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Challenges in Recruitment and Retention

Leveraging Health-Related Antecedents and Information Carrier Factors to Improve Patient Participation in Pancreatic Cancer Research—A Review Article

Tara B. Coffin, PhD, MEd and Barbara J. Kenner, PhD

Abstract: Advancements in pancreatic ductal adenocarcinoma (PDAC) prevention, diagnosis, and treatment rely on representative and robust clinical trial participation. Given the severity of PDAC, along with the lack of effective early detection approaches, the need for accessible screening tools and new treatments is dire. Unfortunately, enrollment barriers often result in low participant accrual rates for PDAC studies and illustrate the challenging terrain researchers are facing. Research participation along with access to preventative care has been further impacted by the coronavirus disease 2019 pandemic. In this review, we use the Comprehensive Model for Information Seeking to discuss underexplored factors that influence patient participation in clinical studies. Adequate staffing, flexible scheduling, effective patient and physician communication, and culturally responsive messaging, along with the use of telehealth, can support enrollment objectives. Clinical research studies are a key component of health care, informing medical advancements, and improving outcomes. By leveraging health-related antecedents and information carrier factors, researchers can more effectively address barriers to participation and implement potential evidence-based mitigating strategies. While this work focuses on the PDAC research context, the lessons delineated here are applicable to the wider cancer research setting.

Key Words: pancreatic cancer, clinical studies, recruitment barriers mitigating strategies, Comprehensive Model for Information Seeking; patient participation in research; improving recruitment and retention in research

(*Pancreas* 2022;51: 1074–1082)

Advancements in cancer care rely on representative and robust clinical trial participation. Unfortunately, enrollment barriers often make this difficult to achieve. These barriers contribute to low patient engagement and participant pools and often exclude those facing the greatest need for healthcare improvements.[1] Despite public health initiatives focusing on increasing participation rates, accrual remains low, with less than 5% of adult cancer patients ever participating in a clinical trial.[2] Importantly, accrual rates drop further when investigating enrollment trends in pancreatic cancer research studies.[3]

From the Kenner Family Research Fund, New York, NY.

Received for publication August 23, 2022; accepted December 18, 2022.

Address correspondence to: Barbara J. Kenner, PhD, Kenner Family Research Fund, 275 East Camp Rd., Germantown, NY 12526 (e-mail: drbken50@gmail.com).

The study was supported by Kenner Family Research Fund.

The authors declare no conflict of interest.

DOI: 10.1097/MPA.0000000000002162

Pancreatic cancer is currently the third leading cause of cancer deaths in the United States.[4] Pancreatic ductal adenocarcinoma (PDAC) makes up more than 90% of all pancreatic malignancies and is most often diagnosed at late stages when there are fewer effective treatment options.[5] Approximately 30% of patients diagnosed with PDAC are found to have locally advanced disease at the time of diagnosis, and more than 50% have metastases when the disease is first diagnosed.[6] This is particularly true for Black communities. Black individuals are statistically more likely to go undiagnosed for longer and face lower survival outcomes.[7] While there are some screening options available for individuals who have a personal or family history of cancer or a known pathogenic variant placing them at higher risk for certain types of cancer, these tools are often out of reach because of insufficient insurance coverage and an inadequate referral system.[8,9]

Given the severity of PDAC, along with the lack of effective early detection approaches, the need for new treatments and accessible screening tools is dire. The absence of cancer prevention services is a complex issue, but one significant contributing factor is low enrollment in clinical trials.[1,3] Participant accrual rates for PDAC research illustrate the challenging terrain researchers are facing. The number of promising clinical trials for PDAC continues to increase, paired with only a slight increase in the number of patients enrolling in these trials (eg, from 3.85% in 2011 to 4.15% in 2014).[10] In other words, the demand for participants in cancer research trials exceeds the number of patients motivated or able to participate. When research enrollment lags to this degree, a key component of health care is lost, innovation suffers, diagnoses continue to occur when it is too late, and investigators are left with a costly and sometimes trial ending problem.[11]

There are many factors that impact access to, and participation in, clinical trials. Different types of studies require different outreach accommodations and modifications. The nature of participant requirements, as well as the risk-benefit ratio associated with participation, should be addressed through enrollment plans. In other words, the approaches that address recruitment for an observational study will not necessarily work for a randomized controlled trial, where subjects are receiving an active study drug. However, there are also important barriers relative to the participant perspective.

