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Payer Coverage for Hereditary Cancer Panels: Barriers, Opportunities, and Implications for the Precision Medicine Initiative

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Abstract

Background: Hereditary cancer panels (HCPs), testing for multiple genes and syndromes, are rapidly transforming cancer risk assessment but are controversial and lack formal insurance coverage. We aimed to identify payers' perspectives on barriers to HCP coverage and opportunities to address them. Comprehensive cancer risk assessment is highly relevant to the Precision Medicine Initiative (PMI), and payers' considerations could inform PMI's efforts. We describe our findings and discuss them in the context of PMI priorities. **Methods:** We conducted semi-structured interviews with 11 major US payers, covering >160 million lives. We used the framework approach of qualitative research to design, conduct, and analyze interviews, and used simple frequencies to further describe findings. **Results:** Barriers to HCP coverage included poor fit with coverage frameworks (100%); insufficient evidence (100%); departure from pedigree/family history–based testing toward genetic screening (91%); lacking rigor in the HCP hybrid research/clinical setting (82%); and patient transparency and involvement concerns (82%). Addressing barriers requires refining HCP-indicated populations (82%); developing evidence of actionability (82%) and pathogenicity/penetrance (64%); creating infrastructure and standards for informing and recontacting patients (45%); separating research from clinical use in the hybrid clinical-research setting (44%); and adjusting coverage frameworks (18%). **Conclusions:** Leveraging opportunities suggested by payers to address HCP coverage barriers is essential to ensure patients' access to evolving HCPs. Our findings inform 3 areas of the PMI: addressing insurance coverage to secure access to future PMI discoveries; incorporating payers' evidentiary requirements into PMI's research agenda; and leveraging payers' recommendations and experience to keep patients informed and involved.

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Background

Identification of hereditary cancer predisposition is an important component of cancer risk management, prevention, and treatment.^{1–3} Its significance was underscored recently by President Obama's Precision

Medicine Initiative (PMI) announced in 2015,^{4,5} with objectives that include advancing inherited cancer genomics.^{6–8} The advent of hereditary cancer panels (HCPs)—defined here as multigene, multisynndrome, next-generation sequencing panels for hereditary can-

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cer testing containing well-studied and less-studied genes—is reshaping clinical cancer risk assessment and igniting cancer genetics research.^{9–13} HCPs represent a transitional step between traditional single-gene/single-syndrome testing and whole-genome/exome sequencing (WGS/WES),^{14–16} and some of the advantages of HCPs serve as a proxy for those of WGS/WES, including more comprehensive and rapid testing than step-wise single-gene assessment, identification of risk not suggested by pedigree, and accelerated data collection for research.^{12,13,15–17} However, the clinical appropriateness of using HCPs instead of pedigree- or phenotype-directed single-gene tests is hotly debated^{17–19}; guidelines recommend caution^{1,2} and some experts consider their broadening clinical use premature.^{14,18,20,21} Nevertheless, HCP commercial offerings proliferate^{9,17,21} and their increasing clinical adoption is viewed by some as “the train that’s left the station.”^{10,11}

Adding to the controversy is the complexity of HCPs’ insurance coverage and reimbursement. Although HCP providers may receive ad hoc payment (eg, when billing with generic or single-gene test codes, or on appeal^{22,23}), payers don’t formally cover HCPs.^{23–25} Our previous review of the 17 largest US private payers’ policies for HCPs containing *BRCA1/2* genes found no positive coverage as of May 2015.²² The absence of formal coverage causes reimbursement inconsistency and uncertainty, impacts patient access, and contributes to practice heterogeneity. Indicating a continued lack of coverage, our more recent data for 5 of the largest private payers from the University of California, San Francisco (UCSF) TRANSPERS Payer Coverage Policy Registry²⁶ showed no or substantially limited HCP coverage (see [supplemental eAppendix 1](#), available with this article at [JNCCN.org](#)). These and other data noted earlier motivated the present study, for which the objective is to elucidate payers’ barriers to HCP coverage and opportunities to address them (the 5 payers in [supplemental eAppendix 1](#) are part of the 11-payer cohort in the present study).

