Improving diverse patient enrollment in clinical trials, focusing on Hispanic and Asian populations: recommendations from an interdisciplinary expert panel

Bhavana Pothuri [1], Premal Thaker,[2] Adrienne Moore,[3] Rosa Espinosa,[4] Kara Medina,[5] Deborah Collyar,[6] Kathleen Lutz,[1] Mihaela C Munteanu,[7] Brian Slomovitz [8]

OPEN ACCESS

[1]NYU Langone Health Perlmutter Cancer Center, New York, New York, USA
[2]Division of Gynecologic Oncology, Washington University School of Medicine, Saint Louis, Missouri, USA
[3]Endometrial Cancer Action Network for African Americans, Atlanta, Georgia, USA
[4]Baptist Health South Florida, Miami, Florida, USA
[5]UC San Diego Health, San Diego, California, USA
[6]Patient Advocates In Research (PAIR), Danville, California, USA
[7]Incyte Corporation, Wilmington, Delaware, USA
[8]Mount Sinai Medical Center and Florida International University, Miami Beach, Florida, USA

Correspondence to
Dr Bhavana Pothuri; bhavana.pothuri@nyulangone.org

Received 16 May 2024
Accepted 12 August 2024

To cite: Pothuri B, Thaker P, Moore A, *et al. Int J Gynecol Cancer* Published Online First: [please include Day Month Year]. doi:10.1136/ijgc-2024-005751

ABSTRACT

Lack of patient diversity in clinical trial enrollment remains an obstacle to achieving equitable healthcare outcomes. Under-representation has resulted in non-generalizable clinical knowledge, inequitable access to treatment, and health disparities among minority and disadvantaged groups. A multidisciplinary panel was convened to consider the challenges of diverse patient accrual and provide actionable solutions to improve representation in clinical trials. The panel was comprised of participants with knowledge in gynecologic oncology and included physician, advanced practice nurse, patient navigator, patient advocate, and pharmaceutical industry representation. Focus was given to recruitment barriers for Asian and Hispanic patients. The panel identified several areas of concern, including explicit and implicit biases for the physician and care teams, language and cultural nuances, inadequate inclusion of family in the decision-making process, and under-representation of women in clinical trials. The panel also identified the important role patient navigators, nurses, and advanced practice providers have in patient recruitment from under-represented populations. The role of study sponsors, and global and regional initiatives, to address historic disparities in clinical trial recruitment were also considered critical. The actionable solutions proposed should enable study sponsors and clinical trial sites to achieve greater diversity in enrollment globally.

INTRODUCTION

Lack of diversity in clinical research is a longstanding issue and a major obstacle to offering patients equitable treatment opportunities. Historically, most patients enrolled in clinical trials, which are predominantly conducted in western countries (primarily the US and Europe), did not accurately represent the population at large.[1 2] This has resulted in clinical knowledge that is not generalizable, unequal access to treatments, and health disparities in outcomes among minority groups. Recently, high-impact journals, including the *New England Journal of Medicine* and the *Journal of the American Medical Association*, have endorsed increased diversity in clinical trial enrollment with guidance on reporting race, ethnicity, and representativeness of study groups.[3]

To better understand practical barriers and brainstorm on ways to improve representation in clinical trials, we convened a multidisciplinary expert panel to discuss challenges and provide actionable solutions. Focus was given to increasing the enrollment of Asian and Hispanic patients, especially in oncology trials. These groups were selected as historically they have received less attention in the literature.[4] This may be attributable to a general lack of data collection for Asian and Hispanic populations and/or a lack of disaggregated data (ie, data are combined with other under-represented groups).[5]

The panel members and authors were selected based on clinical experience (eg, clinical trials, years of practice), organizational leadership roles (eg, Gynecologic Oncology Group (GOG) Foundation, pharmaceutical industry), or experience/leadership as a patient and patient advocate. The multidisciplinary panel was comprised of gynecologic oncology healthcare experts (physicians, advanced practice nurses), patient navigators, patient advocates, and pharmaceutical industry representatives. Although all panel participants focused on gynecologic oncology trial accrual, recommendations arising from this meeting are also applicable to other therapeutic areas.

PHYSICIAN AND CARE TEAM RELATED OBSTACLES

Physicians play a lead role in promoting diversity in clinical trials. The panel identified the importance of ensuring physicians have sufficient time and resources to fulfill this role. Physicians should be provided with the necessary education and training to recognize key demographics, engage patients in a culturally sensitive manner, and avoid personal biases.

Time Constraints, Education, and Training

It is challenging for physicians to set aside the time and effort required to maintain awareness and knowledge of ongoing clinical trials (Figure 1).[6] Demanding clinical productivity benchmarks and the limited time physicians

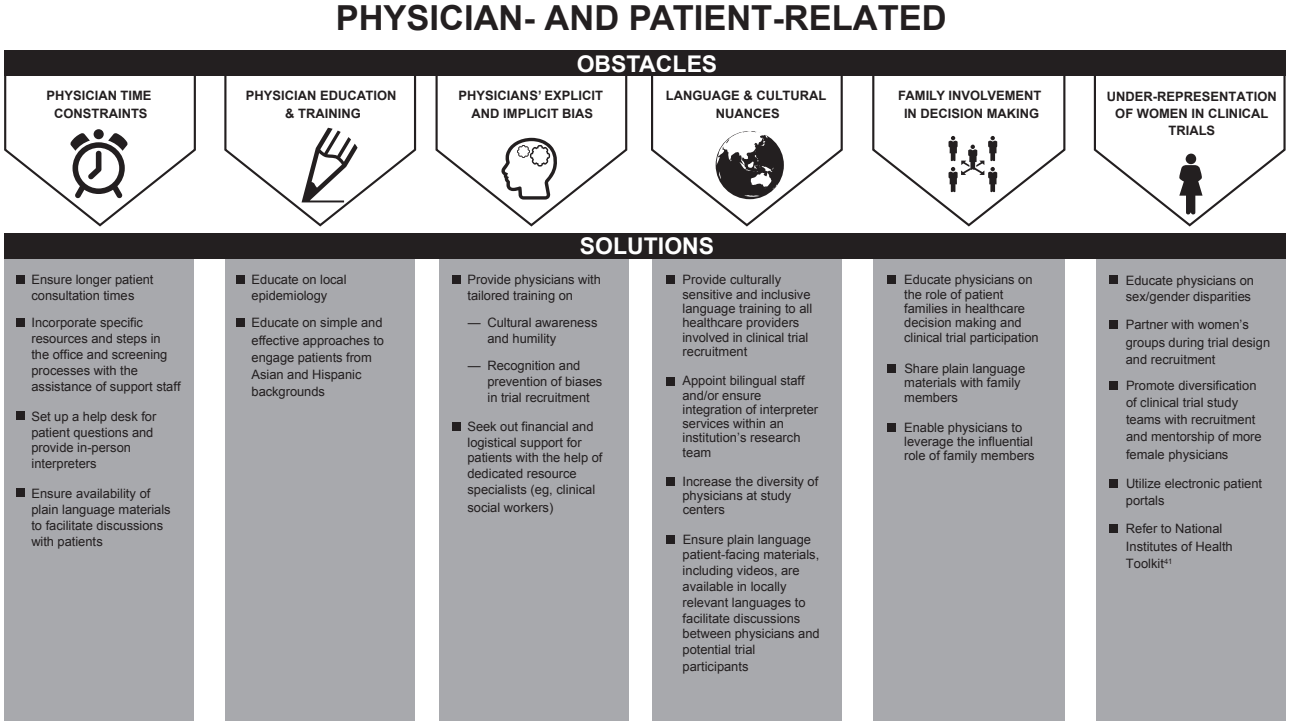

Figure 1 Summary of physician- and patient-related obstacles and recommended solutions to address under-representation of Asian and Hispanic patients in clinical trials.

