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Stakeholders' expectations of precision medicine: A qualitative study to identify areas of (mis)alignment

Background and Aims

To sustainably address challenges in implementing precision medicine (PM), coordinated efforts of different stakeholders are required. Understanding their expectations represents a first key step toward aligning on future actions and strategies. Here, we aimed to explore the expectations of different stakeholders from themselves and each other regarding PM.

Methods

This collaborative qualitative study was initiated by the global multistakeholder consortium From Testing to Targeted Treatments (FT3). Structured interviews were conducted with participants from five stakeholder groups: patients/patient advocates, healthcare providers (HCPs), researchers, policymakers/regulators/payers and industry representatives. A broad reach across geography, roles, experiences, and disease areas was sought. Results were analyzed by grounded theory methodology.

Results

All stakeholders stated that optimal implementation of PM can only be achieved through collaboration; industry representatives were the biggest promoters of collaboration. Stakeholders agreed that PM should be implemented focusing on the patient's best interest; HCPs were seen as important gatekeepers for PM by interacting directly with patients, and policymakers/payers were perceived as the most important drivers of access to PM. Areas of misalignment included the role of industry in clinical trial design and in access to PM (perceived as important by patients, HCPs and policymakers but not by industry representatives), and the stakeholders responsible for elaborating guidelines on PM use (patients indicated policymakers, while researchers indicated themselves). Priorities for optimal PM implementation and suggested actions included the need for enhancing high-level policy focus, improving genomic literacy, optimizing the health technology assessment for PM, advocating for equitable access, promoting collaboration between industry and other stakeholder groups and development of reliable research standards.

Conclusion

Stakeholder expectations revealed in this study suggested that no stakeholder group can drive change on its own; a global, multistakeholder collaborative approach that brings together current programs and best practices to support universal access to PM is needed.

1 INTRODUCTION

The concept of individualizing treatments by taking into account the characteristics of a patient dates back to ancient times and to this day, remains a cornerstone of medical practice.[1, 2] Scientific and technological advancements achieved over the last two decades have allowed the measurement of individual genomic, metabolic, or immune characteristics (collectively known as biomarkers) that could not be evaluated before.[1, 3] The introduction of routine human epidermal

growth factor receptor 2 (HER-2) molecular testing in breast cancer patients is a prominent example of how a biomarker can be used to select an optimal therapeutic approach.[4] This opened the way for the modern concept of precision medicine (PM), which consists of "*a healthcare approach that utilizes molecular information (genomic, transcriptomic, proteomic, metabolomic, etc.), phenotypic and health data from patients to generate care insights to prevent or treat human disease resulting in improved health outcomes*."[3] Through PM, patients are more likely to receive a treatment from which they can benefit. PM allows taking advantage of patient heterogeneity, which is often viewed as a drawback in the context of evidence-based medicine.[2, 5] To date, PM is most commonly applied in the field of oncology,[4, 6-8] and is characterized by developing pairs of companion diagnostic-targeted cancer medicines.[9]

Multiple stakeholders are involved in the pathway from testing to targeted treatments, including patients themselves and patient organizations, treating clinicians and healthcare providers (HCPs), clinical and academic researchers, policymakers, payers, regulators, and industry representatives. While the most important beneficiaries of PM are the patients, its implementation brings advantages to all involved stakeholders and can also result in enhanced disease prevention, more judicious use of healthcare resources, and more efficient clinical trial designs.[3]

Despite the advantages of PM, there is still substantial heterogeneity in the implementation of PM across countries. This leads to increased uncertainty, widely varying practice standards, reimbursement, and regulatory policies, which hamper the optimal implementation of PM.[10, 11] These challenges are numerous and well-documented.[10] However, less information is available on the expectations across and within stakeholder groups. Being aware of what the different stakeholders expect from one another is an essential first step toward establishing a common understanding of PM. Moreover, clarifying expectations would foster collaboration and consensus-building regarding the changes needed for making access to PM possible for all patients who would benefit from it.[11-14]

This research, initiated by the global multistakeholder consortium From Testing to Targeted Treatments (FT3), aimed to explore the expectations, including any potential mismatches, that different stakeholder groups have from each other regarding PM. In addition, the priorities and actions needed to overcome the barriers in PM implementation were identified and summarized for each stakeholder group.

