Current Genetic Medicine Reports (2018) 6:21–27
https://doi.org/10.1007/s40142-018-0134-0

GENETIC COUNSELING AND CLINICAL TESTING (B LEROY AND N CALLANAN, SECTION EDITORS)

How Can We Reach At-Risk Relatives? Efforts to Enhance Communication and Cascade Testing Uptake: a Mini-Review

Rachel Schwiter[1] · Alanna Kulchak Rahm[1] · Janet L. Williams[1] · Amy Curry Sturm[1]

Published online: 19 April 2018

Abstract

Purpose of Review Cascade testing, or screening, is the process of stepwise, systematic genetic testing of at-risk relatives for a genetic variant originally identified in a proband. Cascade testing effectively identifies at-risk relatives who would benefit from early screening and/or medical intervention, and can potentially lead to early diagnoses and disease prevention. However, recent studies highlight the need for additional resources to enhance family communication and improve the cascade testing process. In this mini-review of cascade testing, we discuss various factors that influence the effectiveness of communicating genetic risk information among families, including barriers, provision of additional resources, direct contact, and the role of technology and healthcare providers.

Recent Findings Patients desire and value involvement of healthcare providers in the cascade testing process. Uptake of cascade testing increases when patients are provided with educational materials and technological resources, and when healthcare providers assist with communicating risk to their at-risk relatives.

Summary Through achievable adjustments in patient care, healthcare providers can facilitate family communication and uptake of cascade testing. This can be done by asserting the importance of genetic testing results to at-risk family members when reviewing results with patients and leveraging technological tools and other options for direct contact to maximize the benefits of earlier diagnosis and prevention.

Keywords Cascade screening · Cascade testing · Genetic testing · Family communication · Direct contact · Genetic counseling

Introduction

From the perspective of patients undergoing genetic testing, one of the major benefits to receiving a positive genetic test result is the ability to help family members anticipate health risks [1]. The process of systematic, stepwise testing of at-risk relatives for a previously identified familial variant is referred to as cascade testing or screening. Much of the work on cascade testing has been associated with conditions designated by the Centers for Disease Control and Prevention (CDC) Office of Public Health Genomics as Tier 1 genomic applications, including hereditary breast and ovarian cancer syndrome (HBOC), Lynch syndrome (LS), and familial hypercholesterolemia (FH) [2].

Several different approaches to cascade testing have previously been developed. *Indirect* cascade testing, also known as proband- or family-mediated contact, is commonly used in genetics clinics throughout the USA. In this approach, healthcare providers identify which relatives are at the highest risk to have inherited the genetic variant identified in the proband. Providers then recommend that the proband encourage those relatives to seek genetic testing or appropriate clinical evaluation. Alternatively, *direct* cascade testing, also referred to as "direct contact", occurs when the proband provides informed consent for his or her healthcare team to share pertinent information regarding their genetic test result directly with at-risk relatives. This also involves the proband providing the healthcare team with contact information (e.g., name, mailing address, phone number) for at-risk relatives. Then, clinic staff contact the at-risk relatives and offer information

This article is part of the Topical Collection on *Genetic Counseling and Clinical Testing*

✉ Amy Curry Sturm
asturm@geisinger.edu

[1] Genomic Medicine Institute, Geisinger, Danville, PA, USA

about the genetic risk variant and condition and next steps for cascade testing. An intermediate approach between indirect and direct cascade testing involves proband- or family-mediated contact *with assistance* from a healthcare provider [3]. In this approach, the proband is provided patient-friendly information about their medical condition and genetic testing so that medically accurate information from a healthcare provider can be distributed to their at-risk relatives.

In this mini-review of the recent (past 5 years) literature on cascade testing, we discuss various factors that influence the effectiveness of communicating genetic risk information among families, including barriers, provision of additional resources, direct contact, and the role of technology and healthcare providers.

Where Are We Now?: Success Rates of Cascade Testing Practices

The value of cascade testing is increasingly recognized in the overall process of genetic testing for its potential to lead to earlier diagnoses and preventive management, and for its cost-effectiveness [4]. Herein, we report on recent efforts made by multiple groups to improve family communication and the uptake of cascade testing.

