Introducing eHealth and other innovative options into clinical genetic patient care in view of increased efficiency and maintenance of quality of care

Patients' and providers' perspectives

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Ellen Otten

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Promotores
Prof.dr. I.M. van Langen
Prof.dr. A.V. Ranchor

Copromotor
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Paranimfen
Inge Otten
Yvonne Hoedemaekers

Voor oma

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Chapter 1

General introduction

1.1 CLINICAL GENETICS AND GENETIC COUNSELING

Clinical genetics has been officially registered as a medical specialism in the Netherlands since 1987. However, genetic research and counseling/patient care had been conducted for a long time before the official registration. Clinical genetic patient care focuses on answering patient questions on heritability, which is typically done through genetic counseling and testing. According to the American National Society of Genetic Counselors, genetic counseling means "the understanding and adaptation to the medical, psychological and familial implications of genetic contributions to disease".[1] This process combines three aspects: (1) interpreting medical and family histories to assess the chance of occurrence or recurrence of a certain disease, (2) educating patients/clients about e.g. inheritance, testing, management, and prevention, and (3) counseling to support patients in making informed choices and adapting to a certain risk or condition.[1] In line with this definition, the aspects that are considered important to be taken into account by a genetic counselor in an ideal genetic counseling session are: the ethical implications of genetic issues, relevant information, objectivity (= non-directiveness), assurance of the counselee's understanding, psychological support, informed consent, confidentiality, considering implications for the family, appropriate handling of potential discrimination of testing, and assuring the counselee can make autonomous decisions.[2] There will be some variation in the practice of genetic counseling between countries, but many of the above aspects have been agreed upon internationally.[3] Clinical geneticists follow these same principles in genetic counseling, next to their fulfillment of diagnostic tasks.

The heritability issues that are dealt with in clinical genetics can roughly be divided into three main categories: (1) a patient may have a genetic disease his-/herself, (2) a genetic disease runs in the patient's family, or (3) a patient's child has a congenital anomaly and/or intellectual disability.[4] These categories have some different and some overlapping underlying questions: to learn the recurrence risk of the disease, and the possible options for prevention in (future) offspring, to learn the risk of having or developing the genetic disease that runs in the family, and to learn more about the diagnosis, prognosis and treatment or preventive options.[4] These questions lead on to the various purposes of genetic testing: symptomatic/diagnostic or presymptomatic/screening. The main categories for genetic counseling and testing are oncological, cardiological, neurological, intellectual disability/multiple congenital anomalies, and prenatal genetics.

To receive formal genetic counseling, patients are referred to one of eight university clinical genetics departments in the Netherlands by a medical specialist, midwife, or their general practitioner. Conventionally, a counseling session takes place in-person, between a geneticist or genetic counselor and an individual patient (or several family members together) and his/her partner, parents, or other support person. Counseling is generally provided by staff from a university department at an outpatient clinic of their university medical center or at a regional hospital they serve. In the Netherlands, genetic counseling

and testing for diagnostic purposes and cascade screening are covered by personal health insurance, although the patient may have to pay an own risk on their policy.

A (pre-test) counseling session can be followed by genetic testing if indicated and a patient (or the patient's representative if they are not empowered to make their own decisions) agrees to have the test done. Thereafter, post-test counseling will provide an explanation of the test results and a discussion of the possible consequences and the choices available to the patient and their family members.[5] The counseling process is completed by the counselor sending a summarizing letter to the patient and referring physician, irrespective of whether a genetic test was performed or not. If no definite genetic cause could be found, the patient will generally be asked to inquire again at the department in a few years' time, to see if any new testing possibilities have become available that could be beneficial for them.

When a disease-causing mutation is discovered by symptomatic genetic testing in the first member of a family (called the index patient), presymptomatic or carrier testing of family members becomes possible. If applicable, this process will be initiated by the distribution of a family letter (written by the counselor) by the index patient to their family. This gives relatives the possibility to find out if they are at increased risk of developing the same disease, or whether they carry the risk of having affected (future) offspring. Relatives can benefit from presymptomatic testing because it allows them to make informed choices regarding a future pregnancy, or to take preventive measures and/or undergo regular monitoring, for example in the fields of oncogenetics and cardiogenetics. For oncogenetic and cardiogenetic indications, a family letter will be sent out even if no mutation can be found in the index patient, to inform relatives of their potential risk and to allow them to have genetic counseling and medical follow-up.

This conventional way of providing clinical genetic patient care, based on research outcomes and best practices, meets the current international standard for 'delivering good care'.[5-8]

1.2 CLINICAL GENETICS: DEVELOPING TECHNOLOGY AND KNOWLEDGE

The earliest research in genetics focused mainly on what is now seen as its basis: fundamental research that led to the discovery of how the human body is made up, the way genetic material is stored in human cells and how this material is built-up, and the determination of the different types of inheritance.[9] This research was carried out by scientists and doctors using the limited techniques that were available to them at that time.[9] In the past 60 years, new genetic techniques and diagnostic possibilities have appeared at increasing speed: after the discovery that the human cell contained 46 chromosomes in 1955, it was several more years before cytogenetic chromosomal analyses were introduced, and again

several years before diagnostics could use the molecular genetic technique of Sanger sequencing for analyzing individual genes.[10-16] More recently, new technologies have been developed at a rapid pace. The Human Genome Project, started in 1990 and completed in 2001, has contributed hugely to the increased pace of developments in clinical genetic research, and to the expansion of the number of diagnostic tests offered for various newly discovered disease genes.[17-20] These developments are still ongoing; for example Whole Exome Sequencing (WES) and Whole Genome Sequencing (WGS). WES can currently be applied on a diagnostic basis to more and more patients in an increasing number of genetic centers worldwide. The main advantage of these new technologies is that they can lead to a diagnosis in a larger proportion of patients, but their main disadvantage is that a substantial part of the results cannot yet be well interpreted.[21] The application of both WES and WGS, and thus the implications for clinical diagnostics, will continue to grow in the future, with the increasingly developing knowledge on the human genome.[22]

Genetic knowledge and diagnostic possibilities have enormously increased in the past 60 years and research in clinical genetics now demands professional input from a wide range of disciplines. These disciplines cover a wide range of perspectives from both clinical and non-clinical fields, inside and outside genetics. They cover for example the medical content, psychology, bioethics, statistics/bioinformatics, epidemiology, molecular genetics, health economics, and ICT technology. The collaboration of professionals in all these fields aids the continuing evaluation of the clinical utility of the evolving techniques being used in DNA diagnostics.[23]

Contrary to all the advances in genetic technology and knowledge over the years, the genetic counseling process between a genetic professional and patient has remained almost the same.

1.3 THE DIGITALIZED SOCIETY

The developments in genetic technology are part of wider developments in the field of ICT and technology in society and in health care, that are becoming increasingly widespread accepted and in use. For example, online shopping, online banking, online travel reservations, and online social contact have become standard practice.[24-28] These developments reflect the needs for greater efficiency and ease of use of people with little time to spare in today's busy and demanding society. Besides in society, ICT facilities have also become increasingly important in health care, for example electronic patient files are now being introduced in an increasing number of health care institutions. This contributes to patients increasingly being seen as the 'owners' of their own health/medical information.[29,30] Moreover, patients are better informed via various digital and other resources, and increasingly they can make use of online platforms for creating their own medical records (e.g. http://mymedicalapp.com/) and/or for sharing their experiences and data online (e.g. www.PatientsLikeMe.com). These

developments likely increase patient empowerment and stimulate autonomy and equality in their relations with health professionals.[30] Finally, there is growing interest in 'ehealth' from health care institutions, patients, health insurance companies, and governments.[31-33] Despite the remarkable increase of ICT in the areas of support and management of health care institutions, its application in patient care seems to lag behind, and ehealth is only being used on a small scale so far.

Along with the ICT/technological developments in society and health care, there are other relevant developments in health care and specifically in clinical genetics. These comprise, for example, the continuously increasing possibilities for diagnostic testing and increasing patient numbers attending clinical genetics departments, as well as adverse economic changes resulting in the more limited budgets and more limited opportunities for expanding the number of medical professionals at clinical genetics and other departments. Other ongoing trends that affect health care are a more demanding society and more demanding patients, and the establishment of a 24/7 society.

It seems obvious that the conventional organization of patient care in clinical genetics has, to some degree, to adapt to all these developments in society and health care and to the specific developments in genetics.[34-36] This adaptation should allow for responsible care and maintaining a 'good quality of genetic care' within the current possibilities, challenges and limitations. At the same time, it should meet the increasing demands and enable the provision of efficient and convenient care. The introduction of this adapted care has several sides: the patients' side has been addressed above, but adaptations will probably also affect the genetics professional. They are used to their conventional way of working and might experience less benefit from the adapted care provision than patients will do.[37-39] Many fields outside healthcare and in other medical disciplines are adapting to the changes seen in society, but in clinical genetics the response has so far been rather limited.

1.4 CLINICAL GENETICS: INNOVATIVE CARE

The changes and developments seen in general society, in healthcare, and in clinical genetics specifically, form the basis for the research projects described in this thesis. Does going along with all these developments mean that we should alter or expand the way we provide patient care in clinical genetics? Will such innovations meet the needs of our patients and the professionals involved? And will this lead to increased efficiency and flexibility, and reduced costs of care? The current inability of geneticists to interpret a large part of the test results from new techniques also raises another question: do we – as genetic professionals – now have a greater obligation/responsibility to return to former patients if new, actionable information becomes available, compared to earlier situations? Should we inform them about any new information that might be beneficial for them, perhaps long after the initial diagnostic test has been completed and there is no longer

a clinical relationship? Or should we still place this responsibility fully with the patient? The latter might not be justified because of the increasingly complex testing that is now possible, and the corresponding increase in the number of results of unknown significance, for which interpretations will evolve gradually over time.

We are thus facing a dilemma on how to handle the increasing demand for clinical genetic care in an efficient way and maintain the provision of quality care. Health care changes can take several forms: (1) new content of care that previously did not exist (innovation); (2) the same content of care and the same modality of care provided at a different location and/or with different health care providers (substitution of location of care and/or health care providers); and (3) the same content of care provided through a different modality of care, and/or provided at a different location and/or with different health care providers (substitution of location of care and/or health care providers).[40] The health care change can be applied to the different stages of the process of clinical genetic care (administrative support, pretest counseling, posttest counseling) and to different patient groups (oncogenetic, cardiogenetic, prenatal or other; index patients or presymptomatic relatives). In this thesis, several of the health care changes in clinical genetics will be evaluated. Some of these changes are substitution of care by nature, others are innovations.

1.5 RESEARCH QUESTIONS AND AIMS

In this thesis, we concentrate on the introduction and discussion of several new approaches to the provision of patient care, thereby maintaining the conventional content of care, and the involved professionals. Within this new design of care provision, we focused on changing the location and modality of care provision: group counseling in regional hospitals, and online counseling at patients' homes instead of individual counseling at our regular clinical genetic outpatient departments. Besides this, the increasing possibilities for DNA-testing per se might ask for adaptations in or an extension of the conventional genetic care provision. We evaluated the current knowledge, beliefs and experiences on a clinical genetic care innovation; the systematic recontacting of former patients, regardless of their indication, on new knowledge regarding their genetic disease.

We examined the outcomes of our various new approaches for both patients and care providers, including their satisfaction, practical issues, psychological outcomes and the economic results, with the aim of implementing effective innovations while preserving current quality of care standards:

Chapter 2 describes a cohort study on group genetic counseling of cardiomyopathy index patients. The group sessions were held in regional hospitals in the northern part of the Netherlands, as an alternative for individual genetic counseling at the university medical

center. We measured patients' satisfaction with this type of care and their psychological outcomes.

Chapter 3 is a cost and time analysis of our regional group genetic counseling design compared to our traditional individual genetic counseling, and to several alternative models of group genetic counseling.

Chapter 4 reports an impression of the current availability and use of various telemedicine applications among European clinical genetics professionals. We used an online survey to examine their current practice. We further discuss our vision on the use of telegenetics applications, for both direct and indirect patient care.

Chapter 5 describes a cohort study into online genetic counseling for presymptomatic testing of cardiogenetic and oncogenetic patients, and for urgent prenatal counseling, to patients in their homes. We analysed patient satisfaction, psychological outcomes and the feasibility of the application used.

Chapter 6 reports the counselors' evaluations and the cost and time analysis of the cohort study on online genetic counseling described in chapter 5.

Chapter 7 comprises a systematic review of the literature on the duty to recontact in clinical genetics, in light of new genetic technologies. We provide an overview of the ethical, legal, social and practical issues of recontacting discussed in the literature, to serve as a baseline for future practice and for the development of professional guidelines.

REFERENCES

1. Resta R, Bowles Biesecker B, Bennett RL, et al. A new definition of genetic counseling: National Society of Genetic Counselors' Task Force Report. *J Genet Couns* 2006;15:77-83.
2. Rantanen E, Hietala M, Kristoffersson U, et al. What is ideal genetic counselling? A survey of current international guidelines. *Eur J Hum Genet* 2008;16:445-452.
3. Regulations and practices of genetic counselling in 38 European countries: the perspective of national representatives. *Eur J Hum Genet* 2008;16:1208-1216.
4. Leschot NJ en Brunner HG. Klinische genetica in de Praktijk. In: *Klinische genetica in de praktijk.* Edited by Leschot NJ, Brunner HG, Elsevier/Bunge, Maarssen 1998;1-19.
5. Kääriäinen H, Hietala M, Kristoffersson U, Nippert I, Rantanen E, Sequeiros J, Schmidtke J. Recommendations for genetic counselling related to genetic testing. http://www.eurogentest.org/fileadmin/templates/eugt/pdf/guidelines_of_GC_final.pdf (last access: 1 Sept 2015)
6. Skirton H, Goldsmith L, Jackson L, Tibben A. Quality in genetic counselling for presymptomatic testing – clinical guidelines for practice across the range of genetic conditions. *Eur J Hum Genet* 2013;21:256-260.
7. Skirton H, Goldsmith L, Jackson L, Lewis C, Chitty L. Offering prenatal tests: European guidelines for clinical practice. *Eur J Hum Genet* 2014;22:580-586.
8. http://www.vkgn.org/index.php/vakinformatie/richtlijnen-en-protocollen (last access: 1 Sept 2015)
9. De Nijs Bik H, Schrander-Stumpel CTRM. Enkele historische hoogtepunten en de wetten van mendel. In: *Praktische huisartsgeneeskunde: Klinische Genetica*. Edited by CTRM Schrander-Stumpel, LMG Curfs, JW van Ree. Bohn Stafleu van Loghum, Houten, the Netherlands 2005.
10. Gilgenkrantz S, Rivera EM. The history of cytogenetics. Portrets of some pioneers. *Annales de génétique* 2003;000-000.
11. Tjio J-H, Levan A. The chromosome number of man. *Hereditas* 1956;42:1-6.
12. Caspersson T, Lomakka C, Zech L. The 24 fluorescence patterns of the human metaphase chromosomes – distinguishing characters and variability. *Hereditas* 1971;67:89-102.
13. Van der Ploeg M, Van Duijn P, Bauman JG, Landegent JE, Raap AK. Hybridocytochemistry as a tool for the investigation of chromatin organization. *Basic Appl Histochem* 1985;29(3):181-189.
14. Sanger F, Coulson AR. A rapid method for determining sequences in DNA by primed synthesis with DNA polymerase. *J Mol Biol* 1975;94(3):441-448.
15. Botstein D, White RL, Skolnick M, Davis RW. Construction of a genetic linkage map in man using restriction fragment length polymorphisms. *Am J Hum Genet* 1980;32:314-331.
16. Anderson S, Bankier AT, Barrell BG, et al. Sequence and organization of the human mitochondrial genome. *Nature* 1981;290:457-465.
17. Fields C, Adams MD, White O, Venter JC. How many genes in the human genome. *Nature Genet* 1994;7:345-346.
18. Venter JC, Adams MD, Myers EW, et al. The sequence of the human genome. *Science* 2001;291(5507):1304-1351.
19. http://www.nature.com/omics/index.html (last access: 1 Sept 2015)
20. Collins FS, McKusick VA. Implications of the human genome project for medical science. *JAMA* 2001;285(5):540-544.
21. Atwal PS, Brennan ML, Cox R, et al. Clinical whole exome sequencing: are we there yet? *Genet Med* 2014;16(9):717-719.
22. Roses AD. Pharmacogenetics and the practice of medicine. *Nature* 2000;405:857-865.
23. Clinical utility of genetic and genomic services: a position statement of the American College of Medical Genetics and Genomics. *Genet Med* 2015 march 12.; doi 10.1038/gim.2015.41.epub ehead of print.

24. Centraal Bureau voor de Statistiek: ICT, kennis en economie 2014. http://www.cbs.nl/NR/rdonlyres/4DEFB273-9BC7-459B-8788-44C94175DA4B/0/2014i78pub.pdf (last access: 1 Sept 2015)
25. Centraal Bureau voor de Statistiek 2015. http://www.cbs.nl/nl-NL/menu/themas/vrije-tijd-cultuur/publicaties/artikelen/archief/2015/tablet-verdringt-bord-van-schoot.htm (last access: 1 Sept 2015)
26. Van den Bighelaar S, Akkermans M. Centraal Bureau voor de Statistiek: Bevolkingstrends 2013 – Gebruik en gebruikers van sociale media. http://www.cbs.nl/NR/rdonlyres/06A12225- 495E-4620-80F6-F2A53E819957/0/2013100 1b15art.pdf (last access: 1 Sept 2015)
27. Elskamp G. http://www.pcmweb.nl/nieuws/nederland-heeft-hoogste-aantal-internetaansluitingen.html (last access: 1 Sept 2015)
28. Elskamp G. http://www.pcmweb.nl/nieuws/nederlanders-bankieren-het-meest-online.html (last access: 1 Sept 2015)
29. Peters SG, Khan MA. Electronic health records: current and future use. *J Comp Eff Res* 2014;3(5):512-522.
30. Wicks P, Stamford J, Grootenhuis MA, Haverman L, Ahmed S. Innovations in e-health. *Qual Life Res* 2014;23:195-203.
31. Schippers E, van Rijn MJ. Ministerie van Volksgezondheid, Welzijn en Sport. Kamerbrief ehealth en zorgverbetering 2014. http://www.rijksoverheid.nl/documenten-en-publicaties/kamerstukken/2014/07/02/kamerbrief-over-e-health-en-zorgverbetering.html (last access: 1 Sept 2015)
32. KNMG handreiking artsen en social media 2011. http://knmg.artsennet.nl/Dossiers-9/Dossiers-thematrefwoord/ICT-in-de-zorg-1.htm (last access: 1 Sept 2015)
33. NPCF Visiedocument: Gezondheid 2.0. Toekomst en betekenis van e-health voor de zorgconsument 2008. Nederlandse Patiënten en Consumenten Federatie, Postbus 1539, 3500BM Utrecht.
34. Roche MI. Moving toward NextGeneticCounseling. Genet Med 2012;14(9):777-778.
35. Birch PH. Interactive e-counselling for genetics pre-test decisions: where are we now? *Clin Genet* 2015:87:209-217.
36. Welch BM, Kawamoto K. The need for Clinical Decision Support integrated with the electronic health record for the clinical application of whole genome sequencing information. *J Pers Med* 2013;3:306-325.
37. Whitten P, Holtz B, Laplante C. Telemedicine: what have we learned? *Appl Clin Inform* 2010;5(12):132-141.
38. Barton PL, Brega AG, Devore PA, et al. Specialist physicians' knowledge and believes about telemedicine: a comparison between users and nonusers of the technology. *Telemed J E Health* 2007;13(5):487-499.
39. Grigsby B, Brega AG, Bennett RE, et al. The slow pace of interactive video telemedicine adoption: the perspective of telemedicine program administrators on physician participation. *Telemed J E Health* 2007;13(6):645-656.
40. Silva BMC, Rodrigues JJP, De la Torre Díez I, López-Coronado M, Saleem K. Mobile-health: A review of current state in 2015. *J Biomed Inform* 2015;56:265-272.

Chapter 2

A group approach to genetic counselling of cardiomyopathy patients: satisfaction and psychological outcomes sufficient for further implementation

Ellen Otten, Erwin Birnie, Adelita V. Ranchor,
J. Peter van Tintelen and Irene M. van Langen

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ABSTRACT

The introduction of next-generation sequencing in everyday clinical genetics practice is increasing the number of genetic disorders that can be confirmed at DNA-level, and consequently increases the possibilities for cascade screening. This leads to a greater need for genetic counselling, whereas the number of professionals available to provide this is limited. We therefore piloted group genetic counselling for symptomatic cardiomyopathy patients at regional hospitals, to assess whether this could be an acceptable alternative to individual counselling. We performed a cohort study with pre- and post-counselling patient measurements using questionnaires, supplemented with evaluations of the group counselling format by the professionals involved. Patients from eight regional hospitals in the northern part of the Netherlands were included. Questionnaires comprised patient characteristics, psychological measures (personal perceived control (PPC), state and trait anxiety inventory (STAI)), and satisfaction with counsellors, counselling content and design. In total, 82 patients (mean age 57.5 year) attended one of 13 group sessions. Median PPC and STAI scores showed significantly higher control and lower anxiety after the counselling. Patients reported they were satisfied with the counsellors, and almost 75% of patients were satisfied with the group counselling. Regional professionals were also, overall, satisfied with the group sessions. The genetics professionals were less satisfied, mainly because of their perceived large time investment and less-than-expected group interaction. Hence, a group approach to cardiogenetic counselling is feasible, accessible, and psychologically effective, and could be one possible approach to counselling the increasing patient numbers in cardiogenetics.

INTRODUCTION

With the introduction of next-generation sequencing (NGS) in everyday clinical genetics practice, the number of genetic disorders that can be confirmed at DNA-level increases. This leads to a greater need for genetic counselling and testing of index patients and their close relatives, through cascade screening. However, the number of genetic professionals available cannot increase at the same rate, and other health professionals are generally insufficiently equipped for this task. This imbalance demands us to find new ways to effectively and efficiently accommodate to both the current and anticipated increase in requests for genetic counselling and testing, while maintaining the current levels of quality of care and patient satisfaction. This applies particularly to patients with relatively prevalent diseases, like cardiomyopathies, in which preventive options lead to a decrease in morbidity and mortality.

Hypertrophic cardiomyopathy (HCM) and dilated cardiomyopathy (DCM) are two common subtypes of cardiomyopathy. Prevalences are about 1:500 for HCM and the same or higher for DCM.[1,2] Most HCM cases are familial, with (probable) causative genetic variants being found in up to 60% of familial and in about 30% of sporadic cases, using traditional sequencing techniques.[3] In a Dutch cohort, the overall yield for familial and sporadic cases was 46%.[4] About one-third of DCM cases are familial and a genetic cause can be found in 30-50% of these families.[5,6] Familial cardiomyopathy mostly has an autosomal dominant mode of inheritance with reduced penetrance and variable expression, and preventive and treatment options are available. This makes cascade genetic testing of family members recommended practice.[3] Because NGS further increases the yield of causative genetic variants found in index patients, the number of family members being referred for genetic counselling and testing will also increase.

Group counselling is an attractive way of handling this increasing flow of patients to clinical genetics departments. It has been introduced in several medical disciplines,[7] with the aim of providing information, patients sharing personal experiences, and increasing the efficiency of counselling for professionals. The general goals of genetic counselling are to increase patients' knowledge about their disease and its genetic aspects, and to ensure that patients can control their feelings about their situation/condition, resulting in the ability to make autonomous choices for themselves and their relatives. This is usually done in individual sessions, but could also be achieved group-wise, as has been confirmed by experiences with breast cancer group counselling.[8-11] These studies confirm that the aims and expected advantages of group counselling can be reached.[10] Patient satisfaction and the psychological outcomes of group genetic counselling are also generally positive.[8-10] This oncogenetic group counselling mainly includes small heterogeneous patient groups that include both symptomatic and risk carriers. As far as we are aware, group counselling has not been piloted in cardiogenetics, despite being a rapidly growing segment of referrals.

We therefore piloted group genetic counselling for symptomatic cardiomyopathy patients as part of an intervention to increase access to genetic counselling and testing for patients and cardiologists at small regional hospitals in our service area. Our aim was to deliver adequate quality of care through group counselling. First, we wanted to determine whether the psychological benefits of group counselling were adequate, and at least comparable to the benefits of individual counselling. Second, we investigated both patients' and medical professionals' satisfaction with this type of counselling.

METHODS

Study design and patients

This was a cohort study with pre- and post-counselling measurements, conducted in eight small regional hospitals (mean 326 beds; range 197-642) in the northern part of the Netherlands (total area about 8,304 km^2 with about 1.7 million inhabitants). HCM and DCM index patients who had not attended genetic counselling and testing before, or those who felt the need for a second counselling, were eligible to participate. Thirteen group sessions took place between March 2011 and November 2012.

Study process

In the Netherlands, genetic counselling and testing for cardiomyopathies are performed by clinical geneticists and genetic counsellors employed at eight university medical centers (UMCs), in collaboration with psychosocial workers and dedicated cardiologists. This care is covered by compulsory, Dutch health insurance general policies. Cardiologists in nine regional hospitals within the service area of our university hospital were informed of the possibility of organizing group counselling sessions in their hospital, and the formal referral criteria for genetic counselling and testing for symptomatic HCM and DCM patients were brought to their attention.[12,13] Eight out of nine hospitals decided to participate.

Participating cardiologists and heart failure nurses selected eligible patients and informed them about the possibility of group genetic counselling. Interested patients received a standardized information letter about the possible genetic character of their cardiomyopathy and about the option for group genetic counselling and testing. Individual genetic counselling in the university hospital or at one of our three regular regional outpatient clinics was offered as an alternative. An application form, information-leaflet on group counselling and a stamped return-envelope were added. Patients who applied received an invitation. The preparations for group counselling were similar to those for standard individual care.

The counselling sessions were held in the afternoon or evening, in meeting rooms in the participating hospitals. All patients could bring one relative/partner. At the beginning of the session, each participant was asked to sign a combined "confidence declaration"

and informed consent form to emphasize the confidential nature of the setting. Sessions lasted about two hours, including completing the research questionnaires (taking about 30 minutes) and a break. The legal department of our hospital approved the patient information material we compiled and the group counselling format regarding informed consent and privacy issues. Approval by a medical ethics committee was considered unnecessary because this care modality is also used in regular care.

The counselling team consisted of four professionals: (1) a clinical geneticist-in-training provided the regular cardiogenetic and pre-test information, including a PowerPoint presentation, to patients and answered genetic questions, (2) a social worker was group leader and focused on group interactions and psychosocial issues of patients, (3) a local cardiologist and/or heart failure nurse was present to answer specific cardiological questions, and (4) a clinical geneticist was present to supervise and assist with the short individual discussions after the group session had ended. These took about 5-10 minutes per patient and comprised recording additional personal and family history and discussion of personal considerations in DNA-testing. Immediately after the sessions, blood withdrawal for diagnostic DNA-testing was offered to all patients and performed in those who consented.

Group sessions differed from our standard individual counselling in three respects: (1) groups of unrelated patients were counselled together instead of individually, (2) counselling was done by a team instead of a single counselor assisted by a social worker or cardiologist when necessary, and (3) counselling was given in the regional hospitals instead of at our department or regular outpatient clinics.

Patient measurements

The questionnaires before and immediately after the group counselling session requested the following information.

Patient characteristics

Patient's age, sex, number of offspring, educational level, diagnosis, and age at diagnosis.

Referral for genetic counselling

Patients were asked (1) who initiated their referral for genetic counselling and (2) if they had previously discussed referral for genetic counselling with their cardiologist.

Patient's questions

Before the group session began, patients were asked to indicate which questions they wanted to have answered during the session and if they had any additional questions that they preferred not to have discussed in the group. Afterwards, patients were asked which of their questions had been answered and which not, and if they had heard any information during the session that they would have preferred not to know.

We included five measures in the questionnaires to assess the experienced quality and the psychological outcomes of the counselling sessions in our patients:

Personal Perceived Control (PPC)
The validated nine-item PPC (Dutch version) was used to measure patient's perceived control before and after genetic counselling (α = 0.79-0.81).[14] The response mode is a 0-2 Likert scale. Higher scores indicate higher levels of perceived control.

State and Trait Anxiety Inventory (STAI)
The Dutch six-item short version of the STAI was used to measure patient's experienced anxiety before and after genetic counselling. The response mode is a 1-4 Likert scale, with higher scores indicating higher levels of anxiety. The convergent validity of the Dutch version of the STAI-6 with the full STAI showed a correlation of 0.95.[15,16]

Clinical Genetics Satisfaction Indicator (CGS)
This seven-item questionnaire was adopted by the Clinical Genetics Association in the Netherlands to measure patient satisfaction with genetic counselling. The response mode is a 1-5 Likert scale. Higher scores indicate higher satisfaction. The English version shows excellent internal consistency in a clinical genetics setting (α = 0.91).[17] Internal consistency in the present study was 0.80.

Patient preferences
Before the group counselling session, patients were asked to indicate their preference for the three main characteristics of group and individual counselling: (1) counselling in their local hospital versus counselling in the university hospital, (2) counselling by a team (geneticist, social worker and cardiologist) or by a single genetic counselor, and (3) counselling in a group versus individually. They were also asked to indicate their overall preference for either group or individual counselling based on the three aspects jointly. The five-point response mode ranged from "definite preference for group counselling" to "no preference" to "definite preference for individual counselling".

Evaluation of content and design
Content was defined as both the appreciation of individual parts of the counselling and of the information given. Design concerned: (1) the appreciation of the entire process from referral to counselling, and (2) the composition of the group session itself and the presence of fellow patients. These were evaluated by means of a 20-item ad hoc questionnaire, using a 0-2 Likert scale (totally agree/partly agree/disagree) as response mode. Higher scores indicated higher satisfaction with content and/or design of the group session. "Being satisfied" was defined as "sum-scores" ≥ 80/100.

Professionals' opinions

At the end of the pilot period, all the professionals involved from the regional hospitals were sent an online questionnaire to evaluate the group sessions in terms of (1) their positive and negative experiences with the group sessions, (2) any feedback from patients, (3) suggestions for improvement, (4) willingness to organize further group sessions, and (5) willingness to refer patients to our university hospital for group counselling. We also asked them to rate their overall satisfaction with the group counselling session (1 = very unsatisfied to 10 = very satisfied). The social worker, clinical geneticist, and clinical geneticist-in-training evaluated the group counselling approach informally after each session, and more extensively at the end of the pilot period. Evaluation included feasibility and course of the sessions, interaction during the sessions, and their additional positive and negative experiences.

Analysis

The descriptive statistics used in this study were mean (SD) for variables with normal distributions, median (interquartile range) for variables with skewed distributions, and n (%) for nominal and ordinal variables. PPC, STAI and GCS outcomes were analyzed for patients who completed at least two-third of these questionnaires. Mean item scores per patient were calculated. Changes of PPC and STAI scores within patients were tested using the Wilcoxon rank sum test for skewed variables and the paired Student's t-test for changes with normal distributions. We used the same tests to compare differences in PPC, STAI and CGS outcomes between small and large counselling groups (<7 versus ≥7 patients). Estimated effect sizes were added. Data were analyzed using SPSS statistics v20 (IBM Corporation New York, NY, USA).

RESULTS

Study process and sample

During the study, 121 of the selected/approached patients were invited for a group counselling session (maximum about 80%; the exact number of patients selected/approached is unknown, as this was not fully reported by all cardiologists). Of those invited, 82 patients (68%) attended one of the sessions, with 61 accompanying relatives/partners (Figure 1). Reasons for the 30 patients not attending their scheduled session ranged from not being interested in genetic counselling and testing on second thought (n=4; 13%) to more practical reasons (n=17; 57%; eg, sickness, having no transport, having other obligations at the time of the session), or simply not showing up for unknown reasons (n=9; 30%).

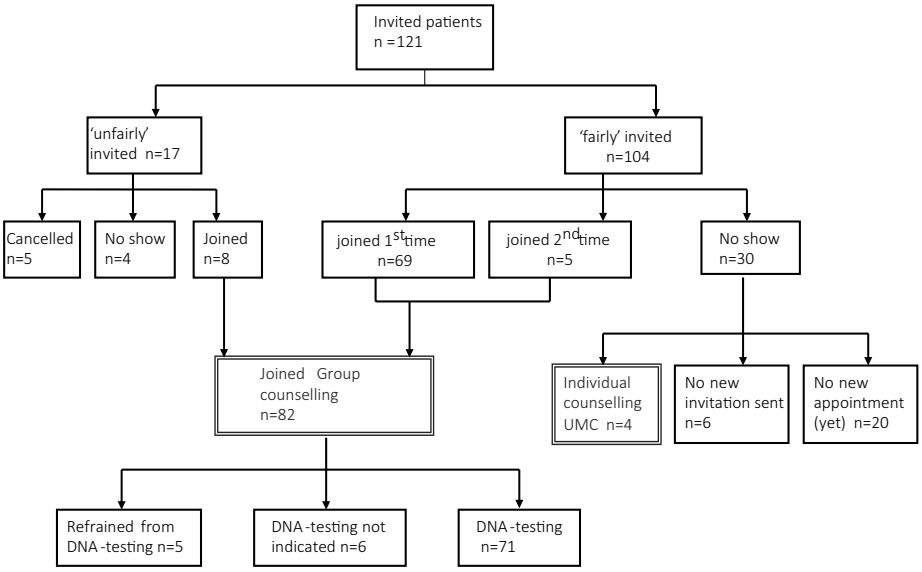

Figure 1. Overview of patients invited for a group counselling session

'unfairly' = patients suspected of having a heritable cardiac disease, but not fulfilling the formal criteria for joining a group counselling session;
'fairly' = patients fulfilling the formal criteria for joining a group counselling session

Median age of patients not showing up was 59.5 years (range 30 to 78), of whom 40% were male and 73% were referred because of DCM. The median age and proportion of DCM of these patients were comparable to the joining patients, whereas the no show-group did contain more females than the patients attending a group session. Median size of the group sessions was six patients (range 3-13 patients), and nine participants including accompanying relatives (range 5-27 persons). Four patients eventually attended an individual session at the university hospital instead of a group session; all because they were unable to be present at the scheduled group session and chose to attend the UMC for an individual session at short-term rather than waiting for a next group session at their own hospital. Patient characteristics are shown in Table 1. In total, 75 of 82 patients (91%) completed both sets of questionnaires before and after the counselling session, whereas 81 of 82 patients completed at least one set. At the end of the pilot period, four cardiologists and two heart failure nurses from five of eight cooperating hospitals completed the professionals' evaluations.

Table 1. Characteristics of all patients attending group counselling sessions

Characteristic	
Age (yr); median (range)	57.5 (20-79)
Sex; number male/female (%)	45/37 (55/45%)
Patients with offspring (% yes)	71 (89%)
Educational level Number of patients (% of total)*	
Low	11 (14%)
Intermediate	58 (73%)
High	11 (14%)
Cardiac disease Number of patients (% of total)	
DCM	52 (63%)
HCM	24 (29%)
Other	6 (7%)
Time since diagnosis (yr); median (range) *	2.0 (0-25)

yr = year; DCM = dilated cardiomyopathy; HCM = hypertrophic cardiomyopathy; *n = 2 unknown

Patient measurements

Referral for genetic counselling

Thirteen patients (16%) reported having discussed genetic counselling with their doctor previously, but they did not attend/were not referred for genetic counselling until group genetic counselling was offered in their regional hospital. Three patients had been previously counselled individually at our university hospital and had DNA-testing initiated, but nevertheless wished to attend additional group genetic counselling.

Patient questions

Forty-two patients (51%) reported at least one question they wished to have answered. Most questions addressed the consequences of confirming heritability for the patient and his/her close family members (n = 22 questions; 35% of questions) and cardiologic signs, symptoms and complaints (n = 17; 27% of questions). At the start of the session, one patient reported one topic, her personal situation, which she did not want to discuss during the group session. Afterwards, five patients reported having received general answers to their questions, but no specific answers for their personal situation. Only one patient reported having heard information he/she would have preferred not to know; this concerned the possibility/risk of sudden cardiac death in cardiomyopathy.

Psychological and satisfaction outcomes

Median change scores of the PPC were significantly higher (increased control) and those of the STAI were significantly lower (less anxiety) after counselling for all groups in relation to before the session (related samples Wilcoxon test, $p<0.001$ for both; Table 2), with effect sizes of 1.00 and 0.49, respectively (Table 2). Patients also reported they were satisfied with the counselors (Table 2); 56.5% of patients gave the maximum CGS questionnaire score of 5.0. PPC and STAI change scores and CGS scores did not differ significantly between small and large counselling groups (Independent Mann-Whitney U-test, $p = 0.74$, $p = 0.94$ and $p = 0.31$ respectively; Table 2). The majority of patients indicated that they would join a group counselling session again if genetic counselling would be necessary (87.7%), and would recommend it to family members (81.4%).

Patient preferences

When comparing each main characteristic of our group counselling approach to its corresponding aspect in our individual counselling practice separately, almost half of the patients (48.5%) preferred their local hospital over the university hospital, whereas 40% did not have any preference.

Regarding the involved professionals in each type of counselling, 52% did not have any preference for counselling by the multi-disciplinary team or for counselling by just a single counsellor.

When taking all main characteristics of both counselling types into account, one-fourth of our patients preferred group counselling overall, whereas 30% preferred individual counselling overall. The remaining patients (45.3%) did not have a clear overall preference for one of both counselling types.

Evaluation of content and design

Almost three-quarters of our patients reported being satisfied with the content (74.3%) and design (73.4%) of the group counselling session (Figure 2). One patient reported the design of the group session process being overall insufficient (score 41 of 100). The items with mean lowest success scores in all patients (range 1-5) were “usefulness of discussing DNA-testing with fellow-patients” (mean score 1.26) and “experiencing support from fellow patients” (mean score 1.11).

Professionals’ evaluations

Regional professionals reported they were satisfied overall with the course of the group counselling at their hospital (mean score 7.8). No negative reactions from their patients were reported. Suggestions for improvement were to be clearer about the session aims (emphasis on genetic information, not on cardiac information), to shorten its duration (shorter introduction), and to consider optimal group size (maximum 10 patients) and time of day (symptomatic patients may be too tired by the end of the day). All professionals

Table 2. Psychological outcomes of patients attending group counselling sessions

		All groups	Small groups (< 7 patients)	Large groups (≥ 7 patients)
Outcome measure	**Time point**	**Median score (IQR)**	**Median score (IQR)**	**Median score (IQR)**
PPC	n	64	34	30
	before	0.89 (0.44)	0.89 (0.44)	0.78 (0.50)
	after	1.24 (0.56)	1.39 (0.47)	1.17 (0.44)
	Δ	**0.33** (0.44)	**0.41** (0.42) #	**0.30** (0.47) #
STAI	n	67	36	31
	before	1.67 (0.67)	1.83 (0.67)	1.67 (0.70)
	after	1.67 (0.83)	1.67 (0.63)	1.50 (1.17)
	Δ	**0.17** (0.33)	**0.08** (0.50)	**0.17** (0.33)
CGS	n	69	37	32
	after	5.0 (0.50)	5.0 (0.29)	5.0 (0.71)

PPC = personal perceived control questionnaire; STAI = state and trait anxiety inventory; CGS = clinical genetics satisfaction indicator; n=number of patients; before = at start of session; after = immediately after session; Δ = change between before and after; IQR = interquartile range. Significant changes ($p < 0.05$) are displayed in bold, test used = Wilcoxon test, except where indicated, # = Student's t-test.

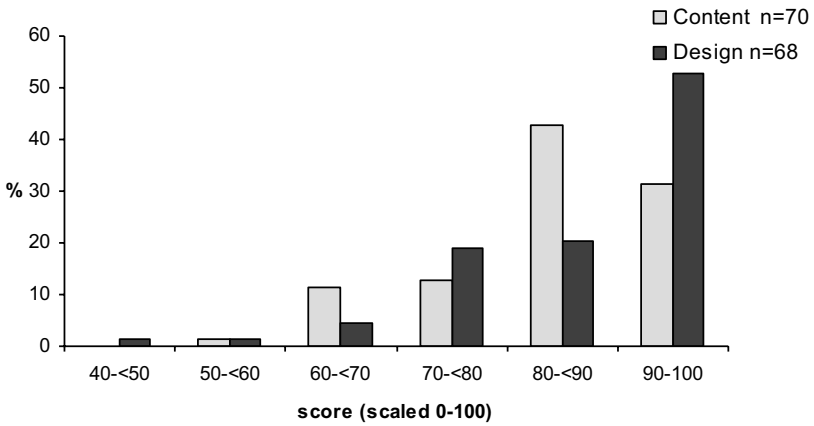

Figure 2. Patient satisfaction with content and design of group counselling sessions

indicated they were willing to organize group counselling sessions for index patients in the future. One of six professionals was not willing to refer patients to the university hospital for group counselling because she thought the regional group concept is more suitable for increasing access to genetic counselling.

