

Patients' and specialist physicians' perspectives on the use of polygenic risk scores in clinical practice: a cross-sectional study

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Abstract

Background: Polygenic risk scores (PRSs), which aggregate the effects of thousands of single-nucleotide variants, can identify individuals at increased genetic risk of common complex diseases. While attracting growing interest for risk-stratified screening and prevention, PRS is not a diagnostic tool, placing responsibility on healthcare providers to interpret results and guide patients in preventive and screening decisions. Although PRS information can support patients, it may also pose a psychological burden.

Methods: In this study, we conducted the first cross-sectional survey of PRS perceptions in the Belgian (Walloon) healthcare context, assessing patients' views in a large cohort (N = 692) alongside specialist physicians' (SPs; N = 52) perspectives on clinical use. The survey evaluated attitudes toward PRS-guided prevention and screening in cancer and noncancer scenarios, as well as perceptions of communication needs and implementation challenges. Descriptive and comparative analyses were used to assess differences between groups and scenarios.

Results: Patients more strongly supported preventive actions in cancer-related scenarios than in noncancer conditions (all FDR-adjusted p-value < 1e-4). In both contexts, they favored earlier and more frequent screening and lifestyle modifications while remaining cautious about preventive pharmacotherapy and prophylactic surgery. Neither patients nor SPs supported reduced screening in the low-PRS groups (all median scores ≤ 50 on a 0-100 scale), and both highlighted concerns about psychological burden and potential discrimination. SPs reported limited time to communicate complex risk information, whereas most patients preferred explanations from a genetics specialist or their attending physician, emphasizing expertise and trust. Individual factors, including age, sex, and family history, further influenced perceptions and willingness to act on PRS-guided interventions.

Conclusions: These findings indicate the need for context-specific implementation strategies and support a model in which a single consultation with a genetics specialist provides a clear interpretation of PRS results, followed by the management of preventive actions by the patient's primary care physician.

Keywords

Polygenic risk scores; genetic risk perception; cross-sectional survey; patient perspectives; clinicians perspectives; preventive medicine; cancer screening; noncancer diseases; clinical implementation.

Background

Genetic research has made significant progress in identifying highly penetrant mutations that explain disease susceptibility in monogenic disorders. However, the risk of developing common complex diseases (CCDs), such as breast cancer or schizophrenia, is not determined by a single gene alone. It is now well established that predisposition to CCDs has a fairly strong genetic component in all human populations and highly polygenic architectures [1]. An individual's genetic risk for CCDs arises from the combined influence of hundreds to thousands of risk variants, most of which contribute only a very small effect to overall disease susceptibility. These per-allele effect sizes are estimated from genome-wide association studies (GWASs) [2], which test genotype–phenotype associations via differences in allele frequencies between affected and unaffected individuals [3].

The genetic predisposition for CCDs is quantified with a polygenic risk score (PRS), calculated as a weighted sum of allele dosages across multiple single nucleotide polymorphisms (SNPs), where weights are estimated effect sizes derived from GWAS summary statistics [4]. PRSs support more targeted prevention strategies and earlier detection of diseases and can outperform traditional risk factors such as family history, providing

greater discriminatory power [5–9]. For example, for women in the UK population, integrated models combining PRS with lifestyle and clinical factors have shown that PRS contributes most to breast cancer risk stratification, followed by mammographic density [10]. PRS also offers a more precise and individualized method of risk stratification that could inform screening recommendations. A large Finnish cohort study of over 450,000 individuals demonstrated that individuals with high PRSs (80–99% and >99%) reached the same cumulative colorectal cancer (CRC) risk as the general population 5 to 11 years earlier [11]. However, the PRS is not a diagnostic tool. It captures only a heritable component of disease risk and excludes nongenetic contributions [6]. Nevertheless, individuals at higher genetic risk can experience greater absolute risk reductions from lifestyle change. For example, in UK Biobank analyses, healthy lifestyle adherence produced similar relative risk reductions across PRS strata, but the absolute benefit was greatest at high PRSs: for type 2 diabetes, maintaining a healthy lifestyle cut the 10-year risk by 12.4% in the top 1% PRS group versus 2.8% in the bottom decile [12].

Despite this progress in demonstrating clinical validity, challenges remain regarding the clinical utility and implementation of PRSs in healthcare, including limited genomic literacy among both patients and healthcare providers (HCPs) [13]. Patients may struggle to interpret PRS results accurately, potentially leading to emotional distress or misconceptions about the genetic nature of the disease. Without appropriate clinician-supported educational guidance, some patients may overestimate the predictive power of the PRS, whereas others may underestimate its clinical relevance [14]. For HCPs, the challenge is to acquire the necessary knowledge to interpret the PRS and communicate results effectively, as the complexity of the PRS often exceeds the scope of traditional medical training [15]. In addition, many HCPs remain cautious because, despite substantial advances in PRS development and growing evidence supporting clinical implementation in selected

conditions, important questions remain regarding equitable implementation across populations and the magnitude of benefit achieved through PRS-informed interventions [16]. This uncertainty may contribute to the relatively low familiarity with PRSs observed in practice; for example, in a UK survey, 49% of general practitioners reported no familiarity with PRSs [17]. Against this backdrop, a growing number of studies have examined attitudes toward PRSs across different countries, which is relevant given that the implementation of PRSs in clinical practice is likely to be country-specific and may vary according to local healthcare systems and societal expectations [18,19].

In this study, we conducted the first cross-sectional assessment of perceptions of PRSs in the Belgian (Wallonia) healthcare context within the ENSEMBLE project, a hospital-based genetic research initiative at the University Hospital of Liège [20]. We aimed to characterize patients' views on the potential clinical use of PRS and to complement these findings with the perspectives of specialist physicians (SPs). Beyond measuring general acceptability, the survey examined how patients and SPs evaluate specific preventive strategies in response to both high and low genetic risk, with differentiation between cancer and noncancer conditions. The questionnaire also explored the benefit–risk balance of the PRS by assessing how patients and SPs weighed potential benefits against possible negative consequences. In addition, we aimed to assess the degree of concordance between patients and SPs regarding how PRS results should be delivered in clinical practice, which may constitute a foundation for the future integration of PRSs into routine clinical care.

Methods

Study settings and data collection

This work was conducted at the University Hospital of Liège (Wallonia, Belgium) within the framework of the ENSEMBLE project, a hospital-based genetic research initiative designed

to calibrate PRSs to the population of the Walloon Region and explore their potential use in healthcare [20]. For clarity, participants who are not healthcare professionals are hereafter referred to as “patients” and healthcare professionals as “specialist physicians” (SPs), emphasizing the distinction between potential PRS recipients and clinicians. A convenience sample was used, with all eligible patients and SPs invited.