Participation barriers are routinely reduced to financial hurdles, scheduling concerns, or a lack of clinical resources necessary to implement research.[12,13] These barriers can be significant. The financial burden patients may face in terms of time away from work can also be a constraining factor. However, limiting research enrollment and retention issues to financial barriers and scheduling issues oversimplify the problem. A patient's choice to become a research participant involves much more than a consideration of bus fare and creative scheduling. In this review, we will discuss the underexplored motivational beliefs and attitudes, along with additional health-related and information carrier factors that influence patient participation in clinical studies. While this work focuses on the pancreatic cancer research context, the lessons described here are applicable to the wider cancer research setting.

Not only do medical advances depend on research, for many patients struggling with conditions that have few treatment options, access to a clinical trial can result in access to health care that would not otherwise be available. For a clinical trial to be accessible, the outreach for that trial must be inclusive, participation financially viable, geographically accessible, and the research team and services provided aligned with patient cultural norms.[14] By conceptualizing research in this capacity, as a key component of health care, we can evaluate access to a clinical trial in the same manner that we would assess access to a routine cancer screening service. This includes considering if the information about the research is communicated effectively to the intended participant. This also means considering if the information is acceptably packaged or if the right information is delivered in the right way at the right time. In other words, the process of ensuring research information that is accessible can be reduced to a health communication challenge, where the researcher is tasked with understanding the demographics, attitudes, and motivational beliefs of the patient.[14] We propose using the Comprehensive Model of Information Seeking (CMIS) to support this objective.

In selecting a construct to guide this discussion, we considered implementing the Health Belief Model (HBM).[15] While HBM originated as a construct to understand preventative health behavior, by defining the desire to avoid illness, alongside with the belief that a health action can help avoid illness, HBM does not explicitly account for the information carrier characteristics that may influence these beliefs. Conversely, the CMIS includes a discussion around how information carrier characteristics may influence health behavior.[16]

The CMIS is a theoretical construct traditionally used to describe how people seek health information, with a focus on understanding patient antecedents and the information carrier characteristics to describe and improve health communication.[16] This model can help the research team better understand their patient population and use this information to guide the development of research outreach and recruitment practices. We adapted the CMIS model to better characterize the choice to enroll in research, with a focus on the critical role that patient attitudes and motivational beliefs play (Fig. 1). As a tool for understanding information seeking and uptake, the CMIS is well suited to help researchers understand and leverage patient attitudes and motivational beliefs, where we will focus much of our discussion, to improve research recruitment and retention.

Under the CMIS model, antecedents include demographic characteristics, patient attitudes and beliefs, and salience of risk and actionability. These factors work together to influence personal choices around information seeking, including acquisition of knowledge and subsequent action related to clinical research studies.[16] In this review, antecedents adapted from Johnson and Meischke,[16] include the following:

1. Demographics: General demographics information, including age, self-identified sex, socioeconomic status (as it relates to availability of resources), education level, race, ethnicity, culture, and geographic location.
2. Direct experience (attitudes) and beliefs (motivational beliefs): Motivational beliefs and attitudes encompass the patient's lived experience. This may include prior interactions with the healthcare system or a health issue that could influence their decision to participate in research or their broader view of pancreatic cancer.
3. Salience: The individual's perception of risk, or how much of a threat they feel pancreatic cancer poses to their own health or the health of someone close to them. This risk perception relates to how likely the person feels this disease will impact them during their lifetime. For healthcare professionals, salience relates to how at risk they believe their patient population to be, which is in turn associated with their understanding of risk factors such as increase in blood glucose level along with recent weight loss.

Among the antecedents noted previously, patient motivational beliefs and attitudes are often poorly defined or neglected in the research setting. However, these are also some of the most important factors to accommodate when developing an effective health communication plan.[17] Given the interdependence associated with motivational beliefs and attitudes, these antecedents will be examined in tandem. Attitudes, or personal experience, encompass experiences that may influence the individual's view toward pancreatic cancer or participation in clinical research more broadly. Beliefs include any motivational beliefs the individual has that may influence their perception of pancreatic cancer and their perception of participation in research.

The research team plays a significant role in building trust and generating engagement from the patient population, shaping patient-facing materials, and influencing outreach.[9,18] Given this influence, the antecedents defined previously will be considered from the perspective of the patient and the investigator. This includes the healthcare provider's personal or professional experience with pancreatic cancer, how at risk they believe their patient population is, and how impactful they believe research participation may be.