The genetics professionals involved were less enthusiastic about the group counselling format than their regional cardiologic colleagues: one positive aspect mentioned was that more, and possibly different, patients were reached and informed by this new approach. Perceived disadvantages were that group counselling in eight hospitals was less efficient than counselling at the university hospital (mainly due to travelling time), that the practical organization of the sessions was difficult and time-consuming, and that it was sometimes difficult to stimulate the group interaction.

DISCUSSION

We evaluated the quality and satisfaction of group genetic counselling for symptomatic cardiomyopathy patients. The outcomes show that the group counselling participants experienced good quality of care, that group counselling was not harmful, and that the psychological aims were met. Moreover, the professionals involved from the regional hospitals were overall positive about this way of providing genetic counselling. Finally, our group counselling approach seemed feasible, acceptable, and satisfied a need in the view of the number of patients that attended group counselling.

As far as we know, we are the first to have piloted and evaluated group counselling in cardiogenetic patients. We included a substantial number of patients to support the reliability of our results. The participants were heterogeneous in terms of gender, age, and educational level, which suggests that, overall, group counselling is acceptable to a wide range of patients. Finally, our pilot study closely mimicked daily practice, that is, the barriers we faced probably also occur in daily practice. This makes our group approach relatively easy being integrated in existing clinical workflow (Figure 3).

Reference PPC and STAI data for cardiomyopathy patients are unavailable. The psychological outcomes of our patients showed suboptimal baseline as well as post-counselling levels of PPC scores, and better STAI scores than reports on individually counselled oncogenetic patients in the Netherlands. However, the improvements in scores between pre- and post-counselling (within patients) were similar.[9,14,18-20] Our PPC results in cardiogenetics are also comparable to group counselling in oncogenetics,[9] and several reports from the United Kingdom about STAI outcomes in oncogenetics show similar improvements in scores as in our patients.[21-23] The psychological outcomes of our patients may have been influenced by group size, group dynamics, and/or the management of questions which they did or did not want to be addressed during the group session. But this all seems unlikely as the psychological outcomes of both the smaller and larger groups in

our study were about equal (Table 2). Only one patient indicated a topic she preferred not to be discussed and only one patient reported having heard some information he would have preferred not to know. This leads us to conclude that our patients overall accept group counselling psychologically and are not harmed by it.

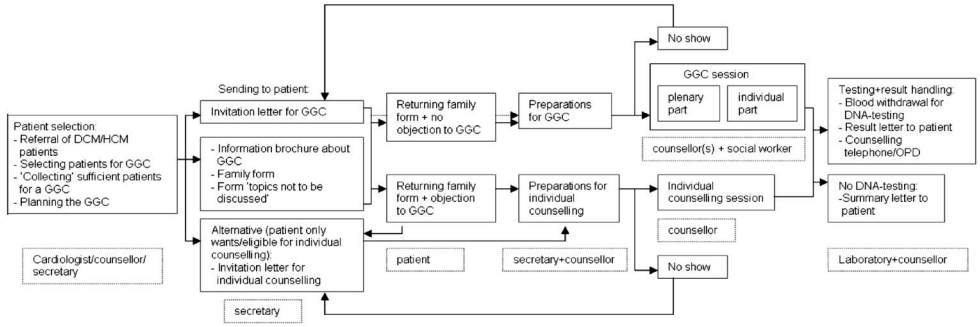

Figure 3. Flow chart – integration of the group genetic counselling (GGC) process into routine care

In addition to the positive outcomes of group counselling reported by the patients and the regional professionals, our approach had some indirect effects. By bringing genetic counselling closer to our patients and the regional professionals, we lowered the threshold for attending genetic counselling, and we provided education and created awareness in the regional professionals, which hopefully will have an ongoing beneficial effect on their referral rates.

Unlike the patients and the regional professionals, the genetics professionals experienced several drawbacks with group counselling, particularly a greater time investment and less interaction amongst patients than expected. Additional research is needed, with regard to time investment, to determine the most appropriate format of the group counselling sessions for both the patients and professionals involved. Sessions could be adapted regarding design, duration, and/or location, to meet the requirements of both patients and professionals. Regarding patient interactions, our expectations were perhaps too much influenced by the literature on repeated group sessions, for example, in diabetic care.[7, 24] A minimum level of group bonding is needed before patients will share thoughts and experiences: this is more likely to evolve over the course of multiple sessions. Moreover, the limited group interaction might also be partly due to the fact that most of these symptomatic patients had already decided for genetic testing before attending the group session, making group interaction less important for them. However, the patient outcomes for the counselling sessions did not suffer from the limited interaction, as shown by the PPC and STAI results. The degree of interaction might be different in group counselling of relatives considering predictive testing, but this has yet to be investigated.

One study limitation is that we cannot be certain that our results are unbiased, owing to the absence of a matched control group that received individual counselling. Moreover, PPC and STAI changes were evaluated directly after the counselling sessions and we did not evaluate the persistence of these benefits in the longer term. Our results may also have been subject to participation bias, as the patients chose to join group counselling rather than refusing this type of counselling outright.

In conclusion, in the near future results of NGS diagnostics will become available for large numbers of HCM and DCM patients, and for patients with other (common) genetic diseases. Because of this anticipated increase, together with growing awareness of these growing possibilities, we should be prepared for an increased demand for genetic counselling and testing of patients and their family members. Fulfilling these needs is important in the light of achieving health gains. Our results support our hypothesis that group genetic counselling in cardiogenetics is a feasible, accessible, and psychologically effective way of counselling large numbers of symptomatic cardiomyopathy patients. Further research is needed to determine which type of counselling will be most suitable in view of increasing patient numbers, thereby satisfying both patients' and professionals' needs, maintaining at least current levels of quality and of access to clinical genetic care, and being cost-effective.

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REFERENCES

1. Maron BJ, Maron MS, Semsarian C: Genetics of hypertrophic cardiomyopathy after 20 years: clinical perspectives. *J Am Coll Cardiol* 2012; 60: 705-715.
2. Mestroni L, Taylor MR: Genetics and genetic testing of dilated cardiomyopathy: a new perspective. *Discov Med* 2013; 15: 43-49.
3. Ackerman MJ, Priori SG, Willems S *et al:* HRS/EHRA expert consensus statement on the state of genetic testing for the channelopathies and cardiomyopathies: this document was developed as a partnership between the Heart Rhythm Society (HRS) and the European Heart Rhythm Association (EHRA). *Europace* 2011; 13: 1077-1109.
4. Hofman N, Tan HL, Alders M *et al:* Yield of molecular and clinical testing for arrhythmia syndromes. Report of 15 years' experience. Circulation 2013;128:1513-1521.
5. van Spaendonck-Zwarts KY, van Rijsingen IA, van den Berg MP *et al:* Genetic analysis in 418 index patients with idiopathic dilated cardiomyopathy: overview of 10 years' experience. *Eur J Heart Fail* 2013; 15: 628-636.
6. Pugh TJ, Kelly MA, Gowrisankar S *et al:* The landscape of genetic variation in dilated cardiomyopathy as surveyed by clinical DNA sequencing. *Genet Med* 2014;16(8):601-608.
7. Jaber R, Braksmajer A, Trilling JS: Group visits: a qualitative review of current research. *J Am Board Fam Med* 2006; 19: 276-290.
8. Ridge Y, Panabaker K, McCullum M, Portigal-Todd C, Scott J, McGillivray B: Evaluation of group genetic counseling for hereditary breast and ovarian cancer. *J Genet Couns* 2009; 18: 87-100.
9. Rothwell E, Kohlmann W, Jasperson K, Gammon A, Wong B, Kinney A: Patient outcomes associated with group and individual genetic counseling formats. *Fam Cancer* 2012; 11: 97-106.
10. Calzone KA, Prindiville SA, Jourkiv O *et al:* Randomized comparison of group versus individual genetic education and counseling for familial breast and/or ovarian cancer. *J Clin Oncol* 2005; 23: 3455-3464.
11. Visser A, Prins JB, Hoogerbrugge N, van Laarhoven HW: Group Medical Visits in the Follow-up of Women with a BRCA Mutation: Design of a Randomized Controlled Trial. *BMC Womens Health* 2011; 11:39.
12. Mestroni L, Maisch B, McKenna WJ *et al:* Guidelines for the study of familial dilated cardiomyopathies. Collaborative Research Group of the European Human and Capital Mobility Project on Familial Dilated Cardiomyopathy. *Eur Heart J* 1999; 20: 93-102.
13. ICIN working group on Hereditary Heart Diseases: Genetic diagnostics and genetic counselling in Hypertrophic Cardiomyopathy (HCM). *Neth Heart J* 2010; 18: 144-159.
14. Smets EM, Pieterse AH, Aalfs CM, Ausems MG, van Dulmen AM: The perceived personal control (PPC) questionnaire as an outcome of genetic counseling: reliability and validity of the instrument. *Am J Med Genet A* 2006; 140: 843-850.
15. van der Bij AK, de Weerd S, Cikot RJ, Steegers EA, Braspenning JC: Validation of the Dutch short form of the state scale of the Spielberger State-Trait Anxiety Inventory: considerations for usage in screening outcomes. *Community Genet* 2003; 6: 84-87.
16. Spielberger CD: Manual for the State-Trait Anxiety Inventory STAI (Form Y). Palo Alto, Consulting Psychologists Press, 1983.
17. Zellerino B, Milligan SA, Brooks R, Freedenberg DL, Collingridge DS, Williams MS: Development, testing, and validation of a patient satisfaction questionnaire for use in the clinical genetics setting. *Am J Med Genet C Semin Med Genet* 2009; 151C: 191-199.
18. Pieterse AH, van Dulmen AM, Beemer FA, Bensing JM, Ausems MG: Cancer genetic counseling: communication and counselees' post-visit satisfaction, cognitions, anxiety, and needs fulfillment. *J Genet Couns* 2007; 16: 85-96.
19. Zilliacus EM, Meiser B, Lobb EA *et al:* Are videoconferenced consultations as effective as face-to-face consultations for hereditary breast and ovarian cancer genetic counseling? *Genet Med* 2011; 13: 933-941.

20. Braithwaite D, Emery J, Walter F, Prevost AT, Sutton S: Psychological impact of genetic counseling for familial cancer: a systematic review and meta-analysis. *Fam Cancer* 2006; 5: 61-75.
21. Brain K, Gray J, Norman P *et al:* Randomized trial of a specialist genetic assessment service for familial breast cancer. *J Natl Cancer Inst* 2000; 92: 1345-1351.
22. Bish A, Sutton S, Jacobs C, Levene S, Ramirez A, Hodgson S: Changes in psychological distress after cancer genetic counselling: a comparison of affected and unaffected women. *Br J Cancer* 2002; 86: 43-50.
23. Cull A, Anderson ED, Campbell S, Mackay J, Smyth E, Steel M: The impact of genetic counselling about breast cancer risk on women's risk perceptions and levels of distress. *Br J Cancer* 1999; 79: 501-508.
24. Raballo M, Trevisan M, Trinetta AF *et al:* A study of patients' perceptions of diabetes care delivery and diabetes: propositional analysis in people with type 1 and 2 diabetes managed by group or usual care. *Diabetes Care* 2012; 35: 242-247.

Chapter 3

A group approach to regional cardiogenetic counseling: evaluation of yields, costs, and cost-effectiveness

Ellen Otten, Adelita V. Ranchor, J. Peter van Tintelen, Irene M. van Langen and Erwin Birnie

Submitted

ABSTRACT

The current ongoing technical developments in molecular genetics lead to more genetically confirmed diagnoses in patients, and hence to an increased pressure on clinical genetic services, also because many eligible patients still are not reached or referred. In cardiogenetics, the identification of mutation carriers leads to preventive options, with potential public health gains. Considering financial constraints, and consequently tight staffing, new ways should be sought to effectively and efficiently serve these increasing numbers of patients. Group counseling could be one option.

We performed a pilot study on group genetic counseling of cardiomyopathy patients in small regional hospitals, to lower the threshold for referral and increase the uptake of genetic counseling. We inventorised the uptake, and the costs and cost-effectiveness of our group counseling approach compared to several alternative approaches.

Our regional group approach included about three times more patients than were referred in previous years. However, this approach turned out to be less efficiently and slightly more costly per patient, at the professionals' side, than several alternative approaches. From the societal perspective, the alternative of individual regional counseling is most preferable because more patients are counseled and tested, at slightly higher costs.

The various advantages and disadvantages for both patients and providers should be weighed against each other in finding the most beneficial way of providing genetic counseling to an increasing number of patients. This study can help us and other professionals in finding the most optimal way of counseling a large number of patients with limited resources.

INTRODUCTION

The increasing availability of next generation sequencing options in diagnostics leads to a larger number of genetic diagnoses being confirmed at the DNA-level. This puts an increased pressure on staff of clinical genetic services. For example, when causative mutations are found in more index patients, this also leads to more genetic counseling and presymptomatic/carrier testing in family members through cascade screening, in accordance with professional guidelines.[1,2]

It is also known that currently genetic services are reaching only part of eligible patients.[3-6] Several factors are likely to contribute to this, e.g., the relative scarcity and limited accessibility of genetic centers, the limited awareness and suboptimal referral of regional professionals, and the personal characteristics, awareness, perceptions and attitudes of patients.

Reaching a larger number of patients is important for two reasons. From the patient's perspective, counseling is important because patients and their relatives receive information about the heritable nature of their disease, and it supports decision making, e.g., on targeted treatment and follow-up. From a public health perspective, a higher uptake could contribute to public health gains, especially for the relatively common genetic diseases for which prevention and treatment options are available. This is for example the case for the heritable heart diseases dilated and hypertrophic cardiomyopathy (DCM and HCM).

New ways should therefore be sought to deal effectively and efficiently with the increasing patient numbers that should be served with genetic counseling and testing while economic resources are limited: One possible approach could be to offer group genetic counseling for selected indications assuming that this will increase cost-effectiveness. This type of counseling has successfully been introduced in several medical disciplines in previous years,[7] and has also been reported to have satisfactory patient outcomes in prenatal and oncogenetics.[8-11]

We recently reported on a successful pilot study on group counseling sessions for index patients with cardiomyopathies in small regional hospitals in the northern Netherlands.[12] By offering group genetic counseling and testing locally, we tried to lower the threshold for referral and uptake of genetic counseling in an efficient way. We found that the outcomes of counseling, i.e. changes in personal perceived control and anxiety of patients participating in group genetic counseling were comparable to previous reports of group and individual oncogenetic counseling, and that patients were satisfied.[12]

In this report we focus on the patient uptake, cost and cost-effectiveness of this group counseling approach compared to several conventional and alternative counseling strategies. We wanted to know if our regional group approach is indeed more cost-effective than individual counseling, and if not, what could be improved to reach optimal cost-effectiveness. The aim of this cost-effectiveness analysis is to frame the multiple

strategies for cardiogenetic counseling in terms of the incremental (health) gains these strategies deliver, compared to the incremental costs associated with these strategies.[13] This is being evaluated from the patient's, professional's, and societal perspectives. As such, comparing these gains and costs can support professionals' decision making.

METHODS

Study setting, design, and participants

In the Netherlands, genetic counseling and testing in most index patients and their relatives is being performed by clinical genetics departments at eight university medical centers (UMCs) throughout the country. The UMC Groningen (UMCG) is the only center in the northern part of the country. From this center, counselors regularly travel to five large regional hospitals to perform outpatient clinics, but the smaller regional hospitals are not covered. Because referrals from smaller regional hospitals were fewer than expected based on the prevalences of DCM and HCM, we invited cardiologists from these hospitals to participate in our pilot project.

Cardiologists from eight smaller regional hospitals participated in our study (maximal distance to the UMC; 87km). They were informed on the formal referral criteria for genetic counseling and testing for DCM and HCM. Eligible index patients were selected by the regional cardiologists and heart failure nurses. Next, they were informed about the possibility of group genetic counseling in their own hospital and the alternative of individual counseling at the UMCG or one of three regular regional outpatient clinics. Interested patients were invited for a group session.[12]

The sessions consisted of: (1) a plenary informational part led by a social worker from the genetics department who concentrated on the group interaction, and a geneticist in training (EO) who focused on the provision of information; (2) short individual discussions after the plenary part regarding family information and considerations on DNA-testing, performed by EO and a geneticist; and (3) the possibility of blood withdrawal for DNA-testing after the session. A regional cardiologist or heart failure nurse was also present and provided cardiological information whenever necessary. Patient questionnaires on satisfaction, preferences, and practical and psychological issues were completed at the beginning and the end of the sessions. The complete session took about two hours.[12] Median group size was six patients (range 3-13) and nine participants (range 5-27) including accompanying relatives.

Referral rate and uptake

The group counseling sessions were performed between March 2011 and November 2012. We compared the number of patients reached by our new approach with the number of referrals by the involved regional cardiology departments to our genetics department in

previous years, from 2007 (onset of genetic testing for cardiomyopathies in our lab) to 2010.

Patient preferences

Patients were asked to report their expectations and evaluations of group genetic counseling, by completing questionnaires both at the start and the end of the group counseling session.[12] These questionnaires contained, among others, several questions concerning patients' preferences for the various characteristics of the group counseling session compared to conventional counseling regarding: (1) the counseling location, (2) the composition of the counseling team, (3) receiving counseling individually or with fellow patients, and (4) their overall preference for the current regional group counseling or individual counseling at the UMC. These questions were asked prior to the onset of the group counseling session. We used this information to estimate the uptake rate when group counseling would have been held at the UMCG.

Cost-effectiveness

We estimated the costs per patient and the cost-effectiveness of group counseling held regionally (current strategy in the pilot), and compared these with several alternative strategies, being explained in detail below, under various assumptions.

Costs

Costs were distinguished into costs of counseling (selection and invitation of patients, preparation and organization of the counseling sessions), patient related costs (time and travel costs) and costs of DNA testing.

Effectiveness

Effectiveness (regarding increased uptake or number of well-informed patients) was expressed as the observed and expected number of patients counseled, as well as the number of patients counseled and tested in each scenario.

The time costs of professionals were based on gross hourly wage rate including taxes and social premiums (excluding departmental and hospital overheads) obtained from the 2013 departmental budget and accounting system. While the cardiologists and nurses were not intended to play a role in the group counseling model we pursue, they are excluded from our cost analyses. Costs of traveling were based on the variable costs of traveling (€0.15/km) and parking costs. The valuation of patient's time was derived from studies on the value (opportunity costs) of travel and leisure time, with valuations ranging between €3 and €15 per hour; for this study we chose the average, being €7.47 per hour. The patient related costs also included the time spent by accompanying family members or spouses. The costs of DNA-testing were estimated €910 including blood withdrawal and included

personnel costs, equipment costs and disposables, but excluding departmental and hospital overheads.

Alternative strategies to cardiogenetic group counseling

We considered that the costs and cost-effectiveness of the applied counseling approach might be affected by the type of counseling (group or individual) by the location of counseling, and by the composition of the counseling team. In view of current regular practice and potential cost reductions, we also varied the counseling teams, being: social worker, clinical geneticist in training, and genetic counselor (team 1); social worker, genetic counselor, and a part-time genetic counselor only present during the individual part of the group session (team 2); and clinical geneticist and genetic counselor (team 3).

Based on the above, we identified various alternative strategies to our current regional group counseling approach, scenario I (with scenario Ia and Ib for different team compositions): Firstly; Group counseling held centrally at the UMC Groningen, assuming that the location of counseling does not affect the uptake of counseling and DNA-testing (scenarios IIa and IIb for different team compositions). Secondly, group counseling held centrally at the UMCG, assuming that the location of counseling reduces the uptake of counseling, but the uptake rate of DNA-testing remains the same (scenario IIc). The rationale of scenario IIc was that traveling to the UMCG and the associated investment of patient time and effort might reduce the uptake of counseling. The estimated reduction of uptake in this scenario was based on patients' answers to the preference questions in the patient questionnaires. And finally scenario III; individual counseling held regionally, assuming that the type of counseling (group or individual) does not affect the uptake of counseling and DNA-testing. We compared the costs and effectiveness of group counseling held regionally (current strategy in the pilot; design I) with these various identified alternative strategies.

RESULTS

Uptake and referral rate

Eight regional cardiology departments in the service area of our UMC participated in the pilot project. Patients ages ranged from 20 to 79 years (median 57.5), 55% of them were male. Educational level was low in 14%, intermediate in 73% and high in 13% of patients. Their (probable) diagnosis was DCM in 63%, HCM in 24% and 'other' in 7% of patients. The time since diagnosis at the time of the group session ranged from 0 to 25 years.

Figure 1 depicts the study profile: After selection, we invited 121 patients in 21 months, of whom 82 patients and 61 accompanying relatives/partners joined one of 13 group counseling sessions, after one or two invitations. Five invited patients eventually had individual counseling at the UMC. For various reasons (e.g., illness, holidays, or funeral of a

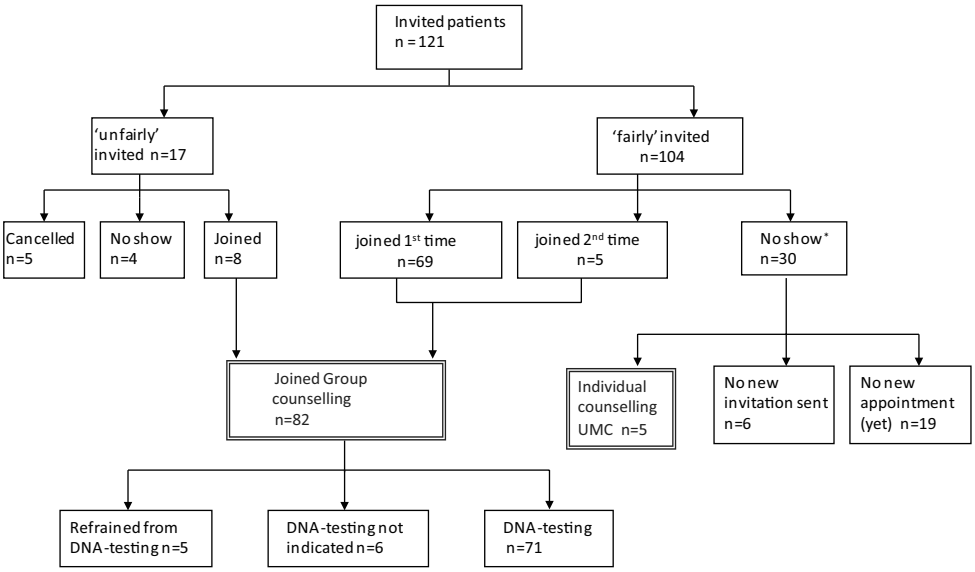

Figure 1. Overview of patients invited for a group counselling session

'unfairly' = patients suspected of having a heritable cardiac disease, but not fulfilling the formal criteria for joining a group counselling session;
'fairly' = patients fulfilling the formal criteria for joining a group counselling session
*: 'no show' included all patients not attending their group session for various known and unknown reasons

close relative) they were unable to attend the group session at their regional hospital at the scheduled time, and did not want to wait for a next group session at their regional hospital.

Before the pilot, between 2007 and 2010 (48 months), 45 DCM and HCM patients were referred by cardiologists from the same eight hospitals to our university department of Genetics. Disregarding eight patients who joined one of our group counseling sessions without the pre-defined justification (they had genetic counseling and testing previously, or another cardiological diagnosis was made) (Figure 1), we reached 3.8 times more HCM and DCM patients from these hospitals with our new approach.

Patient preferences

Of the patients who joined a group counseling session, 48.5% preferred to visit their regional hospital over the university center, 39.7% of patients did not have a preference for one of both locations, while 11.8% preferred the UMC. In summary, 51.5% of the patients who joined group counseling at their own hospital stated to be willing to visit the UMC.

Table 1. Costs per participating patient (in €) and cost-effectiveness (per counseled 'well-informed' patient, or 'well-informed and tested' patient) of group counseling held regionally (current strategy in pilot) compared to several alternative strategies

	CURRENT STRATEGIES		**ALTERNATIVE STRATEGIES**			
COSTS	*Scenario Ia: Group Counseling held regionally* *Team1 uptake 67.8%*	*Scenario Ib: Group Counseling held regionally* *Team2 uptake 67.8%*	*Scenario IIa: Group Counseling at UMCG* *Team1 uptake 67.8%*	*Scenario IIb: Group Counseling at UMCG* *Team2 uptake 67.8%*	*Scenario IIc: Group Counseling at UMCG* *Team2 uptake 34.9%*	*Scenario III: Individual counseling held regionally* *Team3 uptake 71.9%*
Provider-related costs (per patient)	86	76	66	55	63	103
- Preparation, organization	33	33	33	33	41	32
- Counseling session	32	22	32	22	22	54
- Travel and time costs	21	21	0	0	0	18
Patient-related costs (per patient)	45	45	75	75	75	23
Total costs (per patient)	132	121	140	130	138	126
Costs of DNA testing (per patient)	788	788	788	788	788	774
EFFECTIVENESS						
- 'well-informed'	82 patients#	82 patients#	82 patients**	82 patients**	47.2 patients	87 patients**
- 'well-informed' + tested	71 patients#	71 patients#	71 patients**	71 patients**	39.5 patients	74 patients**

* without cardiologist, without clinical geneticist
** assuming that location of counseling does not affect uptake rates
# see Figure 1
Team1 consists of social worker, clinical geneticist in training en genetic counselor
Team2 consists of one social worker, one genetic counselor and one part-time genetic counselor
Team3 consists of clinical geneticist and genetic counselor

Costs and cost-effectiveness

Table 1 shows the costs and effectiveness of our current regional group counseling approach (scenario Ia) and several alternative approaches and team compositions (scenarios II and III). The total costs (= joined costs at patient's and provider's side) of our current group counseling approach were €132 per participating patient, of which €86 (65%) were provider-related and €45 (35%) patient-related. Counseling was performed in 82 of 121 invited patients (uptake 67.8%). Of these, 71 underwent DNA-testing (uptake 86.6%). The total costs per patient of the current group counseling approach could decrease to

€121 when the genetic counseling team is optimized, and thus the costs at the provider's side lowered (applying scenario Ib instead of Ia).

The alternative scenarios IIa/IIb show the costs per patient of group counseling held centrally at the UMCG, assuming the uptake rates and team compositions of scenarios Ia/Ib remain the same. We assumed equal uptake rates because of a higher total number of patients, and a higher frequency of scheduled group sessions in scenarios IIa/IIB, leading to increased possibilities for patients to attend a group session. With scenarios IIa/IIb, the total costs per patient will rise 6-7% compared to scenarios Ia/Ib (€140 vs. €132; €130 vs. €121). The provider-related costs will decrease with 23%-28% (€66 vs. €86; €55 vs. €75) but the patient-related costs increase due to traveling (+67%; €75 vs. €45). This implies that scenarios IIa/IIb are overall more costly than scenarios Ia/Ib but less costly from the professional's perspective, and even less costly when the composition of the counseling team is optimized (scenario IIb vs. IIa).

In scenario IIc, patients' preferences regarding the location of counseling are taken into account: the total costs per participating patient will rise compared to scenario Ib (€138 vs. €121, or +14%) and to scenario IIb (€138 vs. €130, or +6%). The provider-related costs will decrease compared to Ib (€63 vs. €76 or -17%) but will increase when compared to scenario IIb (€63 vs. €55, or +15%). The disadvantage of this scenario is that its effectiveness is assumed to be much lower than in the current approach (scenarios Ia/Ib) since only 51.5% of patients prefer to be counseled at the UMCG. As a result, in this scenario only 47.2 (instead of 82) patients will be counseled, and 39.5 (instead of 71) patients will enter DNA-testing, and thus benefit from potential health gains.

Introducing regional individual counseling for these patients (scenario III) would lower the total costs per patient compared to scenario Ia (€126 vs. €132 or -5%), while the uptake will increase to 87 patients (instead of 82 patients), because 5 patients who would otherwise be counseled individually at the UMC are now seen locally (Figure 1). While the share of patient's costs will be lower (€23 vs. €45, or -49%), the costs per patient from the provider's perspective will rise (€86 v. €103, or +20%).

To summarize: The scenario with lowest total costs per patient is scenario Ib. From the patient's perspective, scenario III, individual counseling held regionally, is the strategy that delivers lowest costs. From the professional's perspective, this is scenario IIb. From the societal perspective, our current group approach with team 2 (scenario Ib) and scenario III are the preferred strategies. Scenario III has the advantage that more patients are counseled and tested, but it is also slightly more costly.

DISCUSSION

Our results show that with our regional group counseling approach we reached considerably more cardiomyopathy index patients in small hospitals who were interested in genetic counseling and molecular testing, than were referred previously to our clinical genetics center by the participating hospitals. By counseling and testing this increased number of patients compared to previous years, consequently also more family members are being informed and become eligible for cascade screening, leading to prevention and public health gains. Also, we demonstrated that the total costs of our current group counseling approach are slightly higher than several other conceivable scenarios for reaching these cardiomyopathy patients in regional hospitals, but costs can be lowered by changing the team and will then be less than with individual counseling. From the patient's perspective, however, regional counselling is preferable in view of lowest costs. Finally, from the societal perspective, regarding total costs and number of patients reached, regional individual counseling will be the optimal scenario.

One limitation of our study concerns the intended/expected uptake of genetic counseling in the outlined alternative scenarios for our current group counseling approach. We used questionnaire data to estimate the patient's uptake rate for counseling in the UMC instead of regionally, answered by our patients who attended the group sessions. However, we cannot be sure that what the patients said they would do ('stated preference') coincides with what they would do in reality ('revealed preference'). Nor can we be sure that the uptake of DNA-testing remains unaltered when the location of counseling (regionally or centrally) or the type of counseling (group or individually) changes, although the only reason for this inconsistency that might occur we can think of is an increased uptake of genetic testing after group counseling compared to individual counseling due to social pressure. However, to avoid this, we discussed their considerations and decisions on DNA-testing individually with patients after the plenary part, in our current group approach. Finally, a point of debate about this study could be the selection we made regarding the patient-related costs and professional-related costs included in our analysis. One could discuss about the preferable level of detail and comprehensiveness to which the included components of the cost-analysis should be assessed, and make other choices than we did in the current analysis.

Previous reports on group counseling in genetics did not detail and systematically analyze the costs and time of regional group counseling, nor did they compare several alternatives from various perspectives, as we did in this study. Only two previous reports do limitly report on a cost and time analysis, showing favorable outcomes of group oncogenetic counseling compared to individual counseling.[8,10] Another issue pointed at in one of these reports was the difficulty and time-consuming way of arranging group appointments.[10] This was also the case in our pilot study, and led to five patients eventually being counselled individually at the UMC instead of having group counseling in their own regional hospital.

This implementation challenge is more often reported in reports of group consultations in other medical disciplines.[14]

Our current regional group approach thus showed an increased number of patients being referred, counseled and tested, and entailing less costs for patients than counseling at the UMC. Increased efficiency could be achieved by counseling in the university center or alternatively, in one of the regular regional OPDs, instead of in the smaller regional hospitals, to decrease traveling time for counselors, and to allow the second geneticist to join only for the short individual discussions after the general group counseling part. The disadvantage of the first scenario is that the patient-related travel costs and time costs increase substantially (67% increase), and that the increased uptake may partially vanish when patients have to travel to the university center. The latter is even more conceivable for some of these affected index patients, while some of them found the regional group sessions already exhausting. Also asking relatives to come along would become more burdensome, while these relatives profit from the information supplied at these sessions as well.

For choosing the optimal approach to genetic counseling, the various advantages, disadvantages, and preferences from the patients', the providers', and the societal perspectives should be weighed against each other: Our previous report on the patient outcomes from our current regional group approach showed that patients were satisfied with group counseling, and that they had similar psychological outcomes as reported previously for individual genetic counseling. It also showed that almost half of involved patients did not have a clear preference for group or individual genetic counseling. Also, the involved local professionals were satisfied with the current group approach.[12] Moreover, our cost-analysis shows that conventional individual counseling held regionally (scenario III) is the preferred strategy from the patient's perspective, but is slightly more costly than regional group counseling with the optimized team (scenario Ib). Scenario III is also the preferred strategy from the societal perspective because it leads to a higher number of patients being counseled and tested compared to the current group approach, and thus allowing for greater public health gains. Our previous report also showed that the genetics professionals were less satisfied, for a substantial part due to greater perceived time investment.[12] From their perspective group counseling held centrally at the UMC (scenario II) is the preferred strategy in view of lower costs for professionals, but a disadvantage is that the impact on uptake rate may be substantial (scenario IIb versus IIc). However, ultimately it is up to the departmental management to decide whether a low-cost, a high-uptake or a compromise scenario will be chosen.

To conclude, the most cost-effective way of reaching eligible patients in regional hospitals for genetic counseling and testing is by performing regional group counseling with an optimized team of a social worker, a genetic counselor and a resident is. Individual regional counseling is still second best. In the near future it is expected that patient numbers at genetics departments will continue to increase, when next generation sequencing

techniques are applied for increasing numbers of patients and an increasing variety of (common) genetic diseases in combination with increasing awareness of the public and non-genetic health professionals. However, the number of genetic professionals is not expected to increase at the same rate. Therefore, we should continue to look for alternative effective and efficient care modalities, with maintenance of the quality of care of our current genetic services. This project has given us insight in the benefits and disadvantages of a regional group approach and several alternative scenarios in cardiogenetics, regarding patient uptake, and involved time and costs from various perspectives. These kinds of detailed analyses can help us and other genetics professionals in finding the optimal way of counseling increasing patient numbers in times of great opportunities but tight staffing.

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REFERENCES

1. ICIN working group on Hereditary Heart Diseases: Genetic diagnostics and genetic counselling in Hypertrophic Cardiomyopathy (HCM). *Neth Heart J* 2010; 18: 144-159.
2. Menko FH, Aalfs CM, Henneman L, Stol Y, Wijdenes M, Otten E, Ploegmakers MM, Legemaate J, Smets EM, de Wert GM, Tibben A; Dutch Society for Clinical Genetics. Informing family members of individuals with Lynch syndrome: a guideline for clinical geneticists *Fam Cancer.* 2013 Jun;12(2):319-24.
3. Delikurt T, Williamson GR, Anastasiadou V, Skirton H. A systematic review of factors that act as barriers to patient referral to genetic services. *Eur J Hum Genet* 2015;23:739-745.
4. Mikat-Stevens NA, Larson IA, Tarini BA. Primary care providers' perceived barriers to integration of genetic services: a systematic review of the literature. *Genet Med* 2015;17(3):169-176.
5. Tan YY, Fitzgerald LJ. Barriers and motivators for referral of patients with suspected lynch syndrome to cancer genetic services: a qualitative study. *J Pers Med* 2014;4:20-34.
6. Hawkins AK, Creighton S, Hayden MR. When access is an issue: exploring barriers to predictive testing for Huntington disease in Britisch Coumbia, Canada. *Eur J Hum Genet* 2013;21(2):148-153.
7. Jaber R, Braksmajer A, Trilling JS: Group visits: a qualitative review of current research. *J Am Board Fam Med* 2006; 19: 276-290.
8. Ridge Y, Panabaker K, McCullum M, Portigal-Todd C, Scott J, McGillivray B: Evaluation of group genetic counseling for hereditary breast and ovarian cancer. *J Genet Couns* 2009; 18: 87-100.
9. Rothwell E, Kohlmann W, Jasperson K, Gammon A, Wong B, Kinney A: Patient outcomes associated with group and individual genetic counseling formats. *Fam Cancer* 2012; 11: 97-106.
10. Calzone KA, Prindiville SA, Jourkiv O *et al:* Randomized comparison of group versus individual genetic education and counseling for familial breast and/or ovarian cancer. *J Clin Oncol* 2005; 23: 3455-3464.
11. Hunter AGW, Cappelli M, Humphreys L, Allanson JE, Chiu TT, Peeters C, Moher D, Zimak A. A randomized trial comparing alternative approaches to prenatal diagnosis counseling in advanced maternal age patients. *Clin Genet* 2005;67:303-313.
12. Otten E, Birnie E, Ranchor AV, van Tintelen JP, van Langen IM. A group approach to genetic counselling of cardiomyopathy patients: satisfaction and psychological outcomes sufficient for further implementation. *Eur J Hum Genet* 2015; Feb 4. doi: 10.1038/ ejhg. 2015.10. [Epub ahead of print]
13. Drummond MF, Sculpher MJ, Torrance GW, O'Brien BJ, Stoddart GL. Methods for the economic evaluation of health care programmes. Oxford University Press, New York. Third edition, 2005.
14. Jones KR, Kaewluang N, Lekhak N. Group visits for chronic illness management: implementation challenges and reccomendations. *Nurs Economics* 2014;32(3):118-147.

Chapter 4

Telemedicine uptake among Genetics Professionals in Europe: room for expansion

Ellen Otten, Erwin Birnie, Anneke M. Lucassen, Adelita V Ranchor and Irene M. van Langen

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ABSTRACT

Today's economic challenges and the changing landscape of clinical genetics are forcing us to consider alternative ways of providing genetic services, to comply with budget limitations and at the same time meeting the demands of increasing patient numbers and patient-centered care delivery. Telegenetics could be an effective and efficient way of counseling, but its use in Europe is not widely reported, nor is there evidence of international collaboration. We conducted an online survey among 929 genetics professionals, to explore the current availability and use of different telegenetics modalities in Europe. Our questionnaire was completed by 104 clinically active European genetics professionals. Telephone genetic counseling was used by 17% of respondents. Videoconferencing facilities were available to 24%, but only 9% of them used these for patient counseling. Various barriers to availability and use were cited, ranging from practical constraints, lack of professional support/knowledge, to lack of perceived suitability and need. The results show that telegenetics modalities are not currently in widespread use by our respondents, in part due to perceived barriers. To meet the changing economic, genetic, and societal circumstances, we recommend consideration of greater integration of telegenetics into regular clinical genetic care, to supplement existing care modalities. Professional cooperation, sharing knowledge, and establishing guidelines on a national and international level could contribute to successful and more widespread implementation of telegenetics. However, the perceived practical and regulatory barriers have to be overcome.

INTRODUCTION

Clinical genetic services are currently facing major challenges: budget limitations, increasing patient numbers, and more tests to communicate, result in ever greater pressure on time. Moreover, patient centeredness is playing an increasingly prominent role. The recent introduction of next-generation sequencing (NGS) techniques illustrates the challenges: NGS has great potential for diagnosing many more syndromic/heritable diseases than with conventional techniques, resulting in more patients being referred for genetic counseling and testing. Moreover, our limited or incomplete ability to interpret NGS results necessitates follow-up contacts. More efficient ways of genetic counseling that maintain high standards of care and facilitate shared decision making are therefore needed. Telemedicine could, in our view, be a mode to achieve this in a substantial part of referrals to clinical genetic centers.

Telemedicine is defined as remote health care to exchange medical information from one site to another via electronic communications to improve a patient's health (http://www.americantelemed.org/about-telemedicine/what-is-telemedicine). It can be used both in communication between professionals and patients, and in communication between professionals about patients. Telemedicine modalities range from telephone consultation as the earliest or simplest form, to communication via a computer and webcam, to using a specialized portable workstation with attached devices to visualize and measure body parts and functions. A common goal of telemedicine applications throughout various medical disciplines is to provide an effective, efficient and patient-friendly way of care.[1-3] Moreover, it can reach patients who are difficult to reach by conventional 'in-person' care methods, for example, due to large distances and travelling costs.[4,5]

Telemedicine has been introduced in various medical disciplines, including clinical genetics, where it has been referred to as telegenetics. The small number of existing reports on telegenetics in oncogenetics and prenatal and dysmorphologic consultations are mainly from outside Europe. Although there are a few UK reports,[6-8] the overall application in Europe is unknown. Reported patient experiences are very positive overall, while those of professionals are moderately positive, influenced to a large extent by technical imperfections.[6-11] No formal international guidelines exist for when and how to use telegenetics in a responsible way. There are also no widespread European or worldwide collaborations on telegenetics, for exchange of knowledge to allow for quality improvement and responsible application of telegenetic modalities. In the United States, there is a national Telegenetics Workgroup to facilitate cooperation and exchange between various regional telegenetics initiatives.