Patient recruitment: patients (participants for the ENSEMBLE project) were recruited on a non-targeted basis from several departments via multiple strategies to minimize selection bias. Individuals aged 18 years or older who understood French were invited to participate during routine consultations, emergency department visits, hospital admissions or when attending the sampling center for a blood test. Patients were recruited by members of the Ensemble research team, as well as by physicians and data managers from departments involved in the project. Additional recruitment was conducted through systematic invitations via email and informational leaflets distributed within the University of Liège and the Liège University Hospital. All patients were provided with standardized study information and participant information sheets. Anonymous questionnaires were sent out between January 2024 and September 2025. The questionnaires were administered primarily as an electronic REDCap survey, with the majority of patients completing it online. A paper version was also available when needed, and these responses were subsequently entered into REDCap. By September 2025, a total of 5,393 patients had been enrolled in the ENSEMBLE project, with a participation agreement rate of > 90% among individuals recruited during in-person encounters. Among the enrolled participants, 3,641 completed the core (mandatory) ENSEMBLE questionnaire. In addition, 590 patients completed both the core questionnaire and the additional PRS acceptability questionnaire, whereas 99 patients completed only the PRS acceptability questionnaire.

SPs' recruitment: All specialist physicians at CHU Liège were eligible to participate, with no restrictions based on their clinical role within specialist practice. Invitations were distributed through the internal mailing list of the University Hospital of Liège communication department and were sent to > 1,000 SPs. However, the exact number of SPs who actually received or saw the invitation is unknown because invitations were distributed via channels that did not allow individual-level tracking of delivery or exposure. The invitation included project information as well as direct links to a training module and a REDCap survey. Reminder emails were sent three times (May, June, and November, 2025), each reiterating the invitation to participate. In total, 67 SPs initiated the questionnaire. Of these, 15 were excluded from the analysis because the completion rate was less than 50%. Among the remaining 52 SPs included in the final analysis, the questionnaire completion rate exceeded 95%.

Survey content and domains

All questionnaires were developed by the research team in collaboration with the Department of Public Health at the University of Liège, based on a literature review and existing validated instruments, and were conceptually informed by domains from the Theoretical Framework of Acceptability (TFA) [21]. The full questionnaires are available in the Supplementary Materials.

Patient survey: in addition to collecting basic demographic information (sex, age), the survey included questions on their personal and family history of CCDs (Additional file 2). The instrument probed general health perceptions and prior awareness of the PRS. The questionnaire then explored four main domains of interest: (1) the intention to access PRS results; (2) the acceptability of PRSs on the basis of perceived benefits relative to perceived burdens; (3) the willingness to adopt PRS-guided screening and prevention strategies; (4) practical conditions and preferences related to implementation (Additional file 3). Patients

rated potential clinical actions for high/low PRS, such as starting screening earlier or more often, and indicated a willingness to adopt preventive strategies (lifestyle changes, medications, or surgery) for cancer and noncancer CCDs. In the noncancer CCD scenario, the terms “*earlier screening*” and “*more frequent screening*” referred broadly to earlier or more intensive clinical surveillance and preventive assessment rather than to any specific population-based screening program. Responses were captured on 0–100 visual analog scales (0 = strongly disagree, 100 = strongly agree).

SPs’ survey and the training module: the training module was designed to provide basic knowledge about PRS (Additional file 4). It covers important concepts, including genetic variation, GWAS, SNP effect estimation, PRS calculation and interpretation, and their clinical use and limitations. The SP survey was developed using a conceptual architecture similar to the patient survey to ensure a parallel structure (Additional file 5). SPs were presented with a scenario in which patients are stratified by their PRS distribution into three groups: high genetic risk (top 10% of PRS values), average genetic risk (middle 80%), and low genetic risk (bottom 10%). SPs then rated their agreement with management statements for patients at high/low genetic risk of cancer and noncancer CCDs on a 0–100 visual analog scale. Additionally, the SPs were surveyed about their perceptions of their potential role in the implementation of risk-stratified screening, as well as the practical challenges of implementation, including time constraints, the need for additional training, the risk of inequalities, and difficulties in interpretation. Finally, the survey explored SPs’ preferences for training formats and the types of information they found most necessary to support PRS integration.

Statistical analysis

All questionnaire items rated on 0–100 visual analog scales were treated as continuous variables. The distributions of the scores were summarized using medians and interquartile ranges (IQRs). Categorical items were described as counts and percentages.

For the five patient-reported self-perception items: (i) perceived susceptibility to developing a chronic illness in the future, (ii) attentiveness to one's health, (iii) being a cautious person, (iv) being an anxious person, and (v) self-reported frequency of illness, differences between patients who expressed interest versus no interest in receiving PRS results were assessed using Mann–Whitney U tests. For comparisons adjusted for age and sex, linear regression models were fitted, with 0–100 scores treated as continuous outcomes, age as a continuous variable, and sex as a categorical variable. For psychological and practical implications of PRS disclosure, associations of patient-reported item scores with age and sex were assessed using linear regression models including both variables simultaneously.

Wilcoxon signed-rank tests were used separately for patients and SPs to assess the five paired comparisons of cancer versus noncancer scenarios regarding preventive behaviors, specifically: (i) earlier screening, (ii) more frequent screening, (iii) lifestyle modification, (iv) preventive drug therapy, and (v) preventive surgery. Because these comparisons were predominantly positively correlated, we further controlled the false discovery rate (FDR) via the Benjamini–Hochberg (BH) procedure, separately for patients and SPs. A $p\text{-value} < 0.05$ was considered statistically significant prior to FDR correction. Nominal $p\text{-values}$ are also reported in the text.

For analyses of associations between family history of specific CCDs and patients' ratings of cancer and noncancer preventive interventions, a single BH-based FDR correction was applied across the full set of tests. Similarly, for all other multiple-testing settings, FDR

correction was applied separately within conceptually defined groups of analyses. These groups were specified a priori according to the analytical objective and included psychological impact items, health-related self-perception items, screening- and prevention-related attitudes.

Descriptive summaries and nonparametric tests were based on all respondents with nonmissing data for the item of interest. For analyses that required adjustment for sociodemographic covariates (age and sex), the sample was restricted to participants for whom these covariates were available. Similarly, models that included family history indicators were fitted only for the subset of respondents with nonmissing family history information. Statistical analyses and graphics were performed via R and Python.

Results

Characteristics of the study participants

For patients, a questionnaire was administered at recruitment, resulting in a total of 692 participants overall. Demographic data (sex and age) as well as family history information were available for 590 patients (64% were women), with a mean age of 47 years (SD = 16). Over 95% of the participants self-reported European ancestry (Additional file 1: Table S1). Across the CHU Liège, 52 SPs responded, 58% of whom were women. The largest group had more than 20 years of experience (46%), followed by 10–15 years (17%) and less than 5 years (13%). The SPs represented a wide range of medical specialties (Additional file 1: Table S2).

Patient interest in PRSs and factors associated with acceptability

Among patients, 18% (n = 124) had heard of PRS prior to the survey. Overall, 92% (n = 637) indicated that they would be interested in accessing PRS results if they became available. Only 2% (n = 14) reported that they would not want to receive PRS results, and 6% (n = 41) were unsure at the time of the survey. Interest in receiving PRS results (yes vs no/unsure) did not differ significantly (p-value = 0.38) between patients who were previously aware of PRS and those who were not (Additional file 1: Figure S1).

Among patients who selected "no" regarding their interest in receiving PRS results, the most common reasons provided in the free-text comments were a lack of interest and a desire to avoid anxiety or excessive worry about the disease. In the group of patients who were unsure, 26% (n = 11) reported needing more time to decide, whereas 48% (n = 20) indicated that they would need more information about the PRS. The requests for additional information focused primarily on what PRS results would mean in practice (which diseases are covered and what actions would follow), the predictive value and reliability of the scores, and potential unintended consequences such as overreaction, overtreatment, or false reassurance. A further 26% of unsure patients provided other reasons, most frequently reflecting concerns about the psychological burden if the results were unfavorable, preferences for disclosure and interpretation by appropriately trained professionals, and broader worries about data use or potential misuse.

