Who should access Germline Genome Sequencing? A mixed methods study of patient views.

Running title: Views on genome sequencing access

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Acknowledgements

The PiGeOn Project is funded by a National Health and Medical Research Council (NHMRC) of Australia Project Grant (ID 1124749). Investigators received the following support: PB, NHMRC Senior Principal Research Fellowship (APP1121630); MCB, Post-Doctoral Research Fellowship from the Cancer Institute

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/cge.13664

of NSW (2017/ECF002); MLB, Cancer Institute NSW Career Development Fellowship (CDF171109); DMT, NHMRC Principal Research Fellowship (APP1104364); No funding body had any input in the design of the study, or collection, analysis, and interpretation of data or in writing the manuscript. The PiGeOn Project consists of the authors listed and Bettina Meiser, Ilona Juraskova, David Goldstein, Katherine Tucker, Timothy Schlub, Richard Vines, Kate Vines, Judy Kirk, and Mary-Anne Young.

Conflict of Interest Statement

No conflict of interest is reported by the authors.

Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ABSTRACT

Implementation of any new medical test, including germline genome sequencing (GS) to inform cancer risk, should take place only when a test is effective, ethically justifiable and acceptable to a population. Little
empirical evidence exists on patient views regarding GS for cancer risk. The aim of this study was to elicit opinions on who should be offered GS and who should pay for it.

Participants with a likely genetic basis for their cancer (n=335) and blood relatives (n=199) were recruited to undergo GS and invited to complete questionnaires at baseline. A subset (n=40) also participated in qualitative interviews about their views regarding access to GS to detect cancer risk.

Our response rate was 92% for questionnaires and 100% for interviews. Participants expressed high enthusiasm overall for access to GS for those with a family history of cancer and anyone who requested testing, but enthusiasm was lower for universal access, if opting out was possible and finances not an issue. Rationales for these

views reflected maximising the sound use of resources. Challenges to introducing community screening via GS to limit cancer burden were raised, including the current limits of science and individual ability to cope with uncertain results.

Participants undergoing GS supported cancer risk testing for those with a family history of cancer but were concerned about the challenges of designing and implementing a population-based GS cancer screening program.

Keywords Genome sequencing, patient views, cancer risk**,** cancer, screening

INTRODUCTION

Cancer is the second leading cause of death globally, responsible for an estimated 9.6 million deaths in 2018.(1) Advances in human germline genome sequencing (GS) and interpretation have been proposed as one way to benefit public health through improving the specificity of population screening for cancer risk, thereby allowing for tailored primary prevention efforts and early detection strategies.(2) Existing (non-genetic) programs offer uniform cancer screening protocols regardless of personal history. While these programs are effective in identifying new cases of cancer, challenges arise from false positive results, over-diagnosis and surveillance-related harms.(3) Stratification of surveillance may create opportunities to achieve high rates of diagnosis and effective early treatment, while advising those identified at average risk to undergo screening less frequently or not at all.(2) While stratified surveillance may reduce overall healthcare costs, in many countries the challenge, in view of finite public funding, is the public policy question of who should be included in the target population.

The cost of GS (including subsequent interpretation and storage of data) remains considerable (6000-1000 AUD per sequence at the time this study commenced, although falling rapidly). Currently, GS is typically offered on a user-pays basis or is provided via a research protocol for individuals who meet relevant clinical inclusion criteria, such as family history, onset of cancer at an early age or multiple primary cancers. GS could be publicly funded through universal offer via a

formal screening program, or via government funding of GS for high risk individuals only.(4) Some jurisdictions in Australia provide limited publicly funded testing for certain well-defined genes in people with a family history,(4) although this does not constitute a comprehensive cancer genetic testing programme. Community-wide GS could address such shortcomings, once existing epidemiological, economic and ethical considerations have been adequately considered.

Publicly funded population screening programs are developed using several criteria and principles, such as an expected medical benefit for those who undergo screening.(5) Similar transparent criteria should be used when determining public resource allocation plans for funding GS. Ethical and social questions about an equitable distribution of healthcare resources will arise in this domain, just as they do for other applications of healthcare. One element necessary for deliberation on GS is accounting for public and patient views on GS for cancer risk. Several authors (6-8) claim that soliciting public involvement is necessary to enable democratization of the resource allocation process in programs such as GS. There will always be representatives of special-interest groups claiming precedence, but, as Foster et al(6) suggest, it may be more helpful to understand which ethical principles (such as equity of access) the public thinks should be applied to inform decision-making.

