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Title: Understanding the reasons for declining to participate in cancer genetics and genomic studies in the United States: a scoping review protocol

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ABSTRACT (Word count 300):

Introduction: Cancer is the second leading cause of death in the United States (US). Cancer genetics and genomic studies have improved our understanding of risk, onset and progression. However, disparities by race and ethnicity have resulted in a lack of representation for minorities in these studies, contributing to unequal reductions in the cancer burden across populations. Moreover, the reasons why some individuals decline to participate in cancer genetic and/or genomic studies across diverse populations remains unclear. This review will summarize the main reasons (concerns) associated with declining to participate in cancer genetics and/or genomics studies for individuals with a history of cancer living in the US and Puerto Rico (PR), considering race and ethnicity.

Methods and Analysis: We will follow the methodology presented by the Joanna Briggs Institute, and the Preferred Reporting Items for Systematic Reviews Statement extended to Scoping Reviews (PRISMA-ScR) to guide manuscript generation. A standardized search strategy developed in collaboration with a health sciences librarian will be deployed in MEDLINE (PubMed), Embase (Ovid), and Scopus from database inception till present. The search strategy consists of three concepts: 1) Cancer; 2) Genetics and Genomics research; and 3) Declination to participate in research studies. Title and abstract screening, followed by full-text review, will be conducted by independent reviewers to determine study inclusion. Only peer reviewed literature in English and conducted in the US and PR will be considered. Findings will be presented as a numerical summary, graphical presentation and narrative review of the literature.

Ethics and Dissemination: Ethical review is not required for scoping reviews. This review aims to facilitate the development of targeted strategies to increase participation in cancer genetics and or genomics studies across diverse populations. Results will be disseminated

through a peer-reviewed publication and conference presentations. The protocol is registered in the Open Science Framework (www.osf.io).

Strengths and limitations of the study:

- This will be the first scoping review to target reasons to decline to participate in cancer genetics and/or genomic research studies in the United States and Puerto Rico across all study designs, considering differences by race and ethnicity.
- The wide breadth and depth of the search strategy increases the likelihood of capturing all relevant literature contained in curated databases.
- Following the guidelines provided by the Joanna Briggs Institute, and the Preferred Reporting Items for Systematic Reviews Statement extended to Scoping Reviews (PRISMA-ScR) enhances the scientific rigor of this scoping review.
- The study is conducted by a multidisciplinary diverse team of researchers that collaborate across the National Cancer Institute Moonshot Initiative supported Participant Engagement—Cancer Genomic Sequencing Network comprising five comprehensive cancer centers with topic expertise.
- The decision to not include gray-literature opens the door to miss potential research relevant to this scoping review.

INTRODUCTION:

Cancer is the second leading cause of death in the United States with 2,001,140 new cancer cases and 611,720 cancer deaths projected to occur in 2024 alone (1). Cancer is a heterogeneous disease. This heterogeneity comes as a result of the complex interplay between multiple risk factors, including environmental and genetic (2). With the rapid development of genomic technologies over the past decades, genetic/genomic testing has become a common practice in clinical settings for identifying individuals at increased risk of inherited conditions as well as for identifying the most effective treatments (3).

Genetic testing encompasses both germline and somatic testing. Germline genetic testing can enhance the understanding of the inheritance pattern of cancer and help manage the cancer risks (4). Centers for Disease Control and Prevention suggests that individuals with a personal or family history of cancer should undergo genetic testing for hereditary cancers, such as breast and ovarian cancer among others, due to their significant genetic influence (5). Genomic testing of the tumor can provide information on the prognosis after a person is diagnosed with cancer, as well as help inform the most optimal cancer treatments, enabling personalized medicine in oncology and ultimately improve survival outcomes (6). Genetic and genomic testing can be further categorized into clinical and research testing. Clinical testing primarily aims to guide diagnosis and treatment at the individual level, whereas research testing focuses on enhancing the global understanding of diseases within, between, and across populations, without directly informing clinical decision-making (7). However, current efforts have a tendency to simultaneously offer clinical and research testing as part of the research study.

Advancements in identifying inherited and tumor genomic and genetic variation in precision oncology emphasize the need to increase the diversity among recruitment in cancer clinical trials. Racial and ethnic minority patients have been grossly underrepresented in large-scale efforts to characterize the cancer genome (8). Moreover, they have also been underrepresented in precision oncology trials. For example, Aldrighetti et al. analyzed 197 precision oncology clinical trial studies and found that 47.2% had appropriate data on race and ethnicity while the remaining 52.8% did not have any information. The 93 studies with reported race and ethnicity data found that of the 5867 enrollees, 82.3% were non-Hispanic White, 10% were Black, 4.1% were Asian, 3.4% were Hispanic, and 0.3% were American Indian and Alaska Native (9). As such, it is inadequate to generalize the presence or absence of biomarkers across populations based on the lack of diversity within cancer clinical trials.

Access to and utilization of health services and specialty care, including genetic services, can improve health outcomes by increasing diagnosis rates among racial and ethnic minority groups, rural communities, people with disabilities, and those with lower incomes (10). A previous systematic review summarized that four primary motivators for pursuing clinical genomic testing were: Interest in the tests' ability to predict cancer occurrence and recurrence risk, inform management decisions, benefit participants' families, and provide participants with a between understanding of their cancer (11). Unfortunately, Asian, Black, Native American, and Hispanic people, are less likely to receive recommended clinical germline genetic testing (12). This not only contributes to disparities in cancer care, but also lack of genetic and genomic research testing in diverse populations can prevent the understanding of health disparities, new discoveries in biology, more accurate matching of diverse patients with safe and effective treatments, and an improved understanding of the impact of genetic variants in cancer risk (13).

Despite information provided by genetic and genomic clinical and research testing, there is still some hesitancy among cancer patients to pursue this type of testing. Therefore, understanding the reasons why participants decline to enroll in genetic and/or genomic cancer studies is important. Moreover, these reasons vary across different regions and populations. A study found that the common reasons for declining genomic sequencing research testing include psychological impact, not interested in research activities, time commitment, and privacy/discrimination (14). Kurian et al. found that only 6.8% patients pursued genetic testing after a cancer diagnosis in California and Georgia, with lower rates among Asian, Black, and Hispanic patients in comparison to Non-Hispanic Whites (15). Another study by Smith-Uffen et al. identified key barriers to genomic testing including concerns about cost, confidentiality, clinical utility and psychological harm (11).