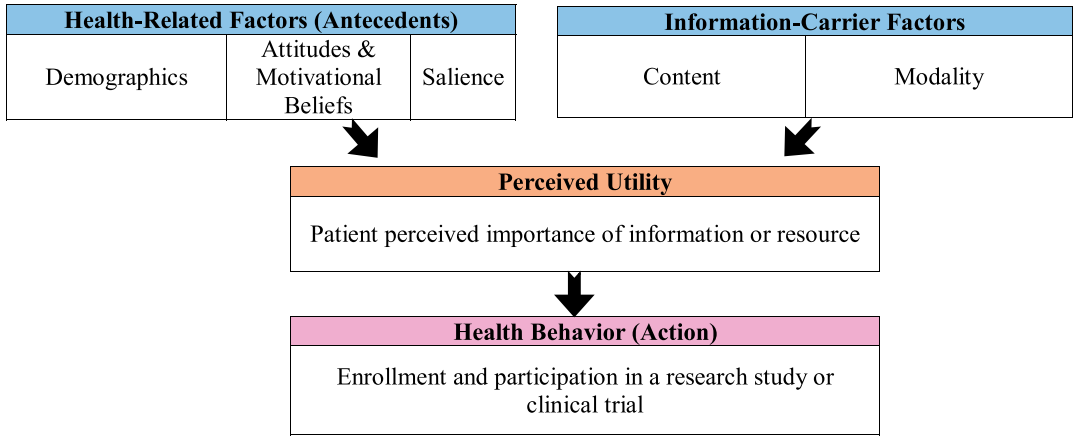

FIGURE 1. Adapted Comprehension Model for Information Seeking, with a focus on the antecedents and information carrier characteristics that influence research enrollment and participation.

In addition to the antecedents described previously, we will explore how information carrier characteristics can be used to facilitate enrollment. Information carrier characteristics are generally defined in the CMIS framework as the tone of the information, how the information is packaged, and how accessible the information is to the intended recipient.[16] In this review, information carrier characteristics include the following:

1. Content: Any content used for the purposes of research outreach or related subject materials. This includes text-based and multimedia content, such as images, video, or Web site.
2. Modality: Any strategies or methods implemented to facilitate the delivery of content. This will include a discussion of logistic barriers and facilitators that may influence the delivery of outreach materials and study information. Modality also includes institutional-level regulatory considerations.

Finally, this review will consider how antecedents and information carrier characteristics coalesce to influence the perceived utility of the information. In this model, perceived utility is defined as how useful the intended audience believes the information is.[16] Perceived utility is dependent on antecedents and information carrier characteristics. This relationship also impacts subsequent action because information perceived as useful is more likely to prompt health behavior action. In other words, when a patient perceives information about a clinical trial as important, they are more likely to consider participation. Likewise, when a primary care doctor perceives a clinical trial as being meaningful to their patients, they are more likely to engage. We propose that by garnering a better understanding of the motivational beliefs and attitudes of the potential participant and how antecedents can be leveraged through strategic outreach, researchers may be better equipped to support participant enrollment and retention.

HEALTH RELATED ANTECEDENTS

Demographics

Current research indicates that patients who report more interpersonal resources to help manage threat-related information are more likely to seek cancer information.[19] Interpersonal resources include anything from family support to critical reasoning and problem-solving skills, encompassing a broad range of resources that support decision making and outcome management. Transposing this finding to enrollment trends in the cancer research setting, patients who become research participants are more likely to have sufficient interpersonal resources that may help support access to research.[19] This may be particularly applicable to research on cancer screening programs. Cancer screening and risk assessment tools may result in actionable findings and impact an individuals' perception of personal risk. If participation in a screening program yields information about disease status or risk, adequate interpersonal resources are key to ensuring the individual has the cognitive tools necessary to manage threat-related information. Of note, current research also indicates that individuals who choose not to enroll in research are more likely to report low self-rated health, and reduced agency or a feeling of helplessness.[20] This may reflect insufficient interpersonal resources.

Sex also seems to play a role in research engagement. Women are statistically more likely to engage with information about research. In contrast, men report a higher rate of health information avoidance, including information about research studies.[21] Trans, nonbinary, and other sex nonconforming people are rarely represented in clinical research trials.[22] This underrepresentation is not an objective reflection of interest in participation but is more likely due to a lack of inclusive practices. Importantly, this population faces poorer health outcomes when compared with cis-gendered people, in part because of exclusionary research and healthcare practices.[22] Other characteristics that seem to align with hesitancy to participate include lower household income and a high school or less education, with the latter influencing health literacy.[12,23]