In order to understand how funding priorities for GS should be set and to explore public views on which populations should have access to GS in the context of limited resources, we conducted a mixed-methods study with a research cohort undergoing germline GS to identify cancer risk.

MATERIALS AND METHODS

Participants

The Genetic Cancer Risk in the Young (RisC) study is recruiting 1,000 individuals with a history of cancer of likely genetic aetiology, and 1,000 first degree blood relatives, to undergo germline GS between 2016 and 2020. Inclusion criteria include: having a histologically confirmed malignancy; aged between 16-40 years at diagnosis, or individual with >1 primary cancer diagnosed <50 years of age

or individual with >2 primary cancers at any age. First degree blood relatives of a proband were also eligible to participate if they were willing and able to comply with all study requirements; and gave written consent to undergo GS.

The Psychosocial Issues in Genomics in Oncology (PiGeOn) Project is a longitudinal, mixed methods psychosocial sub-study of RisC that aims to examine the psychosocial, behavioural and ethical aspects of GS.(9) Participants gave written consent to this sub-study at the same time as giving consent to RisC.

Both RisC and PiGeOn were approved by the St Vincent's Hospital Human Research Ethics Committee (HREC/16/SVH/24).

Data collection

All participants in PiGeOn complete a questionnaire within one month of giving consent, and at 3- and 12-months post-consent. They are informed that results will take at least 15 months to be returned. The baseline questionnaire included questions about access to GS (e.g. for family, those who request it, or the whole community), how age and consent status relate, and questions on knowledge of and attitudes toward GS (see Table 1). A subset of participants from the proband and relative groups were invited to participate in a semi-structured interview at the same time-points. Purposive sampling was used to promote heterogeneity in the interview sample, and recruitment continued until data saturation was reached. Interviews were conducted by trained qualitative researchers (NB and AKS) and explored participants' understanding of GS, and their attitudes towards GS access and return of results (See Table 2 for Interview Schedule). Baseline qualitative interview and quantitative data (prior to receipt of results), relevant to the issue of access to GS, are reported together here.

Analysis

Questionnaire responses were tabulated and summarised using IBM SPSS Statistics Version 25. McNemar's tests were conducted to compare rates of preferences for different groups to have access to GS. Multiple or logistic regression was used to identify demographic and disease predictors of views on access. Demographic and disease variables included in the model were sex, age, education, medical-science

occupation, culturally and linguistically diverse (CALD), Accessibility and Remoteness Index of Australia (ARIA), parental status, cancer diagnosis, time since proband's diagnosis and having a first degree relative diagnosed with cancer. Logistic mixed models and ordinal mixed models were carried out in SPSS, where collinearity checks indicated this was appropriate. Univariate comparisons for each variable were also conducted, for comparison. Mean differences in having the test were compared using t-tests, ANOVA, or chi-squared tests. Differences in age of testing were compared using Mann-Whitney U tests, Kruskal Wallis tests and Spearman's Rank Order correlations.

Interviews were audio recorded and transcribed verbatim. Qualitative data were analysed according to thematic analysis.(10) Using line-by-line coding, a team of multi-disciplinary researchers (from various fields, including medicine, psychology, genetic counselling and bioethics) developed initial codes from the transcripts, which were then grouped to form focused codes which were applied to further transcripts. Using the constant comparative method, new codes were written as required over several meetings and codes were collated into potential themes. Data collection and analysis occurred concurrently as themes were refined and applied to the data. Any differences between researchers' codes were resolved through discussion and negotiated consensus. Rigor was derived from successive discussions and review of the coding process by all researchers until theoretical coding was complete. The varied academic backgrounds of the researchers ensured reflexivity. Comparison of the quantitative and qualitative components of the subject provided triangulation of data.

RESULTS

Quantitative findings

This analysis is of the first 534 respondents in PiGeOn at baseline. A response rate of 92% was achieved for this sample. The combined cohort of probands and relatives (n=534) had a median age of 50 years, with 63.3% female. The characteristics of the sample are shown in Table 3.

