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General Practitioner perspectives on genomics in primary care: using polygenic risk scores to evaluate cancer risk

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Abstract

Background: Polygenic Risk Scores (PRSs) enable personalisation of cancer risk, supporting risk stratification for melanoma, and colorectal, breast, and prostate cancers. Inclusion of PRS in cancer risk assessment can facilitate risk-appropriate cancer screening by incorporating individuals' age, sex, family history and genomic test results. General Practitioners (GPs) are the likely healthcare professionals to order PRS tests and deliver results to patients within existing preventative health models. **Aim**: Elucidate GP perspectives on the use of PRS to tailor cancer screening in the Australian primary care context. **Design and setting:** Thirty GPs were interviewed and were either PRS-naïve or had experience using PRSs in a research context. Participants had a broad spectrum of clinical experience and knowledge of genomics, reflecting the spectrum of experience and knowledge of GPs in Victoria, Australia. **Methods:** Inductive and deductive thematic analysis was conducted and aligned to the Consolidated Framework for Implementation Research (CFIR). **Results:** Common themes identified general practice being the appropriate setting for PRS-based approaches; personalised approaches to cancer risk can prompt discussions about positive lifestyle changes; and tailored risk reports are useful tools for the communication of complex health information. Barriers identified by GPs included time constraints on the delivery of preventative health care; education requirements to upskill GPs in genomics; possible psychosocial harms to patients identified as being at increased risk; life insurance implications; and added pressure on an already struggling health system. **Conclusion:** These findings provide insight into the requirements for implementation of PRSs in primary care, from the perspective of GPs.

How this fits in

PRS-based approaches to cancer risk assessment are being explored, in research settings, as a strategy for risk assessment and screening recommendation for commonly diagnosed cancers including melanoma, colorectal, breast and prostate. We explore the perspectives of General Practitioners, the clinicians most likely to deliver this type of testing, who are PRS-naïve or exposed to PRS through clinical trial involvement. Considering these perspectives is essential for understanding how PRS-based testing could be delivered in primary care.

Research summary

This research explores the perspectives of General Practitioners on the use of Polygenic Risk Scores for cancer risk assessment and personalised cancer screening recommendations in primary care.

Introduction

Polygenic risk scores (PRSs) can predict an individual's risk of developing a range of chronic conditions, including some cancers. A PRS applies multiple common single-nucleotide polymorphisms (SNPs) that have been identified through genome-wide association studies. Each SNP confers a small incremental contribution to an individual's overall risk of developing a specific disease. PRSs have been developed for range of diseases including colorectal (1), breast (2) and prostate (3) cancers and melanoma (4). A PRS can be combined with age, sex and other risk factors to estimate individual risk in absolute terms and relative to the general population. This approach can risk-stratify the population to provide risk-based recommendations for screening activities. For those at greater than average risk, increased cancer screening activities (e.g. more frequent screening, commencing from an earlier age, or utilising more sensitive but potentially invasive screening tests) may be recommended. Conversely, those at less than average risk might delay the starting age for screening or screen less frequently. Such risk-stratified approaches may be more cost-effective than current approaches. (5, 6) The possibility of recommending less screening remains contentious, with clinician (7) and public (5, 8-11) sentiment on its acceptability and feasibility being mixed.

The potential clinical utility of PRS approaches to risk stratification has been demonstrated in breast (12), colorectal (13) and prostate cancer (14). Ongoing large, randomised trials will provide evidence of clinical effectiveness and cost-effectiveness. (15, 16) A recent systematic review of stakeholder perspectives on PRS-based approaches to risk assessment highlights the growing evidence-base and shows that much of the published research originates from Australia and the USA. (17) Survey-based studies from Canada (18) and the UK (19)revealed limited knowledge of PCPs and GPs on PRS-based approaches to breast cancer risk stratification. Participants were concerned about recommending reduced cancer screening activities for those at below average risk, whereas increasing screening for those at increased risk was seen a positive application of PRSs. Barriers to implementing PRS use identified by USA-based PCPs included costs of testing, the absence of clinical guidelines, and concern about insurance discrimination. (20) Australian-based research outputs for PRS-based cancer risk assessment include a number of studies exploring general practice patient (21, 22) or Australian population perspectives. (23) However, there is limited evidence on the views of GPs who have been exposed to PRS-based personalised risk information and risk reports for their patients (7).