spend with patients impair the ability of physicians to provide necessary medical care, let alone the time to discuss the complex nuances of clinical research and trial enrollment with patients. Furthermore, doing so in a culturally appropriate manner, with tailored approaches for Hispanic and Asian patient populations, requires additional time, preparation (eg, coordination with an in-person interpreter), and specific cultural humility training. Combined, these barriers often lead to withholding clinical trial opportunities from potential participants from under-represented groups.[6]

When dealing with diverse patient populations, physician time constraints can be alleviated directly through extended patient consultation times and indirectly by increasing physician efficiency. Improvements in efficiency can take the form of support for patient screening (discussed in the Support and Care Team Involvement section below), scribes, in-person interpreters, and a multilingual help desk to address patient questions. Physicians should also be provided with dedicated time to acquire a general awareness of local epidemiology and catchment area, and to learn simple and effective culturally appropriate approaches to engage patients.[7] One such culturally appropriate approach to encourage patient interest could include promoting improved outcomes for future generations, which is particularly important for Hispanic and Asian populations.[8 9]

Physician and Care Team Explicit and Implicit Biases

Clinical trial recruitment of under-represented groups, including Asian and Hispanic patients, can be affected by physicians' explicit and implicit biases. A recent study based on 91 qualitative interviews (67 White, 13 Asian, and 11 Black clinicians) conducted at five cancer centers in the US showed that clinicians held negative perceptions of racial and ethnic minority study participants, which could contribute to limiting clinical trial opportunities.[6] The negative impact of implicit bias on differential diagnoses, treatments, and patient referrals is well studied; however, its impact on clinical trial recruitment has received less attention.[10] Structural and social determinants of health in the community and workplace (ie, poverty, limited education, limited English proficiency, socioeconomic level) reinforce biased decision making,[6] and assumptions about patients are often made before broaching the topic of clinical trial enrollment.[6] Patients perceive the biases, with Black and Hispanic respondents less likely to report encountering physicians who share or understand their culture versus White respondents; Asian respondents are less likely to report being treated with respect compared with White respondents.[11] In addition, most cancer patients experience some form of financial toxicity, whether or not they enroll in a clinical trial,[12] but minority groups often have disproportionately lower income, potentially creating more financial hardship. Missing work for any treatment, coupled with additional safety visits, long pharmacokinetic schedules, and other time-consuming obligations for trial participants, creates additional burden for patients with limited flexibility. Hispanic patients are more likely to be represented in the service or construction industry and as a result may be less likely to have sick time/leave.[13]

We recommend comprehensive training, such as the American Society of Clinical Oncology (ASCO)/Association of Community Cancer Centers (ACCC) Just ASK™ training program[14] to ensure physicians have the knowledge and skills to avoid implicit biases. This training should be offered to all physicians, nurses, advanced practice providers, and members of clinical trial teams in large health systems, community health centers, and small provider

networks. Ideally, it should also include cultural awareness and cultural humility training, avoidance of stereotyping, and provide examples of successful strategies on inclusivity.

Physicians and their support staff should help to identify financial and logistical support for patients with limited financial resources. This task could be allocated to dedicated resource specialists, such as clinical social workers or navigators (discussed in the Patient Navigators section below).[7] Sponsors can also contract with companies such as Unite Us (https://uniteus.com/) who can connect patients with existing resources within their community. Principal investigators of trials can work with study sponsors to support issues linked to social determinants of health related to trial participation, including loss of wages, childcare, transportation, and housing. Initiation of virtual and decentralized trials by study sponsors removes the need to travel long distances to a central study site and could increase recruitment from rural communities. However, the need for a computer and reliable internet access could present access barriers for some patients in this setting.[15]

PATIENT CONSIDERATIONS

The patient level barriers encountered most frequently by the panel participants in their clinical practice include language and cultural barriers, attitudes and cultural beliefs of family members and inadequate inclusion of family in healthcare decision making, and the under-representation of women in clinical research. Patients frequently rely on family caregivers for support during the consent process to confirm their agreement with participating in the study and support during appointments with healthcare providers.[16] The opinions of family members greatly influence patients' treatment choices and psychological well-being.[17 18] We found that this was especially true in the Asian population and culture, where potential patients rely on family members' or children's views. Research suggests that there are several reasons for the reduced likelihood of women to be enrolled or to enroll in clinical trials, including bias in offering participation,[19] sex-specific eligibility criteria that broadly render women of childbearing age ineligible,[1] family responsibilities, and mistrust of researchers.[20]

Language and Cultural Nuances

With the increase in culturally and linguistically diverse patient populations managed by each provider, language discrepancy between a physician and patient can be a barrier to equitable and effective healthcare in general.[21–24] According to a review of 1597 gynecologic oncology trials registered on ClinicalTrials.gov and conducted between 1997 and 2021, 12% excluded patients because of their spoken language.[21] In a culturally focused psychiatric consultation intervention program for Hispanic Americans with depression, participants agreed that it was more important their providers speak their language than have the same cultural background.[22] Similarly, language access is the number one barrier that prevents Asian Americans from learning about and enrolling in clinical trials.[23] Language barriers can also limit a patient's ability to provide informed consent to participate in a trial, particularly as consent pathways are often complex.[24]

To address these issues, we recommend inclusion of bilingual staff and/or integration of interpreter services within an institution's research team, to be paid at fair market value by the clinical trial sponsor. In addition, we recommend translation of all relevant documents and informed consent forms into the languages spoken by the trial participants by the sponsor or consortium group whenever feasible.[25] To enable sponsors to provide these services in a cost efficient manner across the study, we encourage participating sites to consider and provide accurate feasibility assessments of such needs. This should include in-person interpreters at the initial clinical trial visit (when there are time constraints and a complex and large volume of information to be shared with the patient) to improve lines of communication. Having interpreter services available may increase the workload for trial staff, but will ultimately help to reduce language barriers to ensure all study aspects are well understood by potential study participants.[26] Additionally, having consent and patient materials translated before trial start is very valuable in improving language barriers.[26]