It is conceivable that various local initiatives in Europe do exist, however, and face similar problems, barriers, and challenges, with local professionals trying to solve these by themselves. Given the generally experienced barriers on telemedicine on the one hand, and positive literature reports on telegenetics use on the other, we wanted to get an impression

of the extent and types of telegenetics use throughout Europe and the barriers that are faced, and to aim for collaboration between different centers, as appropriate. To address this, we conducted an international survey among European Society of Human Genetics (ESHG) members to serve as a baseline upon which to superimpose improvements in telegenetics provision.

MATERIALS AND METHODS

Survey design

We composed an online survey in collaboration with the American Telegenetics Workgroup of the National Coordinating Center for the Regional Genetic and Newborn Screening Service Collaboratives (NCC). Our survey questions covered four outcome measures: (1) respondents' professional characteristics, (2) the availability and use of various telegenetics applications by the respondents, (3) reasons for non-availability or non-usage of videoconferencing applications at the respondents' departments, and (4) respondents' interests in telegenetics initiatives and/or collaboration. Design and dissemination of the survey were performed using of the online software tool SurveyMonkey (www.surveymonkey.com; Palo Alto, CA, USA).

Survey distribution

All 929 members of the ESHG for whom the e-mail addresses were available for public use were invited to participate in the online survey between November 2012 and January 2013. The list of e-mail addresses was provided by the ESHG committee and contained no information about the members' professional backgrounds (eg, clinically active or not, working in health care or business). Within the time period, one reminder e-mail was sent to all available members.

Analysis

We excluded respondents from outside Europe and those who were not working in a clinical setting. Data were analyzed using SPSS statistics v22 (IBM Corporation, Armonk, NY, USA). As descriptive statistics we used mean (SD) and median/range, and n (%) for nominal and ordinal variables. We analyzed the outcomes on telemedicine availability and use for the whole group, and for different respondent groups based on the European region in which they were employed.

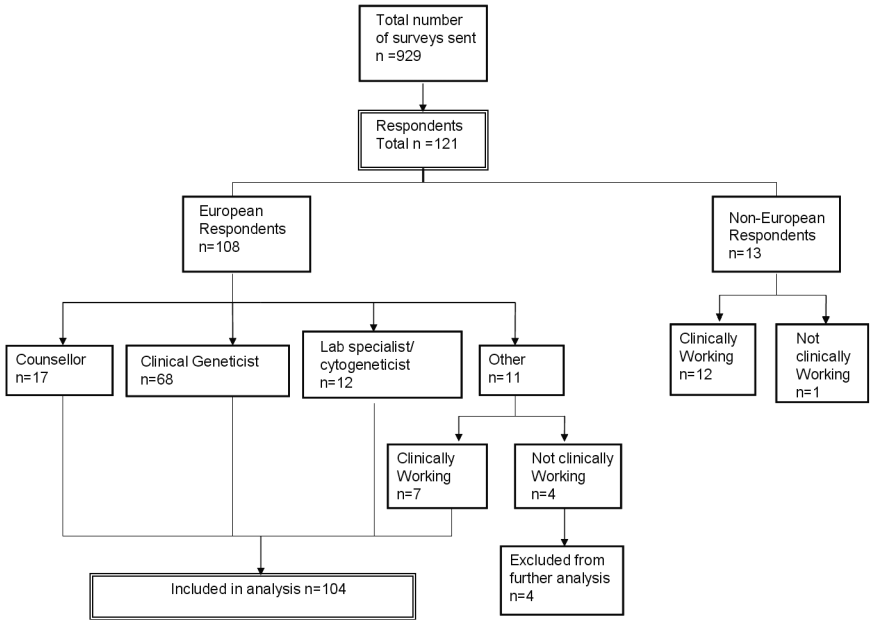

Figure 1. Overview of approached and responded ESHG members

RESULTS

Respondents' characteristics

The survey was fully or partially completed by 121 ESHG members from 92 different institutions in 39 countries, comprising 108 European respondents from 30 different countries (Table 1). We excluded the 13 non-European respondents (of whom one was not working in a clinical setting) and four European respondents who were not working in a clinical setting. This left 104 clinically working European respondents for further analysis. Of these, 65% were clinical geneticist, 16% genetic counsellors, 12% laboratory specialists, and 7% had other clinical specialties (Figure 1). Of these 104 respondents, 86% indicated they worked at a public hospital, while 14% worked in a private clinic. Their working experience ranged from 0 to 40 years (mean 18.6 years).

Table 1. Residence of respondents listed by region, country and location

European respondents (n=108)		
Residence	**Number of respondents**	**Number of locations**
Western Europe (n=36)		
Austria	5	2 (+1 unknown)
Belgium	1	1
France	7	6
Germany	6	5 (+ 1 unknown)
Netherlands	15	7
Switzerland	2	2
Eastern Europe (n=15)		
Bulgaria	2	2
Estonia	2	2
Latvia	1	1
Lithuania	1	1
Poland	1	1
Romania*	7	4
Ukraine	1	1
Northern Europe (n=25)		
Denmark*	4	4
Finland	2	1
Iceland	2	1
Ireland	2	2
Norway	1	1
Sweden	5	3
United Kingdom	9	7
Southern Europe (n=32)		
Croatia	1	1
Cyprus	1	1
Greece	2	2
Italy*	9	8
Macedonia	1	1
Malta	1	1
Portugal	2	2
Slovenia	1	1
Spain*	10	7 (+1 unknown)
Turkey	4	2
Non-European respondents (n=13)		
Residence	**Number of respondents**	**Number of locations**
Africa (n=1)		
Angola*	1	1
Oceania (n=2)		
Australia	2	2
Middle-East (n=5)		
Bahrain	1	1
Iran	2	1
Kuwait	1	1
Saudi Arabia	1	1
South-America (n=1)		
Brazil	1	1
North-America (n=4)		
Canada	1	1
USA	3	3

* One respondent from each of these five countries was excluded from further analyses because of being not working in clinical practice.

Figure 2. Telemedicine modalities in use by European respondents (n=29 respondents)

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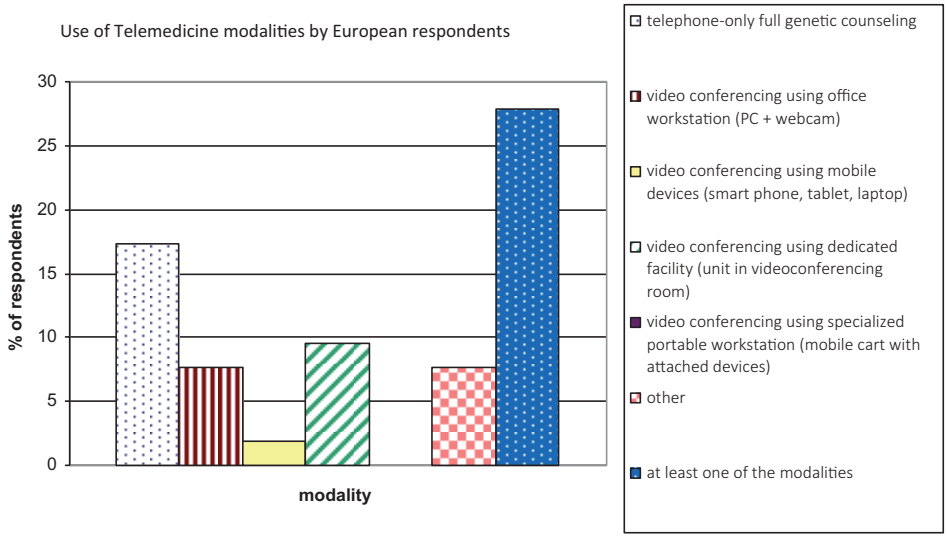

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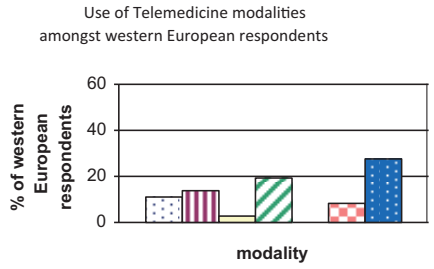

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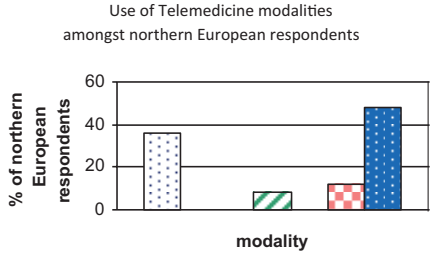

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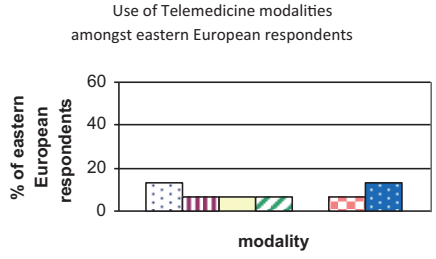

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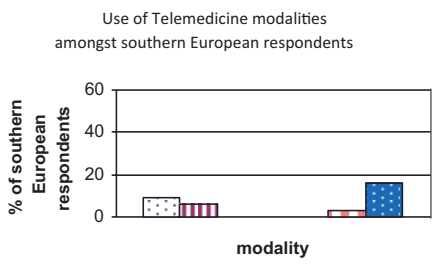


Availability and use of Telegenetics applications

Of all the European respondents, 28% (n=29; of which 17 clinical geneticists, 6 genetic counselors, 4 lab specialists, and 2 'other') indicated that they used at least one subtype of telegenetics. Most users were from northern Europe (41%; n=12) and the smallest proportion was from eastern Europe (6.9%; n=2). Telephone-only genetic counseling was the telemedicine subtype used by the largest number of respondents; 17% of respondents (n=18). Figure 2 shows the geographical location of users. The extent of use varied among respondents from 1 to 25 counseling sessions to over 100 counseling sessions per year, for various indications. Few respondents used videoconferencing, and then most frequently through a telemedicine dedicated facility at their department. This modality was used by 9.6% (n=10) of all respondents (Figure 2) mostly from western European countries (7 of 10 respondents). The frequency of use ranged from 1-25 to 26-50 counseling sessions per respondent per year, for a range of different indications. For each telemedicine modality, we analyzed the relative frequencies of the different types of clinical interactions for which it was used (Figure 3).

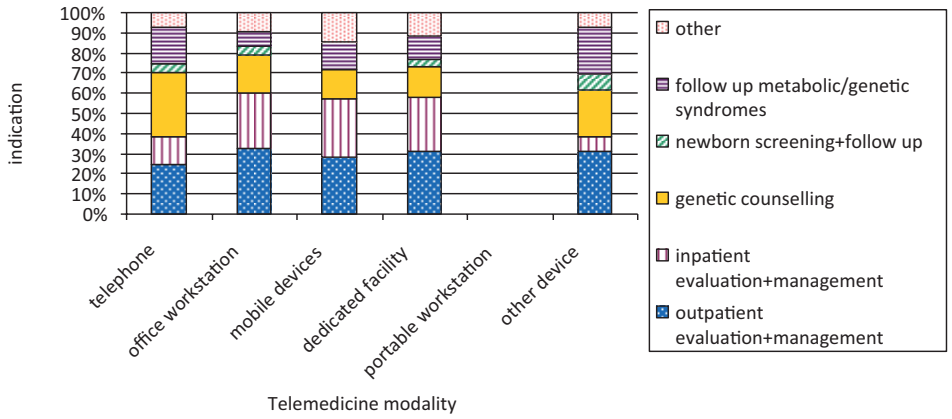


Figure 3. Overview of Telemedicine modalities in use by European respondents, showing their individual roles in online patient communication for various indications

Figure 3 shows that the telephone is most frequently used for genetic counseling, the office workstation and dedicated facility are mostly used for 'outpatient evaluation and management' and 'inpatient evaluation and management' (including, for example, assessing children with mental retardation/multiple congenital anomalies, when admitted to the hospital, or visiting the outpatient department, respectively).

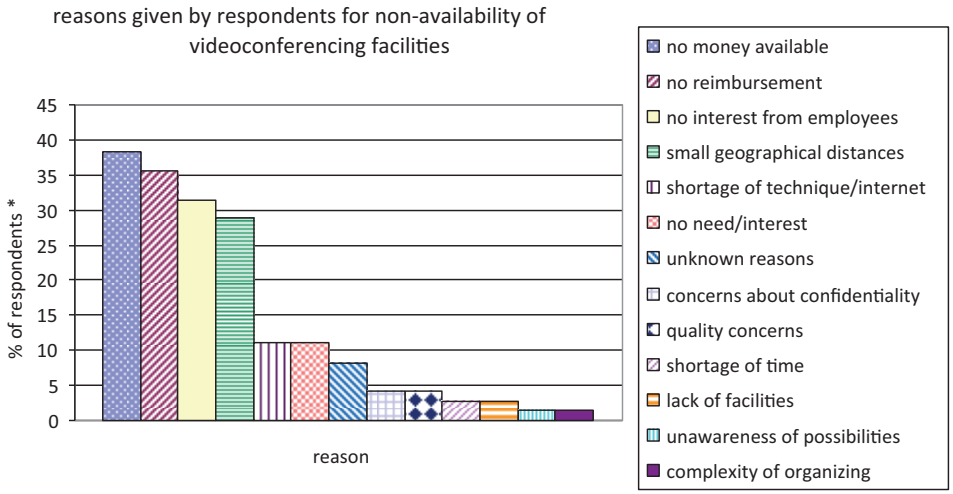
Availability and use of videoconferencing facilities

We investigated which part of respondents had videoconferencing facilities available for performance of patient consultations: 25% (n=24 of 97, of whom 17 clinical geneticists and 4 genetic counselors) had such facilities available for use. These respondents originated from a wide range of countries (n=12), most of them (n=13; 54%) from western Europe. The most frequently indicated reasons for videoconferencing facilities not being available in respondents' departments were lack of money (n=28; 38.4%), lack of reimbursement (n=26; 35.6%), lack of interest by counselors (n=23; 31.5%), and lack of need because of small geographical distances (n=23; 28.8%), but a wide range of other reasons were also mentioned (Figure 4a).

Where videoconferencing facilities were available, we analyzed the extent to which these facilities were actually used, and the reasons for non-usage. Only 8% (2 of 24) of these respondents actually made use of videoconferencing facilities in direct patient care (genetic counseling) rather than in supportive patient care (eg, multidisciplinary consultation or expert consultation; 10 of 24 (41.7% respondents). The reasons given for not using the available facilities in direct patient care were mostly lack of need because of small distances (n=10; 45.5%), and not having a patient population suitable for videoconferencing (n=6; 27.3%) (Figure 4b).

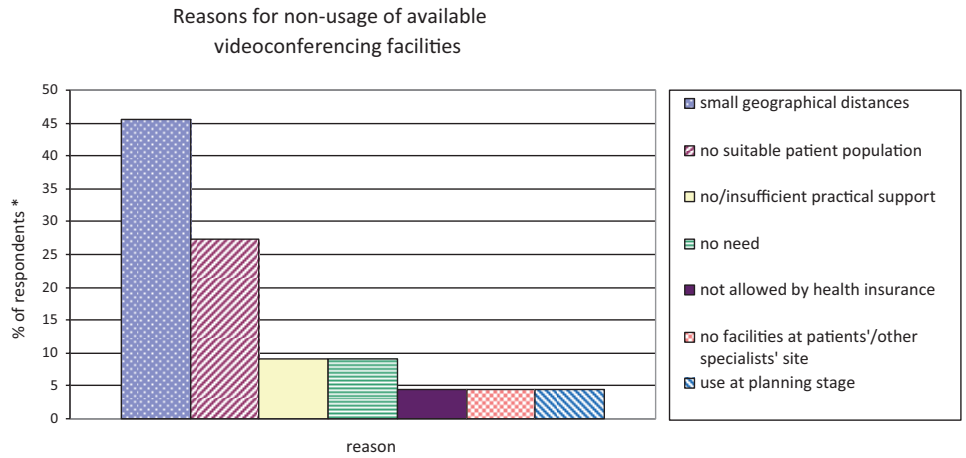
Figure 4.

a.



*: % represents the proportion of respondents who stated each reason relative to the total number of respondents without availability of videoconferencing facilities (n=73). Respondents could indicate more than one reason

b.



*: % represents the proportion of respondents who stated each reason relative to the total number of respondents who had videoconferencing facilities available but did not use them in direct patient care (n=22). Respondents could indicate more than one reason

Interest in Telegenetics initiatives

Respondents were asked whether they would like to participate in a working group or attend a meeting on Telegenetics and 55% of respondents indicated their interest.

DISCUSSION

Our results suggests that clinical genetic services currently have limited availability and use of telemedicine, but also that many of our respondents are interested in learning more about it. Perhaps not surprisingly because of its well-established position in everyday life, the telephone is the most-used modality in direct patient care, used by 17% of respondents, mainly for genetic counseling. Videoconferencing facilities were used by a much smaller proportion, mostly in supportive professional activities and only rarely in direct patient care. Northern and western European respondents had greater availability and therefore more use of telegenetics modalities than those from eastern and southern Europe, although the numbers are too small to draw firm conclusions.

We were unable to determine the response rate of clinically active genetic professionals among the members who received our survey because the professional backgrounds of the non-responders were not known. It is possible our results were biased towards genetics professionals who are interested in telegenetics as they might be more likely to respond. This could mean that professionals' uptake rates of telegenetics are even lower than our survey suggests, but also that the telegenetics uptake rates at the institutional level are actually higher. However, we believe our survey does give a valuable snapshot of current

practice in many European countries and clinical genetic institutions, from which we can conclude that there is room for expansion.

Besides providing value in direct patient care, telegenetics is also seen as a valuable tool in supportive patient care, both being in use by our respondents. Given the expanding discussion about 'mainstreaming' genetics, we believe that telegenetics could be a useful modality and improve genetics engagement by other medical specialisms. It can provide accessible and widely available contact options for multidisciplinary and peer consultation, as well as pre- and post-test online genetic counseling for patients from other medical specialists or general practitioners by trained genetic professionals. Finally, telegenetics could have an important role in recontacting former patients in light of new information from previous diagnostic testing. Using telegenetics to connect laboratories, counselors, patients, and other health-care professionals could facilitate more routine recontacting than currently takes place.[12,13]

We concluded three main points from our survey: First, the current availability and use of telegenetics is limited and could be extended, even without the purchase of new equipment, since there were discrepancies between availability and use. Second, as figure 3 illustrates each different telegenetic modality is used for many types of activities even though respondents might have listed preferential use in particular situations. And third, cooperation, education and finally practical guidelines might be helpful for successful telegenetics application. More widespread use of telemedicine in genetics might be presumed right now, but this seems not to be so. This snapshot of the current state of play and of the barriers professionals experience could be useful in planning future implementation.

Respondents indicated various barriers to greater current use, that could be divided in (1) lack of perceived suitability and need, (2) practical constraints (eg, lack of resources and supportive regulations), and (3) lack of professional support/knowledge. Because both the availability and use of videoconferencing by our respondents were still limited, and consequently most respondents lack experiences with telegenetics, it could be that the barriers they reported were perceived rather than real. This could, for example, be the case for the argument of having no suitable patient population: contrary to the perceptions of respondents, telemedicine is, in our experience, particularly suited to clinical genetics because for many patients, especially in oncogenetics, cardiogenetics, and neurogenetics, the consultation consists largely of communication, rather than requiring technical aids or physical examination. However, online genetic consultation does not preclude examination – dysmorphologic evaluation, among other genetic applications, has been reported as successful.[14-17]

Another reason mentioned by respondents for not using telemedicine facilities is because they did not perceive a need. This could reflect current adequate coverage of their own referral patch by in-person care, or indeed that there is a perception that in-person counseling is the gold standard, and telemedicine should only be applied when in-person

counseling is not possible. This aspect needs further exploration. We consider telegenetics holds potential in terms of improving patient access to health professionals and adapting to their wishes or preferences: It allows patients for example to receive genetic care in their own home at a time convenient to them, thereby avoiding travelling time and costs.[4,18] Moreover, telegenetics could allow for increased flexibility and efficiency for counsellors too. Previous research has shown that perceptions and evaluations of telegenetics vary between patients and professionals: patients mainly judge telegenetics initiatives as very positive, while professionals are generally positive, but are also aware of communication and technical restrictions.[6,7,9,11]

We do not envisage or recommend that telegenetics replaces in-person consultations completely, but it will be important to assess in which situations both patients and professionals might use it as a good alternative or supplement to regular care. While we discussed all telegenetics modalities collectively, in some instances videoconferencing might be preferable to telephone counseling, because it allows for the use of different visual aids and assessment of, at least some, non-verbal communication, which is often considered very valuable in genetic consultation.[19,20] However, telephone counseling has a clearly established role and seems to be effective in satisfying some patient needs,[21,22] and moreover, can be used effectively in conjunction with in-person consultations. It is likely that different situational requirements will require different modalities. For example, certain videoconferencing modalities might be used preferentially to others; videoconferencing-only for a straightforward follow-up discussion, but specialized workstation with attached devices for detailed evaluation and physical examination. Wider discussion on the relative merits of different modalities could help clinically active professionals to plan which telemedicine modality to use and when.

Existing practical barriers, for example, lack of available facilities, money, manpower, and knowledge, are important aspects to address, when considering setting up or expanding telegenetics initiatives. The ways to overcome these barriers will differ in different settings/countries, and influenced for example by geographical distance, economic resources at the professionals' and patients' disposal, the number and distribution of available professionals, and national regulations concerning e-health initiatives. Some obstacles might be overcome by cooperation and exchange of experiences/knowledge between professionals. The introduction of electronic health records in many hospitals in the near future, and parallel developments in the field of hospital-ICT are likely to contribute to increased telegenetics facilitation. Moreover, the use of e-health applications in recent years is being facilitated by several European governments, research funding agencies, and health insurance companies. It will be important to ensure that privacy aspects are well covered in any of these developments. Improving the quality of telegenetics applications, and adapting to data protection requirements of hospitals and health systems will be important. According to the American Telemedicine Association core operational guidelines, a connection should for example at least be encrypted to ensure a secure exchange of sensitive patient information

(http://www.american.telemed.org/docs/default-source/standards/core-operational-guidelines-for-telehealth-services.pdf?sfvrsn=6). Practical experiences by both patients and professionals will clarify and further solve the privacy issues encountered in telegenetics.

A substantial proportion of our respondents were interested to improve their knowledge on telegenetics, suggesting that they are considering or willing to integrate this other way of working in their practice, but need help in achieving it. The importance of gaining more widespread knowledge on telegenetics, and of increasing its prominence and integration with other regular care modalities is underlined by various examples, like positive patient evaluations of telegenetics, developments in present-day society ensuring that more and more people gain access to online resources, the scarcity of genetics professionals in many countries, and the changing context/dynamics within clinical genetics.

To make telegenetics successful genetics professionals will need to be convinced that it can at least be considered equivalent to in-person consultation in some settings and thus part of 'good care', besides being adequately supported in different ways. Only then they will be inclined to implement it in daily practice.[23-25]

We consider that the time has come to integrate telegenetics into patient care more routinely, thereby maintaining quality of care and effectiveness, increasing efficiency, and respecting the importance of patient-centeredness. This survey, as well as the educational satellite meetings on telegenetics we organized during the 2013 and 2014 ESHG conferences in Paris and Milan respectively, are the first steps we took in this respect. We have set up an online telegenetics discussion group on the platform LinkedIn, which currently has 20 members from in and outside Europe (requests for membership to corresponding author). Moreover, it would be valuable to involve both professionals and patients in establishing and expanding telegenetics initiatives and in establishing practical guidelines. In the United States, these have been developed for various medical disciplines by the American Telemedicine Association (http://www.americantelemed.org/resources/standards/ata-standards-guidelines), but in Europe this relevant information has, to the best of our knowledge, not been compiled yet.

To conclude, telegenetics use in Europe seems to be limited in clinical genetics practice so far, with several practical, and possibly also psychological, barriers contributing to this. In our opinion, expanding the use of telegenetics is needed in the light of current developments in genetics and today's society, and there is interest in expansion and sharing of knowledge about telegenetics between genetics professionals at an international level. Establishing a European Working Group on telegenetics and developing guidelines could be the next steps for creating optimal conditions for a wider application of telegenetics facilities and for improving its quality.

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REFERENCES

1. Wade VA, Karnon J, Elshaug AG, Hiller JE. A systematic review of economic analyses of telehealth services using real time video communication. *BMC Health Serv Res* 2010;10:233.
2. Dellifraine JL, Dansky KH. Home-based telehealth: a review and meta analysis. *J Telemed Telecare* 2008;14(2):62-66.
3. Myers KM, Valentine JM, Melzer SM. Child and adolescent telepsychiatry: utilization and satisfaction. *Telemed J E Health* 2008;14(2):131-137.
4. Mehrota A, Paone S, Martich GD, Albert SM, Shevchik GJ. Characteristics of patients who seek care via evisits instead of office visits. *Telemed J E Health* 2013;19(7):1-5.
5. Merell R.C. Editorial:Telemedicine for vulnerable populations. *Telemed J E Health* 2014;20(10):885-886.
6. Gray J, Brain K, Iredale R, Alderman J, France E, Hughes H. A pilot study of Telegenetics. *J Telemed Telecare* 2001;7 suppl 2:68-70.
7. Iredale R, Gray J, Murtagh G. Telegenetics: a pilot study of video-mediated genetic consultations in Wales. *Int J Med Market* 2002;2(2):130-135.
8. Coelho JJ, Arnold A, Nayler J, Tischkowitz M, MacKay J. An assessment of the efficacy of cancer genetic counselling using real-time videoconferencing technology (telemedicine) compared to face-to-face consultations. *Eur J Cancer* 2005;41:2257-2261.
9. d'Agincourt-Canning L, McGillivray B, Panabaker K, et al. Evaluation of genetic counseling for hereditary cancer by videoconference in British Columbia. B C Med J 2008;50(10):554-559.
10. Zilliacus E, Meiser B, Lobb E, Dudding TE, Barlow-Stewart K, Tucker K. The virtual consultation: practitionars' experiences of genetic counseling by videoconferencing in Australia. *Telemed J E Health* 2010;16(3):350-357.
11. Hilgart JS, Hayward JA, Coles B, Iredale R. Telegenetics: a systematic review of telemedicine in genetics services. *Genet Med* 2012;14(9):765-776.
12. Aronson SJ, Clark EH, Varugheese M, Baxter S, Babb LJ, Rehm HL. Communicating new knowledge on previously reported genetic variants. *Genet Med* 2012;14(8):713-719.
13. Hunt K. Individualizing the informed consent process for whole genome sequencing: A patient directed approach [dissertation]. Arizona: Arizona state university, 2013.
14. Hopper B, Buckman M, Edwards M. Evaluation of satisfaction of parents with the use of videoconferencing for a pediatric genetic consultation. *Twin Res Human Genet* 2011;14(4):343-346.
15. Elliott AM, Mhanni AA, Marles SL, Greenberg CR, Chudley AE, Nyhof GC, Chodirker BN. Trends in Telehealth versus on-site clinical genetics appointments in Manitoba: a comparative study. *J Genet Couns* 2012;21(2):337-344.
16. Lea DH, Johnson JL, Ellingwood S, Allan W, Patel A, Smith R. Telegenetics in Maine: successful clinical and educational service delivery model developed from a 3-year pilot project. *Genet Med* 2005;7(1):21-27.
17. Stalker HJ, Wilson R, McCune H, Gonzalez J, Moffett M, Zori RT. Telegenetic medicine: improved access to services in an underserved area. *J Telemed Telecare* 2006;12(4):182-185.
18. Gardner MR, Jenkins SM, O'Neil DA, Wood DL, Spurrier BR, Pruthi S. Perceptions of video-based appointments from the patient's home: a patient survey. *Telemed J E Health* 2014; epub ehead of print.
19. Bradbury AR, Patrick-Miller L, Fetzer D, Egleston B, Cummings SA, Forman A, Bealin L, Peterson C, Corbman M, O'Connell J, Daly MB. Genetic counselor opinions of, and experiences with telephone communication of BRCA1/2 test results. *Clin Genet* 2011;79:125-131.
20. Madlensky L. Is it time to embrace telephone genetic counseling in the oncology setting? *J Clin Oncol* 2014;32:611-612.

21. Platten U, Rantala J, Lindblom A, Brandberg Y, Lindgren G. The use of Telephone in genetic counseling versus in-person counseling: arandomized Study on counselees' outcome. *Fam Cancer* 2012;11(3):371-379.
22. Sutphen R, Davila B, Shappell H, Holtje T, Vadaparampil S, Friedman S, Toscano M, Armstrong J. Real world experience with cancer genetic counseling via telephone. *Fam Cancer* 2010;9(4):681-689.
23. Whitten P, Love B. Patient and provider satisfaction with the use of telemedicine: overview and rationale for cautious enthusiasm. *J.Postgrad Med* 2005;51:294-300.
24. Grigsby B, Brega AAG, Bennett RE, Devore PA, Paulich MJ, Talkington SG et al. The slow pace of interactive video Telemedicine adoption: the perspective of Telemedicine program administrators on physician participation. *Telemed J E Health* 2007;3(6):645-656.
25. Barton PL, Brega AG, Devore PA, Mueller K, Paulich MJ, et al. Specialist physicians' knowledge and beliefs about Telemedicine: a comparison of users and nonusers of the technology. *Telemed J E Health* 2007;13(5):487-499.

Chapter 5

Telegenetics use in presymptomatic genetic counselling: patient evaluations on satisfaction and quality of care

Ellen Otten, Erwin Birnie, Adelita V Ranchor and Irene M. van Langen

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ABSTRACT

In recent years, online counselling has been introduced in clinical genetics to increase patients' access to care and to reduce time and cost for both patients and professionals. Most telegenetics reports so far evaluated online oncogenetic counselling at remote health centres in regions with large travelling distances, generally showing positive patient outcomes. We think online counselling – including the use of supportive tools that are also available during in-person counselling – of presymptomatic patients in their homes can also be feasible and valuable for patients in relatively small regions. We performed a single-centre pilot study of online genetic counselling for 57 patients who were presymptomatic cardiogenetic (n=17), presymptomatic oncogenetic (n=34), and prenatal (3 couples). One-third of presymptomatic patients we approached consented to online counselling. Patient evaluations of practical aspects, satisfaction and psychological outcomes were assessed and compared with a matched control group. Patients managed to fulfil the preparations, were significantly more satisfied with their counsellor and counselling session than controls and were satisfied with the online counselling more than they expected to be beforehand. Psychological outcomes (decreased anxiety and increased control) did not differ with control patients. Technical problems occurred in almost half of online sessions. Nonetheless, online counselling in patients' homes proved to be feasible and was appreciated by a substantial part of presymptomatic patients at our genetics centre in the Netherlands. Based on these outcomes, we conclude online counselling can be a valuable addition to existing counselling options in regular patient care.

INTRODUCTION

Telemedicine applications have recently been introduced in clinical genetics (generally referred to as telegenetics), meaning the remote counselling or evaluation of patients in real time by video and audio applications. The underlying reasons for its introduction concern increased access and efficiency of care.

Currently, genetics departments are facing efficiency measures, cost reductions and shortage of clinical genetic professionals. Simultaneously, the widespread introduction of next-generation sequencing is increasing the number of requests for and yield of genetic counselling and testing. Literature reports suggest that telegenetic care can be useful, patient-friendly, effective, and psychologically acceptable for various indications in the light of economic and personnel scarcity on the one hand, and increasing awareness and counselling requests from patients spread over a large geographical area on the other hand.[1-7]

So far, almost all reports of telegenetics programmes described counselling between professionals at a central clinic and patients at regional clinics, with a genetic counsellor present, in regions with large travelling distances.[1-6,8-11] Our pilot project differs from previous reports by (1) counselling sessions taking place in patients' homes, (2) covering patients in a non-remote area and (3) having cardiogenetic as well as previously reported oncogenetic and prenatal counselling. We think the appliance of telegenetics could also be successful in relatively small countries in the aforementioned respects and, moreover, that online counselling from patients' homes without a counsellor on site could be feasible and advantageous for some of our patients. Therefore, we evaluated our application for online genetic counselling from the patients' perspective. It included various supportive tools that are also available during in-person genetic counselling, for example, simultaneously viewing disease information brochures or supportive drawings and the webcam image of the involved patient and counsellor on-screen. We evaluated the quality of care and patients' satisfaction with the counselling sessions and counsellors: Changes in psychological outcomes and satisfaction with counselling of online patients should be at least similar, on average, to those of controls given regular counselling at our outpatient department (OPD). The satisfaction with online counselling should, on average, be at least equal to patients' expectations, with a moderate or high satisfaction level. This would be in line with the generally reported mean satisfaction level of patients with counselling (≥7 on a 1-10 scale). As part of our evaluation, we also assessed patients' opinions about saliva self-collection for DNA testing.

MATERIALS AND METHODS

Online counselling application

The online counselling application used in our study was established in association with the 'myCoachconnect' company (www.mycoachconnect.com). This secure platform contains several functions in addition to videoconferencing, which aim to support the information exchange during counselling, and to allow future access for patients to this information. These include a notepad for counsellors and notebook for patients, transfer and viewing of disease information brochures and visiting websites together during counselling, and a secured email and patient registration/invitation system (supplemental material figure 1a-f). The application satisfied the safety protocols of our university medical centre (UMC). Privacy protocols were drawn up in consultation with the centre's ICT and personal privacy protection advisors.

Setting and study design

We offered online genetic counselling in the region of northern Netherlands' covered by our department at the UMC Groningen. It has about 6000 new referrals each year, with a mean annual increase of 6% in recent years. Regular outpatient clinics are held in four regional hospitals at mean distance of 78 km. We performed a single-centre matched cohort study, with pre- and post-counselling measurements. We matched by sex and indication (frequency matching), and compared the expectations and outcomes of 57 patients receiving online counselling with those of 71 controls receiving in-person counselling for cardiogenetic and oncogenetic cascade screening for a known familial mutation, and urgent prenatal counselling and testing. Other inclusion criteria were as follows: (1) an appointment comprising a full genetic counselling session; (2) planned at least two days after referral; (3) a maximum of two participants per session on the patient's side; (4) access to a computer with a webcam and internet (for online patients); and (5) verbal consent given by online patients during the first telephone contact and digital consent by creating a personal account in our online platform. Delivery of DNA testing results for both the online and control group was in accordance with the applicable standard for result delivery for each separate indication and test outcome (carrier or non-carrier), and the possible preferences of the involved counselor and/or patient. The study protocol was reviewed by our institutional ethics committee, who found formal ethical consideration not required.

Online patients and procedures

We included online patients between August 2011 and April 2012. The online group was completed first and then the control patients were included until matching to the online group was achieved. Patients were informed by telephone about the study, and asked whether they would be interested in online counselling. Pre-counselling contact with those who agreed included the following (figure 1a): (1) an email with appointment information,

a log-in for the online platform, a telephone number and email address for questions and practical support, and a hyperlink to an instruction video about the online counselling process; (2) an email with a short digital form for family information to complete and return, after patients confirmed their account; (3) telephone contact with a case manager a few days before the session to check their connection and access to the online counselling. Patients were also sent online pre- and postcounselling study questionnaires, and a paper laboratory form with a saliva self-collection kit, which was only suitable for testing of mutations or small deletions. If patients had to be tested for a larger deletion, they were sent a laboratory form for blood withdrawal locally after counselling.

Control patients

Control patients who had conventional counselling at one of our OPDs and had not previously been invited to participate in the online counselling group were included between December 2011 and December 2012 (oncogenetic cardiogenetic) and March to April 2013 (prenatal). In the overlapping period (December 2011 to April 2012), we alternated recruiting online and control patients weekly. Controls were sent online study questionnaires, but for logistical reasons prenatal controls were asked to complete paper questionnaires immediately before counselling, and within a couple of days afterwards.

Patient measurements

The online study questionnaires for both groups had to be completed one week before and within a couple of days after counselling, and covered the following measurements (Table 1):

Table 1. Overview of questionnaire designs

Measurement instrument /aspect	Online before	Online after	Control before	Control after
Personal information	x	x	x	x
PC/internet/online consulting experience	x	x	x	
Online counselling – general	x	x		x
Practical aspects of online counselling		x		
Patient responsibilities		x		x
TSQ	x	x		x
PPC *	x	x	x	x
STAI *	x	x	x	x
CGS *		x		x
Content of counselling session		x		x

* = standard validated questionnaire; TSQ= Telemedicine Satisfaction Questionnaire; PPC = Personal Perceived Control questionnaire; STAI = State-Trait Anxiety Inventory; CGS = Clinical Genetics Satisfaction indicator

Patient characteristics
Data on patients' age (in years), sex, educational level (low/high) and the indication for genetic counselling (cardiogenetic/oncogenetic/prenatal) were recorded. The patients' experience with computers, internet and online communication were assessed by various statements on a 5-point Likert scale (range: "totally disagree" to "totally agree") and by their answers to multiple choice questions on their frequency of use and experience with online communication.

Satisfaction with counselling and content
Patients' satisfaction with genetic counselling was measured using the seven-item Clinical Genetics Satisfaction indicator (CGS), with a 1-5 Likert scale response mode. Higher scores indicate greater satisfaction. The Dutch Clinical Genetics Association adopted the CGS. The English version shows excellent internal consistency in a clinical genetic setting (α=0.91).[12] The internal consistency in our present study was 0.98. Patients also had to indicate how far ten aspects of the genetic disorder concerned were addressed during their counselling session (5-point Likert scale; range "far too little" to "far too much").

Psychological measures
We used the validated Dutch nine-item version of the Perceived Personal Control (PPC) questionnaire to assess perceived control of our patients before and after counselling (α = 0.79-0.81)[13] on a 0-2 Likert scale. Higher scores indicate greater levels of perceived control. We used the Dutch six-item version of the State and Trait Anxiety Inventory (STAI) to assess experienced anxiety by patients before and after counselling, on a 1-4 Likert scale (α =0.83).[14] The STAI has been validated in a clinical genetic setting (α = 0.82).[15] Higher scores indicate greater levels of anxiety.

Expectations and evaluation of online counselling
All patients' expectations of online counselling were rated by various statements (eg, wanting to see the counsellor in-person after online counselling, intending to use online counselling more often in the future) on a 5-point Likert scale (range "totally disagree" to "totally agree"). They were also asked to describe their expected advantages/disadvantages of online versus in-person counselling (eg, time saving, feeling more/less at ease and being more/less focussed on the counselling). Afterwards, online patients were asked about these aspects again, and also to indicate if and how online counselling had to be improved to make it equivalent to OPD counselling, to weigh the advantages of online counselling against its disadvantages and to give an overall judgement of online counselling on a scale of 1-10 (10 being most positive).

Telemedicine satisfaction

The Telemedicine Satisfaction Questionnaire (TSQ) was used to measure expected satisfaction with Telemedicine for all patients and online patients' perceived satisfaction.[16] Higher scores (Likert scale 1-5) indicate greater satisfaction, with 4 representing moderately satisfied and 5 highly satisfied. We translated the validated 14-item English TSQ into Dutch in a validated way, using 'back translation'. We removed item 7 ('I think the healthcare provided via telemedicine is consistent') because it did not apply to our setting. We adapted the item formulation so that we could use the TSQ both before and after counselling. We calculated and compared mean item scores before and afterwards, and had internal consistencies of 0.88 and 0.72 respectively.

Evaluation of practical issues and responsibilities

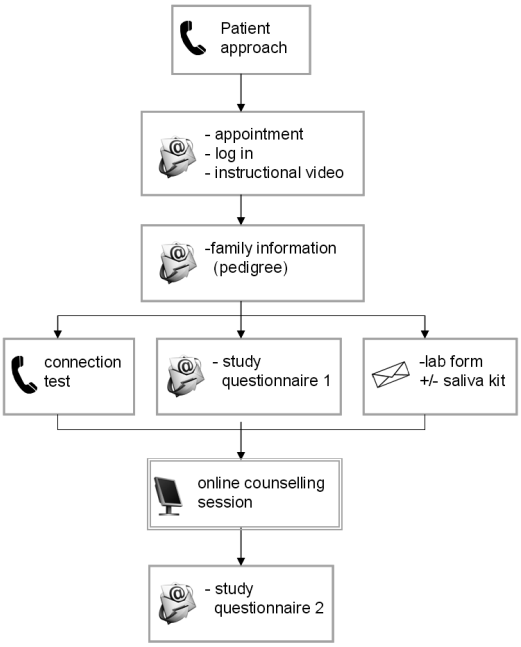
Patients were asked several multiple choice questions about their experiences with preparing for online counselling (eg, clearness of the instruction emails and movie and preparation time required), the occurrence of technical problems during the session (eg, problems occurred yes/no and temporary/continuous, and distracting from counselling yes/no), and their acceptance of patient responsibility for various aspects of online counselling: planning an appointment, preparation before counselling, proper functioning of the application during the session and initiating DNA testing (1-5 Likert scale; range "not acceptable at all" to "very acceptable").