2 METHODS

2.1 Study design and data collection

A qualitative, collaborative, multistakeholder approach was used for this study, where participants were asked to complete a 45–60-min-long structured interview on their expectations and views regarding PM. Additional time was granted for the completion of the interview, if needed. All interviews were conducted by video call, except for one participant who completed the questionnaire offline and returned it via email. The interviews were commissioned by FT3. A stakeholder expectations working group composed of seven industry and patient representatives was established by self-selection to lead the project, formulate the interview questions, and undertake a critical review of interview findings and outputs. Selection of the interviewees and the development of the topic guide were conducted by the FT3 working group in collaboration with an independent healthcare advisory team (Monmouth Partners), which was also responsible for conducting the interviews. Organizations/participants whose experience and expertise could add the greatest value and range of input to the program were approached.

Interviewees were recruited via several contact methods. First, FT3 working group members were informed of the program, and asked to identify potential interviewees, who were contacted in-person, by telephone, or by email to assess their interest in participating. If they agreed, they received an introductory email/invitation, drafted by The Synergist and adapted by Monmouth Partners, which gave interviewees an understanding of the scope and purpose of the survey

Partners, which gave interviewees an understanding of the scope and purpose of the survey.

Second, all interviewees were asked at the end of their interview whether there was anyone in their own networks who could provide a valuable perspective or who they considered to be a good fit for the project. Introductions were made via the interviewee if an appropriate referral was identified.

Finally, interviewees were identified via Monmouth Partners' networks. Emails and conversations were held to present the project to potential participants and invite them to participate. Organizations that are prominent in the field of PM, or those that were identified during the interviews, were also contacted to propose participation in the survey, either via email or LinkedIn.

If a potential interviewee did not respond, they were not contacted again. If they had expressed interest or agreed, they received a follow-up contact, and the interview was scheduled.

Participants were enrolled using a staggered approach, with two pilot interviews conducted, to adapt and refine further upcoming interviews. Pilot interviews took place at the start of August 2021, with the majority of the main interviews being conducted between September 2021 and January 2022. Structured interviews conducted by video call were either transcribed live or video-recorded with the participants' permission and subsequently transcribed; after the interviewees' responses were captured, recordings were deleted. No ethical approval was required. Participants provided their agreement to participate in the study verbally or by email; no informed consent form was signed. An overview of the study stages is presented in Figure 1.

2.2 Interviewee selection and categorization

Five stakeholder groups involved in PM were represented:

- 1.

  patient advocates/groups included individuals or organizations representing patients;

- 2.

  treating clinicians/HCPs included physicians and other HCPs who interact with patients and prescribe PM;

- 3.

  researchers included clinical and academic researchers;

- 4.

  policymakers included organizations that support the development and monitoring of healthcare regulations and policies, along with the organizations that pay or recommend the commissioning of healthcare assets such as drugs, devices, software, and diagnostic services;

- 5.

  industry representatives included those organizations that manufacture and deliver healthcare assets.

Participants across the five stakeholder groups were chosen to be illustrative for North America and Western Europe; other experiences specific to South Africa and other countries (covered by stakeholders with a global role) were also captured. A broad reach across geography, job roles, experiences, and disease areas was aimed. Identifying and selecting participants was done using the quota and snowball sampling techniques.

2.3 Data analysis and interpretation

The interview topic guide covered four major areas: systemic perspective and barriers to PM access; data, research, and best practice; stakeholder expectations; priorities and next steps. Each theme was subcategorized and detailed. Some questions of the interview topic guide were adapted for the different stakeholder groups, to focus on areas where their input was likely to be more consistent. Not all areas/subcategories covered by the interview guide are addressed in this manuscript, which focuses on stakeholder expectations and priorities; other outcomes of the study will be shared elsewhere.

The results were analyzed in-depth using the grounded theory methodology. The comparative quality analysis and the in-depth review were performed by Monmouth Partners. Results were further analyzed and discussed with the stakeholder expectation working group. Stakeholder expectations were formulated based on each group's views of relationships, roles, goals, and responsibilities of their own and other stakeholder groups. Questions from the interview topic guide pertaining to stakeholder expectations are included as a Supplementary Material SI. The collected information is presented as a matrix, where each box describes the expectations of the stakeholder group indicated in the corresponding row from the stakeholder group indicated in the corresponding column.

