

## ARTICLE



# Perceived benefits and barriers to implementing precision preventive care: Results of a national physician survey

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Polygenic risk scores (PRS) may improve risk-stratification in preventive care. Their clinical implementation will depend on primary care physicians' (PCPs) uptake. We surveyed PCPs in a national physician database about the perceived clinical utility, benefits, and barriers to the use of PRS in preventive care. Among 367 respondents (participation rate 96.3%), mean (SD) age was 54.9 (12.9) years, 137 (37.3%) were female, and mean (SD) time since medical school graduation was 27.2 (13.3) years. Respondents reported greater perceived utility for more clinical action (e.g., earlier or more intensive screening, preventive medications, or lifestyle modification) for patients with high-risk PRS than for delayed or discontinued prevention actions for low-risk patients ( $p < 0.001$ ). Respondents most often chose out-of-pocket costs (48%), lack of clinical guidelines (24%), and insurance discrimination concerns (22%) as extreme barriers. Latent class analysis identified 3 subclasses of respondents. *Skeptics* ( $n = 83$ , 22.6%) endorsed less agreement with individual clinical utilities, saw patient anxiety and insurance discrimination as significant barriers, and agreed less often that PRS could help patients make better health decisions. *Learners* ( $n = 134$ , 36.5%) and *enthusiasts* ( $n = 150$ , 40.9%) expressed similar levels of agreement that PRS had utility for preventive actions and that PRS could be useful for patient decision-making. Compared with *enthusiasts*, however, *learners* perceived greater barriers to the clinical use of PRS. Overall results suggest that PCPs generally endorse using PRS to guide medical decision-making about preventive care, and barriers identified suggest interventions to address their needs and concerns.

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## INTRODUCTION

Polygenic risk scores (PRS) have emerged as a promising tool for disease risk stratification in clinical medicine [1–3]. Built on genome-wide association study data, a PRS aggregates small effect sizes from dozens to millions of variants from across the genome to convey a measure of an individual's genetic predisposition to a given disease from common genetic variation. For some diseases, a high PRS value indicates a risk equivalent to that of high-penetrance, single-gene variants associated with monogenic disease [4–6]. Advances in the diversity of available datasets and in computational methods are improving the accuracy of PRS in populations of diverse genetic ancestry [7–9].

As a result of these developments, PRS are now being considered for implementation into clinical medicine. Clinical trials and implementation projects are underway [10–14], and several commercial laboratories already offer PRS products for clinical use [15–17]. Most attention has focused on the potential for PRS to identify high-risk subgroups of patients for whom targeted interventions might improve health outcomes through earlier prevention, detection, or treatment; [4, 10, 18] the potential for PRS to identify low-risk subgroups for whom certain preventive measures might be appropriately deferred remains more theoretical [19, 20].

Whereas preventive medicine is most often the domain of primary care, the successful implementation of PRS for risk stratification and prevention will depend partly on the clinical utility and barriers that primary care physicians (PCPs) perceive to their use. Given the increasing interest in the clinical application of PRS in preventive medicine contexts, it will be important to understand the perspectives of these frontline clinicians. To that end, we fielded a web-based national survey of U.S. PCPs about the potential clinical utility and barriers they perceive to the use of PRS in preventive care.

## METHODS

The study was approved by the Harvard Longwood Campus Institutional Review Board (Protocol #20-2098). We followed the Checklist for Reporting Results of Internet E-Surveys (CHERRIES) in presenting this research (Supplement) [21, 22].

## Population and sampling strategy

We defined the target population as PCPs who care for adult patients, including physicians practicing family medicine, general practice, or internal medicine. We worked with database licensee IQVIA® to recruit respondents from the ONEKEY national physician database of more than 250,000 active

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physicians who have opted in to receiving email survey invitations. The database includes demographic, training, and practice-related data from the American Medical Association (AMA) Physician Masterfile and other sources [23].

### Recruitment

IQVIA sent email invitations with unique web links to the survey to a random sample of 27,000 eligible PCPs from the database. These emails described the questionnaire as an 8–10 minute survey about precision prevention in primary care using genetic risk scores. Recipients were able to opt out of further contact using a link in the invitation email. Respondents could access the survey through a unique web link, hosted by the Qualtrics<sup>SM</sup> Survey Tool (Qualtrics, Provo, UT). The first email invitation was sent April 18, 2021, and offered respondents a \$25 Amazon gift card for completing the survey. On April 27, 2021, a second email offering a \$50 Amazon gift card was sent to PCPs who had opened the first email but not yet accessed the survey link from the first email. The survey was closed on August 27, 2021.

### Survey measures

The survey began with a brief introduction to PRS that included a definition, a comparison to single-gene tests, and the limitations that PRS do not take into account other disease risk factors and have been most extensively studied in populations of European descent (see full survey in Supplement). The survey questions consisted of two major sections. First, a set of clinical case scenarios assessed physicians' medical decision-making with PRS results for atherosclerotic cardiovascular disease prevention and prostate cancer screening; we have previously reported the results of those survey items [22]. The next section assessed PCPs' perceived benefits and barriers to PRS testing, using questions adapted from prior PCP surveys on implementation of genetic and genomic medicine technologies. Specifically, PCP perceived utility of PRS was measured on a 5-point Likert scale ("strongly agree" to "strongly disagree") with questions asking PCPs whether they would use PRS to identify high-risk patients suitable for three "earlier or more intensive" actions: 1) disease screening procedures (e.g. mammography, colonoscopy), 2) recommendations for preventive medications (e.g. statins, aspirin, tamoxifen), and 3) recommendations for lifestyle modifications (e.g. weight loss and smoking cessation) [24–26]. Similarly, PCPs were asked whether they would use PRS to identify low-risk patients who might be able to "delay or discontinue" these three categories of preventive actions. Perceived benefits of PRS, including improvements in patient and provider decision making and patient health outcomes, and PCP confidence in their ability to use PRS were assessed with questions adapted from a prior survey [27]. Perceived barriers to using PRS in clinical practice were assessed by asking PCPs to rate on a 4-point Likert scale from "not a barrier" to "extreme barrier" eight potential implementation barriers adapted from Mikat-Stevens and Lemke [27, 28]. The final questions asked respondents about any prior genetics education beyond the typical medical school curriculum [29] and self-reported race and ethnicity using U.S. Census categories. Other respondent characteristics were obtained by linking individual survey responses to the IQVIA ONEKEY database: age, years in practice, gender, practice specialty, practice size, and geography by state. Data validation, assessment of data completion and careless responding, and the development of composite scores are described in the Supplemental Methods.