Data analysis

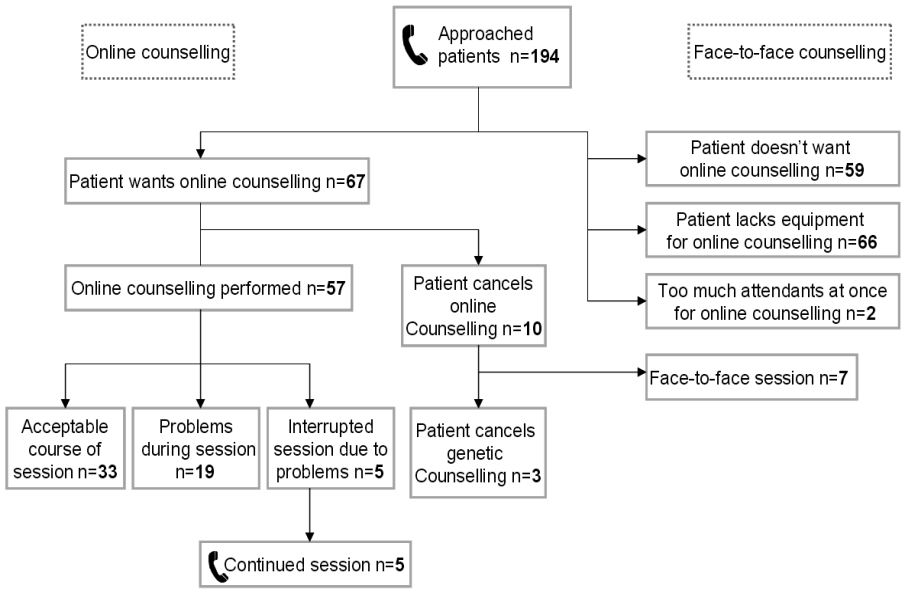
For normally distributed variables we used mean (SD). Median (IQR) was used for variables with skewed distribution and n (%) was used for both ordinal and nominal variables. Mean item scores per patient were calculated for the questionnaires PPC, STAI, CGS and TSQ, if at least two-thirds of each were completed. Adjusted mean differences between groups were estimated with linear regression analysis with mean item score as dependent variable and gender and indication (matching factors), group (online/control) and educational level as independent variables. We calculated effect sizes by dividing the difference of mean scores over time or between groups, by the mean SD of both time points or the pooled SD of both groups. We used paired samples and independent sample t-tests to analyse outcomes of normally distributed variables and Chi-square test or Fisher's exact test for outcomes of all categorical variables.

Figure 1. Flow schemes for the online counselling process

a. online counselling process



b. patient uptake when offered online counselling



RESULTS

Patient outcomes

Of the patients we approached, 35% (n=67) chose for online counselling (Figure 1b); 65% were excluded, because they lacked the proper equipment for online counselling (34%; n=66; mean age 51.5 years; 44% male), or preferred in-person counselling (31%; n=59; mean age 47.2 years; 44% male). Eventually, 57 patients (mean age 44 years; 53% male) had online counselling. Ten patients (mean age 42.9 years; 20% male) cancelled their appointment for various reasons: no longer interest in counselling and testing (n=3), prefer OPD session on second thought (n= 2), join a relative or quicker appointment elsewhere (n=3), or technical problems with home equipment (n=2). Of 102 OPD patients invited to complete the online pre- and post counselling survey, 69.6% (n=71) cooperated and was included in the control group.

Patient characteristics

The online counselling group comprised 57 patients (51 counselling sessions) of which 17 had cardiogenetic (cardiomyopathy, long QT syndrome) and 34 had oncogenetic counselling (BRCA1/2, Lynch syndrome). Three couples (6 patients) had genetic counselling during pregnancy because of foetal anomalies. Online patients and controls did not differ significantly regarding sex, age, educational level or indication for counselling (Table 2). There were also no significant differences between the groups for reported frequency of computer use, experience with online communication for work and/or private purposes, frequency of online communication for work and/or private purposes, and experience with online communication with healthcare professionals other than by email. However, before their counselling session, significantly more patients in the online group had communicated by email with healthcare professionals in general compared to controls (25% versus 10%; p=0.047), and they seemed to be more open and comfortable overall in using and extending their computer use. The mean scores for all related questionnaire items differed significantly between the two groups (Supplementary Table 1).

Table 2. Characteristics of patient groups

	Online	Control
Number of patients	57	71
Sex; % male/female	53/47	51/49
Mean age in years (range)	44 (22-74)	47 (19-74)
Educational level; % low/high	51/49 (4 missings)	68/32 (2 missings)
Indication: % cardiac/oncology/prenatal	30/60/10	24/62/14

Satisfaction with counselling (CGS indicator) and content

Online patients had a significantly higher mean CGS item score (reflecting greater satisfaction) after counselling than controls (Table 3a). However, satisfaction with the counselling content did not differ significantly between the two groups: mean item scores were 2.96 (SD 0.12) for online patients and 2.91 (SD 0.30) for controls. This indicates that both groups found that all aspects of the heritable disease concerned were sufficiently discussed overall.

Table 3. Patient satisfaction and psychological outcomes: differences within and between both patient groups

a. Differences between groups

	Mean item score (SD; n)					
	Online	**Controls**	**Mean difference (SE) adjusted #**	**Mean difference (SE) unadjusted**	**Significance**	**Effect size**
TSQ before	4.11 (0.60;47)	2.84 (0.90;58)	1.21 (0.16)	1.28 (0.15)	**<0.001**	1.66
TSQ after	4.52 (0.40;47)	x	x	x	**x**	x
PPC before	1.15 (0.51;46)	1.07 (0.46;58)	0.11 (0.10)	0.08 (0.10)	0.44	0.17
PPC after	1.45 (0.50;46)	1.29 (0.46;58)	0.19 (0.10)	0.17 (0.10)	0.078	0.33
PPC change	0.30 (0.52;46)	0.21 (0.36;58)	0.07 (0.09)	0.09 (0.09)	0.28	0.21
STAI before	1.74 (0.57;46)	1.98 (0.58;58)	-0.20 (0.11)	-0.24 (0.11)	**0.033**	0.42
STAI after	1.64 (0.55;46)	1.88 (0.59;58)	-0.171 (0.114)	-0.24 (0.11)	**0.033**	0.42
STAI change	0.10 (0.43;46)	0.10 (0.35;58)	-0.03 (0.08)	-0.003 (0.08)	0.97	0.008
CGS after	4.91 (0.23;53)	4.66 (0.91;61)	0.27 (0.14)	0.25 (0.12)	**0.040**	0.42

TSQ= Telemedicine Satisfaction Questionnaire; PPC = Personal Perceived Control questionnaire; STAI = State-Trait Anxiety Inventory; CGS = Clinical Genetics Satisfaction indicator. All outcomes were tested by independent sample t-test; significant differences between groups are shown in bold, significant change P< 0.05; Effect size is difference of mean scores between groups divided by the pooled standard deviation. # Adjusted mean differences were measured by linear regression, adjusted for sex, counselling indication, educational level, and counselling type (online versus in-person at outpatient department).

b. Differences within groups over time

	Mean change (n)	Standard deviation	Significance	Effect size
TSQ change online	0.41 (47)	0.57	**<0.001**	0.82
PPC change online	0.30 (46)	0.52	**<0.001**	0.59
PPC change controls	0.21 (58)	0.36	**<0.001**	0.46
STAI change online	0.10 (46)	0.43	0.132	0.18
STAI change controls	0.10 (58)	0.35	**0.033**	0.17

TSQ= Telemedicine Satisfaction Questionnaire; PPC = Personal Perceived Control questionnaire; STAI = State-Trait Anxiety Inventory. All outcomes were tested by paired samples t-test; significant changes pre-/post-counselling within groups are shown in bold, significant change P< 0.05; effect size is difference of mean scores over time divided by the mean standard deviation of both time points.

Psychological outcomes

The mean change of PPC item score for online patients (after the counselling session compared to beforehand) did not differ significantly from controls (Table 3b). The mean PPC item score for both online and control patients was significantly higher after counselling than beforehand. The respective effect sizes were of moderate magnitude. The mean change of STAI item score after counselling compared to did beforehand not differ significantly between online and control patients. Although the STAI mean item scores only changed significantly for the control group and not for the online group, the effect sizes were both < 0.20, indicating a negligible change in both groups. Notably, the mean STAI item scores of online patients before and after counselling were significantly lower than those of controls. Scores of online patients having and not having technical problems during their session did not differ significantly with respect to their mean CGS item score and mean change of PPC and STAI scores.

Expectations and evaluation of online counselling:

Expectations of online counselling

Online patients' scores on their expectations and experiences on various aspects of online counselling were significantly higher after compared with before their session on feeling comfortable with online counselling and the content-delivery during the session, and significantly lower on wishing to see their counsellor in an additional OPD session (Table 4).

Expected advantages of online counselling mostly mentioned by 42 online patients Were as follows: less time/travelling needed (n=40), lower cost (n=6), increased flexibility (n=5), being in familiar environment/being more relaxed (n=4) and the possibility of recording the session and the online availability of information (n=4). Fifteen online patients expected disadvantages of online counselling beforehand, mostly being less personal contact due to the literal distance between counsellor and patient (n=11), less non-verbal communication (n=3) and dependence on technology functioning well (n=4).

Table 4. General expectations and experiences of online counselling

	Mean score Before # (SD)	Mean score after # (SD)	Mean change# (SD)	Significance*
Comfortable with online talking about genetic testing (n=48)	3.94 (0.84)	4.63 (0.76)	0.68 (8.83)	**<0.001**
Wish to see counsellor in-person on second occasion (n=48)	3.02 (0.91)	2.17 (1.14)	0.85 (1.22)	**<0.001**
Good delivery of content during counselling session (n=47)	4.38 (0.77)	4.85 (0.36)	0.47 (0.80)	**<0.001**
Good emotional interaction during counselling session(n=48)	3.98 (0.86)	4.25 (0.98)	0.27 (1.25)	0.14
Equality of online counselling with in-person counselling (n=48)	3.69 (0.93)	4.04 (1.07)	0.35 (1.28)	0.061

Mean score: 1 = totally disagree, to 5= totally agree; changes measured by t-test; * significant change P < 0.05

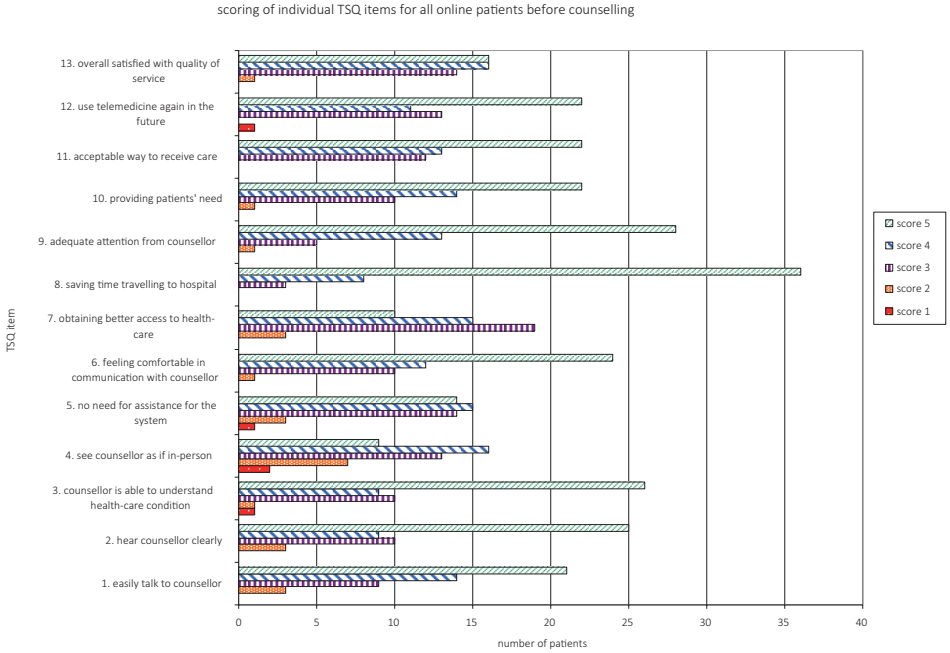
Evaluations of online counselling

After their session, the most raised advantage again was less time/travelling needed (n=43). The advantages of familiar environment (n=12), saving cost (n=9), possibility of recording/ online availability of information (n=4) and no need to take a day off or to arrange a babysitter (n=3) were all mentioned more often after counselling than beforehand. Flexibility (n=3) was mentioned less often. Afterwards, 28 patients indicated disadvantages such af lack of personal contact (n=18), dependence on technology (n=12), installation/complexity of the application (n=2) and less non-verbal communication (n=2).

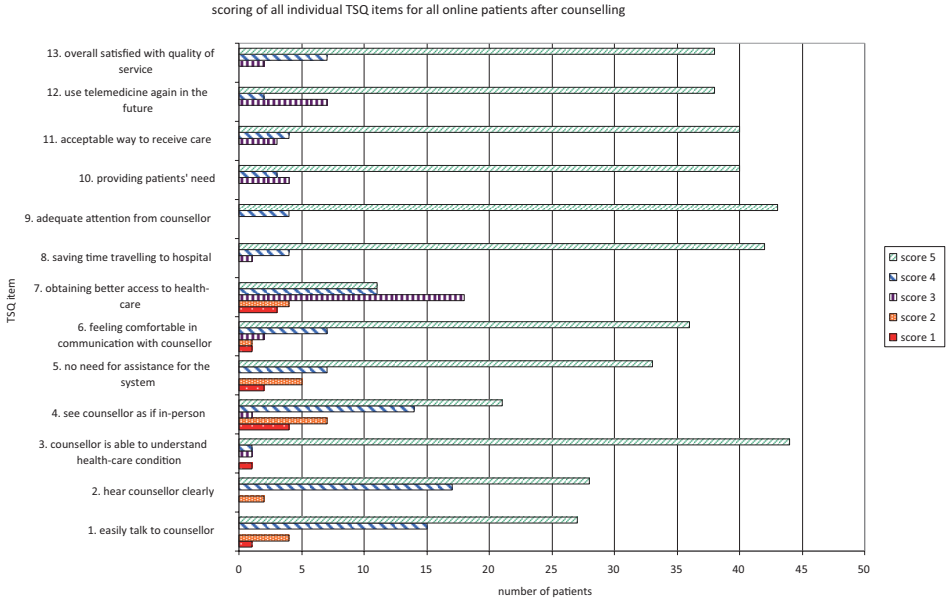
After the counselling session, online patients rated the relative weight they assigned to the advantages and disadvantages of online counselling (1=highly disadvantageous and 10=highly advantageous), and their mean overall score for the session on a 1-10 scale. Mean scores were 8.4 (SD 1.05; range 5-10) and 8.3 (SD 0.95; range 6-10) respectively; perceived advantages overweighed the disadvantages of online counselling and patients were satisfied with their session overall. All patients reported having had enough opportunity to ask questions during the counselling, and 85% would recommend online counselling to friends (mean scores 4.94 (SD 0.24; n=52), and 4.54 (SD 0.75; n=52) respectively, scale 1-5). All online patients' suggestions for improvement were on technical aspects, for example, more stable internet connections, less sound delay and better image quality.

Figure 2. Scores by online patients for individual Telemedicine Satisfaction Questionnaire (TSQ) items

a. Before counselling (n=47)



b. After counselling (n=47)



Telemedicine satisfaction

The mean TSQ item score of online patients before counselling (indicating their expected satisfaction with telemedicine) was significantly higher than that of controls. Online patients were also significantly more satisfied after their session than they had expected to be beforehand (Table 3a and b, Figure 2a and b). Of online patients, 72% had an increased mean score after counselling compared with beforehand. In addition, 91% had a mean itemscore ≥ 4 afterwards (n=47), indicating moderate to high satisfaction. Mean TSQ item score after counselling did not differ between those who had experienced technical problems during their session and those who did not.

The lowest scoring TSQ items, both beforehand and afterwards, were item 4 (seeing my healthcare provider as if in-person; mean score 3.49 and 3.87, respectively) and item 7 (obtaining better access to healthcare by telemedicine; mean score 3.68 and 3.49, respectively). The highest scoring items at both time points were item 8 (telemedicine saves time travelling; mean score 4.70 and 4.87, respectively) and item 9 (receiving adequate attention; mean score 4.45 and 4.91, respectively).

Evaluation of technical issues, DNA-testing, and patient responsibilities

37% of patients (21 of 57) reported technical problems during online counselling: These could be fixed completely during the session for five patients, and partly for four patients. For eight patients the problems could not be fixed, but the session could nevertheless be continued, whereas for four patients the session had to be broken off because of the problems. Some (7 of 21) indicated that the problems distracted them from the counselling. Most patients (n=9; 47%) could fix the problems together with their counsellor. Help from a family member (n=1; 5%), from an employee of the genetics department (n=3; 16%) and fixing the problems by themselves (n=2; 11%) were also reported. Most patients who had technical problems during their online session indicated being satisfied with the degree of support in preparing for the session (instruction emails (80%) and movie (88%) were clear) and managed well in fulfilling the preparations (85% did it all by themselves, 90% needed less than 10 minutes).

Regarding their experience with saliva collection for DNA testing, most (10/11) online patients reported it was easy to do and the kit contained clear instructions. Seven patients would choose DNA testing in saliva over blood in the future, because of the ease of doing it at home in their own time. Two patients would prefer giving a blood sample the next time for fear of doing something wrong and thinking that blood testing was a more exact technique than DNA testing in saliva.

All items addressing the acceptability of patient responsibility in preparing and performing an online counselling session were judged significantly more positively by online patients (after their session) compared to controls (range 82-96% versus 53-57% acceptability; $p<0.001$).

DISCUSSION

Overall, the criteria we set for patient outcomes in our study were met or even exceeded: patients who chose online counselling were satisfied with it, using our application with supportive tools. Moreover, their psychological outcomes (increased control and decreased anxiety) were comparable to controls and their satisfaction level with telemedicine was high, even higher than their positive expectations were beforehand. Despite having similar levels of computer experience, they seemed significantly more open and comfortable in using their computer and in extending its use than controls. They also had lower anxiety levels before and after counselling, and had significantly higher expectations of telegenetics than controls. Technical problems were reported by several online patients, but could mostly be fixed at the beginning or during the session, or the counselling session could still be completed despite the problems.

About one-third of approached presymptomatic patients consented to an online counselling session and were overall satisfied with the online counselling afterwards. One-third of approached patients could not be included, because they lacked the necessary equipment for online counselling. This uptake is comparable with a recent survey of Gardner et al.[17] on patient opinions regarding videoconsultations in patients' homes. In addition, Van de Belt et al.[18] recently reported that 21% of the general Dutch population would like to communicate with a health care provider via a webcam. These numbers will probably increase in the near future, as people become more used to online services and while new devices are generally equipped with a webcam. Our report and review of the literature indicate that patients who have used online consulting applications are satisfied with it.

Our patients' preference for online counselling was not limited to a certain age group or gender, and online patients' satisfaction with telemedicine was significantly higher than their expectations before counselling. This trend or expectation has also been suggested in the literature for professionals,[19,20] and similar outcomes can be expected for future patients who are initially reluctant to use telegenetics. For patients who are unable to use telegenetics, one could think of alternative options: performing online counselling at a location near the patient's home (eg, at their general practitioner's practice) or temporarily supplying patients with webcams upon making an appointment for online counselling. Several authors have warned to be cautious with the overall positive outcomes of online pilot studies, because they report on a selected patient group who are open to online counselling and who might feel privileged to have access to this new service.[20,21] However, as stated by Hilgart et al.,[20] when online counselling is used as an expansion to existing care services rather than as a replacement, the outcomes of patients who are open to adopting new technology are particularly relevant. We thus feel justified in being positive about their evaluations of telegenetics.

The major advantages of online counselling mentioned by our patients were time and cost savings, flexibility and being in their own, familiar environment. A substantial number

of patients experienced technical problems, but only few reported these as a disadvantage of online counselling. The disadvantage of having less personal contact with the counsellor, mentioned afterwards by almost one-third of online patients, was surprisingly not reflected in their mean satisfaction scores afterwards. This could suggest that our patients do not see personal contact with their counsellor as an essential part of genetic counselling and thus find this not necessary to be satisfied.

The psychological outcomes (PPC and STAI) of our online patients did not differ significantly from controls regarding changes after counselling versus beforehand. Moreover, these outcomes are comparable to previous reports on PPC and STAI outcomes for in-person oncogenetic counselling.[1,13,22-25] The mean anxiety level of online patients both before and after counselling was significantly lower than of controls. This might be an indication that patients who choose for online counselling are in general less anxious in nature than patients who choose for in-person counselling. Only three previous reports about online genetic counselling measured patient outcomes using validated standardized psychological measures, partly using the same as we did.[1,5,6] Their usefulness as references for our outcomes is limited. Previous studies reported on the importance of an already established counseling relationship upon performing an online counseling session.[7,19,26] Although without such an existing relationship, our online patients reported to be satisfied and showed similar psychological outcomes as controls. Moreover, although these outcomes were not part of our evaluation study, no online patients did have an additional counselling session apart from their online pre-test session, and the result sessions performed. Only one online patient, who turned out to be carrier of her familial mutation, had multiple contacts with one of the departments' social workers from about a year after testing. In the control group one patient had a single contact with one of the departments' social workers and one patient reported having initiated contact with her occupational social worker, shortly after they both turned out to be carriers from the familial mutations they were tested for. In addition, we assessed the ways testing results were delivered for both patient groups, as part of checking the course of the counselling process. This did not reveal clear differences between both groups. Finally, the only previous study on online genetic counselling from patients' homes did not widely measure psychological patient outcomes.[2] The home-based online counselling of our patients showed to be feasible: Instructions and self-installation were well accepted and technical problems could at least partly be managed, mostly together with genetic professionals. Similar outcomes were reported previously by Meropol et al.[2]

Our study has some limitations: results can be biased by only including patients who were open to and sufficiently equipped for online counselling, and by comparison with a matched control group instead of doing a randomized controlled trial. Furthermore, the positive outcomes in our patient group cannot automatically be assumed on the longer term and for other presymptomatic and symptomatic patient groups: further, more longitudinal research, and in larger and other patient groups, is needed to draw more certain conclusions

about the general quality and acceptability of online genetic counselling. Although, our online patients did not have additional counselling sessions compared with controls, and cardio and oncogenetic patients do comprise a large part of referrals in many genetic clinics. Finally, the inclusion of prenatal couples in our study was problematic due to the different way and urgent nature of referrals.

To conclude, our predefined aims are met, suggesting online counselling as a valuable addition to existing in-person care for some of our patients. Patients who chose for online counselling were satisfied with it, even more than they expected beforehand, despite the current technical imperfections. Moreover, the psychological outcomes of online patients were comparable to controls. Evaluation of our telegenetics application from professionals' and economic perspectives will be logical next steps. Furthermore, technical improvements and cooperation with hospital ICT are needed to improve the quality of our online counselling for future patients and to allow for its implementation in regular patient care.

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REFERENCES

1. Zilliacus EM, Meiser B, Lobb EA, Kirk J, Warwick L, Tucker K. Are videoconferenced consultations as effective as face-to-face consultations for hereditary breast and ovarian cancer genetic counseling? *Genet Med* 2011;13(11):933-941.
2. Meropol NJ, Daly MB, Vig HS et al. Delivery of internet-based cancer genetic counseling services to patients' homes: a feasibility study. *J Telemed Telecare* 2011;17:36-40.
3. Abrams DJ and Geier MR. A comparison of patient satisfaction with telehealth and on-site consultations: A pilot study for prenatal genetic counseling. *J Genet Couns* 2006;15(3):199-205.
4. Stalker HJ, Wilson R, McCune H, Gonzalez J, Moffett M, Zori RT. Telegenetic medicine: improved access to services in an underserved area. *J Telemed Telecare* 2006;12(4):182-185.
5. Coelho JJ, Arnold A, Nayler J, Tischkowitz M, MacKay J. An assessment of the efficacy of cancer genetic counselling using real-time videoconferencing technology (telemedicine) compared to face-to-face consultations. *Eur J Cancer* 2005;41(15):2257-2261.
6. Gray J, Brain K, Iredale R, Alderman J, France E, Hughes H. Letter to the editor: A pilot study of telegenetics. *J Telemed Telecare* 2000;6:245-247.
7. Hawkins AK, Creighton S, Ho A, McManus B, Hayden MR. Providing predictive testing for Huntington disease via telehealth: results of a pilot study in British Columbia, Canada. *Clin Genet* 2013;84(1):60-4.
8. Hopper B, Buckman M, Edwards M. Evaluation of satisfaction of parents with the use of videoconferencing for a pediatric genetic consultation. *Twin Res Hum Genet* 2011;14(4):343-346.
9. d'Agincourt-Canning L, McGillivray B, Panabaker K, et al. Evaluation of genetic counseling for hereditary cancer by videoconference in British Columbia. *BC Med J* 2008;50(10):554-559.
10. Lea DH, Johnson JL, Ellingwood S, Allan W, Patel A, Smith R. Telegenetics in Maine: successful clinical and educational service delivery model developed from a 3-year pilot project. *Genet Med* 2005;7(1):21-27.
11. Gattas MR, MacMillan JC, Meinecke I, Loane M, Wootton R. Telemedicine and clinical genetics: establishing a successful service. *J Telemed Telecare* 2001;7(suppl 2):S2:68-70.
12. Yip MP, Chang AM, Chan J, MacKenzie AE. Development of the telemedicine satisfaction questionnaire to evaluate patient satisfaction with telemedicine: a preliminary study. *J Telemed Telecare* 2003;9(1):46-50.
13. Smets EM, Pieterse AH, Aalfs CM, Ausems MG, van Dulmen AM: The perceived personal control (PPC) questionnaire as an outcome of genetic counseling: reliability and validity of the instrument. *Am J Med Genet* 2006;140:843-850.
14. Van der Bij AK, de Weerd S, Cikot RJ, Steegers EA, Braspenning JC: Validation of the Dutch short form of the state scale of the Spielberger State-Trait Anxiety Inventory: considerations for usage in screening outcomes. *Community Genet* 2003;6:84-87.
15. Marteau TM, Bekker H: The development of a six-item short-form of the state scale of the state scale of the Spielberger State-Trait Anxiety Inventory (STAI). *Br J Clin Psychol* 1992;31:301-306.
16. Zellerino B, Milligan SA, Brooks R, Freedenberg DL, Collingridge DS, Williams MS: Development, testing, and validation of a patient satisfaction questionnaire for use in the clinical genetics setting. *Am J Med Genet C Semin Med Genet* 2009;151C:191-199.
17. Gardner MR, Jenkins SM, O'Neil DA, Wood DL, Spurrier BR, Pruthi S. Perceptions of video-based appointments from the patient's home: a patient survey. *Telemed J E Health* 2015;21(4):281-285.
18. Van de Belt TH, Engelen LJLPG, Berben SAA, Teerenstra S, Samson M, Schoonhoven L. Internet and social media for health-related information and communication in healthcare: preferences of the Dutch general populations. *J of Med Internet Research* 2013;15(10):e220.
19. Zilliacus E, Meiser B, Lobb E, Duddung TE, Barlow-Stewart K, Tucker K. The virtual consultation: Practitioners' experiences of genetic counseling by videoconferencing in Australia. *Telemed J E Health* 2010;16(3):350-357.

20. Hilgart JS, Hayward JA, Coles B, Iredale R. Telegenetics: a systematic review of telemedicine in genetics services. *Genet Med* 2012;14(9):765-776.
21. McDonald E, Lamb A, Grillo B, Lucas L, Miesfeldt S. Acceptability of telemedicine and other cancer genetic counseling models of service delivery in geographically remote settings. *J Genet Counsel* 2014;23:221-228.
22. Rothwell E, Kohlmann W, Jasperson K, Gammon A, Wong B, Kinney A: Patient outcomes associated with group and individual genetic counseling formats. *Fam Cancer* 2012;11:97-106.
23. Pieterse AH, van Dulmen AM, Beemer FA, Bensing JM, Ausems MG: Cancer genetic counseling: communication and counselees' post-visit satisfaction, cognitions, anxiety, and needs fulfillment. *J Genet Couns* 2007;16:85-96.
24. Brain K, Gray J, Norman P *et al:* Randomized trial of a specialist genetic assessment service for familial breast cancer. *J Natl Cancer Inst* 2000;92:1345-1351.
25. Bish A, Sutton S, Jacobs C, Levene S, Ramirez A, Hodgson S: Changes in psychological distress after cancer genetic counselling: a comparison of affected and unaffected women. *Br J Cancer* 2002;86:43-50.
26. Zilliacus E, Meiser B, Lobb E, Barlow-Stewart K, Tucker K. A balancing act – telehealth cancer genetics and practitioners' experiences of a triadic consultation. *J Genet Counsel* 2009;18:598-605.

Chapter 6

Online genetic counseling from the providers' perspective: counselors' evaluations and a cost and time analysis

Ellen Otten, Erwin Birnie, Adelita V. Ranchor and Irene M. van Langen

Submitted

ABSTRACT

Telemedicine applications are increasingly being introduced in patient care in various disciplines, including clinical genetics, mainly to increase access to care and to reduce time and costs for patients and professionals. Most telegenetics reports describe applications in large geographical areas, showing positive patients' and professionals' satisfaction. One economic analysis published thus far reported lower costs than in-person care. We hypothesized that telegenetics can also be beneficial in the above respects in relatively small geographical areas. We performed a pilot study in the northern Netherlands of 51 home-based online counseling sessions for cardiogenetic and oncogenetic cascade screening, and urgent prenatal counseling. Previously, we showed patient satisfaction, anxiety, and perceived control of online counseling to be comparable to in-person counseling. This study focuses on expectations, satisfaction, and practical evaluations by involved counselors, and the impact in terms of time and costs. Most counselors expected disadvantages of online counseling for themselves and their patients, mainly concerning insufficient non-verbal communication; few expected advantages for themselves. Afterwards, counselors additionally raised the disadvantage of insufficient verbal communication, and reported frequent technical problems. Their overall average telemedicine satisfaction itemscore before (mean 3.38) and afterwards (mean 2.95) did not differ significantly, being afterwards slightly below the minimum level we set for a satisfactory result. We estimated reduced time and costs by online counseling with about 8% and 10-12%, respectively. We showed online genetic counseling to be effective, feasible and cost-efficient, but counselors would need to see technical improvements for it to be satisfactory.

INTRODUCTION

Telemedicine is increasingly being applied in many medical disciplines, including clinical genetics. Reasons for its introduction lie mainly in improved access to care, especially for patients in remote areas, avoiding travel time and costs for patients, and increased efficiency for professionals, due to spending less time on patient care and avoiding travelling to regional clinics.[1-4] Efficiency gains in clinical genetics are desirable because of the continuing rise in patient numbers due to the introduction and wider availability of new diagnostic techniques. At the same time, resources (money and staff) are limited and growing at a much slower pace than patient numbers. Several reports on that evaluated the economic aspects of telemedicine applications in- and outside genetics support its favorable cost-effectiveness.[4,5,6] Telemedicine applied in clinical genetics is called telegenetics. Reports on its application have come mainly from countries with large travelling distances. They show positive outcomes on patients' and counselors' satisfaction.[7-14] The only American economic report on telegenetics used by counselors in central clinics and patients in regional clinics showed comparable satisfaction and less costs compared to in-person counseling.[6] In Europe, health-care systems, including the organization of clinical genetic care, and travel distances are different. Therefore it seems useful to evaluate these aspects here.

We performed a pilot study in the northern Netherlands on offering online genetic counseling and testing for presymptomatic cardiogenetic and oncogenetic, and prenatal counseling. The study covered 51 sessions between counselors (at hospital or at home) and patients in their own homes. Patient outcomes showed that our online counseling application is feasible, that patients were satisfied with online counseling, its efficiency, and with the online application we used. Levels of anxiety and personal perceived control were comparable to controls who received regular in-person counseling at our outpatient department (OPD).[15] We hypothesized that telegenetics could, in addition, offer benefits to the professionals regarding efficiency and flexibility, and the costs, even in our small country.

In view of the favorable patient outcome,[15] we believe it is important to determine whether counselors are also willing to accept this new modality, and to identify any barriers to its successful implementation. Here we evaluate the online counseling from the providers' perspective, in terms of counselor's satisfaction with telemedicine, their evaluation of practical aspects of online counseling, and the impact of our online approach in terms of time and costs of counseling compared to regular OPD counseling.

METHODS

Study setting, design and participants

In the Netherlands, clinical genetic care is concentrated in eight university medical hospitals, spread throughout the country. Our department is the only one in the northern Netherlands (area about 8300 km^2 and 1.7 million inhabitants), also holding regular outpatient clinics in five regional hospitals. Although the distances are relatively small compared to many other countries, it still takes time and costs for counselors and patients to travel and perform/receive genetic counseling and testing at regional OPDs. Moreover, for the management this brings travel costs and suboptimal use of medical staff.

We performed a cohort study with before, interim and after measurements for ten counselors from the genetics department of the UMC Groningen, the Netherlands, between November 2011 and June 2012. They represented an average of the total counselors group in our department with regard to age, sex, profession, and attitude towards online counseling. Sessions were performed with patients in their own homes. Counselors performed the sessions from the department, and some sessions from their homes, to test the intended flexibility of online counseling. Patients who were referred for oncogenetic or cardiogenetic cascade screening for a known familial mutation, and several couples referred for urgent prenatal counseling with an appointment planned at least two days after referral, were invited by telephone by the web coordinator and researcher (EO) to participate in an online counseling session. Patients had to have access to a computer with internet and a webcam, and we set a limit of two participants on the patient side per session. We recorded counselors' expectations, their satisfaction with telemedicine, and evaluation of practical issues at baseline, after each counselling session, and at the end of the pilot period, and we estimated the costs of providing this type of care. The institutional medical ethics committee declared the study protocol was exempt from formal review (number M11.108133).

Online counseling application

Counseling sessions were performed through the online platform 'myCoachconnect' (www.mycoachconnect.com), which was adapted for use in our clinical genetics practice and met the UMCG's required safety protocols. Privacy protocols were composed in cooperation with the hospital's ICT and personal privacy protection departments. In addition to video-conferencing, the platform offered several functions intended to support the information exchange during counseling, and to allow for future access to this information for the patients (Supplementary figure a-e): These functions included online file notes for counselors and a notebook for patients, the transfer and viewing of disease brochures, visiting of websites by the counselor and patient together during counseling, and secured email. Before the pilot study began, all ten counselors were trained in a workshop and could practice individually as much as they liked, in order to become familiar with the online application. Support was

provided by a web coordinator, two case managers, and the project researcher (EO). An ICT technician and the myCoachconnect helpdesk were available for supportive services and gave immediate assistance to the professionals whenever needed.

Online counseling procedures

The patients who consented to online counseling, after being fully informed, were evenly allocated to the counselors in order of referral, taking into account counselors' availability and subspecialism. New patients were allocated to the counselor who had previously seen their family members, whenever possible.

Genetics professionals had to prepare as follows before an online counseling session could take place: (1) Indicating the counselors' preferred date and time for the session, (2) Checking if any additional medical information had to be gathered, (3) Registering patients' personal and appointment information on the administrator-side of the application (Supplementary figure f). This automatically generated an email to the patient, including their appointment information, account/login instructions, and a link to an instruction movie. Patients had to complete and return a digital form with family information after creating an account. (4) Processing the received family information forms to update/expand existing family pedigrees. (5) Contacting patients to test the connection a few days before their session. (6) Preparing and sending test kits/forms to patients for them to submit saliva or blood samples for DNA testing after counseling. The researcher and case managers monitored the whole process and contacted patients when necessary. After an online session, counselors made their usual report in the patient's regular paper medical record.

Outcome measures

Counselors' evaluations

Counselors' evaluations were measured at three time points: at the start and end of the pilot study, and in between, immediately after each online session. The online questionnaires contained an ID code to identify each counselor. Table 1 provides an overview of the measures over time:

1) Counselor and counseling characteristics: Date, time and type of counseling (oncogenetic, cardiogenetic, prenatal), location of counseling (at the department, at home, elsewhere), and the sequence number of the online session performed by the counselor.

2) Experience with computers, internet and online communication: Counselors were asked three multiple choice questions on their time spent using internet for private purposes, and their experiences and frequency of use of different online platforms. Moreover, their experience with computer use and online communication were recorded by rating four statements on a 5-point Likert scale ("totally disagree" to "totally agree"): (1) "always looking for new possibilities on my computer"; (2) "expecting to increase working via webcam communication"; (3) "annoying to use a computer when counseling patients" and (4) "I imagine patient feels annoyed when being counseled via a computer".

3) Expectations and evaluations of online counseling: Counselors were asked to rate seven statements on a 5-point Likert scale ("totally disagree" to "totally agree"), and to describe their expected and perceived advantages and/or disadvantages of online counseling over in-person counseling at the OPD, both for themselves and their patients. They were also asked to indicate if and how online counseling had to be improved to make it equivalent to OPD-counseling.

4) Telemedicine Satisfaction Questionnaire (TSQ): The TSQ aims to measure patient satisfaction with telemedicine.[16] We translated the validated 14-item English version into Dutch and adapted it for use amongst counselors (Supplementary figure 1), for measuring both their expected and perceived satisfaction with telemedicine. Previously, we had removed item seven ("I think the health-care provided via telemedicine is consistent") of the original questionnaire because this was inapplicable in our setting.[15] Response mode was a 1-5 Likert scale with higher scores indicate higher satisfaction. Internal consistency (Cronbach's alpha) was 0.88 and 0.72 for the TSQ before and TSQ after counseling, respectively. We set a minimal requirement for a successful counselor evaluation of at least a "neutral" satisfaction with telemedicine (score=3), and a sufficiently technical functioning of the application.

5) Technical issues and patients responsibilities: The occurrence and type of technical problems during the online counseling sessions were recorded. Counselors were also asked to indicate their degree of acceptability regarding several patient responsibilities in the online counselling process: planning an appointment, preparations before counseling, proper functioning of the application during counseling, and self-collection of saliva. The responses were on a 1-5 Likert scale ("not acceptable at all" to "very acceptable").

Table 1. Overview of questionnaire contents for genetic professionals performing online counseling sessions

Aspect measured	counselor online before	counselor online after -interim	counselor online after -end
Counselor information	x	x	x
PC/internet/ online platforms experience	x		x
Online counseling general	x	x	x
TSQ*	x	x	x
Practical aspects of Online counseling		x	
Patient responsibilities			x
Total number of items	36	30	38

* TSQ= telemedicine satisfaction questionnaire

Patient evaluations; analysis of time and cost

Previously we have demonstrated that the psychological outcomes (anxiety and personal control, measured with the STAI and PPC questionnaires) of patients who received online counseling and control patients were comparable.[15] Despite technical problems, online patients perceived a high level of satisfaction with telemedicine, even higher than their positive expectations beforehand.

In view of the comparable patient outcomes, we adopted a cost-minimization analysis as our main analytical framework; implying that the total time and costs spent on the process of online counseling were compared to the in-person counseling process. First, for each stage in the process of online counseling (Figure 1), we estimated the total time spent by counselors, administrative staff, the pilot study team (online process only) and the patients. The time spent by the pilot team members only included care-related time; the time and costs of research activities were excluded. For each professional, the average time spent on conventional OPD counseling per stage was obtained from a detailed workflow and process time sheet. The total time spent on the process of online counseling was extrapolated from the same sheet and added with specific time registrations/measurements and interviews. Patient-related time was based on the digital time-registrations of all online contacts and their estimated travel distance and time based on their postal code. Second, time of professionals was valued at their gross hourly wage (excluding departmental and hospital overheads). Patient time was valued at €3.50 per hour, based on a large variety of national and international time use studies.