Australian-based research is facilitated by Australian government support for evidence-based updates to cancer screening programs, and the development of a policy framework for incorporating genomics in cancer control by 2028 is outlined in the Australian Cancer Plan. (24) General practice has been suggested by clinicians as the most appropriate setting for population PRS testing, (25) with more than 80% of Australians seeing a General Practitioner (GP) each year. (26) Indeed, Australians strongly prefer to receive their cancer risk information in general practice settings. (23) Education for GPs on these new tests could build on existing knowledge of genomics from GP-administered prenatal genomic screening and monogenic variant testing for breast and bowel cancer. (27) In this setting, PRSs could be utilised to extend preventative health through risk stratification, facilitating risk-appropriate screening and encouraging risk mitigating behaviour.

In this qualitative study, we explore the perspectives of GPs as the proposed providers of PRS-based risk information and follow-up care.

Methods

GP Recruitment and Consent

GPs were recruited purposively in association with four distinct, sequential research projects (see Table 1). The first study explored GP views on PRS use in primary care in the context of preventative health, including cardiovascular disease and cancer. The remaining three projects were sub-studies of trials providing PRS results to patients of interviewed GPs, with individualised cancer risks and associated screening recommendations. (21, 28) Patient participants in the three trials were encouraged to discuss their report with their GP. The trials utilised a colorectal cancer or a multi-cancer PRS test (for colorectal, melanoma and prostate, or breast cancer). Trials provided PRS reports developed to communicate cancer risk and promote risk-appropriate screening. Reports contained the same core information and format, including risk-appropriate screening recommendations and information about the risks and benefits of the recommended screening test(s). Each study obtained ethical approval from the University of Melbourne Human Research Ethics Committee, and all participants provided written informed consent. Excluding the first study, the potential pool of GPs was limited to those who had participated in a PRS-based trial.

Table 1. Details of studies that GPs participated in

Study name or acronym	Study type and completion year	Number of GP interviews
Implementation of PRS for common disease in Australian general practice	Qualitative study, 2021	Interviews with 10 PRS-naïve GPs
CRISP DNA (21, 22)	Pilot study of acceptability of a PRS test for colorectal cancer, 2022	Interviews with 12 GPs exposed to a PRS intervention
SCRIPT Trial (28)	Trial of PRS to increase risk appropriate screening for colorectal cancer risk assessment and screening recommendations, 2023	Interviews with 6 GPs exposed to a PRS intervention
MAGPIE Study	Trial of cancer PRS including colorectal, melanoma, breast and prostate cancers, 2024	Interviews with 2 GPs exposed to a PRS intervention

Semi-structured Interviews

Semi-structured interviews were conducted between March 2019 and November 2023 in person, via videocall or phone call. Interviews were recorded and transcribed. Interviews had a duration of approximately 30 minutes. Participants who used PRSs within the clinical trials were asked to share their experience in using the report with their patients, including their opinions on report content and presentation. Interview schedules (*see Supplementary Materials*) addressed domains of the Consolidated Framework for Implementation Research (CFIR) to support exploration of the multidimensional nature of implementation barriers and facilitators. (29)

Qualitative Analysis, including reflexivity

Reflexive thematic analysis, with a mixed inductive and deductive approach, was used to analyse the interview data. (30) Interviews were conducted by authors GR, RB, CW, JJML and SS within their capacity as a research assistant, master's student or PhD student. All interviewers had regular supervision to discuss and reflect on the content raised, the context of the interview (within an overarching trial or with naïve GPs), and the approach of the interviewer themselves.

One to two researchers took the lead for inductive coding and initial grouping into broad categories for each of the four interview groups (authors SS, CW, RB, JJML and GR). Initial coding of the interviews was conducted inductively by systematically reading and rereading the transcripts and coding each concept interviewees discussed. Coding within each sub-study occurred while data collection was taking place to facilitate the iterative additions to and refining of the interview schedules Following completion of initial coding for each sub-study, similar codes within each sub-study's interviews were grouped into themes. These themes were categorised deductively into CFIR domains: characteristics of the intervention; characteristics of the individual; inner setting; outer setting; and implementation process. (29) To combine codes and themes across the four sub-studies, one researcher (GR) identified commonalities and differences between the sub-studies and refined themes with a focus on relevance to the research question and the CFIR domains. A subset of interviews (at least 10%) in each of the four groups underwent co-coding to support consistency, with coding discrepancies discussed and resolved through consensus. Researchers involved in coding also discussed how their varied professional backgrounds and experience impacted their coding choices, ensuring reflexivity was addressed in the analysis process. Some themes spanned two domains, with a consensus approach used to decide whether a single domain or two domains was most appropriate. SS and JE were involved in all projects, ensuring consistency and knowledge of the context in which the interviews took place. NVivo software (version 14) was used to organise codes and themes. (31)

