

'I would like to discuss it further with an expert': a focus group study of Finnish adults' perspectives on genetic secondary findings

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1

2 **Abstract**

3 Background: Lowered costs of genomic sequencing facilitate analysing large segments of genetic
4 data. Ethical debate has focused on whether and what kind of incidental or secondary findings (SFs)
5 to report, and how to obtain valid informed consent. However, people's support needs after
6 receiving SFs have received less attention. We explored Finnish adults' perspectives on reporting
7 genetic SFs.

8

9 Materials and methods: In this qualitative study which included four focus group discussions
10 (N=23) we used four vignette letters, each reporting a genetic SF predisposing to a different
11 disease: familial hypercholesterolemia, long QT syndrome, Lynch syndrome and Li–Fraumeni
12 syndrome. Transcribed focus group discussions were analysed using inductive thematic analysis.

13

14 Results: Major themes were *immediate shock, dealing with worry and heightened risk, fear of being*
15 *left alone to deal with SFs, disclosing to family and identified support needs*. Despite their
16 willingness to receive SFs, participants were concerned about being left alone to deal with them.
17 Empathetic expert support and timely access to preventive care were seen as essential to coping
18 with shock and worry, and disclosing SFs to family.

19

20 Conclusions: Discussion around SFs needs to concern not only which findings to report, but also
21 how healthcare systems need to prepare for providing timely access to preventive care and support
22 for individuals and families.

23

24

1 **Key Words**

2 incidental findings, secondary findings, whole genome sequencing, public perspective, focus group,
3 qualitative vignette study

4

1 Introduction

2 Recent advances in genetics and lowered costs of whole genome/exome sequencing facilitate
 3 analysing large segments of genetic data. This raises the possibility of generating different types of
 4 findings unrelated to the original research question or clinical investigation. These additional
 5 findings are commonly called incidental findings, but this term has been criticized since their
 6 identification requires active analytical effort (Shkedi-Rafid et al., 2014). In this paper we use the
 7 term secondary findings (SFs) (Kalia et al., 2016) to cover both truly incidental and actively sought
 8 findings that are unrelated to the original purpose of genomic sequencing. Amongst other types, SFs
 9 can be single variants suggesting high risk for heritable diseases, including certain cancers and
 10 cardiovascular diseases.

11 There has been intense ethical debate on the reporting back of genetic SFs. Discussion has focused
 12 upon differing ethical principles guiding research and clinical practice (Hallowell et al., 2015),
 13 uncertainty inherent in genetic risk information (Newson et al., 2016), whether and what kind of
 14 SFs to report back (Christenhusz et al., 2013), and how to obtain valid informed consent (Mackley
 15 et al., 2016). Consensus is emerging that scientifically robust, analytically valid, and clinically
 16 actionable findings should be reported back to research participants who have consented to receive
 17 them (Knoppers et al., 2015; Wolf, 2013), and this reflects lay people's preferences (Bollinger et
 18 al., 2012; Daack-Hirsch et al., 2013; Haukkala et al., 2013; Loud et al., 2016; Ormondroyd et al.,
 19 2007). The American College of Medical Genetics and Genomics (ACMG) recommends looking
 20 for and returning SFs in 59 genes during clinical sequencing (Kalia et al., 2016), and the European
 21 Society of Human Genetics recommends involving public perspectives when incorporating genome
 22 sequencing into healthcare (van El et al., 2013).

23 Most research participants wish to receive individual genetic research results and SFs (Facio et al.,
 24 2013; Loud et al., 2016), particularly if they are treatable or preventable. A few studies have looked
 25 at reactions to receiving genetic findings which emerge during research studies (Hallowell et al.,
 26 2013; Haukkala et al., 2013; Lewis et al., 2016; McBride et al., 2016; Ormondroyd et al., 2007;
 27 Sanderson et al., 2017). In a recent Finnish study (Haukkala et al., 2013), biobank participants
 28 received, via letter, unexpected genetic results for long QT syndrome (LQTS) – a treatable, but
 29 potentially fatal, cardiac arrhythmia. Most of the 17 participants were positive about receiving this
 30 information, particularly as preventative measures were available. Likewise ClinSeq participants
 31 who had opted to receive SFs via counselling – primarily related to cancer, cardiomyopathy, LQTS

and familial hypercholesterolemia (FH) – perceived the information as useful for personal and family health after receiving SFs (Lewis et al., 2016). Other studies have observed more ambivalent responses to receiving unexpected genetic risk information (Hallowell et al., 2013; Ormondroyd et al., 2007). While there is a growing literature on individuals’ reactions to receiving SFs, the types of support that people need after receiving SFs has received less empirical attention. In addition, the ways in which people expect healthcare to respond to these needs is largely unexplored.