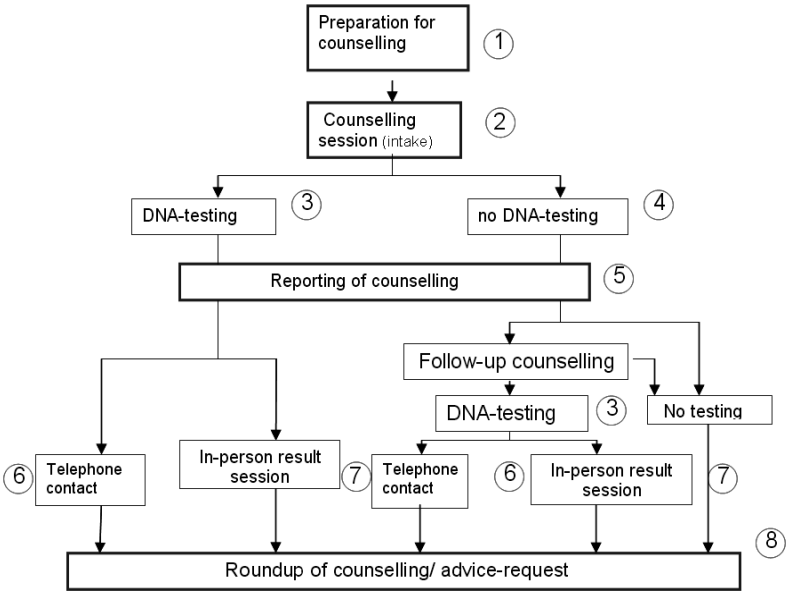


Figure 1. Overview of the general process of online counseling and testing

Analysis

We used the mean, standard deviation (SD) and range as descriptive statistics for quantitative variables and n (%) for nominal and ordinal variables. Mean TSQ item scores within counselors before versus after the pilot study were compared with the paired Student's t-test. This change was also quantified as the effect size, defined as the difference in mean TSQ score before and after counseling, divided by the pooled SD of these mean TSQ scores. An effect size of 0.50 is considered a clinically relevant difference.[17] There were no missing TSQ items. The profiles of counselor's mean TSQ itemscores over the successive online sessions during the pilot study were compared with repeated measurements analysis (mixed linear modeling). The dependent variable was the profile of mean TSQ itemscores; the repeated factor was the counseling session (covariance structure: unstructured); and the covariables were the mean TSQ itemscore at baseline (before the pilot) and the counselor and counseling characteristics. Analyses were performed with SPSS statistics v22, IBM Corporation, New York. A p-value (two-sided) <0.05 was considered a significant difference.

RESULTS

1) Counselors and patients characteristics: Table 2 displays the counselor and patient characteristics. Ten counselors performed a total of 51 counseling sessions with 57 patients, including 16 sessions conducted from counselors' homes. The average number of sessions per counselor was 5 (range 2-7): one prenatal counselor did not perform all five predetermined sessions. Three pairs of patients joined one session for oncogenetic counseling; three couples (six patients) participated in prenatal counseling.

Counselors' evaluations

2) Experience with computers, internet and online communication: At the start of the pilot, five out of ten counselors indicated they spent less then 30 minutes per day on the internet for private purposes, while the other five said they spent between 30 minutes and two hours per day. Seven counselors indicated they had experience with online communication in a manner other than by sending email (e.g. skype, social media), and making use of it from less than once a week to daily. After the pilot, the time spent on the internet overall had increased slightly. In addition, eight instead of seven counselors by then had experience with online communication other than email, with frequencies between less than once a week to daily.

Before the pilot, the mean item scores of the four multiple choice questions regarding computer use were all judged neutrally by the counselor group (mean overall score 3.1; range 1-5). Afterwards, there was no significant change in the item scores overall, although the individual changes reflected a considerable disparity amongst the counsellors. Interestingly, the scoring of items 3 and 4 improved for 5 of the 10 counselors, indicating

Table 2. Counselors and patients characteristics

Counselors (n=10)		
Function	geneticist geneticist in training genetic counselors	1 2 7
Age; mean in years (range)	38.8 (30-53)	
Experience; mean in years (range)	7.2 (2-18)	
Sex	male female	3 7
Counseling indication (number of counselors; number of sessions)	oncogenetic cardiogenetic prenatal	7; 31 3; 17 2; 3
Location of counseling (number of sessions)	department home	36 15
Time of counseling (number of sessions)	during office hours outside office hours	42 9
Patients (n=57)		
Age; mean (range)	44 (22-74)	
Sex	male female	30 27
Indication of counseling (number of patients)	oncogenetic cardiogenetic prenatal	34 17 6

they experienced less annoyance themselves, and imagined less annoyance on their patients' behalf compared to their expectations beforehand.

3) Expectations and evaluation of online counseling aspects: *A) Expectations and experiences* Figure 2 shows the expectations and actual experiences of the counselors regarding various aspects of online counseling: the items 1, 3, 4 and 6, regarding the 'appreciation of performing online counseling', 'feeling need to see patients in person additionally', 'transfer of substantive information', and 'offering recording of the session', scored moderate to sufficient, and remained about the same after the pilot. The mean scores of items 2, 5 and 7 ('feeling pleasant talking to patients via a webcam', 'discussing emotional/ psychological aspects with patients', and 'equality of online counseling to in-person counseling'), were all scored less favorably afterwards compared to before the pilot.

B) Advantages and disadvantages Table 3 shows that before the start of the pilot, few counselors indicated seeing any advantages to online counseling above in-person counseling

Table 3. Advantages and disadvantages of online counseling mentioned by counselors before and after the online counseling period

	Before		After	
Advantages	**for counselor (n=3)***	**for patient (n=9)***	**for counselor (n=8)***	**for patient (n=10)***
Time/cost saving; avoid travelling	2	9	4	10
Increased flexibility	2	3	4	2
Less stressful in case of illness or disability		2		
Better grip on family/ multiple family members counselled by same counsellor		1	1	1
Counselling in familiar environment		1		2
Possibility of watching counselling session again		1		
Disadvantages	**for counselor (n=7)***	**for patient (n=8)***	**for counselor (n=10)***	**for patient (n=10)***
Less non-verbal communication	6	5	7	3
Less extensive information / verbal communication				4
Greater role for /attention to technique	3	4	1	2
Less notion of interaction at patients'side	1			
Less personal contact	1	3	2	1
More working from behind PC	1			
Insufficient verbal communication			7	
Less easy discussing psychological aspects			3	1

Numbers in the table reflect the number of times the particular advantages and disadvantages are being mentioned by counselors; * = (within brackets) the number of counselors included.

for themselves (3 counselors; 4 advantages), whereas most of them saw any disadvantages for themselves (7 counselors; 12 disadvantages). Moreover, for their patients, most counselors saw some advantages (9 counselors; 17 advantages), but also disadvantages (8 counselors; 12 disadvantages) of online counseling. The counsellors saw the time and/or cost savings by not having to travel as the main advantage of online counseling both for their patients

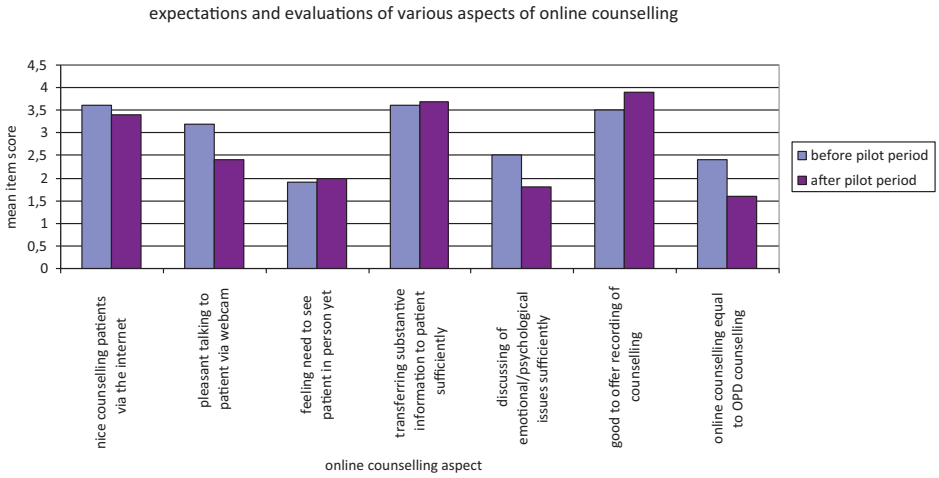


Figure 2. Counselor's judgements on aspects of online counseling before (expectation) and after (evaluation) of the pilot

Itemscore range: 1-5; 1= totally disagree; 3=neutral; 5= totally agree.

and for themselves. The expected disadvantages for their patients and themselves mainly concerned the reduced quality of non-verbal communication in online sessions.

After the pilot period, counselors reported more advantages (8 counselors; 9 advantages), but also more disadvantages (10 counselors; 20 disadvantages) for themselves. Qualitatively insufficient verbal communication was being raised as an additional disadvantage, that was not reported beforehand. The number and balance of advantages and disadvantages seen by the ten counselors for their patients remained about the same (Table 3). The improvements to the online counseling system proposed by nine of the ten counselors – making it more equal to in-person counseling – all concerned technical aspects of the application: e.g. solving the frequently occurring sound delays and echoes during counseling, providing a larger and clearer webcam-image on screen. Two counselors stated that online counseling could never become equal to in-person counseling.

4) Telemedicine satisfaction questionnaire: Figures 3a and 3b show the mean TSQ item scores for each individual counselor before, during and after the pilot. For all the counselors taken together, the mean TSQ item score afterwards did not change significantly compared to that before the pilot (mean (SD) score before: 3.38 (0.68) vs. after: 2.95 (0.96); 1-5 scale; p=.14) (Figure 3a). This was slightly below the minimum level we set beforehand for a successful outcome. The effect size of 0.52, however, points to a clinically relevant change. There were individual differences among counselors, since seven counselors had higher mean TSQ item scores afterwards compared to before, while three had lower scores afterwards.

Figure 3a.

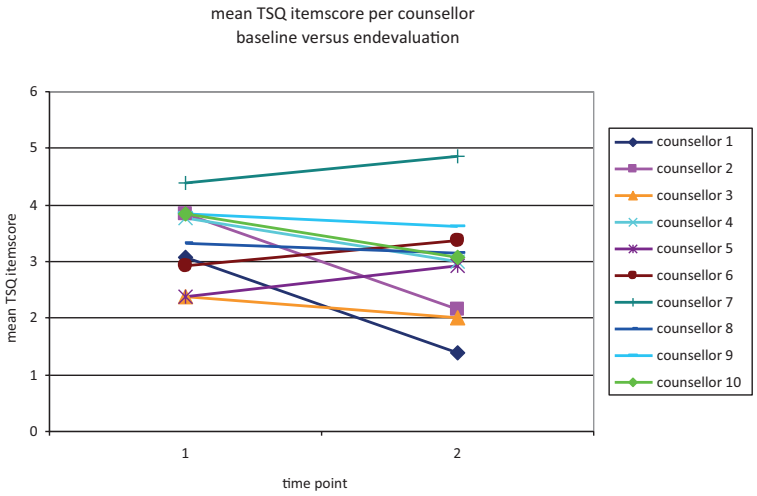


Figure 3b.

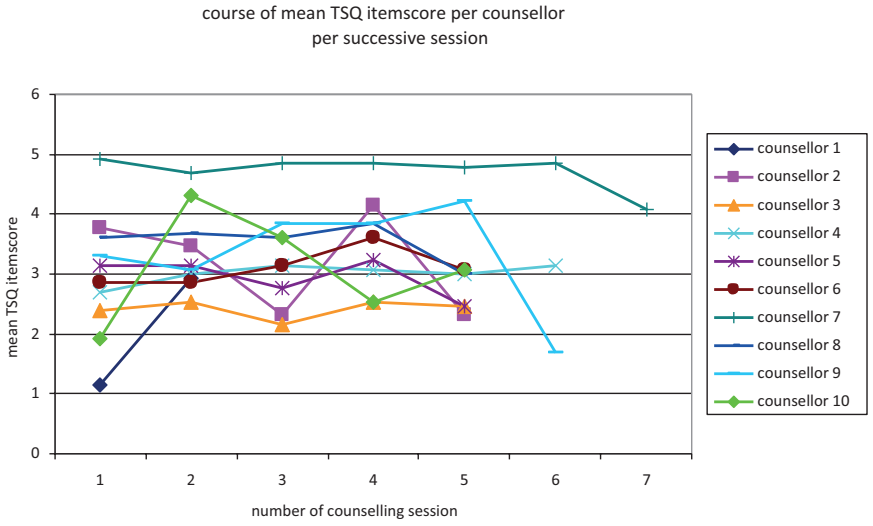


Figure 3b shows the variability in the profiles of mean TSQ item scores among the counselors and over their successive counseling sessions. The overall trend over the successive sessions was positive (increasing TSQ) and significant (beta=0.09, 95%CI: 0.03-0.15, p=0.008). Other significant covariates of the mean TSQ-itemscore were counselor's mean TSQ item score before the start of the pilot (beta=0.69, 95%CI: 0.33-1.04, p=0.002) and the counselor's age (beta=0.03, 95%CI: 0.005-0.50, p=.024), indicating that older counselors reported slightly higher mean TSQ item scores. Other counselor characteristics (gender, years of experience, profession) and counseling session

Figure 4a. TSQ itemscore at the start of the pilot period

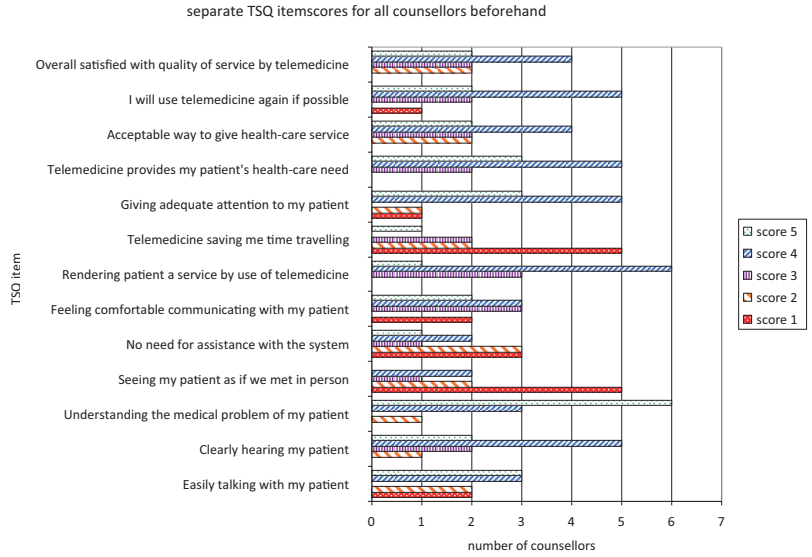
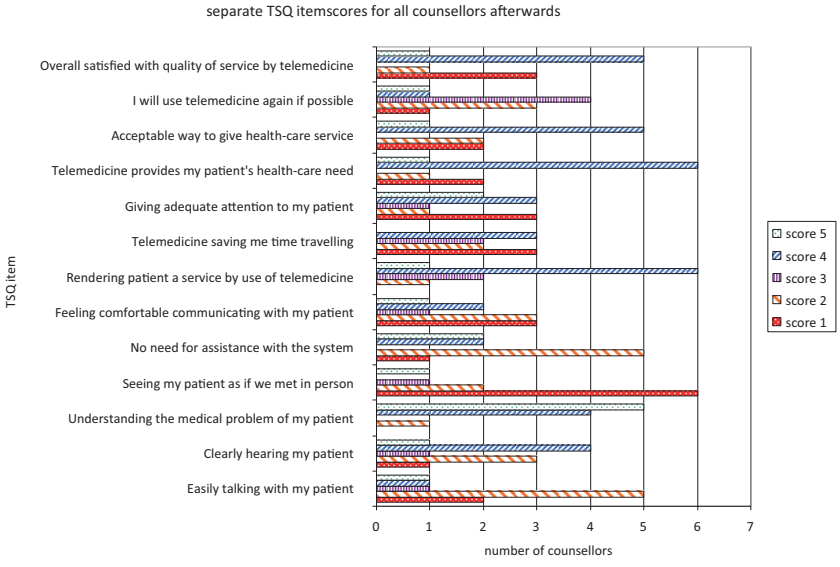


Figure 4b. TSQ itemscore at the end of the pilot period



characteristics (location of counseling, during/outside office hours, technical problems) did not significantly impact the profile of mean TSQ item scores.

Looking at the individual items, the worst-scoring after the pilot were items 1 and 4 'I could easily talk to my patient' (mean score 2.4) and 'I could see my patient as if we met in person' (mean score 1.8). The best-scoring items were items 3 and 7: 'I was able to understand the healthcare condition of my patient' (mean score 4.3) and 'I think I rendered my patient a service by offering telemedicine' (mean scores 3.7) (Figure 4a and 4b).

5) Technical problems and patient responsibilities: In total, counselors reported technical problems in 26 of 51 (51%) sessions, of which 9 were performed from their homes. Problems were related to sound (no sound/too soft sound, echo, delayed sound; 19 sessions (37%)), internet connection (no or broken connection between counselor and patient; 5 sessions (10%)); and webcam image (no image / frozen image; 7 sessions (14%)). Additional remarks referred to the technical imperfections of the online system, as well as its instability, i.e. the sound delay was sometimes reported to be as high as several seconds, greatly hampering the conversation, while at other times there was hardly any delay or echo.

The assignment of shared responsibilities to patients in the online counseling process was judged to be acceptable overall by the counselors for all the given aspects: establishing an appointment by email (mean score 4.8); performing preparatory actions (mean score 3.9); well-functioning system during the session (mean score 4.3); self-collection of saliva for DNA testing (mean score 4.4) (score range 1 highly unacceptable to 5 highly acceptable).

Time and cost analysis

Table 4 compares the costs and time per client spent for online counseling and in-person counseling. Regardless of the indication, professionals had the larger share of the total time spent (about 91%) and costs incurred (about 99%). The estimated time savings from online counseling for the professionals were 7.6% for cardiogenetic/oncogenetic indications and 8.8% for prenatal indications. The cost savings from online counseling for the professionals were 10.2% for cardiogenetic/oncogenetic indications and 12.4% for the prenatal group. Patient time and costs were lower in absolute terms, but their relative cost savings associated with online counseling were substantially higher than for the professionals (88%/89% for the patients vs. 10/12% for the professionals). The type of counseling did not significantly affect the uptake rate of DNA-testing (online group: 54/57 (95%) vs. in-person group: 66/71 (93%); p=0.73). Follow-up showed that health care use after rounding of the counseling was rare in both groups (online group 1/57 (1.8%) vs. in-person group 2/71 (2.8%); p=0.99). Potential cost differences arising by these two factors will not lead to a different cost balance in table 4.

Table 4. Time investments (average per patient) and costs (average per patient, in €) for each process step by counseling type (in-person, online) and indication (cardiogenetic/ oncogenetic, prenatal)

Process step	**Cardiogenetic/ oncogenetic**		**Prenatal**	
	In person / OPD counseling	**Online counseling**	**In person / OPD counseling**	**Online counseling**
Professionals				
1. Preparation	159.5	155.0	130.5	133.0
2. Counseling - traveling - intake*	 20.0 40.0	 none 30.0	 20.0 45.0	 none 24.5
5. Reporting of counseling	147.5	147.5	201.0	201.0
6. Telephone contact	4.0	4.0	4.0	4.0
7+8. in-person/online result session, round up*	30.0	34.0	30.0	30.0
Total time (min)	**401.0**	**370.5**	**430.5**	**392.5**
Total costs (€)	**€ 361.22**	**€ 324.26**	**€ 379.33**	**€ 332.38**
Patients				
Travel time to OPD*	36.0	none	36.0	none
1+2. Preparation and counseling	65.0	70.0	70.0	64.5
6. Telephone contact	4.0	4.0	4.0	4.0
Total time (min)	**105.0**	**74.0**	**110.0**	**69.5**
Total costs (€)	**€ 35.88**	**€ 4.32**	**€ 38.27**	**€ 4.05**

*) observed or reported time

DISCUSSION

Our results show that, though statistically not significant but based on the effect size of the change, counselor satisfaction with telemedicine after the pilot was decreased compared to their baseline scores, being slightly below the minimum acceptable level we had set prior to the study. We also found a large variation in TSQ scores among and within counselors for their start and end scores, and for their scores after each session. Counselors' overall attitudes towards digital communication and their acceptance of the use of various aspects of digital communication remained about the same over the two measurements. After the pilot, the number of advantages and disadvantages of online counseling seen by counselors was more balanced than beforehand. They reported flexibility and cost- and time savings as the main advantages, and insufficient verbal and non-verbal communication as the main disadvantages. Substantial improvements on the technical side of the application were considered a prerequisite by counselors for implementing online counseling in regular patient care. This was supported by their reports of technical problems in half of the counseling sessions. Counselors found the level of patient responsibilities for online counseling acceptable. Finally, our time and cost analysis showed that online counseling involved less time and lower costs for both professionals and patients than in-person counseling, independent from the counseling indication.

Our study has several limitations which could have influenced our results: (1) counseling sessions were performed for a relatively favourable patient group, who consented to online counseling, and thus might have been more open and cooperative than average. This selection allowed for a good evaluation of counselor's experiences, but their evaluations might be less favourable if they had to counsel less well-motivated patients. (2) We only included a few types of indication in the study. Offering online counseling for more indications could also influence the counselors' evaluations. (3) The counselors' questionnaires included mainly non-validated measures, which could have led to biased results. However, the results of the various non-validated measures were largely in agreement with each other.

We recognize that the number of counselors and sessions involved in our study is relatively small for performing statistical analyses, though it is unlikely that the composition of our counselor group influenced the results since they represented a mix of gender, age, and experience with computers and counseling, and their attitude beforehand was average. Only one counselor left the pilot study prematurely because of negative experiences. It seems equally unlikely that the number of sessions played a role: in view of the dominant role of technical problems, more sessions would probably not have led to different insights.

Our outcomes from the counselors' evaluations are in line with previous reports on online counseling regarding the limitations in personal contact and non-verbal communication.[9,10,13,18] However, in the previous reports counselors were positive overall about online counseling despite the limitations, whereas our counselors were less satisfied

overall with online counseling.[9,10,13,18] Our counselors reported many technical problems, which was reflected in their TSQ scores: the items with low scores were related to the system's technical aspects, whereas the items that scored well were system-independent. Surprisingly, patient satisfaction did not appear to be affected by these problems.[15] Still improvements and adjustments to the quality and design of the online system are needed, and would probably improve counselors' satisfaction.

Various explanations might underlie the differences between our counselors and the counselors in previous reports. First, our online approach and system differed from previous reports in that (1) there was no additional counselor on site with the patient, supporting the counseling process as in previous studies[7,11,12,18,19]; (2) counselors used laptops with built-in webcams, and patients used their own equipment at home to run the online application instead of using videoconferencing equipment and television screens[7,9,10,18]; and (3) supportive tools were shown on-screen together with the webcam image, which was an advantage of our system, but it did mean there was only a relatively small image of the patient visible to the counselor rather than a whole-screen image.

Second, in previous reports, online counseling mainly enabled counselors to avoid travelling large distances, thereby saving them a significant amount of time[10,12,13]. This advantage might have meant they were more easily satisfied with the option of online counseling than the counselors in our study in a non-remote area, having less substantial benefit from avoiding travelling and less time saved. In contrast to this, several of our counselors reported that online counseling allowed for increased flexibility, by using counselors' and patients' own laptops/PCs rather than the relatively static videoconferencing systems. Our all-in-one online system has not been reported before, and only one report thus far stated that patients' own home equipment was used, but this did not focus on counselor outcomes.[8]

Finally, we saw a discrepancy between our counselors' and patients' satisfaction levels, with the patients being more satisfied and reporting no negative influence from technical problems.[15] This is likely due to differences in expectations and requirements by the two groups: while patients are likely to see online counseling as an advantage beforehand (no need to travel, being in own environment), counselors are used to conventional counseling at the OPD, and to the generally accepted, and their own standards for and experiences with good quality of counseling.[20-22] Counselors also did multiple online sessions and were thus more vulnerable to repeated technical problems, whereas patients only had one session.

The contrast in our counsellors' and patients' evaluations also points to the issue whose opinion is most important in evaluating the value of this new counseling option in regular care. Our previous study showed that patients were satisfied and showed favourable psychological outcomes similar to controls having in-person sessions, implying that the aims of counseling were met. Our counselors' moderate satisfaction with online counseling in this study does not necessarily imply that the provision of counseling was suboptimal: Most of the identified key aspects of genetic counseling reported by Rantanen et al. were

met.[23] However, we acknowledge that greater counselor satisfaction, e.g. by technically improving the system, and increasing their experience/familiarity with it, would further increase the acceptance of this new option, and contribute to its implementation in regular patient care.[24]

Our study shows time and cost savings for professionals as well as patients, in addition to the favourable patient outcomes in our previous study.[15] Therefore, online counseling can be regarded as the preferred type of counseling in regular clinical genetic care, although one should be cautious about the saving in time and costs that can be realized in practice. In view of the increasing patient numbers it is likely that any time and costs saved will be devoted to new patients. On balance, introducing online counseling will still be beneficial, since more patients can be counseled with the existing staff capacity.

From a manager's viewpoint, there may be more reasons to adopt online counseling. First, it could have a positive effect on patients' access time to genetic counseling (not evaluated in this study). Patients who normally would have had an appointment at one of our regional OPDs could be eligible for online counseling and thereby have faster access to counseling because of more opportunities and flexibility in planning an online appointment. An online approach also offers more flexibility to the counselors, who can counsel from home and outside normal office hours, and avoid travelling. Second, when recontacting former patients becomes part of regular patient care, as we expect it will in the near future, the use of online systems can support this process, with patients being given the new information in an online session.[25,26]

To conclude, it is attractive to implement online counseling in regular care for patients, counselors, and the management. The online application we used is feasible, but it needs technical improvements for use in regular care. We found our way of online counseling leads to more flexibility for counselors, to lower costs and less time investment compared to conventional counseling, and that patients are satisfied with it. Thus, online counseling could have added value for clinical genetic services when the technical requirements are met. It can complement existing genetic counseling services and be offered to (some of) our patients as an additional service, even in small geographical areas.

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Conflict of interest:

The authors declare no conflict of interest.

REFERENCES

1. Mehrota A, Paone S, Martich GD, Albert SM, Shevchik GJ. Characteristics of patients who seek care via evisits instead of office visits. *Telemed J E Health* 2013;19(7):1-5.
2. Merell R.C. Editorial: Telemedicine for vulnerable populations. *Telemed J E Health* 2014;20(10):885-886.
3. Stalker HJ, Wilson R, McCune H, Gonzalez J, Moffett M, Zori RT. Telegenetic medicine: improved access to services in an underserved area. *J Telemed Telecare* 2006;12(4):182-185
4. http://www.americantelemed.org/docs/default-source/policy/examples-of-research-outcomes---telemedicine's-impact-on-healthcare-cost-and-quality.pdf
5. Wade VA, Karnon J, Elshaug AG, Hiller JE. A systematic review of economic analyses of telehealth services using real time video communication. BMC Health Serv Res 2010;10:233.
6. Buchanan AH, Datta SK, Skinner CS et al. Randomized trial of telegenetics vs. in-person cancer genetic counseling: cost, patient satisfaction and attendance. *J Genet Counsel* 2015; April 3. [epub ahead of print] PMID: 25833335
7. Zilliacus E, Meiser B, Lobb AE et al. Are videoconferenced consultations as effective as face-to-face consultations for hereditary breast and ovarian cancer genetic counseling? *Genet Med* 2011;13(11):933-941.
8. Meropol NJ, Daly MB, Vig HS et al. Delivery of internet-based cancer genetic counseling services to patients' homes: a feasibility study. *J Telemed Telecare* 2011;17:36-40.
9. d'Agincourt-Canning L, McGillivray , Panabaker K *et al*. Evaluation of genetic counseling for hereditary cancer by videoconference in British Columbia. *BC Med J* 2008; 50(10):554-59
10. Lea DH, Johnson JL, Ellingwood S, Allan W, Patel A, Smith R. Telegenetics in Maine: Succesful clinical and educational service delivery model developed from a 3-year pilot project. *Genet Med* 2005;7(1):21-27.
11. Elliot AM, Mhanni AA, Marles SL *et al*. Trends in telehealth versus on-site clinical genetics appointments in Manitoba: a comparative study. *J Genet Couns* 2012;21(2):337-44.
12. Gattas MR, MacMillan JC, Meinecke I, Loane M, Wootton R. Telemedicine and clinical genetics: establishing a successful service. *J Telemed Telecare* 2001;7 suppl 2:68-70.
13. Zilliacus E, Meiser B, Lobb E, Dudding TE, Barlow-Stewart K, Tucker K. The virtual consultation: practitioners' experiences of genetic counseling by videoconferencing in Australia. *Telemed J E Health* 2010;16(3):350-357.
14. Hilgart JS, Hayward JA, Coles B, Iredale R. Telegenetics: a systematic review of telemedicine in genetics services. *Genet Med* 2012; 14(9):765-776.
15. Otten E, Birnie E, Ranchor AV, Van Langen IM. Telegenetics use in presymptomatic genetic counseling: patient evaluations on satisfaction and quality of care. *Eur J Hum Genet* 2015; Jul 15.doi:10.1038/ejhg.2015.164.[epub ahead of print]
16. Yip MP, Chang AM, Chan J, Mackenzie AE. Development of the Telemedicine Satisfaction Questionnaire to evaluate patient satisfaction with telemedicine: a preliminary study. *J Telemed Telecare* 2003;9:46-50.
17. Hojat M, Xu G. A visitor's guide to effect sizes: statistical significance versus practical (clinical) importance of research findings. *Adv Health Sci Educ Theory Pract* 2004;9(3):241-249.
18. Iredale R, Gray J, Murtagh G. Telegenetics: a pilot study of video-mediated genetic consultations in Wales. *Int J Med Market* 2002;2(2):130-135.
19. Zilliacus E, Meisser B, Lobb E, Barlow-Stewart K, Tucker K. A balancing act – telehealth cancer genetics and practitioners' experiences of a triadic consultation. *J Genet Couns* 2009;18:598-605.
20. Whitten P, Love B. Patient and provider satisfaction with the use of telemedicine: overview and rationale for cautious enthusiasm. *J Postgrad Med* 2005;51(4):294-300.

21. Grigsby B, Brega AG, Bennett RE et al. The slow pace of interactive video telemedicine adoption: the perspective of telemedicine program administrators on physician participation. *Telemed J E Health* 2007;13(5):487-499.
22. Barton PL, Brega AG, Devore PA *et al*. Specialist physicians' knowledge and beliefs about Telemedicine: a comparison between users and nonusers of the technology. *Telemed J E Health* 2007;13(5):487-99.
23. Rantanen E, Hietala M, Kristoffersson U, et al. What is ideal genetic counselling? A survey of current international guidelines. Eur J Hum Genet 2008;16:445-452.
24. Yi MY, Jackson JD, Park JS, Probst JC. Understanding information technology acceptance by individual professionals: Toward an integrative view. *Information & management* 2006;43:350-363.
25. Aronson SJ, Clark EH, Varugheese M, Baxter S, Babb LJ, Rehm HL. Communicating new knowledge on previously reported genetic variants. *Genet Med* 2012;14(8):713-719.
26. Hunt K. Individualizing the informed consent process for whole genome sequencing: A patient directed approach [PhD thesis]. Arizona: Arizona state university, 2013.

Chapter 7

Is there a duty to recontact in light of new genetic technologies? A systematic review of the literature

Ellen Otten, Mirjam Plantinga, Erwin Birnie, Marian A. Verkerk, Anneke M. Lucassen, Adelita V. Ranchor, and Irene M. Van Langen

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ABSTRACT

Purpose: With rapid advances in genetic technologies, new genetic information becomes available much faster today than just a few years ago. This has raised questions about whether clinicians have a duty to recontact eligible patients when new genetic information becomes available and, if such duties exist, how they might be implemented in practice.

Methods: We report the results of a systematic literature search on the ethical, legal, social (including psychological) and practical issues involved in recontacting former patients who received genetic services. We identified 1,428 articles, of which 61 are covered in this review.

Results: The empirical evidence available indicates that most but not all patients value being recontacted. A minority of (older) articles conclude that recontacting should be a legal duty. Most authors consider recontacting to be ethically desirable but practically unfeasible. Various solutions to overcome these practical barriers have been proposed, involving efforts of laboratories, clinicians, and patients.

Conclusion: To advance the discussion on implementing recontacting in clinical genetics, we suggest focusing on the question of in what situations recontacting might be regarded as good standard of care. To this end, reaching a professional consensus, obtaining more extensive empirical evidence, and developing professional guidelines are important.

INTRODUCTION

Next-generation sequencing technologies are rapidly being introduced into clinical genetic practice. The level of detail at which a person's genetic code can now be analyzed is several thousand times greater than it was just a few years ago, and the costs are decreasing rapidly. Patients seen in the past may have had genetic testing that could now be improved on, whereas for patients who undergo newer testing, the interpretation of clinical diagnoses or predictions may evolve over time. What duties do clinicians have to these patients? This is not a "one-off" problem because the development of genetic testing techniques progresses on an exponential scale. Genetic testing for previously unknown genes may now be available, or results that were previously uninterpretable may now be recognized as pathogenic, with clinical surveillance or even treatment being possible. New, actionable information could change medical policies for patients and offer opportunities for family screening, prevention, and new reproductive choices.

The potential for recontacting in clinical genetics raises several ethical, legal and social (including psychological) issues (ELSI). For example, which new information justifies recontacting? Would recontacting in clinical genetics always be beneficial? How would such activities respect patients' privacy and their putative right not to know? Should recontacting be made a legal obligation? If so, could clinicians face liability claims if they fail to recontact former patients? What practical issues might clinicians face when trying to recontact former patients? And how could these be solved? Who would be responsible for recontacting? What are patients' views on these issues? How is the changing landscape of clinical genetics and communication technologies shaping the debate about a possible duty to recontact? Although many of these questions have been discussed in the literature, there is no overview of what has been published so far. We therefore conducted a systematic review of the literature investigating these issues and of the empirical evidence available. Our results can serve as a starting point for further research and for the possible development of professional guidelines on recontacting in clinical genetic practice.

MATERIALS AND METHODS

Definition of duty to recontact in clinical genetics

We defined the duty to recontact as the ethical and/or legal obligation to recontact former patients about new genetic information. We specifically wanted to explore situations without a current relationship between a health-care professional (HCP) and a patient/client, so we excluded situations in which a treatment relationship was ongoing or recontacting was described in a research setting rather than a clinical setting.

Literature search strategy

We systematically searched the literature on the duty to recontact in clinical genetic practice in four databases: PubMed, Embase, Web of Science, and Google Scholar. In our search strategy we used the key term "genetic", combined by Boolean operators with either the (MeSH) term "duty to recontact" or one of the following synonyms: "duty/obligation/responsibility to warn," "duty/obligation/responsibility to disclose," "duty/obligation/responsibility to recall," and "duty/obligation/responsibility to re-contact." We included all articles published before 1 September 2014 that contained these search terms in their title or abstract (Pubmed, Embase), in their title or topic (Web of Science), or in the whole text (Google Scholar).

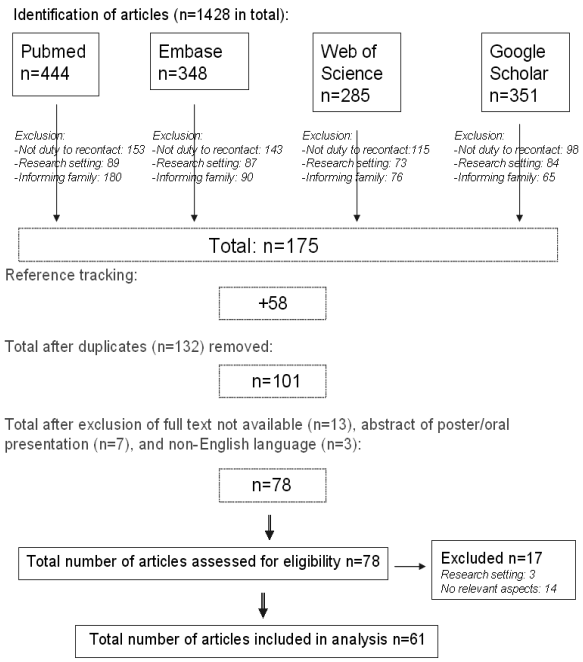

Figure 1. Literature search results for duty to recontact in clinical genetics

Selection of papers

The search was performed by two of the authors (E.O., M.P.); it identified 1,428 articles in total (Figure 1). After reading the titles and abstracts, we excluded 1,253 articles because they (i) did not discuss recontacting at all (n=509); (ii) did not discuss recontacting in clinical genetics but in a research setting (n=333); or (iii) did not discuss recontacting former patients but informing patients' family members or third parties (n=411). When there was any doubt about excluding an article, it was discussed until the two researchers reached agreement. We selected 175 articles for further analysis. Another 58 articles were added

by tracking reference lists. After removing duplicates (n=132) and excluding abstracts of poster or oral presentations (n=7), articles that were not available as full text (n=13), and those that were not written in English (n=3), 78 articles remained.

Analysis

All 78 articles were analyzed independently by two researchers (M.P., E.O.) based on the following eight aspects: (i) From which discipline-specific viewpoints is the duty to recontact discussed (ethical, legal, social, clinical)?; (ii) In which situations is/should recontacting be performed?; (iii) which ELSI and practical issues, for and against a duty to recontact, are put forward?; (iv) Which practical barriers and solutions are being discussed? (v) What conclusion about a duty to recontact is drawn (duty/no duty/not defined)?; (vi) Whose duties are being discussed (laboratory, treating HCP, referring HCP, patient)?; (vii) Is the article written from a theoretical perspective or based on empirical evidence (practical experience/surveys/focus groups) and, if yes, what was the empirical evidence?; and (viii) Do the selected articles mention or make use of any guidelines on the duty to recontact?

After full-text analysis, we excluded another 17 articles because they did not discuss recontacting after all (n=14) or were about recontacting in a research setting only (n=3). We eventually included 61 articles in the review.[1-61] Most of the literature was from the United States (54%), followed by Canada (20%), Europe (20%), Australia (3%), India (1.5%), and Israel (1.5%) (Table 1).

All articles were scored using the eight predetermined aspects covering the main ELSI-related issues discussed in the literature. The scoring system was tested for robustness by four researchers who independently scored seven of the articles, varying with respect to year of publication, discipline, and research type. When scoring all 61 articles, we restricted ourselves to the information given in the articles, which meant that not all the articles could be scored on all aspects. Disagreements on the scoring were discussed until a consensus was reached by the two analyzing researchers and a third independent researcher (I.M.V.L.).

RESULTS

Duty to recontact in clinical genetics: discussion by discipline

The earliest publications about a duty to recontact in clinical genetics date from the 1990s (Table 1). They were all from the United States and Canada except one, and half of these articles addressed a duty to recontact from a legal perspective. Over time, the contributions from other countries increased, the number of legal discussions decreased, and the number of contributions that addressed an ethical perspective increased. An author from a clinical center was involved in more than 80% of the articles, so in the empirical as well as in most of the theoretical articles, the aspects discussed were seen, at least in part, through “clinical eyes.” Contributions primarily written by health psychologists were scarce, although

psychological aspects were mentioned in a substantial number of papers. There were no clear differences between opinions of authors from different countries or disciplines.

In the more recent literature (since 2008), a duty to recontact is often discussed in light of the introduction of next-generation technologies. These articles added two new dimensions to the original discussion about recontacting in clinical genetics: first, a discussion of the issues of large-scale incidental findings and variants of unknown significance (VOUS) associated with these new-generation technologies was initiated, and, second, the introduction and specific characteristics of direct-to-consumer genetic testing were added to the discussion in some articles.[33,41,48] These new developments are believed to further complicate recontacting in clinical genetics.