Results

Thirty GPs based in Victoria, Australia participated in an interview (Table 2). Ten GPs participated in a study exploring the broad use of genomics in primary care (described as 'PRS naïve GPs' below), 12 in the pilot clinical trial using a PRS test for colorectal cancer screening, six in a Randomised Controlled Trial (RCT) using a PRS test for colorectal cancer screening and two in a pilot trial for a multi-cancer (melanoma, colorectal, breast and prostate cancer) PRS test. Of the 72 consented GPs in these trials, 20 completed a post-

trial interview. Barriers to recruitment included the impact of COVID on GP capacity, GPs having left the clinic where the trial took place.

Table 2. Characteristics of participants (*N* = 30)

Characteristic	*n* (%)
Gender	
Woman or Female	16(52)
Man or Male	14(48)
Years of experience in general practice	
1-9	9(30.00)
10-19	6(20.00)
20-29	5(16.67)
30-39	3(10.00)
40+	5(16.67)
Missing	2(6.67)
Clinic location	
Metropolitan	28(93.33)
Rural	2(6.67)

Themes categorised into CFIR domains are summarised in Table 3.

Primary care is the appropriate setting for PRS (Inner Setting)

Most GPs think that general practice settings are the appropriate location for using PRSs.

> *"If there is genomic testing that is shown to be cost effective that is supported by a wraparound health service, then a GP is actually best placed to coordinate that."*
>
> *(GP01, PRS naïve)*

The incorporation of PRS into cancer prevention and screening was reported to align with the preventative health care already being provided by GPs.

> *"We're seeing people for routine check-ups and you're thinking all the preventative health stuff, I have to check their cholesterol, have we done this, have we done that, that might be the time to raise something like this" (GP11, PRS naïve)*

Many GPs thought that genomic testing, including PRS, is something that will inevitably be integrated into routine care.

> *"I could see it become more part of regular screening for other things [beyond colorectal cancer] as well." (GP27, in PRS trial)*

> *"I think that's probably the way, the future of medicine to be honest." (GP28, in PRS trial)*

Some GPs did note that some people are eligible for a 45–49 year old 'health check', covered by a specific government rebate, as a possible opportunity for integration into existing preventative health structures.

> *"…they say 45 is the time most problems start so they come in for general check-ups…" (GP17, in PRS trial)*

PRS information can prompt discussions about lifestyle changes to reduce cancer risk and improve overall health (Intervention Characteristics)

Some GPs thought this information could be useful in encouraging patients to engage with health promoting lifestyle modifications.

> *"…well you say, okay, you're okay for prostate cancer and bowel cancer, but you still have that smoking situation." (GP30, in PRS trial)*

> *"…you can say well actually, you come out high on the genetic score, so I would suggest you change your diet and I would suggest you stop smoking and we're going to do a colonoscopy on you." (GP15, in PRS trial)*

A minority of GPs were less optimistic about the role of PRS in facilitating positive lifestyle changes to reduce cancer risk.

> *"You would have to frame the risk that it was significant…[O]besity was associated with an increased incidence but we know that. Everybody's been publicising, there are about ten cancers that obesity is a known risk factor, but nothing's changed." (GP16, in PRS trial)*

GPs are already trying to fit a lot into short consultations (Inner Setting and Outer Setting)

The short duration of standard consultations and the rarity of patients presenting purely for preventative health was commonly reported as a barrier to PRS implementation.

> *"I think as a GP you have to be very motivated about [preventative health] in order for the patients to get really excited and motivated as well to actually do it." (GP24, in PRS trial)*

Many GPs reported providing cancer screening advice or updating family history only after they had addressed the primary reason for the patient's presentation.

The prospect of needing to provide counselling for patients undergoing genomic testing within standard duration appointments was concerning for some GPs.

