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Personal genomic screening: How best to facilitate preparedness of future clients

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ABSTRACT

Personal genome screening (PGenS) is increasingly being offered as a screen for future health management, and to identify carrier status pertinent to reproductive decision-making. The aim of this study was therefore to explore the experience of individuals who undertook PGenS through the 2014 Sydney "Understand Your Genome (UYG)" event and a 2015 offer of PGenS by Australian biotechnology company Life Letters (LL). Eligible individuals were invited to participate by their clinical geneticist (UYG), or email from Director of LL. Semi-structured telephone interviews with 17 individuals were audio-recorded, transcribed, de-identified and analyzed by two coders using thematic analysis with an inductive approach. Nine participants had genetic/genomics expertise and eight were well-informed health and business professionals. Individual participant PGenS results included: an autosomal dominant condition not previously clinically identified (n = 1); carrier status for recessive condition(s) (n = 8); a number of disease-causing variants associated with an increased susceptibility to an inherited disorder (n = 7); variants of uncertain significance (n = 5); and a few pharmacogenomically-relevant variants (n = 4). The majority of participants described the importance of pre-test genetic counseling, information and/or consent (n = 12). Some barriers to uptake were identified, including scepticism by GPs (n = 6), colleagues (n = 3), and family members (n = 2), as well as privacy concerns (n = 4). Those without genetic/genomics expertise were mostly motivated to have testing by curiosity or interest in personal health (6/8), one seeking a diagnosis for an inherited medical condition and another for future health management. For many with genetic/genomics experience, the motivation was professional interest (8/9) and/or curiosity (5/9), without concern for personal health risk (4/9). On reflection, despite this initial motivation by the latter, the test result had unanticipated personal impact for some of this group, which changed over time (4/5). Several later recognized this, as health problems developed or family history was interrogated more closely. For all participants, disclosure of results to extended family members was limited. Most participants felt personal and family implications and communication (5/17) and/or expectations (3/17) should be addressed at the pre-test session, including more emphasis on residual risk and changes in interpretation with developing phenotypes. Those without genetics/genomics expertise highlighted the need for easy to understand pre-test information and/or an example report to be provided (7/8). These results are consistent with a need to develop more accessible resources, and more personalized counseling approaches to address expectations, dissemination of results, and preparedness for unexpected findings.

1. Introduction

Since the introduction of massively parallel sequencing technologies, there has been an increase in the use of genomic tests in clinical and research settings. Whole exome sequencing (WES) and whole genome sequencing (WGS) have clinical utility in the diagnosis,

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management and treatment of genetic conditions (Biesecker and Biesecker, 2014). In addition, identification of pharmacogenomic variants can inform safe and effective medication regimes (Dunnenberger et al., 2015), (Relling and Evans, 2015); and tumor profiling has led to the identification of treatable targets in cancer (Gagan and Van Allen, 2015), (Johns et al., 2017). Although there have been concerns over patient safety regarding medical errors and limitations of genomic testing (Korngiebel et al., 2016), no associated serious long-term psychological harms from genomic testing have been reported for low risk SNP alleles and common complex condition risk estimates (Bloss et al., 2013). However, PGenS has the potential to identify more severe and more highly penetrant conditions, which could lead to increased risk of anxiety and psychological stress. In addition, challenges remain around the return of results (Knoppers et al., 2015), (Mcguire et al., 2013), (Middleton et al., 2016), (Rahimzadeh et al., 2015) and there are ethical concerns in regard to privacy and confidentiality, inequity of access to genomic testing and the potential for genetic discrimination (Mcclellan et al., 2013). Despite these challenges and concerns, International initiatives to integrate new sequencing technologies into mainstream healthcare are ongoing (Doble et al., 2017), (Haga, 2017), (Kichko et al., 2016).