Race and ethnicity also influence research uptake in critical ways. Black, indigenous, and people of color (BIPOC) are often absent from the clinical research setting.[24,25] They are statistically less likely to participate in research because of mistrust and the continued effects of systemic racism.[26] The subsequent underrepresentation of BIPOC communities in the research setting is particularly critical in PDAC.[27] In the United States for example, Non-Hispanic Black populations have the highest PDAC incidence and mortality rates.[28–30]

Geographic location influences enrollment and information seeking.[31,32] For example, people who enroll in research are statistically more likely to live within proximity to a healthcare setting with sufficient staffing that can accommodate their schedule.[33] Unless participation can take place remotely or there are the necessary resources available to support travel accommodations, participants must have access to a physical healthcare setting that can support research activities. As a result, most individuals who choose to enroll in cancer research studies live in larger metropolitan areas, where major and academic centers are located.[34] Healthcare deserts, or geographic locations that are medically underserved, pose a significant barrier to research participation.[35,36] This is particularly an issue for BIPOC communities.[37] At present, nearly 80% of rural United States is designated as medically underserved, a term that includes access to research participation.[35,36] Access to the research setting may also influence wait times for patient enrollment. This is important because longer enrollment times are associated with higher rates of attrition.[38]

Healthcare providers and investigators need to consider demographics that influence enrollment and retention. These factors include the clinic setting, and the time limitations and staffing needs inherent to that setting.[39] Such variables may influence the investigators' ability to dedicate time to recruitment activities and trial support. While other healthcare provider demographics may influence clinical trial outreach practices, and subsequent enrollment practices, this area is relatively under explored. More research is needed to better understand the role physician demographics may play in achieving enrollment goals and generating investigator engagement.

Attitudes and Motivational Beliefs

In the healthcare and clinical research context, the patient's lived experience defines their attitudes and motivational beliefs, as well as how that experience influences their healthcare decisions.[40,41] This lived experience may include health issues that they have dealt with or that they have seen a friend or family member experience.[42] It also includes any prior interactions they have had with a healthcare provider or a healthcare system more broadly that may affect how much they trust a healthcare clinic or provider.[43,44] Trust is an important indicator of successful enrollment.[33] This is particularly true for BIPOC communities and other marginalized populations.[43] People who feel safe where they receive health care and who express interest in medical affairs report an existing positive attitude toward clinical research and believe that they will receive better care in the research setting, a perspective that data support.[41] They are also more likely to enroll in research. Those who enroll also tend to have a positive relationship with their primary care provider, supported by experienced-based trust that their provider can solve a problem.[45,46] This relationship depends

on proximity to an approachable and acceptable healthcare provider or healthcare setting. Among enrollees who have access to a provider or setting they trust, there is a preference for university hospital settings where research is more likely to be routinely conducted, over general hospitals or community health centers.[41] These variables align with the issue of trust. Those who do not enroll report a lack of trust and view research studies as a risker source of healthcare.[45] When an individual is not able to trust the healthcare system serving them, or when they have not received a referral from a trusted healthcare provider, enrollment suffers. It is imperative that researchers strive to establish trust within the communities they wish to serve, rebuilding it where it is broken. While bus fare may be a part of recruiting research participants, to build trust and meet recruitment goals researchers must have a clear understanding of the attitudes and motivational beliefs of their intended audience. This requires ongoing collaboration with patient advocates, community gatekeepers, and other stakeholders who can leverage their lived experience and social networks to improve patient outreach.

Referrals from a trusted care provider are critical to successful recruitment.[47] This is particularly true for underserved communities, for whom trust plays a critical role in accessing health care.[32] A positive patient-provider relationship can also improve the appropriateness and acceptability of the care provided, improving patient retention and engagement.[14] People who enroll in research indicate that their healthcare team often notified them about a specific research study, highlighting the importance of garnering support from primary care providers. When primary care providers view research favorably, know what research studies may be applicable to which patients, and understand the broader impact of a study, they are better equipped to support research outreach and enrollment. A referral from a trusted care provider can also reassure patients who may be hesitant to join a research study or provide an opportunity to address concerns about the perceived risks of the research as well as potential adverse effects associated with participation in the research study.

Individuals who participate in research are also more likely to report a personal or family history of cancer.[42] Personal experience with a cancer shifts an individual's perception of risk, as well as their interest in prevention and screening initiatives. In other words, direct experience with cancer contributes to positive attitudes toward cancer research from the perspective of personal gain and altruism.[48] Being diagnosed with cancer, or reporting a family history of cancer, also increases an individual's likelihood of being engaged in cancer research by way of provider referrals or via a patient advocacy group.[49] In contrast, individuals who do not have a personal connection with cancer may be less motivated to take part in cancer research, and their healthcare team is less likely to make them aware of research initiatives.