3 RESULTS

3.1 Demographics

Overall, 30 interviews were conducted; the number of interviewees within each stakeholder group ranged between four and eight, with a median of six. Interviewees represented diverse disease areas, including general oncology, various oncology specializations (hereditary tumors, anaplastic lymphoma kinase-positive [ALK+] and nonsmall cell lung cancer, colorectal cancer, breast cancer, leukemia, and lymphoma), autoimmune disorders, renal diseases, respiratory conditions, cardiovascular diseases, rare diseases, teratology, neuroscience, and microbial science. Stakeholder groups where obtaining engagement was challenging included HCPs and the genetic counselor community, as well as regulators and policymakers (sometimes due to restrictions related to their professional role).

Most stakeholders were from the United States ($n = 9$), followed by stakeholders with a global role ($n = 6$), those from the United Kingdom ($n = 4$), and from Canada ($n = 3$). Other specific views and experiences were captured from the Netherlands and the European Union region ($n = 2$ for each) and from Belgium, Lithuania, South Africa, and Spain ($n = 1$ for each). A breakdown of the number of interviewees according to stakeholder group and geography is presented in Figure 2. Additional details on the roles of the interviewees in each stakeholder group can be found in Table 1.

Table 1. Roles of the participants by stakeholder group.

Stakeholder group (*N*)	Role (*n*)
Patient advocates/groups (7)	• – patient organization representatives (3) • – patient advocates (2) • – patient and patient organization representative (2)
	• – consultant clinical geneticist (1) • –

Treating clinicians/HCPs (5)	genetic counsellor (1) • – representative of a professional body for genetic counsellors (1) • – medical oncology fellow (1) • – family medicine physician and human genetics specialist (1)
Researchers (4)	• – consultant clinical geneticist and professor of medical translational genetics (1) • – biomedical researcher, professor of pathology and molecular medicine, and research portfolio lead for cancer (1) • – professor of cancer biology and genetics, and director of cancer genomics (1) • – director of research, genomics (1)
Policymakers (8)	• – member of a government commission for integrating reimbursement criteria for drugs and companion diagnostics (1) • – healthcare commissioner (1) • – expert evaluator to the EU Commission (1) • – funder of genomic research (1) • – former legislative assistant/economist in biotechnology (1) • – vice-president of science policy (1) • – director of strategy and engagement for genomics and health (1) • – commissioner of a cancer center network (1)
Industry (6)	• – executive director of oncology policy and healthcare systems (1) • – head of precision medicine and oncology (2) • – global director of oncology market access (1) • –

	executive director of precision medicine and companion diagnostics (1) • – global medical lead (1)

3.2 Stakeholder expectations

Results for each participating stakeholder group are included in the stakeholder expectation matrix (Figure 3). Below, a summary of the stakeholder views is presented.

3.2.1 Collaboration among stakeholders

All stakeholder groups seemed to believe that PM can only be advanced through collaborative efforts. Many participating stakeholders expected a collaborative approach from industry representatives, manifested by aiding the work of patient advocacy groups, contributing to HCP education and supporting research in the field of PM. Taking an open, sustainable approach to PM, with greater transparency and enhanced data sharing was also expected from the industry.

3.2.2 Industry representatives

In agreement with the expectations expressed by the other participating stakeholder groups, participating industry representatives appeared to be the biggest promoters of collaboration between stakeholder groups. While they seemingly understood and agreed with the benefits of sharing more research information (e.g., in rare diseases), they expressed that doing this can be difficult in a competitive environment.

3.2.3 HCPs

HCPs were seen as the important gatekeepers of PM, on whom patients rely and whom they trust with their healthcare journey. Several interviewed stakeholders expressed the expectation that HCPs should keep up-to-date with the fast-paced advancements in the field of PM; however, it was also acknowledged that this is difficult in practice, due to the speed at which PM is developing, its complex nature, or disparities in HCP motivation/understanding. Therefore, universal up-to-date knowledge of PM among HCPs was seen by the interviewees more as an ideal or a desire, rather than a realistic expectation that could be implemented in practice. Nevertheless, HCPs are expected by all other participating stakeholders to educate their patients, to support them in making informed choices, and to promote and facilitate their access to PM. In addition, the role of HCPs in connecting patients with the researchers conducting clinical trials, in advocating the benefits of PM to payers, and in assisting industry representatives in PM implementation was also mentioned by the different stakeholder groups.

3.2.4 Patient advocates/groups

Patients would like researchers to share how they used and benefited from their data, which could motivate more patients to participate in research in the future.