In addition to the use of WES/WGS in a disease setting, personal genome screening (PGenS) is being offered to healthy individuals in clinical, research and commercial settings (Biesecker and Biesecker, 2014), (Linderman et al., 2016) (Sanderson et al., 2016a), (Vassy et al., 2017), (Genome.One), (Illumina Inc), (Partners Healthcare), (XomeDX) (Invitae). PGenS can provide individuals with personalized risk information for rare monogenic diseases, pharmacogenomic responses, and inform reproductive planning (Kauffman et al., 2017), (Linderman et al., 2016), (Pillar et al., 2015), (Sanderson et al., 2016a), (Vassy et al., 2015). Polygenic risk assessments, although preliminary, are anticipated to become more robust as longitudinal population genotype phenotype databases are developed (Khera et al., 2018). As these are healthy individuals, there is some debate over which results should be returned. Therefore, it is important to explore not only the clinical validity and utility of such testing, but also participant attitudes and perceived personal value of testing. Many studies to date differ in participant demographics, results returned, choice regarding the types of result to be returned, and whether participant opinions were assessed pre- or post-testing. Participant motivations and barriers, expectations, concerns, preferences, information needs, and perceived utility of results have also been explored in a variety of small studies to inform how best to support informed decision-making and consent, given the uncertainty around potential findings (Adams et al., 2016), (Delaney et al., 2016), (Lerner et al., 2017), possible misconceptions, and unrealistic expectations (Facio et al., 2013), (Hylind et al., 2018), (Lupo et al., 2016), (Robinson et al., 2016), (Sanderson et al., 2016a), (Sanderson et al., 2017), (Suckiel et al., 2016). Recommendations for PGenS implementation internationally that have been postulated also include the need for information to aid decision-making (Suckiel et al., 2016) given the lack of genetic/genomic literacy in the general population (Middleton et al., 2016) to better prepare participants undergoing PGenS in the future. In this study, we explored the views, preferences and information needs of those who undertook PGenS in Australasia, which may inform recommendations for implementation of PGenS in this setting. Participants included clinicians and laboratory/bioinformatician experts with experience in genetic and genomic testing, individuals who had previously undertaken genetic/genomic testing, professionals with a governance or commercial interest in the potential integration of genomic technologies into public or private healthcare systems, or well-read individuals with an interest in the topic, or a personal or family history of an inherited condition.

2. Methods

This was an interview-based study with individuals who had undergone PGenS in Sydney, Australia from April 2014 to April 2015. Participants were recruited from two events, both requiring written consent.

(1) An Illumina 'Understand Your Genome' (UYG) event for stakeholders in genomics and healthcare, held in April 2014. In contrast to other international UYG events, participants were required to undergo pre- and post-test genetic counseling with a clinical geneticist (via general practitioner (GP) referral). Participants received their raw data, available on a searchable browser on an iPAD with an interactive MyGenome App or a hard drive, with clinical interpretation of 1600 associated disease genes. Clinically-reported results were significant findings and carrier status in the categories of pathogenic, likely pathogenic and VUS (within 1600 genes). Participants could see all other variants (within and outside the clinical report) as part of the interactive MyGenome App and in their hard drive files if they had the expertise to search these. There was also the option to mask unactionable results. Most participants also attended a two-day education event involving seminars, workshops and Q&A sessions on applications of genomic medicine including pharmacogenomics, cancer diagnosis and testing; analysing and accessing personal genomic data on the MyGenome App; ethical and legal issues surrounding genomic data; and future potential for use, sharing and updating of participant genomic information.
(2) An offer of PGenS through Australian biotechnology company Life Letters (LL) for business professionals was launched in April 2015, with testing also performed by Illumina. Pre- and post-test genetic counseling was provided by a genetic counselor or GP. Participants received their individual raw sequence data from Illumina as above, but with clinical interpretation of 2000 genes.