Genetic risk information is received in different individual, social and cultural contexts. McBride et al.’s (McBride et al., 2016) qualitative study explored how research participants and their relatives reacted to receiving a letter that revealed a variant linked to Li–Fraumeni syndrome (LFS), which predisposes to several cancers. Their results emphasize the importance of timing and individuals’ life situation when receiving unanticipated findings. For example, in the presence of a newly diagnosed cancer in the family individuals said they were less able to process genetic risk information (McBride et al., 2016). We argue that besides personal life situation, concerns and needs around receiving SFs may be shaped by wider sociocultural structures, such as availability of social welfare and types of healthcare systems, and cultural ideals (Press et al., 2000). Arguably, people’s contextualized needs and concerns following the receipt of SFs need to be better understood when designing clinical and research procedures for disclosing this type of information.

The aim of our study was to explore Finnish adults’ perspectives on the reporting of genetic SFs via letter, more specifically high risk single variants linked to serious but actionable diseases. It extends previous literature by exploring not only people’s willingness to receive SFs, but also their potential support needs and concerns following the receipt of SFs in a hypothetical situation, contextualized in a society with a tax-funded public healthcare system.

Materials and Methods

To explore people’s concerns and support needs we used a qualitative vignette study design, which employed focus group discussions (Barbour, 2008). Members of the public were recruited by the Helsinki area Metro newspaper, which ran an advertisement about the study on three days in April–May 2016. The advertisement headed ‘*How should hereditary risk information be delivered*’, called for 18–64-year-old volunteers (compensation: two cinema tickets). There were no exclusion criteria, but the participants needed to be able to speak Finnish. Interested volunteers (N=32) were e-mailed an online survey with consent form, demographic questionnaire, and open-ended writing

1 task. The writing task was completed by 29 adults, of whom 23 attended focus group discussions.
 2 This paper only reports data from focus group discussions.

3 The writing task asked participants to read a vignette letter (Table 1), which revealed a genetic SF
 4 generated during a clinical examination, and imagine themselves receiving this letter in real life.
 5 Four versions of the letter were constructed and these were randomly assigned. Each reported a
 6 variant linked to either familial hypercholesterolemia (FH), long QT syndrome (LQTS), Li-
 7 Fraumeni syndrome (LFS), or Lynch syndrome (LS). We chose these diseases since they are all on
 8 the ACMG list of variants to be reported back following WGS (Kalia et al., 2016), and we had
 9 previous experience of disclosing incidental LQTS findings (Haukkala et al., 2013), and of directly
 10 contacting LS families for genetic testing (Aktan-Collan et al., 2007). To vary the diseases in terms
 11 of their treatability, we chose another cardiovascular disease FH, which is relatively common but
 12 undertreated in Finland (Lahtinen et al., 2015), and another cancer syndrome LFS, which has fewer
 13 prevention possibilities (Schneider et al., 1993). Table 2 describes the diseases and their treatment
 14 options (this table was not given to the study participants).

15 After reading one of the four letters, participants (N=29) were asked to write down their initial
 16 thoughts upon receiving the letter, and describe what they would do in this hypothetical situation
 17 (Table 1). Between 0–7 days later, 23 participants attended focus group discussions (N=4); these
 18 contained 4–7 participants each. In each session, the participants discussed one letter on cancer
 19 (either LS or LFS) and one letter on cardiovascular disease (either FH or LQTS), one of which each
 20 participant had read during the earlier writing task. MV and KA-C led and moderated the
 21 discussions using a topic guide, which focused upon: first reactions to the letter, perceptions of
 22 disease and risk, searching for information, family, recommendations for implementation, and
 23 consent. Participants were encouraged to discuss the topic broadly. Sessions lasted between 94–125
 24 min (mean 114). Approximately 45 min into the discussion, KA-C, a medical doctor, introduced a
 25 slide show (14–32 min, 13 slides), providing further information on the two diseases under
 26 discussion, and answered questions about these diseases. We started the discussions before
 27 presenting more information to first discuss participants' initial reactions to their hypothetical
 28 results. The aim was to mimic a realistic process, in which first impressions might change after
 29 receiving more information on the condition via counseling.