Dilzell et al. evaluated educational materials provided to patients diagnosed with Lynch syndrome to facilitate communication with their relatives about their inherited risk [5]. A variety of materials were provided to relatives, including genetic counseling notes, a family letter, a personal note from the proband, laboratory information, online resources, and support group information. A survey of 50 probands and 24 relatives evaluated satisfaction and use of the different materials. Probands indicated that they had informed 88% of available first-degree relatives and 64% of available second-degree relatives of the family risk. The educational material probands reported sharing most often was the genetic counseling note. Eighty-three percent of relatives reported receiving at least one of the educational materials. This study demonstrated that sharing at least one educational material was associated with increased cascade testing follow-up, i.e., more first-degree relatives had genetic testing (51 vs. 19%, $p = 0.012$) and cancer screening (69 vs. 29% $p = 0.001$) when they received educational material compared to relatives who did not [5]. Both probands and relatives also reported a desire for additional information, such as a brochure or link to a website describing Lynch syndrome, related cancer risks, and recommended cancer screening.

A 2015 study by Bell et al. reported improvement in cascade testing uptake for FH with a program coordinated through a dedicated centralized approach set within an Australian healthcare system [6•]. The centralized approach follows the cascade testing recommendations outlined in the model of care document from a consensus group established by the FH Australasia Network [7]. The Australian model calls for formal identification of at-risk family members using "pedigree drawing and information management systems" and written information resources that can be distributed to at-risk family members. Contact may be through the proband, a clinical service, or both. However, contact by both the proband and clinical service, "dual efforts," are likely to be most acceptable and successful in reaching at-risk family members. Notification of at-risk relatives by clinical services is recommended to occur with consent of the proband. For probands who are reluctant to consent to sharing with relatives, efforts should be made to build a relationship with the proband and better understand the reasons for their reticence to share. Provisions made in 1988 to the Australian Commonwealth Privacy Act allow for contact of at-risk relatives without consent in the case of genetic information which could address a life-threatening condition in relatives. However, in this model of FH care, providers are cautioned to contact relatives without proband consent only as a last resort, as privacy legislation differs among states and local regulations may not allow providers to contact relatives without proband consent. Bell et al. reported that this centralized approach increased detection of FH by 2–3 family members per proband [6•]. The protocol tested identified probands seen in a specialty clinic, followed by outreach by a trained nurse to first-degree relatives, then second-degree and third-degree relatives. After seeking written consent from the proband for notifying relatives of their risk, a letter and an information sheet were sent directly to family members and/or delivered through the proband. If no response was obtained, clinic staff contacted relatives by telephone. In the first 100 consecutive patients in the FH program, 1267 at-risk relatives were identified, 366 were tested, and 188 were found to have the FH variant. A median of 4 family members were tested per proband and 2 new FH cases per proband were detected. Of 84 kindreds in which 3 or more family members were tested, a median of 3 new cases per proband were detected.

A recent qualitative study assessed healthcare providers' and patients' opinions on family letters that were intended to inform relatives about their risk to have an inherited cancer or cardiac condition [8]. In general, healthcare providers reported that family letters fulfilled their responsibility to inform at-risk relatives and were an easy method of communication for the proband. However, healthcare providers had difficulty deciding on an appropriate tone for the letters. A letter that was too vague might not motivate at-risk relatives to pursue cascade testing, yet a strongly worded letter might be too directive, anxiety-provoking, or beyond an acceptable reading level. Healthcare providers also discussed the possibility that patients might not distribute family letters appropriately, thereby mistakenly encouraging cascade testing in relatives who are

not at risk or who are obligate carriers. From the patient perspective, many reported feeling burdened with the obligation to inform relatives about their risks in addition to the emotional impact of learning their own genetic diagnosis. Based on their results, the authors suggest that healthcare providers review the logistics of the family communication process with their patients and specifically identify which relatives should receive family letters and the reasoning behind this. The authors also concluded that direct contact of relatives could be an alternative or additional resource to family letters due to the stress reported by patient participants around delivering these letters.

