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Genetic health professionals' experiences returning results from diagnostic genomic sequencing to patients

Running title: Experiences returning sequencing results

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ABSTRACT

Despite widespread use of genomic sequencing (GS) in clinical care, there has been little exploration of actual experiences of genetic health professionals (GHPs) using GS in clinical practice worldwide. To address this, semi-structured interviews were conducted with 31 clinical geneticists and genetic counselors across Europe, Australia and Canada to explore their experiences with returning results from GS to patients. GHPs remarked that patients' reactions to receiving causative results varies; some patients are relieved or appreciative at identification of a genetic cause, whilst others express frustration that finding an answer does not lead to a treatment. GHPs discussed the importance of managing expectations in pre-test counseling to minimise disappointment. Although some patients experience mild distress, they generally cope well receiving unsolicited findings and appreciate being informed of their increased risk. While many GHPs felt patients understand what a variant of uncertain significance (VUS) means, a proportion found VUS quite difficult to convey and had concerns for patients' level of understanding. A proportion mentioned concerns regarding potential negative repercussions of non-genetic clinicians misinterpreting the significance of VUS. These results provide important insights into the challenges GHPs can experience returning GS results to patients, highlighting a need for additional training for GHPs and non-genetic clinicians.

Keywords: next generation sequencing; genetic counseling; bioethics; incidental findings; unsolicited findings; variants of uncertain significance

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INTRODUCTION

Genomic sequencing (GS), including exome, genome and condition-specific panels, is now well embedded into clinical care, and its implementation has brought many benefits. Use of GS is increasing the rate of identification of genetic causes of diseases, with 'hit rates' using exome/genome sequencing ranging from 25-57%, depending on the genetic condition being investigated and the selection criteria used (Daoud et al., 2016; Lee et al., 2014; Soden et al., 2014; Stark et al., 2016; Yang et al., 2013; Yang et al., 2014). This increased success rate decreases the time to diagnosis, leading to reductions in unnecessary and potentially invasive tests and improved patient care (Stark et al., 2018). In addition, evidence is increasing for the importance of GS in changing medical management and providing genetic counselling options for patients, particularly for causative results but also when no genetic cause is identified (Matias et al., 2019). Yet it can also create a number of challenges for genetic health professionals (GHPs) across a range of different dimensions compared with previous approaches to testing. These include aspects such as the increased volume of data and number of variants that arise from the analysis, the uncertainty associated with determining the clinical relevance of many of these variants, and the subsequent complexity of the reports issued by laboratories (Biesecker & Green, 2014; Biesecker, Nussbaum, & Rehm, 2018; Vears, Senecal, & Borry, 2019). GS also impacts on workload; an Australian census of 354 genetic counselors and clinical geneticists identified that exome/genome sequencing added an additional 2.75 and 2.25 hours to their workload per patient (Nisselle et al., 2019). Although in some countries GS is in widespread use by large proportion of

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GHPs (Nisselle et al., 2019), in others, use of GS in clinical care may still be relatively new and GHPs may have limited experience integrating GS into their practice. In addition, GS techniques are under constant refinement and GHPs may experience difficulty keeping abreast of the latest technological developments.

GHPs need to provide patients with sufficient information to make informed choices about which results they want to receive, or at least prepare patients for the potential test outcomes (Ayuso, Millán, Mancheno, & Dal-Ré, 2013). To achieve this, GHPs themselves have a responsibility to have a good understanding of the likelihood of particular types of results – such as variants of uncertain significance (VUS) and unsolicited findings (UF) – being identified during analysis and then potentially reported. The fact that that laboratory practices are inconsistent regarding whether VUS or UF are reported may make it challenging for GHPs who use multiple laboratories to keep track of which results will end up on the report (D.F Vears, K. Sénécal, & P. Borry, 2017; D. F. Vears, K. Sénécal, & P. Borry, 2017). Park et al. also identified in interviews with genetic counsellors that the increased uncertainty associated with exome/genome sequencing compared to standard genetic testing also made the pre-test counselling process more challenging (Park, Zayhowski, Newson, & Ormond, 2019).

As GS becomes more widespread, it is important to understand the experiences of GHPs using this technology and the challenges that they are facing in their practice, in order to adapt training programs to best accommodate any new skills that are required. Although there has been some investigation of the experiences of GHPs returning results to patients

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in the research context (Wynn et al., 2018), to our knowledge, there has been no exploration of their experiences integrating these technologies into their practice in the clinical setting. To address this, we sought to interview clinical geneticists and genetic counselors across Europe, Australia and Canada about their experiences counseling patients in response to GS. This follows on from interviews conducted with laboratory personnel conducted across these regions (D.F Vears et al., 2017; D. F. Vears et al., 2017).