30 Focus group discussions were transcribed verbatim and analysed using inductive thematic analysis
 31 (Braun and Clarke, 2006). The analysis aimed to capture implicitly expressed meanings in addition

to explicitly stated opinions (Braun and Clarke, 2006) on the following: What are lay people's concerns and needs related to receiving genetic SFs linked to serious but actionable conditions? MV coded the transcripts and discussed the emerging codes and their grouping into larger themes at length with KA-C, who had co-facilitated the focus groups and thoroughly familiarized herself with the transcripts. KA-C agreed with MV's interpretation of the data. The overall thematic structure was further discussed in a number of data discussion meetings that included MV, KA-C and NH. Chosen data extracts were translated into English during manuscript writing.

Results

Focus group participants (N=23) were between 20–64 years old, primarily middle-aged (mean age 50; 19/23 over 40) and female (21/23). Their educational and professional backgrounds were diverse: 9/23 had a university degree, and 3/23 reported working in the healthcare sector (nurses, personal assistants). Approximately half of participants (N=12) had children. In focus groups, several participants spontaneously brought up a family history of cancer, heart disease or high cholesterol; one participant was waiting for a genetic test for a heart related condition (other than FH or LQTS).

The study scenario (Table 1) assumed that the participant, hypothetically, had already given their consent to receiving SFs. The study participants approached the topic from this perspective, and rather discussed the aftermath of receiving SFs than whether or not they would like to receive them. In general, participants were in favour of receiving SFs, but some had mixed feelings. Particularly towards the end of the lengthy focus group discussions, participants tended to express more ambivalence, seemingly because they were slightly overwhelmed by all the complexities involved in the matter.

Presenting more information on the diseases in the midst of the session did not drastically change the course of discussion. However, participants suggested that some modifications to the vignette letters could prevent misunderstandings. For example, they suggested effectiveness of preventive measures to be emphasized more, in order to reduce distress and potential avoidant reactions. Also, participants discussed whether and how commonness or uncommonness of the syndrome might play a role in how it could be managed in the healthcare system. With regard to potential concerns and needs after receiving SFs, we identified five major themes within focus group discussions: *immediate shock, dealing with worry and heightened risk, fear of being left alone to deal with SFs,*

1 *disclosing to family and identified support needs.* These contained a number of subthemes as
 2 outlined below.

3 Immediate shock

4 Negotiating the level of shock was participants' first reaction to reading the letter. Many
 5 participants described receiving the letter as a 'surprise', 'shock' or 'bomb' (e.g. below,
 6 A7=seventh speaker of the first session), although a minority said they 'did not take it very
 7 seriously' (D1). In particular, participants commented that receiving SFs could be difficult for
 8 certain groups: younger people, females, and those who tend to worry in general.

9 Despite acknowledging that SFs could be shocking, participants disapproved of being too worried
 10 about one's health. To resolve this conflict of being shocked, but also wanting to appear reasonable
 11 and capable of coping with risk information, participants defended and normalized their own
 12 (hypothetical) emotional reactions to the letter by emphasizing the severity of the disease.

13 *A7: but in any case this is like a bomb to anyone [A2: yeah!] there's no such person to*
 14 *whom this is not like a bomb.*

15 However, focus groups also implied that one was expected to manage the situation eventually.
 16 Participants actively distanced themselves from 'those people' who would panic altogether upon
 17 reading this type of letter. Being rational and open to receiving risk information were considered
 18 desirable traits, instead of 'panicking' or 'sticking one's head in the sand' (D3), i.e. choosing to live
 19 in denial of one's risk status. The following interchange shows how D2 and D3 distanced
 20 themselves from 'those' irrational, weak or fearful people who tend to panic.