2.1. Recruitment

Recruitment of participants from the UYG cohort was via email from clinical geneticists (n = 7) after the post-test counseling session, in October 2014, with reminders sent in May 2015 and June 2016 through the administration office at the Garvan Institute of Medical Research, which hosted the UYG event. Recruitment of participants who undertook PGenS through Life Letters was via email from the Director of the company in 2015. Individuals interested in participating provided written consent, prior to participation in a semi-structured telephone interview conducted by JF.

2.2. Data collection

A semi-structured interview schedule was developed by the research team, including questions about motivation to undergo PGenS; genetic counseling and referral experience; reaction to and confidence in results; information needs and preferences; and perceived benefits and disadvantages of the technology. Basic demographic information was also obtained. Interviews were audio recorded, transcribed and de-identified prior to analysis.

2.3. Data analysis

A code list was developed and refined by two coders (JF and KBS) and updated using an iterative approach. Both coders analyzed three transcripts (with inter-coder reliability of > 90% concordance), JF coded the remainder of the transcripts. The data was then analyzed thematically by JF and KBS using an inductive approach (Braun and Clarke, 2006).

3. Results

Seventeen (UYG = 15: Life Letters = 2) of the estimated total of 70

Table 1
Participant demographics.

Age (years)	
• 31-40	2
• 41-50	7
• 51-60	1
• > 60	7
Participants with children/grandchildren	
• Children	15
• Grandchildren	4
Profession	
• Medical Specialist	5
• Clinical researcher	4
• Bioinformatician	1
• Medical educator	3
• Research governance	3
• Administration	3
• Philanthropist	4
• Medical/health entrepreneur	3
• Consumer	1
• Executive/businessperson	2
Work in State/Territory	
• New South Wales	13
• Other: Victoria, Western Australia and New Zealand	4

individuals who undertook PGenS (UYG (n ~ 50); Life Letters offer (n ~ 20)) were interviewed between October 2014 and January 2017 (response rate ~ 28%). Nine participants were considered to have genetics/genomics expertise defined as a role in bioinformatics, clinical genetics, medical specialist/medical education and/or involvement/experience in genetic/genomic testing (genetics professionals). Eight participants were considered not to have expertise in this area, however the majority had tertiary level education in medicine or science or had a commercial interest or governance/administration role in a medical field (non-genetics professionals) (Table 1).

Participants self-reported clinically significant results including: an autosomal dominant condition, for which no personal or family history was known prior to testing (n = 1), autosomal recessive conditions, most known prior to testing (n = 4), carrier status for a number of recessive conditions (n = 8), variants associated with an increased susceptibility for an inherited disorder (e.g. cancer, thrombophilia and Alzheimer disease) (n = 7), pharmacogenomic variants (n = 5), and a number of variants of uncertain significance in genes associated with medically significant conditions (n = 4). One participant reported there were no findings in the report (see Table 2). Most described themselves as healthy, beyond reproductive age (> 40–50 years), "bulletproof", or having attained a certain age without significant health issues (> 60 years). Some participants also perceived that 'knowledge is power' and many opted to receive all results. However, a few masked their results, though two participants reanalyzed their raw data.

Five themes were identified: 1) Rationale for being an early adopter; 2) Barriers to participating in PGenS; 3) Views on pre-test counseling; 4) Opinions on the post-test results session and 5) Information needs and preferences.

3.1. Theme 1: rationale for being an early adopter

The majority of participants were motivated by professional interest (11/17), and/or curiosity (7/17).

"curiosity. …. experience what it would feel like. I wanted to know what it felt like to go through the consent process, to wait for the results and to have the results" (P07, genetics professional)

Most non-genetics professionals were additionally motivated by personal or family health concerns, future health management or to achieve a genetic diagnosis (7/8).

"… it [PGenS] was important for me to know about my health and how I can proactively manage my health through my genome" (P12, non-genetics professional)

A number of participants (n = 7) reported they were keen to contribute to medical research and/or to share their results to increase knowledge, understanding and the ability to interpret genomic data.