In addition to language barriers, cultural barriers may also limit patient access and interest in clinical trials. For example, many patients prefer to be treated by a physician from their own racial or ethnic group. However, according to a 2016 analysis from ASCO, only 2.3% of practicing oncologists self-identified as Black, and 5.8% of practicing oncologists self-identified as Hispanic (vs 13% and 18% of the US population, respectively), and~13% identify as Asian vs 6% of the US population.[27]

Increasing the diversity of physicians and other clinical research study members could enhance recruitment of under-represented minorities. In a recent survey, Black respondents (n=323) were more interested in participating in a clinical trial when they were presented with a photograph of a Black investigator, with perceived trustworthiness a key factor influencing this finding.[28] However, increasing the diversity of clinical trial staff is not always possible, highlighting the importance of providing cultural humility and inclusive language training to all physicians and the research team involved in clinical trial recruitment.[9]

Plain Language and Patient-Facing Materials

Clinical trial material, and medical material in general, can be complex and lengthy, making it difficult to comprehend, even for educated patients communicating in their primary language. Plain language, culturally appropriate patient-facing materials, designed to be understood quickly and easily by matching health literacy levels (ideally eighth grade language) should be used to facilitate discussions between physicians and potential trial participants.[29] These materials should be translated into commonly spoken languages that are site specific. Videos in Spanish and local Haitian and Asian languages introducing a specific trial and the rationale for enrollment in a clinical trial can be helpful.[30] These materials should also provide an adequate explanation of the scientific and medical terminology used in clinical research (eg, in placebo-controlled trials, there should be a clear explanation of what a placebo is and why treatment is administered in a blinded fashion, as patients may not realize that they will receive the best standard of care at minimum).[9] Availability of these patient-facing materials can help address health misinformation that is spread via social media networks, an issue that appears to disproportionally affect Hispanic communities.[31] In agreement with these recommendations, development of culturally appropriate recruitment materials (ie, patient brochures) was recommended as a strategy by the Diversity Working Group of the IRONMAN registry to enhance minority engagement in prostate cancer clinical trials.[25] In addition,

the eXamining the Relevance of Articles for You (XRAY; https://www.facingourrisk.org/XRAY) program reviews cancer topics reported in the media to improve health literacy and counter inaccurate or misleading reporting.

To support adoption of patient-friendly language in the clinical research setting, the US Food and Drug Administration (FDA) has produced a glossary of common terms used in oncology clinical trials that patients find difficult to understand[32]; other similar glossaries are also available, including the National Cancer Institute Dictionary of Cancer terms,[33] within the Investigator's Toolbox produced by the National Institute on Aging,[34] and the Multi-regional Clinical Trial Center of Brigham and Women's Hospital and Harvard.[35]

Critical Role of Family in Decision Making

For some patient populations, the beliefs and attitudes of their families can be as important as their own for healthcare decision making.[17] In focus group studies, positive opinions of family and friends were cited as an important facilitator for clinical trial enrollment among Asian patients with breast cancer in Singapore,[17] whereas cultural beliefs regarding stigma and shame were described by Chinese American women as a barrier to sharing a breast cancer diagnosis or positive screening result with family members.[18] Similarly, in Hispanic populations, many patients look to family members for approval or agreement when deciding whether to participate in a cancer clinical trial.[16]

A physician's ability to leverage the influential role of family members can improve recruitment and retention of diverse patient populations. Decision making patterns observed in pediatric clinical trials (including exclusionary, informative, collaborative, and delegated behaviors)[36] are a good starting place for understanding the role of families in decision making for patients of all ages and cultural backgrounds. Depending on the role family members will take—functioning as a gatekeeper, making decisions while informing the patient, screening information for the patient, or simply providing support for patient decisions—appropriate efforts can be made to include and inform family members rather than hold isolated discussions with the patient. Clear communication with the patient while inviting them to their appointments or engaging them via telephone during consultation is key.

Under-representation of Women in Clinical Research

Although female participation in clinical trials has increased in recent years, under-representation remains, particularly within certain disease areas, including cardiology,[37] and remains uneven in cancer. For example, in a review of completed cardiovascular trials registered in ClinicalTrials.gov from 2010 to 2017, only one-third of patients were women,[37] despite heart disease being the leading cause of death for women in the US and worldwide.[38] Furthermore, in a similar analysis of cancer clinical trials completed between 2003 and 2016, female patients represented 41% of trial participants overall, despite higher prevalence rates (compared with male patients) for many cancers, including colorectal and lung cancer.[39]

To address the ongoing bias that contributes to under-representation of female patients, we recommend adopting new initiatives, such as electronic patient portals that invite patients to participate in clinical research and circumvent potential implicit bias in offering participation.[19] Study sponsors and personnel involved in trial recruitment should also refer to the National Institutes of Health Toolkit, which includes a range of strategies designed to engage, recruit, and retain women in clinical research.[20] Additional strategies include education of physicians on sex/gender disparities, partnership with women's groups, and diversification of clinical trial study teams with recruitment and mentorship of more female individuals in STEM and medicine,[1] which some patients may consider more trustworthy and be more comfortable with. In a recent literature review, female authorship of clinical trial publications (specifically if both first and senior authors were women) was correlated with higher female enrollment in clinical trials compared with male authorship.[40] The importance of using gender neutral language in clinical trial protocols to increase sexual and gender minority recruitment in cancer trials has also been highlighted recently.[41]

SUPPORT AND CARE TEAM INVOLVEMENT

The panel discussed the important role that patient navigators and advanced practice providers can play in referring patients from under-represented populations to clinical trials and in supporting, educating, and guiding patients through the process of trial enrollment and participation.

Patient Navigators

In recent years, patient navigation, which involves providing educational and facilitative services to patients, has emerged as an important tool to enhance recruitment and retention of under-represented groups in clinical trials.[7]

Navigators are well positioned to help Asian and Hispanic patients identify suitable trials (Figure 2). Through carefully tailored one-to-one support, these members of the healthcare team may play an important part in presenting clinical research as an option and in helping patients understand the potential risks and benefits of participating in clinical trials. For example, for patients with ovarian cancer, navigators in the community can direct patients to the Ovarian Cancer Research Alliance (OCRA) and Clearity Foundation. These entities have information on clinical trials on their websites and the option to speak with a counselor about trial options and connect with other individuals with the same diagnosis with similar racial/ethnic backgrounds.[42] Project IMPACT showed that when patient navigation services were provided, 80% of eligible Black patients with cancer enrolled in a clinical trial and 75% completed the trial, compared with 38% who did not receive navigation support ($p<0.001$).[43] In a recent survey of research associates conducted by NRG Oncology, more than 44% of respondents cited the use of patient navigators as one of the most effective methods of improving recruitment of under-represented patient populations into oncology clinical trials, particularly in terms of clinical trial education.[44]

A key function of navigators is to develop and maintain deep relationships with patients and their families during the whole clinical trial process. In an interview-based study of patients' experiences with navigation for cancer care (n=35; 69% White, 20% Black, and 6% Hispanic), providing emotional support, "being there," and providing helpful information were identified as the most valuable aspects of navigation, highlighting the importance of trust in the patient–navigator relationship.[45] Patients also value their presence as "insiders" to the healthcare system.[45] Patient navigators have been shown to address issues related to patient distrust (as has been reported for Black patients[46]), modestly improve cancer clinical trial knowledge and participation among Chinese patients,[47]