### Analysis

Analyses were conducted in R (v4.0.3, R Foundation, Vienna, Austria) and Stata (v17.0, StataCorp, College Station, TX, USA). Respondent characteristics and survey responses are presented descriptively. All structural modeling and other analyses are presented with relevant test statistics, *p*-values, and confidence intervals where appropriate. To identify subgroups of respondents based on similarities and differences in response patterns, we used latent class analysis (LCA), an exploratory latent variable modeling method that leverages data patterns to indirectly measure a categorical latent construct composed of distinct homogeneous classes [30]. The final indicator set included seven dichotomous items, and examination of model fit and interpretability favored a 3-class model. Additional details are included in the Supplemental Methods.

## RESULTS

### Participant characteristics

The invitation was sent to 27,000 physician email addresses, of which 1197 were returned due to invalid addresses. Of the 25,803 physicians who received the email invitation without bounceback,

2776 opened the email (email open rate 10.8% by CHERRIES reporting standards) and 409 participants clicked the hyperlink to view the survey (survey view rate 409/2,776, 14.7%). Of PCPs who viewed the survey, 394 consented to study participation (participation rate 394/409, 96.3%), 369 completed the initial case scenarios questions (Q1–Q6), and 367 completed all questions other than the optional demographics questions (completion rate for this report 367/394, 93.1%). Among these 367 respondents, 232 (63.2%), 73 (19.9%), 12 (3.2%), and 5 (1.4%) self-reported white, Asian, Black/African-American and Native Hawaiian/Other Pacific Islander race, respectively; 15 (4.1%) self-reported Hispanic/Latinx ethnicity. The majority (329, 89.6%) reported no additional genetics training beyond medical school. Respondents had similar characteristics to non-respondents (Supplementary Table 1).

### Perceived utility of PRS for preventive actions

Figure 1 shows PCPs' reported likelihood of using PRS to identify patients for whom they might change their medical decision-making about categories of preventive actions. The majority of PCPs (63%–93%) somewhat or strongly agreed that they would use PRS for all clinical actions queried except for using a low-risk PRS to identify patients who might be able to delay or discontinue recommendations for lifestyle modification (41% somewhat/strongly agreeing). Across composite scores associated with the 3 classes of preventive actions (disease screening procedures, preventive medications, and lifestyle modification), respondents endorsed stronger preference for taking earlier or more intensive action for high-risk patients than with delaying or discontinuing action for low-risk patients (all Wilcoxon signed rank test  $p < 0.001$  across composite and pairwise comparisons, Supplementary Table 2).

### Perceived benefits of PRS

The large majority of respondents agreed that PRS could help them (89% somewhat/strongly agreeing) and their patients (91% somewhat/strongly agreeing) improve their medical decision-making (Fig. 2). A smaller majority (77%) somewhat or strongly agreed that PRS could help improve their patients' health outcomes. Supplementary Fig. 1 shows respondent interest in using PRS for specific diseases, ranging from 88 to 91% agreement for prostate, colorectal, and breast cancer to 48–52% agreement for obesity, atrial fibrillation, and depression.

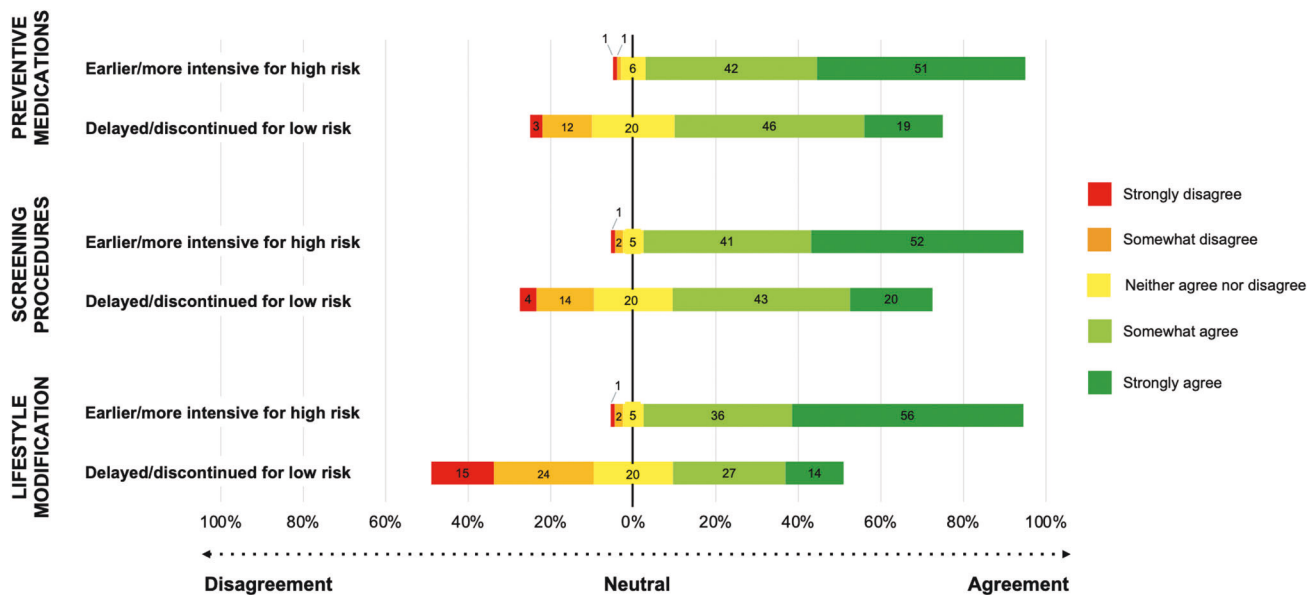
### Perceived barriers to PRS implementation

Figure 3 shows the significance respondents ascribed to potential barriers to using PRS in practice. Of the eight items, possible out-of-pocket cost to patients was most often chosen as a moderate or extreme barrier (86%), while insufficient time to explain PRS to patients was chosen least often (34%). All other potential barriers were chosen by the majority of respondents (51%–66%) as moderate or extreme barriers. Only 42% somewhat or strongly agreed with that statement "I am confident in my ability to use genetic risk score results."