3.2. Theme 2: barriers to uptake of PGenS

While UYG participants were supposed to consult a GP for referral to a clinical geneticist for pre- and post-test counseling, a few genetics professionals sought referral from specialists or did not seek a GP referral. Those who were referred by a GP reported neutral or negative experiences including scepticism (7/10) with some GPs referring to PGenS as: "like GATTACA", "opening a can of worms", or "madness". A few also reported scepticism from clinical geneticists/medical specialists (3/17), or lack of interest from family members (3/17), and two participants expressed uncertainty about the clinical utility of PGenS (2/17).

"GP thought it was criminally insane … GP thought it was nuts and no good would come of it" (P15, non-genetics professional)

Many commented on GP lack of awareness and knowledge (10/17), and many did not support the requirement of a GP referral for pre- and post-test genetic counseling suggesting this was paternalistic, unnecessary, or a waste of money, and one participant did not want linkage of having testing to the electronic medical record.

"Most GPs would I think, not really know what to do with it and may be threatened by it. I'm not sure they would be adding to the process and may be taking away from it" (P01, genetics professional)

"It would be great to be in a world where GPs could make a meaningful contribution. I don't think we live in that world yet" (P15, non-genetic professional)

Two participants suggested that GPs needed further training and education in genomics. One GP also queried their role in referral of a healthy individual to a clinical geneticist, as they considered this was not appropriate.

" [GP said] this is not my role, this is clearly a research thing. not really something that is of high need for your health" [P16, non-genetics professional]

However, a few participants did support GP referral for PGenS counseling and testing as they felt it reflected the GP gatekeeper role in the current health system model in Australia - others felt GPs may have knowledge of the family history and rapport with the client (4/17).

Privacy of medical records/databases (4/17) and cost (3/17) were also raised as barriers. One participant voiced concerns about privacy of medical records or other databases.

"I didn't want to go to my GP and ask for a referral . I didn't want it to be part of the medical record … it's my concern about the privacy of this information and what it might mean for my children" (P04, genetics professional)

3.3. Theme 3: views of pre-test genetic counseling

About half found the pre-test counseling session beneficial and reported it was a positive experience (8/17). Although many genetics professionals felt it was unnecessary for them (4/9), they appreciated it would be important for a non-expert.

"It was really perspective and nuance … to emphasize how the information was handled and some of the pitfalls" (P08, genetics professional)

One participant who had counseling through a GP for PGenS through LL, reflected that this was not ideal and a genetics professional

Table 2
Variant characteristics and reactions.

Variant type	Inheritance	Penetrance	Cancer Susc.	N.	Symptoms	Reaction to results	Concerns
Mendelian disorder	AD	High	Yes	1	Minor symptoms (identified. post PGenS).	Surprised. Interesting and unexpected result. Information was considered beneficial, and important.	Some concern for children including ethical challenges: time of testing, when to provide results, and potential for harm.
	AR		No	4	1 (family history)	Interested/useful results. Three had a previous genetic/clinical diagnosis.	Unconcerned about results, unlikely to be life threatening.
	AR carrier		No	8	0	Beneficial/useful for children, for future reproductive planning.	No concern.
Cancer susceptibility	AD	Unknown	Yes	1	0	Beneficial results: potential for early detection and treatment.	Adopted regular screening to reduce personal risk.
		Low risk	Yes	1	0	Uninterested.	Unconcerned for self, supported testing of child.
Multifactorial condition		High	No	1	Family history (identified. Post-PGenS)	Surprised. Researched and sought specialist advice.	Concerned about implications for children. Lifestyle changes to reduce personal risk.
		Unknown	No	2	1	Underwhelmed/unsurprised had previous diagnosis.	No concern. Had already adopted lifestyle changes to reduce personal risk.
				1	0	Intrigued.	No concerns. No lifestyle changes required.
				1	1	Interested/useful results. Initial symptoms recognized post PGenS, impact QOL.	Concerned: Sought specialist advice and may contact researchers in the field.
Variant of uncertain significance	AR	Unknown	No	2	0	Personal interest potentially associated with personal/family history of clinically relevant conditions.	Interrogation of, and meditation on, results. Consideration of genetic/clinical testing to confirm association, management/treatment implications, right of family members not to know. One participant had significant anxiety and concern, but information considered valuable.
	Common polymorphisms	Unknown	No	1	0	Interested. Interrogation of a number of VUS.	No concern after interrogation of VUS as identified to be common polymorphisms.
	Unknown	Unknown	No	3	0	Interested. One participant found the information confusing.	No concerns after further consideration and/or professional advice.
	Susceptibility locus	Unknown	No	1	1	Personal history of associated mild condition. Searched literature.	No concerns.
Pharmacogenomic			No	5	0	Interested/beneficial results.	No concern. Considered information might be useful in the future.