Largely, there was agreement between what interviewed patient advocates/groups saw as their role and other participating stakeholders' expectations of them; the most commonly cited ones were providing patient education and advocating for access to PM. Furthermore, most interviewed stakeholders agreed that the patients' voice needs to be heard, and that all stakeholders must ensure that PM implementation is focused on the patients' best interest.

3.2.5 Areas of expectation misalignment

Several expectations expressed by other stakeholder groups from industry representatives were not specifically mentioned by the interviewed industry representatives themselves. These included designing trials that are more inclusive with regard to age and ethnicity (e.g., adaptive, enrichment, basket, or umbrella trials), a view expressed by participating patient

advocates/groups and policymakers, and improving access to PM, mentioned by participating HCPs and policymakers.

Clinical researchers seemed to consider themselves responsible for elaborating guidelines on translating use of PM to clinical practice; however, participating patient advocates/groups expected this to be done by policymakers. Interviewed policymakers recognized their role as important drivers of PM, a view that was also shared by other participating stakeholder groups (HCPs and researchers).

Researchers appeared to consider policymakers as the hardest stakeholder group to convince about the benefits of PM; this was mostly due to difficulties in demonstrating the cost-effectiveness of PM versus a population-based approach within the existing reimbursement frameworks. Furthermore, industry representatives seemed to believe that policymakers should be involved earlier in the creation of value frameworks.

3.3 Priorities in optimal implementation of PM and suggested actions

For most participants, optimal implementation of PM was characterized by universal access for all eligible patients, increased efficiency through greater application of already-available technologies and therapies across a wider range of diseases, and improved sharing and application of clinical research data.

Challenges and barriers identified by the different stakeholder groups were often specific to different points in the patient's journey from diagnosis to receiving personalized therapy, as depicted in Figure 4. In response to the identified barriers, several priorities and suggested actions for each stakeholder group emerged (Figure 5). Many of these seemed to reflect expectations for a patient-centered approach from all stakeholders, as the proposed actions included “supporting patients,” “ensuring actions are in the patients' interest,” “advocate to health system[s] for patients,” “share with patients how their data is being used,” “be transparent with research data,” and “widen access to poorer communities.”

Stakeholder groups appeared to be generally aligned in their thoughts on how access to PM could be improved and on ways to address the identified systemic barriers. Responses were grouped into six themes, detailed below. For each theme, relevant quotes from the interviewed stakeholder groups are presented.

- 1.

  High-level policy focus and emphasis from the government

  Interviewed stakeholders seemed to agree that optimal implementation of PM should start at the top, with policymakers/payers.

  > Researcher representative: *“First action: funding for infrastructure and therapy budgets. Governments need to understand the importance of PM: that it is changing the face of cancer, that it can bring significant benefits.”*

  > Industry representative: *“One place it falls down mostly is the payer environment. If I could instigate one change, it would be putting together the discussions that happen about the diagnostic and drug together. Separately and without that link [it] is non-sensical.”*

  > Patient representative: *“There are many systemic barriers to access currently. There is a lack of awareness among patients, providers and policymakers. Greater education among policymakers is required re: biomarker testing. There is a lot happening, but more can be done.”*

  To support the uptake of PM, policymakers/payers could provide incentives or penalties

To support the uptake of PM, policymakers/payers could provide incentives or penalties (financial or mandated policies) to HCPs, as well as incentives to industry representatives to focus on PM product development.

> Policymaker/regulator representative: *"Let's provide, in legislation and policy, incentives for the system to bring PM forward. Providers and payers. Evidence that this is the best way to go to provide better care and bring down long-term healthcare costs. This requires appropriate investment."*

Policymakers should ensure that guidelines are widely and rapidly adopted into clinical practice. Payers could invest into basic research to better understand early-stage disease, individual responses to treatment, combinations of therapies, and tumor biology. As PM clinical trials are challenging to design, fund, and regulate, more resources should be allocated for an increased volume and delivery of such trials.

> Industry representative: *"It is great to say that individual-focused, personalized care is more valuable than a population-based approach. However, the system is designed for a 'one size fits all' solution. Now to say let's pay for value, that takes an investment and change in the way things have been done. Investment in funding and investment in change."*

Patients and patient advocates could lobby regulatory bodies to ensure PM is a priority and there is sufficient funding provided for scientific research, testing infrastructure, training of skilled workers in PM, and treatment reimbursement for all eligible patients.