### Latent class structure

A detailed description of LCA model fitting is described in the Supplementary Results. Table 1 presents predicted class prevalences with 95% confidence intervals for the selected 3-class solution. Item-response probabilities associated with the final LCA model are presented in Supplementary Table 3.

**Class 1 (Skeptics).** Nearly one-quarter of survey response patterns (22.8%, 95% CI 16.9% to 30.0%) were characterized by high endorsement probabilities for barriers to PRS use, including that PRS would result in unnecessary testing or treatment (0.799, 95% CI 0.680, 0.882) and are less studied in non-European populations (0.790, 95% CI 0.666, 0.876). These patterns suggested only moderate agreement that PRS could improve clinical decision-



**Fig. 1 Perceived utility of PRS for preventive actions.** Data indicate respondent agreement that they would use PRS in their clinical practice to identify high-risk patients who might need earlier/more intensive preventive action in three categories (preventive medications, screening procedures, and lifestyle modification) or to identify low-risk patients who might be able to delay/discontinue these preventive actions. Examples given were statins, aspirin, tamoxifen (preventive medications); mammography and colonoscopy (screening procedures); and weight loss and smoking cessation (lifestyle recommendations).

making (0.585, 95% CI 0.463, 0.698) and endorsed uncertainty around or disagreement with the statements that PRS could improve patient health outcomes (0.148, 95% CI 0.041, 0.410) and that respondents could confidently use PRS in medical practice (0.084, 95% CI 0.036, 0.183). We labeled this latent class *skeptics*.

**Class 2 (Learners).** Approximately one-third of response patterns (33.5%, 95% CI 26.0% to 42.0%) were also characterized by high endorsement probabilities for barriers to PRS, but their response patterns were distinguished by very high endorsement of the statements that they had insufficient understanding about how to use PRS (0.987, 95% CI 0.889, 1.000) but that PRS could improve both medical decision-making (0.977, 95% CI 0.885, 0.996) and patient outcomes (0.999, 95% CI 0.999, 1.000). These patterns were also associated with uncertainty or disagreement that respondents could confidently use PRS in their clinical practice (0.329, 95% CI 0.241, 0.432). We labeled this latent class *learners*.

**Class 3 (Enthusiasts).** The remainder of response patterns (43.7%, 95% CI 36.2% to 51.6%) aligned with fewer endorsed barriers to using PRS (all item-response probabilities < 0.350) and suggested high to very high agreement that PRS could improve medical decision-making (0.978, 95% CI 0.910, 0.995) and patient outcomes (0.908, 95% CI 0.830, 0.952). These respondents were confident in their ability to use PRS results in practice (0.670, 95% CI 0.577, 0.752). Given the inclination toward fewer barriers, heightened utility, and confident use of PRS, we labeled this latent class *enthusiasts*.

#### Characteristics of latent classes

Table 1 shows characteristics by latent class. High agreement was observed between estimated class prevalences and predicted class memberships among respondents: 83 (22.6%) *skeptics*, 134 (36.5%) *learners*, and 150 (40.9%) *enthusiasts*. Between-class differences in demographics, professional history, and practice location were not statistically significant. Slightly higher proportions of female respondents were observed among *skeptics* (38.6%) and *learners* (44.0%) compared to *enthusiasts* (30.7%,  $p = 0.065$ ). *Enthusiasts* were more likely to report additional

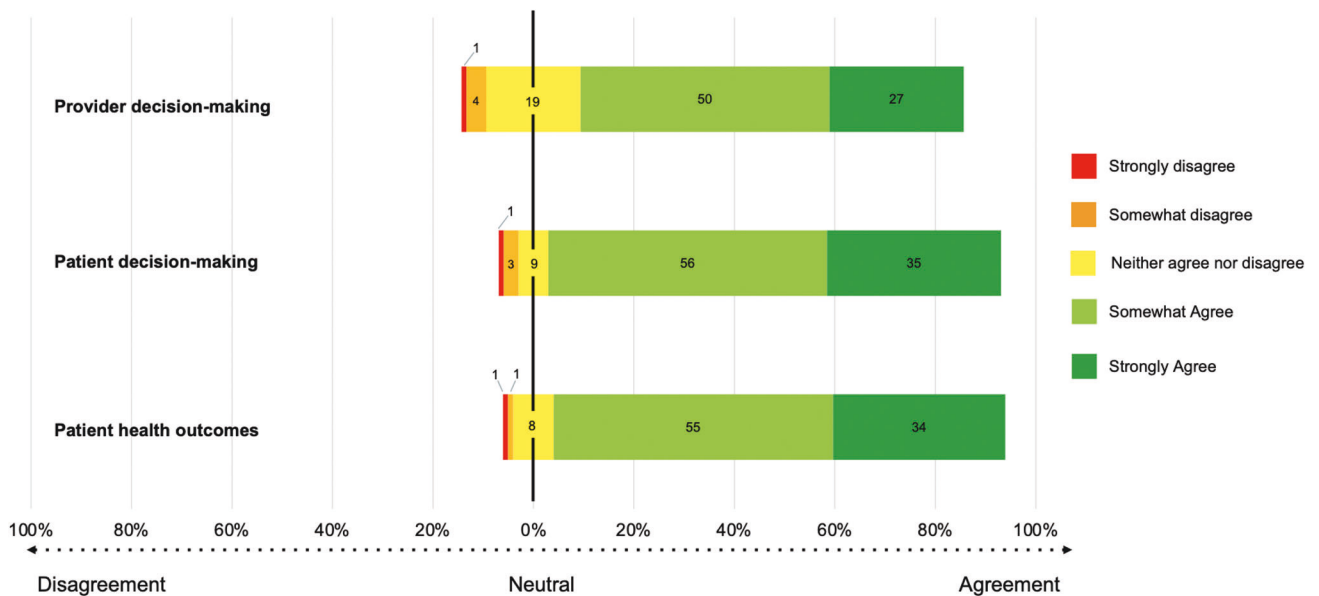
genetics training beyond medical school (14.7%) than *learners* (6.7%) or *skeptics* (8.4%,  $p = 0.073$ ).