would have been more informative.

The importance of family communication as an important concept for discussion at the pre-test counseling session, and the need to consider the impact for children was highlighted by some (5/17)

"… did you really want to do this? Could you handle it, the results if they weren't perfect . And thinking that it could affect your children"

(P09, non-genetics health professional)

"*I would like to think I would give them the choice …. if I found out a few things from my genome, 'there are some interesting things with consequences for the family would you like me to tell you' – so make it their choice. Bit more difficult for kids" (P16, non-genetics professional)*

A few also highlighted the importance of realistic expectations (3/17), and the possibility of a significant finding (4/17) and suggested this needed to be explored as part of the consent process.

"I would imagine the lay person may have unrealistic expectations that it will pick up everything…. I'll expire in 79 [years] and 3 days and I will develop type II diabetes at 65, and so on and so forth" (P06, genetics professional)

Two participants noted the need to discuss possible ambiguity and uncertainty related to results and the option for reannotation – others suggested that being aware of the difficulties in interpretation of results was important to discuss (6/17).

"a broad sense of why it might be difficult to interpret and there will be a degree of uncertainty, a degree of uncomfortable knowledge, some of which is uncertain but you can't, it's not going to sink into anybody until you get some, until we can tell something specific, ….. and we will find some stuff that will be slightly useful and it will be grey.: (P16 non genetics professional)

Given the limitations of the technology: one participant proposed a two-step consent process: an initial consent to participate in PGenS with an understanding of the limitations and ambiguity of data, followed by a second consent to pursue specific results if this was of interest. Three participants also felt it was important to be given information and options to encourage decision-making and informed choice (for example whether or not to receive unactionable results).

3.4. Theme 4: views on post-test results session

Two genetics professionals noted anxiety immediately prior to receiving the results despite not undergoing PGenS for personal reasons.

"I started thinking I haven't given it a lot of thought … I wonder what is going to come up?. I sort of got nervous. Just a sense of 'Oh I wonder'…"

(P07, genetics professional)

A number of genetics professionals also found that despite expressing their motivation for testing in intellectual terms, they described being surprised by the subjective impact of unexpected results (5/9). Many genetics professionals in this study had privileged access to resources, expert advice and information to help them interpret their results.

"I guess I reacted very strongly to some particular results with a gene that immediately grabbed my attention and I raced away and read as much as I could and talked to a couple [of specialists] I work with"

(P01, genetics professional)

There were a range of responses to disclosure of one or more VUS (see Table 2). On reflection and consideration of the meaning of the results, all were comfortable with the ambiguity and uncertainty associated with VUS and no regret regarding receipt of VUS results was reported. More generally, genetics professionals had conflicting views regarding return of VUS to lay individuals: some suggested VUS may cause anxiety or could be misinterpreted or misunderstood by a lay person, alternatively some thought lay individuals may experience less anxiety and concern based on an inability to analyze the raw data. One participant felt all VUS should be returned as future reclassification may be possible.

Overall, five participants reported their initial reaction to their results was disappointment at underwhelming, boring or uninteresting results, including one participant who received no results and regretted participation in PGenS.