Understanding payers’ coverage decision-making is critical for clarifying the HCP reimbursement state for patients and physicians, informing genetic research, and ultimately enabling access to these potentially transformative modalities. Barriers to HCP coverage foreshadow those of WGS/WES, and ad-

ressing them may facilitate future access to WGS/WES as science evolves. Further, payers’ HCP coverage considerations have particular relevance to the PMI and its effort to assemble and study an unprecedented cohort of ≥ 1 million volunteers (PMI cohort, or the All of Us Research Program) who will contribute genomic, clinical, and lifestyle data to accelerate genetic science.^{4,5,7} Incorporation of increasingly comprehensive genomic testing into our understanding of cancer risk and approaches to treatment is integral to the PMI,²⁷ which will likely contribute to further development of multigene testing technologies. Thus, challenges to insurance coverage of these technologies must be understood and addressed proactively to ensure effective translation of future PMI results into care. Payer evidentiary requirements for HCPs could inform PMI’s research agenda and increase future relevance of research outcomes to payers’ coverage decisions. This article describes our study findings and discusses their implications for the PMI.

Methods

The study was approved by the UCSF Institutional Review Board. We adapted the framework approach of qualitative research^{28,29} for study design and data analysis as an effective method for eliciting stakeholders’ perspectives (including payers and clinical experts) and examining coverage issues, previously used by us and other researchers.^{30–37}

We first conducted semi-structured interviews with 12 clinical experts possessing direct knowledge of and experience in HCP research and clinical applications; development of the expert interview guide ([supplemental eAppendix 2](#)) was informed by literature review. The interviews focused on identifying characteristic HCP features, HCP advantages compared with single-gene testing, and HCP controversies and challenges ([supplemental eAppendix 2](#)). Phone interviews took 45 to 55 minutes each and were taped, transcribed, and analyzed for common themes, according to the framework approach, by 2 independent investigators. Discrepancies were resolved by discussion and consensus. Resulting themes were summarized into an HCP Case Study (Table 1), and helped formulate the structure and content of the payer interview questions ([supplemental eAppendix 2](#)).

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Table 1. HCP Case Study: Features, Benefits, and Controversies^a

HCP ^b Characteristics	Description
HCP features ^{9,10,15,21,22}	
Disease scope	One cancer, multiple syndromes (eg, panels for hereditary breast cancer, testing for HBOC, Li-Fraumeni, Cowden, and Peutz-Jeghers syndromes) Multiple cancers, multiple syndromes
Number of genes	Range from 6 to >100 genes
Familiarity of genes	Well-studied genes: high familiarity and evidence on pathogenicity, cancer risk, and/or intervention outcomes (eg, <i>BRCA1/2</i>) Less-studied genes: lower familiarity, less evidence on pathogenicity, and/or risk level
Testing results	Pathogenic variant: results in a dysfunctional protein, consistent with a disease phenotype VUS: sequence variant (usually subtle, such as a single nucleotide polymorphism or other missense change) that may or may not result in a dysfunctional protein and a disease phenotype Normal: no variation from normal sequence
Gene penetrance	High penetrance: alterations confer high lifetime risk of cancer (40%–80%) Medium penetrance: alterations confer medium lifetime risk of cancer (20%–40%)
HCP advantages vs single gene testing ^{1,10,13,17,22}	
Address syndrome heterogeneity and overlaps	Increasing understanding that pedigree may not be suggestive of particular alterations HCPs identify alterations that would not have been evaluated in phenotype-directed testing
Testing efficiency effectiveness	Streamlines testing compared to step-wise, single-gene testing; prevents testing fatigue for patients and clinicians; sequences more genes for comparable cost
Accelerate research in a hybrid research/clinical setting	The setting of combined research and clinical use is emerging, resembling the evolution of clinical <i>BRCA1/2</i> testing Considered an effective way to advance research on less-studied genes and reclassify VUS to clinically useful results, which would otherwise take decades and vast patient cohorts
Expedite application of future research	Inclusion of less-studied genes allows to expediently identify and recontact relevant patients when new evidence becomes available
HCP controversies and challenges ^{1,9–11,16,18,20}	
Debate on how to determine actionability	Should management of less-studied alterations with moderate to high cancer risk (1) be similar to that of well-studied alterations or (2) be studied to prove outcomes?
Require a different genetic counseling model	HCPs require extensive pretest and posttest genetic counseling, but the current counseling paradigm based on single-gene testing is not adequate for HCPs
Emerging state of evidence and guidelines	Scarce validity and utility/actionability data for many HCP genes, and lack of consistency and clarity in guidelines have not prevented HCP clinical adoption