Observed endorsements of items not included in LCA modeling aligned as expected with predicted survey response patterns and class memberships (Fig. 4). *Skeptics* consistently endorsed lower agreement with individual items regarding the use of PRS for earlier or delayed preventive action, expressed the most concern that patient anxiety and insurance discrimination were also significant barriers, were less likely to agree that PRS could help patients make better health care decisions. *Learners* and *enthusiasts* generally expressed higher levels of agreement that PRS could be used for either earlier or delayed clinical action and that PRS could help patient decision-making. Compared to *enthusiasts*, however, *learners* acknowledged greater barriers to using PRS across all items and were most likely to consider absence of guidelines as the primary barrier to using PRS in practice. All three classes noted out-of-pocket costs as a barrier.

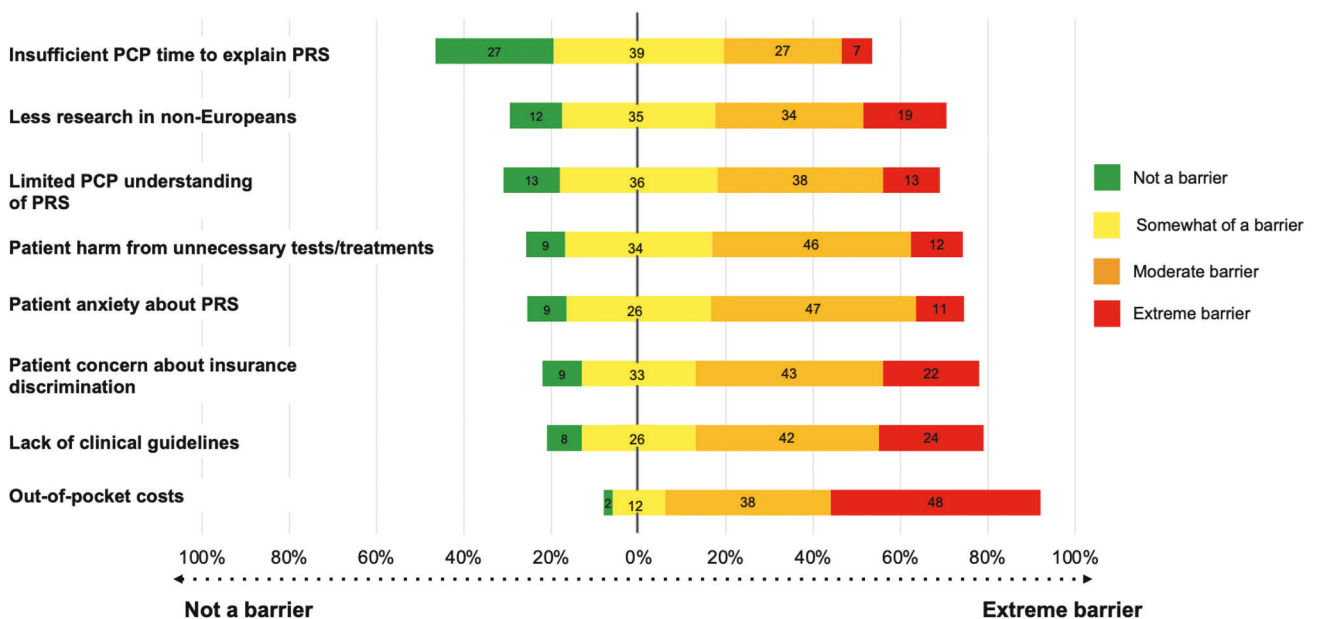
Between-class differences were also observed for both early preventive action composite scores for high-risk PRS (Kruskal-Wallis rank sum test  $p < 0.001$ ) and delayed action composite scores for low-risk PRS ( $p = 0.005$ ). Pairwise comparisons demonstrated less overall propensity to favor earlier or delayed preventive action among *skeptics* compared to *learners* (early action  $p < 0.001$ ; delayed action  $p = 0.005$ ) and *enthusiasts* (early action  $p < 0.001$ ; delayed action  $p = 0.005$ ). No statistically significant median differences were observed between *learners* and *enthusiasts* (early action  $p = 0.081$ ; delayed action  $p = 0.848$ ). Within all classes, respondents favored more clinical action for high-risk PRS results over less action for low-risk results (*skeptics*  $p < 0.001$ ; *learners*  $p < 0.001$ ; *enthusiasts*  $p < 0.001$ ).

#### DISCUSSION

We observed general endorsement among PCPs for using PRS to guide medical decision-making about preventive medicine actions. Respondents favored earlier action for high-risk individuals more than delayed action for low-risk individuals. They also endorsed certain barriers to the clinical implementation of PRS, and fewer than half reported confidence in their ability to use PRS.



**Fig. 2 Perceived benefits of PRS.** Data are respondent agreement with the statements “Genetic risk scores could help improve my medical decision-making in the care of patients;” “Genetic risk scores could help my patients make better decisions about their healthcare;” and “Genetic risk scores could improve my patients’ health outcomes.”



**Fig. 3 Perceived barriers to PRS implementation.** Data are respondent ratings of the significance of each item as a barrier to using PRS in clinical practice.

Latent class analysis suggested 3 classes of PCPs with regard to the utility and barriers they perceived for PRS: *skeptics* who heavily weighted the barriers to and potential harms of PRS; *learners* who perceived both barriers and benefits to implementation; and *enthusiasts* who perceived benefit and self-confidence in the use of PRS. These observations suggest policy and system interventions to optimize the implementation of PRS into preventive care.

A primary focus of the survey was whether and how PCPs anticipated using PRS to make medical decisions. The majority reported they would use PRS results to change their recommendations for preventive actions, suggesting some degree of PCP acceptance of PRS as actionable results. However, among respondents overall and within each latent class, we observed a clear preference for doing more for high-risk results than doing

less for low-risk results. This pattern might represent commission bias among respondents, an inclination towards clinical action even when inaction might result in equivalent or more favorable outcomes [31, 32]. It might also reflect their concerns, observed in studies of risk-stratified breast cancer screening [33, 34], about whether PRS have sufficient accuracy to justify reducing recommended screenings at the risk of delaying detection. The current or proposed implementation of PRS also reflects this bias towards action. PRS for breast cancer and coronary artery disease are proposed as tools (or *risk-enhancing factors*) to identify high-risk patients eligible for screening and statin therapy, respectively, that traditional risk stratification methods miss [15, 18]. Whether PRS are used in the future as *protective factors* to help patients safely defer preventive care will require strong evidence of benefit