METHODS

Participants

Qualitative methods were used to explore the experiences of GHPs requesting GS for patients. GHPs were recruited using a purposive sampling strategy to identify both genetic counselors and clinical geneticists returning results from different types of GS, including targeted large and small gene panels, exome and genome sequencing, to patients, primarily in the diagnostic setting. Sampling aimed to recruit participants with representation across different countries (within Europe) and States/Provinces (within Australia and Canada), yet also enrich for services recognized by peers (i.e. experts in the field) as having considerable experience with offering GS to patients (as identified through our previous research with laboratory specialists). To achieve this, potential participants were identified using three strategies: 1) internet searches to identify genetic services - potential participants were approached via email if the researcher (DV) gauged from their online profile that they were offering GS to patients; 2) snowball sampling – GHPs were asked to suggest other potential participants at the completion of their interview; 3) participants from a previous study of

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laboratory personnel (D. F. Vears et al., 2017) were asked to suggest GHPs that they knew of offering GS to patients.

Procedures

Interviews were semi-structured and conducted either by telephone or in person (at the request of the interviewees) by one member of the research team (DV) between November 2018 and August 2018. These interviews explored a range of different topics, including the types of patients for whom GHPs request GS, which types of GS they request, which results they receive from laboratories, and their experiences returning results to patients.

Data analysis

Interviews were audio-recorded, transcribed verbatim and analysed using inductive content analysis in which content categories were derived from the data, rather than pre-determined (Downe-Wamboldt, 1992; Graneheim & Lundman, 2004; Schamber, 2000).

Transcripts were coded into broad content categories. Sections of the data within the categories were compared and more specific subcategories were developed. All interviews were coded by DV; KS and PB coded a subset to confirm the coding scheme.

This study was approved by the SMEC Review Board (Social and Societal Ethics Committee), KU Leuven and by the Research Ethics Board of the Faculty of Medicine, McGill University.

RESULTS

Participant characteristics

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Thirty interviews were conducted with 31 genetic health professionals (24 clinical geneticists and 7 genetic counselors), which included participants from 30 different institutions in Europe (15), Australia (10), and Canada (5). Participants had a mean of 9.5 years (1– 30 years) experience in their current role and 14.3 years (3.5 – 38 years) experience in the field of genetics. Eight were involved in the analysis and interpretation of genomic sequencing data as part of their role and an additional nine assist with patient review at multidisciplinary team (MDT) or similar meetings with their local laboratory. One participant only requested and returned results from large panels and another used a laboratory that only used genomes. The remaining 29 participants requested varying combinations of exomes and panels (either virtual/bioinformatic or exon capture). For those that used exon capture-based panels, these investigated conditions such as cancers, connective tissue disorders, cardiac conditions and hearing loss, to name a few. Here we report data focussing on the experiences of GHPs returning causative results, negative results, UF, and VUS from GS to patients.

Returning causative results

GHPs often remarked that patients' or parents' reactions to receiving results varied with many giving examples of both positive and negative reactions. Participants explained that often patients are happy, relieved, or appreciative at the identification of a genetic cause for the condition.

It does vary depending on where they are in terms of their journey.

We've tested a lot of families that have been on a diagnostic odyssey

for a long time and they've certainly been very appreciative because

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it's something that they've struggled with for a number of years and they have been through a number of other investigations and a long period of uncertainty and anxiety and stress.

Participant 16, clinical geneticist

Yet other parents express more negative emotions, such as shock that the condition is genetic, devastation at the severity of the prognosis, ambivalence because they are still dealing with their sick child, or frustration that despite having identified the cause, the answer does not lead to a treatment or cure.

Other people have different expectations going into the testing process. In other words, their expectation is that a result will mean that there's a higher likelihood of a treatment or a cure and those kinds of people who have different expectations going into the testing will often be disappointed.

Participant 22, clinical geneticist

Two GHPs described how difficult it can be to tell patients or parents about a finding that confers a more severe prognosis for the child than anticipated.

For me the hardest thing is when the diagnosis is more heavy, so more brutal than it seemed in the first place. For example, if we have somebody with epileptic seizures which are quite OK managed for now but...then it turns out it's Rett Syndrome or something like that and it's not only epilepsy.

Participant 5, clinical geneticist

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Two GHPs specified that they find it challenging that there is often very little information about the diagnosis because the condition is rare and emphasised the importance of connecting patients with support networks.