Patients who wished to receive their genetic risk reported greater perceived susceptibility to developing a chronic illness in the future (for example, diabetes, cancer, inflammatory bowel disease, hypertension) than those who did not wish to receive it or were unsure (median = 69 [IQR 50.0–88.0] versus 50 [IQR 50.0–66.0] on a 0–100 scale; p-value = 0.0016; FDR-adjusted p-value = 0.008; Additional file 1: Figure S2). However, this association lost statistical significance after adjustment for sex and age (p-value = 0.05;

FDR-adjusted p-value = 0.26), whereas increasing age was significantly associated (p-value = 0.003) with lower perceived susceptibility to developing a chronic illness in the future. No significant differences were observed between interest groups for items related to being a cautious/anxious person, attentiveness to health, or self-reported frequency of illness (n = 687; Additional file 1: Figure S3-6).

Patient-reported psychological and practical implications of PRS disclosure

Figure 1 shows patients' scores regarding the potential psychological impact of disclosing their genetic risk and any associated concerns (n = 690). Across all the items, the median scores were above the midpoint of the 0–100 scale (>50), indicating that responses generally leaned towards the higher end of the scale. The least positive responses were observed for the item addressing potential “*discrimination by an employer and/or health insurer*” (left end) versus “*adaptation of working conditions and/or fair insurance access*” (right end): median = 53 [IQR 50.0–84.0]. The highest median score was reported for “*I would not know what to do with the results*” versus “*allow me to be an actor in my health*” (median = 87 [IQR 70.0–100.0]).

For me, knowing the results of PRS will be associated with:

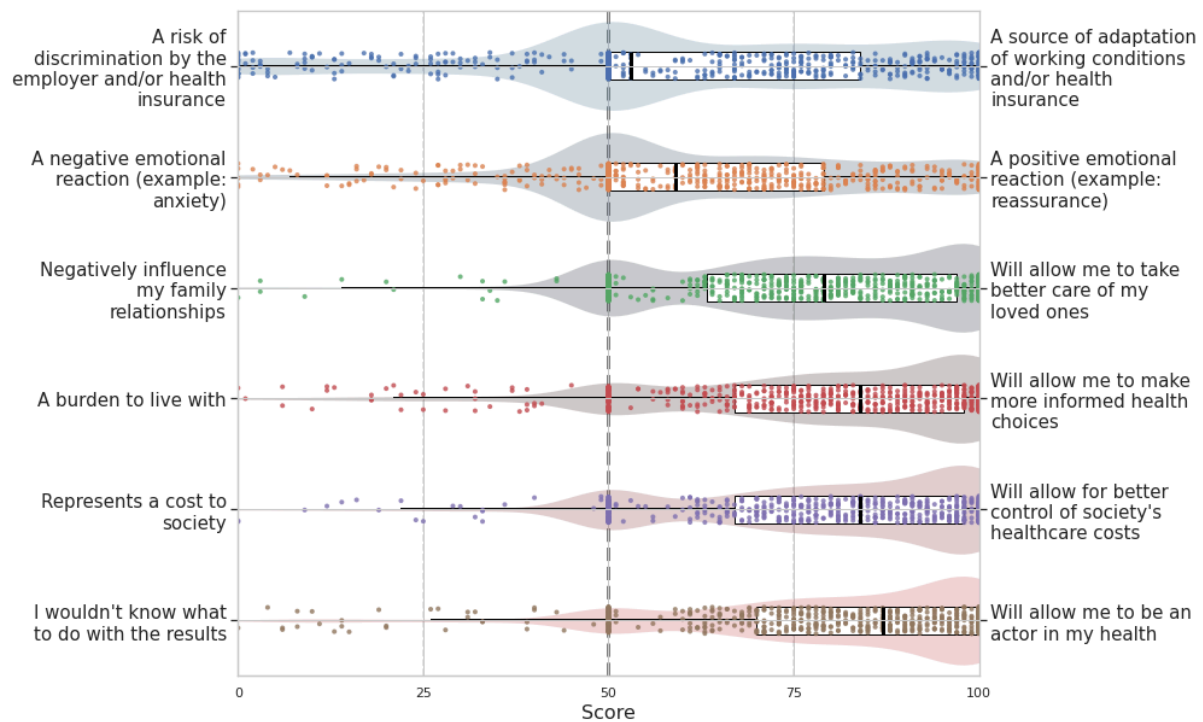


Figure 1. Patient-reported psychological impact and practical implications of PRS disclosure.

Points represent individual responses on a 0–100 scale anchored by paired statements (lower values correspond to the left-hand statement; higher values correspond to the right-hand statement). Half-violins illustrate response distributions, and boxplots indicate medians and interquartile ranges.

Regarding impact of age, we identified a tendency toward more negative expectations with increasing age for three items (Additional file 1: Figure S7): with each additional year at recruitment, the score is shifted by 0.17 (95% CI: -0.286 to -0.052; $n = 590$) toward “*negative emotional reaction*” (p -value = 0.005; FDR-adjusted p -value = 0.017), 0.14 (95% CI: -0.247 to -0.04; $n = 589$) toward “*negatively influencing my family relationships*” (p -value = 0.006; FDR-adjusted p -value = 0.017), and 0.15 (95% CI: -0.265 to -0.038; $n = 590$) toward “*I would not know what to do with the results*” (p -value = 0.009; FDR-adjusted p -value = 0.017). For these last two items, an association with sex was also observed: women tended to respond +4.5 points (95% CI: +1.243 to +7.74; $n = 589$) toward “*allow me to take better care of my loved ones*” (p -value = $6.7\text{e-}03$; FDR-adjusted p -value = 0.02) and +4.9 points (95%

CI: +1.38 to +8.44; $n = 590$) toward “*allow me to be an actor in my health*” (p -value = $6.4e-03$; FDR-adjusted p -value = 0.02) in comparison with men.

Patient willingness to adopt PRS-guided screening and prevention

For items concerning “*earlier screening*” and “*more frequent screening*” in the context of high genetic risk of cancer, patients' scores ($n = 690$) were strongly shifted toward agreement: median = 97 [IQR 82–100] and median = 97 [IQR 81.25–100], respectively (Fig. 2). In contrast, the agreement was less pronounced for “*preventive drug therapy*” (median = 75 [IQR 50–97]) and “*preventive surgery*” (median = 53 [IQR 50–86]).