21 *D2: but there are people who don't need but the zero point zero something per cent*
 22 *risk and still the anxiety, the fear hits them and they collapse, you know that kind of*
 23 *people*

24 *D3: on my part I certainly would think about the odds*

25 *D2: but that indicates courage. Then there are those who start to be fearful straight*
 26 *away before there is really anything at all*

27 *D3: yeah, but I just wanted to make clear, that I would not like push it away, like*
 28 *because of fear, but instead like through reason*

1 Discussions such as these suggest that in the aftermath of receiving SFs there is more than the shock
 2 to deal with. Individuals may experience pressure to manage their emotional reactions in a socially
 3 desirable way, to appear strong, rational, and capable of dealing with bad news. Focus group
 4 participants made no explicit statements that overtly displaying emotional distress would be
 5 shameful. Yet, since participants actively attempted to avoid falling into the category of ‘those
 6 people’ who are not able to handle their emotions, a threat of shame over one’s emotionality was
 7 apparent. Hence, individuals may have to deal with their shock of receiving SFs, but also the
 8 implicit shame of experiencing and displaying distress. Finally, some participants recognized that
 9 receiving SFs could be seen as a positive event; as a ‘wake up call’, as it might remind one to ‘live
 10 one’s life to the fullest’ (A6).

11 Dealing with worry and heightened risk

12 Participants also identified the possibility that receiving SFs could generate enduring anxiety and
 13 discussed how receiving SFs could evoke ‘stress’, ‘placebo effect’, or ‘energy’ that might in turn
 14 trigger the genetic risk and cause the illness.

15 *A6: if we learn about a possibility to develop some illness, and then we give it both*
 16 *our own energy and our relatives’ worry energy, and start to like dwell on it (--) so*
 17 *are you like actively activating the gene*

18 Dealing with worry and heightened risk was seen as a threat to holistic wellbeing. Indeed, some
 19 disapproval was voiced about vigorous attempts to control health risks:

20 *A7: everything has to be so controlled (--) and then you just hysterically follow*
 21 *[guidelines of authorities] (--) like common sense is all lost [these days]*

22 In sum, participants described how receiving a letter suggesting an unanticipated inherited risk for
 23 cancer or cardiovascular disease was emotionally confronting and had the potential to cause
 24 ongoing distress. This distress arose partially because they were afraid they might be left on their
 25 own to deal with this information.

1 Fear of being left alone to deal with secondary findings

2 Participants' overarching concern was that it would be distressing to be left on their own to make
3 sense of the SF and cope with the shock and worry. Concerns about being left alone to deal with
4 SFs were related to a) immediate situation of receiving the letter, b) one's personal life situation,
5 and c) structure and equity of healthcare system.

6 *Immediate situation*

7 Many participants felt that being left alone to cope with 'horror scenarios' that SFs might evoke was
8 unacceptable. While some said they were happy to receive the information in a letter, many said
9 they would prefer to receive SFs in person or by phone.

10 *D5: No letter! This is somehow so sterile and you collapse after this. At first you will*
11 *be like, 'Aha, yeah ok', but when you start going through it in your head, like 'Help',*
12 *you panic*

13 While participants were pleased that the vignette letters provided (hypothetical) contact details
14 suggesting where they might access further information and support, some participants worried
15 about finding the time to call and discuss this issue in the midst of a busy life.

16 *Personal life situation*

17 One's previous experiences, current life situation, and future prospects were all seen to affect the
18 meaning of the SFs, and the extent to which one would feel threatened by this information. Again,
19 younger people were perceived as more vulnerable because it was reasoned that receiving SFs at a
20 young age could complicate future life decisions and isolate one from peers.

21 *D2: how on earth would a [15-year-old] person who wants to be like everyone else*
22 *bear having this kind of very rare thing [risk for LFS], so it would be even worse, at a*
23 *certain age*

24 At older ages, the threat of illness was seen as more commonplace, less stigmatizing, and hence not
25 as threatening to social relations like friendships, romantic relationships and family planning.

1 *Structure and equity of healthcare system*

2 Fear of being left alone to deal with SFs was also influenced by views of the wider societal
3 structure. Participants explicitly linked the acceptability of reporting SFs to the stability and
4 justness of healthcare system and society in general. Trust towards society, science, and healthcare
5 appeared important for feeling safe and cared for after receiving SFs.

6 *A7: we have exceedingly skilled clinical professionals, and our doctors and research*
7 *and everything are really top-notch, like the care one receives in Finland is so good*
8 *so I definitely wouldn't be worried one bit*

9 It was argued that in an equal, stable and just society that ensures access to treatment and care,
10 disclosing SFs would be more acceptable compared to an unequal, poorly structured society where
11 not everyone has access to proper healthcare. In the latter case, information about SFs was
12 perceived as potentially benefiting those who are well-off, and further harming the disadvantaged.
13 Ensuring a sense of safety and being taken care of, and simultaneously supporting individual
14 autonomy were emphasized.