Given the heterogeneity of the results from studies that report on reasons for declining participation in genetic or genomic studies, and the importance of understanding these reasons, a comprehensive synthesis of the sociodemographic characteristics and external factors associated with people who decline participation in these studies is necessary. Currently, only a few existing published syntheses have reported on the reasons why individuals choose to opt out of pursuing genetic and/ or genomic testing in cancer research (11,14,15). However, these studies

have not considered racial and ethnic disparities and how these disparities could impact the decision to participate. Therefore, we propose to conduct a scoping review with the goal of identifying and synthesizing the existing reasons for declining participation in cancer genetic and/or genomic testing, with special consideration of differences by race and ethnicity, as well as other sociodemographic factors.

Prior to the development of this scoping review protocol, we conducted a thorough search of MEDLINE (Pubmed), Embase (Ovid), Scopus, PROSPERO, the Cochrane Database of Systematic Reviews, Open Science Framework, and JBI Evidence Syntheses. No previous registered, published, or ongoing scoping reviews or systematic reviews on an equal or similar topic were identified.

The primary objective of the current review is to examine the reasons (concerns) why persons decline to participate in cancer genetics and genomic studies for individuals with a history of cancer living in the United States (US) and Puerto Rico (PR). A secondary objective is to examine reasons why persons decline to participate in cancer genetic and/or genomic research considering race and ethnicity, age at diagnosis, gender, health insurance, nativity/immigration status, socio-economic status, family history of cancer, cancer characteristics (i.e., primary, metastatic; treatment status; cancer site; stage at diagnosis), and co-morbidities. We aim to leverage the findings from this review to facilitate the development of target strategies to increase participation in cancer genetics and/or genomics research across diverse populations in the US and PR.

METHODS AND ANALYSIS:

Protocol design, registration and reporting:

This scoping review will follow the guidelines generated by the Joanna Briggs Institute (JBI) in the JBI Manual for Evidence Synthesis (16), this manual leverages the foundational methodology constructed by Arksey and O'Malley (17) with close consideration of the enhancement provided by Levac et al (18) and enables the generation of a review that will align with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) (19). In addition, this protocol was developed in accordance with the guidance and checklist published by Peters et al (20). This scoping review protocol is registered online with the Open Science Framework (www.osf.io)

Review questions/objectives:

Scoping review studies aim to rapidly map key concepts underpinning a specific research area/question (21). In this review, we target three out of the four common reasons to undertake a scoping review as stated by Arksey & O'Malley. Specifically, we will: 1) examine the extent, range, and nature of research activity in relation to reasons to decline to participate in cancer genetics and/or genomic cancer studies in the US and PR; 2) summarize and disseminate our research findings to the broader scientific community, stakeholders, and community representatives; and 3) identify research gaps in the existing literature in relation to reasons to decline to participate in cancer genetics and/or genomic cancer research in the US.

Motivated by these reasons to conduct this review, we propose the following research questions:

I. What are the reasons (concerns) expressed by persons with a history of cancer who decline to participate in cancer genetic and/or genomic studies in the US and PR?
II. What are the socio-demographic attributes among individuals with a history of cancer who decline to participate in cancer genetics and/or genomic studies in the US and PR?
III. What are the cancer-specific characteristics among persons with a history of cancer who decline to participate in cancer genetics and/or genomic studies in the US and PR?
IV. Do the reasons (concerns) to decline to participate in cancer genetics and/or genomic studies differ by race and ethnicity and cancer type?

Eligibility/Inclusion criteria:

Types of Participants/Population:

This scoping review will consider for inclusion readily available peer-reviewed literature that reports on adults (≥18 years of age) with a current or previous diagnosis of cancer (either primary or metastatic) who have been approached in intra- or extra-hospital settings to participate in cancer genetic and/or genomic studies in the US and PR and have declined to partake in such studies. This criterion does not exclude participants based on how the diagnosis-status was obtained (e.g., clinical, histological, self-report). Moreover, we will not exclude literature that reports on participants with a history of cancer diagnosis who have comorbidities or coexisting conditions (e.g., pregnancy).

Concept:

In this study, we target literature that examines the reasons (concerns) why individuals with a prior cancer history decline to participate in cancer genetics and genomic studies in the US and PR. This primary objective is decomposed into three concepts defined as follows:

1) *Cancer*: To describe cancer, we adhere to the recent definition demarcated by Brown et al, which defines cancer as a "disease of uncontrolled proliferation by transformed cells subject to evolution by natural selection" (22).
2) *Genetics and/or Genomics studies*: The World Health Organization defines “genetics” as the study of hereditary patterns of inheritance among organisms with a focus on the specific gene structure and variations to form a clear picture of the potential for a condition. While “genomics” is defined as the study of the genome and its actions; it refers to all the DNA contained in a cell including the nuclear and mitochondrial DNA (23). Thus, genomics involves the analysis of the full DNA sequence of an organism whereas genetics interrogates the functioning and composition of one or more genes. Therefore, for the purpose of this review, we define cancer genetics and/or genomic studies as the investigational efforts conducted in individuals with a history of a cancer diagnosis to elucidate the molecular elements that influence cancer presentation, progression, and outcomes. This research leverages genetic and/or genomic testing technologies to inform

the biological basis of different cancer types, develop targeted therapies and interventions, discover genomic biomarkers of drug response and resistance, provide targeted genetic counseling, and potentially guide clinical decision-making (24).

3) *Declination/Refusal to participate*: We operationally define a "declination to participate" as the non-coerced negative from protocol-eligible subjects to partake in cancer genetics and/or genomics research studies at any capacity. Thus a "decliner" is defined as a potential participant that directly or indirectly (e.g., through a family member) informed the study staff they were unwilling or unable to participate after being contacted for recruitment. The "declination to participate" decision may occur before, during, or shortly after informed consent, depending on the project's protocol, but will always take place before the "decliner" is subject to any study-related activities (14).

Context:

The context of this review will be settings with individuals with a positive history of cancer diagnosis residing either in the US or in PR at the time they choose to not participate in a cancer genetic and/or genomic study.