If my PRS shows that I have an increased risk of developing cancer:

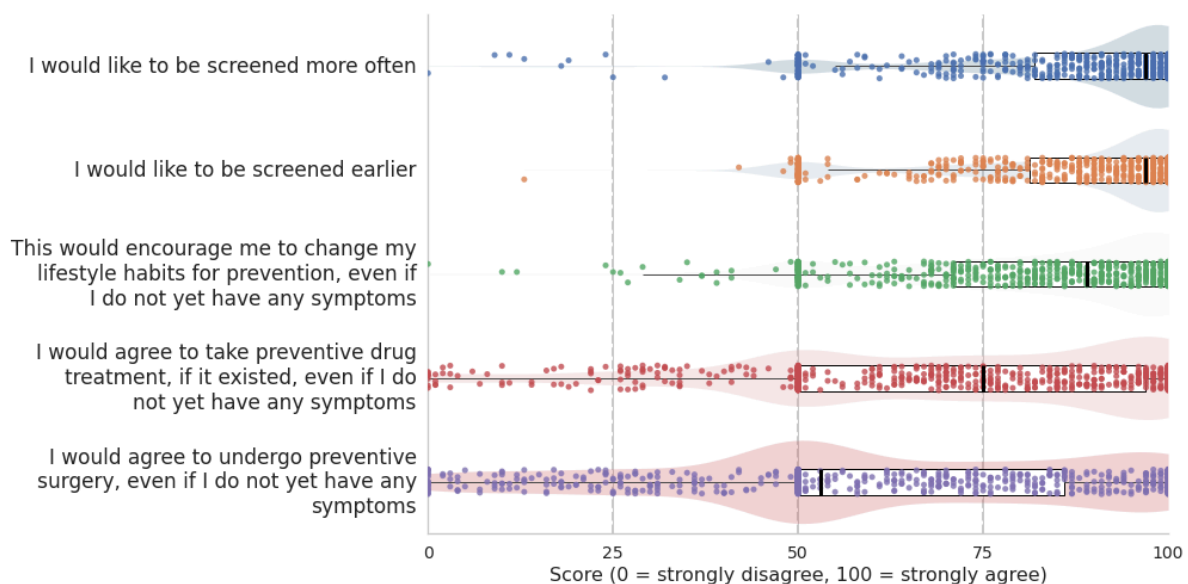


Figure 2. Patient willingness to pursue preventive actions given a high polygenic risk of cancer.

Each point represents one participant's 0–100 agreement score (0 = strongly disagree, 100 = strongly agree). Half-violins illustrate response distributions, and boxplots indicate medians and interquartile ranges.

Age dependence was observed for “*earlier and more frequent screening*” items in the context of high genetic risk of cancer (Additional file 1: Figure S8). With each additional year of age at recruitment, scores shifted toward disagreement by 0.19 points (95% CI: -0.28

to -0.09; $n = 590$) for “*earlier screening*” ($p\text{-value} = 9.8\text{e-}05$; FDR-adjusted $p\text{-value} = 2.4\text{e-}04$) and by 0.21 points (95% CI: -0.3 to -0.12; $n = 589$) for “*more frequent screening*” ($p\text{-value} = 2.8\text{e-}06$; FDR-adjusted $p\text{-value} = 1.4\text{e-}05$).

For high genetic risk of noncancer CCDs, patients presented a broadly similar response profile to that of the cancer context; however, there was systematically and statistically significantly lower agreement overall (Fig. 3). For “*earlier screening*”, the median was 93 [IQR 71–100] (paired Wilcoxon signed-rank $p\text{-value} = 2.0\text{e-}12$; FDR-adjusted $p\text{-value} = 5\text{e-}12$), and for “*more frequent screening*”, the median was 94 [IQR 73–100] ($p\text{-value} = 1.3\text{e-}09$; FDR-adjusted $p\text{-value} = 2.2\text{e-}09$). For “*preventive drug therapy*”, patients showed a median score of 70 [IQR 50–93] ($p\text{-value} = 2.1\text{e-}09$; FDR-adjusted $p\text{-value} = 2.6\text{e-}09$), while for “*preventive surgery*” the median = 50 [IQR 36–74] ($p\text{-value} = 2.2\text{e-}24$; FDR-adjusted $p\text{-value} = 1.1\text{e-}23$).

If my PRS shows that I have an increased risk of developing non-cancer diseases:

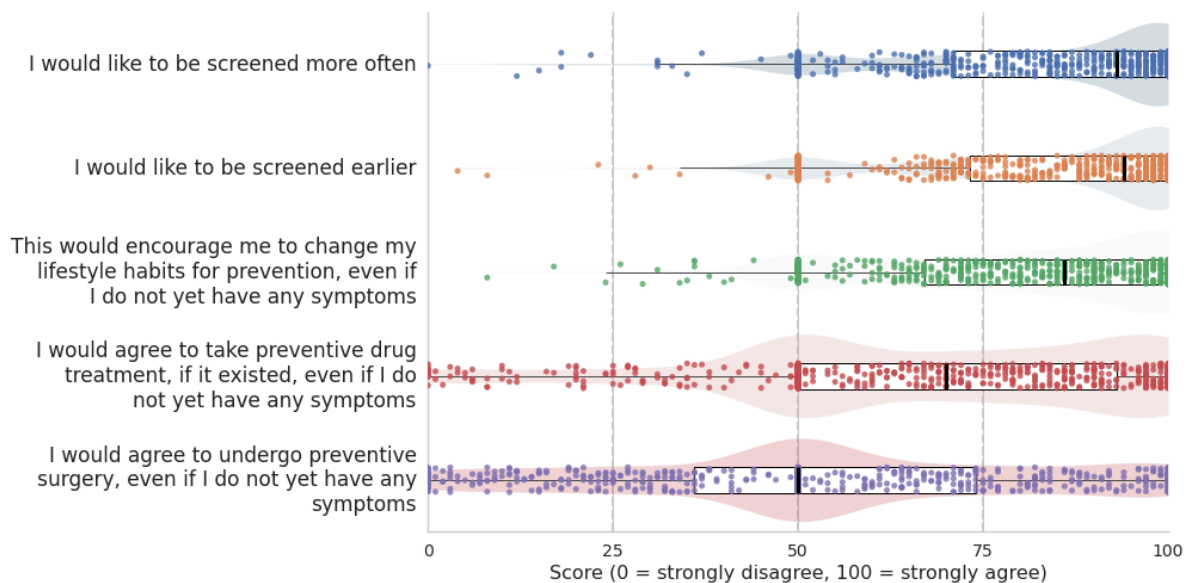


Figure 3. Patient willingness to pursue preventive actions given a high polygenic risk of common noncancer diseases. Each point represents one participant’s 0–100 agreement score (0 = strongly disagree, 100 = strongly agree). Half-violins illustrate response distributions, and boxplots indicate medians and interquartile ranges.

As in the cancer context, an age-related trend was observed (Additional file 1: Figure S9): for each additional year at recruitment, scores shifted by 0.13 points (95% CI: -0.23 to -0.03; $n = 589$) toward disagreement with “*earlier screening*” (p -value = 0.012; FDR-adjusted p -value = 0.03) and by 0.21 points (95% CI: -0.31 to -0.12; $n = 590$) toward disagreement with “*more frequent screening*” (p -value = 6.6×10^{-6} ; FDR-adjusted p -value = 3.3×10^{-5}) in the high-risk noncancer CCDs scenario.

For items concerning low genetic risk of cancer, patients did not support “*delaying or less frequent screening*”: median = 47 [IQR 13.0–66.0] and median = 39 [IQR 14.0–60.75], respectively (Additional file 1: Figure S10). Comparable patterns were observed for noncancer diseases: “*delaying screening*” with a median = 50 [IQR 19.0–71.0] and “*less frequent screening*” with a median = 50 [IQR 18.0–66.0] (Additional file 1: Figure S11).