**Table 1.** Latent class prevalence and participant characteristics.

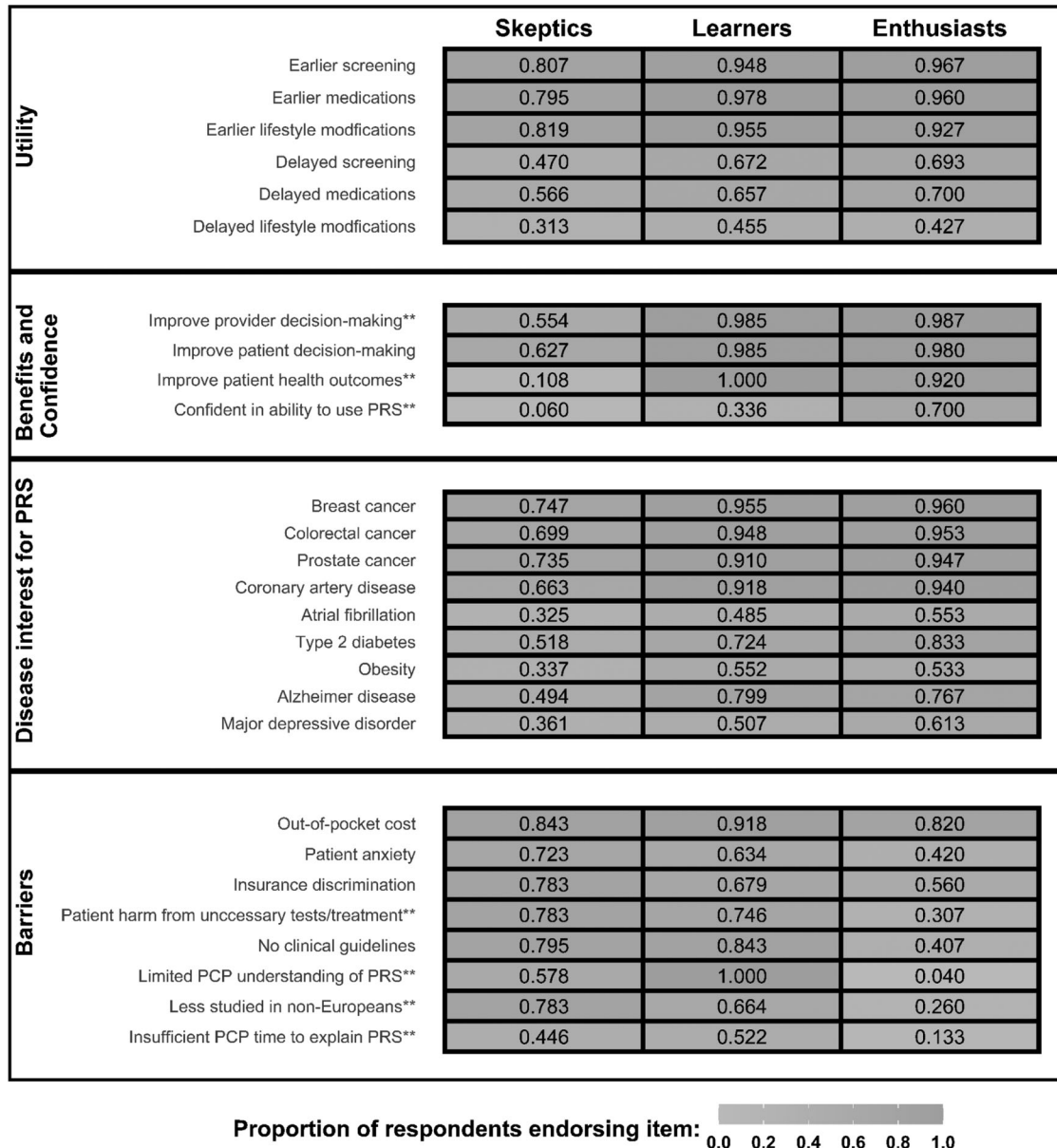
Classes					
Class distribution (95% CI) <sup>1</sup>	Total sample	Skeptics	Learners	Enthusiasts	
Class prevalence	-	0.228 (0.169, 0.300)	0.335 (0.260, 0.420)	0.4371 (0.362, 0.516)	
Modal posterior probability	-	0.226	0.365	0.409	
Average posterior probability	-	0.907 (0.873, 0.940)	0.886 (0.868, 0.904)	0.957 (0.943, 0.971)	
Total <i>N</i>	367	83	134	150	
Demographic information	Total sample	Skeptics	Learners	Enthusiasts	<i>p</i> <sup>3</sup>
Age, years, Mean (SD)	54.9 (12.9)	53.3 (14.0)	54.2 (12.8)	56.5 (12.3)	0.126
Time since medical school graduation, years, Mean (SD)	27.2 (13.3)	25.7 (14.4)	26.5 (12.9)	28.7 (13.0)	0.188
Gender, <i>n</i> (%)					
Female	137 (37.3%)	32 (38.6%)	59 (44.0%)	46 (30.7%)	0.065
Male	230 (62.7%)	51 (61.4%)	75 (56.0%)	104 (69.3%)	
Self-reported race, <i>n</i> (%)					
Asian	73 (19.9%)	15 (18.1%)	34 (25.4%)	24 (16.0%)	0.647
Black or African American	12 (3.2%)	4 (4.8%)	5 (3.7%)	3 (2.0%)	
Native Hawaiian/Pacific Islander	5 (1.4%)	0 (0.0%)	2 (1.5%)	3 (2.0%)	
White	232 (63.2%)	54 (65.1%)	78 (58.2%)	100 (66.7%)	
Multiracial	7 (1.9%)	1 (1.2%)	2 (1.5%)	4 (2.7%)	
Prefer not to answer/Other/Missing	38 (10.4%)	9 (10.8%)	13 (9.7%)	16 (10.7%)	
Self-reported ethnicity, <i>n</i> (%)					
Latinx or Hispanic	15 (4.1%)	2 (2.4%)	6 (4.5%)	7 (4.7%)	0.733
Not Latinx or Hispanic	330 (89.9%)	74 (89.1%)	122 (91.0%)	134 (89.3%)	
Prefer not to answer/Other/Missing	22 (6.0%)	7 (8.4%)	6 (4.5%)	9 (6.0%)	
Specialty, <i>n</i> (%)					
Family medicine	159 (43.3%)	31 (37.3%)	60 (44.8%)	68 (45.3%)	0.301
General practice	8 (2.2%)	0 (0.0%)	3 (2.2%)	5 (3.3%)	
Internal medicine	200 (54.5%)	52 (62.7%)	71 (53.0%)	77 (51.4%)	
Genetics training beyond medical school, <i>n</i> (%)					
Additional training	38 (10.4%)	7 (8.4%)	9 (6.7%)	22 (14.7%)	0.073
No additional training/Missing	329 (89.6%)	76 (91.6%)	125 (93.3%)	128 (85.3%)	
US Region					
Midwest	82 (22.3%)	16 (19.3%)	35 (26.1%)	31 (20.1%)	0.701
Northeast	83 (22.6%)	21 (25.3%)	30 (22.3%)	32 (21.3%)	
South	97 (26.4%)	21 (25.3%)	30 (22.4%)	46 (30.7%)	
West	105 (28.6%)	25 (30.1%)	39 (29.1%)	41 (27.3%)	
Rurality <sup>2</sup>					
Rural	28 (7.6%)	4 (4.8%)	14 (10.4%)	10 (6.7%)	0.302
Urban	339 (92.4%)	79 (95.2%)	120 (89.6%)	140 (93.3%)	