We acknowledge that the reasons for declining participation in cancer genetic/genomic studies may vary between clinical and research testing. In this review, both types of testing will be considered for inclusion, with notations added to distinguish the rationale behind the specific type of testing conducted when possible.

An itemized inclusion/exclusion criteria table is provided as Supplementary Table 1.

Information sources:

This scoping review will consider all observational, interventional and review study designs including: analytical cross-sectional studies; prospective, retrospective, ambidirectional cohort studies; case-control studies and its variations according to methods of control sampling (i.e., nested case-control study using risk-set sampling, case-cohort sampling, and cumulative case-control study); randomized controlled trials; controlled clinical trials; qualitative studies; quantitative studies, mixed-methods studies; systematic reviews; meta-analyses; and narrative reviews.

The databases to be searched will include MEDLINE (PubMed), Embase (Ovid), and Scopus. Both Embase and Scopus cover the search of "gray" literature (i.e., conference abstracts, symposia articles, book chapters, etc.). If abstracts or symposia articles are detected, an effort to identify peer-reviewed publications derived from these sources will be made. If none are available, the entries will not be included. Databases will be interrogated from inception to the present, with only literature published in English considered for inclusion.

Search strategy:

The search strategy was developed in collaboration with an expert health sciences librarian (JD) from the Keck School of Medicine at the University of Southern California. An initial search was conducted in MEDLINE (PubMed) to identify relevant articles on the topic. Keywords were

extracted from the titles, abstracts and manuscript body, and were utilized in combination with the index terms to develop a full search strategy for MEDLINE (PubMed) (Supplementary Table 2). The proposed search strategy encompasses three main concepts: “cancer”, “genetics and/or genomics studies”, and “declination/refusal to participate”. These concepts are decomposed into terms indexed in the National Library of Medicine, controlled vocabulary thesaurus (MesH, Medical Subject Headings) (https://www.ncbi.nlm.nih.gov/mesh/). This search strategy will be adapted to each information source. References cited in articles that met inclusion criteria will be reviewed to identify additional literature for inclusion and supplemented with hand searching. Following JBI recommendations (16), a pilot test screening of eligible studies will be conducted by two independent reviewers, the search strategy will be updated accordingly.

Selection of sources of evidence:

Identified records from all sources of evidence will be collated and uploaded into Covidence, an online screening and data extraction tool for systematic reviews (https://www.covidence.org). Duplicate records will be removed. A two-stage screening process will ensue to select studies for this review: 1) Title and abstract screening, retrieved literature of potentially eligible studies will be screened against inclusion and exclusion criteria and labeled as “include”, “exclude”, or “uncertain”; 2) Full-text review, we will extract full-text publications from studies labeled as “include” or “uncertain” to evaluate against the inclusion and exclusion criteria. All studies will be independently reviewed by at least two reviewers, with conflicts resolved by a third independent reviewer. For literature labeled as “exclude” after full-text review is conducted, the reasons for exclusion will be documented.

Full-text publications from studies that meet the inclusion criteria will be imported into Zotero v.6.02.0 for citation management. The results of the selection process will be presented in the final scoping review as a PRISMA flow diagram (25).

Critical appraisal of individual sources of evidence:

Scoping reviews are not required to conduct an assessment of the methodological quality of the retrieved literature (20). As the primary goal of this review is to examine the extent, range and nature of available evidence in our topic of interest, we have opted to not critically appraise the studies we will include.

Data charting process:

Data will be extracted by two reviewers into Covidence following the fields specified in a standardized data extraction tool (Supplementary Table 3). The tool will be piloted by three reviewers who will independently chart data from the first five studies, with adjustments made accordingly after a discussion among the team. Additionally, the data extraction tool may be iteratively updated to ensure that unforeseen data is usefully captured. Modifications made to the presented tool (Supplementary Table 3) will be recorded and mentioned in the full scoping review manuscript.

We will extract information from the following categories: 1) publication details, 2) study characteristics, 3) study methods, 4) socio demographics of study participants, 5) clinical

characteristics of study participants, and 6) study results. Specifically, the study results will focus on the following: participation rate-, reasons for declining to participate-, sociodemographic and clinical characteristics of decliners-, and strategies to enhance participation- in cancer genetics and/or genomic studies.

Collating summarizing, and reporting the results:

Studies will be grouped by design into qualitative, mixed methods, and quantitative research, with the latter further stratified into cross-sectional and longitudinal studies. Data will be summarized following this stratification, with results presented in three blocks of information by study type as follows: 1) Studies that deployed qualitative and/or mixed methods, 2) Studies that report on quantitative research efforts (stratified into cross-sectional and longitudinal), and 3) Studies that were not initially conducted to evaluate reasons for declining to participate in cancer genetics and/or genomics studies but meet inclusion/exclusion criteria and report sufficient results to be included in the scoping review.

After grouping the included literature into these three categories, we will present the data using the following strategies:

1. Descriptive numerical summary:

This includes the publication details, study characteristics, and study methods as described in the data extraction tool (Supplementary Table 3). Namely, publication year, publication source, study design, study setting/location, study sponsor/funding source, sampling method, if an incentive for participation was offered, primary vs. secondary data analysis, sequencing platform/technology utilized to obtain the genetic and/or genomic information, time commitment for participation in the study, study activities, and method of recruitment.

2. Graphical presentation of the charted information:

The reasons and factors associated with the decision to decline participation in cancer genetics and/or genomic research will be collected and presented in bar graphs. The x-axis will display the reasons and factors, while the y-axis will show the number of studies reporting on these reasons and factors. Results will be stratified according to the three blocks of information previously constructed. If possible, efforts will also be made to present results by race and ethnicity subcategories.

3. Narrative review of the literature

Studies will be grouped thematically according to the reported reasons and factors associated with the decision to decline to participate in cancer genetics and/or genomic studies. For studies of qualitative nature, a narrative review of the findings will be provided, with similarities and differences in the different methodological efforts to increase participant accrual emphasized. In addition, clinical and sociodemographic characteristics of the study participants that cannot be quantitatively presented, and that may be associated with study participation rates will be described in this section.