Personal and family history of cancer influences motivation, but it also affects health literacy. Those who do not enroll in research studies report lower health literacy, a lower threshold for cancer information overload, and a limited understanding of research opportunities.[50,51] Without a clear understanding of why research is important, either from the perspective of how research may benefit them or their families, or medicine more broadly, motivation to participate suffers. People who report lower health literacy may also feel a sense of powerlessness on matters concerning health and illness, lacking a clear understanding of the potential positive impact of research participation for themselves or others.[41]

Attitudes and motivational beliefs start with the experiences and relationships the patients walk in with. These antecedents inform cultural responsiveness and can be used to drive the development of approachable and acceptable outreach materials.[14] While it is important to describe these factors, understanding patient perception of risk and actionability is also necessary to improve patient outreach and encourage health behavior action.

Salience

Personal experiences with cancer and health literacy both influence motivational beliefs and attitudes, but fueling these perspectives is salience. The experience of seeing a loved one undergo a cancer diagnosis and be successfully treated through participation in a clinical trial may highlight the importance of research.[42] Similarly, seeing a parent or family member struggle with pancreatic cancer, a person worried about their own risk of the disease, may be motivated to look for a research study. Alternatively, a person who received a late-stage cancer diagnosis may discuss with their friends and family the importance of early detection initiatives and cancer screening.

Altruism can be a powerful motivator, driving participation. It includes more direct patient impact, for example, a patient participating in a research study may directly benefit their family members, which may be the case for a study that involves genetic testing. However, it also includes less direct patient impact, such as knowledge that their participation may benefit others in the future. Current research indicates that patients may be more inclined to participate in a research study if they recognize a clear benefit to others.[48] Where altruism or understanding of personal impact is not a factor, financial incentives can offer alternative motivation.

Patients may be more likely to participate in clinical research if they are being compensated for their time or reimbursed for travel expenses related to study participation.[52–54] Compensation can be a tricky area from a regulatory perspective, leaving the study team tasked with striking the balance between adequate compensation versus coercive compensation. Financial compensation is not considered a "benefit" from a regulatory perspective but rather is intended to offset risks associated with time loss and other personal resources spent.[55] In these situations, regulations require a careful analysis of the risk and benefit to subjects, in interest of protecting participants from coercion.

At the cornerstone of salience is again health literacy, by way of personal experience, health information seeking, or communication with a provider. These concepts are interdependent and require a clear understanding of cancer risk on the part of the patient and the primary care provider, as well as a grounded sense of actionability. Whereas patients who feel helpless are less likely to enroll, those who understand the risk associated with pancreatic cancer, understand the severity of the disease, and believe that they can take steps to reduce their risk, are those who are most likely to engage in preventative health behavior, including supporting clinical research.[20,56] Likewise, primary care providers who understand risk factors associated with PDAC, have an up-to-date knowledge of current screening recommendations, and are informed about relevant research efforts, are those who are most likely to refer patients to research.[33,57] For research enrollment to occur, both patients and physicians must have the resources necessary to strike a balance between enough fear of the disease to prompt action, but enough hope to take control and act.

Patient demographics, direct experience, beliefs, and their perception of risk and belief in their ability to take action heavily influence attitudes toward clinical research and motivations to participate. Importantly, these antecedents also dictate their response toward information about a clinical research trial. These antecedents inform the development of patient outreach. In this next section, we will discuss leveraging these antecedents to improve recruitment and retention through information carrier factors.

INFORMATION CARRIER FACTORS

Patient and physician demographics, salience, attitudes, and motivational beliefs all influence research enrollment and retention.

These factors also inform outreach and recruitment practices, including content and modality. Content focuses on what kind of information is important to patients and physicians. Modality, or delivery, focuses on other system-related factors that impact when and how a patient receives information about a research study. While many of these factors are interdependent, they are delineated below as system-related information carrier factors, physician information carrier factors, and patient information carrier factors.