Regarding current family history (FH) of disease and willingness to undertake preventive measures under the high genetic risk scenario, we found that patients with FH of myocardial infarction ($n = 159$ with FH; $n = 434$ without FH) were more inclined to adopt “*lifestyle modification*” if a high genetic risk of cancer was identified, with the association remaining statistically significant after adjustment for age and sex (p -value = 3.6×10^{-4} ; FDR-adjusted p -value = 0.011). For the high genetic risk scenario for noncancer diseases, the association was similar (p -value = 8×10^{-4} after adjustment for age and sex; FDR-adjusted p -value = 0.02).

Another finding concerned patients with FH of Parkinson’s disease ($n = 45$ with FH; $n = 548$ without FH): these individuals reported a greater inclination toward “*earlier screening*” in the high genetic risk of cancer scenario (p -value = 2.7×10^{-4} after adjustment for age and sex; FDR-adjusted p -value = 9×10^{-3}). The association was weaker in the noncancer scenario (p -value = 0.03 after adjustment for age and sex; FDR-adjusted p -value = 0.29).

For cancer, a significant association was also observed among women with a family history of ovarian cancer ($n = 21$ with FH; $n = 572$ without FH), who reported a greater inclination toward “*preventive surgery*” if a high genetic risk of cancer was identified (p -value = $2.4e-04$ after adjustment for age and sex; FDR-adjusted p -value = $9.3e-03$). No other statistically significant associations were observed after correction for multiple testing.

Patient preferences for PRS implementation in clinical care

Regarding patients’ preferences for the disclosure of PRS results, responses to the multiple-choice item “*If you want to receive PRS results, who would you prefer to receive them from?*” indicated that most patients would prefer disclosure either by a physician specializing in genetics (geneticist or genetic counselor) (54.9%) or by their attending physician (51.2%). Notably, 26.3% of the patients indicated that they would consult only a physician specializing in genetics, whereas 22.0% would consult only their attending physician. A smaller proportion, 17.1%, reported that they would seek guidance from any member of the broader medical staff (Additional file 1: Figure S12).

For the single-choice question “*In your opinion, from what age should these polygenic risk scores be calculated and communicated to patients?*”, most patients indicated that the PRS should be calculated and communicated from childhood at the parents’ request (33.3%) or from age 18 (30.1%). Fewer patients selected “from age 40” (16.1%) or “from age 50” (4.8%), whereas 14.3% of the patients answered “I don’t know”, and 1.3% preferred not to answer (Additional file 1: Figure S13).

For the single-choice question “*How much would you be willing to pay to have these polygenic risk scores done and to know your risk of developing common complex diseases?*”, the most common response was “I don’t know” (30.2%), whereas 3.4% of the patients preferred not to answer. Among patients who selected a specific amount, the option chosen

most frequently was €50 (24.4%), followed by €25 and €100 (16.7% each). €0 and more than €100 were each selected by 13.5%, whereas €75 and €10 were less frequently selected (8% and 7.1%, respectively; Additional file 1: Figure S14).

SPs' support for PRS-guided screening and prevention

Among SPs, support for “*preventive drug therapy*” and “*preventive surgery*” was substantially lower in comparison with screening and lifestyle measures (Fig. 4). Although this pattern mirrors the patient survey, responses from SPs showed lower acceptance of preventive drug therapy and surgery, with medians of 50 [IQR 27–69] and 50 [IQR 35–69], respectively.

Patients with a HIGH polygenic risk score for cancer:

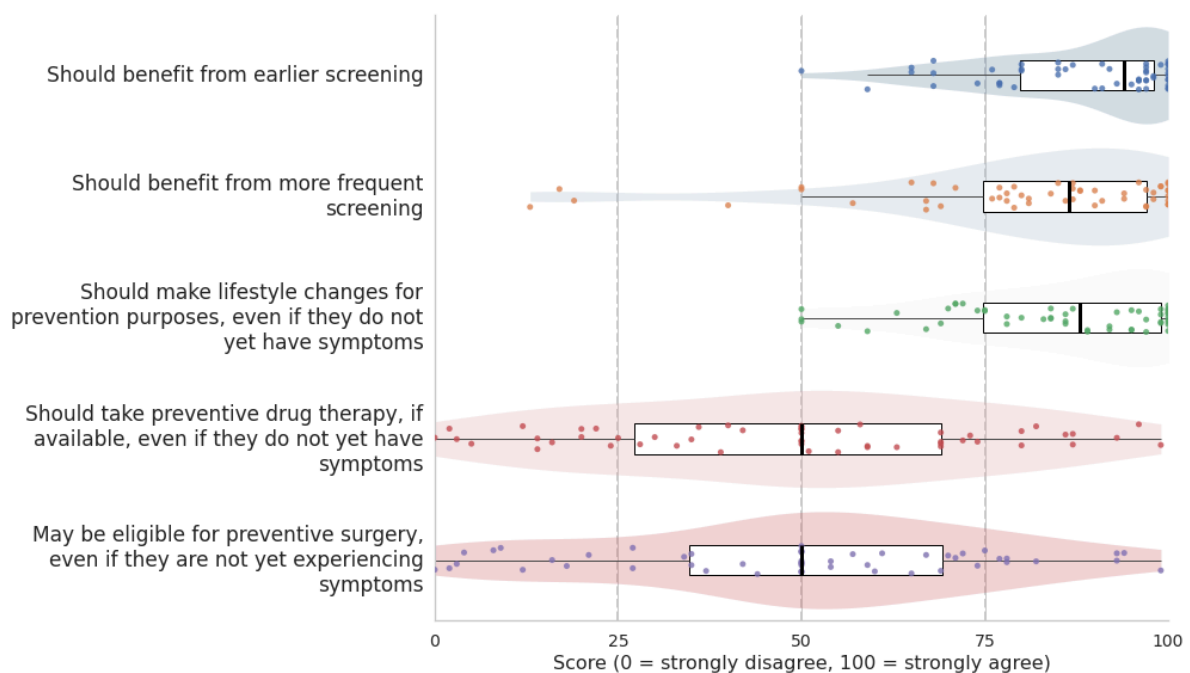


Figure 4. Clinician agreement with preventive actions for cancer patients at high polygenic risk.

Each point represents one clinician's 0–100 agreement score (0 = strongly disagree, 100 = strongly agree). Half-violins illustrate response distributions, and boxplots indicate medians and interquartile ranges.

SPs reported lower median scores for screening modifications in the noncancer than in the cancer scenario (Additional file 1: Figure S15): the “*earlier screening*” item had a median = 83 [IQR 72–98] (paired Wilcoxon signed-rank p-value = 0.023; FDR-adjusted p-value = 0.029 for cancer versus noncancer CCDs), whereas the “*more frequent screening*” item had a median = 77 [IQR 66–92] (p-value = 0.015; FDR-adjusted p-value = 0.027). In contrast, for the “*lifestyle modification*” item, the scores were higher but showed no evidence of a difference between cancer and noncancer risk (median = 92 [IQR 77–99], p-value = 0.29). SPs were also more in agreement with “*preventive drug therapy*” for high-risk noncancer CCDs (median = 61 [IQR 39–73], p-value = 0.016; FDR-adjusted p-value = 0.027), whereas patients remained comparatively more reserved than in the cancer context. In comparison, responses for “*preventive surgery*” in high-risk noncancer CCDs were shifted toward disagreement and differed from those in the cancer scenario (median = 38 [IQR 18–50], p-value = 1.6e-04; FDR-adjusted p-value = 8e-04).