15 *B1: if the society is like just and equal, then people might be more ready to receive the*
16 *[SF] information, because they would feel they are safe (pause) but if it's a very*
17 *unequal society, and everything is like going in a bad way (pause) then it could be, it's*
18 *hard to say, then everyone acts more (pause) from their own stances. Some flush their*
19 *lives down the toilet and some [other interviewee: pull themselves together] yeah, pull*
20 *themselves together*

21 In sum, being left alone to deal with SFs was a major concern in several ways. Uncertainty about
22 who they could discuss SFs with added to such concerns, indeed, seeking support from family
23 members was considered problematic since the information also concerned them.

24 *Disclosing to family*

25 Participants were concerned about a potential lack of support when it came to disclosing SFs to
26 their relatives. Concern for the family included worries about family members' health, and also the
27 worry that disclosure could harm family relations. In addition, participants expressed concerns since
28 they perceived conflicting responsibilities to both disclose SFs and to protect family from worry.

1 Disclosing SFs was described as a difficult task for a professional, let alone a lay person who lacked
 2 expertise in genetics, medicine, or communication. Participants felt responsible to disclose
 3 information to family members, but also responsible to support their relatives following disclosure.

4 *C4: it would be very hard as a lay person to inform another person about this kind of*
 5 *possibility to a serious hereditary illness, because you don't have all the information,*
 6 *(--) you really have no answers to questions that could arise in that situation, so it*
 7 *would be quite a scary situation, I mean informing others, how to then do it so that the*
 8 *other one doesn't panic altogether*

9 Parents' responsibility to be able to take care of and support their children was particularly
 10 emphasized. Participants implied that in these situations the parents' own emotions and needs were
 11 no longer the focus, but instead their role as a responsible caregiver.

12 *D5: the parent has to be able to like be strong then, and there for the child and*
 13 *listening and, and like safe*

14 Participants acknowledged that whatever one might perceive as the right time and way to disclose
 15 the information to children in principle, in practice, it might be difficult to keep SFs secret. On the
 16 one hand, children and young people were seen as vulnerable and therefore, in need of protection
 17 from worry about risk. On the other hand, it was argued that 'growing up knowing' about risk might
 18 enable children to avoid the shock of unexpectedly finding out this information later:

19 *A2: That way it will not startle you if everything is thought through beforehand, that*
 20 *you might get it from [this or that side of the family] [A3 and A4 agree] discussed*
 21 *beforehand around the kitchen table so even if grandchildren are there to hear it, it*
 22 *will not be striking (laughter)*

23 Identified support needs

24 To cope with shock and worry, and to be able to make the best possible decisions for themselves
 25 and their relatives, participants said they needed timely access to expert support, including:
 26 information, access to care and empathetic communication.

1 *Information and access to care*

2 Reliable and reassuring information was seen as enabling individuals to cope with the initial shock
3 of receiving SFs. Rapid access to reliable information was particularly emphasized since ‘these days
4 you can find all kinds of [scary and unreliable] things on the internet’ (D1), which could easily be
5 misinterpreted. Timely information about preventive methods and cures was seen as a means to
6 tackle uncertainty and fear of the unknown, to gain control of the situation.

7 *A5: at first you panic, but the more you get to know about the matter, the easier it*
8 *gets. And then if you know, like (pause) how it’s treated. To me that’s always the most*
9 *important, that I know how to go forward, and how I can survive this (pause) so, I*
10 *think this letter is very good. And the fact that you can contact, probably I would*
11 *contact them (pause) so (pause) I would like to discuss it further with an expert*

12 However, perceptions of reliable information sources varied and covered more than professional
13 knowledge. Some participants wished for peer support to access emotional support and to gain
14 relevant information that ‘a doctor won’t tell’ (A5). In addition, one participant brought up the
15 possibility of seeking information on alternative treatments, since she did not ‘trust chemical,
16 artificial medicine unconditionally’ (C4). Other participants had a practical approach, and felt that
17 the possibility to do something immediately would relieve anxiety. This is why they endorsed
18 prompt and detailed advice on what to do and whom to contact.