"So there were no results of value and no discussion or anything about them my absolutely crystal clear recollection of it is a big fat zero. It was not as the hoopla up front led me to expect"

(P17, non-genetics professional)

The majority of participants (13/17) were confident about positive results.

"I have a pretty good knowledge of what they did. I have confidence in the positive results" (P08, genetics professional)

Several genetics professionals were less confident about the negative results (3/9), referring to limitations of the technology; the fact that some mutations may be missed; sequencing or alignments may be incomplete; and the potential for some ambiguity in annotation.

On the other hand, about half of all participants found negative results reassuring (8/17) and reported they engendered a feeling of promising future good health.

All participants informed close family (partners, siblings or children), but most did not inform extended family, particularly about carrier status for autosomal recessive conditions.

"I have told my partner and child. I asked my parents if there was any known history of the disease, and they said no … I thought about telling my cousins"

(P15, non-genetics professional)

Some passed on their report to a GP or specialist (6/17), whereas a few informed everyone (3/17).

Many of the genetics health professionals used their technical knowledge and explored the data further (5/9), and two unmasked results, from the raw data that was provided, which they had originally opted not to receive. This was possible as they had the expertise and data to do this.

"I have sat down with a genome reader and looked very carefully at all the different individual reads and looked for strand bias and all the sorts of things you look at …. " (P01, genetics professional)

3.5. Theme 5: information needs and preferences

Many participants commented on the technical nature of the reports, the complexity and the use of scientific jargon (13/17). Many also suggested that less technical information was required at the pre-test counseling session, such as a brief genetics primer, video, assessment tool/decision aid or website information. Standardization of counseling and use of an example report at pre-test counseling was also recommended. Some wanted a more personalized report, which focused not only on clinical outcomes, but also highlighted the reduced risk of other common conditions of relevance to the individual - based on their demographics (i.e. breast cancer risk for women). One participant felt that more of a "black box approach" could be used in the counseling of participants given the diverse range of genetic/genomic literacy in the general population. For example, "I drive a car, and I don't really know what works, as long as the engine works".

About half were concerned that results could cause distress (7/17) and four participants emphasized the need for follow up, to assess psychological impact of results and to provide advice or information,

and a plan for re-analysis. Six participants voiced concerns about dissemination of results and two did not share their results on a research database, as anonymity could not be assured. However, those with a personal or family history of an inherited condition felt this was "a moral obligation" (4/17). At the time of this study, the majority of genetics professional participants felt WGS should only be offered to symptomatic individuals or those with a family history. For two clinicians, this was based on a long-standing conviction, for others it was not clear if this was a prior belief or based on their PGenS experience.

The vast majority of participants believed in the benefits of PGenS if good management, education, access to qualified practitioners and uptake of lifestyle/behavior changes were in place (15/17). A few clinicians also felt experience of PGenS had improved their understanding of the challenges of variant interpretation, the time required to curate results, and how best to advise their patients. However, some believed that technology was ahead of healthcare systems and that it was too early to introduce this technology. There were also concerns about return of results (ROR) given difficulties in variant interpretation, the risks of false negative and false positive results, the potential for psychosocial impact of unexpected or uncertain results and the lack of follow up procedures. Life insurance implications and potential for discrimination and challenges in not overstating the capacity of the technology were also mentioned. Some worried about equity and accessibility, given the high cost of PGenS. Several non-experts felt the results were not personalized enough, requiring more information on what results meant for future health and actionable lifestyle options.