They are really, really very rare disorders and we just don't have a lot of patients and not a lot of experience ourselves because we just see one patient in our lifetime perhaps. So, getting the proper information to the patients about really rare disorders, I think that is also very important and I think that the fact that there are a lot of Facebook groups of parents and initiatives that are founded by parents or patient groups, those things are, I think, very important and keep getting more important in the future.

Participant 30, clinical geneticist

Returning negative results

GHPs described that patients were often disappointed or distressed at the lack of a causative result being identified, particularly after a long diagnostic odyssey.

I think one of the most challenging things for me is about patients that have been seeking a...genetic diagnosis for a long time...and you do this exome test that covers as much as we possibly can test for and look at and uses all the knowledge that is available today and we still can't find an answer. So, I think the disappointment around that can be really challenging.

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Participant 18, genetic counselor

Four participants stressed the importance of managing expectations in the pre-test counseling session to minimise this disappointment.

We usually give an estimate of what the chance of making a diagnosis is. So, I hope that most people go into the test with realistic expectations... Certainly the ones who have been through our service, I make a point of telling what I think the yield is likely to be. So, I think they're usually pleasantly surprised that we've got a diagnosis, rather than the other way around.

Participant 16, clinical geneticist

Further investigations, such as through research collaborations, or reanalysis down the track might also be mentioned to provide patients with hope for an answer in the future.

I would say that even though we haven't found anything, and I would reinforce that it's because our limit in knowledge. We can only analyse the genes that we know so far. And we can always go back to their genome in the future to reanalyze it when new genes are being discovered, for their primary condition I'm talking about. So, I emphasize that there's hope there.

Participant 16, clinical geneticist

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In contrast, some patients or parents express relief that a genetic cause had not been identified. While one GHP was concerned that this was a marker of a lack of understanding, it may also be because patients then feel they have done everything that they can for now.

They're also happy when you can feed back any results, either positive or negative afterwards. So, I'm sure that patient,...they will be relieved as well, and that they feel that we have done everything that we could do to come to a result, even though it's a negative result and we didn't find anything. But sometimes also a negative result is reassuring.

Participant 29, clinical geneticist

Returning unsolicited findings (UF) or secondary findings (SF)

Four participants gave examples of experiences where they felt that receiving UF or SF had been either challenging or unhelpful for the patient. More commonly, however, GHPs felt that even though some patients or families experience a degree of distress, they generally cope quite well with receiving UF/SF and appreciate receiving information about their increased risk.

How have the families been? Worried but often appreciative of the information which could make a difference for other family members... I don't want to paint a picture of it being all kind of a rosy situation. I mean, I think some of the families are quite worried. Have I had anyone who's gotten angry about it? Or become extremely distressed? No. Has there been some distress, potentially about their own health or the health of their other children? Yes. But the families seem to still

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be, not happy that they pursued it, but content with their decision for that information. And some have been very appreciative.

Participant 20, genetic counselor

They all like it. I never had a negative experience on that, even in cases where I myself was very surprised and very worried about these unsolicited findings, how to communicate them and what kind of effect that could have on the patient. They were much more relaxed than me, in fact, and they really appreciate it every time.

Participant 3, clinical geneticist

Although some GHPs highlighted the importance of good pre-test counseling, as this participant illustrated, sometimes that is not enough to help prepare patients for receiving a UF, flagging the need for good post-test counseling.

When I first started doing this I was like, yep it's all about the pre-test counseling. It's all about preparing people for possible outcomes and sheltering them and making sure that they're ready for anything and so on. But I think because they're living the experience of some really bad conditions, I don't think that they have capacity to think about anything else... Sure, we have to mention it and obviously make people as prepared as possible. I think it's OK to then come back and kind of be there to pick up the pieces in a post-test counseling session.

Participant 14, genetic counselor

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Returning variants of uncertain significance

Almost half of the GHPs specified that patients generally understand what a VUS means when it is conveyed to them as a result from their test. Participants drew on a number of 'markers' of comprehension as evidence of this, such as patients' responses to questions checking their understanding, how patients summarise their results, whether patients come back 1-2 years later to check reclassification of the variant, and a lack of anger at the result.

I think many of the families, and we see quite a diverse population here, but my perception is that most of them do understand (their VUS result). When those situations arise, and they certainly arise frequently, I don't perceive that we get a lot of anger, you know, with families saying 'I didn't know this could happen. Why didn't you prepare me beforehand?' So, I think they do.