Views on access to GS are shown in Table 4. Significantly more probands thought that if available, GS should be offered to: a) their *relatives* (91%) compared to *everyone* (66%) (a difference of 25%: 95% CI: 20% to 31%, χ^2=72.74, $p < 0.001$), and b) to '*anyone who requests it'* (91%) rather than *everyone* (66%), (a difference of 25%: 95% CI: 21% to 31%, χ^2=76.86, $p < 0.001$).

Similarly, among the relatives' cohort, more people thought that GS should be offered to: a) their *relatives* (94%) compared with *everyone* (73%) (a difference of 21%, 95% CI: 15% to 26%), χ^2= 38.03, $p < 0.001$), and b) to *anyone who requests it* (96%) compared with *everyone* (73%), (a difference of 23%: 95% CI: 16% to 28%. χ^2=40.09, $p < 0.001$).

Almost all participants (probands and relatives) thought that GS should be performed with appropriate consent in place, with only 0-2% of participants suggesting that adolescents and adults should have GS without their consent (see Table 4). Slightly more thought that GS in newborn babies and children without parental consent would be appropriate (11-22%). The most popular age for GS was newborn babies and children <16 (40-65% across cohorts and scenarios), followed by adults between the ages of 20-30 (19-33% across cohorts and scenarios).

Three multinomial logistic regression analyses (see Supplementary Tables 1-3) were conducted to examine associations between demographic/disease variables and views on who should have access to GS (*relatives, everyone* and *anyone who asks for it*). The odds of probands thinking that access to GS should be given to: a) *relatives,* were higher among females than males (p = .044) and those living in an urban versus remote/rural area *(*p = .028); and b) *everyone,* were higher among probands with a lower educational background (p = .048) and with less time since their diagnosis (p = .018). No variables were significantly associated with probands' views on whether *anyone who asks for it* should have access. There were no variables significantly associated with relatives' views on all three outcomes.

Three ordinal regression analyses (see Supplementary Tables 1-3) were conducted to examine the relationship between demographic/disease predictors and age at which people believe GS should occur (that is, newborn babies and children <16 years, teenagers 16-19 years, adults between ages 20-30 and adults 30 years and over) for *relatives, everyone* and *anyone who asks for it*. The ordered odds of probands preferring testing at an older rather than younger age in: a) *relatives*, were higher among participants with a medical-science occupation ($p < .001$), with a family member diagnosed with cancer ($p = .029$), and not having a CALD background ($p = .029$); b) *everyone,* were higher among participants with a medical-science occupation ($p < .001$); and c) *anyone who wants it*, were higher among participants with a medical-science occupation ($p =.004$) and with a higher education ($p = .037$). Relatives were significantly more likely to think that testing should be done at an older age in anyone wants it, if they had a cancer diagnosis ($p = .046$), and less time since their probands' diagnosis ($p = .04$). Univariate results for these analyses can be seen in Supplementary Tables 4-6.

Qualitative findings

Twenty participants were interviewed from each group (probands and relatives). At interview, participants were asked who should be prioritised for GS for hereditary cancer risk in the case of limited financial resources. Themes identified in responses were (1) Greatest perceived need; (2) Greatest perceived benefit; (3) Open to everyone; and (4) Reservations.

(1) <u>Greatest perceived need</u>

Many participants felt access to GS should be based on level of need, i.e., prioritising those with the highest risk of cancer or a family history, because they were most likely to have a pathogenic variant.

> *'[you should test] anyone who is at risk of developing an illness … being given an opportunity to find out whether they will be affected, and if so, what steps they can take to avoid it … to overcome that situation, and I guess, warn or better prepare the others that would be affected.' (Female 51 years)*

Some relatives suggested GS prior to childbearing, to inform reproductive decision-making, and to protect future generations.

> *'Probably it could be worthwhile if I'd had this by the time I was 30…I suppose when you're getting married and going to have kids, would be the time wouldn't it?' (Male, 71 years)*

However, some probands with a family history had previously rejected accessing GS due to cost.

> *'I think many people would like to [have GS]…I haven't done any gene testing just because I can't afford it… it was looking like a $10,000 venture, and I just don't have that.' (Female 41 years)*

The proviso was given that, while GS could be offered to those with a family history of cancer, opting out should be possible.

> *'I guess there's not harm in offering – and then people can decide for themselves.' (Female, 53 years).*

Some commented that the markers of a genetic basis for cancer (young age at cancer onset and multiple cancer diagnoses- the eligibility criteria for the RisC study) increased perceived vulnerability and loss of trust in bodily health, increasing the need for GS to address worry about other encroaching illnesses.