System-Related Information Carrier Factors

Research engagement places significant demands on the study team, but these demands also affect peripheral staff, including primary care providers tasked with supporting recruitment.[58] Without mitigating strategies, research program sustainability and recruitment suffer. One way to address this burden is to secure opportunities for direct guidance from the principal investigator.[38] While this requires more work on the front end, it also ensures that support staff understands research objectives. Another important step is to ensure support staff are recognized for their contributions to the study. This messaging should include a clear statement about the wider impact of the research, building on feelings of altruism.[59]

Trial design and eligibility criteria can also be a system barrier to participation. It is important for research teams to consider the inclusion of specific groups that may otherwise be excluded, such as certain racial-ethnic groups, non-English speakers, or other vulnerable populations. For adults lacking capacity or pregnant patients, this also means a careful consideration of the risk-benefit ratio and available safety and efficacy data. While it can be an ethical concern to include some of these populations, it is also a justice issue to potentially limit access through exclusion, which limits the generalizability of findings.[60]

Another system-related factor has to do with patient wait time. Current literature indicates that by reducing patient wait time during any specific study related visit, they are more likely to continue participation.[61] This relates to convenience but keeping wait times down also demonstrates respect toward the patient, supporting a positive relationship between patient and practice. Keeping wait time short at other intervals is also critical, from the point of first contact to enrollment, or any wait time between visits or study procedures.[40,53] Adequate staffing can support timeliness and reduce clinic resource demands.

Patient concerns about coronavirus disease 2019 (COVID-19) exposure, and other infectious diseases, can also serve as a barrier to participation that can be overcome through system-level mitigating strategies.[62,63] Patients may be more willing to participate in research if they are provided with information related to the clinic or medical center's procedures for assuring patient safety and welfare.[64] These issues along with other system-related information carrier factors that may hinder or facilitate enrollment are summarized in Table 1.

TABLE 1. System-Related Strategies for Improving Participant Recruitment and Retention

Potential Barriers	Mitigating Strategies
Clinic resource burden	• Include patient input in the design of clinical trial • Recognition of staff who open trials and recruit patients • Systematic prescreening of incoming patients for trial eligibility • Readily available guidance from principal investigator • Engage patient advocacy groups
Participant wait time	• Once appropriate trial is identified, time for consent minimized • Minimize patient appointment wait time
Concerns about COVID-19 or other infectious diseases	• Clear communication about steps to ensure patient safety

Physician-Related Information Carrier Factors

There are a variety of information carrier factors connected to the referring or participating physician (Table 2). Healthcare providers outside of the immediate research team often play a key role in supporting research engagement and enrollment.[18,47,57] A primary care physician, for example, can only refer patients to research if they know that the research is going on and if they believe that it could positively impact their patients. When a healthcare provider has limited awareness to a research study, their commitment supporting that trial falters. This barrier can be addressed through strategic communication.[65]

By providing healthcare providers with succinct information about the research objectives, focusing on the most salient information, researchers can improve trial awareness.[18,47,53] This is best accomplished through a one-page factsheet, focusing on research objectives along with potential benefits of participation not only for the individual patient but also for the community more broadly. Physicians also benefit from receiving clear and succinct information about patient eligibility criteria.[66] Finally, it is important to encourage enthusiasm and to ensure support staff have an opportunity to understand the impact of the research, both by communicating objectives from the start and by providing a copy of any study results when published.[38] This ensures that individuals who are involved even with early stages of the research have an opportunity to appreciate their impact.

The time burden imposed on healthcare providers who are asked to engage with the research can be minimized by completing usability testing on any subject facing materials. Usability testing is an effective way to assess the acceptability and functionality of communication tools and delivery systems, optimizing them before utilization, and is a key step to ensure materials are appropriate for the intended audience.[67] Usability testing often involves selecting a small group of participants who reflect the target audience and have them review the outreach materials, providing feedback about the accessibility and effectiveness of the review item. This feedback informs changes to outreach materials.

While usability testing can streamline communication systems and reduce some of the time burden inherent to supporting research, there are also instances where it may be appropriate to offer compensation to physicians or a recruitment bonus.[68] Recruitment bonuses are defined as an additional payment offered to a site or an investigator that is provided in response to reaching a specific number of enrolled participants. This payment is separate from any reimbursement or payment received for participating in the research as an investigator and can be an important mitigating strategy for engaging clinic settings and physicians that cater to underserved populations. While this strategy can be an effective way to incentivize physician engagement, it requires careful review and approval by the institutional review board (IRB) or independent ethics committee, because it potentially may create a conflict of interest that could influence patient safety and welfare. In certain situations, regulatory authorities may determine that the use of an investigator recruitment bonus is unethical and disapprove the use of this mitigation strategy.