Participant 20, genetic counselor

GHPs highlighted the importance of discussing VUS in the pre-test counseling session in order to pre-empt the possibility so, if one is identified, this is not new information for the patient.

I think they have a lot more tools to then receive the information and process it. Because if you go through the consent process and you're presented with what the options are, at least while the test is being done you either consciously or unconsciously process what you would do with each one of the options. So, the next time that you meet is a revisit in which you are discussing, 'OK, remember we told you there

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are three options? This is the option that happened.’ Whereas the ones that don’t get a good pre-testing consent kind of come to that session and say, ‘oh, well I didn’t really expect this to be a possible outcome’.

Participant 26, clinical geneticist

However, eight participants felt that some of their patients do not understand when they receive the result of a VUS, despite this being explained in the pre-test counseling session.

I think in the consent process people just, you know, say ‘yes’ and smile. ‘Yes, we understand that’. But when it actually comes to explaining it with the real variant, a portion of people don’t understand why we can’t clarify it further.

Participant 13, clinical geneticist

Participants also flagged factors that seemed to make it more challenging for patients to understand the significance (or lack thereof) of their VUS, such as the need for segregation studies, being required to undergo surveillance, and the extent of their diagnostic odyssey.

For people who have been searching and where it’s not likely to be disease-causing, I find that they’re the ones that perhaps might really cling onto that result... and perhaps don’t get that nuance of how to interpret that result for them. So, I do wonder if it’s often linked to how much they’re interested in the result. And how invested they are for their family about how much they choose to understand this.

Participant 18, genetic counselor

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Thirteen participants expressed that VUS could be quite difficult to convey to patients for a range of reasons and many gave examples of how they explained VUS. Several GHPs discussed issues targeting the level of information to the patient's needs and one highlighted that conveying the concept of VUS was particularly challenging when using an interpreter. Some GHPs drew on analogies to make the concept of a VUS more accessible to patients. Others provide less elaborate descriptions, focusing more on the fact that they were unsure what the variant meant at this point in time and suggesting other investigations that should be done to try to clarify this further.

I would say 'we haven't been able to say one way or the other. But if it's looking like it's probably likely to be the answer, we'll need to do further testing. So that's when I talk about segregation, if we haven't done that already. Or I would talk about further functional studies if that's an option. Or I would talk about, 'at this point in time we don't know more but contact us in 12 months and we'll get the lab to have another look at it'.

Participant 14, genetic counselor

While there was acknowledgment that communicating VUS to patients was not specific to the context of GS, the increased likelihood and frequency of identifying them is challenging, as is needing to develop sufficient competence to explain them to patients.

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Uncertainty's not new. The VUS, those aren't new. I mean, I remember talking with families 30 years ago about marker chromosomes and uncertainty and unexpected findings... [It's] probably the volume of data...with potentially findings in genes that I have little or no familiarity with and the amount of work it takes to become competent at communicating that kind of information.

Participant 19, genetic counselor

Seven GHPs mentioned how they discuss their own interpretation of the significance of the VUS in relation to the patient's clinical presentation with the patients.

I mean, there are 'variants' and 'variants'. In some cases, I had the feeling that we could work on that and that maybe they could become something significant in time and that's the way I communicate it to the patients. In other cases, I thought, well, these are kind of polymorphic variants, so we simply need to know a little bit more about the occurrence of this variant in the general population, so I did not stress that too much.

Participant 3, clinical geneticist

While some GHPs indicated that they do not necessarily inform their patients about every variant reported by the laboratory if they do not consider them to be clinically significant, many participants felt it was important to discuss all of the reported VUS to some degree. This was for several reasons, including that the VUS may become the causative variant in

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the future, they may want to enlist other family members for segregation studies, patients will receive a copy of the report, and also that the report will be seen by other non-genetics clinicians.

So I would say it's pretty rare that we don't talk about a variant at all, especially since these reports go in the clinical chart and we've had situations where, even though we've explained to the patients about these variants, they go see another physician who is not a geneticist and, even though it says 'variant of unknown significance' it still says 'variant in gene whatever'. And so sometimes they're misinterpreted by other physicians as a cause for their condition.

Participant 25, clinical geneticist

In fact, 14 of our 31 participants mentioned challenges they had either experienced personally or heard from colleagues associated with non-genetics clinicians misinterpreting, or over-interpreting a VUS, and conveying this information to patients, which could have negative repercussions.