Conclusions for the full scoping review will be drawn from all these three strategies. This will enable the identification of predominant factors that may influence decision-making in cancer genetic and/or genomic research, potentially transforming them into actionable strategies to improve recruitment in future research efforts.

Patient and public involvement:

No patient or public representatives were involved in the design, conduct, reporting or dissemination of this protocol.

Ethics and dissemination:

Ethical review is not required for scoping reviews as only secondary data analyses from publicly available data are conducted. Results will be disseminated with a peer-reviewed publication and conference presentations.

Data availability statement:

All data supporting the development of the scoping review protocol is available within the paper and its Supplementary Information.

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Supplementary Table 1. Inclusion and exclusion criteria across phases of study selection for scoping review.

Selection Phase	Inclusion Criteria	Exclusion Criteria
1) Title and abstract screening	1.- Study is conducted in humans. 2.- Study is conducted in the United States and/or Puerto Rico. 3.- Study is focused on individuals with a history of cancer diagnosis. 4.- There is a mention of genetics and/or genomics for cancer research.	1.- Study is not a peer-reviewed publication. 2.- There is no mention of genetic and/or genomic testing. 3.- Study was not conducted in the United States. 4.- Study is not reported in English. 5.- Study does not include participants with a history of cancer diagnosis.
2) Full-text review	1.- A genetic and/or genomic assay was performed in at least a subset of the study participants. 2.- Reasons and/or concerns associated with the decision to decline to participate in a study are provided either with a numerical summary or narrative description. 3.- Study reports sociodemographic characteristics of study participants. 4.- Study reports clinical characteristics of study participants.	1.- No information is provided on reasons and/or concerns associated with the decision to decline to participate. 2.- The clinical and sociodemographic characteristics of the study participants are not described (i.e., the population under study is not described). 3.- The genetic and/or genomic assay that was utilized is not described. 4.- No information on funding sources and conflicts of interest is provided.

Supplementary Table 2. Search Strategy for scoping review.

Search	Concept	Query	Records Retrieved
#1	Cancer (humans)	((((("Neoplasms"[MeSH Terms] OR "Neoplasm"[All Fields] OR "Neoplasia"[All Fields] OR "Neoplasias"[All Fields] OR "Tumors"[All Fields] OR "Tumor"[All Fields] OR "Tumoral"[All Fields] OR "tumour"[All Fields] OR "Tumours"[All Fields] OR "Cancers"[All Fields] OR "Cancer"[All Fields] OR "Malignant Neoplasm"[All Fields] OR "Malignant Neoplasms"[All Fields] OR "neoplasm malignant"[All Fields] OR "neoplasms malignant"[All Fields] OR "Malignant"[All Fields] OR "Malignancy"[All Fields] OR "Malignancies"[All Fields] OR "Malignant Tumor"[All Fields] OR "Malignant Tumours"[All Fields] OR "tumor malignant"[All Fields] OR "tumor s"[All Fields] OR "Tumoral"[All Fields] OR "tumorous"[All Fields] OR "Tumour"[All Fields] OR "Neoplasms"[MeSH Terms] OR "Neoplasms"[All Fields] OR "Tumor"[All Fields] OR "tumour s"[All Fields] OR "tumoural"[All Fields] OR "tumourous"[All Fields] OR "Tumours"[All Fields] OR "Tumor"[All Fields]) AND ("malign"[All Fields] OR "malignance"[All Fields] OR "malignances"[All Fields] OR "Malignant"[All Fields] OR "malignants"[All Fields] OR "malignities"[All Fields] OR "malignity"[All Fields] OR "malignization"[All Fields] OR "malignized"[All Fields] OR "maligns"[All Fields] OR "Neoplasms"[MeSH Terms] OR "Neoplasms"[All Fields] OR "Malignancies"[All Fields] OR "Malignancy"[All Fields])) OR "Oncology"[All Fields] OR "Medical oncology"[MeSH Terms]) AND "humans"[MeSH Terms]) AND (humans[Filter])	3,920,224

#2	Genetics and/or genomics research (humans)	(("genetic research"[MeSH Terms] OR "research genetic"[All Fields] OR "genomic research"[All Fields] OR "genetics research"[All Fields] OR "genomics research"[All Fields] OR "genetic testing"[MeSH Terms] OR "genetics testing"[All Fields] OR "genetic profiling"[All Fields] OR "genomic profiling"[All Fields] OR "genomics profiling"[All Fields] OR "genome testing"[All Fields] OR "genomic testing"[All Fields] OR "genomics testing"[All Fields] OR "Whole-genome sequencing"[All Fields] OR "exome sequencing"[All Fields] OR "exomic sequencing"[All Fields] OR "sequence analysis dna"[All Fields] OR "genome sequencing"[All Fields] OR "genomic sequencing"[All Fields] OR "genomic sequencing"[All Fields] OR "genomic sequence"[All Fields] OR "genetic sequencing"[All Fields] OR "genetics sequencing"[All Fields] OR "genetic sequence"[All Fields] OR "clinical sequencing"[All Fields] OR "genetic carrier screening"[All Fields] OR "carrier screening"[All Fields] OR "genetic screening"[All Fields] OR "genetic susceptibility testing"[All Fields] OR "genomic risk profiling"[All Fields] OR "genome-based testing"[All Fields] OR "genomic medicine"[All Fields] OR "genetic counseling"[All Fields] OR "genetic information"[All Fields] OR "genetic diagnosis"[All Fields] OR "genomic diagnosis"[All Fields] OR "genetic diagnoses"[All Fields] OR "genomic diagnoses"[All Fields] OR "precision medicine"[All Fields] OR "individual genetic"[All Fields] OR "individual genomic"[All Fields] OR "individual genomics"[All Fields] OR "individual genome"[All Fields]) AND "humans"[MeSH Terms]) AND (humans[Filter])	280,114