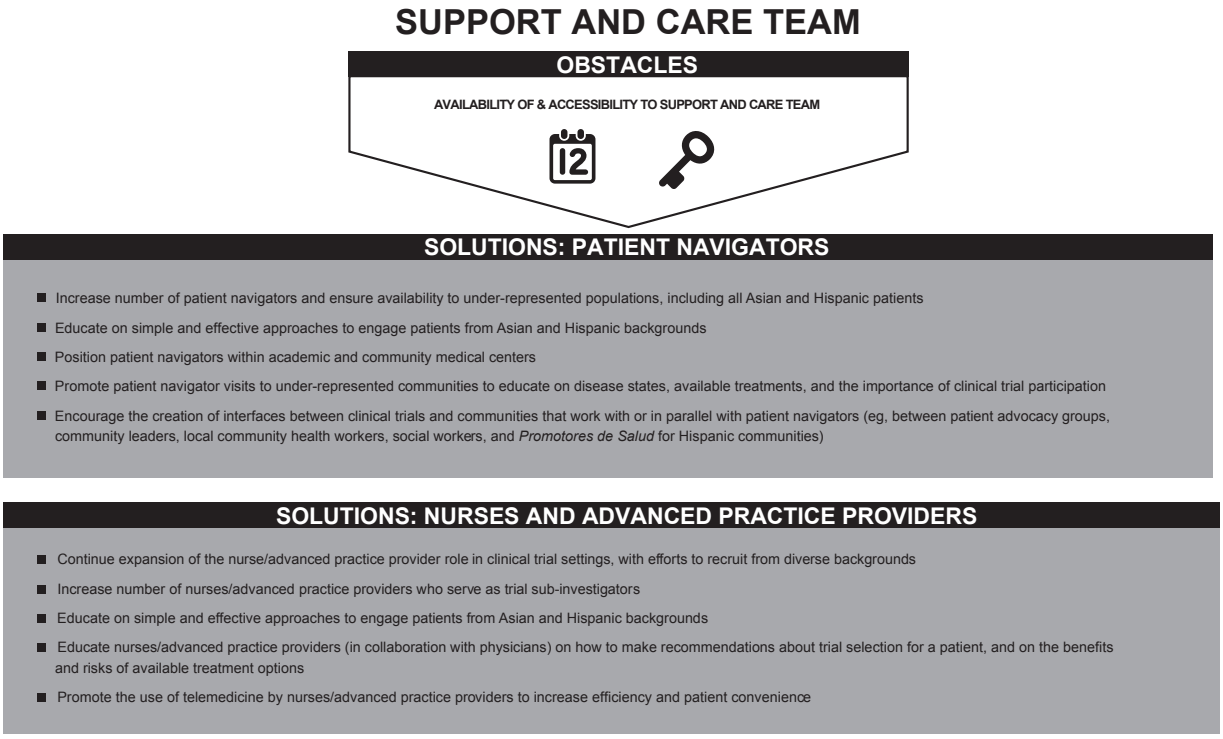

Figure 2 Summary of support and care team–specific obstacles and recommended solutions to address under-representation of Asian and Hispanic patients in clinical trials.

and improve participation and retention of Hispanic patients in clinical trials.[48]

Once a patient has agreed to participate in a clinical trial, navigators can continue to act as an intermediary between the patient and clinical care staff, as well as support patients and their families from the beginning of their clinical trial journey. Navigators can guide patients through the maze of protocol-required testing and patient-reported outcome forms, schedule medical and testing appointments as required by the study, provide information about various financial and social support resources, such as child support, and arrange transportation for research appointments, while working around caregivers' and patients' daily schedules. In addition, they can provide reassurance to family members about their relative enrolling in a clinical trial.

Patient navigation has received a huge boost in recent years with the Centers for Medicare and Medicaid Services recently approving financial compensation for navigation services in the US.[49] Navigators can also extend outside of medical centers by visiting minority communities to educate on disease states, available treatments, and the importance of trial participation and biospecimen donation.

Community Outreach

Patient advocacy groups, community leaders (local and with shared ethnicity/race), local community health workers, and social workers may be best suited to deliver education on clinical trials, as they are often perceived to be trusted pillars of each community. Patient advocacy groups may have a good understanding of how to identify trusted community leaders—including religious leaders, business figures, politicians, or other society leaders—and can put physicians in touch with target community contacts. Furthermore, community events and outreach activities can provide a valuable opportunity for promoting clinical trials.[7] To promote community involvement in science and research, the Community Based Participatory Research (CBPR) program has been established by the National Institute on Minority Health and Health Disparities with the aim of strengthening community engagement in addressing health disparities in socially disadvantaged groups.[50] As documented for Native American patients, culturally aware patient navigators and community research representatives can increase trial enrollment by liaising between medical center staff and communities.[30] In addition, recognizing and expanding the established roles of Promotores de Salud for Hispanic communities (front-line public health workers who are trusted members of and/or have an especially close understanding of the community) can also provide successful strategies for increasing recruitment. Finally, healthcare systems should recognize the importance of navigators and provide reimbursement for their services, which includes Patient Illness Navigation (PIN) services, as highlighted recently by the Centers for Medicare and Medicaid Services.[49]

Nurses and Advanced Practice Providers

Nurses and advanced practice providers are an integral part of the support and care team, providing the primary point of contact for many patients. In a recent survey of advanced practice providers, of which more than two-thirds were nurses, 98% recognized the importance of trials in improving standard of care, 78% stated they were comfortable discussing clinical trials in general with their patients, and 73% expressed an interest in becoming more involved in the clinical trial process.[51]

Compared with physicians, nurses and advanced practice providers typically have more time to spend with patients and

can develop strong relationships with patients and their families throughout the clinical trial process. An assessment of family and friend support systems at the initial visit is vital for successful trial recruitment. Nurses and advanced practice providers can also provide education and reassurance to patients and their families about the clinical research protocol and participant expectations. Advanced practice providers with appropriate clinical trial training, in collaboration with the physician, can make recommendations about trial selection for a patient and help with understanding the risks and benefits of available treatment options.

The role of advanced practice providers in the clinical trial setting continues to expand, which is reflected by an increase in advanced practice provider positions, especially at larger academic centers, and their role as sub-investigators managing patients at some study sites.[51] Alongside this role expansion, as with physicians, efforts must be directed at increasing the recruitment of advanced practice providers from diverse backgrounds. According to recent data from the US, the most common race/ethnicity of nurse practitioners is White (77.5%), followed by Hispanic or Latino (6.7%), Asian (6.3%), and Black (4.7%; vs 59%, 19%, 6%, and 14%, respectively, based on the 2020 US Census).[52] In addition to increasing the number of nurses and advanced practice provider positions, the use of telemedicine can help increase efficiency and access, allowing time to discuss trials with patients and facilitating prompt trial evaluation and initial screening, particularly for patients who are internal referrals.[51]

ROLE OF STUDY SPONSORS

Study sponsors from pharmaceutical companies have an important role in improving diverse patient enrollment in clinical trials by providing multilingual help desks to respond to patient questions, developing plain language materials, translating educational and patient-facing materials to locally relevant languages, supporting virtual navigators to help patients through the clinical trial process, supporting in-person patient navigator and community outreach, and designing more inclusive and decentralized trials.