19 *C2: I don’t necessarily understand so much about these genes, but I also wouldn’t*
20 *have needed, that they would have explained it all through, (--) to me there was*
21 *enough information and advice what to do and so on*

22 *Empathetic communication*

23 In addition to a need for knowledge and concerns about access to care, the need for expert support
24 was linked to an emotional need to be taken care of and treated in a respectful manner, which
25 promotes feelings of safety and being valued. These needs were clearly connected to previous
26 hurtful experiences of healthcare. Needs for information and emotional support were tightly
27 intertwined; content of information and communicating it in a respectful, sensitive manner were
28 considered equally important. Experience of being taken care of was perceived as strongly
29 supporting coping with SFs.

D4: it has an enormous impact, what kind of (pause) conversation you can create then, and plan for further care, that gets you through everything

Participants emphasized that considerate and easy to understand wordings in the letters or possible other written information materials were essential. Nevertheless, they explicitly underlined that no matter how informative and reassuring such materials might be, a possibility for a human contact would be crucial after receiving SFs, either in person or by phone:

D5: someone has to call then, and have time [to discuss the SF], I mean at least call or tell you face to face (--)

D2: And this letter is very well formulated anyway, there is nothing wrong with that. You can't really put it any more nicely [D5: yeah you can't really], that type of information

Discussion

We examined Finnish adults' potential concerns and needs related to receiving serious but actionable genetic SFs via letter. Despite a general positive attitude towards receiving SFs, concern about being left alone to deal with this information was widely expressed. Empathetic expert support and prompt access to preventive care and treatment were seen as essential to coping with immediate shock, heightened risk and potential prolonged worry, as well as to being able to disclose SFs to family in an appropriate way. While the results of the current study support previous findings that stress the importance of practical guidance (Daack-Hirsch et al., 2013) and quick retesting (Haukkala et al., 2013), they provide new insight into how contextual factors, such as the structure of healthcare system, may shape how people expect the healthcare to respond to their needs for treatment and support after receipt of SFs.

Access to empathetic expert support and further care were considered as means to cope with emotional distress caused by the SF's implications for oneself and family members. Participants depicted shock as an understandable first reaction to receiving SFs that could be overcome if, and only if, appropriate support and information are available. There is some evidence that distress following receipt of information on LS variants or BRCA variants (linked to breast and ovarian cancers) eases after a few weeks (Aktan-Collan et al., 2013; van Oostrom et al., 2003). However, when family members of Australian Ovarian Cancer Study participants received an unexpected

1 letter stating that a BRCA variant had been detected in their family, they described themselves as
2 more distressed than the original research participants (Hallowell et al., 2013). Further research is
3 needed to examine whether unexpectedness and potential unfamiliarity with the diseases associated
4 with the SFs might cause more enduring distress. Moreover, the subtle threat of shame about overly
5 emotional reactions that was implied in our participants' responses, might also discourage
6 individuals from expressing negative reactions in research interviews or clinical encounters. This
7 reaction may be culturally specific as stubborn perseverance in the face of difficulties is generally
8 highly valued in Finnish culture (Lahti, 2013). Yet, potential for similar pressure to appear strong
9 and capable of coping should be taken into account also in other cultures that value individual
10 agency in managing one's life.

11 Similarly, access to care and clear clinical procedures and processes were seen as crucial to long
12 term coping with SFs. This finding is in line with previous studies' conclusions that people wish
13 information about SFs to be accompanied with a practical plan (Daack-Hirsch et al., 2013), and that
14 prolonged processes in re-test practices may cause distress (Haukkala et al., 2013). Professionals
15 have expressed reluctance about returning SFs, due to lack of comprehensive practice framework,
16 uncertainty in interpreting genomic results, the need to update consent practices, and the fact that
17 the finding concerns not only the individual but the whole family (Gourna, 2016). Our results
18 endorse these reservations, suggesting that those who receive SFs expect timely support and clear
19 procedures.

20 Expert support was also seen as needed to help with disclosing SFs to family. A similar wish was
21 identified in a previous Finnish study within LS families (Aktan-Collan et al., 2011). Our
22 participants considered delivering SFs a demanding task even for a professional, due to dual
23 demands of expertise and empathy. Still, in line with previous research (Hallowell et al., 2003;
24 Vavolizza et al., 2015), they felt responsible for disclosing the information about genetics to their
25 family. At the same time, they felt responsible for coming to terms with the IF on their own at first,
26 so that they would be able to support others. Parents' responsibility to take care of their children
27 was particularly emphasized, to the extent that it could even overwhelm parents' own needs. These
28 results shed light to previous contradictory observations that suggest that perceived responsibility
29 for one's children may encourage willingness (Christenhusz et al., 2014), ambivalent feelings
30 (Haukkala et al., 2013; Wright et al., 2014), or reluctance towards receiving SFs (Richards et al.,
31 2003). In addition to parents, receiving SFs was perceived as distressing for young people, whose
32 friendships and family planning receiving SFs might complicate. Overall, our results emphasize

1 McBride et al.'s (McBride et al., 2016) remarks on the importance of an individual's life situation
2 when receiving SFs.