4. Discussion

4.1. Motivations and barriers

Motivations for participating in personal genome screening reported mirror those reported in other studies: curiosity, professional development, to identify personal disease risk, early detection/disease prevention, to adopt a healthy lifestyle, and to contribute to research (Hylind et al., 2018), (Linderman et al., 2016). However, contrary to other cohorts, the main motivation for the majority of genetics professionals in this study was not to identify personal health risk, but for professional development. This may reflect the characteristics of the cohort and their expectations. Participants also identified a number of potential barriers to having PGenS. Many GPs were reported to be sceptical of the technology, and most participants rated GP knowledge poorly. This mirrors the experience of participants undergoing direct-to-consumer testing (Van Der Wouden et al., 2016), and it has been reported that engagement of primary care physicians (PCPs) in PGenS will require further professional training and education in genomics, and access to comprehensive information (Vassy et al., 2015). Other obstacles to uptake of PGenS identified by this cohort included: privacy concerns, cost and genetic discrimination, as reported previously (Lindor et al., 2017),(Mahlmann et al., 2016). Despite these perceived barriers, only one participant in this study had regret regarding PGenS uptake.

4.2. Return of results

Initial and subsequent reactions to return of results were mixed and included "surprise", "disappointment", or "as expected" responses. As the majority of participants were motivated by professional interest, a few were surprised by the emotional impact of unexpected results that had immediate or future personal or family health implications. On reflection, some participants said they did not feel they had "thought this through fully", despite their genomics knowledge and experience. It has been postulated that given these are ostensibly healthy individuals return of a clinically actionable variant is comparable to an incidental finding (Lindor et al., 2017). The majority of participants felt consent was as expected, however, it has been reported that fully informed consent is challenging (Tomlinson et al., 2016). One participant suggested a two-step process, with consent at pre-test and post-test counseling sessions, to enable more informed decision-making at step two when consent to ROR could be based on known findings.

Many participants in this study were initially disappointed or underwhelmed by their results, and the limited number of genes that were interpreted, as previously reported (O'neill et al., 2015). Although the majority of participants were motivated by curiosity and professional interest, rather than personal health risk, most opted to receive all results. A few elected not to receive unactionable results, although two participants later re-analyzed their raw data to retrieve these results. Many recognized the complex nature of uncertain findings, and the potential for PGenS to cause distress in members of the general population. O'Neill reported ~20% of participants in a US study exhibited a negative emotional response to learning their genomic risk for a genetic disease. In contrast, positive effects can enhance decision-making, and understanding of information (O'neill et al., 2015).

4.3. Genetic counseling and information needs

The majority of participants valued the pre-test genetic counseling session, if not for themselves then for those with less genomic knowledge. As individuals have different expectations at different stages of life, a more personalized genetic counseling approach was recommended. For example, more emphasis on conditions relevant to the client's personal or family history, a reference to risk of developing a condition including common conditions relevant to the client that were not identified in the result. Different models (e.g. client-centered or education-focused) and approaches (e.g. message framing, tailoring and anticipatory counseling) have been suggested as a way to increase positive emotions, uptake of recommendations, and communication of results (Khan et al., 2015), (Lindor et al., 2017), (Suckiel et al., 2016). It has also been suggested that an assessment tool to identify those at risk of psychological issues may be valuable (Schmidlen et al., 2014). Although it has been reported that traditional pre- and post-test counseling sessions are unlikely to be sustainable due to workforce and time issues (Suckiel et al., 2016) in this study, pre- and post-test genetic counseling was valued. Many participants highlighted the need to address unrealistic expectations, promote informed-decision making and support individual choice. In some studies where counseling was optional, only ~6% chose to have genetic counseling to discuss ROR (Schmidlen et al., 2014); decliners had no concerns or perceived they understood results. Our results suggest that pre- and post-test genetic counseling is essential, even where the individual perceives that they have high genomics literacy.

In addition to genetic counseling, most non-genetics professionals in this study highlighted the need for more easily accessible, less technical information about PGenS. Genetics professionals also felt the information provided in this study was too complex for a non-expert, but not themselves. Provision of more easily accessible information is also appropriate given low genomic awareness and low genomic literacy reported in the general population (Lanie et al., 2004), (Meisel et al., 2015), (Schmidlen et al., 2014). Currently videos, website information and Apps to support informed decision-making and consent, and patient and PCP friendly reports are being developed and evaluated (Haga, 2017), (Khan et al., 2015), (Sanderson et al., 2016b), (Suckiel et al., 2016), (Vassy et al., 2015). As non-genetics professionals in this study had almost 100% confidence in positive and negative results, clear and accurate information regarding limitations of testing is also essential.