Table 1. Articles included in the review, by country and by discipline

Nr.	First author	Year of publication	Country	Discipline(s)			
				Ethical	Legal	Social	Clinical
1.	Pelias	1991	USA	-	+	-	+
2.	Andrews	1991	USA	-	+	-	-
3.	Andrews	1992	USA	-	+	-	-
4.	Hecht	1992	USA	-	-	-	+
5.	Pelias	1992	USA	-	+	-	+
6.	Patenaude	1996	USA	-	-	+	-
7.	Almqvist	1997	Canada	-	-	-	+
8.	Andrews	1997	USA	-	+	-	-
9.	Bernard	1999	Canada	-	-	-	+
10.	Hirschhorn	1999	USA	-	-	-	+
11.	Sharpe	1999	Canada	-	-	-	+
12.	Fitzpatrick	1999	USA/Canada	-	-	-	+
13.	Harris	1999	Europe	-	-	-	+
14.	Dean	2000	Europe	-	-	-	+
15.	Hunter	2001	Canada	-	-	-	+
16.	Knoppers	2001	Canada	-	+	-	-
17.	Peshkin	2001	USA	-	-	-	+
18.	Godard	2003	Europe	-	-	-	+
19.	Wertz	2003	Europe	+	-	-	-
20.	Letendre	2004	Canada	+	+	-	-
21.	Doheny	2004	USA	-	-	-	+
22.	Milunsky	2004	USA	-	-	-	+
23.	Brown	2006	USA	-	-	-	+
24.	Guzauskas	2006	USA	+	-	-	+
25.	Kausmeyer	2006	USA	-	-	-	+
26.	Hunter	2006	Canada	-	-	-	+
27.	Nagaraja	2006	India	-	-	-	+
28.	Griffin	2007	USA	-	-	-	+

Nr.	First author	Year of publication	Country	Discipline(s)			
				Ethical	Legal	Social	Clinical
29.	Peshkin	2007	USA	+	-	-	+
30.	Sexton	2008	Australia	-	-	-	+
31.	Rubinstein	2008	USA	-	-	-	+
32.	Rantanen	2008	Europe	-	-	-	+
33.	Shirts	2008	USA	+	-	-	+
34.	Sexton	2008	Australia	-	-	-	+
35.	Hampel	2009	USA	-	-	-	+
36.	Mezer	2009	Israel	-	-	-	+
37.	Resta	2009	USA	-	-	-	+
38.	Ali-Khan	2009	Canada	-	-	-	+
39.	Dondorp	2010	Europe	+	-	-	-
40.	Elger	2010	Europe	+	-	-	-
41.	Pyeritz	2011	USA	-	-	-	+
42.	Sijmons	2011	Europe	-	-	-	+
43.	Sharp	2011	USA	+	-	-	-
44.	Murray	2011	USA	-	-	-	+
45.	Hastings	2012	Europe	+	-	-	+
46.	Trakadis	2012	Canada	-	-	-	+
47.	Aronson	2012	USA	-	-	-	+
48.	Thorogood	2012	Canada/Europe	+	-	-	+
49.	Townsend	2012	Canada	+	-	-	+
50.	Van El	2013	Europe	+	-	-	+
51.	Vanacker	2013	Europe	-	-	-	+
52.	Reiff	2013	USA	-	-	-	+
53.	Bean	2013	USA	-	-	-	+
54.	Clayton	2013	USA	+	+	+	+
55.	Hazin	2013	USA	+	-	+	+
56.	Quaid	2013	USA	+	-	-	+
57.	Ayuso	2013	Europe	-	-	-	+
58.	Hunt	2013	USA	+	-	-	-
59.	O'Connor	2014	USA	-	-	-	+
60.	Semaka	2014	Canada	-	-	-	+
61.	Wagner	2014	USA	-	-	-	+

Recontact in clinical genetics: in which situations?

For each article, we analyzed the situations in which a duty to recontact was thought to apply (Table 2). We scored each article on whether one or more of four recontacting situations were mentioned: (i) new treatment option or screening recommendation; (ii) new technique or genetic test available; (iii) new laboratory information (e.g., new interpretation of former test results or new gene associated with a disease formerly tested for); (iv) VOUS. In 13 articles recontacting was discussed in light of new genetic information

without defining what this new information entailed. Recontacting in situations where new treatment options or screening recommendations were available was discussed in nine of the (mostly older) articles. In about 50% of the older articles, recontacting situations included the availability of new tests (e.g., direct testing for Huntington disease, *FMR1* testing, *BRCA1/2* large rearrangement testing) and, consequently, new genetic information being available to former patients. By contrast, the more recent articles did not discuss the availability of whole-genome sequencing (WGS) as a new test/technique but rather discussed the consequences of applying this new test/technique in relation to recontacting, in the sense of new laboratory information becoming available.

Table 2. Discussed duties in the clinical genetic setting

Discussed duty in which situation?						**Discussed duty for whom?**			
	New treatment/ Screening recommendation	**New technique/ test**	**New lab information***	**VOUS**	**New informa-tion undefined**	**Lab**	**Treating HCP**	**Referring HCP**	**Patient**
1.					+		+		+
2.	+	+	+				+		
3.		+	+				+		
4.	+	+					+		
5.					+		+		+
6.		+	+				+		
7.		+					+		+
8.		+	+				+		
9.		+					+		
10.	+	+					+	+	+
11.		+					+		+
12.		+	+				+		+
13.		+					+		
14.					+		+	+	+
15.		+	+				+		+
16.					+		+		
17.			+	BRCA1/2			+		+
18.					+		+		+
19.					+		+		
20.		+	+				+		+
21.					+		+		+
22.		+					+	+	+
23.	+		+	BRCA1/2			+	+	+
24.					+		+		
25.					+		+	+	+
26.	+	+					+	+	+

	Discussed duty in which situation?						Discussed duty for whom?			
	New treatment/ Screening recommendation	New technique/ test	New lab information*	VOUS	New informa-tion undefined	Lab	Treating HCP	Referring HCP	Patient
27.	+				+		+		+
28.					+		+		
29.	+	+	+				+		+
30.			+				+		
31.		+					+	+	+
32.	+						+		
33.			+	WGS		+			
34.		+					+		
35.		+					+		+
36.					+		+	+	
37.			+			+	+		+
38.			+	WGS			+	+	+
39.			+	WGS			+		+
40.	+				+		+		
41.			+	WGS			+	+	+
42.		+	+				+		+
43.			+	WGS			+		
44.			+	BRCA1/2			+		+
45.			+	WGS			+		
46.			+	WGS			+		
47.			+	HCM a.o.		+	+		+
48.			+	WGS			+		
49.			+	WGS			+		+
50.			+	WGS			+		
51.			+	WGS		+	+		
52.			+	array			+		+
53.		+	+	BRCA1/2		+			
54.			+				+		+
55.			+	WGS		+	+		
56.		+	+				+		+
57.			+	WGS			+		+
58.			+	WGS		+			+
59.		+	+			+	+		+
60.			+				+		+
61.			+	WGS		+	+		

a.o., and other (diseases); BRCA1/2, Breast Cancer gene 1/2; HCM, Hypertrophic Cardiomyopathy; HCP, health-care Professional; VOUS, variant of unknown significance; WGS, whole-genome sequencing.

Most articles (36 in total, including all articles from 2011 onwards) referred to the situation in which new laboratory information becomes available; the issues of changes in classification of monogenetic test outcomes from VOUS to known pathogenic or non-pathogenic outcomes or the expansion or reinterpretation of results from WGS based on extended knowledge were often raised (Table 2).

ELSI issues regarding the duty to recontact

ELSI, as well as practical issues, were raised when discussing whether recontacting should be considered a duty (Table 3). Ethical and legal issues were raised as arguments both in favor of and against a duty to recontact, whereas social and practical issues were mostly seen as counterarguments. Overall, counter-arguments are discussed in the literature more often than arguments in favor of recontacting. This did not, however, lead authors to conclude that recontacting in clinical genetics is undesirable. Many articles, in fact, start by proposing that recontacting in clinical genetics is to some extent desirable. The arguments for why this is believed to be so are not always mentioned explicitly. Counterarguments, on the other hand, usually are mentioned explicitly. From the overview of pro and contra arguments (Table 3), one can therefore not (always) conclude whether authors are in favor of or against a duty to recontact in clinical genetics.

The ethical arguments that were most often cited on both sides of the discussion were respect for patient autonomy, beneficence (do good), and nonmaleficence (do no harm). Regarding patient autonomy, it was often reasoned that recontacting former patients with new actionable information may promote autonomy because such information may offer new opportunities to former patients.[15] Another argument put forward regarding patient autonomy was that consent to be recontacted can never be truly autonomous because patients do not know what kind of information might be disclosed.[20] The more recent literature relatively more often raised ethical arguments against a duty to recontact, thereby emphasizing respect for patient autonomy, which is thought to become even more important in light of WGS.[49,54] Hunter et al.[15] stated that there is a greater justification for recontacting former patients with definite, significant information about a life-threatening disease than for a small increased risk for a slowly progressive disease. They also noted that information may affect people differently, and therefore recontacting might be beneficial for some, whereas it might be harmful to others. The disease in question and the nature and timing of the information will most probably influence this impact.

Legal arguments for and against recontacting were raised primarily in the older articles. Liability issues were discussed most often. It was argued that recontacting could prevent professionals from being held liable for negligence by former patients, who might claim a need to know any new, medically relevant information.[1,5,15,28,59] The opposite issue – that patients could sue their HCP because recontacting breached their right not to know – was not explicitly addressed in the literature, although the importance of a patient's right not to know was often mentioned. Liability was, however, discussed as a counterargument by

Letendre and Godard,[20] reasoning that professionals may make themselves vulnerable if they cannot satisfy the expectations raised by embracing a recontacting policy. In the more recent literature focusing on recontacting in relation to WGS, legal arguments are rarely discussed. With respect to the persistently increasing relevance of incidental findings from WGS, Clayton et al.[54] stated there is no existing case law and a duty to recontact is unlikely to extend in perpetuity or to require more than reasonable effort.

The social aspects of recontacting were addressed repeatedly (Table 3), mainly focusing on psychological issues. Psychological arguments in favor of recontacting were discussed in only three articles. According to Sharpe,[11] one can argue in favor of recontacting because it may correspond to "patients' informational, communicative, emotional, and psychological needs." Sexton and Metcalfe[34] and O'Connor[59] mentioned the reduction of uncertainty to patients as a psychological argument in favor of recontacting. In 15 articles the presumed psychological impact of recontacting was, however, put forward as an argument against imposing a duty. The main arguments comprised potentially increased anxiety, stress, and negative effects on self-image and relationships/family relations. These authors considered that, as long as the psychological consequences of recontacting former patients are unclear, one should be cautious in implementing a recontacting policy. The negative psychological consequences of recontacting former patients regarding relations with their family members, and the consequences for the family members themselves, were mentioned by several authors.[8,11,23,29,33,41] Because familial implications are an important aspect of genetic counseling and testing in general, these should also be considered in the case of recontacting. In addition to psychological counter-arguments, a minority of articles also mentioned other social arguments, for example, financial impact and consequences for insurance.[8,15,30,34]

Ultimately, however, it is the practical aspects, such as knowing which patients to recontact and the availability of an infrastructure for recontacting, that were put forward most often as counterarguments for imposing a duty to recontact. These were the main reasons for many authors to conclude that although recontacting might be desirable, it cannot be regarded as a legal duty.

Recontact in clinical genetics: practical barriers and solutions discussed

About 75% of the articles addressed practical barriers to recontacting. Various barriers were distinguished, for example, lack of infrastructure for efficiently tracking files/data of former patients;[16,23,42,51,57] deciding on/selecting which patients to recontact,[24,33,35,37,38] lack of time, money, and staff to perform recontacting;[6,11,12,14,15,23,26,36-39,41-43,49,52,57] and lack of up-to-date patient addresses.[10,22,44]

However, about two-thirds of the articles also mentioned solutions to overcome these barriers. In the older literature about half of the articles that mentioned a solution suggested involving patients in the process of recontacting.[1,7,10,12,18,21,23,25] Patients could contribute by, for example, contacting the department regularly to inquire about new genetic information,

keep the genetics department up to date regarding address and personal information, and checking for new genetic developments on websites. Fitzpatrick et al.[12] suggested including informing the media, support groups, and other health professionals in the recontacting process. Establishing databases or computerized registries were also mentioned as possible solutions in several of the older articles.[3,5,6,11,13,14,19] Ensuring patient privacy was, however, mentioned as a major concern in this respect. Finally, Hunter et al.[15,26] suggested recording patient preferences regarding recontacting as part of the informed consent procedure at the initial consultation.

In the more recent articles (since 2008), the main solutions being discussed involve communication technologies and (digital) storage of information.[38,41-43,45-47,49-51,53-55,58,59] Hunt[58] discussed combining digital storage of patient information and involving patients in the recontacting process by establishing an electronic health system in which patients are in control of their own (WGS) data over time. Several authors also reported on pilot or implemented digital communication systems between laboratories, clinicians, and patients.[46,47]

Wagner et al.[61] proposed a solution that could avoid large-scale recontacting concerning WGS results: Treating WGS like every other diagnostic test by focusing only on the data concerning the actual diagnostic question and discarding all other data avoids a large number of potential recontacting-required findings. If a new diagnostic question arises in the future, a new WGS test can be performed. Hastings et al.[45] also mentioned this approach with regard to privacy/confidentiality issues of patient data storage, relative to the costs of repeating WGS.

Recontact in clinical genetics: duty or not?

Although the situations authors referred to when discussing a duty to recontact in clinical genetics varied, we tried to score articles by the conclusions given by the authors. Table 3 presents an indication of the extent to which recontacting was considered to be a duty in clinical genetic practice (columns 4-6). Half of the articles drew no clear conclusion about whether recontacting should be considered a duty in clinical genetics. Of the 28 articles that did formulate a conclusion, 6 concluded that a duty to recontact does apply and 22 concluded that it does not.

This scoring should be interpreted with caution because authors' interpretations of what constituted a duty varied. For example, some authors confined the discussion to legal considerations, whereas others focused on broader moral, ethical, or professional duties. All six articles that concluded that there is a duty to recontact in clinical genetics were older articles. Four were written from a legal perspective in the early 1990s by two different researchers.[1-3,5] They concluded a duty to recontact may be expected in the field of clinical genetics on the basis of US case law on clinical practice in other medical specialties. An often cited case in this respect is that of *Tresemer versus Barke*, in which a physician was held responsible for not warning his patient of the possible dangers of an

intrauterine device when he learned that the device, which he had previously inserted in his patient, was proving dangerous.[1,62] Andrews,[3] for example, argued that "courts may hold that professionals who undertake genetic diagnostic procedures, even if they had only a fleeting contact years earlier, have a duty to update patients about subsequently discovered meanings of those tests."

In the fifth article that concluded that a duty to recontact does apply in clinical genetics, Wertz et al.[19] consider recontacting former patients to be a moral duty and extend this to a responsibility to at-risk family members. They reasoned that a "professional's ethical duty extends beyond those individuals who have presented themselves for care. Ideally, all family members at genetic risk should be informed of all new developments, provided that it is possible to find them and that they are willing to be informed."[19] Finally, in the sixth article in favor of a duty to recontact in clinical genetics, Rubinstein[31] discussed recontacting in the context of specific patient groups in certain situations: recontacting to inform breast cancer patients of the availability of chemoprevention; recontacting patients who earlier had not met the criteria for *BRCA1/2* testing, but would do so now; and recontacting to inform patients who had previously been tested for *BRCA1/2* about the availability of more comprehensive tests for *BRCA1/2*. She concluded that in these situations there was a duty to recontact, but recommended careful selection of eligible patients.[31]

In the more recent articles, no authors concluded that a duty to recontact in clinical genetics applies. First, it was argued that there are no American or Canadian legal precedents that support a duty to recontact former patients in clinical genetics.[20,26,54] Although American courts have speculated about the creation of a duty to recontact former patients about subsequently discovered risks, in the more recent literature this speculation was given less support. It was argued that recontacting in light of genetic advances should be regarded as a different legal (and ethical) situation than recontacting because of errors in the application of knowledge or the use of a technical procedure that was valid at the time of initial consultation.[26] The situations in which a legal duty had been found to apply were all related to side effects of medical interventions instead of new/incidental information from diagnostic or screening tests.[54] Second, in many articles the clinician's practical ability to fulfill such a duty was questioned. Although a physician's obligation to a patient is to exercise a reasonable degree of care, it was argued that the "nature and scope of a physician's obligations will be adjusted to the particular facts and exigencies of a medical situation."[26] Therefore, in the field of clinical genetics a "reasonable degree of care" has not yet involved a legal duty to recontact.

Table 3. ELSI arguments and conclusions regarding duty to recontact in clinical genetics

Article nr.	Arguments								Conclusion: professional duty to recontact in clinical genetics		
	Pro				Contra						
	E	L	S	Pr	E	L	S	Pr	Yes	No	Not defined
1.		+							+		
2.		+							+		
3.		+							+		
4.								+			+
5.		+		+					+		
6.	+							+		+	
7.	+				+						+
8.						+	+			+	
9.	+										+
10.								+			+
11.	+	+	+		+		+	+			+
12.	+	+				+	+	+		+	
13.											+
14.							+	+			+
15.	+	+			+		+	+		+	
16.		+			+	+		+		+	
17.											+
18.								+			+
19.	+							+	+		
20.	+	+			+	+	+	+		+	
21.	+	+						+		+	
22.											+
23.	+						+	+		+	
24.	+				+	+	+	+		+	
25.										+	
26.	+	+			+	+	+	+		+	
27.											+
28.	+	+					+	+			+
29.	+				+						+
30.											+
31.							+		+		
32.											+
33.	+										+

Article nr.	Arguments								Conclusion: professional duty to recontact in clinical genetics		
	Pro				Contra						
	E	L	S	Pr	E	L	S	Pr	Yes	No	Not defined
34.			+				+				+
35.	+									+	
36.	+				+			+			+
37.					+			+			+
38.	+							+		+	
39.	+				+						+
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60.	+						+	+			+
61.											+

Abbreviations: E, ethical; L, Legal; Pr, practical; S, social

In two-thirds of the articles (19 of 29) published since 2008, the duty to recontact was discussed in light of WGS and/or VOUS. The discussion in these articles, however, has shifted from the original recontacting discussion that highlights availability of new treatments or tests to a discussion about the management of complicating/resulting issues of incidental findings and VOUS associated with performing a new test. This complicates the discussion on the duty to recontact yet also puts it in a new light.

Whose duty to recontact is being discussed?

Table 2 summarizes who was considered to have a duty to recontact. Almost all the articles focused on whether an HCP has a duty toward a patient. In the six articles that concluded a duty to recontact does exist, this was narrowed down to a duty of the treating physician. Ten of 61 articles also suggested that the referring physician had a duty in the process of recontacting former patients with new information. Patient duties were referred to in 33 articles, in which it was reasoned that the responsibility for recontacting should not be limited to the professional level, but instead shared with the patient. Finally, the duties of the laboratory in informing HCPs and patients about new findings or conclusions were discussed in nine recent articles, of which five were about a duty to recontact in light of WGS.[33,51,55,58,61] Laboratory staff were thought to have a particular duty to keep physicians and counselors up to date on changes in test interpretations so that information could be appropriately offered to patients. Shirts and Parker[33] discussed the duty of the laboratory directly to the patient in light of direct-to-consumer testing, for which there is no intervening HCP.

Empirical evidence on the duty to recontact

Ten articles covered in our review provided empirical evidence on recontacting in clinical genetics (Table 4). Four presented their practical experiences with recontacting;[9,30,31,35] in each case, the recontact was initiated by a clinician from the genetics department by telephone or letter, but three of four studies did not report whether consent for recontacting had been requested at the initial consultation. Despite the difficult consequences that might accompany new information, the majority of patients that participated in these studies were happy to be recontacted because they were now better informed. Some patients, however, expressed negative feelings about being recontacted because it meant they had to cope with new information and/or fears.[9,30]

The other six articles presented data from surveys and focus groups about the implementation of recontacting from the perspective of both counselors and patients.[12,14,25,28,49,59] These studies described opinions on recontacting as part of standard care; possible benefits, burdens and methods; and professional opinions about using genetic registries for recontacting patients. These data showed that opinions of professionals and patients generally differed on who is responsible for recontacting and on the ethical principles of recontacting. A substantial proportion of patients considered the HCP responsible for updating them about new information and wanted regular contact/recontact. Most professionals considered recontacting to be desirable and the shared responsibility of professionals and patients. Only Townsend et al.[49] reported on the duty to recontact in light of WGS; patients' and professionals' opinions were in accordance with the other empirical articles.

Table 4. Empirical evidence on the Duty to Recontact (DtR) in clinical genetics

Article nr.	Study type	Perspective	Study population/content	Conclusion(s)
9.	DtR in practice	Patient	39 patients at risk for Fragile X premutation; recontacting for availability of FMR1 testing	For the majority of patients, getting information seems to outweigh their need for privacy
12.	Survey	Counselor	Randomly selected genetics professionals (n=1,000) (ASHG members); survey on opinions about DtR	Most respondents regard recontacting of patients ethically desirable but not feasible. Suggestions for the development of guidelines by (closely involved) professionals are made
14.	Survey	Counselor	Consultant members of the UK Clinical Genetics Society (n=77); survey on use of genetic registers	The majority of clinical geneticists in the UK regard recall and review through genetic registers as an important part of clinical genetic centers function
25.	Survey	Patient	Patients who received cancer genetic counseling from 1998 to 2004 at Penn State Cancer Institute (n=340); survey about patient expectations, experiences, and satisfaction with counseling process	The majority of patients view the genetic counselor as responsible for updating them about new discoveries
28.	Survey	Patient	Cancer genetics patients (n=851) previously seen in a clinic or who participated in a gene testing study; provided with written update, survey about their opinions on this way of recontact	Substantial portion of patients want an ongoing relationship with geneticist, with regular contact. Preferred way of contact: tailored letter
30.	DtR in practice	Patient	Nine parents of deceased children with mitochondrial disease; oral interviews about experiences with recontacting	Be aware of the widely variable impact of genetic information between patients. Patients wanted information despite difficult consequences
31.	DtR in practice	Counselor	BRCA patients attending genetics clinic from 1996 to 1998; recontacting by letter for availability of MLPA test	Duration of responsibility to patients must be considered, and standards made, to accommodate to changes in standards of care
35.	DtR in practice	Counselor	Patients who had tested negative for BRCA (n=319); recontacting patients by letter for availability of BRCA large rearrangement test	Recontact is possible, but careful preparation is needed. Professional and patient responsibilities are unclear. Practice guidelines are recommended
49.	Focus groups	Counselor and patient	Ten genetics professionals, 8 parents of “genetic” patients, 10 laypersons; three focus groups exploring issues on disclosure of incidental findings in clinical whole-exome sequencing.	Professionals and laypersons have opposite viewpoints regarding ethical principles. Pre-test discussions should reflect the shift to patients as fully informed partners, being a shared venture built on trust and responsibility.
59.	Survey	HCP and patient	Patients (n=254) and cancer genetics providers (n=216); patient survey on expectations and preferences for recontact, professionals survey on current practices, methods, and opinions about recontacting	Patient survey : patients held their genetics provider and specialists responsible for recontact, preferably by personalized letter, with new information to appropriate patients Professionals survey: 67% of genetics providers do perform recontacting, and 63.8% think they have an ethical duty, but a majority also put responsibility for recontacting on the patients. There is a need of formal guidelines on recontacting.

ASHG, American Society of Human Genetics; BRCA, breast cancer; DtR, duty to recontact; FMR1, fragile-X mental retardation 1; MLPA, multiplex ligation-dependent probe amplification.

Existing guidelines on the duty to recontact

Finally, we examined whether professional guidelines on the duty to recontact exist and what was mentioned in the literature. The only guideline we found was the 1999 policy statement of the American College of Medical Genetics and Genomics on the duty to recontact,[10] which was referred to by several authors. In this statement the primary-care physician is considered responsible for alerting patients to the need for recontact because medical geneticists do not usually maintain ongoing contact with patients and would therefore have problems relocating and recontacting prior patients. In the 2007 revision of the American College of Medical Genetics and Genomics recommendations for standards for interpreting and reporting of sequence variations (referred to by Shirts and Parker[33]), it was, however, argued that the position described in the 1999 statement could be problematic for information on novel sequence variants, for example. Because these variants are by definition rare, such knowledge is often restricted to the laboratory. According to the 2007 revision, it was the testing laboratory that should make an effort to contact physicians of previously tested patients if new information changes the initial clinical interpretation of a sequence variant.

The scarcity of guidelines for recontacting in clinical genetics was also apparent from a 2008 review of European countries' national regulations and practices of genetic counseling.[32] This review showed that the application of recontacting in clinical genetic practice was not usually regulated by legislation or mentioned in guidelines and needs further discussion. In addition, two papers referred to two other guidelines when addressing the duty to recontact,[28,34] but after careful scrutiny neither of these guidelines explicitly addressed the duty to recontact.

DISCUSSION

Summary

This systematic review provides an overview of the ELSI as well as practical issues raised in the literature on recontacting former patients in clinical genetic practice and the available empirical evidence. Our review shows that most of the included articles are written from an ethical and clinical perspective. In general, no clear differences between the opinions of authors from different countries or disciplines were apparent, although the few articles that concluded a duty to recontact does exist were written mostly from a legal viewpoint. Most articles discussed recontacting for situations in which new laboratory information related to new test options or techniques becomes available. In the more recent literature the issue of recontacting was also discussed in relation to VOUS and WGS. Ethical and legal arguments were raised both in favor of and against a duty to recontact, whereas social and practical issues were mainly used as counterarguments. Most authors regarded recontacting to be ethically desirable, although it was argued that there is no legal basis for a duty to

recontact in clinical genetics. Legal precedents are lacking, and recontacting is currently not regarded as a "reasonable degree of care." The greatest obstacles for implementing a general recontacting policy lie in the practical issues, such as tracking and selecting patients, and the time, money and staff required. Various solutions have, however, been proposed and piloted. Many articles suggest involving patients in the recontacting process; although the responsibility of the treating HCP is central in the recontacting discussion, many articles stated that the patient also has a responsibility in the recontacting process. Finally, our review shows that empirical evidence and formal guidelines about recontacting in clinical genetics are currently sparse.

Study limitations

By using broad search terms and a thorough research process, we aimed to make our review as complete as possible. However, we did find 13 references for which no full-text article was available (mostly "gray" literature from Google Scholar), and we excluded three articles not published in English. Furthermore, we will have missed local or national guidelines on the duty to recontact that were not published in peer-reviewed journals. So, despite our thorough approach, we may have missed some relevant articles or information.

Conclusions

When comparing the discussed situations, arguments, and conclusions of professionals regarding recontacting in the literature, it can be concluded that the weight of ELSI issues in favor of and against recontacting varies for different circumstances and, as a result, the justification for recontacting varies accordingly. This justification seems more obvious for definite and actionable information than for less certain information. A general duty to recontact in clinical genetics will therefore not be applicable. However, future circumstances can be envisaged in which recontacting former patients with new information might be regarded as a "reasonable degree of care."

Furthermore, patient perspectives have to be included in shaping the debate on recontacting in clinical genetics. Although the empirical evidence on implementing a duty to recontact in clinical genetics is sparse, patient experiences that have been described were mainly positive. From another perspective, one can ask how free patients are to decide whether they would like to be recontacted in different circumstances.

Most of the articles we reviewed addressed only the theoretical issue of recontacting and pointed to practical problems as the major challenge. These problems form an important argument against establishing a duty to recontact. Various solutions to overcome these barriers have, however, been raised in the literature. Solutions should also include delineating the roles of all stakeholders and adequate communication between laboratories and clinicians. New digital technologies might offer opportunities for this, and few successful pilots have already been reported. We recognize, however, that the

practical constraints also have an ethical component and that resource restrictions will limit recontacting policies in both these dimensions. Clearly, these issues need to be taken into account when developing professional guidelines.

Finally, there are currently few international guidelines on recontacting former patients when new genetic information becomes available. Further debate is required to determine whether any international guidelines could be sufficient to deal with national and/or local differences in practice or with different national legal systems.

Based on our review, we conclude that there is no generally held legal basis for recontacting in clinical genetics, although it is often considered desirable by both HCPs and patients. General views on the scope of recontacting are unclear, but it was felt that both HCPs and patients should play a role. Patient wishes need to be incorporated in a satisfactory way; some may (temporarily) not wish to hear future updates or new interpretations. Using eHealth technologies in recontacting systems could help solve this issue, but further elaboration on how to best address patient wishes is needed. To make progress in implementing recontacting in clinical genetics, we suggest moving on from the current discussion of whether there is a general duty to recontact in clinical genetics and focusing on the question of in which specific situations recontacting might be regarded as a good standard of care. To this end, we call for a debate between HCPs and patients on future recontacting policies and practices. Moreover, reaching a professional consensus, obtaining more extensive empirical evidence, and developing professional guidelines are important in present-day clinical genetics. This may improve the medical and psychological benefits of new genetic technologies for our patients and their family members.

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REFERENCES

1. Pelias MZ. Duty to disclose in medical genetics: a legal perspective. *Am J Med Genet* 1991; 39(3):347-54.
2. Andrews LB. Legal aspects of genetic information. *The Yale Journal of Biology and Medicine* 1991;64:29-40.
3. Andrews LB. Torts and the double helix: malpractice liability for failure to warn of genetic risks. *Houst Law Rev* 1992;29(1):149-84.
4. Hecht F. Duty to disclose to family members in medical genetics. *Am J Med Genet* 1992;42(5):758-758.
5. Pelias MZ. The duty to disclose to relatives in medical genetics – response. *Am J Med Genet* 1992;42(5):759-760.
6. Patenaude A.F. The genetic testing of children for cancer susceptibility: Ethical, legal, and social issues. *Behavioral Sciences and the Law* 1996;14:4(393-410).
7. Almqvist E, Adam S, Bloch M, Fuller A, Welch P. Risk reversals in predictive testing for Huntington disease. *Am J Hum Genet* 1997;61:945-952.
8. Andrews LB. The genetic information superhighway: rules of the road for contacting relatives and recontacting former patients. In: Knoppers BM, editor. Human DNA: Law and Policy: International and Comparative Perspectives? The Hague: Kluwer Law International, 1997:133-143.
9. Bernard LE, McGillivray B, Van Allen MI, Friedman JM, Langlois S. Duty to re-contact: a study of families at risk for Fragile X. *J Genet Couns*. 1999;8(1):3-15.
10. Hirschhorn K, Fleisher LD, Godmilow L, et al. Duty to re-contact. *Genet Med.* 1999;1(4):171-2. Erratum in: *Genet Med* 1999;1(5):186.
11. Sharpe NF. The duty to recontact: benefit and harm. *Am J Hum Genet*. 1999;65(4):1201-4.
12. Fitzpatrick JL, Hahn C, Costa T, Huggins MJ. The duty to recontact: attitudes of genetics service providers. *Am J Hum Genet*. 1999;64(3):852-60.
13. Harris R, Harris H. Knowledge about medical genetics in health care. *Community Genet* 1999;2:115–117.
14. Dean JCS, Fitzpatrick DR, Farndon PA, Kingston H, Cusine D. Genetic registers in clinical practice: a survey of UK clinical geneticists. *J Med Genet* 2000;37:636-640.
15. Hunter AG, Sharpe N, Mullen M, Meschino WS. Ethical, legal, and practical concerns about recontacting patients to inform them of new information: the case in medical genetics. *Am J Med Genet.* 2001;103(4):265-76.
16. Knoppers BM. Editorial comment: Duty to recontact: a legal harbinger? *Am J Med Genet* 2001;103:277.
17. Peshkin BN, DeMarco TA, Brogan BM, Lerman C, Isaacs C. BRCA1/2 testing: complex themes in result interpretation. *J Clin Oncol* 2001;19(9):2555-2565.
18. Godard B, Kääriäinen H, Kristofferson U, Tranebjaerg L, Coviello D, Aymé S. Provision of genetic services in Europe: current practices and issues. *Eur J Hum Genet* 2003;11 (Suppl 2): S13–S48.
19. Wertz DC, Fletcher JC, Berg K. Review of ethical issues in Medical Genetics. Report of consultants to WHO. Geneva: World Health Organization, Human Genetics Programme, 2003.
20. Letendre M, Godard B. Expanding the physician's duty of care: a duty to recontact? *Med Law* 2004; vol.23.
21. Doheny DO, Leon de D, Raymond D. Genetic testing and counseling. In: Brin MF, Comella C, Jankovic J, editors. Dystonia: Etiology, Clinical Features and Treatment. Philadelphia: Lippincot Williams & Wilkins, 2004:23-32.
22. Milunsky A, Milunsky JM. Genetic counseling: preconception, prenatal and perinatal. In: Milunsky A, editor. Genetic Disorders and the Fetus: Diagnosis, Prevention and Treatment. Baltimore: JHU Press, 2004:1-65.
23. Brown KL, Moglia DM, Grumet S. Genetic counseling for breast cancer risk: General concepts, challenging themes and future directions. *Breast Disease* 27 (2006, 2007);69-96.

24. Guzauskas GF, Lebel RR. The duty to re-contact for newly appreciated risk factors: fragile X premutation. *J Clin Ethics* 2006;17(1):46-52.
25. Kausmeyer DT, Lengerich EJ, Kluhsman BC, Morrone D, Harper GR, Baker MJ. A survey of patients' experiences with the cancer genetic counseling process: Recommendations for cancer genetics programs. *J Genet Couns* 2006;15(6):409-431.
26. Hunter A, Sharpe NF, Mullen M, Meschino WS. Ethical, legal, and practical concerns about recontacting patients to inform them of new information: The case in medical genetics. In: Sharp NF, Carter RF, editors. Genetic Testing: Care, Consent and Liability. Hoboken: John Wiley & Sons, Inc., 2006:415-424.
27. Nagaraja SM, Sanjeev J, Muthane UB. Perspectives towards predictive testing in Huntington disease. *Neurology India* 2006;54(4):359-362.
28. Griffin CA, Axilbund JE, Codori AM, et al. Patient preferences regarding recontact by cancer genetics clinicians. *Fam Cancer.*2007;6(3):265-73.
29. Peshkin BN, and Burke, W. Bioethics of genetic testing for hereditary breast cancer. In: Isaacs C and Rebbeck TR, editors. Hereditary Breast Cancer. New York: Informa Healthcare USA, Inc., 2007:35-49.
30. Sexton AC, Sahhar M, Thorburn DR, Metcalfe SA. Impact of a genetic diagnosis of a mitochondrial disorder 5-17 years after the death of an affected child. *J Genet Couns* 2008;17(3):261-73.
31. Rubinstein WS. Roles and responsibilities of a medical geneticist. *Fam Cancer* 2008;7(1):5-14.
32. Rantanen E, Hietala M, Kristoffersson U, et al. Regulations and practices of genetic counselling in 38 European countries: The perspective of national representatives. *Eur J Hum Genet* 2008;16(10): 1208-1216.
33. Shirts BH, Parker LS. Changing interpretations, stable genes: responsibilities of patients, professionals, and policy makers in the clinical interpretation of complex genetic information. *Genet Med* 2008;10:778–783.
34. Sexton AC, Metcalfe SA. Disclosing genetic research results after death of pediatric patients. *JAMA* 2008;300(14):1693-1695.
35. Hampel H. Recontacting patients who have tested negative for BRCA1 and BRCA2 mutations: how, who and why? *J Genet Couns* 2009;18(6):527-529.
36. Mezer E, Wygnanski-Jaffe T. Ethical issues in ocular genetics. *Curr Opin Ophthalmol* 2009;20(5):382-386.
37. Resta RG. Unprepared, understaffed, and unplanned: thoughts on the practical implications of discovering new breast and ovarian cancer causing genes. *J Genet Counsel* 2009;18:521-523.
38. Ali-Khan, SE, Daar AS, Shuman C, Ray PN, Scherer SW. Whole Genome Scanning: Resolving Clinical Diagnosis and Management Amidst Complex Data. *Pediatr Res* 2009;66(4):357-363.
39. Dondorp WJ, De Werth GMWR. Health Council of the Netherlands. The 'thousand-dollar genome': an ethical exploration. Monitoring Report Ethics and Health 2010/2. The Hague: Centre for Ethics and Health, 2010.
40. Elger B, Michaud K, Mangin P. When information can save lives: the duty to warn relatives about sudden cardiac death and environmental risks. *Hastings Cent Rep* 2010;40(3):39-45.
41. Pyeritz RE. The coming explosion in genetic testing -is there a duty to recontact? *N Engl J Med* 2011;365(15):1367-9.
42. Sijmons RH, Van Langen IM, Sijmons JG. A clinical perspective on ethical issues in genetic testing. *Account Res* 2011;18(3):148-62.
43. Sharp RR. Downsizing genomic medicine: Approaching the ethical complexity of whole genome sequencing by starting small. *Genet Med* 2011;13(3):191-194.
44. Murray ML, Cerrato F, Bennett RL, Jarvik GP. Follow-up of carriers of BRCA1 and BRCA2 variants of unknown significance: Variant reclassification and surgical decisions. *Genet Med* 2011; 13(12):998-1005.
45. Hastings R, Werth de G, Fowler B, et al. The changing landscape of genetic testing and its impact on clinical and laboratory services and research in Europe. *Eur J Hum Genet* 2012;20:911-916.

46. Trakadis YJ. Patient-controlled encrypted genomic data: an advance to approach clinical genomics. *BMC Medical Genomics* 2012;5(31).
47. Aronson SJ, Clark EH, Varugheese M, Baxter S, Babb LJ, Rehm HL. Communicating new knowledge on previously reported genetic variants. *Genet Med* 2012;14(8):713-719.
48. Thorogood A, Knoppers BM, Dondorp WJ, De Wert GMWR. Commentary: Whole genome sequencing and the physician. *Clin Genet* 2012;81:511–513.
49. Townsend A, Adam S, Birch PH, Lohn Z, Rousseau F, Friedman JM. "I want to know what's in Pandora's box": comparing stakeholder perspectives on incidental findings in clinical whole genome sequencing. *Am J Med Genet Part A* 2012;158A:2519–2525.
50. Van El CG, Cornel MC, Borry P, et al. Whole-genome sequencing in health care. Recommendations of the European Society of Human Genetics. *Eur J Hum Genet* 2013;21:580-584.
51. Vanakker OM, De Paepe A. Review: Pharmacogenomics in Children: Advantages and Challenges of Next Generation Sequencing Applications. *Int J Pediatr* Vol.2013 (2013).
52. Reiff M, Ross K, Mulchandani S, et al. Physicians' perspectives on the uncertainties and implications of chromosomal microarray testing of children and families. *Clin Genet* 2013;83:23–30.
53. Bean LJH, Tinker SW, da Silva C, Hedge MR. Free the data: One laboratory's approach to knowledge-based genomic variant classification and preparation for EMR integration of genomic data. *Hum Mutat* 2013;34(9):1183-1188.
54. Clayton EW, Haga S, Kuszler P, Bane E, Shutske K, Burke W. Managing incidental genomic findings: legal obligations of clinicians. *Genet Med* 2013;15(8):624-629.
55. Hazin R, Brothers KB, Malin BA, et al. Ethical, legal, and social implications of incorporating genomic information into electronic health records. *Genet Med* 2013; 15(10):810-816.
56. Quaid KA. Molecular testing: Ethical and legal issues. In: Cheng L, Zhang DY, Eble JN, editors. Molecular genetic pathology. New York: Springer science and business media, 2013:1083-1090.
57. Ayuso C, Millán JM, Mancheño M, Dal-Ré R. Informed consent for whole-genome sequencing in the clinical setting. Proposed recommendations on essential content and process. *Eur J Hum Genet* 2013; 21(10):1054-1059.
58. Hunt K. Individualizing the informed consent process for whole genome sequencing: A patient directed approach. Dissertation, Arizona State University: Phoenix, Arizona, 2013.
59. O'Connor MR. Patient and genetics health care providers attitudes regarding recontact. Thesis, University of Pittsburgh: Pittsburgh, PA, 2014.
60. Semaka A, Hayden MR. Evidence-based genetic counselling implications for Huntington disease intermediate allele predictive test results. *Clin Genet* 2014:85:303-311.
61. Wagner JK, Mozersky JT, Pyeritz RE. "Use it or lose it" as an alternative approach to protect genetic privacy in personalized medicine. *Urol Oncol* 2014;32(2):198-201.
62. Berg D, Hirsch HL. Duty to recall. *Southern Med J* 1980;73(8):1041-1045.

Chapter 8

Summary

The aim of this research was to investigate promising innovations in clinical genetic patient care to find new and more effective ways of providing genetic counseling and information to our patients, while maintaining the quality of care. We aimed to determine patient outcomes and evaluations, and professionals' opinions and evaluations, including cost aspects, on three types of innovations in our clinical genetic care: (1) group genetic counseling; (2) telegenetics application in general, and online genetic counseling specifically, and (3) the recontacting of former genetic patients. This chapter provides an overview of our main findings.

