] D.T. Miller, M.P. Adam, S. Aradhya, et al., Consensus statement: chromosomal microarray is a first-tier clinical diagnostic test for individuals with developmental disabilities or congenital anomalies, *Am. J. Hum. Genet.* 86 (5) (2010) 749–764, <https://doi.org/10.1016/j.ajhg.2010.04.006>.
- [8] Y.G. Weber, S. Biskup, K.L. Helbig, et al., The role of genetic testing in epilepsy diagnosis and management, *Expert Rev. Mol. Diagn.* 8 (2017) 739–750.
- [9] K.A. Myers, D.L. Johnstone, D.A. Dymont, Epilepsy genetics: current knowledge, applications, and future directions, *Clin. Genet.* 95 (2019) 95–111.
- [10] J.D. Symonds, A. McTague, Epilepsy and developmental disorders: next generation sequencing in the clinic, *Eur. J. Paediatr. Neurol.* 24 (2020) 15–23.
- [11] J. Haddow, G. Palomaki, ACCE: a model process for evaluating data on emerging genetic tests, in: M. Khoury, J. Little, W. Burke (Eds.), *Human Genome Epidemiology: A Scientific Foundation for Using Genetic Information to Improve Health and Prevent Disease*, Oxford University Press, Oxford, UK, 2004, pp. 217–233.
- [12] S. Shostak, R. Ottman, Ethical, legal, and social dimensions of epilepsy genetics, *Epilepsia* 47 (2006) 1595–1602.
- [13] R. Ottman, S. Hirose, S. Jain, et al., Genetic testing in the epilepsies—report of the ILAE genetics commission, *Epilepsia* 51 (2010) 655–670.
- [14] C.B. Caminiti, D.C. Hesdorffer, S. Shostak, et al., Parents' interest in genetic testing of their offspring in multiplex epilepsy families, *Epilepsia* 57 (2016) 279–287.
- [15] J.O. Okeke, V.E. Tangel, S.T. Sorge, et al., Genetic testing preferences in families containing multiple individuals with epilepsy, *Epilepsia* 55 (2014) 1705–1713.
- [16] S. Shostak, D. Zarhin, R. Ottman, What's at stake? Genetic information from the perspective of people with epilepsy and their family members, *Soc. Sci. Med.* 73 (2011) 645–654.
- [17] D.F. Vears, K.L. Dunn, S.A. Wake, I.E. Scheffer, "It's good to know": experiences of gene identification and result disclosure in familial epilepsies, *Epilepsy Res.* 112 (2015) 64–71.
- [18] J.M. Wilmschurst, W.D. Gaillard, K.P. Vinayan, et al., Summary of recommendations for the management of infantile seizures: task force report for the ILAE commission of pediatrics, *Epilepsia* 56 (2015) 1185–1197.
- [19] O. Devinsky, M. Asato, P. Camfield, et al., Delivery of epilepsy care to adults with intellectual and developmental disabilities, *Neurology* 85 (2015) 1512–1521.
- [20] R. Resta, B.B. Biesecker, R.L. Bennett, et al., A new definition of genetic counseling: national society of genetic counselors' task force report, *J. Genet. Counsel.* 15 (2006) 77–83.
- [21] L. Madlensky, A.M. Trepanier, D. Cragun, B. Lerner, K.M. Shannon, H. Zierhut, A rapid systematic review of outcomes studies in genetic counseling, *Genet. Med.* (2017) 361–378.
- [22] M. McAllister, K. Payne, R. Macleod, S. Nicholls, Dian Donnai, L. Davies, Patient empowerment in clinical genetics services, *J. Health Psychol.* 13 (2008) 895–905.
- [23] M. McAllister, A. Wood, G. Dunn, S. Shiloh, C. Todd, The Genetic Counseling Outcome Scale: a new patient-reported outcome measure for clinical genetics services, *Clin. Genet.* 79 (2011) 413–424.
- [24] M. McAllister, A. Dearing, Patient reported outcomes and patient empowerment in clinical genetics services, *Clin. Genet.* 88 (2015) 114–121.
- [25] J.S. Voorwinden, M. Plantinga, W. Krijnen, et al., A validated PROM in genetic counseling: the psychometric properties of the Dutch version of the Genetic Counseling Outcome Scale, *Eur. J. Hum. Genet.* 27 (2019) 681–690.
- [26] J.S. Voorwinden, M. Plantinga, M. Ausems, et al., Cognitive and affective outcomes of genetic counselling in The Netherlands at group and individual level: a personalized approach seems necessary, *Eur. J. Hum. Genet.* 28 (2020) 1187–1195. Publication ahead of print.
- [27] T.M. Marteau, H. Bekker, The development of a six item short form of the state scale of the Spielberger State Trait Anxiety Inventory (STAI), *Br. J. Clin. Psychol.* 31 (1992) 301–306.