Barriers to Cascade Testing

Communication Barriers

The process of communicating positive genetic testing results and their implications to relatives can be complex, depending on the inheritance, disease risks, and severity of a condition, as well as family dynamics. In the setting of FH, for example, a commonly cited barrier to cascade testing uptake is that probands may not feel prepared with enough information to talk about genetic testing or other recommended screenings with their relatives [9]. Regarding cascade carrier testing for family members of individuals with cystic fibrosis, McClaren et al. report that lack of information on the availability of cascade testing translates to many relatives simply being unaware of their genetic risk to be a carrier, or affected, and the options for cascade testing [10].

In an effort to better understand the issues influencing cascade testing uptake in familial long QT syndrome, researchers in Australia surveyed patients enrolled in Heart Disease Clinics to assess psychosocial wellbeing, socioeconomic status, and family communication [11•]. All reported communicating with at least one first-degree relative, 73% with at least one second-degree, and 60% with at least one third-degree relative. However, by 4 years after the proband received a positive genetic testing result, only about half of all first-degree relatives completed cascade testing. Probands reported using multiple modes of communication with at-risk family members, including in-person, phone, and letter. Reasons probands reported sharing genetic information included a sense of obligation that the information would be useful to family members, family members need to know their risk, and that they wanted to encourage family members to get tested. Factors that aided probands in communicating included having a good understanding of the results and having a good relationship with family members. This study also found the effectiveness of family communication was influenced by the proband's psychological adaptation (i.e., depressive symptoms or anxiety) to a positive genetic testing result. In addition, the study pointed to potential access inequities for those with lower socioeconomic status and low educational attainment. The authors call for greater education and improved practice guidelines for healthcare providers to promote referral to genetics services due to the gap between reported family communication and actual uptake of cascade testing. They suggest that greater emphasis on discussion with genetic counselors might facilitate more directive approaches to family communication or referral options to clinical psychologists.

Geographic Barriers

The previous study discussed the likely gap in access to genetic testing services for individuals of lower socioeconomic status and education. This may relate to the geographical area where the patient lives. Many genetic counseling services are part of large urban medical centers or university hospitals [12]. Far distances and travel time may also limit the likelihood of completing cascade testing. The lack of easy access to genetic specialists has been noted to cause frustration within families [13]. This access issue can be addressed with technology via telephone and telemedicine counseling for individual or group counseling sessions. Existing evidence suggests that genetic counseling provided via telephone and telemedicine may be as effective as face-to-face genetic counseling [14–16].

Policy Barriers

Systemic barriers to cascade testing include little recognition by many healthcare providers of the need for accurate hereditary risk assessment, lack of genetics expertise especially in underserved regions, low levels of reimbursement for comprehensive genetic counseling that includes cascade counseling and testing, and the health system focus on care of the individual (versus the family) in guidelines and coverage policies [17]. Based on current service delivery models and reimbursement protocols, there is little financial incentive for genetic counseling programs to provide services that include comprehensive and active cascade screening programs, as direct outreach to at-risk relatives will not be reimbursed. Few genetic specialists find themselves with the time, support, and resources to fully pursue cascade screening for all at-risk relatives of their patients [11•].

George et al. proposes that cascade testing could be incentivized though policy changes that recognize the health value of identification of high-risk individuals [17]. The authors also suggest the possibility of aligning with public health models which offer reduced or no-cost testing for other public health issues. Greater use of registries could also help relatives to learn of their genetic risk and facilitate cascade testing.