> Industry representative: *"Advocates need to be louder"*.

- 2.

  More experienced workforce and improved genomic literacy

  Participating stakeholders seemed to agree that there is a need to support HCPs in being comfortable dealing with diagnostic results and applying these in clinical decision-making, to improve genetic literacy of patients, and to address the current skill shortage in the workforce engaged in PM. Professional bodies with substantial reach (e.g., the American Society of Clinical Oncology [ASCO], the European Society for Medical Oncology [ESMO], the American Association for Cancer Research [AACR] or disease-specific organizations/journals) were mentioned as the best channels to keep HCPs' knowledge up-to-date by providing access to quality bitesize education.

  The need for supporting clinicians in understanding the role of testing and the robustness/suitability of the tests was highlighted; this support includes recognizing the need for the ongoing educational need of HCPs, as well as investing in systems/platforms to run the analysis and help interpret the results, ideally integrated into electronic health records (EHRs). Genomic science could be included in the medical training curriculum.

  > Researcher representative: *"Some work is being done to incorporate clinical decision support within EHR systems related to biomarker testing and PM but there is still a way to go. It would be good if clinicians received alerts, e.g., if [a] patient has [a] particular condition, the alert would suggest specific biomarker tests. Results tend to come back with [a] whole suite of options; alerts could suggest further treatments based on [the] test results. Alternatively, where no treatment option exists, the alert could suggest a specific clinical trial for which a patient may be eligible. If this type of support could be built into a physician's workflow, it could go a long way to improving access."*

  > Researcher representative: *"Some testing companies provide very detailed results to clinicians and include potential treatment options or clinical trials, but a lot of this is*

> *not directly within [the] EHR. The clinician may be required to log in to a different system. Documentation, workflows, and EHR seems like a simple thing, but if all integrated properly it makes a big difference. Ultimately, [it] make[s] it easier for [the] clinician to interpret results and direct [the] patient to the right treatment."*

> Patient representative: *"Lack of physician knowledge is also a barrier. Some physicians have questioned why they would do biomarker testing when they wouldn't know what to do with the results when they came back. Community oncologists in smaller towns, treating whatever type of cancer comes to them, won't keep up with every innovation. It is difficult for oncologists to keep up with that in multiple kinds of cancers."*

Proposals to improve genomic literacy among patients included promoting some of the high-quality resources that already exist around PM to patients and patient organizations and ensuring that the level of information is appropriately tailored to this audience. Skill shortages could be addressed by applying a multidisciplinary approach that routinely involves specialists in complex treatments. Furthermore, funding would be needed to address skill gaps such as lack of genetic counselors in hospitals or insufficient statistics and data analytics skills in clinical research; this should also include providing sufficient remuneration that would motivate trained people to take on and maintain such roles.

The role of molecular tumor boards (MTBs) in providing advice to clinicians should be expanded, and MTBs should be founded in countries where they do not exist yet; virtual specialist support models, where specialists can be accessed online, could also be considered. A hub and spoke setup, in which information from the central hub is distributed to several spokes, could be used to support the upskilling of HCPs.

- 3.

  Understanding the health technology appraisal process for PM

  Interviewed stakeholders seemed to agree that with PM, the value assessment pathway needs to account for a more complex set of decision-making that spans from biomarker testing to treatment. Specific examples of a successful solution could not be given, but participating stakeholders proposed several criteria that should be fulfilled by such a solution.

  First, it should focus on demonstrating cost-effectiveness and affordability of PM, by also considering the wider benefits of PM implementation, i.e., reduced burden on health services on both short- and long-term. For this, value (in terms of benefits and outcomes), as well as metrics for success and the type of data needed, should be clearly defined.

  Second, an optimal solution should support a collaborative value framework where advanced diagnostics and other healthcare assets that are not a drug or device (e.g., MTBs or genetic counselors) are considered integral to the care approach and associated value streams. Such an approach would increase demand on the system to effectively appraise the economic and clinical benefits of nontraditional therapy options. To overcome this, innovativeness and a change of perception are needed within the system, to move away from code-based funding. Currently, value assessment pathways for PM and established criteria for funding exist only for drugs, but not testing. Therefore, either the way value is assessed, or the budgets allocated need to change; the latter could be optimized through finding innovative payment solutions together with industry stakeholders (e.g., risk-share- or outcome-based payment models).

