



# Navigating the uncertainty of precision cancer screening: The role of shared decision-making

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## ABSTRACT

**Objective:** Describe how applying a shared decision making (SDM) lens to the implementation of new technologies can improve patient-centeredness.

**Methods:** This paper argues that the emergence of polygenic risk scores (PRS) for cancer screening presents an illustrative opportunity to include SDM when novel technologies enter clinical care.

**Results:** PRS are novel tools that indicate an individual's genetic risk of a given disease relative to the population. PRS are anticipated to help identify individuals most and least likely to benefit from screening. However, PRS have several types of uncertainty, including validity across populations, disparate computational methods, and inclusion of different genomic data across laboratories.

**Conclusion:** Implementing SDM alongside new technologies could prove useful for their ethical and patient-centered utilization. SDM's importance as an approach to decision-making will not diminish, as evidence, uncertainty, and patient values will remain intrinsic to the art and science of clinical care.

**Innovation:** SDM can help providers and patients navigate the considerable uncertainty inherent in implementing new technologies, enabling decision-making based on existing evidence and patient values.

## 1. Introduction

As genetic testing has become more common in recent years, concerns have arisen regarding how patients and their families can reasonably understand the strengths and limitations of the options available to them. Just as technological innovations may require restructuring or reprioritizing resources in healthcare, the proliferation of genomic testing options has outpaced both the clinical genetics workforce capacity and development of clinical guidelines. In addition, DNA-based information is distilled from large amounts of data, and there are several types of uncertainty that must be addressed when contemplating the integration of such data into clinical care [1-3]. This paper argues for the proactive consideration of shared decision making (SDM) as a way to incorporate discussions about novel genomic tests, namely polygenic risk scores, in cancer screening.

## 2. Context of SDM

### 2.1. Shared decisionmaking and cancer screening

Sharing decisions, as opposed to paternalism, has gained significant prominence in health care policy and practice in recent decades [4,5]. Briefly, shared decision making (SDM) may be understood as a process through which clinicians share the best available evidence, patients are supported to achieve informed preferences that are in accordance with their values, and a final decision takes both evidence and preferences into account [6]. Recommendations for SDM attempt to put into practice preference-informed, individually-tailored decisions in liminal circumstances for which clinical utility is not clearly defined. The growth of SDM in policy and practice results from current ethical mores prioritizing

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patient autonomy and from accruing evidence that patient involvement in decision-making has multiple benefits [7].

SDM is commonly endorsed in cancer screening. All screening guidelines aim to balance population-level benefits and harms, but there are often subgroups (e.g., earlier age categories) for which the population-level benefit is unclear. Thus, current guidelines often recommend anchoring the decision to screen on the individual patient’s goals and values [8-14]. The United States Preventive Services Task Force, the American Cancer Society, and other professional organizations’ guidelines for cancer screenings frequently recommend SDM for certain cancers and select patient populations (e.g., prostate cancer screening for individuals with prostates aged 55-69; breast cancer screening for cisgender women in their 40s). When appropriate, clinical empirical risk models are also incorporated into screening discussions, and their inclusion in providing personalized information to patients can help guide how other personalized risks may be discussed in the screening context.

2.2. Integrating SDM can be a patient-centered way to use new technologies

One central reason for engaging in SDM is the uncertainty of benefits and risks for the individual patient. Clinical equipoise is generally invoked when there are multiple options equally supported by a large evidence base; however, SDM is similarly useful for the ethical introduction or utilization of novel interventions, technologies, and screening tools [15]. Consistent with SDM as “perfected informed consent,” [16] SDM can be used when discussing experimental or newly approved tests, procedures, and medications. That is, SDM can be used for situations in which there is a lack of evidence supporting the options, not only when there is a plethora of evidence. Applying an SDM lens to the implementation of uncertain genetic services could prove useful for providers and patients until sufficient evidence has been found to guide more definitive recommendations. Even then, however, the decision whether or not to undergo genomic testing for screening purposes will remain highly preference-sensitive. Moreover, someone who decides against genomic testing may revisit their decision at a later time.