For items concerning “*delaying screening*” in patients at low genetic risk, responses were shifted toward disagreement in both the cancer and noncancer contexts, similar to the patient survey results: median = 30 [IQR 14–51] and median = 33 [IQR 16–55], respectively (Additional file 1: Figure S16-17). Similarly, for the “*less frequent screening*” item, SPs reported low acceptance of this option.

SPs’ expectations about the psychological and behavioral impact of PRS disclosure and readiness to implement PRS

Next, we included questions capturing SPs’ views on the psychological aspects of how patients might perceive PRS results (Additional file 1: Figure S18). For patients at high genetic predisposition to cancer, scores were shifted toward “*negative emotional reaction*” rather than “*positive emotional reaction*” (median = 28 [IQR 14–43]). The responses likewise

leaned toward “*concerns about the risk of discrimination by the employer and/or insurance*” rather than “*ensuring a suitable working environment and fair access to insurance benefits*” (median = 33 [IQR 11–50]). In contrast, for lifestyle impact, scores favored “*more proactive preventive behaviors*” over “*negative consequences for lifestyle*” (median = 73 [IQR 67–83]). Finally, for the item contrasting “*a complete misunderstanding and desire to consult a doctor*” (0) versus “*a complete understanding of the results and next steps*” (100), scores were centered around the midpoint of the scale, with a slight shift toward the left end (median = 50 [IQR 32–63]).

We assessed the situation with respect to the SPs' willingness to use the PRS in their clinical practice (Fig. 5). The results showed that SPs are generally willing “*to recommend PRS to their patients*”: median = 74 [IQR 60–89, min score > 50]. However, their “*confidence in their ability to explain PRS to patients*” is less strong: median = 67 [IQR 50.0–77]. Next, SPs reported high agreement across all questions related to post-disclosure patient support (median scores 73–77).

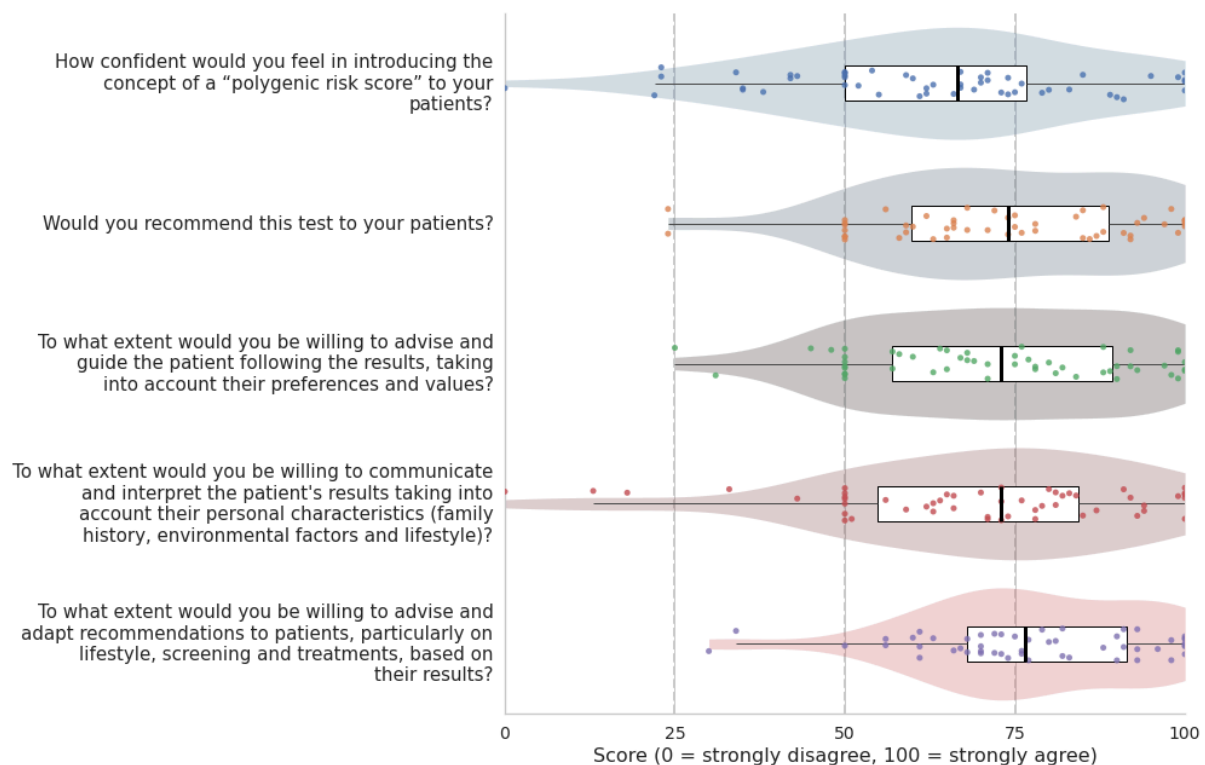


Figure 5. SPs' readiness to recommend, explain, and operationalize PRSs in practice. Each point represents one clinician's 0–100 agreement score (0 = strongly disagree, 100 = strongly agree). Half-violins illustrate response distributions, and boxplots indicate medians and interquartile ranges.

We also surveyed SPs about their concerns regarding the implementation of PRSs in clinical practice (Additional file 1: Figure S19). The highest median score was observed for limited time available for discussing and explaining risk score results to patients (87 [IQR 73–98]), followed by the need for continuing education on risk scores (82 [IQR 65–93]). More than half of the SPs identified online courses and webinar training as the most preferred learning modes (35% each). Next in priority were consultation with a geneticist/genetic counselor and mobile applications (24% each), followed by national guidelines and in-person training workshops (17% each). Additional concerns included inequalities in access to PRSs among economically disadvantaged and underrepresented ethnic groups (median scores 80 [IQR 62–95] and 81 [IQR 64–92], respectively).

Discussion

Overall, in a large sample of nearly 700 patients within the University Hospital of Liège healthcare context, the PRS was well accepted, with participants expressing strong interest in receiving information about their genetic risk. This aligns with their prior agreement to participate in a hospital-based genetic research project, suggesting that they may represent early beneficiaries of PRS in clinical practice. The majority of the SPs also reported that they would be willing to recommend PRS in clinical practice. This smaller sample of approximately 50 SPs may be subject to bias, and the low participation likely reflects time constraints and the fact that many SPs remain unfamiliar with PRSs or do not yet perceive them as directly relevant. Nevertheless, these SPs can be considered a pioneering group of doctors in adopting PRSs. Preventive actions were more strongly supported by patients in

cancer-related scenarios than in noncancer scenarios. In both contexts, they favored earlier and more frequent screening and lifestyle modifications while remaining cautious about preventive pharmacotherapy and prophylactic surgery, which was also observed in SP responses. As expected, individual factors such as age, sex, and family history influenced attitudes, intentions, and perceived psychological impact. Finally, concerns regarding communication, emotional responses, and equity underscore the importance of clinician guidance, as patients recognized both potential risks and substantial benefits. These findings go beyond overall PRS acceptability, offering a structured view of decision-making across patient and SP perspectives. They suggest a gradient of acceptance that varies by disease context and type of intervention.