  Third, assessing evidence for clinical integration should account for the PM-specific environment, where different patients respond differently to therapies, leading to smaller groups of potential patients

groups of potential patients.

Fourth, the solution should consider the cost implications of companion diagnostic assays versus local laboratory-derived biomarker tests quality monitoring; for this, regulatory and data access challenges need to be overcome.

Fifth, it should include educating regulators and payers on the value propositions, benefits, and risks of implementing PM, with a focus on providing clinical evidence that PM works and results in improved outcomes for patients. However, the payers' perspective on what information they consider important for decision-making should also be considered. Pilot projects could generate more practice-based real-world evidence, while in the United States, a national identifier system for genetic tests was proposed to support the coding and billing system.

> Policymaker/regulator representative: *"Where we need to focus strategies now is providers and then payers. These two stakeholder groups control access to these new technologies, to get them to patients and [to be] used in the clinical setting. The challenge with providers is the scope, variability, and diversity of [the] different kinds of providers. There are trailblazers and elite organizations implementing personalized medicine at a high level, but the bulk are behind."*

- 4.

  Advocating for equitable access

  Universal access was described by most participating stakeholders as a crucial component of optimal PM implementation. A suggested action for industry representatives consisted of adjusting the availability of technologies globally, by focusing on improving ability to scale instead of solutions only available to certain populations. Industry representatives could explore opportunities for collaboration with the state and private sectors to support access to testing in developing countries (e.g., by offering package deals to private laboratories), which could also support upskilling of local expertise in molecular test interpretation.

  The process of identifying relevant clinical trials/eligible patients could be improved; the proposed solutions included designing decentralized clinical trials, facilitating identification of clinical trials based on biomarker testing, integrating clinical trials into the HCPs' workflow, removing the barriers that stand in the way of increasing trial participant diversity, advocating for insurance-covered testing (which in turn will also support access to clinical trials based on molecular testing). Telehealth and remote access technologies could support decentralized clinical trials (that enable more people to participate) and could provide online support for HCPs and patients in certain stages of PM trials. Understanding the role of local laboratory testing versus companion assays may have an impact on cost and accessibility for developing countries.

- 5.

  Industry and collaboration

  Industry representatives seek to collaborate with other stakeholders at various points in the PM development process, and other stakeholders also expect greater collaboration from industry. Industry stakeholders participating in this study proposed greater involvement of payers earlier on in the development process, while some of them wished for a shift in the overall drug development mindset, from a single drug approval focus to a whole end-to-end diagnostic to therapy solution.

  > Industry representative: *"We can't do it alone. It is a team game. We need all of the stakeholders working together to take anything from concept to delivery. We cannot*

> *do it without the science, the treating community, patients, payers. Everyone has to play their part: multi-disciplinary. We have a streamlined process in clinical trial testing, working hand in glove with regulators. But once ready to launch, it feels like it passes into a different realism. There is more work needed to prepare the ground. Payer discussions need to be had earlier so they are ready to receive it when regulators approve."*

Researchers seemed to wish for greater collaboration of data sharing in a pre-competitive environment, while industry representatives asked for greater sharing of patient databases. In addition, representatives of the pathology community and some payers would like to see tissue samples being shared, to compare laboratory assays with companion assays, and review the cost-effectiveness of both testing options.

- 6.

  Research, data, and clinical standards

Interviewed stakeholders seemed to agree that standardization of genomic nomenclature and increased regulation of testing providers would be needed, along with guidelines for clinical data. The need for transposing real-world evidence/large scale clinical validation and population-level clinical data into guidelines for policymakers and regulatory agencies was highlighted.

Participating stakeholders believed that models and the consent process for clinical data sharing should be reviewed, and data standards that support integration and sharing of data should be developed and widely adopted. Such data standards would comprise technical standards (to support technology agnostic integration), standardization of reports and nomenclature, optimal integration of EHRs with molecular test results, and technology that supports patient ownership of their data and enables them to set permissions on that data. Examples of data sharing where countries own their own data but provide access rights to eligible parties via application programming interfaces (APIs) were mentioned (e.g., the international Global Alliance for Genomics and Health [GA4GH] organization,[15] which provides a genomics data toolkit including Data Connect API and a data passport specification). In addition, the need for better and trustworthy methods of obtaining patients' consent to secondary research use of their data was highlighted.