- [28] E. Otten, E. Birnie, A.V. Ranchor, JP Van Tintelen, IM Van Langen, A group approach to genetic counselling of cardiomyopathy patients: satisfaction and psychological outcomes sufficient for further implementation, *Eur. J. Hum. Genet.* 23 (2015) 1462–1467.
- [29] J. Cohen (Ed.), *Statistical Power Analysis for the Behavioral Sciences*, second ed., Academic Press, New York, USA, 1988.
- [30] D. Revicki, R.D. Hays, D. Cella, J. Sloan, Recommended methods for determining responsiveness and minimally important differences for patient-reported outcomes, *J. Clin. Epidemiol.* 61 (2008) 102–109.
- [31] F. Angst, A. Aeschlimann, J. Angst, The minimal clinically important difference raised the significance of outcome effects above the statistical level, with methodological implications for future studies, *J. Clin. Epidemiol.* 82 (2017) 128–136.
- [32] A. Costal Tirado, A.M. McDermott, C. Thomas, et al., Using patient-reported outcome measures for quality improvement in clinical genetics: an exploratory study, *J. Genet. Counsel.* 26 (2017) 1017–1028.
- [33] A. Inglis, D. Koehn, B. McGillivray, S.E. Stewart, J. Austin, Evaluating a unique, specialist psychiatric genetic counseling clinic: uptake and impact, *Clin. Genet.* 87 (2016) 218–224.
- [34] K. Borle, E. Morris, A. Inglis, J. Austin, Risk communication in genetic counseling: exploring uptake and perception of recurrence numbers, and their impact on patient outcomes, *Clin. Genet.* 94 (2018) 239–245.
- [35] C. Slomp, E. Morris, A. Inglis, A. Lehman, J. Austin, Patient outcomes of genetic counseling: assessing the impact of different approaches to family history collection, *Clin. Genet.* 93 (2018) 830–836.
- [36] E. Morris, J. Best, A. Inglis, J. Austin, Impact of the physical environment on patient outcomes of genetic counseling: an exploratory study, *J. Genet. Counsel.* 28 (2019) 760–766.
- [37] S. Gerrard, A. Inglis, E. Morris, J. Austin, Relationships between patient- and session-related variables and outcomes of psychiatric genetic counseling, *Eur. J. Hum. Genet.* (2020). Online ahead of print.
- [38] J. Yuen, S.Y. Lee, E. Courtney, Evaluating empowerment in genetic counseling using patient-reported outcomes, *Clin. Genet.* 97 (2020) 246–256.
- [39] HE Ison, SM Ware, T. Schwantes-An, The Impact of Cardiovascular Genetic Counseling on Patient, *J. Genet. Couns.* 28 (2019) 570–577, <https://doi.org/10.1002/jgc4.1050>.
- [40] N. Davison, K. Payne, M. Eden, et al., Exploring the feasibility of delivering standardized genomic care using ophthalmology as an example, *Genet. Med.* 19 (2017) 1032–1039.
- [41] C. Thomas, M. Mc Allister, Establishing the minimum clinically important difference for the genetic counseling outcome scale (GCOS-24), *J. Genet. Counsel.* 28 (2019) 1003–1010.
- [42] C.D. Spielberger, R.L. Gorsuch, R. Lushene, P.R. Vagg, G.A. Jacobs (Eds.), *Manual for the State-Trait Anxiety Inventory*, Consulting Psychologists Press, Palo Alto, CA, 1983.
- [43] C. Forsberg, H. Bjirvell, Swedish population norms for the GRHI, HI and STAI-state, *Qual. Life Res.* 2 (1993) 349–356.
- [44] R.G. Knight, H.J. Waal-Manning, G.F. Spears, Some norms and reliability data for the state-trait anxiety inventory and the zung self-rating depression scale, *Br. J. Clin. Psychol.* 22 (1983) 245–249.
- [45] L.J. Julian, Measures of anxiety, *Arthritis Care* 63 (2011) 1–11.
- [46] H.L. Bekker, F. Legare, D. Stacey, A. O'Connor, L. Lemyre, Is anxiety a suitable measure of decision aid effectiveness: a systematic review? *Patient Educ. Counsel.* 50 (2003) 255–262.
- [47] L. Dinc, F. Terzioglu, The psychological impact of genetic testing on parents, *J. Clin. Nurs.* 15 (2006) 45–51.
- [48] M. Lingen, L. Albers, M. Borchers, et al., Obtaining a genetic diagnosis in a child with disability: impact on parental quality of life, *Clin. Genet.* 89 (2016) 258–266.
- [49] J. Wynn, R. Ottman, J. Duong, et al., Diagnostic exome sequencing in children: a survey of parental understanding, experience and psychological impact, *Clin. Genet.* 93 (2018) 1039–1048.
- [50] Y. Baruch, B.C. Holtom, Survey response rate levels and trends in organizational research, *Hum. Relat.* 61 (2008) 1139–1160.