Abbreviations: HBOC, hereditary breast and ovarian cancer syndrome; HCP, hereditary cancer panel; VUS, variant of uncertain significance.

^aThis case study describes illustrative features, advantages, and challenges of HCPs and does not represent a comprehensive analysis of HCPs.

^bHCPs are defined here as next-generation sequencing assays that simultaneously test multiple genes for susceptibility to multiple cancer syndromes, sequence both well-studied and less-studied genes, include high and moderate penetrance alterations, and return VUS.

Subsequently, semi-structured interviews were conducted with 11 private US payers. We focused the study on private payers because they collectively cover nearly two-thirds of the insured US population,³⁸ and their policies impact the public health plans they manage, such as some state Medicaid and Medicare Advantage programs.³⁹

We used purposive sampling⁴⁰ to assemble the payer and clinical expert interview cohorts, both recruited via the UCSF TRANSPERS Evidence and Reimbursement Policy Advisory Council. All member-payers chose to participate in the study. The payer cohort included senior executives with coverage

decision-making responsibilities from the 8 largest US private payers and 3 regional payers, collectively covering >160 million enrollees.⁴¹

An interview guide, including the HCP Case Study (Table 1) and interview questions ([supplemental eAppendix 2](#)), was provided before the interviews. The semi-structured phone interviews with payers were conducted between February and June 2015. Two investigators performed independent thematic coding and analysis, resolving disagreement by discussion and consensus. We used simple frequencies to further describe identified themes.

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Results

Payer interviews revealed a range of themes reflecting payers' perspectives on barriers to positive HCP coverage and suggested opportunities to overcome them. The following sections describe the findings by categories of barriers and opportunities (summarized in Table 2).

HCPs Do Not Fit Payer Coverage Frameworks

Most payers (73%) stated that they understood why novel HCP features present unique appeal to clinicians and patients. Payers recognized that the inclusion of less-studied genes in panels promotes research and helps future dissemination of new genetic knowledge via patient recontacting (64%). They also acknowledged limitations in our current understanding of phenotype/genotype associations and agreed that multisymptom testing may identify alterations unsuspected from pedigree (73%). However, interviewees explained that these very features make positive coverage challenging, because they do not fit exist-

ing coverage frameworks. Because HCPs include both well-studied (“medically necessary”) and less-studied (“experimental/investigational”) genes, they don't fit either category; thus, an entire panel is deemed experimental. Although all payers noted this barrier, only 18% believed that coverage frameworks should be modified to align with panel features and benefits. Three other payers (27%) contemplated potential approaches to HCP coverage, including separating billing/coding for medically necessary from experimental/investigational genes in one HCP and paying only for those medically necessary, and/or requiring that a test provider establish a registry studying experimental/investigational genes within a panel, with demonstrated research rigor and data-sharing practices.

Similarly, interviewees described that the departure from phenotype-directed testing conflicts with the current concept of predefined medical necessity of specific suspected genes, and will likely lead to indiscriminant genetic screening (91%). However, they signaled their willingness to expand testing populations and relax testing criteria if evidence of

Table 2. Payers' Perspectives on Barriers to HCP Insurance Coverage and Opportunities to Address Barriers