#3	Declination/refusal to participate (humans)	(("patient participation"[MeSH Terms] OR "refusal to participate"[MeSH Terms] OR "decision making"[MeSH Terms] OR "patient decision making"[All Fields] OR "patients decision making"[All Fields] OR "participant decision making"[All Fields] OR "participants decision making"[All Fields] OR "participation factors"[All Fields] OR (("reason"[All Fields] OR "reasonable"[All Fields] OR "reasonably"[All Fields] OR "reasons"[All Fields]) AND ("decline"[All Fields] OR "declined"[All Fields] OR "decliner"[All Fields] OR "decliners"[All Fields] OR "declines"[All Fields] OR "declining"[All Fields])) OR "reasons for participation"[All Fields] OR "enrollment barriers"[All Fields] OR "enrollment"[All Fields] OR "participate"[All Fields] OR "decline"[All Fields] OR "declining"[All Fields] OR "declining to participate"[All Fields] OR "risk perception"[All Fields] OR "participation factors"[All Fields] OR "decisional preferences"[All Fields] OR "participant preferences"[All Fields] OR "concern"[All Fields] OR "concerns"[All Fields] OR "barriers"[All Fields] OR "cancer worry"[All Fields] OR "genetic discrimination"[All Fields] OR "trial participation"[All Fields] OR "recruitment"[All Fields] OR "facilitators"[All Fields] OR "return of results"[All Fields]) AND "humans"[MeSH Terms]) AND (humans[Filter])	1,108,448
#4		#1 AND #2 AND #3	4,656
Search developed for MEDLINE (Pubmed), conducted on July 19th, 2024. Filters: Species, Humans			

Supplementary Table 3. Data extraction instrument.

Publication Details	Study characteristics	Study Methods	Study participants sociodemographic characteristics	Study participants clinical characteristics	Study Results
1.- Paper ID (Covidence ID) 2.- Publication source (database) 3.-Year of publication. 4.- First author (last name, name) 5.- Senior author (last name, name) 6.- Academic affiliation first author (industry, academic, foundation, government). 7.- Academic affiliation corresponding author (industry, academic, foundation, government)	1- Study design (cross-sectional, cohort study, case-control, clinical trial, review, qualitative, mix methods). 2.- Study aims. 3.-Study setting/location. 4.-Study sponsor/funding source (industry, academia, foundation, government). 5.- Period under study.	1.- Sampling method (i.e., method of participant identification/inclusion). 2.- Incentive of participation. 3.- Inclusion criteria. 4.- Exclusion criteria. 5.- Primary vs. secondary data analysis. 6.- Sequencing platform/technology. 7.- Time commitment. 8.- Study activities (surveys, interviews, specimen donation). 9.- Method of recruitment (electronic/digital, phone, phase-to-phase contact, mail, etc).	1.- Sample size. 2.- Racial and ethnic composition. 3.- Gender distribution. 4.- Age and/or age range. 5.- Socioeconomic status. 6.- Income level. 7.- Nativity (US-born vs. non-US-born). 8.- Region of origin. 9.- Insurance. 10.- Marital status. 11.- Level of education.	1.- Tumor site. 2.-Tumor type. 3.- Tumor stage at diagnosis. 4.- Tumor grade at diagnosis. 5.- Primary vs. secondary recurrence. 6.- Treatment phase (pre-, during-, post-treatment). 7.- Family history of cancer (positive vs. negative first degree relative). 8.- Time since diagnosis to treatment. 9.- Time since diagnosis to study recruitment.	1.- Decline participation (i.e., participation rate). 2.- Reasons for declining participation. 3.- Characteristics of decliners (i.e., sociodemographic and clinical characteristics) 4.- Strategies to increase participation (i.e., enhance participation rate).

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Understanding the reasons for declining to participate in cancer genetics and genomic studies in the United States: a scoping review protocol

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Title: Understanding the reasons for declining to participate in cancer genetics and genomic studies in the United States: a scoping review protocol

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ABSTRACT (Word count 300):

Introduction: Cancer is the second leading cause of death in the United States (US). Cancer genetics and genomic studies have improved our understanding of risk, onset and progression. However, disparities by race and ethnicity have resulted in a lack of representation for minorities in these studies, contributing to unequal reductions in the cancer burden across populations. Moreover, the reasons why some individuals decline to participate in cancer genetic and/or genomic studies across diverse populations remains unclear. This review will summarize the main reasons (concerns) associated with declining to participate in cancer genetics and/or genomics studies for individuals with a history of cancer living in the US and Puerto Rico (PR), considering race and ethnicity.

Methods and Analysis: We will follow the methodology presented by the Joanna Briggs Institute, and the Preferred Reporting Items for Systematic Reviews Statement extended to Scoping Reviews (PRISMA-ScR) to guide manuscript generation. A standardized search strategy developed in collaboration with a health sciences librarian will be deployed in MEDLINE (PubMed), Embase (Ovid), and Scopus from database inception till present. The search strategy consists of three concepts: 1) Cancer; 2) Genetics and Genomics research; and 3) Declination to participate in research studies. Title and abstract screening, followed by full-text review, will be conducted by independent reviewers to determine study inclusion. Only peer reviewed literature in English and conducted in the US and PR will be considered. Findings will be presented as a numerical summary, graphical presentation and narrative review of the literature.

Ethics and Dissemination: Ethical review is not required for scoping reviews. This review aims to facilitate the development of targeted strategies to increase participation in cancer genetics and or genomics studies across diverse populations. Results will be disseminated

through a peer-reviewed publication and conference presentations. The protocol is registered in the Open Science Framework (www.osf.io).

Strengths and limitations of the study:

- This scoping review will follow the guidelines provided by the Joanna Briggs Institute, and the Preferred Reporting Items for Systematic Reviews Statement extended to Scoping Reviews (PRISMA-ScR) to enhance the scientific rigor.
- The study is conducted by a multidisciplinary team of researchers that collaborate across the National Cancer Institute Moonshot Initiative, Participant Engagement—Cancer Genomic Sequencing Network comprising five comprehensive cancer centers with topic expertise.
- Although no gray literature will be included in the review, an effort will be made to identify peer-reviewed publications derived from abstracts and symposia articles to consider for inclusion.

INTRODUCTION:

Cancer is the second leading cause of death in the United States with 2,001,140 new cancer cases and 611,720 cancer deaths projected to occur in 2024 alone[1]. Cancer is a heterogeneous disease. This heterogeneity comes as a result of the complex interplay between multiple risk factors, including environmental and genetic[2]. With the rapid development of genomic technologies over the past decades, genetic/genomic testing has become a common practice in clinical settings for identifying individuals at increased risk of inherited conditions as well as for identifying the most effective treatments[3].