> *"…[this] often takes more…than the allocated 15 minutes, just to see where they're coming at with it, what experiences they've had with a relative or a friend. Things where I'm not necessarily referring them onto the service but trying to work out if there are risk factors to warrant sending them on." (GP29, in PRS trial)*

GPs need evidenced-based education about genomics and how to use PRS with their patients (Intervention Characteristics and Implementation Process)

While most interviewees viewed genomic tests as becoming a component of personalised medicine in the future, they reported requiring additional education to further their understanding of genomics and how PRS-based approaches can be integrated into routine practice.

> *"[A] lot of education and training will be required because you have a huge cohort of GPs who are at different stages of their careers…I work with colleagues here coming towards the tail end of their career and so this didn't even exist in terms of medicine whenever they were coming through." (GP28, in PRS trial)*

Many respondents highlighted the need for governing body endorsed guidelines before any significant practice change could be made, which would reassure GPs about the value of using PRS-based approaches.

> *"I would want to see national guidelines…some synthesised sort of evidence, what the state of play was, how it might be useful in general practice and what resources would be available." (GP07, PRS naïve)*

> *"I'd want to know what the guidelines are about who should have the testing, when and how, etc. … [a]nd then I would use it according to guidelines." (GP23, in PRS trial)*

GPs want clear and accessible referral pathways for those identified as being at increased risk (Implementation Process)

Several respondents voiced concern about how increased cancer screening activities for those identified as being at increased risk, could burden the health system. Those identified as being at increased risk for a type of cancer would require more frequent or more invasive screening (e.g. screening via colonoscopy every five years rather than biennial immunochemical faecal occult blood test [iFOBT]) may add pressure to the health system.

> *"…it would actually bring more burden into healthcare or it would help? I'm not sure." (GP21, in PRS trial)*

> *"So I'd be very wary that it could potentially squeeze things in maybe the tertiary centres, perhaps, but then what happens at the bottleneck?" (GP29, in PRS trial)*

Will genomic testing be introduced in a way that ensures equitable access to preventative health? (Outer Setting and Implementation Process)

While some GPs thought patients may be willing to pay an out-of-pocket fee to receive an individualised PRS, many GPs expressed concern about the cost of testing and the risk that those of lower socioeconomic status missing out and amplifying health disparities.

> *"…on a population level, it's tricky… the people who want to do preventative health activities will do them, and those who don't want to do them, or because of other*

socioeconomic barriers, will still proceed to miss out as a result of it." (GP28, in PRS trial)

Many interviewees highlighted the need for evidence to support the use of PRS in the Australian setting through cost-benefit analysis of PRS-informed risk-stratified screening.

"…you've got to hang in there for the next ten years and see how many of the people get cancer, you know, before you can actually say yes it did in fact save lives. And that's what governments want to know. And, what's more, governments actually want to know if it saves them money." (GP15, in PRS trial)

They stated that the government should fund such a test only if there was sufficient evidence to justify the use of PRSs to inform screening, removing the need for patients to pay out of pocket.

"…it would definitely have a role if it was cost-effective as well and was covered by the government…I think cost is a huge influence in whether a patient decides to opt for that investigation. And the doctors as well, as a result." (GP21, in PRS trial)

PRS results may cause psychological harm for patients stratified into above average risk categories (Intervention Characteristics)

Some GPs expressed concern about PRS results being a source of anxiety for some patients, especially those stratified into higher risk categories.

"…the downside would be that it does cause more patients anxiety when people think they're at higher risk and people's understanding of risk varies" (GP23, in PRS trial)

While some GPs saw pre- and post-test counselling as falling within their scope of practice, others thought that access to genetic counselling services would be an essential part of the implementation process.

"I'm sure there's not all that many genetic counsellors on the ground. So that's going to be the problem is what to do with the results when they come back." (GP30, in PRS trial)

However, some GPs reported that their experience of patients who had an increased risk identified from the PRS did not display significant anxiety, partly due to clear recommendations for risk-appropriate screening activities to manage the risk.

> *"I think that can be contained because if they do have increased risk they will probably be advised to have the colonoscopy… so I think those concerns were probably less than they were, having seen [the report]." (GP14, in PRS trial)*

Importantly, this sentiment endured for GP who were exposed to the multi-cancer PRS trial reports, where patient-participants were informed that they were at above average risk for up to three cancers (melanoma, colorectal and breast or prostate cancer).