Further efforts of pharmaceutical companies should also include determining the incidence and prevalence of the patient population to be studied (eg, in terms of sex, age, race, ethnicity, location, disabilities, socioeconomic status) through careful review of the published literature, real-world data, and population registries; setting a priori race/ethnicity recruitment goals; and financing clinical trial diversity initiatives. Pharmaceutical companies can also consider diverse recruitment goals when planning and developing clinical protocols, biospecimen collections, and patient-reported outcome measures. Lack of diversity in biospecimen collections and clinical trial recruitment has created gaps in our understanding of diseases and treatment effectiveness across subgroups within each population, and this lack of diversity also extends to the collection of patient-reported outcome data.[53] There is an urgent need to enable more comprehensive evaluation of the benefit–risk profile of investigational drugs across an appropriately diverse population that is reflective of contemporary patient populations expected to use the medicine. Setting enrollment goals and sex/gender data collection proactively creates measurable accountability.[54]

In addition, in ongoing discussions with the FDA and other health authorities, sponsors can promote expansion of post-marketing trial eligibility criteria to facilitate more diverse patient populations, even if they were excluded from earlier phase trials. Improvements in recruitment diversity will also hopefully be achieved with the 2022 US Food and Drug Omnibus Reform Act (FDORA), which requires pharmaceutical companies to submit diversity action plans, including information on their diversity enrollment goals, rationale for their goals, and how they intend to meet their goals, for all late-stage trials planned for regulatory submission.[55]

GLOBAL EFFORTS TO ADDRESS DIVERSITY

Under-representation of racial and ethnic minority groups in clinical trials persists despite concerted efforts, including the National Institutes of Health Revitalization Act of 1993, which called for increased representation of minorities in all clinical research.[56] Clinical trials in oncology are no exception, and accrual of underserved communities remains low.[2 46] Various initiatives are being undertaken regionally and globally to address historic disparities in clinical trial recruitment. A plenary presentation on inclusion, diversity, equity and access was part of the Gynecologic Cancer Intergroup (GCIG) first Endometrial Cancer Consensus Conference held in Incheon/Seoul, Korea, in 2023 and will be included in all future endometrial cancer trial designs. The topic of diversity was also discussed in a brainstorming session at the 2024 GCIG Meeting (https://gcigtrials.org/node/3941), and statements on equity, inclusion, and diversity in cancer clinical trials will be forthcoming.

United States

Examples of US-focused initiatives include FDA draft guidance and strategies that support enrollment of participants from underrepresented populations in clinical trials using online videos[57]; FDORA, which includes several provisions intended to promote diversity in clinical trial enrollment, encourage growth of decentralized clinical trials, and streamline clinical research (Box 1)[55]; and joint initiatives between ASCO and ACCC,[58] and between ASCO and Friends of Cancer Research (endorsed by the FDA),[59] aimed at overcoming the lack of equity, diversity, and inclusion in cancer clinical trials. The ASCO/ACCC resources include the free-of-charge Just ASK training program and Site Self-Assessment tool to help research sites identify their specific barriers to participation in cancer clinical trials.[14] Improving enrollment of patients from diverse backgrounds through inclusion, diversity, equity, and access (IDEA) was also the recent focus of a joint statement published by the Gynecologic Oncology Group Foundation and the Society of Gynecologic Oncology.[60] Finally, the White House Office of Science and Technology Policy (OSTP) is also leading a whole-of-government approach to bolster clinical trial capacity in the US and includes among its aims the realization of more diverse participation in clinical trials through increased community outreach and creation of a diverse workforce.[61]

Europe

Demographic and socioeconomic characteristics continue to evolve in European populations. Western European countries in particular have experienced a high growth in immigration in recent years, and many European countries now have sizable immigrant populations of both European and non-European descent.[62] To address a diversifying population, the European Union Clinical Trial Regulation was initiated in 2014, coming into full effect in 2022, and aims to

Box 1 Summary of key points to promote clinical trial diversity included in the FDA guidance[57] and US Food and Drug Omnibus Reform Act (FDORA) 2022[55]

FDA draft guidance 2022[57]

Study sponsors are required to submit a 'race and ethnicity diversity plan'

Enrollment goals for under-represented racial and ethnic participants should be defined as early as practically possible.

Race and ethnicity diversity plan should include the following:

⇒ Assessment of any data that may indicate the potential for a drug to have differential safety or effectiveness associated with race or ethnicity

⇒ Collection of sufficient pharmacokinetic, pharmacodynamic, and pharmacogenomic data from a diverse population to inform analyses of drug exposure and response

⇒ Description of planned assessments of race and ethnicity

⇒ Specify the study design features that will support analyses to inform on safety and effectiveness of the drug in the relevant racial and ethnic populations (in the case of known data that indicate the drug may perform differently across populations)

⇒ If there are no data that indicate that race or ethnicity will impact safety or effectiveness, enrollment should reflect the epidemiology of the disease

⇒ An outline of how data will be collected to explore the potential for differences in safety and/or effectiveness associated with race and ethnicity throughout the entire development life cycle of the drug and not just during the pivotal trial(s) or studies

FDORA 2022[55]

Sponsors must submit to the FDA 'diversity action plans' for certain late-stage trials, including all phase 3 trials, unless otherwise waived or excepted.

Diversity action plans should include the following:

⇒ Goals for enrollment in the clinical study

⇒ Rationale for the above goals

⇒ Explanation of how the goals will be met

The US Department of Health and Human Services must update guidance on diversity action plans for clinical studies and host public stakeholder workshops focused on enhancing clinical study diversity.

As applicable, the US Department of Health and Human Services must issue or revise guidance on the appropriate use of decentralized clinical studies in the development of drugs and devices and how digital health technologies can be best used in clinical trials to facilitate inclusion of diverse and under-represented populations.

FDA, US Food and Drug Administration.

promote more equitable representation of sex and age groups in clinical trials.[63] The regulation requires that, unless otherwise justified in the protocol, clinical trial participants represent the population groups (eg, sex and age groups) that are likely to use the medicinal product investigated in the clinical trial.