Patient Confidentiality

In 1996, the Health Insurance Portability and Accountability Act (HIPAA) outlined limits to sharing a defined set of a patient's protected health information (PHI) to protect patient privacy. However, the nature of cascade testing requires willingness from a proband to share PHI (e.g., genetic testing results, pedigree, personal and family risk information) with relatives to ensure they are aware of their risk and that the most appropriate testing is ordered. Cascade testing also requires relatives' willingness to act on the genetic information, thus creating a tension between the "duty to warn" from the proband's perspective and the personal autonomy of relatives and their "right *not* to know." This makes communication of risk and the availability of genetic testing to clarify that risk for at-risk family members a delicate balance for both healthcare professionals and patients, as HIPAA is typically interpreted to partition health information about the proband from other individuals, including family members, unless explicit consent is provided. This protected patient right of privacy and confidentiality can be counter to their at-risk relatives' "right *to* know" health information about risk for conditions in which preventive action could be taken. Genetics professionals have developed methods to work within the confines of HIPAA by preparing materials for their patients to share with their at-risk family members. As previously noted in this mini-review, this proband-mediated approach has had mixed results, with under-ascertainment of at-risk relatives even in the context of high-risk conditions, despite probands reporting a sense of responsibility or duty to warn relatives about their health risks [18]. Safarova and Kullo proposed a potential option for sharing information among families by permitting proxy access to family history information in the electronic health record [19].

Direct Contact

It has been suggested previously that clinical genetics services should consider a more active approach, or "direct contact" of at-risk relatives, for cascade screening [3, 20•]. A previous literature review of cascade screening for FH concluded that most studies support direct contact of relatives via letter, mailed from the provider, and that provider-initiated communication more often results in relatives undergoing testing when compared with other methods of communication [21]. It is important to note that in Australian studies of direct contact, improvement in cascade testing uptake was dependent on trained nurses who proactively contacted, consented, and scheduled at-risk family members into clinics where subsequent counseling and cascade testing were accomplished [6•].

Direct contact can be accomplished in accordance with HIPAA when the proband provides consent for his or her relevant health information to be discussed with at-risk relatives [19, 22]. Through direct contact, informational letters to relatives can consist of a general notification of a positive genetic testing result in the family and omit PHI such as the proband's name, specific condition, or genetic variant [23]. More specific information could then be shared once family members connect with the proband's healthcare team and agree to learn more information.

Previous research has shown that when asked about cascade screening for FH, 77% of respondents, who were individuals from the general public in Western Australia, indicated a desire to be informed of their risk by the clinic involved in the FH screening program [24]. This showed evidence of community support for direct contact policies, where clinical program staff contact relatives of probands to inform them of their risk. To maximize support for such a program, consent from probands to share their PHI may be required and is preferable, as reported above [7, 24].

The question "how disturbing is it to be approached for a cascade screening program for FH?" has been investigated by assessing the views and psychological impact of a family-based screening program for FH [25]. In this program, performed in the Netherlands, at-risk relatives were actively approached and screened by the genetic service. Consent for release of the name of the proband was obtained prior to approaching the at-risk relatives, who were invited to participate in the screening program via mail. A week later, the relatives were telephoned by a "Genetic Field Worker" to determine whether they wished to participate. Of those approached, 2% did not participate, because they were either not interested, were already clinically diagnosed with FH, or were afraid of insurance consequences. Overall, less than 5% were critical of the approach. Twenty percent expressed feelings of social pressure by agreeing with the statement "The circumstances made me feel like I was more or less forced to participate in the screening programme" while 89% agreed with the statement "I felt free to choose whether I would participate or not." Effects on mood and quality of life effects were minimal to absent [25].

Attitudes toward direct contact as an alternative to family-mediated dissemination have also been explored in individuals at risk for other inherited cardiac conditions, including hypertrophic cardiomyopathy and long QT syndrome [26]. In this study, most relatives saw advantages in direct contact from health professionals and supported it in principle, with the consent of the affected relative. The advantage as a first-line approach was also recognized, especially in the context of strained family relationships where resentment and estrangement were cited as barriers to informing others. In addition, the "right to know" was specifically cited by at-risk relatives, and some expressed the view that they would have appreciated third party contact if the alternative was to remain in ignorance. In addition, participants felt that providing a

point of contact and written information would be an essential part of a direct contact program since receiving a letter informing you of your potential risk could be anxiety-provoking. Direct contact was also felt to have the potential to reinforce information previously provided to family members from the proband, which may overcome the proband's feeling of not being taken seriously enough when communicating this risk information to family members.