Barrier Categories; % of Payers Noting at Least One Challenge (N=11)	Payers' Description of Specific Barriers (N=11)	Payer Recommendations to Address Barriers (N=11)
HCPs don't fit payers' coverage frameworks (100%)	HCPs don't fit definitions of “medically necessary” and “investigational” (100%)	Align the coverage frameworks to enable evaluation of new tests, such as HCPs (18%) Adjust the coverage frameworks to account for non-direct clinical benefits, such as ease of use (18%)
	HCPs move genetic testing toward genetic screening vs testing in preselected populations (91%)	Prove existence and prevalence of syndrome/gene heterogeneity (73%) Better define subpopulations indicated for HCP to avoid universal screening and develop panels for these subpopulations (82%)
Gaps in evidence (100%)	Lacking evidence of pathogenic significance and penetrance of many variants in panels (100%)	Must have evidence of significance and penetrance for all genes on an HCP (64%) Develop standards and decision tools for patients and clinicians to deal with less proven variants in HCPs (27%)
	Lacking definition and data on actionability of cancer genetic alterations (82%)	Define criteria when penetrance data are sufficient, and when outcomes data are needed (36%) Evidence of penetrance is sufficient to determine actionability (27%)
Hybrid research/clinical setting for HCPs is not acceptable by payers (91%)	Lack of research rigor and transparency (82%)	Develop a novel, rigorous, transparent model for the hybrid approach, delineating research and standard care (44%)
	Hybrid means de facto coverage/reimbursement for research (73%)	Hybrid should separate funding of research vs standard care (36%)
Patient engagement in HCP testing (82%)	Lack of transparency to patients (73%)	Increase transparency to patients on the state of evidence for HCPs and related interventions (73%) Capture and accommodate patient preferences for testing and recontacting (45%) Determine patient utility of HCPs via patient reported outcomes research (36%)
	Patient recontacting with new data is ad hoc, not standard (64%)	Establish and standardize process, infrastructure, and accountability for recontacting (45%)

Abbreviation: HCPs, hereditary cancer panels.

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syndrome heterogeneity were provided (73%), and the relevant populations were more precisely defined to avoid “universal testing” (82%). Payers noted specific end points for these evidentiary requirements, including identifying which syndromes overlap and in what combinations; determining prevalence of overlaps compared with single-syndrome prevalence; and elucidating characteristics of populations with overlaps to indicate appropriateness of panel testing.

Gaps in Evidence on HCPs, and Views on Genetic Alteration Actionability

All interviewees stated that a major impediment to HCP coverage is insufficient evidence on less-studied genes, specifically evidence of clinical validity with respect to pathogenicity (association with a cancer syndrome) and penetrance (degree of cancer risk). Although most payers (64%) would require this evidence for all genes in an HCP, a minority (27%) stated they could cover panels with less-studied genes if specific protocols and tools were developed for patients/families and clinicians to guide posttest decisions and prevent unnecessary testing, interventions, and anxiety.

Most payers (82%) also noted the scarcity of data on HCP clinical utility, particularly actionability of alterations in less-studied genes. However, their opinions varied on how actionability should be defined, specifically, (1) whether management of alterations in less-studied genes conferring moderate to high cancer risk should be similar to that of alterations in well-understood genes (eg, *BRCA1/2*), or (2) whether management strategies should be studied for alterations in each newly tested gene to prove their effectiveness. Only a minority of payers (36%) would require that the outcomes of interventions for alterations in each new gene be studied if these interventions are already proven for alterations in other genes related to the same syndrome. Conversely, other payers stated that outcomes studies of alterations in each newly tested gene are not necessary: 27% regarded the “similar management” approach as reasonable, whereas another 36% suggested a mixed model, which would require outcome studies for some but not all genes, based on “plausibility of similarity in outcomes with alterations in known genes” and on syndrome prevalence. Lack of agreement between medical societies on how to de-

fine an actionable mutation was noted as a barrier by 82% of interviewees.

Nine payers (82%) shared perspectives on what study designs may constitute evidence acceptable for HCP coverage (data are not shown in Table 2). They noted that randomized control trials may not be required; observational studies, registries, and pooled studies could be acceptable, as long as they are large enough to demonstrate statistical power and significance of findings. A total of 18% would require at least one additional study to confirm original findings, citing particular importance of the “do no harm” in asymptomatic populations. Although 82% of payers would require the studies to be published in peer-reviewed journals, they did not share preferences for particular journals, and 27% would take guidance from medical societies to assess reputability of published results.