<sup>1</sup>Average posterior probabilities > 0.70 indicate well-separated classes. <sup>2</sup>Inferred from practice 5-digit ZIP code and USDA Rural-Urban Commuting Area Codes categorizations (4–10 considered rural; Micropolitan area with primary flow to urban clusters < 50,000 population). <sup>3</sup>*p*-value estimate associated with differences in demographic features among predicted classes. ANOVA test used to compare continuous values and chi-square test or Fisher's exact test used to compare categorical demographic features depending on cell sizes.

and effective communication to PCPs and patients that doing so is to reduce preventive care-related risks and not about rationing health care [34, 35].

The barriers to clinical PRS implementation that PCPs selected are consistent with prior studies, in which common concerns about the use of PRS included lack of knowledge or confidence [36–38], insufficient evidence or guidelines to support their use [37, 39–41], and insurance discrimination and other ethical issues [36, 37, 41, 42]. In the present survey, it is noteworthy that out-of-pocket costs and concerns about patient insurance discrimination were among the three most commonly selected barriers to PRS

implementation. Respondents brought their own information and perceptions in these responses, as the survey did not inform them about the cost of PRS testing or about the Genetic Information Nondiscrimination Act of 2008, which prohibits discrimination on the basis of genetic information in employment and health insurance, but not in life or disability insurance [43]. The majority (73%) of respondents categorized insufficient time to explain PRS to patients as at least somewhat of a barrier; however, given concerns about PCP burnout, it is striking that this was the least often selected potential barrier. Barrier response patterns varied among the 3 latent classes of PCP identified from the data.



**Fig. 4 Observed survey item endorsements by predicted class membership.** Data are proportions of respondents endorsing greater agreement or barrier significance for selected dichotomized items. \*\*Item included in final latent class analysis model.

*Enthusiasts* generally endorsed few barriers to the use of PRS beyond out-of-pocket costs, while *skeptics* and *learners* also often identified patient anxiety, unintended harms, insufficient understanding, and the lack of studies among non-European populations as concerns. *Learners* were distinguished from *skeptics* in their agreement that PRS might help improve health decision-making and outcomes.

These findings point to a research and policy agenda to promote the appropriate uptake of PRS into preventive care. First, additional research is needed to clarify the benefits and harms of PRS-informed risk stratification. The necessary evidence will need to detail the specific diseases and patient populations for which PRS might have the most favorable benefit-to-harm ratio. This evidence will likely come from a combination of clinical epidemiology and modeling studies, select randomized trials, and clinical implementation projects and should prioritize important clinical outcomes. Second, this evidence should inform the development of clinical guidelines from relevant

professional organizations for the appropriate use of PRS in clinical care. Given the proliferation of PRS, it will be beneficial for such organizations to state proactively the benchmarks that a PRS must meet to prove beneficial for the preventive care of their diseases of interest, even if they do not find the evidence supports such use at the present time. If guidelines do endorse the use of PRS, they should include both recommendations for appropriate management and identification of what they would consider inappropriate management, to check any overinterpretation of results that might occur among the *believers* in our study. Such guidelines would also address the *learners* who wanted guidance on how to use PRS and the *skeptics* who were concerned about their uncertain utility and the harms and unnecessary tests and treatments that might result. They could also be incorporated into clinical decision support tools within the electronic medical record to promote appropriate usage. Third, educational initiatives including medical school curricula, continuing medical education, and genetics specialist

consultations should be developed to support the *learners* in our study and others with lower understanding of and confidence in using PRS [44]. Fourth, professional organizations and healthcare systems should summarize information about cost and insurance discrimination to PCPs ordering PRS testing. This information is complex, dynamic, and variable by country and U.S. state [45], but providers and patients will need accurate information to make informed decisions.

One limitation of this study is its hypothetical nature. Few respondents likely have actual clinical experience with PRS, and their responses might not reflect their actual practice patterns as PRS become more commonplace. Second, although this is the largest national physician survey about PRS to date, only 10.8% of invited PCPs opened the survey invitation email. This rate compares favorably with those of other large national physician surveys, including those about genetic testing and precision medicine [26, 38, 46–48]. Response rate is not the best indicator of non-response bias [49], and our comparison of the sample to the target population gives some support for its representativeness. The invitation described the study as a “survey on precision prevention in primary care.” Respondents may have had more interest in PRS than average PCPs, but we nonetheless observed a range of positive and negative attitudes.

In conclusion, data from a national survey about PRS to date suggest that PCPs see utility in using PRS in preventive medicine. The pressing needs for the future of PRS implementation include evidence and guidelines to support their appropriate use by PCPs and clarity around their financial consequences.

## DATA AVAILABILITY

The dataset supporting the current study has not been deposited in a public repository but is available from the corresponding author on reasonable request.