> *'Because at that time, dealing with a diagnosis like that when it's completely out of the blue, you can't help but wonder - are there any other issues that you have in your body or part of your DNA that - you know the likelihood or the risk of contracting some kind of different form of cancer or whatever later on in life or even other diseases, …I would like to be informed… I'd like to know if there is anything, I can do to change that, or not.' (Female 39 years).*

Conversely, some suggested those NOT at high risk might potentially benefit more from GS, since they lacked the family history to cue awareness of cancer and the need for preventive behaviours:

> *'I suppose [if] you choose who's more … at risk then they're more likely to come up with something …, but they might already be aware of their health risk and eating well and exercising versus someone who might not have had any idea*

and no family history, who then might come up with something and could then make preventative action if there is something that can be risk that can be mitigated.' (Female 37 years)

A number of relatives felt that cancer patients were the group with the greatest need because GS may lead to discovery of a cancer cure, which demonstrates misunderstanding of the purpose of GS.

2. Greatest perceived benefit

Some participants prioritised access for people who they thought would most likely benefit from GS, using what could be described as a utilitarian calculus; that is greatest benefit for the greatest number. Young people were mentioned as a group most likely to benefit, and most deserving of public healthcare expenditure.

'I think personally that age has a factor in there, you know… that they do have a lot more life ahead of them to live.' (Male 37 years)

Others thought decisions should be based on severity of potential genetic illness, such as whether the condition is life-threatening. The need for results to be clinically actionable (that could inform modifiable prevention behaviours) was also a consideration:

'I'm pausing because I'm really into the greater good, so I would say things that affect healthy people, that can kill them, but we think we can influence.' (Female 43 years)

Underlying these statements was a presumption that prevention is cheaper than treatment.

'I think it's [GS] still cheaper than having the cancer actually occur and then the government has to actually pay for the cost of reacting to it than be proactive. So, my answer would really be, be proactive and put your money there.' (Female 40 years)

3. Open to everyone

GS was seen as sufficiently valuable by some participants that it should be open to everyone – regardless of family history.

> *'Knowledge is important…If people are given the opportunity to actually explore their health, then it should almost be open to anyone, really.' (Male, 47 years)*

Cost was acknowledged to be a problem, and several solutions were suggested for this, including subsidising testing according to income for those who wanted GS or the government subsidising test costs for all citizens, to ensure accessibility to all.

> *'If you could pay for it, you'd pay. [But if you couldn't pay], means test [i.e. government subsidy based on income], I suppose.' (Female 74 years).*

Some participants suggested those with "self-inflicted" disease should not be eligible, such as smoking-related lung cancer.

> *'If someone smokes and they're likely to get cancer, they're the people doing it to themselves, so it's really hard…I don't know, it might not be fair to say one person gets it for free and another doesn't. I'd have to think about that.' (Female, 40 years)*

Others felt a focus on cost was missing the point. For this cohort, with personal experience of living with cancer, the cost was irrelevant if the test was going to make a difference.

> *'When you're faced with it [cancer] you're probably thinking, well, it doesn't really matter how much it's going to cost me, if it's going to help – going to help me live longer or – or my family live longer well… you just pay what you have to pay.' (Female, 64 years)*

4. Reservations about universal GS

Not all participants were in favour of population GS. Several reasons were given for this, including hesitations based on the current limits of scientific knowledge:

> *'[In the past], I thought that was probably a good thing [to have everyone sequenced], but I'm less certain now… the therapeutics for individually tailored*

> *treatment haven't caught up with the ability to individualise people and their disease. .. like all tests, it needs to have a clear indication, and be addressing clear clinical problems for which we have a means to solve. … there's this idea that…. genetic information will be the panacea or be …the lock that they're looking for in the keys available, but it's not that simple…. my feeling is it should be a tool that should be available, it should be [government] funded, when it's indicated, but lots of thought needs to go into how that's rolled out*.' *(Male 35 years)*

Regarding potential public funding of GS, some participants felt GS should be contingent on a person's willingness to act on results, or at least their ability to cope with 'bad news':

> *'… everything's driven by cost and who pays for that, is it the government, is it the person?…, and then, the people's mental wellbeing, you do have to be able to mentally cope with it, and also taking preventative measures, some of the preventative measures are quite severe, like, people lopping off body parts that aren't diseased.' (Female 69 years)*

The idea that not all people would want to know, or would be able to cope with, genetic knowledge, was mentioned several times, further reinforcing that universal access with the opportunity to opt out was preferred.