3 While international guidelines for managing SFs are formulated, it should be noted that, in practice,
4 such guidelines will be applied in nuanced societal and cultural contexts, in which responsibilities
5 of different actors may be emphasized differently. Results of the current study highlight a need to
6 evaluate the practices of reporting SFs in the context of the healthcare system. Disclosing SFs is
7 never an isolated act but contextualized within the relationship of the disclosing institution/person
8 and the patient/research participant/family member. Consistent with previous literature (Daack-
9 Hirsch et al., 2013), current participants perceived managing SFs as a shared responsibility between
10 professionals and patients. They implied that whoever discloses the information is, to some degree,
11 responsible for taking care of the recipient of the information. The nature and degree of perceived
12 responsibility appears to stem from the relationship between the disclosing institution/person and
13 the recipient. Not only were parents seen as responsible for their children, but also the healthcare
14 system was seen as responsible to provide support and further care for the families who received
15 this information. Our study participants expected healthcare to provide support and equal access to
16 treatment for everyone after receipt of SFs, but were concerned whether there would be resources to
17 manage this appropriately. These expectations and concerns reflect the Finnish context where tax-
18 funded public healthcare is available and, in general, takes some responsibility for citizens' health
19 and wellbeing. We hypothesise that in countries without public healthcare systems, people might
20 expect and seek support from other sources.

21 Since disclosure happens within a particular relationship, the act and way of disclosure may also
22 influence that relationship. In line with previous research (Vavolizza et al., 2015), our study
23 participants identified potential for strengthened family ties, but also isolation after disclosing SFs
24 to family members. Similarly, disclosing SFs may affect relationships between healthcare
25 system/research and the patient/participant. The widely expressed fear of being left alone to
26 understand and deal with the emotional and practical sequelae of SFs suggests that adverse
27 reactions and distrust towards research and healthcare may arise, if the ways of reporting SFs and
28 referral for treatment/prevention are perceived as disrespectful, disorganized, or unequal.
29 Communication and collaboration between research and clinics should be attended to (Lohn et al.,
30 2014). When practices of reporting SFs are formulated, societies with public healthcare systems
31 need to allocate resources to psychosocial support and preventive treatment.

1 Methodological considerations

2 Participants in this study were asked to imagine a situation in which they received serious, but
3 actionable, genetic SFs via letter. The use of hypothetical scenarios has been criticized, since
4 imagined accounts do not necessarily match actual behaviour (Persky et al., 2007). In response, we
5 argue that the vignette approach of this study had some significant advantages. We assume
6 participants were not as distressed as they might be in a real situation, and thus, these focus group
7 discussions offered them a safe space to explore a broad variety of points of views on the topic. In
8 addition, the use of hypothetical scenarios meant that we could interview people only days after
9 they ‘received’ SFs.

10 Some previous studies of the feedback of SFs to research participants during a counselling session
11 (Lewis et al., 2016) or via letter (Haukkala et al., 2013) have reported almost exclusively neutral or
12 positive reactions. A longer time between receiving SFs and interviews could explain this
13 difference, but it should be noted that in those previous studies, only 31/46 and 17/27 invited
14 individuals, respectively, participated in the studies. Since it is challenging to recruit interviewees
15 who do not wish to receive genetic risk information in the first place (Richards et al., 2003), it is
16 possible that those who experience more distress avoid participating in studies after receiving SFs.
17 Further research is needed to explore whether adverse reactions to receiving SFs discourages
18 participation, which might bias research on reactions.

19 The scenario presented in this study concerned reporting SFs in clinical practice. Clinical patients
20 and genetic research participants go through genome sequencing for different reasons and with
21 different expectations (Sanderson et al., 2015). Similarly, people’s expectations for support after
22 receiving SFs may vary across contexts. Previous research, however, suggests that to lay people the
23 underlying meaning of SFs is similar regardless of the setting (Daack-Hirsch et al., 2013); hence,
24 needs for empathetic expert support and access to care can be expected to be comparable across
25 contexts.