I have a lot of experience with...clinicians who request gene panel analysis themselves. And also, they don't refer their patients to our department. But they discuss the results themselves. There's a lot of over-interpretation...and it has certainly led to under-diagnosis, because when you decide you have found a cause then you don't ask for any further tests.

Participant 7, clinical geneticist

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GHPs felt that this predominantly came down to a lack of genetics training in other specialties and many had implemented strategies attempting to prevent this misinterpretation. This included providing clear summaries on reports or patient letters, only giving non-genetic clinicians a copy of the patient letter rather than the full report or giving patients a copy of the report. Some had also implemented training, either formal or informal, or make themselves available to assist non-genetics clinicians with report interpretation. Some noted this added considerably to their workload, particularly when non-genetics clinicians can order their own tests.

It has been a huge burden on the genetic service for the variants of unknown significance. And it has been hard for us to really get through to the administration of the hospital that we need more resources for genetic counselors if we are really giving independence to those services to order the test because when they find VUS, then they expect us as geneticists to come in, become involved to explain them and to help them interpret them.

Participant 26, clinical geneticist

DISCUSSION

One of the most prominent concepts that emerged from the interviews with GHPs was the importance of managing patient expectations regarding the nature and likelihood of different types of results from GS in the pre-test counseling session. This finding aligns with results of a similar study conducted in the research setting (Wynn et al., 2018), and two other studies

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that focused on GHPs experiences with pre-test counselling and obtaining informed consent (Bernhardt et al., 2015; Park et al., 2019). Our participants viewed management of expectations as essential to prepare patients for the likelihood that a genetic cause for their condition would not be identified. This was flagged as particularly important when patients have already experienced a long pathway attempting to identify the genetic cause, often referred to as the 'diagnostic odyssey' (Rosenthal, Biesecker, & Biesecker, 2001). Although, historically, negative results are quite common in genetics, there was a sense that patients have inflated expectations of the chances of gene identification using GS, potentially due to the hype of exome/genome sequencing being framed as the "best technology". While giving patients realistic information about the likelihood of GS identifying the genetic cause is crucial, given the fact that our knowledge is increasing so rapidly in this area it would be important to counsel patients that GS is, in fact, not their "last hope" and that even if they do not identify the genetic cause now, future reanalysis or retesting may find the answer. While genetic counselors have highlighted this as important to cover during the pre-test counseling process (Park et al., 2019), it would also be important to address again when returning results.

Our participants felt that it was also important to prepare patients for the fact that a positive result may not be the answer they were expecting, either regarding the prognosis of their child or the potential for changes in disease management. This finding that obtaining a genetic diagnosis may not provide the relief one might anticipate supports that of a case report from the Undiagnosed Disease Network (UDN) in the US, in which the identification of a genetic cause led to a different outlook for the patient that the parents were not anticipating (Macnamara et al., 2019). Despite this, our GHPs flagged the importance of having a name for

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the condition in order to connect patients/families with other patients or support groups, as highlighted by others (Gilmore, 2018; Gundersen, 2011; Strehle & Middlemiss, 2007). However, the nature of GS which increases our ability to both detect rare disorders and identify new ones leads to situations where there is even less information about the condition to give to families. This reflects another case from the UDN where a diagnosis in a child resulted in feelings of frustration for the parent at the lack of support networks for an ultra-rare condition (Macnamara et al., 2019). Although the lack of actionability of gene identification in rare disease is not necessarily new or specific to GS, the increased rate of previously undetectable variants means this is becoming more commonplace. As such, it is more important than ever that patients with complex clinical pictures are prepared for this as a potential outcome, and that GHPs provide suggestions for how to connect with support, such as broader rare disease networks or forming their own Facebook groups (Macnamara et al., 2019).

Preparing patients to receive UFs was also highlighted as an important component of the pre-test counseling session, although some questioned whether patients could truly comprehend the potential significance of UF at this point in time. Despite this, our GHPs generally felt that patients/families cope quite well with receiving UFs identified during the analysis and that they seem to appreciate receiving information that allows them to take steps to improve their future health. This conflicts with the findings of Wynn and colleagues, where GHPs report that returning SF can provoke anxiety and confusion for patients (Wynn et al., 2018). However, our GHPs viewed situations where analysis identified an unrelated disease-causing UF, but no causative variant, as a 'double blow' and are therefore particularly challenging, for both the

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patient and the clinician returning the result. Interestingly, several GHPs said they experience more difficulties with 'unexpected findings' which identify the cause of the condition in the patient yet confer a worse prognosis than originally anticipated. This scenario is perhaps more common with the introduction of GS where genes that would not previously have been sequenced are now included in the analysis. This suggests that, training should prepare GHPs to counsel patients for this possibility, as well as the focus on returning UF.