Participating stakeholders felt that a better integration of research into clinical care would lead to treatments being more rapidly applied within health systems. For this, systems for profiling and risk modeling should be improved; an adequate information technology (IT) infrastructure of primary and secondary care could allow accessing patient cohorts and fitting PM into treatments. Better integration of health records was perceived as critical for the aggregation of healthcare data that increases the efficacy of medical research, for enabling iterative analysis of a patient's care and treatment options as new discoveries and guidelines are made, and for supporting more effective reimbursement processes. The need for improved guidelines and standardization of tissue sample collection and clinical data was also mentioned.

4 DISCUSSION

The main goal of our study was to assess the expectations of each stakeholder group from each other and themselves when it comes to PM. This knowledge can be used to identify and address any mismatches in this area and to improve communication between the involved parties, as a step in harmonizing PM implementation and supporting the multistakeholder collaboration. The negative effects of failing to obtain an alignment in stakeholder expectations and perspectives have already been highlighted.[16, 17] The results of the stakeholder expectation matrix presented here will be further used to inform the FT3 program strategy and activities.

The interviews suggested that all participating stakeholders consider optimal implementation of PM a priority and acknowledge that this can only be done through a collaborative effort with the

PM a priority and acknowledge that this can only be done through a collaborative effort with the other stakeholders. However, there still appears to be a lack of clarity and some misalignment regarding the perceived roles and expectations of the different stakeholder groups in driving PM. Similar attempts have been made to discover differences between various stakeholder groups in terms of perceptions and expectations regarding patient engagement in medicines development,[18] prognostic-based genomic testing,[16] barriers to optimal implementation of PM,[19] or the optimal components of value frameworks.[11] Results of these studies are in line with those of our stakeholder expectation matrix, highlighting the need for improved communication and collaboration between all stakeholders if harmonization of PM implementation is desired.

Stakeholder expectations seemed to be aligned regarding the important role played by patients in PM implementation. The driving force of patient-centered approaches toward PM has been illustrated by successful initiatives of patient oncogene groups in developing relationships and partnerships with other stakeholder groups (i.e., HCPs, researchers, industry representatives, and other advocacy organizations for addressing unmet patient needs).[20]

No stakeholder group designated themselves as the leaders of PM implementation, although policymakers appeared to be considered as drivers of access to PM by their own group and by other groups. A tendency to expect other stakeholders to take the lead was observed, suggesting that a collaborative leadership to align on a shared goal and common priorities should be aimed for. This is in line with the findings of a similar study published in 2018 that explored different perceptions and expectations regarding patient engagement.[18] In this study, perception of HCPs regarding their role in connecting the different stakeholder groups was in agreement with the views of the other stakeholders when PM implementation was concerned. However, with regards to patient engagement, HCPs did not consider their role of connecting different stakeholder groups as essential, even if they were perceived as such by other stakeholder groups.[18]

All stakeholder groups seemed to recognize the value of collaboration in overcoming the challenges of PM implementation; this is also well described in other recent publications.[21, 22] A multidisciplinary approach supports not only the raising of awareness and education of the various stakeholder groups, improved access to PM, and more efficient collection and interpretation of large amounts of complex data, but can also contribute to controlling issues with patient data privacy or ethical aspects of PM.[13, 23-25] Several international multistakeholder coalitions can provide platforms for such a collaboration, including the European Patients' Academy on Therapeutic Innovation (EUPATI),[26] the Patient-Centered Outcomes Research Institute (PCORI),[27] the Clinical Trials Transformation Initiative (CTTI),[28] the GA4GH,[15] the Patient-Focused Medicines Development (PFMD),[29] the European Cancer Organization (ECO),[30] the International Exchange Experience with Patient Organizations (IEEPO),[31] and FT3.[32] While other coalitions concentrate more on patient engagement in the drug development process/clinical trials, FT3 is a collaborative program focused specifically on improving patient access to PM. Other examples of collaboration in PM include Access to Comprehensive Genomic Profiling (ACGP),[33] a coalition of molecular diagnostics companies and laboratories, as well as the Precision Cancer Consortium (PCC),[34] which facilitates broader collaboration across industry.

Another major theme that emerged was the need for equitable access to PM. The importance of this topic has been highlighted before through the voice of patient organizations.[35] Our results suggest that concerns over universal access to PM are present in all stakeholder groups. Concerns have been previously formulated that in a healthcare environment already burdened by significant discrepancies in access, as well as in the quality of available healthcare services, which vary based on geographical location, ethnicity, or socioeconomic status, introduction of PM could deepen such inequities.[35, 36] Due to its global scope and collaborative multistakeholder approach, FT3 can play an important role in promoting universal access to PM regardless of country, condition, socioeconomic status, and beyond.