Genetic testing encompasses both germline and somatic testing. Germline genetic testing can enhance the understanding of the inheritance pattern of cancer and help manage the cancer risks[4]. Centers for Disease Control and Prevention suggests that individuals with a personal or family history of cancer should undergo genetic testing for hereditary cancers, such as breast and ovarian cancer among others, due to their significant genetic influence[5]. Genomic testing of the tumor can provide information on the prognosis after a person is diagnosed with cancer, as well as help inform the most optimal cancer treatments, enabling personalized medicine in oncology and ultimately improve survival outcomes[6]. Genetic and genomic testing can be further categorized into clinical and research testing. Clinical testing primarily aims to guide diagnosis and treatment at the individual level, whereas research testing focuses on enhancing the global understanding of diseases within, between, and across populations, without directly informing clinical decision-making[7]. However, current efforts tend to simultaneously offer clinical and research testing as part of the research study.

Advancements in identifying inherited and tumor genomic and genetic variation in precision oncology emphasize the need to increase the diversity among recruitment in cancer clinical trials. Racial and ethnic minority patients have been grossly underrepresented in large-scale efforts to characterize the cancer genome[8]. Moreover, they have also been underrepresented in precision

oncology trials. For example, Aldrighetti et al. analyzed 197 precision oncology clinical trial studies and found that 47.2% had appropriate data on race and ethnicity while the remaining 52.8% did not have any information. The 93 studies with reported race and ethnicity data found that of the 5867 enrollees, 82.3% were non-Hispanic White, 10% were Black, 4.1% were Asian, 3.4% were Hispanic, and 0.3% were American Indian and Alaska Native[9]. As such, it is inadequate to generalize the presence or absence of biomarkers across populations based on the lack of diversity within cancer clinical trials.

Access to and utilization of health services and specialty care, including genetic services, can improve health outcomes by increasing diagnosis rates among racial and ethnic minority groups, rural communities, people with disabilities, and those with lower incomes[10]. A previous systematic review summarized that four primary motivators for pursuing clinical genomic testing were: Interest in the tests' ability to predict cancer occurrence and recurrence risk, inform management decisions, benefit participants' families, and provide participants with a between understanding of their cancer[11]. Unfortunately, Asian, Black, Native American, and Hispanic people, are less likely to receive recommended clinical germline genetic testing[12]. This not only contributes to disparities in cancer care, but also lack of genetic and genomic research testing in diverse populations can prevent the understanding of health disparities, new discoveries in biology, more accurate matching of diverse patients with safe and effective treatments, and an improved understanding of the impact of genetic variants in cancer risk[13].

Despite information provided by genetic and genomic clinical and research testing, there is still some hesitancy among cancer patients to pursue this type of testing. Therefore, understanding the reasons why participants decline to enroll in genetic and/or genomic cancer studies is important. Moreover, these reasons vary across different regions and populations. A study found that the common reasons for declining genomic sequencing research testing include psychological impact, not interested in research activities, time commitment, and privacy/discrimination[14]. Kurian et al. found that only 6.8% patients pursued genetic testing after a cancer diagnosis in California and Georgia, with lower rates among Asian, Black, and Hispanic patients in comparison to Non-Hispanic Whites[15]. Another study by Smith-Uffen et al. identified key barriers to genomic testing including concerns about cost, confidentiality, clinical utility and psychological harm[11].

Given the heterogeneity of the results from studies that report on reasons for declining participation in genetic or genomic studies, and the importance of understanding these reasons, a comprehensive synthesis of the sociodemographic characteristics and external factors associated with people who decline participation in these studies is necessary. Currently, only a few existing published syntheses have reported on the reasons why individuals choose to opt out of pursuing genetic and/ or genomic testing in cancer research[11,14,15]. However, these studies have not considered racial and ethnic disparities and how these disparities could impact the decision to participate. Therefore, we propose to conduct a scoping review with the goal of identifying and synthesizing the existing reasons for declining participation in cancer genetic and/or genomic testing, with special consideration of differences by race and ethnicity, as well as other sociodemographic factors.

Prior to the development of this scoping review protocol, we conducted a thorough search of MEDLINE (Pubmed), Embase (Ovid), Scopus, PROSPERO, the Cochrane Database of Systematic Reviews, Open Science Framework, and JBI Evidence Syntheses. No previous registered, published, or ongoing scoping reviews or systematic reviews on an equal or similar topic were identified.

The primary objective of the current review is to examine the reasons (concerns) why persons decline to participate in cancer genetics and genomic studies for individuals with a history of cancer living in the United States (US) and Puerto Rico (PR). A secondary objective is to examine reasons why persons decline to participate in cancer genetic and/or genomic research considering race and ethnicity, age at diagnosis, gender, health insurance, nativity/immigration status, socio-economic status, family history of cancer, cancer characteristics (i.e., primary, metastatic; treatment status; cancer site; stage at diagnosis), and co-morbidities. We aim to leverage the findings from this review to facilitate the development of target strategies to increase participation in cancer genetics and/or genomics research across diverse populations in the US and PR.

METHODS AND ANALYSIS:

Protocol design, registration and reporting:

This scoping review will follow the guidelines generated by the Joanna Briggs Institute (JBI) in the JBI Manual for Evidence Synthesis[16], this manual leverages the foundational methodology constructed by Arksey and O'Malley[17] with close consideration of the enhancement provided by Levac et al[18] and enables the generation of a review that will align with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR)[19]. In addition, this protocol was developed in accordance with the guidance and checklist published by Peters et al[20]**.** This scoping review protocol is registered online with the Open Science Framework (www.osf.io). We will start the proposed review on March 3rd, 2025 and complete it by November 3rd, 2025.

Review questions/objectives:

Scoping review studies aim to rapidly map key concepts underpinning a specific research area/question[21]. In this review, we target three out of the four common reasons to undertake a scoping review as stated by Arksey & O'Malley. Specifically, we will: 1) examine the extent, range, and nature of research activity in relation to reasons to decline to participate in cancer genetics and/or genomic cancer studies in the US and PR; 2) summarize and disseminate our research findings to the broader scientific community, and community representatives; and 3) identify research gaps in the existing literature in relation to reasons to decline to participate in cancer genetics and/or genomic cancer research in the US.