In more detail, despite low prior awareness of the PRS among patients, the acceptability of PRS disclosure was high, in line with a previous study [22], and prior awareness was not associated with interest in receiving results. Our findings and previous evidence raise the possibility that the expressed interest in PRSs may not reflect a clear understanding of how PRSs are interpreted but may instead be partly driven by limited knowledge about the role of PRSs in predicting disease risk. However, because only self-reported familiarity with PRSs was assessed, this interpretation requires further investigation.

Regarding changes in screening behavior, an important observation is that patients prioritize genetic risk for cancers over risk for noncancer conditions. This pattern is consistent with the widely recognized “fear of cancer” in the general population [23–25]. A similar pattern was observed among the SPs, possibly reflecting a professional view of cancer screening as an important tool for preventing advanced disease. At the same time, the SPs emphasized that lifestyle changes are more important in cases of high genetic risk for noncancerous diseases than for oncological diseases, while patients continue to prioritize

cancer. This pattern may in part reflect a notable imbalance: there is substantial enthusiasm and investment in drug treatments and invasive screening procedures for cancers, whereas preventive strategies, including behavioral interventions and the necessary patient support to implement them, receive comparatively little attention [26]. Meanwhile, cancer risk is also related to lifestyle factors [27], although the strength of these associations varies considerably across cancer sites—most notably, strong associations have been observed for lung, head and neck, and esophageal cancers, whereas links appear weaker or subtype-specific for prostate and ovarian cancer [12,28–30].

For preventive pharmacotherapy and surgery before symptom onset, acceptance was lower than for screening and lifestyle for both patients and SPs, which is an expected gradient, as pharmacotherapy and surgery are more invasive interventions. In the context of cancer versus noncancer diseases, patients continue to prioritize cancer, whereas SPs show a greater tendency to recommend preventive medications for high genetic risk of noncancer CCDs but remain more cautious about preventive surgery. Notably, findings on SPs' opinions should be interpreted cautiously, given the smaller and specialty-diverse sample, in which not all SPs may be fully aware of the nuances distinguishing cancer prevention from noncancer prevention.

In low-risk situations, our results, which revealed that both patients and SPs remained cautious about reducing screening, are consistent with previous studies [17,31]. These results may be explained by patients' tendency to request the best management, even when only a small proportion would be expected to benefit. Among SPs, this cautious approach may partly reflect the fact that very few true experts in organizing screening programs participated in the survey—those who would be most aware of the economic limitations inherent in healthcare systems. This may also indicate a lack of confidence in the PRS when its use could lead to missed diagnoses or harm to patients' health. While PRSs may theoretically support

more efficient allocation of screening resources by identifying individuals at lower risk, our findings suggest that this application may face greater challenges in clinical implementation. Risk stratification toward de-escalation of preventive interventions may require stronger evidence, clear clinical guidelines, and effective communication strategies before being accepted in routine care.

Although our study is the first to directly compare cancer and noncancer diseases in the context of using PRSs to guide screening, lifestyle, and pharmacotherapy/surgery decisions, disaggregated by intervention category, the observed pattern can be compared with findings from previous works. Among SPs, a national U.S. survey of primary care physicians revealed greater interest in using PRSs for cancer (88–91% for prostate, colorectal, and breast) than for noncancer conditions (48–52% for obesity, atrial fibrillation, and depression) [31]. For patients, while direct head-to-head comparisons of preferences for PRS-based risk assessment across cancer and noncancer conditions remain limited, analyses from the U.S. Health Information National Trends Survey (HINTS) have shown that individuals who perceived genetic information as important for cancer prevention and early detection were more likely to report cancer genetic testing [32]. Regarding differences in patient perceptions of screening, lifestyle, and pharmacotherapy/surgery interventions, another study examining willingness to accept genetic risk among participants in the Swedish CARDIOpulmonary bioImage Study (Swedes aged 50–64 years) reported that respondents preferred lifestyle changes over surgery and medication as preventive measures [33]. This was explained by the participants' perception that information requiring lifestyle changes might be more empowering than information requiring surgery or medication.

Regarding psychological impact items, patients acknowledged the possibility of negative emotional reactions to PRS disclosure. However, recent evidence suggests that the actual psychological impact of receiving PRS results in clinical settings is generally limited

[19]. By contrast, studies of direct-to-consumer (DTC) testing have reported more frequent negative emotional reactions, including confusion and anxiety, particularly when results are returned without healthcare professional involvement [34]. Findings from other psychological impact items suggest that patients consider PRS information beneficial in areas they perceive to be within their control. Considering patients with a high genetic risk, SPs similarly recognized potential negative emotions but saw opportunities for increased personal control and proactive preventive behavior, which is consistent with prior surveys. In a U.S. national sample, 91% of primary care physicians agreed that PRS could help patients make better decisions, and 77% believed that PRS could improve patient outcomes [31]. Likewise, an international survey of health professionals (Australia, Canada, and the U.S.) revealed that, despite noted concerns, most judged the benefits of polygenic testing to outweigh the harms (66% agree or strongly agree), highlighting stronger prevention uptake as a key advantage [35]. SPs also expected that many patients would require assistance in interpreting PRS results and would seek medical consultation. It has been shown previously that poorer understanding of PRSs was associated with experiencing a negative reaction from receiving the information [34]. This is consistent with the findings of another study, where patients understood a key takeaway that they should ask their primary care provider about actions to lower their disease risk [14]. Together, these findings suggest that clinician support and genetic counseling may play an important role in mitigating potential adverse psychological effects associated with PRS disclosure.

SPs expressed high willingness to provide postdisclosure support, although some reported limited confidence in explaining and interpreting PRSs. Many highlighted the need for ongoing training via workshops, conferences, or online modules, which is consistent with previous surveys [17]. Their main concern was insufficient time to discuss results in routine care, in contrast with a survey of primary care physicians, where time was rarely seen as a

barrier [31]. These issues reflect challenges of feasibility within busy clinical workflows and economic pressure and suggest that involving genetic counsellors in interpretation may be an effective pathway to implementation. Notably, most patients preferred results to be explained either by a genetics specialist or their attending physician, emphasizing both expertise and trust. Taken together, these findings suggest a model in which a single consultation with a genetics specialist provides clear recommendations, with subsequent follow-up by the patient's primary care physician.

An additional key finding was that perceptions of PRS information are likely influenced by individual characteristics and prior experiences with disease risk. In our study, older age was associated with more cautious perceptions of PRS disclosure, which may reflect differences in perceived opportunities for prevention [36]. Women tended to give more positive ratings on items related to family relationships, as well as perceived ability to maintain control over one's life, which is consistent with previous observations that women often report greater engagement with genetic risk information [37]. Finally, the association between family history and willingness to undertake preventive measures supports the established role of personal disease experience in shaping risk perception and preventive decision-making [38]. However, whether these findings translate into real changes in health behavior should be evaluated in prospective implementation studies.