These findings represent the opinions and recommendations of a more highly educated, knowledgeable population, motivated more by curiosity and professional development than an interest in future health or wellbeing. Therefore, it is possible that they do not reflect the opinions of future participants in PGenS. However, concerns such as confidentiality and privacy of personal data, cost, genetic discrimination and lack of knowledge in ostensibly 'healthy' individuals have been

Table 3
Recommendations for pre- and post -test counseling.

Pre-test counseling	Post-test counseling	General
Important to discuss/promote: • family communication • realistic expectations • potential for: significant findings, impact for children, ambiguity and uncertainty of results • insurance implications • consent • informed choice and decision-making Client resources: • less technical information	Return of results: • nuanced variant interpretation • more personalized reports • promotion of beneficial lifestyle behaviors • plan for re-analysis of results – what next? Psychosocial factors: • exploration of psychosocial impact of results • follow up to address potential client concerns post-testing	Education and training • increase primary care physician/GP knowledge • standardize information from qualified health professionals Improve: • community genomic awareness and literacy • equity of access to genomic screening • security of genomic databases Develop legal strategies/guidelines: • to address genetic discrimination and insurance concerns

reported previously (Vassy et al., 2015), (Lindor et al., 2017), (Mahlmann et al., 2016). In addition, the importance of accessible and current information to address the potential for unexpected clinically significant or uncertain results, implications for family, and disappointment due to lack of expected results will likely impact a percentage of individuals undertaking PGenS to assess future health and wellbeing. Nevertheless, we believe the recommendations from this study, as summarized in Table 3, are valid. They are informed by experienced clinicians, who are well-placed to comment on difficulties that might be experienced by patients, those with poor genetic/genomic health literacy, or asymptomatic individuals: as well as experienced stakeholders in the governance/commercial arena, who have contemplated the clinical utility and strategies required to support PGenS within public/private healthcare models in Australia.

4.4. Limitations

This study was not representative of the general population in Australia. There were only a small number of participants, they were highly educated, and the majority were over 40 years with children. Although the number of respondents was small, they appeared to be closely representative of those invited to participate. However non-responders included more non-genetics professionals (~64% medical/genetics professionals, ~80% non-medical professionals). Respondents were also slightly younger than the majority attending the Garvan UYG (mostly 50 + years), however age ranges for the Life Letters screening were not available but likely younger than UYG. Most non-respondents and respondents were from NSW as expected. In addition, some had undergone previous genetic testing (through 23 and me, preconception carrier screening, exome sequencing, whole genome sequencing and individual genetic testing for specific inherited conditions), so for some the findings from PGenS were already known.

5. Conclusion

Motivations for undertaking PGenS varied in this study, and some were not motivated by personal health risk or a desire to keep well. Concerns and barriers included: lack of primary healthcare physician acceptance, knowledge and understanding of the technology; privacy and confidentiality of data on shared databases; genetic discrimination and cost. Consumers valued genetic counseling support and would have appreciated more personalized reporting, with additional follow up and support. Given the limits of genomic literacy in the general population and non-genetics health professional workforce, there was a perceived need for more accurate and accessible educational resources, with some concern regarding the appropriateness of offering PGenS for asymptomatic individuals at this time.

Conflict statement

Bronwyn Terrill held a part-time role with Genome.One, a commercial, wholly-owned subsidiary of the Garvan Institute of Medical Research that offers clinically-accredited genomic testing services. Associate Professor Edwin Kirk and Associate Professor Kristine Barlow-Stewart were honorary advisory board directors for biotechnology company Life Letters.

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