Rest of World

The World Health Organization (WHO) has provided draft guidance on best practices for clinical trials, devoting an entire section to addressing under-represented subpopulations, emphasizing that strenuous efforts are needed to recruit diverse populations in clinical trials through appropriate patient, public, and community engagement.[64] The Australian Clinical Trials Alliance program was initiated to advance clinical trial engagement, involvement, and participation for people from culturally and linguistically diverse backgrounds.[65] In addition, recent draft guidance from Health Canada on the collection and analysis of disaggregated data in clinical trials also stipulates the need for sponsors to report on the diversity of clinical trial participants for each drug product.[66]

In the field of cancer, minority under-representation in clinical research is further exacerbated by the fact that cancer research is heavily skewed toward high income countries, with disproportionately less research conducted in low and middle income countries.[64] Expansion of recruitment efforts outside of the US and Europe will be critical to addressing minority under-representation of Hispanic and Asian patients in clinical research. The WHO guidance on best practices for clinical trials includes a call to promote and advance clinical trials in low and middle income countries.[64] Some progress has been made on this front in recent years, with an increase in representation in Latin American and Asian countries in clinical trial development, although more work is still needed.[67 68]

FUTURE CONSIDERATIONS

Looking toward the future, addressing the issues that currently impede enrollment of racial and ethnic minority groups in clinical trials will be important as the use of artificial intelligence to identify patients for clinical trial recruitment increases. Artificial intelligence has the potential to improve clinical trial recruitment in general, providing more rapid identification of potential patients based on analyses of medical records, including patient demographics and laboratory results, and has the potential to operate without bias if established to be truly data driven and trained carefully to overcome system barriers that currently exist, instead of perpetuating them. Although several barriers need to be addressed (generally related to data availability, maintaining high standards, and a need for regulatory guidance), it will be essential to begin with representative patient population models and to couple existing and future artificial intelligence–based recruitment methods with real-world outreach and recruitment strategies that are proven effective.[69]

CONCLUSIONS

The actionable solutions to improve diversity and minority enrollment in clinical trials identified and discussed by our expert panel are not intended to be a roadmap to success, but rather a set of considerations that may allow study sponsors and clinical trial sites to tailor specific recruitment strategies and implement site-specific tools to foster improvement in diverse patient enrollment globally. We acknowledge that some of the proposed solutions are more difficult to implement than others, and some may require additional funding. Ultimately, with time, many different approaches will be adopted by the medical community to improve diversity and ensure study populations accurately reflect those who are affected by the disease. It is critical that we address this issue globally to improve diversity and ensure access to trials to achieve health equity.

X Brian Slomovitz @gyncancermd

Acknowledgements Writing assistance was provided by ICON (Blue Bell, PA) and was funded by Incyte Corporation (Wilmington, Delaware, USA).

Contributors All authors participated in the conceptualization, writing-review, and editing, and approved the final manuscript.

Funding The panel discussion and writing support for the manuscript were supported by Incyte Corporation.

Competing interests BP has received grants from Tesaro/GSK, Merck, Astra Zeneca, Karyopharm Therapeutics, Incyte, Toray, VBL Therapeutics, InxMed, Agenus, Clovis Oncology, Roche/Genentech, Mersana, Celsion/Immunon, I-Mab, Takeda, Onconova, Celgene, Sutro Biopharma, Novocure, Seagen, NRG Oncology, Duality Bio, Xencor, Immunogen, Eisai, Acrivon, and Alkermes; consulting fees from Tesaro/GSK, Astra Zeneca, Merck, Immunogen, GOG Foundation, Seagen, Lilly, Eisai, Signatera, Celsion, Sutro Biopharma, Imvax, Incyte, InxMed, Onconova Therapeutics, R-Pharm, Regeneron, and Duality Bio; honoraria from Bioascend, PERS, Vanium, Curio, OncLive, Yale University, and PeerView; support for attending meetings and/or travel from GOG Partners; participated on data safety monitoring boards (DSMBs) or advisory boards for Sutro Biopharma, Astra Zeneca, GOG Foundation, Celsion/Immunon, Toray, InxMed, Onconova, Imvaz, I-Mab, Tesaro/GSK, Merck, Mersana, Nuvation, and BioNTech; and served as SGO Clinical Practice Committee Chair, SGO Board of Directors, SGO COVID-19 Taskforce Co-chair, GOG Partners, and NYOB Society Second Vice President. PT has received grants (paid to the institution) from Merck and GSK; participated on DSMBs or advisory boards for Iovance, Astra Zeneca, Verastem, GSK, Seagen, Immunon, Immunogen, Mersana, Novocure, Zentalis, Caris, and Merck; and holds stock or stock options in Immunon. AM has received honoraria and travel fees from Foundation for Women's Cancer and served as President of Endometrial Cancer Action Network for African Americans. KM has received consulting fees from Eisai. DC has received honoraria from Antibacterial Resistance Leadership Group (ARLG); grants from Duke University for COMET study (cancer) Patient Leadership Group, UCSF for STORMing Cancer Patient Advocate Team, and MD Anderson for PRECISION Patient Advisory Involvement Panel; consulting fees from SimBioSys, MaxisHealth, Health Literacy Media (HLM; as Patient Advisor), Apellis Pharmaceuticals, and Kinnate Biopharma; honoraria and travel support from HMP Education; support for travel from Agile Falcon Strategic Group, DGE Events, and Informa; participated on DSMBs for American Society for Clinical Oncology and on Patient Partner Council for Evidera; has a role on Executive Group for Metastatic Breast Cancer Alliance and a role as committee member for Alliance for Clinical Trials in Oncology; and received manuscript writing support from IQVIA through Regeneron. KL has received fees for participation on advisory boards for Astra Zeneca, Merck, and Eisai. MCM is an employee and stockholder of Incyte. BS has received consulting fees from Astra Zeneca, Clovis, GSK, Genentech, Lilly, Novartis, Gilead, Seagen, Karyopharm, Addy, Circulogene, GOG Foundation, Merck, Imvax, EQRx, and Nuvation; and honoraria from Seagen.

Patient consent for publication Not applicable.

Ethics approval Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

ORCID iDs
Bhavana Pothuri http://orcid.org/0000-0003-4578-2061
Brian Slomovitz http://orcid.org/0000-0002-7241-3096