Direct contact may have additional support benefits for the proband. First, it can alleviate the burden of notifying at-risk relatives from the affected probands, who have reported feeling that they have insufficient authority or control to persuade family members to attend screening and welcome greater hospital assistance for contact with their at-risk relatives [20•]. Second, it increases accuracy and efficiency of information to relatives, as errors may occur in proband-mediated communication in families [27]. Furthermore, multiple studies have shown that when direct contact was employed, significantly higher numbers of at-risk relatives had their genetic status clarified, compared to the numbers when risk notification was proband-mediated [23, 28]. In a study focused on HBOC families, a protocol directly informing relatives nearly doubled the number of relatives tested and was also found to be psychologically safe [28]. It is hypothesized this impact on the uptake of testing in direct contact was due to increased accuracy and efficiency of information communicated to at-risk relatives.

Technology

Despite the acknowledgement of cascade testing as important (and necessary) to the cost-effectiveness of genetic testing and to realizing the promise of broad public health benefit [29], uptake of cascade testing remains sub-optimal [3]. There have been several calls to action for improving the reach into immediate and extended families to expand utilization of cascade testing, as detailed above. No matter the process for contacting relatives, studies have suggested that technology could play a crucial role in facilitating contact, communication, and education throughout families. However, there is a dearth of existing technological options and evidence about effectiveness of using technology for this purpose. Therefore, opportunities exist to develop and disseminate effective technological communications to improve family communication and uptake of cascade testing.

In a 2013 commentary, Jasperson called for improvement in cascade testing for LS, specifically through the creation and enhancement of online interventions, and offered solutions based on existing options available at the time [30]. One option highlighted, KinTalk (http://kintalk.org/), is an online social networking site to improve family communication about LS, and even allows family members to securely exchange test results and other medical information. Per the commentary, at least one advocacy group, Lynch Syndrome International, also supported communication throughout families via Facebook and Twitter platforms. Other research reviewed by Jasperson noted that early studies of HBOC families found that probands were interested in multiple resources to help with family communication, from booklets and letters to educational websites, as well as family sessions and support groups [30].

In 2014, Lynch and colleagues summarized the existing literature on advances in technology for counseling probands and communicating cancer risk through families [22]. They noted opportunities for improvement, particularly in identifying at-risk family members. This review pointed to the effectiveness of technological alternatives to face-to-face genetic counseling in reaching family members and overcoming geographic barriers. Telephone and videoconferencing were shown to be viable alternatives; however, most studies suffered from significant limitations in their comparators as well as lack of sustainability in practice.

A barrier to use of technology, however, could be due to perceived lack of utility by genetic counselors rather than probands and family members. A pilot study in the Netherlands of 51 home-based videoconferencing pre-test counseling sessions for cascade testing and other indications found comparable levels of patient satisfaction, anxiety, and perceived personal control between the online and face-to-face sessions [31]. The researchers in this study also examined this technology (a videoconferencing platform called mycoachconnect.com) from the genetic counselors' perspective. Despite an 8% estimated reduction in counselor time and a 10–12% lower cost, counselor satisfaction with the online tool was lower after the pilot—mostly due to technical difficulties with the platform [31]. Genetic counselors also cited disadvantages over in-person sessions of limited non-verbal communication cues.

Per a commentary by Sturm, tools to improve cascade screening should "provide education, offer support, and provide attainable next steps" to help probands and family members understand risk and take action [3]. While different types of technological solutions offer great opportunity and potential to address these points, there is still limited data on the effectiveness and acceptability of the use of technology to facilitate family communication and cascade testing. However, different technologies could enhance cascade testing by facilitating the development and provision of educational materials, videos, and other online content for easy distribution to at-risk relatives by probands and/or providers. Non-specific web-based content focused on the general importance of cascade testing could also be easily accessed by family members. Therefore, this is an opportune time to develop and test affordable and sustainable technological solutions with potential for broad dissemination to positively impact communication of genetic testing results to at-risk relatives and subsequent uptake of cascade testing services.