VUS was raised as a major challenge by a considerable number of participants. Although many GHPs felt that patients understand the concept of VUS, others found explaining what a VUS is, and the uncertainty associated with the variant, to be one of the most challenging aspects of returning results from GS to patients. Previous research with genetic counselors have also suggested that VUS are a source of uncertainty that they find challenging to discuss with patients in pre-test counselling (Park et al., 2019). Again, although uncertainty is not a new concept in the field of genetic counselling, the scale of the testing is increasing the chance of identifying VUS, making it more important that patients are prepared for this as a potential outcome of the test (Park et al., 2019). While participants described different strategies for explaining VUS, such as various analogies, a proportion found success in focusing on what identification of the variant means for the patient and any next steps for further variant classification (e.g. obtaining samples from other family members or engaging with research laboratories for functional studies). While uncertainty of results is not new to GS, the nature of the test does increase the chance that a VUS will be identified – a reason likely to be behind recommendations that discussion of VUS should be a requirement for obtaining informed consent for GS (Ayuso et al., 2013; Vears, Niemiec, Howard, & Borry, 2018).

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GHPs discussed using their clinical judgment regarding returning VUS to patients. First, while some discuss all reported variants with their patients, others make judgments about which VUS to convey. Second, some explained how they give weightings to VUS when they discuss them with patients, based on their view about the variant's likelihood of being the genetic cause. These examples highlight the importance of the expertise held by these genetically trained specialists for interpreting the relevance of results and conveying this to their patients. This was emphasised by the difficulties relayed relating to working with non-genetics clinicians where misinterpretation of the significance of variants impacted on both their workload and patient care.

Study limitations

While the exploratory nature of our study does not lend itself to generalisability, it provides key insights into the types of challenges being experienced by GHPs when returning GS results to patients. We chose to only sample participants from across Europe, Australia and Canada as a follow on from interviews conducted with laboratory personnel conducted across these regions (D.F Vears et al., 2017; D. F. Vears et al., 2017) which means we cannot comment on the experiences of GHPs practicing in other parts of the world. While we attempted to recruit more genetic counselors, we were restricted by the number of counselors who were able to request GS for patients, particularly in Australia and parts of Europe.

Practice implications

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Our findings stress the importance of pre-test counseling to prepare patients and their families for the full spectrum of possible results from GS. This includes managing expectations around the likelihood of finding a causative result and the potential lack of clinical utility of identifying a causative variant, particularly in patients with very rare disease. VUS were seen by some as particularly difficult to convey in a way that patients understand, which may have implications for activating family members to assist further variant classification. In addition, the challenges these GHPs are facing regarding working with non-genetic clinicians has important implications for mainstreaming (ie, where GS is being offered, requested, and returned to patients by non-genetics specialists) and the likely impact that this will have on GHP workload in the future. This suggests a real need for training of non-genetics clinicians who are likely to be using GS in their practice to enable them to be less reliant on GHPs or to recognise when they need GHP support.

Research recommendations

As these interviews highlighted concerns of GHPs about patients' understandings of VUS and UF, it would be worthwhile exploring the experiences of patients (and parents) who have received GS, with both pre- and post-test counseling, to see if these concerns are warranted.

AUTHOR CONTRIBUTIONS

Danya Vears made a substantial contribution to the conception and design of the work, and the acquisition, analysis, and interpretation of the data for the manuscript. She also wrote the first draft of the manuscript and gave final approval of the version to be published. Karine Sénécal made a substantial contribution to the conception and design of the work, assisted

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with the analysis and interpretation of the data for the manuscript, revised the manuscript critically for important intellectual content, and gave final approval of the version to be published. Pascal Borry made a substantial contribution to the conception and design of the work, revised the manuscript critically for important intellectual content, and gave final approval of the version to be published. Danya Vears, Karine Sénécal and Pascal Borry all give agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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CONFLICT OF INTEREST

Danya F Vears, Karine Sénécal and Pascal Borry have no conflicts of interest to declare.

HUMAN STUDIES AND INFORMED CONSENT

This study was approved by the SMEC Review Board (Social and Societal Ethics Committee), KU Leuven and by the Research Ethics Board of the Faculty of Medicine, McGill University and conforms to recognized standards. All participants gave their informed consent prior to their inclusion in the study.

ANIMAL STUDIES

No non-human animal studies were carried out by the authors for this article.

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