## REFERENCES

- Lewis ACF, Green RC, Vassy JL. Polygenic risk scores in the clinic: Translating risk into action. *Hum Genet Genomics Adv* 2021;2:100047.
- Lewis CM, Vassos E. Polygenic risk scores: from research tools to clinical instruments. *Genome Med*. 2020;12:44.
- Lambert SA, Abraham G, Inouye M. Towards clinical utility of polygenic risk scores. *Hum Mol Genet*. 2019;28:R133–42.
- Khera AV, Chaffin M, Aragam KG, Haas ME, Roselli C, Choi SH, et al. Genome-wide polygenic scores for common diseases identify individuals with risk equivalent to monogenic mutations. *Nat Genet*. 2018;50:1219–24.
- Conti DV, Darst BF, Moss LC, Saunders EJ, Sheng X, Chou A, et al. Trans-ancestry genome-wide association meta-analysis of prostate cancer identifies new susceptibility loci and informs genetic risk prediction. *Nat Genet*. 2021;53:65–75.
- Mavaddat N, Michailidou K, Dennis J, Lush M, Fachal L, Lee A, et al. Polygenic Risk Scores for Prediction of Breast Cancer and Breast Cancer Subtypes. *Am J Hum Genet*. 2019;104:21–34.
- Wojcik GL, Graff M, Nishimura KK, Tao R, Haessler J, Gignoux CR, et al. Genetic analyses of diverse populations improves discovery for complex traits. *Nature*. 2019;570:514–8.
- National Human Genome Research Institute. Polygenic Risk Methods in Diverse populations (PRIMED) Consortium. Accessed July 2, 2021. <https://www.genome.gov/Funded-Programs-Projects/PRIMED-Consortium>
- Ruan Y, Lin YF, Feng YCA, Chen CY, Lam M, Guo Z, et al. Improving polygenic prediction in ancestrally diverse populations. *Nat Genet*. 2022;54:573–80.
- Hao L, Kraft P, Berriz GF, Hynes ED, Koch C, Koratgeri P, et al. Development of a clinical polygenic risk score assay and reporting workflow. *Nat Med*. 2022;28:1006–13.
- National Human Genome Research Institute (NHGRI). Electronic Medical Records and Genomics (eMERGE) Network. Published February 23, 2020. Accessed November 9, 2022. <https://www.genome.gov/Funded-Programs-Projects/Electronic-Medical-Records-and-Genomics-Network-eMERGE>
- Widén E, Junna N, Ruotsalainen S, Surakka IDA, Mars N, Ripatti P, et al. How Communicating Polygenic and Clinical Risk for Atherosclerotic Cardiovascular Disease Impacts Health Behavior: an Observational Follow-up Study. *Circ Genomic Precis Med*. 0:CIRCGEN.121.003459. <https://doi.org/10.1161/CIRCGEN.121.003459>
- Maamari DJ, Brockman DG, Aragam K, Pelletier RC, Folkerts E, Neben C, et al. Clinical Implementation of Combined Monogenic and Polygenic Risk Disclosure for Coronary Artery Disease. *JACC Adv*. 2022;1:100068.
- Muse ED, Chen SF, Liu S, Fernandez B, Schrader B, Molparia B, et al. Impact of polygenic risk communication: an observational mobile application-based coronary artery disease study. *NPJ Digit Med*. 2022;5:30.
- Hughes E, Tshiabla P, Wagner S, Judkins T, Rosenthal E, Roa B, et al. Integrating Clinical and Polygenic Factors to Predict Breast Cancer Risk in Women Undergoing Genetic Testing. *JCO Precis Oncol*. 2021;5:PO.20.00246. <https://doi.org/10.1200/PO.20.00246>
- Mujwara D, Henno G, Vernon ST, Peng S, Domenico PD, Schroeder B, et al. Integrating a polygenic risk score for coronary artery disease as a risk-enhancing factor in the pooled cohort equation: A cost-effectiveness analysis study. *J Am Heart Assoc*. 2022;11:e025236.
- Xu J, Resurreccion WK, Shi Z, Wei J, Wang CH, Zheng SL, et al. Inherited risk assessment and its clinical utility for predicting prostate cancer from diagnostic prostate biopsies. *Prostate Cancer Prostat Dis*. 2022;25:422–30.
- O'Sullivan JW, Raghavan S, Marquez-Luna C, Luzum JA, Damrauer SM, Ashley EA, et al. Polygenic risk scores for cardiovascular disease: A scientific statement from the American Heart Association. *Circulation*. 2022;146:e93–e118.
- Kiflen M, Le A, Mao S, Lali R, Narula S, Xie F, et al. Cost-effectiveness of polygenic risk scores to guide statin therapy for cardiovascular disease prevention. *Circ Genom Precis Med*. 2022;15:386–95.
- Callender T, Emberton M, Morris S, Eeles R, Kote-Jarai Z, Pharoah PDP, et al. Polygenic risk-tailored screening for prostate cancer: A benefit-harm and cost-effectiveness modelling study. *PLoS Med*. 2019;16:e1002998.
- Eysenbach G. Improving the quality of Web surveys: the Checklist for Reporting Results of Internet E-Surveys (CHERRIES). *J Med Internet Res*. 2004;6:e34.
- Kerman BJ, Brunette CA, Harris EJ, Antwi AA, Lemke AA, Vassy JL. Primary care physician use of patient race and polygenic risk scores in medical decision-making. *Genet Med*. 2023. <https://doi.org/10.1016/j.gim.2023.100800>
- Fraze TK, Lewis VA, Wood A, Newton H, Colla CH. Configuration and Delivery of Primary Care in Rural and Urban Settings. *J Gen Intern Med*. 2022;37:3045–53.
- Physician Survey on Cancer Susceptibility Testing. Accessed March 9, 2022. <https://healthcaredelivery.cancer.gov/susceptibility/>
- National Survey of Primary Care Physicians' Recommendations & Practice for Breast, Cervical, Colorectal, & Lung Cancer Screening. Accessed March 9, 2022. [https://healthcaredelivery.cancer.gov/screening\\_rp/](https://healthcaredelivery.cancer.gov/screening_rp/)
- Grant RW, Hivert M, Pandiscio JC, Florez JC, Nathan DM, Meigs JB. The clinical application of genetic testing in type 2 diabetes: a patient and physician survey. *Diabetologia*. 2009;52:2299–305.
- Lemke AA, Amendola LM, Kuchta K, Dunnenberger HM, Thompson J, Johnson C, et al. Primary care physician experiences with integrated population-scale genetic testing: A Mixed-Methods Assessment. *J Pers Med*. 2020;10:165.
- Mikat-Stevens NA, Larson IA, Tarini BA. Primary-care providers' perceived barriers to integration of genetics services: a systematic review of the literature. *Genet Med J Am Coll Med Genet*. 2015;17:169–76.
- Christensen KD, Vassy JL, Jamal L, Lehmann LS, Slashinski MJ, Perry DL, et al. Are physicians prepared for whole genome sequencing? a qualitative analysis. *Clin Genet*. 2016;89:228–34.
- Collins LM, Lanza ST. *Latent Class and Latent Transition Analysis: With Applications in the Social, Behavioral, and Health Sciences* | Wiley.; 2009. Accessed March 22, 2022. <https://www.wiley.com/en-us/Latent+Class+and+Latent+Transition+Analysis%3A+With+Applications+in+the+Social%2C+Behavioral%2C+and+Health+Sciences-p-9780470228395>
- Musiienko A Commission Bias. In: Raz M, Pouryahya P, eds. *Decision Making in Emergency Medicine: Biases, Errors and Solutions*. Springer; 2021:77–82. [https://doi.org/10.1007/978-981-16-0143-9\\_13](https://doi.org/10.1007/978-981-16-0143-9_13)
- Blumenthal-Barby JS, Krieger H. Cognitive Biases and Heuristics in Medical Decision Making: A Critical Review Using a Systematic Search Strategy. *Med Decis Mak*. 2015;35:539–57.
- Laza-Vázquez C, Codern-Bové N, Cardona-Cardona À, Hernández-Leal MJ, Pérez-Lacasta MR, Carles-Lavila M, et al. Views of health professionals on risk-based breast cancer screening and its implementation in the Spanish National Health System: A qualitative discussion group study. *PLoS One*. 2022;17:e0263788.
- McWilliams L, Woof VG, Donnelly LS, Howell A, Evans DG, French DP. Risk stratified breast cancer screening: UK healthcare policy decision-making stakeholders' views on a low-risk breast screening pathway. *BMC Cancer*. 2020;20:680.
- Hall AE, Chowdhury S, Hallowell N, Pashayan N, Dent T, Pharoah P, et al. Implementing risk-stratified screening for common cancers: A review of potential ethical, legal and social issues. *J Public Health*. 2014;36:285–91.
- Hauser D, Obeng AO, Fei K, Ramos MA, Horowitz CR. Views Of primary care providers on testing patients for genetic risks for common chronic diseases. *Health Aff Proj Hope*. 2018;37:793–800.