26 Finally, participants of this study were self-selected, primarily female and middle-aged, and
27 possibly more interested in health risk management than the average citizen. Children and young
28 adults were seen as vulnerable to receiving SFs, but it should be noted that most participants were
29 middle-aged themselves. Diversity of educational and professional backgrounds, however, resulted
30 in broad variety of points of views on receiving SFs.

1 Conclusions

2 Results of the current study suggest potential for shock and prolonged worry after receiving genetic
3 SFs linked to serious but actionable diseases, and that the lack of available expert support or timely
4 referral to treatment are likely to increase this distress. Discussion around SFs should focus not only
5 on what type of SFs to disclose, but also on how disclosure should take place, and how to further
6 support the recipient. Procedures that follow reporting SFs need to be carefully formulated and
7 communicated to patients/research participants, in order to ensure that people will not feel left alone
8 to deal with SFs. Participants of the current study wished for expert support to make informed,
9 autonomous decisions regarding their own and their family member's health after receiving SFs;
10 hence, shared decision making is encouraged (Fried, 2016).

11

1 **Compliance with Ethics Guidelines**

2 **Conflict of Interest**

3 Marleena Vornanen, Katja Aktan-Collan, Nina Hallowell, Hanna Konttinen, and Ari Haukkala
4 declare that they have no conflict of interest. Helena Kääriäinen works part time as Clinical
5 Geneticist in Docrates Clinic (a private cancer clinic), and as a Clinical Consultant in Blueprint
6 Genetics laboratory. Helena Kääriäinen has received (September 2016) an honorarium from Orion
7 Pharma (a presentation in a Symposium for Gynaecologists; the topic was genetic testing).

8 **Ethical approval**

9 All procedures followed Declaration of Helsinki ethical guidelines on research with human
10 participants. Informed consent was obtained from all participants for being included in the study.
11 Study protocols were approved by University of Helsinki Ethical Review Board in the Humanities
12 and Social and Behavioural Sciences.

13

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38

Table 1. Online writing task.

Please read the following and write down what You would think and do in the situation.

Dear Madam/Sir,

You have been to a university hospital, where your blood sample was collected to examine a disease, and the sample was used to sequence your whole genome (genes were spelled out letter by letter). When genes are spelled out letter by letter, it is possible that also other health related genetic mutations are found.

Before giving the blood sample, You signed a consent form stating that you can be contacted if also other health related findings were found during the examination.

Your recently analyzed results indicate [susceptibility to LS, LFS, LQTS, or FH].

[Brief description of the disease, its inheritance and relevance to family members, and preventive methods.]

[Recommendations to contact genetics clinic of the university hospital for LS and LFS / laboratory of the healthcare center for LQTS and FH.]

If You have any questions, you can contact the healthcare personnel below.

[Hypothetical contact details for personnel at the university hospital]

Please imagine this situation and write down what You would think and do in this situation.

(Open responses)

We ask you to imagine being in the situation described in the letter until you come to the focus group discussion, and to think about how you would act, after first reactions, to receiving the letter.

Table 2.
Description of diseases at study focus.

Disease; abbreviation	Disease OMIM number	Description	Mode of inheritance	Typical age of onset	Surveillance/Treatment
Familial hypercholesterolemia; FH ¹	143890	Elevated cholesterol leading to coronary artery disease after age 30	Autosomal dominant	Myocardial infarction after age 30 in heterozygotes, childhood in homozygotes	Medication to lower cholesterol (statins) and other preventive measures: cessation of smoking, increased physical activity, reduced intake of saturated fats and increased intake of daily soluble fibre
Long QT syndrome; LQTS ²	192500 613688	Potentially fatal cardiac arrhythmia	Autosomal dominant	before 20, sometimes before 40	Medication, pacemaker
Lynch syndrome; LS ³	120435	Different neoplasia, primarily colorectal (CRC), endometrial (EM)	Autosomal dominant	44–61 years CRC 48–62 years EMC	Colonoscopy every 1–3 years, gynaecological examinations
Li–Fraumeni syndrome; LFS ⁴	151623	Different neoplasia, including breast, sarcomas, adrenocortical cancer	Autosomal dominant	Childhood , early adulthood	(1) Children and adults undergo comprehensive annual physical examination. (2) Women undergo breast cancer monitoring, with annual breast MRI and twice annual clinical breast examination beginning at age 20–25 years.

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