> *'Whether or not people are mentally stable or strong enough to be able to cope with the outcomes [should be taken into account]. Some people don't need to know…because all it would do is prey on their mind… [But] if people are given the opportunity to explore their health, then it should be open to anyone.' (Male 47 years)*

Finally, some participants suggested that GS, like other tests, should just be available at the specific recommendation of the doctor as guided by expert-generated clinical indications.

> *'Your doctor has to be the point where they will brief you and tell you what's available. …There must be a reason for it [requesting testing] and whether that be family history or whatever, so be it.' (Female, 63 years)*

DISCUSSION

This study of participants with a cancer history of likely genetic origin who had themselves taken up an offer of GS, showed high support for access to low- or no-cost GS for cancer families and those who requested it, although there was less support for universal population GS. The reduced support for universal screening could be explained by themes such as reduced need for and potential benefit of GS for the general population, cost, and the current limitations of the science behind GS. These concerns mirror those reported in other studies, describing significant challenges due to the rapid introduction of GS into routine clinical practice occurring at a time when there is scientific uncertainty about the clinical utility of such testing, with incomplete understanding about the implications of many gene variants, and some cancer risks not well defined. (11-14).

Statistical analysis identified only a few demographic/disease variables associated with probands' views on who should have access to GS (*relatives, everyone* and *anyone who asks for it*) and when, and these associations were not always easy to explain. Perhaps due to the small variability within samples, having a medical/ science background was the only variable consistently associated with these views, with these participants advocating for access at an older age. These individuals may have recognized that little could be done to address risk until a person had reached a certain age, or that results could be a burden with which older people would better cope. Increased female interest in giving relatives access to GS could be associated with the increased fear of cancer recurrence in that group. Further qualitative research is planned to investigate these findings.

Of interest was that the majority of our participants who were in favour of wide access to GS for each subgroup (family, those who request it, and the general population) thought it should be conducted before adulthood, while 11-22% thought this should be conducted on newborns and children <16 years old without requiring parental consent. A small number (1%) even thought that it should be conducted on adolescents aged 16-19 without their consent. In Australia, the age of consent and assent varies according to the context, and this may reflect lay perception that consent is not possible until age 18 years. Cancer screening is complicated by the fact that the number of mutation carriers who will develop

disease (penetrance) is incomplete and onset is often in adulthood, with widespread variation. Claims in support of newborn GS therefore need to show that overall benefits outweigh the harms.(15, 16) Our participants' support for testing in newborns and children may also reflect familiarity with the widely-accepted and routine practice of biochemical newborn screening in Australia, which screens for rare but serious conditions including phenylketonuria, hypothyroidism and cystic fibrosis. Nevertheless, it should be noted that distinctions between biochemical and genetic screening, and aspects such as the economic implications of universal genomic newborn screening as well as current limits to the science, were not discussed. These views should be considered as an initial snapshot of views, which may change with further deliberation. It is likely that the challenge to autonomy, particularly for adult-onset disorders, and the complexity of reporting individual results, would pose significant barriers that need to be addressed prior to implementing population germline GS for cancer risk. (17, 18)

It is not unexpected that a cohort of individuals with a history of cancer which is potentially familial would agree that their family members should be offered publicly funded GS. The qualitative data in this study corresponds with the quantitative results: participants were significantly more likely to agree that GS should be offered to their relatives than to other groups. There is evidence that genetic risk perception, illness perception, and psychological responses to genetic risk information are strongly influenced by personal experience.(19, 20) In the context of inherited cancer, there is some evidence that patients who have received a genetic diagnosis through Clinical Genetic Services have a sense of empowerment and improved family functioning.(21) As a result, our findings could represent participants' desire to ensure that family members have the opportunity to choose among available preventative actions. There is evidence that individuals who are found to have a pathogenic genetic variant, including those for inherited cancer, are more likely to engage in surveillance/prevention behaviour if they have a family history of the inherited disease.(22-25) In considering genomic testing more generally, Juengst and colleagues suggest that such engagement with results is necessary for patient empowerment.(28) Acting on results is necessary for the benefits of GS to be realised. Participants such as those in RisC would be logical cohorts to include if government-sponsored screening were available and if

values such as “greatest need” and “high likelihood of acting on results”, were used to decide access, as suggested by interviewees.