HCPs' Hybrid Clinical/Research Setting is Concerning

Payers recognized that HCPs are used in a hybrid research/clinical setting, in which increasing HCP clinical use generates data to elucidate validity and utility of less-studied genes, in turn enhancing HCP clinical use. Interviewees acknowledged that this approach may accelerate data collection and that it enabled the past evolution of *BRCA1/2* testing. Nonetheless, payers considered the hybrid setting inappropriate as either a clinical or a research model (91%), because as a clinical setting, it uses unproven testing, and as a research setting, it lacks rigor and transparency, putting resulting data into question (82%). Additionally, 73% of interviewees were concerned that if they cover HCP clinical use, they will be paying for research in the hybrid setting. They commented that financing research, either by covering experimental technologies or by direct funding, conflicts with payers' mandate to cover only nonexperimental technologies, causes objection from employers (customers of the payers), and confers legal implications. However, interviewees understood that traditionally designed research studies in asymptomatic patients may require decades and large patient cohorts, and realized that the research paradigm is changing. Therefore, they may be willing to support the hybrid HCP setting if it is transformed to a more rigorous, transparent model clearly delineating research from standard care (45%). Additionally, payers shared how they could support research with-

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out directly funding it, including (1) obtaining grants from payer company foundations; (2) paying for standard care within a research study, as required by the Affordable Care Act; (3) encouraging collaborations between researchers and payers' clinical analysts to develop combined data sets and shorten the research cycle; and (4) identifying large self-insured employers who may be willing to work with a payer to underwrite a research study, if interested in HCPs for their employee base.

Concerns About Patients' Understanding and Engagement

Most interviewees (82%) expressed concerns about the impact of HCP testing on patients, and stated that these concerns influenced their coverage decisions. They believed that despite informed consent and genetic counseling, patients may not understand the immature state of evidence about numerous genes within panels (73%) and that their data are used for research, to which many would object if better informed. Payers' suspicion that many patients do not receive pretest and/or posttest genetic counseling exacerbated these concerns.

In payers' opinions, the merit of hereditary panel testing may be overpromised to patients by clinicians and test providers. One interviewee noted, "Genetics is met with breathless excitement that's not backed by solid evidence, and not demystified for patients." One such unfounded promise is to capture less-understood alterations now, and later, when more definitive knowledge about their significance becomes available, recontact patients with relevant alterations and offer medical management without retesting. Although 73% of payers agreed that this may be beneficial, 64% were skeptical about the feasibility of fulfilling this promise and about variability of recontacting practices across clinicians and genetics laboratories. Addressing these issues will require creating an industry-wide secure recontacting infrastructure, developing standard evidence thresholds and analytics for recontacting, and establishing approaches to honoring patients' data storage and recontacting preferences.

Discussion

This study examined private payers' perspectives on barriers and opportunities for insurance coverage of

HCPs. Identified barriers included poor fit of HCPs with coverage frameworks, evidence gaps on cancer risk and actionability for numerous genes in panels, insufficient rigor of the HCP's hybrid clinical/research setting, and concerns about appropriate patient transparency and involvement in HCP testing. Payers also shared opportunities to overcome barriers, suggesting evidence that could both meet coverage requirements and be feasible to obtain, outlining improvements to the hybrid HCP setting and approaches to informing patients, and even indicating a possibility of adjusting the diagnostic coverage frameworks. This work builds on our previous study on challenges to coverage for tumor sequencing,³⁴ and expands prior findings by identifying coverage barriers unique to HCPs and providing payers' perspectives on potential solutions. This section discusses the study's relevance to the present and future of HCP and cancer multigene testing. We also discuss implications for the PMI, because of its paramount importance, breadth, and potential to frame solutions to evidentiary and policy challenges, including those of HCPs.