Motivated by these reasons to conduct this review, we propose the following research questions:

I. What are the reasons (concerns) expressed by persons with a history of cancer who decline to participate in cancer genetic and/or genomic studies in the US and PR?
II. What are the socio-demographic attributes among individuals with a history of cancer who decline to participate in cancer genetics and/or genomic studies in the US and PR?
III. What are the cancer-specific characteristics among persons with a history of cancer who decline to participate in cancer genetics and/or genomic studies in the US and PR?
IV. Are there different reasons (concerns) to decline to participate in cancer genetics and/or genomic studies by cancer type or race and ethnicity?

Eligibility/Inclusion criteria:

Types of Participants/Population:

This scoping review will consider for inclusion readily available peer-reviewed literature that reports on adults (≥18 years of age) with a current or previous diagnosis of cancer (either primary or metastatic) who have been approached in intra- or extra-hospital settings to participate in cancer genetic and/or genomic studies in the US and PR and have declined to partake in such studies. This criterion does not exclude participants based on how the diagnosis-status was obtained (e.g., clinical, histological, self-report). Moreover, we will not exclude literature that reports on participants with a history of cancer diagnosis who have comorbidities or coexisting conditions (e.g., pregnancy) (Table 1).

Table 1. Inclusion and exclusion criteria across phases of study selection for scoping review.

Selection Phase	Inclusion Criteria	Exclusion Criteria
1) Title and abstract screening	1.- Study is conducted in humans. 2.- Study is conducted in the United States and/or Puerto Rico. 3.- Study is focused on individuals with a positive history of cancer diagnosis. 4.- There is a mention of genetics and/or genomics for cancer research.	1.- Study is not a peer-reviewed publication. 2.- There is no mention of genetic and/or genomic testing. 3.- Study was not conducted in the United States or Puerto Rico. 4.- Study is not reported in English. 5.- Study does not include participants with a history of cancer diagnosis.
2) Full-text review	1.- A genetic and/or genomic assay was performed in at least a subset of the study participants. 2.- Reasons and/or concerns associated with the decision to decline to participate in a study are provided either with a numerical summary or narrative description.	1.- No information is provided on reasons and/or concerns associated with the decision to decline to participate. 2.- The clinical and sociodemographic characteristics of the study participants are not described (i.e., the population under study is not described).

	3.- Study reports sociodemographic characteristics of study participants. 4.- Study reports clinical characteristics of study participants.	3.- The genetic and/or genomic assay that was utilized is not described. 4.- No information on funding sources and conflicts of interest is provided.

Concept:

In this study, we target literature that examines the reasons (concerns) why individuals with a prior cancer history decline to participate in cancer genetics and genomic studies in the US and PR. This primary objective is decomposed into three concepts defined as follows:

1) *Cancer*: To describe cancer, we adhere to the recent definition demarcated by Brown et al, which defines cancer as a "disease of uncontrolled proliferation by transformed cells subject to evolution by natural selection"[22].
2) *Genetics and/or Genomics studies*: The World Health Organization defines “genetics” as the study of hereditary patterns of inheritance among organisms with a focus on the specific gene structure and variations to form a clear picture of the potential for a condition. While “genomics” is defined as the study of the genome and its actions; it refers to all the DNA contained in a cell including the nuclear and mitochondrial DNA[23]. Thus, genomics involves the analysis of the full DNA sequence of an organism whereas genetics interrogates the functioning and composition of one or more genes. Therefore, for the purpose of this review, we define cancer genetics and/or genomic studies as the investigational efforts conducted in individuals with a history of a cancer diagnosis to elucidate the molecular elements that influence cancer presentation, progression, and outcomes. This research leverages genetic and/or genomic testing technologies to inform the biological basis of different cancer types, develop targeted therapies and interventions, discover genomic biomarkers of drug response and resistance, provide targeted genetic counseling, and potentially guide clinical decision-making[24].
3) *Declination/Refusal to participate*: We operationally define a “declination to participate” as the non-coerced negative from protocol-eligible subjects to partake in cancer genetics and/or genomics research studies at any capacity. Thus a “decliner” is defined as a potential participant that directly or indirectly (e.g., through a family member) informed the study staff they were unwilling or unable to participate after being contacted for recruitment. The “declination to participate” decision may occur before, during, or shortly after informed consent, depending on the project’s protocol, but will always take place before the person who declines to participate is subject to any study-related activities[14].

Context:

The context of this review will be settings with individuals with a positive history of cancer diagnosis residing either in the US or in PR at the time they choose to not participate in a cancer genetic and/or genomic study. Thus, studies that did not performed a genetic and/or genomic test, or were no information is provided vis-à-vis a genetic and/or genomic assay will be excluded (Table 1)

We acknowledge that the reasons for declining participation in cancer genetic/genomic studies may vary between clinical and research testing. In this review, both types of testing will be considered for inclusion, with notations added to distinguish the rationale behind the specific type of testing conducted when possible.

Information sources:

This scoping review will consider all observational, interventional and review study designs including: analytical cross-sectional studies; prospective, retrospective, ambidirectional cohort studies; case-control studies and its variations according to methods of control sampling (i.e., nested case-control study using risk-set sampling, case-cohort sampling, and cumulative case-control study); randomized controlled trials; controlled clinical trials; qualitative studies; quantitative studies, mixed-methods studies; systematic reviews; meta-analyses; and narrative reviews.

The databases to be searched will include MEDLINE (PubMed), Embase (Ovid), and Scopus. Both Embase and Scopus cover the search of "gray" literature (i.e., conference abstracts, symposia articles, book chapters, etc.). If abstracts or symposia articles are detected, an effort to identify peer-reviewed publications derived from these sources will be made. If none are available, the entries will not be included. Databases will be interrogated from inception to the present, with only literature published in English considered for inclusion (Table 1).