37. Puryear L, Downs N, Nevedal A, Lewis ET, Ormond KE, Bregendahl M, et al. Patient and provider perspectives on the development of personalized medicine: a mixed-methods approach. *J Community Genet*. 2018;9:283–91.
38. Nisselle A, King EA, McClaren B, Janinski M, Metcalfe S, Gaff C, et al. Measuring physician practice, preparedness and preferences for genomic medicine: a national survey. *BMJ Open*. 2021;11:e044408.
39. Woof VG, McWilliams L, Donnelly LS, Howell A, Evans DG, Maxwell AJ, et al. Introducing a low-risk breast screening pathway into the NHS Breast Screening Programme: Views from healthcare professionals who are delivering risk-stratified screening. *Womens Health Lond Engl*. 2021;17:17455065211009746. <https://doi.org/10.1177/17455065211009746>
40. Carroll JC, Makuwaza T, Manca DP, Sopcak N, Permaul JA, O'Brien MA, et al. Primary care providers' experiences with and perceptions of personalized genomic medicine. *Can Fam Physician*. 2016;62:e626–35.
41. Erdmann A, Rehmann-Sutter C, Bozzaro C. Patients' and professionals' views related to ethical issues in precision medicine: a mixed research synthesis. *BMC Med Ethics*. 2021;22:116.
42. Hamilton JG, Abdiwahab E, Edwards HM, Fang ML, Jdayani A, Breslau ES. Primary care providers' cancer genetic testing-related knowledge, attitudes, and communication behaviors: A systematic review and research agenda. *J Gen Intern Med*. 2017;32:315–24.
43. Green RC, Lautenbach D, McGuire AL. GINA, genetic discrimination, and genomic medicine. *N. Engl J Med*. 2015;372:397–9.
44. Slunecka JL, van der Zee MD, Beck JJ, Johnson BN, Finnicum CT, Pool R, et al. Implementation and implications for polygenic risk scores in healthcare. *Hum Genomics*. 2021;15:46.
45. Joly Y, Huerne K, Arych M, Bombard Y, Dove E, Granados Moreno P, et al. The Genetic Discrimination Observatory: confronting novel issues in genetic discrimination. *Trends Genet TIG*. 2021;37:951–4.
46. Bonter K, Desjardins C, Currier N, Pun J, Ashbury FD. Personalised medicine in Canada: a survey of adoption and practice in oncology, cardiology and family medicine. *BMJ Open*. 2011;1:e000110.
47. Hickner J, Thompson PJ, Wilkinson T, Epner P, Sheehan M, Pollock A, et al. Primary care physicians' challenges in ordering clinical laboratory tests and interpreting results. *J Am Board Fam Med JABFM*. 2014;27:268–74.
48. Haga SB, Kim E, Myers RA, Ginsburg GS. Primary Care physicians' knowledge, attitudes, and experience with personal genetic testing. *J Pers Med*. 2019;9:29.
49. Davern M. Nonresponse rates are a problematic indicator of nonresponse bias in survey research. *Health Serv Res*. 2013;48:905–12.

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CRediT category: Conceptualization: JLV, BJK; Data curation: EJH, KI, TY; Formal analysis: CAB; Funding acquisition: JLV, BJK; Investigation: JLV, BJK, EJH; Methodology: JLV, BJK, EJH, AAL, MLC, JLV; Project administration: EJH, AAA; Software: EJH, TY, CAB; Supervision: JLV; Validation: EJH, CAB; Visualization: JLV, BJK, EJH, KI, TY, CAB; Writing - original draft: JLV, CAB; Writing - review & editing: JLV, BJK, EJH, AAL, MLC, AAA, KI, TY, CAB.

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## COMPETING INTERESTS

The authors declare no conflicts of interest. JLV, MLC, AAA, TY, and CAB are employees of the U.S. Department of Veterans Affairs (VA). The views expressed in this manuscript do not represent those of the U.S. government or VA.

## ETHICAL APPROVAL

The study was approved by the Harvard Longwood Campus Institutional Review Board (Protocol #20-2098). All participants consented to participation in the research.

## ADDITIONAL INFORMATION

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