Patient-Related Information Carrier Factors

There are several logistical barriers facing eligible patients as noted hereinafter in Table 3. Perhaps one of the most frequently

TABLE 2. Physician-Related Barriers and Strategies for Improving Recruitment and Retention

Potential Barriers	Mitigating Strategies
Limited awareness or waning commitment	• Encourage leadership engagement • Recognition for contributions to study
PCP attitude toward patient participation	• Factsheet that outlines study objectives and potential benefits • Access to published results of study
Staff limitations	• Recruitment incentives • Relay patient eligibility criteria • Usability testing where applicable

PCP indicates primary care physician.

cited barriers involves their geographic distance to a participating site, making it difficult to schedule required study visits and travel to study locations.[31,32,34] One way to overcome these barriers is to limit in-person requirements, when possible, by using electronic consent processes and telehealth visits. This approach also addresses patient concerns about COVID-19 or other disease exposure. Institutional review board approval is required for an alternative or remote consent process, but the research that is considered greater than minimal risk also must use a consent platform that is title 21 of the Code of Federal Regulations Part 11 compliant. Remote consenting processes have been used for many years and are now becoming more common in the wake of the COVID-19 pandemic and the increase demands for telehealth services.[69]

While remote recruitment and enrollment processes can help overcome geographic barriers, current research indicates that it may not be the panacea researchers hope for. For example, BIPOC individuals continue to be underrepresented across research studies relying on remote consent and participation, with many expressing a preference for in-person interactions and direct engagement with trusted healthcare providers.[32,33,46]

Alternatively, a central research location may benefit from using home health visitors, local community sites that are closer to participants, or satellite clinics to reduce travel time.[70] When these alternatives are not attainable, participants should be reimbursed for any study-related travel expenses. Reimbursement is different from compensation; however, both must be reviewed and approved by the IRB or independent ethics board to ensure that financial incentives are not coercive.[55] While patient compensation, like investigator compensation, can support enrollment and retention, it can prompt ethical concerns. Excessive compensation can also raise safety fears in patients and negatively impact enrollment as a result.

Patients may have trouble taking time away from work or family obligations to attend study visits. These and other patient scheduling barriers may be resolved by using flexible scheduling, clearly communicating scheduling requirements to participants at the beginning of their participation and embedding frequent reminders about upcoming appointments.[38,54] Ultimately, competing scheduling demands are a complex barrier to participant retention that cannot be reduced to logistical-focused solutions but must also take patient motivational beliefs and attitudes into consideration when seeking resolution.

Motivated patients are more likely to have interest in and find time for participation. Simply put, when patients have a limited understanding of research and why it is important to themselves, their families, or the community more broadly, they are less inclined to participate in research.[38,54] Conversely, patients with a solid foundation in health literacy and who appreciate why research is important are more likely to enroll and refer others. Culturally responsive subject materials that accurately delineate research objectives and put a "face" to the research team, through personal and supportive communication, support patient engagement.

TABLE 3. Patient-Related Barriers and Strategies for Improving Recruitment and Retention

Potential Barriers	Mitigating Strategies
Geographical distance	• Limit in-person requirements • Use local community sites, home visitors, or telehealth options • Reimbursement for travel expenses
Scheduling burden	• Use flexible scheduling • Clearly communicate study and time requirements • Appointment reminders • Patient compensation or patient referral bonus
Outreach	• Patient-facing materials succinctly communicate main information about study • Include patient advocacy groups in the design process and dissemination of all research materials • Post materials over a variety of platforms and media, include social media, print (when appropriate), Web site, etc
Limited awareness or health literacy barriers	• Accessible, culturally responsive study materials • Include community stakeholders on study team or as consultants • Approachable study team (provide biosketch card of study team) • Practice of using empathetic communication • Personal interactions
Concern about risk of participation (includes physical risk, confidentiality risk, etc)	• Clearly communicate risk/benefit ratio • Encourage discussion with medical staff and family members about the research • Clearly communicate confidentiality and privacy protections
Lack of interest in research or hesitancy in enrolment	• Initiate contact via different modalities, including email or phone call • PCP or investigator initiate direct outreach when possible • Emphasize scheduling flexibility and personalized communication • Lack of expressed interest

PCP indicates primary care physician.

The inclusion of community gatekeepers and patient stakeholders as members of the research team is quintessential to the development of culturally responsive patient-facing materials.[14] Research outreach is conceptualized as the beginning of the consent process, so it is important that any subject facing materials emphasize the voluntary nature of the research through thoughtful content and tone, to avoid undue influence, and create opportunities for continued conversation.[52] Participants should be reminded that voluntary participation means they can withdraw from the research at any time, respecting the autonomy of the individual.[52] From a regulatory perspective, this means that any subject materials are free of misleading information and strive to avoid a therapeutic misconception.