> *"I think I was impressed with the lack of anxiety that the slightly increased risk group displayed when they came [to see me] … Like whether the counselling had been quite good, or you know, they were kind of not, they weren't, no one came back paranoid… Which was a bit of a worry with the test, I was worried that would happen. I was worried that I would get some people who it could potentially tip their health anxiety over the edge" (GP29, in PRS trial)*

Will there be insurance implications for those who undergo PRS testing? (Implementation Process)

Concern about insurance implications, especially for people who return greater than average risk results was a common, but no participants reported knowledge of the Australian Memorandum on Genetic Tests in Life Insurance. (32)

> *"I think it's knowing if that person has an increased risk, what an insurance company might do with that in terms of premiums and whether… they should disclose that or not." (GP14, in PRS trial)*

> *"If I was a 20-year-old professional, I would be not doing the test 'til I've got income protection and so forth." (GP29, in PRS trial)*

Communication tools for risk information and recommendations are helpful (Intervention Characteristics)

Eighteen of the 30 participants were exposed to a PRS report for their patients in the context of a research study. See Figures 1 and 2 for an example of the Personalised Risk Report provided to participants (patients and GPs).

> *"[B]ased on my normal conversation with people [about colorectal cancer screening] … if I don't have this kind of visual representation and just based on my, I suppose, verbal education to them, or whatever, maybe there's a less of an uptake. So I think certainly, this is a useful tool to guide their decision making" (GP19, in PRS trial)*

Additionally, the design of the report with reinforcement of screening recommendations by their GP resulted in patients clearly understanding next steps.

> *"…the report, I think, must have been very good and readable, because I think that's why the patients weren't particularly anxious for themselves, and as long as I was endorsing that [same screening recommendation], that's why they were probably quite relaxed." (GP29, in PRS trial)*

The report was a conversation starter and reduced discomfort around subjects such as bowel function and faecal sample collection in the context of colorectal cancer screening.

> *"I think it probably made them more comfortable to talk about it... I think that was definitely an easier approach." (GP27, in PRS trial)*

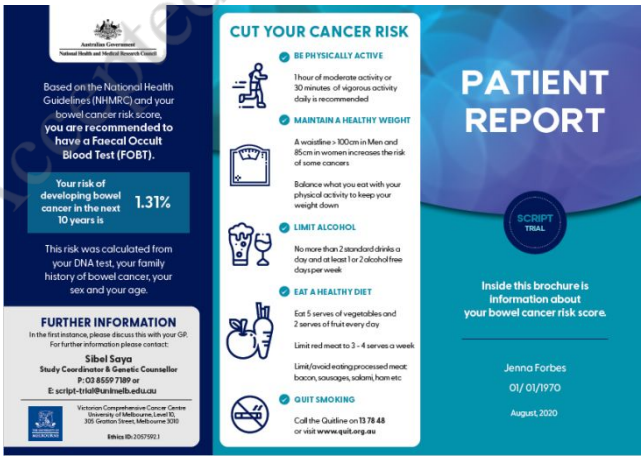

Figure 1. Example PRS report for colorectal cancer risk (28)

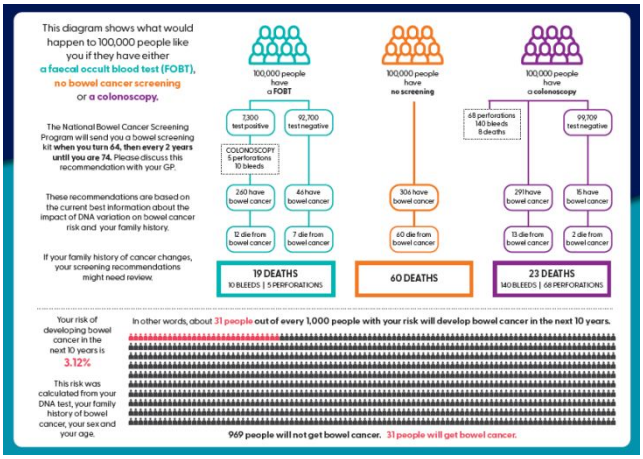

Figure 2. Example PRS report risk communication for personalised colorectal cancer risk (28)

Discussion

Summary

GPs in this study foresaw genomics being integrated into their future practice and general practice as the most appropriate setting for PRS-based approaches. They acknowledged the potential for returning personalised risk information to motivate patients to positively modify their behaviour. GPs also identified several barriers to implementing PRS including the need for education and training, evidence-based guidelines to inform appropriate PRS use and timely access to secondary care for those identified at increased risk of cancer. Availability of psychosocial support for individuals at increased risk was also an important implementation consideration.