The Role of Healthcare Providers in Facilitating Cascade Testing

Healthcare providers can facilitate cascade testing by asserting the importance of the genetic testing result to at-risk family members when discussing results with a proband. For example, healthcare providers can state, "You were born with this genetic risk variant, and your children, siblings, and parents could have this risk, too. It is important for them to have this information so they can pursue genetic testing and take steps to reduce their risks now." Such statements can reinforce to the proband that genetic information has implications for the whole family. Professional groups such as the National Lipid Association [32] and the American College of Obstetricians and Gynecologists (ACOG) advocate cascade testing [33]. Specifically, ACOG recommends that obstetrician-gynecologists should be aware of who is eligible for cascade testing and understand its value [33].

Given that a common barrier to cascade testing is a proband's sense of inauthority or a lack of accurate information and knowledge about a genetic testing result, genetic counselors can assist in the cascade testing process by further educating probands, directing probands to additional resources, and enhancing their communication skills to empower them to relay appropriate genetic risk information to relatives [34]. Cascade testing conversations between healthcare providers and the proband should be ongoing, especially in families where there are young children—in other words, it is not a one-time conversation, but one that should be revisited over time by multiple healthcare providers. Genetic counselors can discuss with parents techniques on how to share age-appropriate genetic information with their children [35]. For adult-onset conditions, cascade testing may not be appropriate for children and adolescents, and not all individuals with positive genetic testing results have regular follow-up with a genetics clinic. Therefore, it is important that other healthcare providers, especially primary care providers and specialists who focus on these hereditary conditions, continue the conversation so that most, if not all, at-risk relatives are informed and provided access to cascade testing. With the combined efforts of healthcare professionals and their patients to encourage family communication about genetic risk, cascade testing can become universally available to enable family members to realize the health benefits of early diagnosis and risk-reducing measures.

Conclusions

The time is now to address the cascade testing barriers noted in this mini-review via further research into the development, testing, and dissemination of technology-based tools for family communication of genetic testing results. It is also critical to conduct research into direct contact methods with greater involvement from the healthcare professional to assist the proband in communication.

Compliance with Ethical Standards

Conflict of Interest All authors declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

References

Papers of particular interest, published recently, have been highlighted as:

- • Of importance

1. Hallowell N, Jenkins N, Douglas M, Walker S, Finnie R, Porteous M, et al. A qualitative study of patients' perceptions of the value of molecular diagnosis for familial hypercholesterolemia (FH). J Community Genet. 2017;8:45–52. https://doi.org/10.1007/s12687-016-0286-0.
2. Centers for Disease Control and Prevention, Office of Public Health Genomics. Tier 1 genomics applications and their importance to public health. 2013. Available from https://www.cdc.gov/genomics/implementation/toolkit/tier1.htm
3. Sturm AC. Cardiovascular cascade genetic testing: exploring the role of direct contact and technology. Front Cardiovasc Med. 2016;3. doi:https://doi.org/10.3389/fcvm.2016.00011.
4. Hampel H. Genetic counseling and cascade genetic testing in Lynch syndrome. Familial Cancer. 2016;15:423–7. https://doi.org/10.1007/s10689-016-9893-5.
5. Dilzell K, Kingham K, Ormond K, Ladabaum U. Evaluating the utilization of educational materials in communicating about Lynch syndrome to at-risk relatives. Familial Cancer. 2014;13:381–9. https://doi.org/10.1007/s10689-014-9720-9.
6. • Bell DA, Pang J, Burrows S, Bates TR, van Bockxmeer FM, Hooper AJ, et al. Effectiveness of genetic cascade screening for familial hypercholesterolaemia using a centrally co-ordinated clinical service: an Australian experience. Atherosclerosis. 2015;239:93–100. https://doi.org/10.1016/j.atherosclerosis.2014.12.036. **This report outlines the process of a centralized cascade testing service in Australia and provides evidence for the improved effectiveness of a centralized service**
7. Watts GF, Sullivan DR, Poplawski N, van Bockxmeer F, Hamilton-Craig I, Clifton PM, et al. FH: a model of care for Australasia. Atherosclerosis Supp. 2011;12:221–63.
8. Dheensa S, Lucassen A, Fenwick A. Limitations and pitfalls of using family letters to communicate genetic risk: a qualitative study with patients and healthcare professionals. J Genet Couns. 2017; https://doi.org/10.1007/s10897-017-0164-x.
9. Benson G, Witt DR, VanWormer JJ, Campbell SM, Sillah A, Hayes SN, et al. Medication adherence, cascade screening, and lifestyle patterns among women with hypercholesterolemia: results from the WomenHeart survey. J Clin Lipidol. 2016;10:937–43.
10. McClaren BJ, Aitken M, Massie J, Amor D, Ukoumunne O, Metcalfe SA. Cascade carrier testing after a child is diagnosed with cystic fibrosis through newborn screening: investigating why most relatives do not have testing. Genet Med. 2013;15(7):533–40. https://doi.org/10.1038/gim.2012.175.