This study has several limitations. The scope of this project did not allow for conducting a sufficient number of interviews that could represent views of an entire stakeholder group globally.

While a conscious effort was made to include a broad range of interviewees and to capture the typical views of each stakeholder, opinions cannot be considered to fully represent those of the whole stakeholder group. Instead, the results should be considered as representative of the interviewees themselves, rather than of the stakeholder group they are part of. Obtaining engagement from genetic counselors and HCPs was particularly challenging. Each structured interview was allocated a time of 45–60 min; where necessary, some of the interviews were extended upon agreement with the interviewee. In cases where this was not possible, not all interview questions were completed, and time was preferentially spent focusing on areas of most relevance to the interviewee's experience and expertise. Stakeholder groups encompass a wide range of job roles, functions, and geographies. Stakeholders often held roles that did not fall neatly into just one stakeholder category and sometimes straddled more than one. Therefore, stakeholder groups contain a wide range of diverse views themselves.

The main strengths of the study lie in its collaborative approach and its multistakeholder perspectives and interviews. Members of the patient community were actively involved in designing the study and writing the manuscript. This study was initiated by FT3, a global nonprofit, multistakeholder initiative that is connecting people with relevant backgrounds and building a neutral forum that aims to make PM accessible for all patients who could benefit from it.[14] The FT3's mission is to be a global convener, accelerator, and connector that enhances the understanding and uptake of PM, with the goal of improving patient outcomes and quality of life. In this study, FT3 sought input from the different stakeholder groups relevant to practical PM implementation.

5 CONCLUSIONS

Stakeholder groups were generally aligned in their thoughts on how access to PM could be improved, on priorities and actions needed to overcome barriers, and in their desire for collaboration; however, expectations of stakeholder groups are not yet fully aligned. There was agreement that no stakeholder group can drive change on its own, and a global collaborative approach to implement PM in the healthcare system is needed. There was a call for a more structured approach and additional guidance; no stakeholder group felt they should be the main drivers of PM implementation but instead were looking to other stakeholders to take the lead. Multistakeholder collaboration that aims to bring together current programs and best practices to support more universal access to PM globally is a priority.

AUTHOR CONTRIBUTIONS

Tanya Knott: conceptualization; methodology; validation; writing—review & editing. **James Creeden**: conceptualization; methodology; validation; writing—review & editing. **Benjamin Horbach**: conceptualization; methodology; validation; writing—review & editing. **Maximiliane Rauch-Zumbrägel**: conceptualization; methodology; project administration; supervision; validation; writing—review & editing. **Lidewij Vat**: conceptualization; methodology; validation; writing—review & editing. **Helena Harnik**: conceptualization; methodology; validation; writing—review & editing. **Zorana Maravic**: conceptualization; methodology; validation; writing—review & editing.

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Teleconferences and meetings for manuscript development were organized by FT3. FT3 was involved in the selection of the interviewees and the development of the topic guide but not in the collection, analysis, and interpretation of data. Authors did not receive payment for their contribution to the development of the manuscript. Further information about the governance structure of the FT3 Program (including funding, membership, and the decision-making process of the organization) is available at: https://www.fromtestingtotargetedtreatments.org/governance/.

CONFLICTS OF INTEREST STATEMENT

Tanya Knott reports support for meeting attendance/speaker from Roche Products Ireland. Roche & Illumina grants for World CUP Awareness Week, and a leadership or fiduciary role in the FT3 board. Benjamin Horbach is an employee of and holds stock options in F. Hoffmann-La Roche Ltd. James Creeden is an unpaid independent advisor to the FT3 board and owns Roche stock. Maximiliane Rauch-Zumbrägel, Lidewij Vat, and Helena Harnik are collaborating with The Synergyst, a non-profit organization, of which programs, including the FT3 program, are sponsored by the industry (list available at https://www.fromtestingtotargetedtreatments.org/). Zorana Maravic's organization received grants from BMS, Astellas, Daiichi-Sankyo, Bayer, BI, Pierre Fabre and Seagen.

ETHICS STATEMENT

No ethical approval was required for this study.

TRANSPARENCY STATEMENT

Maximiliane Rauch-Zumbrägel affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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