3. The emerging technology of polygenic risk scores: an example of SDM for healthcare innovations

Polygenic risk scores (PRS) are novel tools that assess a patient’s genetic risk of a number of cancers and might therefore help make cancer screening more precise [17]. PRS leverage data from genome-wide association studies (GWAS), which identify common genetic variants (or single-

nucleotide polymorphisms, SNPs) across the entire genome, each associated with a small change in risk for a particular disease [18-21]. A PRS for a given disease sums the weighted effects of these individual variants, and can be used to describe an individual’s genetic risk of the disease relative to the overall population [22]. To be clinically useful, PRS can be presented as risk percentiles, relative risks, and, in some cases, absolute risks [23]. This is in contrast to more traditional monogenic risk testing, which evaluates cancer risk by examining variation in an individual high-risk gene (e.g., BRCA1, HER2). However, genomic factors represent only one of several disease risk factors, and PRS can only capture part of these genomic contributions. They can, however, play an important role in improving existing risk prediction models that use high-risk monogenic variants, family history, and personal history to predict disease risk [23-26].

Although early in their implementation, PRS are predicted to have numerous potential benefits and risks for precision population health [19,27]. Potential benefits include enhancing prediction of disease risk, progression, and recurrence; reducing overdiagnosis; development of precision therapeutics; and improved efficiency of population-level screening [28-33]. Prostate cancer screening is a useful example (Fig. 1). Because the potential benefits of screening for reducing prostate cancer morbidity and mortality do not convincingly outweigh the potential harms of overdiagnosis and overtreatment at the population level [34,35], current guidelines recommend SDM around screening for those between the ages of 55-69 rather than universal screening for all individuals with prostates [9,36]. An active area of research is whether a prostate cancer PRS could help distinguish patients most likely to benefit from screening from those least likely to benefit [37,38]. Similar research is ongoing for screening of breast, lung, and colorectal cancers [39-42]. Cancer screening SDM is already complicated for patients and providers; it stands to become more so in an era of precision screening.

3.1. Types of uncertainty in PRS development

When thinking about how both providers and patients can understand PRS, it is important to note that uncertainty abounds. The most prominent types of uncertainty in this instance relate to stochastic processes (i.e., those related to measurement) [43]. First, multiple PRS have been proposed for a given disease, which vary in statistical methods and number of constituent SNPs, ranging in number from dozens to millions [44,45]. Second, PRS and their computation will change with innovations in the field [46]. Third, a PRS developed in one population might have variable predictive accuracy in other populations, based on between-population differences in genomic substructure and environmental exposures [47]. That is, different

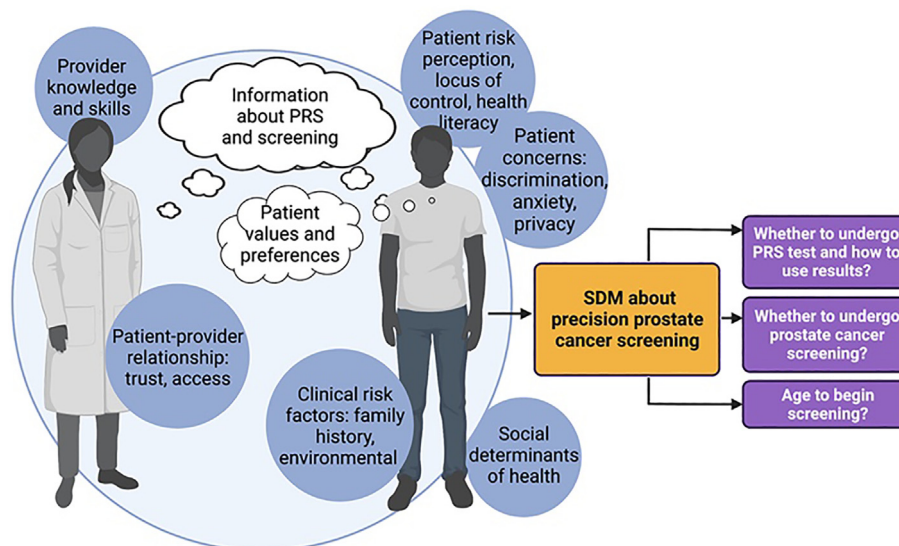


Fig. 1. Shared decision making conversation about precision prostate cancer screening.