In *Chapter 2* we described the results of a cohort study on group genetic counseling of cardiomyopathy index patients, as carried out in various regional hospitals in the northern part of the Netherlands. Counseling sessions consisted of a main plenary (informational) part, short individual discussions, and the possibility of giving blood for DNA testing. In total 13 group sessions were held in 8 regional hospitals, for 82 symptomatic cardiomyopathy patients and their partners/relatives. Patients reported they were overall satisfied and their questions had been answered. Their changes in perceived personal control and anxiety were comparable to previous reports of group genetic counseling and individual oncogenetic counseling. Regional cardiologists and heart failure nurses were also satisfied with this new approach, whereas the genetic professionals involved were less satisfied, mainly due to the large time investment on their part and the more limited than expected group interaction during the sessions. However, the reported patient outcomes showed that this could be an acceptable type of care from the patients' perspective as an alternative care modality to individual genetic counseling at the University Medical Center. However, the optimal design of this new type of care, taking into account both patients' and providers' perspectives, still has to be determined. The composition of the counseling team, as well as the number of professionals involved in these group sessions may be reconsidered to reduce the professional's total time investment.

Chapter 3 covered the economic analysis of our group genetic counseling design in regional hospitals, in terms of patient uptake, the percentage of counseled patients having their DNA tested, and the resultant quality of life effects (in terms of anxiety and perceived control) of our new approach. In addition, we compared our new group approach to conventional, individual counseling given in regular regional outpatient clinics and in the UMC, and to two alternative models of offering genetic counseling: group genetic counseling at the UMC and individual counseling at patients' local hospitals. This analysis showed that our regional group counseling reached substantially more patients than had been referred to the UMC in previous years. Moreover, the total differences in costs of the various scenarios of group or individual cardiogenetic counseling were relatively small, although individual counseling given locally is the preferred scenario from the patients' and societal perspective. From the provider's perspective, group counseling should preferably be held at the UMC, but

it is unclear to what degree the hospital setting, and the travel time and cost would then impact the referral rate, and attendance rate of patients. Overall, group counseling as a care modality could be an appropriate addition to current clinical genetic care, but the composition of the team, location of the group sessions, and optimal group size may need some reconsideration.

Chapter 4 reported the results of an online survey amongst European genetic professionals on the current availability and use of various telemedicine applications among clinically working genetics professionals. The survey revealed three main points: telemedicine applications are only limitedly available and have an even more limited use throughout a substantial number of European countries, which could both be extended; each telemedicine application is being used for various activities; and cooperation, education and guidelines might be helpful in successfully increasing the use of telegenetics. Three main groups of barriers to its use were reported by respondents, most of whom did not have personal experience with using telemedicine: lack of perceived suitability and need, practical constraints, and lack of professional support/knowledge. These could be indications that the opportunities of telegenetics are so far largely unseen, and thus unused. We concluded that there is sufficient ground to extend the use of Telegenetics applications in Europe, both in direct and indirect patient care. To achieve this, the perceived practical and regulatory barriers should be overcome, and we need to raise awareness of the possibilities and likely advantages of telegenetics amongst genetics professionals.

Chapter 5 reported the results of a matched cohort study with pre- and post-measurements for online genetic counseling for cascade screening of cardiogenetic and oncogenetic patients, and for urgent prenatal counseling. Online counseling was given to patients in their own homes, at a relatively short distance from the hospital. Patients needed to undertake various preparations. Genetic counseling was given using a dedicated online platform with supportive tools that were available during counseling, in addition to a webcam image on screen. Patient outcomes on satisfaction, perceived personal control and anxiety showed that those involved in online genetic counseling were satisfied and the changes in their levels of perceived personal control and anxiety were, on average, similar to those of patients undergoing conventional, in-person counseling at the outpatient department. The patient evaluations showed that this self-prepared online care in patients' homes is feasible, and that the main advantages for patients afterwards were the decreased time investment/travelling and having counseling in a familiar environment.

Chapter 6 reported the professionals' perspective on online genetic counseling for presymptomatic testing of cardiogenetic and oncogenetic patients, and urgent prenatal counseling, and gave a cost and time analysis of this type of care. We performed a cohort study with pre- and post-measurements in ten genetic counselors, studying their

satisfaction with telemedicine, and the impact on cost and time of this type of counseling. Counselors considered our current online application to be qualitatively inadequate for use in regular care, mostly because of the technical characteristics and imperfections, and because of the relative lack of personal contact. On the positive side, online counseling allowed them to have more flexibility in work processes, to possibly avoid travelling time to regional hospitals, and allowed them to monitor cascade screening in families living all over the country. The time and cost analyses showed that less time and lower costs were involved in this new type of counseling than for conventional in-person counseling at the outpatient clinic. However, when we continue the use of the current external provider of the application upon its implementation in regular care, we will need additional investments in terms of licenses and technical support. Altogether, online counseling could reasonably be offered as an addition to the current spectrum of genetic care options to that group of our patients who have the required facilities and are open to use online options. However, technical imperfections mean that online counseling at this stage cannot be regarded as a full alternative to in-person counseling. Technical improvements and adaptations need to be made before this application will be considered sufficient by counselors for adopting on a larger scale in regular patient care.

Finally, *Chapter 7* covered issues surrounding the duty to recontact former patients in clinical genetics. We performed a systematic review of 61 articles published up to 1 September 2014, and selected from 1428 hits in four different databases. Articles were included when they reported about the duty to recontact in clinical genetics, and the ethical, legal, social and practical aspects were discussed in the light of new genetic diagnostic technologies. Our review showed that most authors consider recontacting to be ethically desirable, but that they saw practical concerns as the main barriers. Various solutions to these barriers have been proposed in the literature, but so far there is little empirical evidence on recontacting in practice, for example reporting evaluations of preferred/feasible methods for recontacting, and patient opinions and outcomes of being recontacted. The available empirical studies show that most patients appreciated being recontacted for various indications and time spans since their counseling. We concluded that reaching a professional consensus and obtaining more empirical evidence – by performing pilot projects – on the specific situations in which recontacting is regarded as a good standard of care, and establishing guidelines are important next steps. The preferred method of recontacting, both from the patients' and providers' perspectives, should be determined, taking into account the psychological impact, the ethical and legal preconditions, the possibility of dynamic consent, and the feasibility and costs of a recontacting system, for example. Using an online tool to achieve some of these requirements could be a next step in the research into the introduction of recontacting practice in clinical genetics.

Chapter 9

General Discussion

COMMON THEMES OF THE INNOVATIONS IN CLINICAL GENETICS

Opposing viewpoints

The innovations described in this thesis revealed various opposing viewpoints held by the parties involved, as is frequently the case in innovative changes. Both our group counseling and online counseling approaches were attractive from the patients' perspective, as shown by their reported satisfaction and their psychological outcomes. Our review on recontacting former patients also showed that overall patients appreciated being recontacted. However, our studies also revealed that these positive evaluations were not shared by all the parties: for all the innovations we studied, the genetics professionals were less satisfied than patients were with the new options. For group counseling, the professionals' drawbacks mainly reflected their time investment and the lack of group interactions, while online counseling was judged as less positive by counselors because of technical problems and the reduced quality of communication compared to conventional counseling. Seen in a broader perspective, the genetics professionals' less positive expectations of online applications was also illustrated by their limited use of such applications in patient care throughout Europe, even when they had the opportunity and facilities. Finally, regarding recontacting, professionals' and patients' views differed widely in that the professionals mainly perceived recontacting as being nearly impossible to implement in practice.

Our new approaches in clinical genetic care thus have various sides: the provision of accessible patient-centered care, the related time and cost investments, and the drawbacks seen by the genetics professionals. The professionals' viewpoints were mainly based on their experiences with conventional counseling, which they consider as their standard of care and acknowledge as 'good care provision'.[1-3] However, from the patients' viewpoint, convenience and efficiency are becoming increasingly important in society in general – as seen in the rapid rise in the availability and use of all kinds of online services.[4-7] Accordingly, we should expect an increasing consumer interest in digital and online oriented health service delivery and organization of care. It is therefore conceivable that an increasing number of patients will also be interested in online genetic counseling, if this service is offered as part of regular care. If we want to aim at keeping up with developments in society, with our patients' wishes and needs, and if we want to take future developments and the economic constraints in health care and genetic services into account, then the current gap in user satisfaction between our subset of patients open to online counseling, and the counselors has to be bridged. To reach this aim, we need better quality of our online technology, but it is equally important to promote a change in the attitude of counselors/professionals. This aspect will be addressed in detail in the next section.

Other perspectives addressed in our studies were the management and societal perspectives, in which it is important to deliver qualitatively acceptable and low-cost efficient care, and reach a high uptake both in terms of patient attendance and of DNA-testing with a view to achieving health gains. The specific counseling modality used might influence

these uptake rates.[8-10] Opposing viewpoints of patients and regional professionals, and the genetics management became apparent in our study on group genetic counseling. From the management viewpoint, group counseling should preferably be performed centrally – at the UMC – to avoid counselors travelling from the UMC to regional hospitals. In contrast, patients and regional professionals appreciated our local approach, which was also shown by increased referral rates. Here, the interest of a third party also plays a role: local care provision could stimulate the referral and uptake (patient attendance of group counseling), allowing for more family members of patients to be informed and to take preventive measures if necessary. Although half of the patients indicated they would be willing to travel to the UMC, and almost all regional professionals were willing to refer patients for group counseling at the UMC instead of in their own hospital, it is unclear if the higher uptake realized with the local approach would be continued in that case. It seems plausible that the increased uptake was, for a substantial part, caused by our active approach to regional professionals, thereby stimulating their cooperation and awareness, rather than by increased patient willingness to participate in local group counseling instead of our conventional approach. These opposing viewpoints could be reconciled if group counseling is held centrally at the UMC, and if alternative ways of continuing and efficient cooperation between regional and UMC professionals can be reached, to maintain and increase local awareness, and allow as many patients and their families as possible to take advantage of our clinical genetic care. Perhaps regular, online, interprofessional consultations would help support this aim. Even the provision of online group consultations to patients could be considered.

Finally, we pinpointed opposing views of the genetics management and counselors in the online counseling project. To increase the flexibility and efficiency of care provision, and to serve more patients over a larger geographical area, online counseling could be an attractive modality and a useful addition to regular care services, despite genetic professionals' initial hesitation, reluctance or even negative opinions.[9,11-13]

Implementation in regular care

Another common theme arising from our research was the issue of implementation in regular care. Would this be beneficial for all the surveyed innovations? And if so, how should we position these new types of care? Should they completely replace conventional care (for selected indications)? Or should they only be extensions to existing care services? And which patients or groups should be offered these new types of care? Our studies showed that the patient and cost outcomes of group and online genetic counseling are at least similar to regular care. Although these two new types of care should not be regarded as care modalities that will completely replace current ways of providing genetic counseling. Given that clinical genetics covers a wide range of diseases and serves a large range of patients, there will be, and continue to be, categories of patients that benefit more from one type of care than another. This could, for example, be influenced by the number of

relatives attending counseling, the indication for counseling, personality characteristics, or co-morbidity. Also, In addition, some patients will not have the required facilities for online counseling, and/or will dislike/refuse to have a certain type of care.[14,15] Therefore, a mix of different counseling modalities will be needed in the future. This increases the flexibility for both patients and providers, provided the hospitals we are working with facilitate these options through implementing state-of-the-art ICT-facilities, and our medical secretariat is able to manage the greater organizational complexity of this mode of care.

Group genetic counseling

Our studies on group genetic counseling to cardiomyopathy patients do not justify implementing it in regular patient care in the design we offered (we found no clear gains in terms of lower cost or less time investment, a modest evaluation from the genetic professionals involved, and no clear patient preference for the group session features). Alternative designs of group counseling in terms of team composition, group size and location, and an assessment of location-dependent uptake could be considered. However, the studies did reveal that our active approach led to an increased awareness and cooperation in regional professionals and higher patient uptake, and thus to better informed index patients and potential health benefits for their family members. For these reasons the benefit of increased referral and uptake of symptomatic patients should be maintained. Future research should indicate the best way of providing genetic counseling to this patient group, with regard to a balanced time/cost and uptake rate.

If the current regional approach would be continued, changing the composition of the counseling team could be one way to reduce the cost of group counseling, which would help justify this approach.[8,16] The main requirement for the professionals is to be able to deal with groups of patients instead of individual patients, and to have sufficient knowledge of the genetic disease for which the group is being counselled. To reach these aims, various combinations of a social worker, a resident and a genetic counselor, under the supervision of a distant clinical geneticist and a cardiologist could be possible.[8]

Apart from the reasons of efficiency and costs, the ideal group size with a view to psychological patient outcomes and optimal group interaction should be determined before possible further implementation. We included groups from 3 to 13 patients, and found no differences regarding psychological outcomes and satisfaction for smaller (<7 patients) or larger (≥7 patients) group sizes. Obviously, larger groups are more efficient due to the economies of scale. Groups of about eight patients were regarded as optimal by the genetic professionals involved, taking into account the beforementioned purposes. However, amongst the limited publications available on group genetic counseling, there are no reports about what is regarded as the ideal group size for group genetic counseling. Moreover, it seems unreasonable to aim for any extensive group interaction in our setting of a single group session, in which the participants do not know each other. In this respect, our one-off group counseling sessions are different from those reported in other medical

disciplines which mostly concern multiple consecutive group sessions for chronically ill patients.[17-21] In these multiple sessions, interaction and peer support can develop in the course of time. Although genetic and familial aspects were not discussed extensively during our single group sessions, the patients' exchange of experiences on their medical history and treatment did suggest a potentially positive role for group counseling in cardiologic care. However, the advantages of providing more information for patients by attending a group instead of an individual session also applies to our setting, and assessing the optimal interactive circumstances in our specific genetic setting could be an aspect of further research into our group approach.

Finally, an important aspect to consider, if group counseling is to be implemented, is to which patient/disease groups or type of patients it should be offered. Several reports on oncogenetic group counseling sessions for combined symptomatic/presymptomatic breast and ovarian cancer patients showed successful patient outcomes.[22-24] One report exists on group prenatal counseling, but to our knowledge, experiences with other patient groups have not been reported thus far.[25] Besides playing a role in the counseling of these 'conventional' patient categories, a possible role could be considered for group counseling associated with the new diagnostic technologies. When recontacting former patients becomes part of standard care, group sessions at the UMC might be used as one of the approaches for informing several patients at the same time about new and relevant knowledge for their genetic disease or on their previous genetic testing. Group counseling could also be used in pre-test counseling for population screening related to pregnancy, such as expanded preconception screening and non-invasive prenatal testing (NIPT). The use of next generation sequencing in these situations necessitates relatively extensive and skilled counseling of couples/patients.

Telegenetics applications and online counseling

From the perspectives of patients, society, and management, it seems justified to implement online counseling – or more generally, telegenetics applications – in regular patient care. Mainstreaming clinical genetics is a topical issue for genetic professional's organizations.[26,27] Telegenetics could make a valuable contribution to effective and efficient mainstreaming, not only in regular direct patient-counselor interactions, but also in indirect patient care, in communication between health care professionals for various purposes by offering easy access and widely available contact options. Our studies revealed rather hesitant and negative attitudes and opinions among involved counselors, but they may have different opinions about telemedicine to support interprofessional communication.

The literature mentions some general steps in the implementation of innovations, and various factors influencing the success and professionals' and patients' levels of acceptance.[28-32] These should all be applied and taken into account when implementing online counseling, including introducing the innovation gradually; setting up consecutive phases of orientation (creating awareness, interest, and involvement), insight

(understanding of the innovation), acceptance (positive attitude, motivation/intention to change), change (applying in practice), and preservation (integration of the innovation in routines).[28] In every phase, influencing factors – either stimulating or hindering – may be related to individual professionals (e.g. their skills, attitudes, norms and values), the social context (e.g. attitude and behavior of colleagues and patients, opinions of leaders and key figures) or organizational context (e.g. logistics, policies, task distribution), or the economic and legal context (e.g. reimbursement, regulations).[28]

Furthermore, the psychological Theory of Planned Behavior, the Innovation Diffusion Theory, and the Technology Acceptance Model, agree that various factors, including attitude, perceived usefulness, ease of use, and perceived subjective norm all play a part in professionals' acceptance of telemedicine.[29,31-33] Moreover, the theoretical domains framework identifies 14 domains, which also cover the factors stated by these theories, that are of importance in regulating or changing the behavior of health care professionals.[34,35] However, this framework does not indicate the causal processes that explain how the factors or constructs in the various domains influence the regulation or change of behaviors. Based on the above theories, having and/or gaining experience is likely to contribute to a positive change in opinion, provided that the right conditions are met, and recognizing its usefulness (which is partly being influenced by perceived ease of use) is a major factor in the adoption of telemedicine applications.[28,29,31,32] Moreover, acceptance can be facilitated by identifying and actively involving those professionals who particularly like to adopt the new technology, by establishing a social network, and by providing adequate resources and training of skills.[28,29,32] Finally, according to Kuo et al, it helps to use different strategies for experienced and inexperienced professionals to effect such a change.[36] All these above factors could provide the basis for drawing genetics professionals over the line to accept online counseling as part of regular clinical genetic practice.

In line with the above, creating support amongst professionals at the institutional, national and international level, and ensuring its utility and ease of use are needed for a successful implementation of online counseling, in addition to guaranteeing the quality of care provision, and removing practical barriers.[28-33,36] One way to create support could be to make online counseling part of the genetic professional standard in general, thereby making it more normal, and creating more acceptance. This could, for example, be done by making telegenetics a specific spear point of the European Society of Human Genetics, e.g. by giving it a more pronounced role at the yearly international conference, by organizing dedicated meetings of the ESHG Professional and Public Policy Committee aiming at establishing guidelines, or by establishing an ESHG working group. The results of our European telegenetics survey, together with our experience in organizing seminars at ESHG meetings, showed that professionals are interested in learning more about telegenetics and in attending meetings or participating in a working group. Initiatives at the national level might also be beneficial in this respect.[37] By exchanging experiences and research outcomes, the best ways for providing online genetic care regarding quality of care,

patient- and provider friendliness, and the most suitable patient groups could be identified most effectively and efficiently. It is desirable to perform this under the umbrella of the Dutch professional organization *VKGN*, with representatives from each university hospital participating in a telegenetics working group, and possibly collaborating with commercial partners in the field, to facilitate optimal cooperation and exchange amongst all the Dutch university genetic centers.

Another important issue at the national level is that the government and health insurance companies need to create the proper conditions to allow for the successful implementation of telegenetics, for example, by supporting digitalization in health care and ensuring reimbursement of online consultations, preferably at the same rate as in-person consultations. Currently, in the Netherlands, e-health initiatives are supported by the government by regulations and research grants in this area.[38] However, in regular patient care, only follow-up online sessions but no initial online sessions are being reimbursed by health insurance companies. This suffices for various medical disciplines that mostly need physical and additional investigations in their patients at first appointments, and which aim to apply online sessions for the follow-up and coaching of their chronically ill patients. But for clinical genetics, where patients are mostly seen only once or twice and counseling is the main activity for most patients, this arrangement does not suffice. So, reimbursement should also be provided for first online sessions, to make online counseling in clinical genetics a real added value to existing clinical genetics patient care.

Moreover, the genetics field should discuss what is a good quality of care, and if or how online counseling and/or other telegenetics applications could meet this standard of good care. According to Rantanen et al, who based their report on 56 guidelines of 29 global and European organizations, an ideal genetic counseling should comprise nine salient aspects (at least).[39] If we accept these criteria as a starting point to judge online genetic counseling, we should assess if, and to what extent, these aspects are/could be covered by this type of care. Furthermore, if aspects are not or only partly covered by telegenetics application, we should discuss how this would affect optimal patient care. Such a discussion should also be conducted with patients.

From table 1 it seems that the key aspects identified are almost completely covered in our online and group counseling approaches. It should be noted that the key aspects of Rantanen et al[39] address mainly the quality of counseling and to a lesser extent the outcomes of counseling. On the one hand, the aspects not sufficiently covered by our new approaches (#4 in online counseling; #6 and #9 in group counseling) can be taken into account when selecting patients or indications for online counseling, or other telegenetic services in regular care. On the other hand, when online counseling becomes part of regular care, and is offered alongside in-person counseling, we expect patients will also be able to decide for themselves whether their personal needs will be better met by online counseling or in-person counseling.

Table 1. The key aspects of genetic counseling being addressed in the various innovative types of care, according to our research outcomes

	Innovations in clinical genetic patient care		
Key aspects of ideal genetic counseling*	**Group counseling**	**Online counseling**	**Recontacting**
1. appropriately trained professional with understanding of genetics and ethical implications	+	+	+
2. relevant and objective information	+	+	+
3. assurance of the counselee's understanding	+	+	+/-
4. offering psychological support	+	+/-	+
5. informed consent	+	+	+
6. confidentiality of genetic information	+/- #	+	+
7. considering familial implications	+	+	+
8. appropriate handling of potential discrimination of testing	+	+	+
9. assuring autonomous decision-making by the counselee	+/-	+	+

*: according to Rantanen et al, *Eur J Human Genet* 2008[39];
confidentiality between patients during/after counseling

Recontacting former patients

From a professional and ethical viewpoint, recontacting former patients in regular clinical genetics care should be considered, and it will probably be implemented in the future.[40,41] However, the shaping, scope and circumstances for this process are still unclear. One issue remaining from our literature review was if recontacting should become standard practice over the entire width of clinical genetics, or only for selected patient groups or circumstances (e.g. new testing options available, reclassification of mutations/variations). Before this question can be answered, the multiple aspects included in recontacting, e.g. the psychological impact for patients and their relatives, the ethical and legal preconditions, and the feasibility and cost of a regular recontacting system, should be assessed. This should preferably be done by performing pilot studies. From our systematic review it became clear that there is only limited experience with recontacting patients in clinical genetics thus far,[40,42-44] although several authors from more recent papers do point to ICT technologies /systems as a possible way to do this systematically and efficiently.[45-50] However, when systematically recontacting in this way is technically feasible, the questions remain if this would be good care (although Table 1 shows that recontacting seems to address most of the key aspects of counseling), if this care is necessary, what would be the most beneficial

approach, under what conditions and circumstances, and how patients would value this. To gain more insight into these aspects of recontacting, we need more empirical evidence on various possible approaches. One of these approaches will be the topic of a pilot study by the ELSI research group at the Department of Genetics at the UMCG in Groningen. Recontacting of former patients will be performed by using an online application with two separate modules: one for communication between clinicians and patients that allows for dynamic patient consent to recontacting; and a second for communication between laboratory- and clinical professionals. Patients' evaluations concerning the above aspects will be assessed for two aims: (1) assessing and minimizing the psychological impact for patients of being recontacted, and (2) optimizing the design of the application that will be used.

Another aspect that has to be elaborated is reaching professional consensus on whether to recontact or not in various situations. Which patients should be recontacted and for which indications? It would be desirable to eventually capture these consensuses in guidelines, to ensure that patients at different genetic centers/services receive the same genetic care and to avoid confusion amongst patients and their referring physicians. Such guidelines should also cover the responsibilities of the laboratories in the process of enabling recontacting, for example, regarding the systematic tracking of reclassifications of mutations, and updating the clinicians of the respective patients.

METHODOLOGICAL ISSUES

Some methodological aspects of our studies are worth critical reflection. Firstly, we evaluated patients' and professionals' acceptance of group and online genetic counseling by means of cohort studies with pre-post comparisons instead of randomized controlled trials (RCT). This might have led to two types of bias in the online and group counseling studies. First, selection bias may have occurred because patients only participated in online or group counseling when they were interested, had given their explicit consent, and fulfilled all the inclusion criteria. Second, our study designs could have led to information bias: possibly in our online counseling study due to a lack of comparability between the study and control groups; and especially in our group counseling study because we lacked a control group. In our online counseling study we reduced information bias by comparing the outcomes of the online group with a matched control group, and by statistically adjusting for differences between these groups. Information bias was more likely in the studies of online counselors' evaluations and the time and cost evaluations of both types of care. In our group counseling study, the costs and attendance rates of the comparative designs were based on estimations and in one design on patients' stated preferences. Finally, in our online study, the counselors' evaluations were partly based on the outcomes of the telemedicine satisfaction questionnaire, which was originally for measuring patient satisfaction instead of counsellors' outcomes.

The above selection bias could have led to more favorable outcomes in both studies, while the patients involved in the evaluations had at least a neutral or positive attitude towards these types of care. An advantage of RCTs is that the study group is compared to a randomized control group, but selection bias through selective participation and/or strict inclusion/exclusion criteria may still occur. If we aimed to replace the current regular genetic care provision completely by these new methods of care, our selection of patients would not have been representative. However, if we offer the two new types of care as an extension of current clinical genetic services instead of completely replacing it, selection bias is a limiting factor to a much lesser extent. In view of our goals, the opinions and outcomes of patients who are open to these new types of care are of specific importance. With the fast developments in this field, we think it is justified to consider these results as sufficient ground from the patients' perspective for implementation of both types of care, despite the lack of firm evidence that could have been obtained through RCTs.

Second, the relatively small patient numbers we used was another limiting factor in both our patient evaluation studies, especially because our implicit expectations were that there would be no difference with standard genetic care. To prove statistically that the differences between our study groups and control group or standard of care are small (effect sizes <0.20), we would have needed much larger sample sizes. As an alternative, we provided additional information by comparing the effect sizes of outcomes between groups.

The third methodological issue concerns the questionnaire based outcomes of our studies. In both our group counseling and online counseling study we used questionnaires containing non-validated measures in addition to several validated outcome measures for assessing patients' evaluations. This might have had an effect on the validity and reliability of our study outcomes. However, the non-validated and ad-hoc measures were only used for characterizing our patients groups, and as secondary outcomes. For determining the results of our pre-set primary outcome measures, we only used validated measures, except for measuring satisfaction with telemedicine. No validated Dutch questionnaire is available for this measure, and we therefore decided to rely on our non-validated translations and adaptations of the Telemedicine Satisfaction Questionnaire.[51]

As reported in a review article by Payne et al, many different outcome measures are being used for evaluating various genetic counseling outcomes.[52] The psychological (PPC and STAI) and satisfaction (CGS) measures we used have been used before in clinical genetics in general, but only in a very limited way in the genetic counseling modes we studied.[24,53-57] Consequently, there were only limited reports available to which we could compare our patients' outcomes, and thus the issue of reliability and value of our study outcomes might play a role in this respect, too.

From our own literature search on reported patient outcomes for various modes of genetic counseling, and from the review by Payne et al,[52] it became clear that a variety of measures have been applied in evaluating clinical genetic services, of which the outcomes could be compared to greater or lesser extent. To increase the comparability of patient

outcomes, and thus the validity of clinical genetic studies, it is desirable to use more uniform outcome measures. One measure that could be used for this purpose is the Genetic Counseling Outcome Scale (GCOS-24), which contains items regarding various aspects of patients' outcomes from genetic counseling (e.g. satisfaction, impact and control), and it has already been validated in English.[58] Our ELSI research group at the UMCG is currently working on validating this questionnaire in Dutch and on creating a reference database containing various patient categories in clinical genetics: this work is being done with colleagues from the University Medical Center Utrecht. Translations in several other languages are available, but have not yet been published. It would be valuable to further extend its validation and use in other countries and languages in a responsible way, to allow for more sharing of data, comparable to initiatives seen in molecular medicine.[59-61] Finally, the recent initiatives of the ESHG Genetic Services Quality Committee for the External Quality Assessment (EQA) of genetic counseling services could be helpful in this respect.

FUTURE PERSPECTIVES ON CLINICAL GENETIC PATIENT CARE – 'CLINICAL GENETICS OF THE FUTURE'

In line with our research outcomes and the issues discussed, we can ask how clinical genetics (and health care in a broader sense) will look in, for example, ten years. While currently the preference for using online services among patients is still relatively low,[14,15] it is likely that this will increase in the near future when the younger generations become care consumers, because they will have long been accustomed to using all kinds of online applications and services.[4,5] At the same time there will be more use made of WES/WGS techniques, putting an increasing pressure on genetic centers, particularly because many results are not yet well understood (and may therefore need recontacting of the patients in the future). So, will online services in clinical genetics and other medical specialisms be the order of the day in ten years' time, and will they thus have become completely integrated into healthcare? And will genetic services be increasingly patient-centered, and focused on meeting the characteristics and wishes of the various types of patients? In this respect, one could think of various options for patients to choose their own ideal type of genetic care, e.g. whether they desire pragmatic care or personal care; or patients wanting fast and efficient care versus those desiring extended time when receiving care; those patients who have a need to share their experiences with peers or not; those desiring to get 'complete' information from a genetic professional and wanting to discuss their options versus those preferring to read the relevant information online for themselves and make use of online decision aids; and those who want to be recontacted with any new information versus those preferring to make their own searches for new information and who will contact the department if desirable. And finally, will the medical discipline of clinical genetics still exist in the way we know it today? Or will it be integrated into other medical disciplines?

Given the current trends in society and health care, and the reports in the literature, this could all be seen in the future: we indeed foresee an ongoing increase in the digitalization in both direct and indirect patient care and in the role of telegenetics. In the coming years, the quality of applications and the extent to which they are embedded in an institution's ICT systems will definitely increase, which in turn will increase convenience, flexibility and efficiency for both patients and professionals, and probably their satisfaction with its use too.[62] To aid a further extension of these effects, the possibilities and options for patients in telegenetics applications within the various steps in the provision of patient care should be expanded, which will lead to a much stronger patient-oriented approach, tailored to an individual's needs and wishes.[63,64] By implementing ehealth more widely in health care it is conceivable that a model will be adopted that places the patient in a central position, and that creates a web of all the health care professionals, psychosocial support and private contacts around the patient.[48,65,66] In this way, medical information can be efficiently transferred digitally between various contacts in the web via the patient, and with the patients' consent, thus promoting patient responsibility and empowerment, and cooperation between professionals.[66-70] In this scenario, for example, a digital referral letter from the general practitioner can be transferred by the patient to a genetics department, upon making an appointment online. Subsequently, depending on the specific indication for clinical genetic care, the patient should have the opportunity to have pre-counseling online information tailored to their specific situation,[71] to complete digital family forms and other pre-counseling forms, to have online counseling, and/or to view online decision aids regarding genetic testing.[72] After the genetic testing, the results could be made available online to the patient, depending on patients' wishes, so that they also become available – via the patient – to others in the digital web, and can be discussed with other health professionals. Finally, patients should be given the options to save their preferences online regarding future recontacting, and to change these over time. A more prominent role for patients in their own health care is supported by various national and international organizations, but how far patients are really willing and capable to take this increased responsibility, and the possible interference with equity aspects has to be assessed more extensively.[38,73-77]

Besides these changes in the provision of patient care, we think the role of genetics related to other medical disciplines will change. Genetics will increasingly become an integrated part of some medical disciplines, and clinical geneticists and genetic counselors will therefore have to claim their role as content experts; they will increasingly act as a consulting specialist in a multidisciplinary manner.[78,79] For example, a consulting role should be applied increasingly in cooperation with primary care givers and in regard to pharmacogenetics.[27]

Along with expanding online consumerism in general society and in health care, it is conceivable there will be an increase in the use of Direct-To-Consumer (DTC) testing, although its current use is limited, and also legally restricted.[80] This may have an effect on

clinical genetics services, in the sense of increasing numbers of patients seeking advice or more detailed explanation of their DTC test results, or it may be the other way round, with fewer patients actually attending genetic counseling services.[81,82] In general, many DTC testing services do not yet meet the criteria for providing a 'good quality of care' as assessed by the society of clinical genetics professionals.[83-85] As long as there are no international regulations, consumers will have access to various kinds of DTC tests offered by these companies. In the consumers' interest, the clinical genetics profession should ensure care of the responsible use of such tests and of for providing post-test care of sufficient-quality. This could be reached by cooperation with the DTC companies in offering online decision aids, for example, and/or by striving for more extensive regulations covering responsible DTC provision, and by establishing multidisciplinary guidelines (for general practitioners, genetic professionals) for providing post-DTC-test-result care in regular health care.[86-88] Finally, a designated role for the genetic professionals' societies in further shaping and regulating this care provision and assuring its quality is conceivable.[83]

However, in ten years' time we will be able to see what the field of clinical genetics looks like and how far the developments described here have taken effect. In Groningen, we will continue our research studies into, and the implementation of, innovations in this rapidly changing field, to help facilitate responsible changes in clinical genetic practice.

REFERENCE LIST

1. Grigsby B, Brega AG, Bennett RE, et al. The slow pace of interactive video telemedicine adoption: the perspective of telemedicine program administrators on physician participation. *Telemed J E Health* 2007;13(5):487-499.
2. Barton PL, Brega AG, Devore PA *et al*. Specialist physicians' knowledge and beliefs about Telemedicine: a comparison between users and nonusers of the technology. *Telemed J E Health* 2007;13(5):487-99.
3. Whitten P, Love B. Patient and provider satisfaction with the use of telemedicine: overview and rationale for cautious enthusiasm. *J Postgrad Med* 2005;51(4):294-300.
4. http://www.cbs.nl/NR/rdonlyres/4DEFB273-9BC7-459B-8788-44C94175DA4B/0/2014i78pub.pdf p75-114. (last access: 7 Sept 2015)
5. http://www.cbs.nl/nl-NL/menu/themas/vrije-tijd-cultuur/publicaties/artikelen/archief/2015/tablet-verdringt-bord-van-schoot.htm (last access 1 Sept 2015)
6. http://www.comscore.com/dut/Insights/Data-Mine/Nearly-2-in-3-Dutch-Internet-Users-visit-Banking-Sites (last access 7 Sept 2015)
7. http://www.comscore.com/dut/Insights/Data-Mine/UK-Leads-Online-Engagement-across-Europe (last access 7 Sept 2015)
8. Visser A, van Laarhoven HW, Govaert PHM, Schlooz MS, Jansen L, van Dalen T, Prins JB. Group medical consultations in the follow-up of breast cancer: a randomized feasibility study. *J Cancer Surviv* 2015; doi 10.1007/s11764-014-0421-z [epub ahead of print]
9. Buchanan AH, Datta SK, Sugg Skinner C, et al. Randomized trial of telegenetics vs. in-person cancer genetic counseling: cost, patient satisfaction and attendance. *J Genet Counsel* 2015; doi 10.1007/s10897-015-9836-6.
10. Schwartz MD, Valdimarsdottir HB, Peshkin BN, et al. Randomized noninferiority trial of telephone versus in-person genetic counseling for hereditary breast and ovarian cancer. *J Clin Oncol* 32:618-626.
11. Hawkins AK, Creighton S, Hayden MR. When access is an issue: exploring barriers to predictive testing for Huntington disease in British Columbia, Canada. *Eur J Hum Genet* 2013;21:148-153.
12. Doarn CR, Merell RC. Editorial: The business side of telemedicine. *Telemed Ehealth* 2014;20(11):981-983.
13. Hilgart JS, Hayward JA, Coles B, Iredale R. Telegenetics: a systematic review of telemedicine in genetic services. *Genet Med* 2012;14(9):765-76.
14. Van de Belt TH, Engelen LJLPG, Berben SAA, Teerenstra S, Samson M, Schoonhoven L. Internet and social media for health-related information and communication in healthcare: preferences of the Dutch general populations. *J of Med Internet Research* 2013;15(10):e220.
15. Gardner MR, Jenkins SM, O'Neil DA, Wood DL, Spurrier BR, Pruthi S. Perceptions of video-based appointments from the patient's home: a patient survey. *Telemed J E Health* 2015;21(4):281-285.
16. Benusiglio PR, Di Maria M, Dorling L, Jouinot A, Claret B, Boinon D, Lejri D, Caron O. Hereditary breast and ovarian cancer syndrome: successful, large-scale implementation of a group-based approach to genetic counselling. Oral presentation at European Society of Human Genetics Meeting, Glasgow, June 8, 2015; https://www.eshg.org/fileadmin/www.eshg.org/conferences/2015/downloads/ESHG2015_Abstracts_May_19.pdf p.39 (last access 7 Sept 2015)
17. Watts SA, Strauss GJ, Pascuzzi K, O'Day ME, Aron DC, Kirsh SR. Shared medical appointments for patients with diabetes: Glycemic reduction in high-risk patients. *J Am Assoc Nurs Pract* 2015;doi: 10.1002/2327-6924.12200 [epub ehead of print]
18. Seesing FM, Drost G, Groenewoud J, Van der Wilt GJ, Van Engelen BGM. Shared medical appointments improve QOL in neuromuscular patients: a randomized controlled trial. *Neurology* 2014;83(3):240-246.
19. Bartley KB, Haney R. Shared medical appointments: improving access, outcomes, and satisfaction for patients with chronic cardiac diseases. *J Cardiovasc Nurs* 2010;25:13-19.
20. Reed SC, Partridge AH, Nekhlyudov L. Shared medical appointments in cancer survivorship care: A review of the literature. *J Oncol Pract* 2015;11(1):6-11.

21. Jaber R, Braksmajer A, Trilling JS. Group visits: a qualitative review of current research. *J Am Board Fam Med* 2006;19:276-290.
22. Calzone KA, Prindiville SA, Jourkiv O, et al. Randomized comparison of group versus individual genetic education and counseling for familial breast and/or ovarian cancer. *J Clin Oncol* 2005;23(15):3455-3464.
23. Ridge Y, Panabaker K, McCullum M, Portigal-Todd C, Scott J, McGillivray B. Evaluation of group genetic counseling for hereditary breast and ovarian cancer. *J Genet Counsel* 2009;18:87-100.
24. Rothwell E, Kohlmann W, Jasperson K, Gammon A, Wong B, Kinney A. Patient outcomes associated with group and individual genetic counseling formats. *Fam Cancer* 2012;11:97-106.
25. Hunter AGW, Cappelli M, Humphreys L, Allanson JE, Chiu TT, Peeters C, Moher D, Zimak A. A randomized trial comparing alternative approaches to prenatal diagnosis counseling in advances maternal age patients. *Clin Genet* 2005;67:303-313.
26. Martin G, Currie G, Finn R. Bringing genetics into primary care: findings from a national evaluation of pilots in England. *J Health Serv Res Policy* 2009;14(4):204-211.
27. Bennett CL, Burke SE, Burton H, Farndon PA. A toolkit for incorporating genetics into mainstream medical services: Learning from service development pilots in England. *BMC Health Serv Res* 2010;10:125.
28. Grol R, Wensing M. Implementatie, effectieve verbetering van de gezondheidszorg. Reed Business Education, vijfde druk, Amsterdam 2013.
29. Rogers EM. Diffusion of Innovations. The Free Press, New York, NY, 1995.
30. Obstfelder A, Engeseth KH, Wynn R. Characteristics of successfully implemented telemedical applications. *Implementation Science* 2007;2:25.
31. Chau PYK and Hu PJ. Investigating health care professionals' decisions to accept telemedicine technology: an empirical test of competing theories. *Information & Management* 2002;39:297-311.
32. Yi, MY, Jackson JD, Park JS, Probst JC. Understanding information technology acceptance by individual professionals: Toward an integrative view. *Information & Management* 2006;43:350-363.
33. Ajzen I. The theory of planned behavior. *Organizational behavior and human decision processes* 1991;50:179-211.
34. Michie S, Johnston M, Abraham C, Lawton R, Parker D, Walker A, on behalf of the "Psychological Theory" group. Making psychological theory useful for implementing evidence based practice: a consensus approach. *Qual Saf Health Care* 2005;14:26-33.
35. Cane J, O'Connor D, Michie S. Validation of the theoretical domains framework for use in behaviour change and implementation research. *Implementation Science* 2012;7:37.
36. Kuo K, Talley PC, Lee C, Yen Y. The influence of telemedicine experience on physicians' perceptions regarding adoption. *Telemed J E Health* 2015;21(5):388-394.
37. KNMG handreiking artsen en social media 2011. http://knmg.artsennet.nl/Dossiers-9/Dossiers-thematrefwoord/ICT-in-de-zorg-1.htm (last access 1 Sept 2015)
38. Schippers E, van Rijn MJ. Ministerie van Volksgezondheid, Welzijn en Sport. Kamerbrief ehealth en zorgverbetering 2014. http://www.rijksoverheid.nl/documenten-en-publicaties/kamerstukken/2014/07/02/kamerbrief-over-e-health-en-zorgverbetering.html (last access 1 Sept 2015)
39. Rantanen E, Hietala M, Kristoffersson U, et al. What is ideal genetic counselling? A survey of current international guidelines. *Eur J Hum Genet* 2008;16:445-452.
40. Rubinstein WS. Roles and responsibilities of a medical geneticist. *Fam Cancer* 2008;7(1):5-14.
41. Wertz DC, Fletcher JC, Berg K. Review of ethical issues in Medical Genetics. Report of consultants to WHO. Geneva: World Health Organization, Human Genetics Programme, 2003. Report number WHO/HGN/ETH/00.4
42. Bernard LE, McGillivray B, Van Allen MI, Friedman JM, Langlois S. Duty to re-contact: a study of families at risk for Fragile X. *J Genet Couns*. 1999;8(1):3-15.
43. Sexton AC, Sahhar M, Thorburn DR, Metcalfe SA. Impact of a genetic diagnosis of a mitochondrial disorder 5-17 years after the death of an affected child. *J Genet Couns* 2008;17(3):261-73.
44. Hampel H. Recontacting patients who have tested negative for BRCA1 and BRCA2 mutations: how, who and why? *J Genet Couns* 2009;18(6):527-529.