REFERENCES

1 Filbey L, Zhu JW, D'Angelo F, *et al*. Improving representativeness in trials: a call to action from the Global Cardiovascular Clinical Trialists Forum. *Eur Heart J* 2023;44:921–30.
2 Reid MM, Davis SP, Henry ON, *et al*. Demographic diversity of US-based participants in GSK-sponsored interventional clinical trials. *Clin Trials* 2023;20:133–44.
3 Rubin E, ed. Striving for diversity in research studies. *N Engl J Med* 2021;385:1429–30.
4 Asare M, Flannery M, Kamen C. Social determinants of health: a framework for studying cancer health disparities and minority participation in research. *Oncol Nurs Forum* 2017;44:20–3.
5 Champion CD, Thomas SM, Plichta JK, *et al*. Disparities at the intersection of race and ethnicity: examining trends and outcomes in Hispanic women with breast cancer. *JCO Oncol Pract* 2022;18:e827–38.
6 Niranjan SJ, Martin MY, Fouad MN, *et al*. Bias and stereotyping among research and clinical professionals: perspectives on minority recruitment for oncology clinical trials. *Cancer* 2020;126:1958–68.
7 Mesa RA, Ramirez AG. Chapter 12. Overcoming barriers for Latinos on cancer clinical trials. In: *Advancing the Science of Cancer in Latinos*. Springer, 2019.
8 Dreyfus B, Kuri L, Ferri M, *et al*. Understanding Hispanic/Latino participation in clinical trials and observational studies, and strategies to increase participation: a targeted literature review. *J Health Care Poor Underserved* 2023;34:399–424.
9 Ma GX, Seals B, Tan Y, *et al*. Increasing Asian American participation in clinical trials by addressing community concerns. *Clin Trials* 2014;11:328–35.
10 Popkin R, Taylor-Zapata P, Bianchi DW. Physician bias and clinical trial participation in underrepresented populations. *Pediatrics* 2022;149:e2021054150.
11 Paguio JA, Golbin JM, Yao JS, *et al*. Self-reported cultural competency measures among patients with diabetes: a nationwide cross-sectional study in the United States. *Lancet Reg Health Am* 2022;7:100158.
12 Chino F, Zafar SY. Financial toxicity and equitable access to clinical trials. *Am Soc Clin Oncol Educ Book* 2019;39:11–8.
13 US Bureau of Labor Statistics. Labor force characteristics by race and ethnicity. 2021. Available: https://www.bls.gov/opub/reports/race-and-ethnicity/2021/ [Accessed 06 Mar 2024].
14 Association of Community Cancer Centers (ACCC). Community oncology research. ASCO-ACCC initiative. Available: https://www.accc-cancer.org/home/learn/community-oncology-research/asco-accc-initiative [Accessed 06 Mar 2024].
15 Rosa C, Marsch LA, Winstanley EL, *et al*. Using digital technologies in clinical trials: current and future applications. *Contemp Clin Trials* 2021;100:106219.
16 Fischer SM, Kline DM, Min SJ, *et al*. Apoyo con cariño: strategies to promote recruiting, enrolling, and retaining Latinos in a cancer clinical trial. *J Natl Compr Canc Netw* 2017;15:1392–9.
17 Lee GE, Ow M, Lie D, *et al*. Barriers and facilitators for clinical trial participation among diverse Asian patients with breast cancer: a qualitative study. *BMC Womens Health* 2016;16:43.
18 Lee-Lin F, Menon U, Nail L, *et al*. Findings from focus groups indicating what Chinese American immigrant women think about breast cancer and breast cancer screening. *J Obstet Gynecol Neonatal Nurs* 2012;41:627–37.
19 Kannan V, Wilkinson KE, Varghese M, *et al*. Count me in: using a patient portal to minimize implicit bias in clinical research recruitment. *J Am Med Inform Assoc* 2019;26:703–13.
20 National Institutes of Health. NIH inclusion outreach toolkit: how to engage, recruit, and retain women in clinical research. Available: https://orwh.od.nih.gov/toolkit/recruitment [Accessed 06 Mar 2024].
21 Lee SS, Dinicu AI, Arthurs L, *et al*. Demographic reporting and language exclusion in gynecologic oncology clinical trials. *Am J Obstet Gynecol* 2024;230:73.
22 Trinh N-HT, Hagan PN, Flaherty K, *et al*. Evaluating patient acceptability of a culturally focused psychiatric consultation intervention for Latino Americans with depression. *J Immigr Minor Health* 2014;16:1271–7.
23 Asian and Pacific Islander American Health Forum (APIAHF). Clinical trial diversity and Asian Americans, Native Hawaiians and Pacific Islanders. Available: https://www.apiahf.org/wp-content/uploads/2021/01/Clinical-Trial-Diversity-Factsheet-v7_1.6.2021.pdf [Accessed 06 Mar 2024].
24 Lee JS, Pérez-Stable EJ, Gregorich SE, *et al*. Increased access to professional interpreters in the hospital improves informed consent for patients with limited English proficiency. *J Gen Intern Med* 2017;32:863–70.
25 McKay RR, Gold T, Zarif JC, *et al*. Tackling diversity in prostate cancer clinical trials: a report from the Diversity Working Group of the IRONMAN Registry. *JCO Glob Oncol* 2021;7:495–505.
26 Staples JN, Lester J, Li A, *et al*. Language as a barrier to cancer clinical trial accrual: assessing consenting team knowledge and practices for cancer clinical trial consent among low English fluency patients. *Appl Cancer Res* 2018;38.
27 American Society of Clinical Oncology. Facts & figures: diversity in oncology. Available: https://society.asco.org/news-initiatives/current-initiatives/diversity-oncology-initiative/facts-figures [Accessed 06 Mar 2024].
28 Alsan M, Campbell R, Leister L, *et al*. *Investigator Racial Diversity and Clinical Trial Participation*. HKS Working Paper No. RWP23-029.2023:1–48.