laboratories could each develop a PRS for a specific disease but use different SNPs and populations on which to base their risk estimates. A majority of datasets in use today come from those of European ancestry, although initiatives are currently underway to include other genetic ancestries. In addition, a PRS (and therefore an individual's genetic risk estimate) from one laboratory could change as the test evolves. Finally, the cutpoint that determines "high" vs. "low" risk is somewhat arbitrary, and the point-estimates of risk within the "normal" range might feel different to patients (e.g., a 30%ile population risk and a 70%ile risk might both be in the "normal" range).

Use of PRS may require a shift in perspective from prioritizing 'clinical utility,' the overall impact on mortality and morbidity, to 'personal utility,' the whole-person impact including economic, psychological, socio-cultural, lifestyle, and familial sequelae [48]. While the hope is a measurable influence on all of these outcomes, it remains unclear whether PRS will become clinically useful for cost-effective cancer screening given an absence of robust evidence, effects of differential ancestry on score interpretation, economic costs for potential interventions, and uncertain future uses of the gathered genomic data [49]. Some of the challenges to full integration include preserving whole-person approaches to care, maintaining respect for persons and communities, and translating the genomic risk into clinical actionability. In order to measure and address these expansive impacts and other unforeseen effects of genomic testing, a patient-centered approach holds great value. To that end, SDM's prioritization of progressive dialogue towards a fact and value-informed decision provides a useful format for precision cancer screening.

### 3.2. SDM, genetic counselors, and the continued increase in genomic testing

One might ask about the role of genetic counselors, as SDM already is aligned with genetic counseling's historical focus on non-directive care [50-52]. However, the rise in the number and type of genomic tests means that the already-limited genetic counseling workforce will be stretched further. Progress is being made to bolster the coverage of the genetic counseling workforce through genetic counseling assistants, telehealth-delivered genetic counseling, and innovative technologies such as chatbots [53-56]. While these recent modifications take effect, tests are still likely to be ordered, interpreted, and explained by non-genetics-specialized providers. Given that PCPs are highly trusted sources of cancer screening guidance [62], it is likely that PCPs in particular will remain influential and important when discussing PRS and screening. For example, current *BRCA1/2* testing guidelines recommend suitable genetic counseling can be provided by trained PCPs [57]. While genetic counselors, unlike most other providers, receive extensive training in SDM, risk communication, and non-directive methods of decision making, they may struggle in the near future to meet the growing need to provide this care.

## 4. Discussion and conclusion

### 4.1. Discussion

SDM will remain an important component of cancer screening decision making and will likely become even more complicated for both providers and patients as more genomic tests become available in primary care. Successful interventions will likely need to occur at system-wide levels rather than focusing on small-scale changes to clinical practice. Recent work has indicated both patient- and observer-measured increases in SDM when providers receive training in addition to systematic deployment of patient decision aids [58,59].

### 4.2. Innovation

Proactively conceptualizing how SDM can fit into discussions about PRS is both innovative and prudent. As PCPs will need to become facile with content knowledge of PRS and skills around SDM, increasing the ability of PCPs to initiate genomic care through additional training in both could

broaden access to genomic testing while facilitating greater collaboration with geneticists and genetic counselors [60,61]. In addition, explicitly broadening the application of SDM to new technologies and other areas where data is sparse, rather than contexts in which data is voluminous, is an innovation in how SDM is typically discussed and implemented.

### 4.3. Conclusion

Health systems could similarly facilitate the uptake of precision screening through thoughtful and anticipatory provision of supports and training needed for providers, patients, and families. It is not certain what precision cancer screening will look like even 10 years from now, but SDM's importance as an approach to decision-making will serve patients and providers well, as evidence, uncertainty, and patient values will always be intrinsic to the art and science of clinical care.

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