Strengths and limitations

Self-selection of interview participants, and GP clinics for participation in the overarching trials, may have introduced a bias towards GPs with an interest in genomics, cancer screening or preventative medicine. GPs' knowledge of PRSs is likely to have evolved over the five years of data collection. Though this study was not designed to explicitly explore this, evaluating GP perspectives over a period of five years in serial studies and demonstrating enduring themes provides useful information for policy makers and those involved in the implementation of risk-stratified cancer screening programs. Participating GPs were primarily delivering care in metropolitan settings, meaning perspectives of GPs

practicing in remote or regional Australia are underrepresented. The small number of rural GPs rendered comparisons of opinions between geographical location not possible.

Most participating GPs also had experience with PRS reports through receiving individualised reports for their patients involved in research, which does not represent the experience of most GPs. However, this allowed for exploration of the impact of exposure to PRS on GPs' perspectives. The commonality in themes expressed by both groups, and the diversity in knowledge of and experience with genomics among Australian GPs, suggests that barriers identified in this study require consideration before the introduction of routine PRS use in general practice.

While this study includes the perspectives of Australian-based GPs, findings are useful in understanding factors that support and impede the implementation of PRS-based approaches in other countries, particularly those with comparable health systems.

Comparison with existing literature

Our findings regarding the use of PRS in colorectal cancer and multi-cancer tests are aligned with related work exploring Australian GP perspectives on PRS use for melanoma, where GPs conveyed the need for practice guidelines to underpin any change to clinical practice and the importance of preventing psychological harms. (33)

GP concerns identified that appropriate referral pathways and health system capacity should be considered with such a practice change. Educational strategies and clinical guidelines may improve GP capacity to provide PRS-guided care and inform how to better manage those with high-risk PRS results including referral to specialty genetics services as required. While concerns were raised regarding possible referral bottlenecks, GPs engage in patient-centred care and use clinical judgement that includes balancing preventative health activities with other patient priorities. A US study demonstrated that primary care providers consider a patient's individual circumstances before deciding to change their clinical management based on genomic results. (34) Genomic information can be used by GPs as an additional tool in the decision-making process rather than replacing clinical decision making.

PRS-based approaches to cancer risk differ from single gene or monogenic approaches that have been the major focus of genetics services, suggesting that preparedness of clinical geneticists, genetic counsellors and others involved in care may be lacking. Evaluation of Australian clinicians' preparedness to expand their practice to include PRS indicated that even those with a comparatively high level of relevant genomics knowledge felt only 'somewhat prepared' (45.7%) or 'not at all prepared' (43.8%). (35) This highlights the importance of whole system strategies to prepare for the use of PRS-based cancer risk assessments and associated risk-informed cancer screening encompassing education for GPs, clinical geneticist, genetic counsellors and others across the health sector. (36) (37)

While numerous participants expressed concern about possible psychological harm arising from genomic testing, several participants reflected that this did not occur for their patients who were identified as being at increased cancer risk within the PRS trial they participated in. The level of concern expressed by GPs was inversely related to level of previous exposure to PRS, particularly when their patients were stratified into above average risk categories. This is concordant with findings from a systematic review of studies providing PRS to individuals, which did not find significant psychological distress in participants after receiving their PRS results. (38) While most individuals who receive genomic-informed risk results will not experience psychological harm, pathways must be developed to ensure that those who do receive appropriate and timely support. The option for a telephone call with a genetic counsellor has been tested in the context of melanoma PRS in Australia, with participants reporting a high level of satisfaction. (39) This may provide a suitable option for individuals requiring support beyond what can be delivered by their GP. Concerns around psychological safety also highlight the importance of how genomic risk is communicated to patients. Providing risk information in multiple formats (e.g. verbal, graphs and icon arrays) facilitates effective content communication for people with varied health literacy (40), an approach being used in colorectal (28) and multi-cancer contexts (41).