This study has several limitations. First, although ENSEMBLE participants are typical hospital patients with a high agreement rate (Methods), those who agreed to participate in the genetic risk assessment project (and subsequently complete the questionnaire on PRS acceptability) may have initially been more interested in or positively disposed toward genetic testing and prevention than the broader patient group was, potentially limiting generalizability. Participation in such a study may have prompted patients to hold more optimistic expectations about their adherence to recommended preventive actions than might

have occurred in practice. Second, the study did not assess participants' genomic literacy or understanding of the PRS. Consequently, responses may reflect a partial or inaccurate understanding of PRS. Future research should better evaluate genomic literacy as a determinant of attitudes and a factor in PRS implementation. Third, the study relies on responses to hypothetical scenarios, which capture stated intentions rather than actual behaviors. The extent to which these responses reflect real-world decisions and emotional reactions following PRS disclosure remains uncertain. In addition, responses to psychological impact items capture anticipated emotional reactions to a hypothetical PRS disclosure scenario and cannot assess how these reactions may evolve over time, including potential longer-term effects. Therefore, prospective clinical studies are needed to evaluate the real-world psychological impact of PRS implementation. Such studies should include the disclosure of actual PRS-informed risk estimates and follow participants over time to assess both short- and long-term psychological responses, as well as changes in preventive behaviors and adherence to screening recommendations. Further, participants' views on screening may have been influenced by differences in current healthcare practices between cancer and noncancer conditions. In Belgium, organized screening programmes are available for several cancers but are not widely implemented for most noncancer CCDs. As a result, participants may have been more familiar with cancer screening, which could have influenced their expectations regarding PRS-based screening strategies. Next, although the survey was distributed to all medical doctors holding a specialist position at CHU Liège, responding required both completing the educational module and the questionnaire. Therefore, our sample of SPs is likely biased toward those who initially expressed a greater interest in PRS, potentially overestimating enthusiasm and perceived readiness for implementing PRS into everyday practice. Finally, given the large number of questionnaire items and statistical tests performed, our analyses should be considered exploratory, and

individual p-values should be interpreted with appropriate caution rather than as definitive evidence.

Despite these limitations, our study has several important strengths. To our knowledge, it is the first to directly compare the acceptability of PRSs for cancer and noncancer diseases across both patients and healthcare specialists. The study goes beyond assessing willingness to receive or recommend PRSs by examining their acceptability across different clinical applications. Finally, the combination of quantitative data with qualitative comments provides deeper insight into the factors influencing PRS acceptability.

Conclusions

In conclusion, this study provides evidence supporting the clinical acceptability of polygenic risk scores among patients and specialist physicians, while also revealing clear context-dependent differences in attitudes toward prevention. It also highlights key implementation challenges, including limited time among specialist physicians to communicate complex genetic risk information. The findings highlight the importance of structured implementation pathways that integrate specialist genetic interpretation with primary care follow-up.

List of abbreviations

PRS: polygenic risk score; GWAS: genome-wide association studies; SNPs: single nucleotide polymorphisms; FH: family history; CCDs: common complex diseases; ENT: ear, nose, and throat (Otorhinolaryngology); SPs: specialist physicians; HCPs: healthcare providers; CHU: Centre Hospitalier University (University Hospital); IQR: interquartile range; FDR: false discovery rate; BH: Benjamini–Hochberg; REDCap: research electronic data capture; DTC: direct-to-consumer.

Declarations

Ethics approval and consent to participate

The study protocol was approved by the Hospital-Faculty Ethics Committee of Liège University Hospital (approval number: 2023/270), and written informed consent was obtained from all participants prior to enrolment. The study was conducted in accordance with relevant guidelines and regulations, including the principles of the Declaration of Helsinki.

Consent for publication

Not applicable

Availability of data and materials

The datasets generated and/or analysed during the current study are not publicly available due to ethical and data protection restrictions (GDPR), but are available from the corresponding author upon reasonable request and subject to approval by the relevant ethics committee.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

A.N., J.B., A-F.D., B.P., S.V. and E.L. contributed to the conceptualization of the study. Methodology was developed by A.N., A-F.D., B.P., and S.V. Investigation was performed by A.N. and G.J. Data curation was carried out by J.B. and S.A. A.N. conducted the formal analysis and prepared the visualizations. A.N. and J.B. drafted the original manuscript. All authors (A.N., J.B., G.J., A-F.D., S.R., E.L., B.P., and S.V.) contributed to manuscript review and editing. Supervision was provided by E.L., B.P., and S.V. Project administration was managed by S.V. and E.L., who also secured funding for the study. S.V. and B.P. contributed equally to this work. All authors read and approved the final manuscript.

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Supplementary information

Additional file 1

File format: PDF (.pdf)

Title of data: Supplementary tables and figures

Description of data: Table S1. Patients characteristics; Table S2. Specialist physicians characteristics; Figure S1. Patient interest in receiving PRS results by prior awareness of PRS; Figure S2. Patient interest in receiving PRS results by perceived risk of developing a chronic disease (among those without a current diagnosis); Figure S3. Patient interest in receiving PRS results by self-reported attention to health compared to peers; Figure S4. Patient interest in receiving PRS results by self-reported cautiousness compared to peers; Figure S5. Patient interest in receiving PRS results by self-reported frequency of illness compared to peers; Figure S6. Patient interest in receiving PRS results by self-reported tendency to worry compared to peers; Figure S7. Mean agreement scores by age group among patients for psychological and practical implications of PRS disclosure; Figure S8. Mean agreement scores by age group among patients for preventive actions in the context of a high PRS for cancers; Figure S9. Mean agreement scores by age group among patients for preventive actions in the context of a high PRS for noncancer diseases; Figure S10. Patients' agreement with proposed screening modifications in the case of low polygenic risk of cancers; Figure S11. Patients' agreement with proposed screening modifications in the case of low polygenic risk of noncancer diseases; Figure S12. Distribution of patients' responses regarding their preferred healthcare professional for explaining PRS results; Figure S13. Distribution of patients' responses regarding the appropriate age for PRS assessment; Figure S14. Distribution of stated willingness to pay for PRS assessment among patients; Figure S15. Specialist physicians' agreement with preventive actions for patients at high polygenic risk of common noncancer diseases; Figure S16. Specialist physicians' agreement with

proposed screening modifications for patients at low polygenic risk of cancers; Figure S17. Specialist physicians' agreement with proposed screening modifications for patients at low polygenic risk of common noncancer diseases; Figure S18. Specialist physicians' expectations about patients' psychological and practical responses to a high cancer PRS; Figure S19. Specialist physicians' concerns about implementing PRS in routine care.

Additional file 2

File format: PDF (.pdf)

Title of data: Patient phenotypes survey

Description of data: Survey instrument used to collect patient phenotypic and clinical characteristics.

Additional file 3

File format: PDF (.pdf)

Title of data: Patient PRS acceptability survey

Description of data: Questionnaire assessing patients' perceptions and acceptability of polygenic risk scores.

Additional file 4

File format: PDF (.pdf)

Title of data: Specialist physicians PRS educational material

Description of data: Educational course material provided to specialist physicians regarding polygenic risk scores.

Additional file 5

File format: PDF (.pdf)

Title of data: Specialist physicians PRS acceptability survey

Description of data: Questionnaire assessing specialist physicians' perceptions and acceptability of polygenic risk scores.