Implications for Practices and Reimbursement of Cancer Multigene Testing: Present and Future

The current HCP reimbursement is complex and confusing for clinicians and patients: although payers formally do not cover HCPs, they may still pay for them, depending on how HCPs are billed or whether they are appealed.^{22,23} This creates payment uncertainty among payers and among patients within one payer, impeding the ability of medical institutions to develop consistent ordering and clinical protocols and exacerbating heterogeneity of related clinical decisions and practices. Further, variability of HCP reimbursement may increase already existing disparities in access to cancer genetic testing,⁴²⁻⁴⁴ particularly for medically and socioeconomically vulnerable patients unable to pay out-of-pocket for the more contemporary multigene tests. Our study's findings clarify the confusing HCP reimbursement environment and could help medical institutions' shorter-term efforts to reduce the exposure to reimbursement uncertainty and address the challenges described. For instance, understanding payers' reasons for the lack of HCP coverage could inform clinicians' appeal approaches, and recognizing HCP clinical applications potentially acceptable by payers may inform insti-

tutional criteria for HCP use (eg, for patients with multicancer phenotype).

To achieve long-term sustainable coverage and reimbursement, concerted multi-stakeholder efforts are needed, especially as multigene testing expands from HCPs to WGS/WES. Because HCP and WGS/WES share key features, such as inclusion of well-studied and less-studied genes and testing not indicated by pedigree, they may also encounter similar challenges.^{14–16} In fact, our findings suggest that HCP coverage challenges may also indicate barriers to coverage for WGS/WES. Of particular importance is the requirement of coverage frameworks that all genes within a test be medically necessary, which may deem WGS/WES noncoverage permanent. Indeed, a CMS official noted that WGS is “something that CMS would never cover,”⁴⁵ later amending this remark to state that it would be “very, very challenging” to collect convincing data.⁴⁶ However, several payers in our study signaled willingness to adjust coverage frameworks for multigene testing, and suggested specific approaches to evidence development and potential HCP coverage. This may serve as a start of a broader multi-stakeholder dialogue and policy effort to facilitate evidence generation and update assessment, coverage, and reimbursement approaches for HCPs, and ultimately for WGS/WES.

Implications for the PMI

Addressing HCP Insurance Coverage: The PMI’s vision includes developing policy pathways to support PMI-based research and translation into care, with an emphasis on modernizing the regulatory evaluation and approval of genomic sequencing technologies.^{4,5,8} Payer coverage for sequencing tests, including HCPs, should also be addressed as a critical link in the precision medicine policy pathway. Shorter-term, positive coverage may enable generation and availability of genomic data to be contributed by the PMI cohort (in addition to data from sequencing for some cohort participants, as being planned to be potentially paid by the PMI²⁷), whereas the lack of coverage may considerably limit this opportunity. Longer-term, payer coverage will be a key factor in access to modalities developed by the PMI. Additionally, according to the PMI’s vision, new genetic results will be shared with cohort participants who are expected to discuss implications of results, potential further tests, and interventions

with their physicians.²⁷ Lack of insurance coverage for these tests and interventions will create a conundrum for patients, clinicians, payers, and the PMI.

Thus, addressing the barriers of coverage policy may be as crucial to the PMI’s success as optimizing the regulatory policy. Notably, genomic sequencing challenges the frameworks of payer coverage and regulatory policy in similar ways. Our findings indicate that sequencing tests (exemplified by HCPs), which report multiple genetic results that are not defined in advance of testing and vary in the strength of evidence, often do not fit payers’ frameworks of medical necessity for coverage. The FDA reported, and experts noted, that these features also strain its regulatory methodology, which was developed for traditional single-gene tests capturing predefined data points anticipated before testing.^{47–49} This commonality provides an opportunity for expanding the PMI’s policy scope to include payer coverage and developing a comprehensive policy framework suitable to evaluate and approve genomic sequencing tests from the regulatory and coverage perspectives. Importantly, the PMI calls for modernization of the regulatory framework for genomic sequencing. Whether coverage policy frameworks require modernization should be debated, and at least 3 major payers in our study signaled their openness to a dialogue.