45. Trakadis YJ. Patient-controlled encrypted genomic data: an advance to approach clinical genomics. *BMC Medical Genomics* 2012;5(31).
46. Aronson SJ, Clark EH, Varugheese M, Baxter S, Babb LJ, Rehm HL. Communicating new knowledge on previously reported genetic variants. *Genet Med* 2012;14(8):713-719.
47. Bean LJH, Tinker SW, da Silva C, Hedge MR. Free the data: One laboratory's approach to knowledge-based genomic variant classification and preparation for EMR integration of genomic data. *Hum Mutat* 2013;34(9):1183-1188.
48. Hunt K. Individualizing the informed consent process for whole genome sequencing: A patient directed approach [PhD dissertation]. Arizona: Arizona State University, 2013.
49. Ali-Khan, SE, Daar AS, Shuman C, Ray PN, Scherer SW. Whole Genome Scanning: Resolving Clinical Diagnosis and Management Amidst Complex Data. *Pediatr Res* 2009;66(4):357-363.
50. Pyeritz RE. The coming explosion in genetic testing – is there a duty to recontact? *N Engl J Med* 2011;365(15):1367-9.
51. Yip MP, Chang AM, Chan J, Mackenzie AE. Development of the telemedicine satisfaction questionnaire to evaluate patient satisfaction with telemedicine: a preliminary study. *J Telemed Telecare* 2003;9:46-50.
52. Payne K, Nicholls S, McAllister M, MacLeod R, Donnai D, Davies LM. Outcome measurement in clinical genetics services: a systematic review of validated measures. *Value Health* 2008;11(3):497-508.
53. Zilliacus EM, Meiser B, Lobb EA, Kirk J, Warwick L, Tucker K. Are videoconferenced consultations as effective as face-to-face consultations for hereditary breast and ovarian cancer genetic ounseling? *Genet Med* 2011;13(11):933-941.
54. Smets EM, Pieterse AH, Aalfs CM, Ausems MG, van Dulmen AM: The perceived personal control (PPC) questionnaire as an outcome of genetic counseling: reliability and validity of the instrument. *Am J Med Genet* 2006;140:843-850.
55. Pieterse AH, van Dulmen AM, Beemer FA, Bensing JM, Ausems MG: Cancer genetic counseling: communication and counselees' post-visit satisfaction, cognitions, anxiety, and needs fulfillment. *J Genet Couns* 2007;16:85-96.
56. Brain K, Gray J, Norman P *et al:* Randomized trial of a specialist genetic assessment service for familial breast cancer. *J Natl Cancer Inst* 2000;92:1345-1351.
57. Bish A, Sutton S, Jacobs C, Levene S, Ramirez A, Hodgson S: Changes in psychological distress after cancer genetic counselling: a comparison of affected and unaffected women. *Br J Cancer* 2002;86:43-50.
58. McAllister M, Wood AM, Dunn G, Shiloh S, Todd C. The genetic counseling outcome scale: a new patient-reported outcome measure for clinical genetic services. *Clin Genet* 2011;79(5):413-424.
59. Wild D, Grove A, Martin M, Eremenco S, McElroy S, Verjee-Lorenz A, Erikson P. Principles of good practice for the translation and cultural adaptation process for Patient-Reported Outcomes (PRO) measures: Report of the ISPOR task force for translation and cultural adaptation. *Value Health* 2005; 8(2):94-104.
60. Wild D, Eremenco S, Mear I, et al. Multinational trials- recommendations on the translations required, approaches to using the same language in different countries, and the approaches to support pooling the data: the ISPOR patient-reported outcomes translation and linguistic validation good research practices task force report. *Value Health* 2009;12(4):430-440.
61. Beaton D, Bombardier C, Guillemin F, Bosi Ferraz M. Guidelines for the process of cross-cultural adaptation of self-report measures. *SPINE* 2000;25(24):3186-3191.
62. Zhang K, Liu W, Locatis C, Ackerman M. Mobile videoconferencing apps for Telemedicine. *Telemed E Health* 2015. doi:10.1089/tmj.2015.027 [epub ahead of print]
63. Hilgart J, Haywart JA, Iredale R. E-genetics: exploring the acceptability and feasibility of using technology in cancer genetics services. *Clin Genet* 2012;81:514-520.
64. Mehrotra A, Paone S, Martich GD, Albert SM, Shevchik GJ. Characteristics of patients who seek care via evisits instead of office visits. *Telemed ehealth* 2013;19(7):1-5.
65. http://www.hereismydata.com/ (last access 7 Sept 2015)
66. Aarts JWM, Vennik F, Nelen WLDM, Van der Eijk M, Bloem BR, Faber MJ, Kremer JAM. Personal health communities: a phenomenological study of a new health-care concept. *Health Expect* 2014 Mar 19. doi:10.1111/hex.12177. [Epub ahead of print]

67. Tozzi AE, Carloni E, Gesualdo F, Russo L, Raponi M. Attitude of families of patients with genetic diseases to use m-health technologies. *J Telemed Ehealth* 2015;21(2):86-89.

68. Crouch PC, Rose CD, Johnson M, Janson SL . A pilot Study to evaluate the magnitude of association of the use of electronic personal health records with patient activation and empowerment in HIV-infected veterans. *Peer J* 2015;3:e852; DOI10.7717.

69. Le PN. Patient engagement solutions. Why physicians should care. *Health Manag Technol* 2104;35(11):18-19.

70. Van der Eijk M, Faber MJ, Aarts JWM, Kremer JAM, Munneke M, Bloem BR. Using online health communities to deliver patient-centered care to people with chronic conditions. *J Med Internet Res* 2013 Jun 25;15(6):e115.

71. Albada A, Van Dulmen S, Otten R, Bensing JM, Ausems MGEM. Development of E-info gene(ca): A website providing computer-tailored information and question prompt prior to breast cancer genetic counseling. *J Genet Counsel* 2009;18:326-338.

72. Birch PH. Interactive e-counselling for genetics pre-test decisions: where are we now? *Clin Genet* 2015;87:209-217.

73. Heldoorn M. NPCF Visiedocument: Gezondheid 2.0. Toekomst en betekenis van e-health voor de zorgconsument. Nederlandse Patiënten en Consumenten Federatie, Utrecht, 2008.

74. Bierma L, Heldoorn M. Het persoonlijk gezondheidsdossier. De visie van patiëntenfederatie NPCF. Nederlandse Patiënten en Consumenten Federatie, Utrecht, 2e druk, juni 2013.

75. Monteagudo Pena JL, Gil OM. E-health for patient empowerment in Europe. Report from the ehealth ERA project, 2007. http://www.ehealthnews.eu/images/stories/pdf/eh_era-patient-empower.pdf (last access 7 Sept 2015)

76. Kontos E, Blake KD, Chou WS, Prestin A. Predictors of ehealth usage: insights on the digital divide from the information national trends survey 2012. *J Med Internet Res* 2014;16(7):e172.

77. Atzori W, on behalf of the European Patients Forum (EPF). Ehealth and patient empowerment: a patient perspective. Oral presentation at PALANTE conference, Brussels, 6 November 2013. http://www.ehma.org/files/PALANTE%20midterm.%20Walter%20Atzori%20-%20eHealth%20and%20patient%20empowerment.pdf (last access 7 Sept 2015)

78. Bensend TA, McCarthy Veach P, Niendorf KB. What's the harm? Genetic counselor perceptions of adverse effects of genetic service provision by non-genetics professionals. *JGenet Counsel* 2014;23:48-63.

79. Nippert I, Julian-Reynier C, Harris H, Evans G, van Asperen CJ, Tibben A, Schmidtke J. Cancer risk communication, predictive testing and management in France, Germany, the Netherlands and the UK: general practitioners' and breast surgeons' current practice and preferred practice responsibilities. *J Community Genet* 2014;5:69-79.

80. Borry P, van Hellemondt RE, Sprumont D, Fittipaldi Duarte Jales C, Rial-Sebbag E, Spranger TM, Curren L, Kaye J, Nys H, Howard HC. Legislation on direct-to-consumer genetic testing in seven European countries. *Eur J Hum Genet* 2012;20:715-721.

81. Bloss CS, Schork NJ, Topol EJ. Direct-to-consumer pharmacogenomic testing isassociated with increased physician utilisation. *J Med Genet* 2014;51:83-89.

82. Boeldt, DL, Schork NJ, Topol EJ, Bloss CS. Influence of individual differences in disease perception on consumer response to direct-to-consumer genomic testing. *Clin Genet* 2015;87:225-232.

83. Borry P. Statement of the ESHG on direct-to-consumer genetic testing for health-related purposes. *Eur J Hum Genet* 2010;18:1271-1273.

84. Howard HC, Borry P. Survey of European clinical geneticists on awareness, experiences and attitudes towards direct-to-consumer genetic testing. *Genome Medicine* 2013;5:45.

85. Howard HC, Avard D, Borry P. Are the kids really all right? Direct-to-consumer genetic testing in children: are company policies clashing with professional norms? *Eur J Hum Genet* 2011;19:1122-1126.

86. Jackson L, Goldsmith L, Skirton H. Guidance for patients considering direct-to-consumer genetic testing and health professionals involved in their care: development of a practical decision tool. *Family Practice* 2014;31(3):341-348.

87. Goldsmith L, Jackson L, O'Connor A, Skirton H. Direct-to-consumer genomic testing from the perspective of the health professional: a systematic review of the literature. *J Community Genet* 2013;4:169-180.
88. Hawkins AK, Ho A. Genetic counseling and the ethical issues around direct to consumer genetic testing. *J Genet Counsel* 2012;21:367-373.

Chapter 10

Supplementary figures & tables

Nederlandse samenvatting

Dankwoord

Over de auteur

List of publications

Research Institute SHARE

Supplementary figures & tables

SUPPLEMENTS TO CHAPTER 5

Glossary

CGS = Clinical Genetics Satisfaction indicator
OPD = Outpatient Department
PPC = Personal Perceived Control
STAI = State and Trait Anxiety Inventory
TSQ = Telemedicine Satisfaction Questionnaire
In-person counselling = counselling at the outpatient department; synonym: face-to-face counselling
Online application = the specific application in use for performance of Telegenetics
Online counselling = conducting a counselling session via a computer and webcam, including the use of supportive tools that are also available for in-person genetic counselling
Telemedicine = the general term used for various types of remote healthcare when medical information is exchanged between locations via electronic means, in order to improve a patient's health.
Telegenetics = the overall term for different kinds of telemedicine facilities in use in clinical genetics, including synchronous and asynchronous online communication between a professional and patient, and between professionals.
Videoconferencing = communication between a counsellor and patient (or between professionals/counsellors), via a computer and webcam but without having integrated supportive tools in the application used.

Supplementary **Table 1.** Patients' experience with computers, internet and online counselling

	Online patients* Before counselling	**Control patients* Before counselling**	**Significance of difference between groups**	**Online patients* After counselling**
1. "I am always looking for new possibilities on my computer"	3.58 (1.18)	2.54 (1.43)	**<0.001**	
2. "I think I will do more communication via PC and webcam in the future"	3.63 (1.03)	2.10 (1.16)	**<0.001**	3.49 (1.37)#
3. "I think I will find it annoying to use a computer while talking to a doctor"	2.23 (1.04)	3.34 (1.44)	**<0.001**	1.68 (0.96)#
4. "I think the doctor will find it annoying to use a computer while talking to a patient"	2.56 (0.94)	3.06 (0.91)	**<0.001**	2.36 (1.01)#

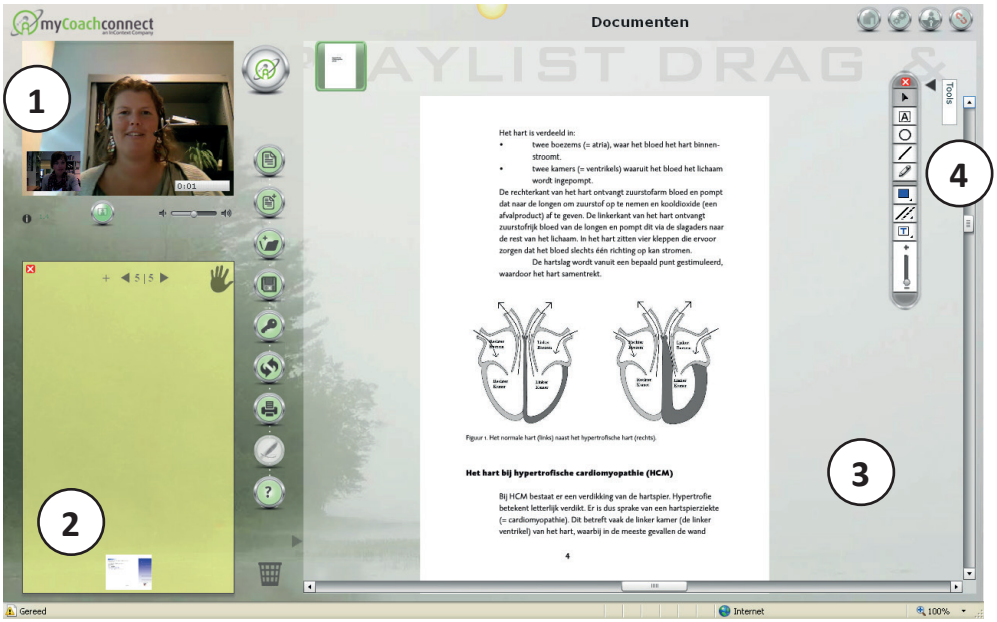
* All outcomes are mean scores (SD); significant change P<0.05

Significance of changes in item scores of online patients after their counselling session relative to beforehand: item 2, P=0.44; item 3, P=0.03; item 4, P=0.25

SUPPLEMENTS TO CHAPTERS 5 AND 6

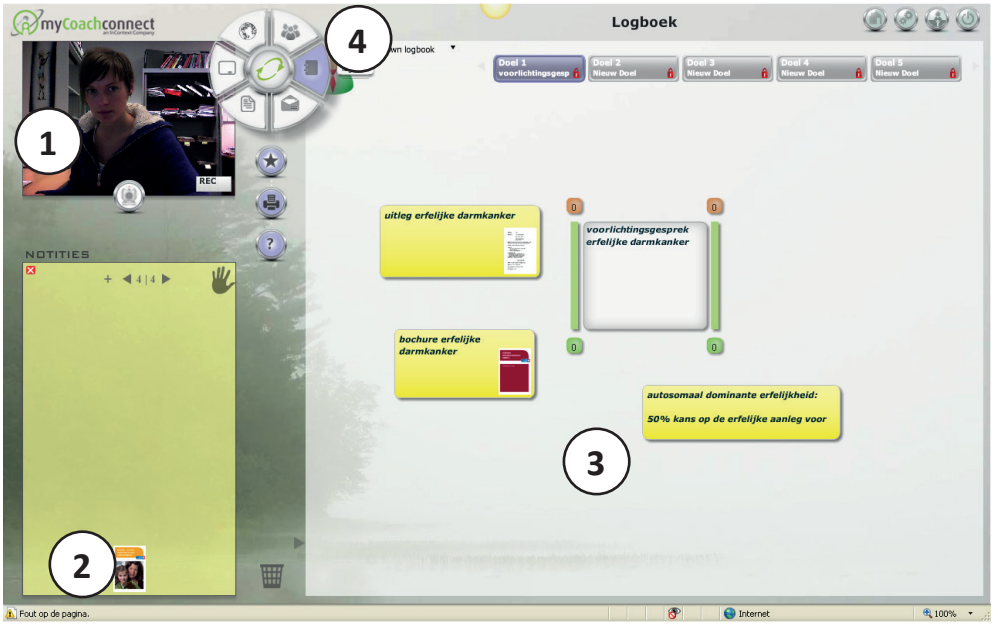
Supplementary Figures a-f. Screenshots of the online counselling application used in our pilot (www.myCoachconnect.com)

a. Both the conversation participants and disease brochure are simultaneously visible on screen.



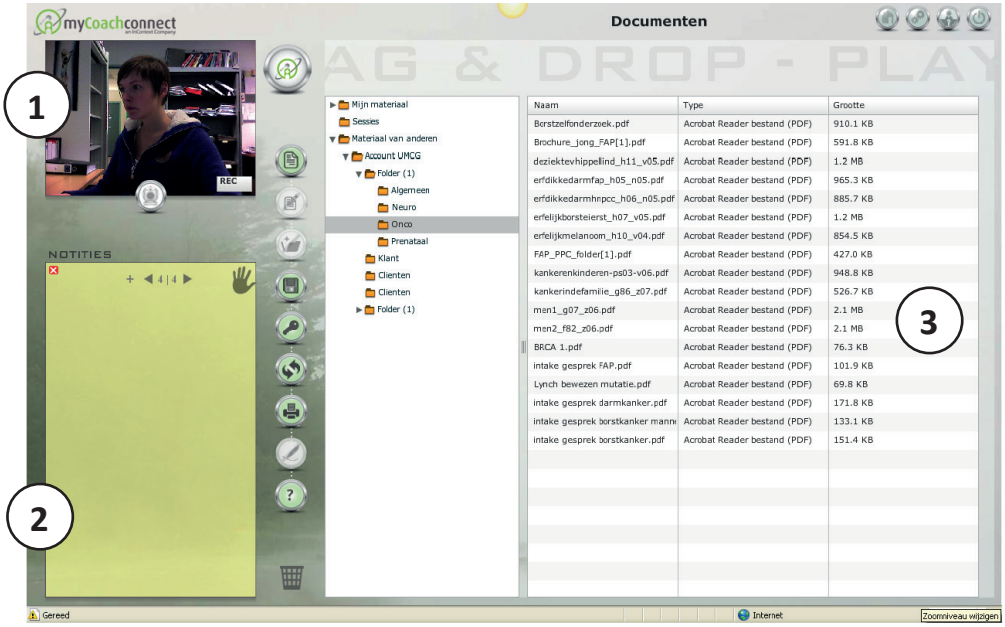
1. Webcam images of conversation partners during online counselling session;
2. Notepad for counsellor (not visible to patient);
3. Disease brochure visible to both patient and counsellor during session;
4. Drawing tools

b. Screenshot of notebook for patients



1. Webcam image of conversation partner during online counselling session;
2. Notepad for counsellor (not visible to patient);
3. Notebook for patients (also visible to counsellor during the session): information can be transferred from the counsellors' notepad to here, and remains available to patients after their session. In this screenshot, an information picture, a disease brochure in PDF format and some written information are transferred to the patient's notebook;
4. Menu button to switch between tools (e.g. between notebook/document viewing/co-browsing) during the counselling session.

c. Screenshot of the document list for counsellors: disease brochures that can be transferred to the patient's notebook during the counselling session



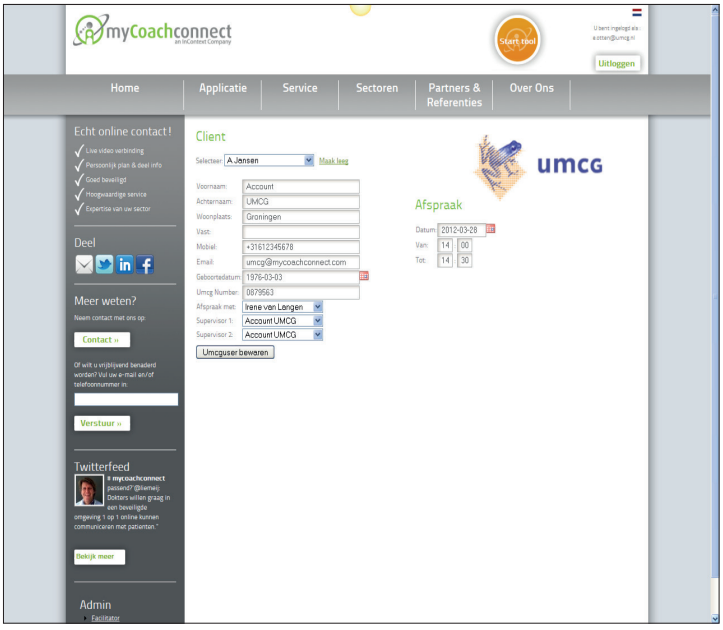
1. Webcam image of conversation partner during online counselling session;
2. Notepad for counsellor (not visible to patient);
3. Document list (not visible/accessible to patients): this contains a wide variety of disease brochures and explanatory figures for transfer to the patient's notebook and for use during the counselling session.

d. Screenshot of the co-browsing tool, showing a patient information website, which is visible to both the counsellor and patient during the counselling session

1. Webcam image of conversation partner during online counselling session;
2. Notepad for counsellor (not visible to patient);
3. Internet browsing tool in the application, visible to both counsellor and patient during the counselling session;
4. Button for saving a list of three ‘favorite’ websites.

e. Screenshot of the landing page of the myCoachconnect platform (*in Dutch*), containing information and an instruction movie for the patient about the online counselling process

f. Screenshot of the management side of the myCoachconnect platform, showing the patient registration screen for commencing the online counselling process



SUPPLEMENTS TO CHAPTER 6

Supplementary figure 1: Original English version of the Telemedicine Satisfaction Questionnaire by Yip et al*, with item 7 being removed in our Dutch version

1. I can easily talk to my health-care provider
2. I can hear my health-care provider clearly
3. My health-care provider is able to understand my health-care condition
4. I can see my health-care provider as if we met in person
5. I do not need assistance while using the system
6. I feel comfortable communicating with my health-care provider
7. *I think the health-care provided via telemedicine is consistent*
8. I obtain better access to health-care services by use of telemedicine
9. Telemedicine saves me time travelling to hospital or a specialist clinic
10. I do receive adequate attention
11. Telemedicine provides for my health-care need
12. I find telemedicine an acceptable way to receive health-care services
13. I will use telemedicine services again
14. Overall, I am satisfied with the quality of service being provided via telemedicine

* Yip MP, Chang AM, Chan J, MacKenzie AE: Development of the telemedicine satisfaction questionnaire to evaluate patient satisfaction with telemedicine: a preliminary study. *J Telemed Telecare* 2003;9:46-50.

Nederlandse samenvatting

Klinische genetica is het medisch specialisme dat zich primair richt op het beantwoorden van patiëntenvragen die te maken hebben met erfelijkheid. Dit gebeurt in de vorm van het uitvoeren van genetische counseling en DNA tests. Een genetische counseling bevat verschillende kernaspecten, zoals het bespreken van relevante informatie, nagaan van implicaties voor familieleden, bieden van psychologische steun, objectiviteit en geïnformeerde toestemming ("informed consent"). Ondanks dat er kleine individuele verschillen kunnen zijn, bestaat er zowel nationaal als internationaal grotendeels overeenstemming over de inhoud van een counseling. Een regulier counselingsgesprek vindt plaats tussen een counselor en een patiënt met één of meerdere begeleidende familieleden en/of partner, op de polikliniek van een academisch ziekenhuis of in een regionaal ziekenhuis waar de counselors vanuit het academisch ziekenhuis spreekuur houden. Deze manier van counselen is door de tijd heen constant gebleven.

In de afgelopen jaren is de samenleving echter veranderd: we leven steeds meer in een gedigitaliseerde wereld. Het online regelen van zaken en doen van aankopen, en het onderhouden van sociale contacten online is heel normaal geworden. De digitalisering neemt ook toe in de gezondheidszorg, bijvoorbeeld in de vorm van online beschikbaarheid van informatie over allerlei aandoeningen, het online maken van afspraken, en de invoer van digitale patiënten dossiers. Binnen de genetica zijn er daarnaast, door de voortschrijdende ontwikkelingen in de techniek, steeds meer en uitgebreidere mogelijkheden ontstaan voor het doen van erfelijkheidsonderzoek, en komen er mede daardoor steeds meer mensen in aanmerking voor erfelijkheidsvoorlichting en -onderzoek. Tegelijkertijd kan door economische beperkingen het aantal klinisch genetische counselors niet in dezelfde mate toenemen als het aantal patiënten dat wordt verwezen voor erfelijkheidsvoorlichting.

De huidige tijd vraagt om nieuwe manieren van erfelijkheidsvoorlichting en de organisatie daarvan, om aan de eisen/wensen van deze tijd te voldoen en om de zorgverlening op een efficiëntere manier te laten verlopen. In dit proefschrift worden verschillende manieren beschreven om deze innovatieve zorg vorm te geven, waarbij evaluaties plaatsvinden vanuit het perspectief van de patiënt, de zorgverlener, en het management van de afdeling genetica.

In *hoofdstuk twee* worden de resultaten beschreven van het onderzoek waarbij erfelijkheidsvoorlichting werd gegeven aan groepen patiënten met een hartspierziekte in regionale ziekenhuizen in Noord-Nederland. Deze groepsvoorlichting vormde een alternatief voor

erfelijkheidsvoorlichting aan individuele patiënten in het UMCG. 13 groepsvoorlichting sessies werden gehouden in 8 verschillende ziekenhuizen, waaraan in totaal 82 patiënten en hun partners/familieleden deelnamen. Bij het onderzoek werden de patiënttevredenheid met dit type zorg en de psychologische uitkomsten van de patiënten gemeten. Patiënten gaven aan tevreden te zijn met de geleverde zorg, en een antwoord te hebben gekregen op hun vragen. De psychologische uitkomsten van de patiënten, op het gebied van ervaren angst en controle over hun situatie, waren vergelijkbaar met eerdere studies betreffende groeps- en individuele voorlichting over erfelijke kanker. Ook de betrokken cardiologen en verpleegkundigen van de deelnemende ziekenhuizen waren tevreden, terwijl de klinisch genetische medewerkers minder tevreden waren door de grote tijdsinvestering en beperkte groepsinteractie tijdens de sessies. De patiënten resultaten toonden aan dat dit een acceptabel alternatief is voor individuele counseling in het UMCG, maar de meest optimale vormgeving waarbij ook het perspectief van de zorgverlener wordt meegenomen, moet nog worden vastgesteld.

Hoofdstuk drie beschrijft de economische analyse van deze manier van groepsvoorlichting in regionale ziekenhuizen wat betreft patiënten deelname en het percentage geteste patiënten, en de hieruit voortvloeiende gezondheidswinst. Hierbij wordt vergeleken met de gebruikelijke manier van individuele counseling en enkele alternatieve scenario's voor het geven van groepscounseling, namelijk groepscounseling in het UMCG en individuele counseling in de regionale ziekenhuizen. De analyse toonde aan dat aanzienlijk meer patienten zijn bereikt met de groepsvoorlichting in regionale ziekenhuizen, dan het aantal patiënten dan in de voorafgaande jaren door deze ziekenhuizen naar het UMCG werd verwezen. Daarnaast zijn de kostenverschillen van de verschillende scenario's relatief klein, waarbij regionale individuele counseling het voorkeursscenario is vanuit patiënten- en maatschappelijk perspectief, en groepscounseling in het UMCG de voorkeur heeft vanuit het zorgverleners perspectief. Al met al zou groepscounseling een goede aanvulling op de huidige klinisch genetische zorgverlening zijn, maar verdient de teamsamenstelling, de lokatie van de sessies en de optimale groepsgrootte nog een nadere overweging.

In *hoofdstuk vier* worden de uitkomsten beschreven van een online enquête onder Europese professionals die werkzaam zijn binnen de genetica om een impressie te krijgen van de huidige stand van zaken betreffende de beschikbaarheid en het gebruik van verschillende online toepassingen in de kliniek. De belangrijkste punten die hierbij naar voren komen zijn dat Telemedicine toepassingen slechts beperkt beschikbaar zijn, en in nog beperktere mate worden gebruikt in een groot aantal Europese landen; iedere Telemedicine applicatie wordt gebruikt voor verschillende doeleinden; en samenwerking, scholing en richtlijnen zouden van waarde kunnen zijn bij het succesvol uitbreiden van het gebruik van telegenetics. De drie voornaamste vormen van barrières voor het gebruik ervan, die door de respondenten – die over het algemeen zelf geen ervaring met telegenetics hadden – werden genoemd,

zijn een ervaren gebrek aan geschiktheid en noodzaak, praktische beperkingen en een gebrek aan professionele ondersteuning en kennis. Dit kan erop wijzen dat de mogelijkheden van telegenetics tot dusver grotendeels niet worden gezien, en dus niet gebruikt. Wij concluderen uit de enquête dat er voldoende grond is om het gebruik van telegenetics binnen Europa uit te breiden, zowel in de directe als in de indirecte patiëntenzorg. Om dit te bereiken moeten de ervaren barrières op het gebied van praktische uitvoer en regelgeving worden opgelost, en dient bewustwording te worden gecreëerd onder genetische professionals, over de mogelijkheden en mogelijke voordelen van telegenetics.

Hoofdstuk vijf beschrijft de resultaten van een onderzoek over het geven van online erfelijkheidsvoorlichting via een webcam aan niet-aangedane patiënten. De patiënten zitten hierbij thuis achter de computer en dienen vooraf verschillende voorbereidingen te treffen. Het betreft patiënten bij wie in de familie een erfelijke hartziekte of erfelijke kanker voorkomt, en paren waarbij met spoed erfelijkheidsvoorlichting tijdens de zwangerschap plaatsvindt. Genetische counseling vindt plaats via een online platform, waarbij naast het webcam beeld verschillende ondersteunende opties beschikbaar zijn tijdens de counseling. De patiënten uitkomsten tonen dat de patiënten die online counseling ondergaan tevreden zijn en dat de mate van verandering van hun ervaren controle en angst, na counseling ten opzichte van ervoor, gemiddeld gelijk is aan die van patiënten die de reguliere manier van counseling op de polikliniek ondergaan. De evaluatie toont aan dat deze manier van online zorgverlening bij de patiënt thuis uitvoerbaar is, en dat de verminderde reistijd en het worden gecounseld in een vertrouwde omgeving worden gezien als de grootste voordelen door patiënten.

Hoofdstuk zes beschrijft het zorgverleners perspectief op onze manier van online counselen, en laat de kosten en tijdsanalyse voor deze online counseling op onze afdeling klinische genetica zien. De tien counselors die de online counselingen uitvoerden vinden de huidige online applicatie kwalitatief onvoldoende voor gebruik in de reguliere zorg, vooral door de technische kenmerken, en suboptimale werking van de applicatie en het relatieve gebrek aan persoonlijk contact. Aan de andere kant geeft deze manier van counselen hen meer flexibiliteit in hun werk, leid het voor hen tot vermindering van reistijd, en geeft het hen de mogelijkheid om familieonderzoek bij familieleden verspreid over heel Nederland te monitoren. De tijd en kosten analyse laat zien dat deze vorm van counseling minder tijd en kosten met zich mee brengt dan de reguliere manier van counselen op de polikliniek. Echter, de implementatie van deze specifieke toepassing van online counseling in de reguliere zorg zal extra kosten met zich meebrengen in de vorm van abonnementen en technische ondersteuning. Al met al kan online counseling redelijkerwijs worden aangeboden als een uitbreiding van het huidige spectrum aan klinisch genetische zorg aan die groep van patiënten die de juiste faciliteiten hiervoor heeft, en die open staat voor deze zorgvorm. De technische problemen leiden er echter toe dat dit nog niet als volwaardig

alternatief kan worden gezien voor reguliere counseling, en dat op dit vlak verbeteringen en veranderingen nodig zijn voordat de applicatie op grotere schaal in de reguliere zorg kan worden toegepast.

In *hoofdstuk zeven* wordt een systematisch literatuuronderzoek beschreven waarin 61 gepubliceerde artikelen tot 1 september 2014 zijn opgenomen, geselecteerd uit 1428 hits in vier medische literatuur databases. De artikelen werden geïncludeerd als ze betrekking hadden op het opnieuw contact opnemen met oud-patiënten in de klinische genetica in het licht van de nieuwe technische diagnostische mogelijkheden en de ethische, juridische, sociale en praktische aspecten die hiermee samenhangen. Ons review laat zien dat de meeste auteurs het hercontacteren ethisch wenselijk vinden, maar dat zij praktische bezwaren als de grootste barrières zien hierbij. Verschillende oplossingen voor deze barrières worden in de literatuur aangedragen, maar tot nu toe is er weinig wetenschappelijk bewijs met betrekking tot het uitvoeren van hercontacteren in de praktijk, bijvoorbeeld over de voorkeursmethode van hercontacteren, en meningen en effecten ervan op patiënten. Uitvoerende studies laten zien dat de meeste patiënten hercontacteren waarderen voor verschillende indicaties en termijnen sinds hun genetische counseling. Wij concluderen dat het een belangrijke volgende stap is om professionele overeenstemming te bereiken en meer bewijs te krijgen op basis van praktische studies, over de specifieke situaties waarin hercontacteren als goede zorg wordt gezien. De optimale manier van hercontacteren, zowel vanuit patiënten als professionals perspectief, dient te worden bepaald, waarbij o.a. rekening moet worden gehouden met de psychologische impact, de ethische en juridische voorwaarden, de mogelijkheid van dynamische toestemming, en de uitvoerbaarheid en kosten van het hercontactering systeem. Het gebruik van een online toepassing om aan een aantal van deze gestelde voorwaarden te voldoen kan een goede vervolg stap zijn in het onderzoek naar de invoering van hercontactering in de klinisch genetische praktijk.

Dankwoord

Na een tijd van hard werken is het eindresultaat van mijn onderzoek nu daar: mijn proefschrift! De weg naar dit einddoel toe heeft heel wat hobbels gekend, maar ook vele mooie, uitdagende, en leerzame momenten. Die hoefde ik gelukkig niet allemaal alleen te ervaren; er waren heel veel ondersteunende, deskundige en lieve mensen om mij heen. Op deze plek wil ik iedereen bedanken die – op welke manier dan ook – heeft bijgedragen aan het tot stand komen van mijn proefschrift. Hoewel ik me ervan bewust ben dat het onmogelijk is om iedereen in dit dankwoord persoonlijk te benoemen, wil ik dit hieronder toch voor een deel van de mensen doen.

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Over de auteur

Ellen Otten werd op 7 juli 1981 geboren te Emmen. Ze groeide op in Sleen en behaalde in 1999 haar VWO diploma aan de Gemeentelijke Scholen Gemeenschap te Emmen. Daarna studeerde zij enige tijd aan de Hanzehogeschool te Groningen, waar ze haar propedeuse Verpleegkunde behaalde. In 2001 startte ze met haar studie Geneeskunde aan de Rijksuniversiteit Groningen. Tussen haar doctoraal en haar co-schappen deed ze 2 maanden een Public Health stage in het Misikhu Mission Hospital in Kenia. Vervolgens liep ze haar co-schappen in het Scheper Ziekenhuis te Emmen en het Röpke Zweers Ziekenhuis te Hardenberg. Haar afsluitende keuze coschap kindergeneeskunde liep ze deels in het Wilhelmina Ziekenhuis te Assen en deels in het Sint Joseph's Hospital te Nguludi, Malawi. In augustus 2007 behaalde ze haar artsenbul.

Per januari 2008 startte Ellen als ANIOS op de afdeling klinische genetica van het Universitair Medisch Centrum Groningen en schreef zij haar eerste publicaties – op het gebied van de cardiogenetica – onder supervisie van dr. J.P. van Tintelen. In januari 2011 startte ze op deze afdeling tegelijkertijd met de opleiding tot klinisch geneticus (opleider prof.dr. I.M. van Langen) en met haar promotieonderzoek, onder supervisie van prof.dr. I.M. van Langen, prof.dr. A.V. Ranchor en dr. E. Birnie, dat tot dit proefschrift heeft geleid.

List of publications

Otten E, Ranchor AV, van Langen IM, Birnie E. A group approach to regional cardiogenetic counseling: evaluation of yields, costs and cost-effectiveness. *Submitted.*

Otten E, Birnie E, Ranchor AV, van Langen IM. Online genetic counseling from the providers' perspective: counselors' evaluations, and a time and cost analysis. *Submitted*.

J.E.H. Bergman, **E. Otten**, J.B.G.M. Verheij, H.E.K. de Walle. Folic acid supplementation influences the distribution of neural tube defect subtypes: a registry-based study. *Submitted*.

Otten E, Birnie E, Ranchor AV, van Langen IM. Telegenetics use in presymptomatic genetic counselling: patient evaluations on satisfaction and quality of care. *Eur J Hum Genet.* 2015. doi: 10.1038/ejhg.2015.164.[Epub ahead of print]

Saskia M. Maas, Adam C. Shaw, Hennie Bikker, Hermann-Josef Lüdecke, Karin van der Tuin, Magdalena Badura-Stronka, Elga Belligni, Maria Teresa Bonati, Daniel R Carvalho, JanMaarten Cobben, Stella A. de Man, Nicolette S. Den Hollander, Nataliya Di Donato, Livia Garavelli, Sabine Grønborg, Anne Herkert, Jeanette Hoogeboom, Aleksander Jamsheer, Anna Latos-Bielenska, Anneke Maat-Kievit, Cinzia Magnani, Carlo Marcelis, Inge Mathijssen, Maartje Nielsen, **Ellen Otten**, Lilian B Ousager, Jacek Pilch, Astrid Plomp, Gemma Poke, Anna Poluha, Renata Posmyk, Claudine Rieubland, Margharita Silengo, Marleen Simon, Elisabeth Steichen, Connie Stumpel, Katalin Szakszon, Jenneke van den Ende, Antony van der Steen, Ton van Essen, Arie van Haeringen, Annet van Hagen, Joke Verheij, Marcel M. Mannens, Raoul C. Hennekam. Phenotype and genotype in 103 patients with Tricho-Rhino-Phalangeal syndrome. *Eur J Med Genet.* 2015;58(5):279-292.

Otten E, Birnie E, Lucassen AM, Ranchor AV, Van Langen IM. Telemedicine use among Genetics Professionals in Europe: room for expansion. *Eur J Hum Genet.* 2015. doi:10.1038/ejhg.2015.83. [Epub ahead of print]

Otten E, Birnie E, Ranchor AV, van Tintelen JP, van Langen IM. A group approach to genetic counselling of cardiomyopathy patients: satisfaction and psychological outcomes sufficient for further implementation. *Eur J Hum Genet.* 2015;23:1462-1467.

Otten E, Plantinga M, Birnie E, Verkerk MA, Lucassen AM, Ranchor AV, Van Langen IM. Is there a duty to recontact in light of new genetic technologies? A systematic review of the literature *Genet Med*. 2015;17(8):668-678.

Menko FH, Aalfs CM, Henneman L, Stol Y, Wijdenes M, **Otten E**, Ploegmakers MM, Legemaate J, Smets EM, de Wert GM, Tibben A; Dutch Society for Clinical Genetics. Informing family members of individuals with Lynch syndrome: a guideline for clinical geneticists *Fam Cancer.* 2013;12(2):319-24.

Otten E, Lekanne Dit Deprez RH, Weiss MM, van Slegtenhorst M, Joosten M, van der Smagt JJ, de Jonge N, Kerstjens-Frederikse WS, Roofthooft MT, Balk AH, van den Berg MP, Ruiter JS, van Tintelen JP. Recurrent and founder mutations in the Netherlands: mutation p.K217del in troponin T2, causing dilated cardiomyopathy. *Neth Heart J.* 2010;18(10):478-85.

Otten E, Asimaki A, Maass A, van Langen IM, van der Wal A, de Jonge N, van den Berg MP, Saffitz JE, Wilde AA, Jongbloed JD, van Tintelen JP. Desmin mutations as a cause of right ventricular heart failure affect the intercalated disks. *Heart Rhythm* 2010;7(8):1058-64.

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