There is the potential for PRS-based approaches to provide opportunities to encourage appropriate screening activities, including for those at average risk, and protective lifestyle modifications. Internationally, there is mixed evidence on the behavioural impact of

personalised risk estimates alone, (38, 42, 43) however compelling arguments have been made for trialling of risk assessments have been integrated with proven and behavioural-theory based interventions (38, 44). The value of GP endorsement of cancer screening has been shown, internationally, to increase uptake of breast (45) and colorectal cancer screening. (46) While individuals may not act on this advice, primary care clinicians suggest that recommendations regarding cancer prevention may be more impactful than prevention for other chronic conditions. (25) This may present an opportunity to increase participation in Australian population screening programs, which currently report participation rates as 50% for breast cancer (47) and 41% for colorectal cancer (48). Additionally, PRS-approaches that include age, sex and family history, require up-to-date family history details which can lead to identification of people who should be offered increased screening options, referral to familial cancer services and testing for high-risk monogenic variants regardless of their PRS results. (49)

Insurance implications of genomic testing for risk stratification was also a concern reported by GPs and reflects a broader discourse in Australia about how genomic test results should be used by insurers to limit the value or type of coverage people can obtain. (32) Currently, a moratorium preventing insurance companies from using genomic test details for risk-rating life insurance policies, up to monetary thresholds, exists in Australia. (50) Further announcements regarding a permanent, forthcoming ban on insurers using genetic test results in this manner are expected. (51) This necessitates further work to reassure patients and their treating clinicians that genomic testing will not result in insurance issues and safeguards to ensure insurers comply with their obligations. (52)

Implications for research and practice

There is consistent GP support for their involvement in using PRS to support risk-stratified cancer screening. This spans GPs with little prior exposure to genomic testing to those who have experience through PRS-based cancer risk reports in a clinical research context. Future research is needed to test scalable models of implementation of PRS in general practice. This needs to occur while policy frameworks for risk-stratified cancer screening are

developed. (24) (53) Consideration of how to refine existing screening programs to include evidence-based, cost-effective changes in an already stretched health system is essential.

For multi-cancer PRS approaches, estimates of the number of individuals that will be categorised into higher risk groups across multiple cancer types and developing appropriate referral pathways for those with more complex risk profiles will be important.

This work is directly informing current clinical trials of multi-cancer PRS use in general practice in terms of resources and support provided for participating GPs and strategies for communicating risk to both GPs and patients. Acting on this feedback and adapting the multi-cancer PRS intervention to meet the needs of end users in general practice is an essential step in ensuring its suitability within this environment. (54) A RCT aiming to provide further evidence for the clinical utility and cost-effectiveness of using PRSs to tailor cancer screening in Australian general practice is currently underway. (16)

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Ethics Approval

Table 3. Results summary: themes of GP perspectives on the use of PRS for cancer in general practice categorised by Consolidated Framework for Implementation Framework domain

Intervention Characteristics	Individual Characteristics	Inner Setting	Outer Setting	Implementation Process
• GPs want evidence-based guidelines for using PRS • GPs exposed to PRS in a trial context view content and format as useful in communicating risk to their patients • Risk of PRS results causing distress • PRS may encourage health promoting behaviour change	• Varied understanding and experiences with genetic or genomic testing • Focus on preventative health • GP perception of patients' willingness to make healthy lifestyle changes • GPs need education about PRS before implementation can occur	• General practice as the appropriate setting for PRS use • Relative priority of preventative health activities when patients usually present when unwell • Limitation of appointment duration on providing thorough explanation of PRS	• Risk of referral bottlenecks if many patients classified as being at increased risk • Pressure on GPs to fit increasingly more into 'standard consultations' • Insurance implications • Risk of exacerbating health inequities	• General practice as the appropriate setting for PRS • Evidence-based endorsed guidelines (with clear referral pathways for those at increased risk) are essential • Equitable access to PRS with minimal or no out-of-pocket expense for patients

All studies were conducted in line with the 1964 Declaration of Helsinki and received separate ethical approval by the University of Melbourne Human Research Ethics Committee [PRS in General Practice ID 20721; CRISP DNA ID 1749826; SCRIPT ID:2057592.1; MAGPIE ID: 25128].

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Competing Interests

Author JE is a medical advisor to GeneType (Rhythm Biosciences Ltd., formerly Genetic Technologies Ltd.) who have commercially available PRS products. Genetic Technologies Ltd. provided support through goods and services for the CRISP DNA, SCRIPT and MAGPIE studies, but had no input in interpretation of study findings.

All other authors declare no completing interests.

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