29 Thominet L, Hamel LM, Baidoun F, *et al*. Physicians' use of plain language during discussions of prostate cancer clinical trials with patients. *Patient Educ Couns* 2022;105:3453–8.
30 Nouvini R, Parker PA, Malling CD, *et al*. Interventions to increase racial and ethnic minority accrual into cancer clinical trials: a systematic review. *Cancer* 2022;128:3860–9.
31 Hernandez D. Clinical Leader. Tackling health misinformation among Hispanics for better clinical research & patient data., Available: https://www.clinicalleader.com/doc/tackling-health-misinformation-among-hispanics-for-better-clinical-research-patient-data-0001 [Accessed 06 Mar 2024].
32 US Food and Drug Administration. Patient-friendly language for cancer clinical trials. Available: https://www.fda.gov/about-fda/oncology-center-excellence/patient-friendly-language-cancer-clinical-trials [Accessed 06 Mar 2024].
33 National Cancer Institute. NCI dictionary of cancer terms. Available: https://www.cancer.gov/publications/dictionaries/cancer-terms [Accessed 05 Apr 2024].
34 National Institute on Aging. NIA glossary of clinical research terms. Available: https://www.nia.nih.gov/research/dgcg/nia-glossary-clinical-research-terms [Accessed 06 Mar 2024].
35 Multi-regional Clinical Trials Center of Brigham and Women's Hospital and Harvard. Clinical research glossary. Available: https://mrctcenter.org/glossary/ [Accessed 05 Apr 2024].
36 Snethen JA, Broome ME, Knafl K, *et al*. Family patterns of decision-making in pediatric clinical trials. *Res Nurs Health* 2006;29:223–32.
37 Jin X, Chandramouli C, Allocco B, *et al*. Women's participation in cardiovascular clinical trials from 2010 to 2017. *Circulation* 2020;141:540–8.
38 World Heart Federation. Women & CVD. Available: https://world-heart-federation.org/what-we-do/women-cvd/ [Accessed 06 Mar 2024].
39 Duma N, Vera Aguilera J, Paludo J, *et al*. Representation of Minorities and Women in Oncology Clinical Trials: Review of the Past 14 Years. *J Oncol Pract* 2018;14:e1–10.
40 Chhaya VY, Binion CC, Mulles SM, *et al*. Gender Bias in Clinical Trial Enrollment: Female Authorship Matters. *Ann Vasc Surg* 2023;95:233–43.
41 Gupta G, Myint Z, Yan D, *et al*. Use of gender-neutral language in clinical trial protocols in select cancers. J Clin Oncol 2023;41:1574.
42 Clearity Foundation. Cancer connections. Available: https://www.clearityfoundation.org [Accessed 06 Mar 2024].
43 Fouad MN, Acemgil A, Bae S, *et al*. Patient navigation as a model to increase participation of African Americans in cancer clinical trials. *J Oncol Pract* 2016;12:556–63.
44 Cook ED, Yeager KA, Cecchini RS, *et al*. Recruitment practices for U.S. minority and underserved populations in NRG oncology: results of an online survey. *Contemp Clin Trials Commun* 2018;10:100–4.
45 Carroll JK, Humiston SG, Meldrum SC, *et al*. Patients' experiences with navigation for cancer care. *Patient Educ Couns* 2010;80:241–7.
46 Awidi M, Al Hadidi S. Participation of Black Americans in cancer clinical trials: current challenges and proposed solutions. *JCO Oncol Pract* 2021;17:265–71.
47 McClung EC, Davis SW, Jeffrey SS, *et al*. Impact of navigation on knowledge and attitudes about clinical trials among Chinese patients undergoing treatment for breast and gynecologic cancers. *J Immigr Minor Health* 2015;17:976–9.
48 Ramirez AG, Chalela P. Equitable representation of Latinos in clinical research is needed to achieve health equity in cancer care. *JCO Oncol Pract* 2022;18:e797–804.
49 Center for Health Law and Policy Innovation of Harvard Law School (CHLPI). Review of new medicare payment policies addressing health-related social needs under the calendar year 2024 physician fee schedule. Available: https://navigationroundtable.org/wp-content/uploads/Review-of-CY-2024-PFS-Final-Rule-CHLPI-11-03-23.pdf [Accessed 06 Mar 2024].
50 Community-Based Participatory Research Program, US Department of Health and Human Services, National Institutes of Health. Community-based participatory research program. Available: https://www.nimhd.nih.gov/programs/extramural/community-based-participatory.html [Accessed 06 Mar 2024].
51 Braun-Inglis C, Boehmer LM, Zitella LJ, *et al*. Role of Oncology Advanced Practitioners to Enhance Clinical Research. J Adv Pract Oncol 2022;13:107–19.
52 Zippia. Nurse practitioner demographics and statistics in the us. Available: https://www.zippia.com/nurse-practitioner-jobs/demographics [Accessed 06 Mar 2024].
53 Calvert MJ, Cruz Rivera S, Retzer A, *et al*. Patient reported outcome assessment must be inclusive and equitable. *Nat Med* 2022;28:1120–4.
54 Cullen MR, Lemeshow AR, Amaro S, *et al*. A framework for setting enrollment goals to ensure participant diversity in sponsored clinical trials in the United States. *Contemp Clin Trials* 2023;129:107184.
55 Peloquin D, Barnes M, Lam C. Congress enacts legislation requiring guidance on clinical research diversity and modernization. Ropes & Gray. Available: https://www.ropesgray.com/en/insights/alerts/2023/01/congress-enacts-legislation-requiring-guidance-on-clinical-research-diversity-and-modernization [Accessed 06 Mar 2024].
56 Freedman LS, Simon R, Foulkes MA, *et al*. Inclusion of women and minorities in clinical trials and the NIH Revitalization Act of 1993–the perspective of NIH clinical trialists. *Control Clin Trials* 1995;16:277–85; .
57 US Food and Drug Administration, US Department of Health and Human Services. Diversity plans to improve enrollment of participants from underrepresented racial and ethnic populations in clinical trials: guidance for industry. Draft guidance. Available: https://www.fda.gov/media/157635/download [Accessed 06 Mar 2024].
58 Oyer RA, Hurley P, Boehmer L, *et al*. Increasing racial and ethnic diversity in cancer clinical trials: an American Society of Clinical Oncology and Association of Community Cancer Centers joint research statement. *J Clin Oncol* 2022;40:2163–71.
59 Kim ES, Uldrick TS, Schenkel C, *et al*. Continuing to broaden eligibility criteria to make clinical trials more representative and inclusive: ASCO-Friends of Cancer Research joint research statement. *Clin Cancer Res* 2021;27:2394–9.
60 Pothuri B, Blank SV, Myers TK, *et al*. Inclusion, diversity, equity, and access (IDEA) in gynecologic cancer clinical trials: a joint statement from GOG Foundation and Society of Gynecologic Oncology (SGO). *Gynecol Oncol* 2023;174:278–87.
61 Sipes G. A stronger clinical trial infrastructure for better health outcomes. The White House. Available: https://www.whitehouse.gov/ostp/news-updates/2023/10/26/a-stronger-clinical-trial-infrastructure-for-better-health-outcomes [Accessed 06 Mar 2024].
62 European Commission. Statistics on migration to Europe, Available: https://commission.europa.eu/strategy-and-policy/priorities-2019-2024/promoting-our-european-way-life/statistics-migration-europe_en#migration-to-and-from-the-eu [Accessed 06 Mar 2024].
63 European Commission. Clinical trials - regulation EU no 536/2014. Available: https://health.ec.europa.eu/medicinal-products/clinical-trials/clinical-trials-regulation-eu-no-5362014_en#transparency [Accessed 06 Mar 2024].
64 World Health Organization. WHO guidance for best practices for clinical trials: draft for public consultation. Available: https://cdn.who.int/media/docs/default-source/research-for-health/2023-07_who-guidance-for-best-practices-for-clinical-trials_draft-for-public-consultation.pdf?sfvrsn=7a5c9fa5_4 [Accessed 06 Mar 2024].
65 Australian Clinical Trials Alliance. Advancing clinical trial engagement, involvement, and participation for people from culturally and linguistically diverse backgrounds. Available: https://clinicaltrialsalliance.org.au/wp-content/uploads/2023/05/20230502_ACTA_CALD-in-Clinical-Trials-Reccomendations.pdf [Accessed 06 Mar 2024].
66 Health Canada. Draft guidance document on the collection and analysis of disaggregated data in clinical trials: overview. Available: https://www.canada.ca/en/health-canada/programs/consultation-proposed-agile-regulations-guidance-licensing-drugs-medical-devices/draft-collection-analysis-disaggregated-data-clinical-trials.html#objective [Accessed 06 Mar 2024].
67 Ali S, Egunsola O, Babar ZUD, *et al*. Clinical trials in Asia: a World Health Organization database study. *Perspect Clin Res* 2019;10:121–4.
68 Gössling G, Rebelatto TF, Villarreal-Garza C, *et al*. Current scenario of clinical cancer research in Latin America and the Caribbean. *Curr Oncol* 2023;30:653–62.
69 Askin S, Burkhalter D, Calado G, *et al*. Artificial intelligence applied to clinical trials: opportunities and challenges. *Health Technol (Berl)* 2023;13:203–13.