The use of GS for population screening programs was raised by some participants. In the event of limited public funding, in our survey cohort, two thirds expressed approval for free universal GS. Most interviewees’ responses were less enthusiastic about the notion of universal screening. Concerns related to the limits of genetic knowledge and the risks of testing without clear clinical indications, cost, and the theoretical risks of difficulty coping with uncertain results or results showing no actionable variant. Juengst and colleagues(26) point out that while handing responsibility for the patient’s long-term disease outcome over to the patient may be beneficial in terms of reducing healthcare paternalism, it may be problematic if this leads to social and health service institutions reducing interventions that promote health-risk reducing behaviours. Additionally, ongoing challenges such as the lack of ethnic diversity in the genomic record will need to be addressed,(27) and a focus on genomics for patient self-care arguably overlooks the fact that there will be population variations in health literacy, as well as the social determinants of health: not everyone is going to have the personal, familial or social resources necessary to take on this kind of responsibility. These issues also illustrate equity concerns that will be raised if GS is available only to ‘those who request it’, as only those who know enough to ask for testing will receive it. Lack of genomic knowledge among groups such as primary care providers can also create challenges in ensuring that results are accurately interpreted and appropriate actions recommended.(28) Widening of GS access would therefore require careful consideration before implementation. This statement echoes the view of the American College of Medical Genetics and Genomics, which did not recommend GS for general population screening in 2017.(29)

In interviews, participants’ rationales for access to free GS varied. We found that the main foundations considered in this group were greatest perceived need or greatest perceived benefit, both of which are common responses to healthcare rationing questions.(30)

Underlying the greatest need and greatest benefit arguments was the idea that, if wider use of GS was implemented, it should be applied in such a way as to

maximise benefit from expenditure of public funds. This was also the case for those who supported universal access.(31) Andermann and colleagues (32), reviewing the criteria for public health screening in the genetic era, note that all these points should be considered before implementing genetic screening programs, but that essentially the final decision will be a political one, as increasing pressure is applied to contain healthcare budgets. Although genetic programs are likely to improve public health and support biotechnology sectors, the infrastructure required to support such programs, including education, counselling, interventions and follow-up represents a possibly greater expense. They conclude that public opinion and a good evidence base are required to identify target populations.

Limitations to this study include the small amount of information given to participants about the utility and ongoing interpretation of results of GS. Some participants could have made their decision to undergo GS based on the assumption that GS is a test with no limitations. Participants had all decided to have GS, and therefore were likely to be biased towards GS. On the other hand, our findings provide a novel insight into participants' real-life experience of grappling with this decision. This is a population subgroup with knowledge and interest in GS, and further research in more diverse populations is indicated.

Conclusion

The availability of cheaper and faster technology raises questions such as whether GS should be freely available and who should be offered GS. This study has presented the views of a cohort with a likely genetic basis for cancer, a group whose views deserve to be a part of the ongoing debate regarding access to GS. The general principle of value for (public) money was preferred. Introduction of widespread GS in a public health program would require evidence of efficacy in a targeted population, and identification of safeguards to ensure quality assurance and informed choice.(2)

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Table 1: Questionnaire excerpt showing questions relevant to this paper

If whole genome sequencing was available to predict cancer do you think it should be done on:

a) Your first degree relatives (mother,	□ Yes – please indicate at what age
father, brothers or sisters, or children)?	□ No

Age

□ Newborn babies and children (<16 years), ***without*** parental consent

□ Newborn babies and children, requiring parental consent

□ Teenagers aged 16-19, ***without*** their consent

□ Teenagers aged 16-19, only with their consent

□ Adults between ages 20-30 years, ***without*** their consent

□ Adults between ages 20-30 years, only with their consent

□ Adults 30 years and over, ***without*** their consent

□ Adults 30 years and over, only with their consent

(Question replicated for: b) anyone who requests it, and c) everyone)

Table 2: Interview Schedule (Probands*)

1. How did you come to know about the study?
2. Tell us what you know about the blood test you had for the study.
3. Had you heard of germline genomic screening before the study?
4. Why do you think you were offered the opportunity to be in this study?
5. Do you think genomic sequencing should be offered to people like you?
6. How do you think we should decide who gets these tests, if a public healthcare system can't fund them for everyone?
7. What do you think makes genetic information valuable to people?
8. Is there anything else you would like to say about genomic sequencing?
9. Do you have any advice about how this topic should be discussed with other patients?