Patient-facing materials can also address concerns about potential adverse events or risks related to study procedures.[71] It is important for research coordinators to clarify protocol information and consult with the overseeing IRB to ensure accurate and transparent communication about risks. Patients should also be encouraged to discuss their concerns with the medical staff, including their primary care provider, along with friends and family. These conversations can be supplemented via a one-page summary of the research study, described earlier under physician-related factors, or a study Web site.[54] Similarly, research teams must discuss confidentiality and privacy concerns with their patients and provide supports needed for patients to answer questions they have about health insurance coverage and cost concerns.

Just as it is important to communicate research results and impact to supporting physicians, it is also important to delineate research milestones to patients. This can be done through newsletters or thank you notes, but current literature also highlights the value of sharing published research results or updates. These materials should take an altruistic tone and encourage patients to reach out to their healthcare team with any questions or concerns.[47,48]

Despite the mitigating factors listed previously, there are still going to be patients who fail to respond or indicate a lack of interest in the study. For these difficult to reach populations, enrollment trends may improve by sending out alerts via their health portal when feasible or through direct phone calls.[64,72] Response to physical mailings can be improved by using a large colored or textured envelope when mailing a recruitment letter and study fact sheet. The use of mailing services, like FedEx, can also improve uptake, by implying a sense of importance or distinguishing the mailing from "junk mail." Envelopes should be handwritten or use a typeface that appears handwritten, and physical mailings benefit from an email before and a phone follow-up after the letter is received. For these more labor-intensive, multipronged recruitment techniques, it is important to implement a triaging system to help direct recruitment investments.[73] This could include a prescreening tool to explore interest in clinical trials or implement a tiered approach that focuses on easier outreach first, before moving on to those that place a heavier burden on study resources. Ultimately, the more personal, direct, and culturally responsive outreach materials are going to be not only the most labor intensive but also the most effective.

CONCLUSIONS

Medical advances require equitable, representative participation in research studies. Unfortunately, recruitment goals are one of the most difficult research objectives to meet. Our ability to overcome this barrier is further limited by the paucity of research exploring recruitment and retention of research participants, especially historically underserved communities. Traditionally, researchers have focused on addressing basic logistic barriers, providing reimbursement for travel-related expenses, or have invested in publishing recruitment materials to different media platforms with variable success. While these strategies are important, research teams also need to consider the diverse motivational beliefs, attitudes, demographics, and risk perceptions of their target audience. The Comprehension Model for Information Seeking is well positioned to support research teams in establishing this important knowledge base about the community they wish to serve, with a focus on using patient motivational beliefs and attitudes as antecedents to drive research outreach and influence health behavior.[16] Using these antecedents, outreach materials and methods can be tailored to the patient population. This approach may result in culturally responsive content, delivered via routes of most impact, addressing the multidimensional nature of accessible and effective healthcare messaging.[14] For pancreatic cancer, where there is frequently rapid progression and clinical deterioration, timing is critical. Importantly, while this approach may indicate the need for more initial recruitment investment, the use of a thoughtful triaging system can ensure there is a return on investment.

An important limitation to this work is that many of the evidence-based strategies included in this review are based on pre–COVID-19 research. As patient perceptions of, access to, and trust in health care has changed since early 2020, system opportunities and patient attitudes toward research participation have changed along with it.[62] The magnitude and effect of this terrain change are yet to be fully apparent. Some patients may be disinclined to sign up for a clinic visit unrelated to their routine medical care, but they may also have a better understanding in the importance of clinical trial participation. Research teams may find geographic barriers easier to overcome through the utilization of remote visits and remote monitoring, as the application of telehealth has become routine and more widely accepted by medical practices and the general population.[69] However, participants may possibly lose the valued personal connection with the medical team, one that supports trust building, which could affect both recruitment and retention.[26] Depending on the research objectives, the research context, the study design, currently available treatments, attitudes of the target patient audience, along with other important variables, best practices behind patient outreach and recruitment will vary by study. Ultimately, the burden falls to the research team to develop a keen understanding of the health-related and information carrier factors of their target audience and use that knowledge to identify the best route to engagement.

ACKNOWLEDGMENTS

The authors thank the following individuals for their support and input in the development of this article: Vay Liang Go, MD; Jennifer Carney, MA, MPH; Suresh Chari, MD; Sudhir Srivastava, PhD, MPH, MS; Jo Ann Rinaudo, PhD; Lynn Matrisian, PhD, MBA; Eva Shrader, MS, CCRP; Laura Rothschild, MBA; and Ann Goldberg, BA. Most of all, the authors thank the dedicated research coordinators who willingly shared their recruitment and retention experiences and ideas.

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