11.• Burns C, McGaughran J, Davis A, Semsarian C, Ingles J. Factors influencing uptake of familial long QT syndrome genetic testing. Am J Med Genet A. 2015;170A:418–25. https://doi.org/10.1002/ajmg.a.37455. **This study identified barriers to cascade testing and addressed family communication of genetic testing**

12. Hawkins AK, Hayden MR. A grand challenge: providing benefits of clinical genetics to those in need. Genet Med. 2011;13:197–200. https://doi.org/10.1097/GIM.0b013e31820c056e.

13. Bernhardt BA, Zayac C, Pyeritz RE. Why is genetic screening for autosomal dominant disorders underused in families? The case of hereditary hemorrhagic telangiectasia. Genet Med. 2011;13(9):812–20. https://doi.org/10.1097/GIM.0b013e31821d2e6d.

14. Interrante MK, Segal H, Peshkin BN, Valdimarsdottir HB, Nusbaum R, Similuk M, et al. Randomized noninferiority trial of telephone vs in-person genetic counseling for hereditary breast and ovarian cancer: a 12-month follow-up. JNCI Cancer Spectrum. 2017;1. doi:https://doi.org/10.1093/jncics/pkx002.

15. Buchanan AH, Datta SK, Skinner CS, Hollowell GP, Beresford HF, Freeland T, et al. Randomized trial of telegenetics vs. in-person cancer genetic counseling: cost, patient satisfaction and attendance. J Genet Couns. 2015;24(6):961–70. https://doi.org/10.1007/s10897-015-9836-6.

16. Schwartz MD, Valdimarsdottir HB, Peshkin BN, Mandelblatt J, Nusbaum R, Huang AT, et al. Randomized noninferiority trial of telephone versus in-person genetic counseling for hereditary breast and ovarian cancer. J Clin Oncol. 2014;32(7):618–26. https://doi.org/10.1200/JCO.2013.51.3226.

17. George R, Kovak K, Cox SL. Aligning policy to promote cascade genetic screening for prevention and early diagnosis of heritable diseases. J Genet Couns. 2015;24:388–99. https://doi.org/10.1007/s10897-014-9805-5.

18. Hallowell N, Jenkins N, Douglas M, Walker S, Finnie R, Porteous M, et al. Patients' experiences and views of cascade screening for familial hypercholesterolemia (FH): a qualitative study. J Comm Genet. 2011;2(4):249–57. https://doi.org/10.1007/s12687-011-0064-y.

19. Safarova MS, Kullo IJ. Lessening the burden of familial hypercholesterolemia using health information technology. Circ Res. 2018;122:26–7. https://doi.org/10.1161/CIRCRESAHA.117.312319.

20.• Hardcastle SJ, Legge E, Laundy CS, Egan S, French R, Watts GF, et al. Patients' perceptions and experiences of FH, cascade genetic screening and treatment. Int J Beh Med. 2015;22:92–100. **This paper supports direct contact based on analysis of patients' attitudes and experiences with cascade testing**

21. Allison M. Communicating risk with relatives in a familial hypercholesterolemia cascade screening program: a summary of the evidence. J Cardiovasc Nurs. 2015;30(4):E1–12.