*****Wording of the interview schedule was amended slightly for first degree blood relatives to ensure it remained appropriate.

Table 3. Demographics

Demographic Variables	Probands (n=335)	Interviews (n=20)	Relatives (n=199)	Interviews (n=20)
Sex (n,%):				
Female	220 (66%)	13 (65%)	118 (59%)	11 (55%)
Age (years):				
Median (IQR)	39 (15)	42 (15)	64 (11)	63(9)
Mean (SD)	41.72 (13.75)	46.10 (12.55)	63.04 (8.43)	62.65 (6.66)
Range	16-83	32-78	31-87	49-74
Education (n,%):				
Primary School	0	0	1 (0.5%)	0
Year 7 or 8	2 (0.6%)	0	9 (5%)	0
Year 9 or 10	23 (7%)	1 (5%)	38 (19%)	3 (15%)
Year 11 or 12	40 (12%)	2 (10%)	17 (9%)	1 (5%)
Vocational Training	53 (16%)	4 (20%)	40 (20%)	2 (10%)
University - did not graduate	29 (9%)	1 (5%)	13 (7%)	1 (5%)
University - graduated	187 (56%)	10 (50%)	79 (40%)	12 (60%)
Unknown	1 (0.3%)	2 (10%)	2 (1%)	1 (5%)
Medical-science occupation (n, %)	27 (8%)	3 (15%)	16 (8%)	1 (5%)
Culturally and Linguistically Diverse (CALD) (n,%)	74 (22%)	3 (15%)	18 (9%)	2 (10%)
Accessibility and Remoteness Index of Australia (ARIA) (n,%):				
Urban	314 (94%)	17 (85%)	168 (84%)	19 (95%)
Biological children (n, %)	175 (52%)	17 (85%)	197 (99%)	20 (100%)
Cancer Diagnosis (n,%)	335 (100%)	20 (100%)	48 (24%)	4 (20%)
Time since Probands' Diagnosis (years)				
Mean (SD)	7.47 (9.39)	12.81 (12.47)	4.51 (5.29)	3.39 (2.55)
Range	0-52.17	0.83-41.83	0.08-35.30	0.83-9.20
Family member diagnosed with cancer (n,%)	164 (49%)	18 (90%)	199 (100%)	20 (100%)

Table 4: Survey results- Who should be tested?						
If whole genome sequencing was available to predict cancer do you think it should be done on _ (n%)*	**Your Relatives**		**Everyone**		**Anyone who Requests it**	
	Probands	**Relatives**	**Probands**	**Relatives**	**Probands**	**Relatives**
Yes	306 (91%)	186 (94%)	220 (66%)	146 (73%)	305 (91%)	190 (96%)
If yes, at what age?	**(n=302)**	**(n=184)**	**(n=219)**	**(n=143)**	**(n=299)**	**(n=187)**
Newborn babies and children (<16 years), without parental consent	32 (11%)	33 (18%)	32 (15%)	32 (22%)	34 (11%)	27 (14%)
Newborn babies and children (< 16 years), requiring parental consent	122 (40%)	79 (43%)	89 (40%)	62 (43%)	87 (29%)	63 (34%)
Teenagers (16-19 years), without their consent	3 (1%)	0	1 (0.5%)	1 (0.7%)	2 (0.7%)	2 (1%)
Teenagers (16-19 years), only with their consent	51 (17%)	20 (11%)	34 (15%)	14 (10%)	60 (20%)	38 (20%)
Adults between ages 20-30 years, without their consent	1 (0.3%)	3 (2%)	2 (0.9%)	3 (2%)	6 (2%)	4 (2%)
Adults between ages 20-30 years, only with their consent	77 (25%)	38 (21%)	51 (23%)	24 (17%)	94 (31%)	42 (22%)
Adults 30 years and over, without their consent	1 (0.3%)	0	0	0	0	1 (0.5%)
Adults 30 years and over, only with their	15 (5%)	11 (6%)	11 (5%)	7 (5%)	16 (5%)	10 (5%)

consent						