Informing PMI Research Priorities and Methods:

Both payers and regulators evaluate evidence of analytic and clinical validity for genomic tests,^{23,30,35,50–52} and generating validity data is one of the PMI’s objectives.²⁷ However, payers also require evidence of clinical utility^{23,34}—how effective and actionable genetic results are in care decisions and interventions—which is beyond the regulatory domain and the current PMI scope. Proving clinical utility of genetic tests to payers has been challenging, partly because of variation in payers’ definitions of utility and expectations about the quality of relevant studies.^{23,30,34} We found that HCPs are no exception, in that payers’ evidence requirements for actionability differ, and evidence developed in a hybrid clinical/research setting may not meet the required rigor. Including studies of clinical utility/actionability of genomic testing within the PMI’s priorities and considering payers’ methodological concerns when designing the PMI Cohort studies would produce the evidence required by payers and accelerate coverage of PMI-derivative tests. However, a consensus across medical societies and payers should

be reached first on what constitutes utility and actionability. Although this may be a difficult task, some collaborative efforts have produced cross-payer recommendations for evidence and coverage of genomics, such as tumor sequencing.⁵³ The PMI has the scale, authority, and clout to reach this consensus in areas relevant to its priorities.

Enhancing PMI Approaches for Participant Involvement and Transparency: Informed and engaged participants are a hallmark of the PMI cohort.^{6,8,27,54} Participants' involvement will reflect their preferences and include receipt of their individual genomic information as well as potential recontacting to offer participation in further studies.²⁷ Acknowledging the challenges associated with return of genetic results, especially less-studied variants, the PMI is considering means to ensure that patients' preferences are defined in an informed fashion, they fully understand returned results, and results do not lead to unnecessary testing or interventions.²⁷ Approaches considered by the PMI to mitigate these challenges include an effective consent process to clarify the implications of preferences, and accompanying the return of genetic results with interpretative or genomic counseling services.²⁷ Payers are keen on addressing these challenges and have undertaken efforts to ensure that patients are informed and appropriately counseled.⁵⁵⁻⁵⁸

Participants in our study strongly recommended that qualified genetic counseling be provided not only posttesting but also pretesting, and that genetic counseling approaches and guidelines be developed to handle preferences and processes for return of multigene, mixed-validity results. The capacity, process, and cost of providing these services to PMI cohort participants may seem prohibitive, but working with private payers who have successfully tackled these issues could provide a solution. For example, several private payers have developed the capacity to provide effective and scalable pretesting and posttesting genetic counseling to their enrollees, including coverage for telephonic genetic counseling.⁵⁹⁻⁶² These approaches could be leveraged by the PMI and extended to the cohort volunteers.

As the PMI solidifies the patient recontacting process, it should consider its obligation to notify participants when new research concerning their already captured alterations becomes available. Recom-

mendations provided by payers in our study could be incorporated and detailed by PMI to create a robust recontacting process and enrich participants' understanding of their genomes with newly available data in an appropriate fashion.

The limitation of our study is the relatively small payer interview cohort. However, payers in our cohort have a large national impact based on their share of the US population, including the 8 largest national private payers. Their policies are monitored and often followed by other payers, and they manage an important portion of the US public plans, such as some Medicaid and Medicare Advantage plans. Although our study identified opportunities to address barriers to positive coverage of HCPs, future efforts, within and outside the PMI, to build on our findings and detail these opportunities are necessary to transform them into actionable solutions and seek consensus across payers.

Conclusions

We found barriers to insurance coverage for HCPs, including poor fit with coverage frameworks, insufficient rigor and gaps in evidence on cancer risk and actionability, and concerns about transparency to patients. Opportunities to address barriers included developing payer-suggested evidence end points that are feasible for insurance coverage; approaches to better inform patients about the potential for identifying aberrations in genes with unknown or evolving clinical validation, along with methods for recontacting patients in future; and a possibility of adjusting coverage frameworks. Our findings can inform the PMI in 3 areas: (1) addressing insurance coverage barriers to secure access to future PMI discoveries; (2) incorporating payers' evidentiary requirements into the PMI research agenda to increase relevance of research to future coverage decisions; and (3) leveraging payers' recommendations and experience to keep patients informed and engaged. Integration of these perspectives into the PMI's agenda and priorities will contribute to its success and enable ultimate access to its discoveries.

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