22. Lynch HT, Snyder C, Stacey M, Olson B, Peterson S, Buxbaum S, et al. Communication and technology in genetic counseling for familial cancer. Clin Genet. 2014;85:213–22. https://doi.org/10.1111/cge.12317.

23. Suthers GK, Armstrong J, McCormack J, Trott D. Letting the family know: balancing ethics and effectiveness when notifying relatives about genetic testing for a familial disorder. J Med Genet. 2006;43:665–70. https://doi.org/10.1136/jmg.2005.039172.

24. Maxwell SJ, Molster CM, Poke SJ, O'Leary P. Communicating familial hypercholesterolemia genetic information within families. Genet Test Mol Biomarkers. 2009;13(3):301–6. https://doi.org/10.1089/gtmb.2008.0138.

25. Van Maarle MC, Stouthard MEA, Marang-van de Mheen PJ, Lkazinga NS, Bonsel GJ. How disturbing is it to be approached for a genetic cascade screening programme for familial hypercholesterolaemia? Psychological impact and screenees' views. Comm Genet. 2001;4(4):244–52. https://doi.org/10.1159/000064200.

26. Ormondroyd E, Oates S, Parker M, Blair E, Watkins H. Pre-symptomatic genetic testing for inherited cardiac conditions: a qualitative exploration of psychosocial and ethical implications. Eur J Hum Genet. 2014;22:88–93. https://doi.org/10.1038/ejhg.2013.81.

27. Vos J, Stiggelbout AM, Oosterwijk J, Gomez-garcia E, Menko F, Collee JM, et al. A counselee-oriented perspective on risk communication in genetic counseling: explaining the inaccuracy of the counselees' risk perception shortly after BRCA1/2 test result disclosure. Genet Med. 2011;13(9):800–11. https://doi.org/10.1097/GIM.0b013e31821a36f9.

28. Sermijn E, Delesie L, Deschepper E, Pauwels I, Bonduelle M, Teugels E, et al. The impact of an interventional counselling procedure in families with a BRCA1/2 gene mutation: efficacy and safety. Familial Cancer. 2016;15(2):155–62. https://doi.org/10.1007/s10689-015-9854-4.

29. Ademi Z, Watts GF, Pang J, Sijbrands EJG, van Bockxmeer FM, O'Leary P, et al. Cascade screening based on genetic testing is cost-effective: evidence for the implementation of models of care for familial hypercholesterolemia. J Clin Lipidol. 2014;8:390–400.

30. Jasperson K. Cascade genetic testing in Lynch syndrome: room for improvement. Nat Rev Gastroenterol Hepatol. 2013;10:506–8. https://doi.org/10.1038/nrgastro.2013.122.

31. Otten E, Birnie E, Ranchor AV, van Langen IM. Online genetic counseling from the providers' perspective: counselors' evaluations and a time and cost analysis. Eur J Hum Genet. 2016;24:1255–61. https://doi.org/10.1038/ejhg.2015.283.

32. Goldberg AC, Hopkins PN, Toth PP, Ballantyne CM, Rader DJ, Robinson JG, et al. Familial hypercholesterolemia: screening, diagnosis and management of pediatric and adult patients: clinical guidance from the National Lipid Association Expert Panel on Familial Hypercholesterolemia. J Clin Lipidol. 2011;5:S1–8. https://doi.org/10.1016/j.jacl.2011.04.003.

33. American College of Obstetricians and Gynecologists. ACOG Committee Opinion No. 727: cascade testing testing women for known hereditary genetic mutations associated with cancer. 2018. doi:https://doi.org/10.1097/AOG.0000000000002457.

34. Campbell M, Humanki J, Zierhut H. A novel approach to screening for familial hypercholesterolemia in a large public venue. J Comm Genet. 2017;8:35–44. https://doi.org/10.1007/s12687-016-0285-1.

35. Raspa M, Edwards A, Wheeler AC, Bishop E, Bailey DB Jr. Family communication and cascade testing for fragile X syndrome. J Genet Couns. 2016;25:1075–84. https://doi.org/10.1007/s10897-016-9940-2.