Search strategy:

The search strategy was developed in collaboration with an expert health sciences librarian (JD) from the Keck School of Medicine at the University of Southern California. An initial search was conducted in MEDLINE (PubMed) to identify relevant articles on the topic. Keywords were extracted from the titles, abstracts and manuscript body, and were utilized in combination with the index terms to develop a full search strategy for MEDLINE (PubMed) (Supplementary Table 1). The proposed search strategy encompasses three main concepts: "cancer", "genetics and/or genomics studies", and "declination/refusal to participate". These concepts are decomposed into terms indexed in the National Library of Medicine, controlled vocabulary thesaurus (MesH, Medical Subject Headings) (https://www.ncbi.nlm.nih.gov/mesh/). This search strategy will be adapted to each information source. References cited in articles that met inclusion criteria will be reviewed to identify additional literature for inclusion and supplemented with hand searching. Following JBI recommendations[16], a pilot test screening of eligible studies will be conducted by two independent reviewers, the search strategy will be updated accordingly.

Selection of sources of evidence:

Identified records from all sources of evidence will be collated and uploaded into Covidence, an online screening and data extraction tool for systematic reviews (https://www.covidence.org). Duplicate records will be removed. A two-stage screening process will ensue to select studies for this review: 1) Title and abstract screening, retrieved literature of potentially eligible studies will be screened against inclusion and exclusion criteria and labeled as "include", "exclude", or "uncertain"; 2) Full-text review, we will extract full-text publications from studies labeled as "include" or "uncertain" to evaluate against the inclusion and exclusion criteria. All studies will be

independently reviewed by at least two reviewers, with conflicts resolved by a third independent reviewer. For literature labeled as "exclude" after full-text review is conducted, the reasons for exclusion will be documented.

Full-text publications from studies that meet the inclusion criteria will be imported into Zotero v.7.0.11 for citation management. The results of the selection process will be presented in the final scoping review as a PRISMA flow diagram[25].

Critical appraisal of individual sources of evidence:

Scoping reviews are not required to conduct an assessment of the methodological quality of the retrieved literature[20]. As the primary goal of this review is to examine the extent, range and nature of available evidence in our topic of interest, we have opted to not critically appraise the studies we will include.

Data charting process:

Data will be extracted by two reviewers into Covidence following the fields specified in a standardized data extraction tool (Supplementary Table 2). The tool will be piloted by three reviewers who will independently chart data from the first five studies, with adjustments made accordingly after a discussion among the team. Additionally, the data extraction tool may be iteratively updated to ensure that unforeseen data is usefully captured. Modifications made to the presented tool (Supplementary Table 2) will be recorded and mentioned in the full scoping review manuscript.

We will extract information from the following categories: 1) publication details, 2) study characteristics, 3) study methods, 4) socio demographics of study participants, 5) clinical characteristics of study participants, and 6) study results. Specifically, the study results will focus on the following: participation rate-, reasons for declining to participate-, sociodemographic and clinical characteristics of decliners-, and strategies to enhance participation- in cancer genetics and/or genomic studies.

Collating summarizing, and reporting the results:

Studies will be grouped by design into qualitative, mixed methods, and quantitative research, with the latter further stratified into cross-sectional and longitudinal studies. Data will be summarized following this stratification, with results presented in three blocks of information by study type as follows: 1) Studies that deployed qualitative and/or mixed methods, 2) Studies that report on quantitative research efforts (stratified into cross-sectional and longitudinal), and 3) Studies that were not initially conducted to evaluate reasons for declining to participate in cancer genetics and/or genomics studies but meet inclusion/exclusion criteria and report sufficient results to be included in the scoping review.

After grouping the included literature into these three categories, we will present the data using the following strategies:

1. Descriptive numerical summary:

This includes the publication details, study characteristics, and study methods as described in the data extraction tool (Supplementary Table 2). Namely, publication year, publication source, study design, study setting/location, study sponsor/funding source, sampling method, if an incentive for participation was offered, primary vs. secondary data analysis, sequencing platform/technology utilized to obtain the genetic and/or genomic information, time commitment for participation in the study, study activities, and method of recruitment.

2. Graphical presentation of the charted information:

The reasons and factors associated with the decision to decline participation in cancer genetics and/or genomic research will be collected and presented in bar graphs. The x-axis will display the reasons and/or factors, while the y-axis will show the number of studies reporting on these reasons and factors. Results will be stratified according to the three blocks of information previously constructed. Efforts will also be made to stratify the results by sociodemographic or clinical characteristics of the populations under study (e.g., sex, race and ethnicity, socioeconomic status, cancer type) if feasible.

3. Narrative review of the literature

Studies will be grouped thematically according to the reported reasons and factors associated with the decision to decline to participate in cancer genetics and/or genomic studies. For studies of qualitative nature, a narrative review of the findings will be provided, with similarities and differences in the different methodological efforts to increase participant accrual emphasized. In addition, clinical and sociodemographic characteristics of the study participants that cannot be quantitatively presented, and that may be associated with study participation rates will be described in this section.

Conclusions for the full scoping review will be drawn from all these three strategies. This will enable the identification of predominant factors that may influence decision-making in cancer genetic and/or genomic research, potentially transforming them into actionable strategies to improve recruitment in future research efforts.

Patient and public involvement:

No patient or public representatives were involved in the design, conduct, reporting or dissemination of this protocol.

Ethics and dissemination:

Ethical review is not required for scoping reviews as only secondary data analyses from publicly available data are conducted. Results will be disseminated with a peer-reviewed publication and conference presentations.

Data availability statement:

All data supporting the development of the scoping review protocol is available within the paper and its Supplementary Information.

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Supplementary Table 1. Search Strategy for scoping review.

Search	Concept	Query	Records Retrieved
#1	Cancer (humans)	((((("Neoplasms"[MeSH Terms] OR "Neoplasm"[All Fields] OR "Neoplasia"[All Fields] OR "Neoplasias"[All Fields] OR "Tumors"[All Fields] OR "Tumor"[All Fields] OR "Tumoral"[All Fields] OR "tumour"[All Fields] OR "Tumours"[All Fields] OR "Cancers"[All Fields] OR "Cancer"[All Fields] OR "Malignant Neoplasm"[All Fields] OR "Malignant Neoplasms"[All Fields] OR "neoplasm malignant"[All Fields] OR "neoplasms malignant"[All Fields] OR "Malignant"[All Fields] OR "Malignancy"[All Fields] OR "Malignancies"[All Fields] OR "Malignant Tumor"[All Fields] OR "Malignant Tumours"[All Fields] OR "tumor malignant"[All Fields] OR "tumor s"[All Fields] OR "Tumoral"[All Fields] OR "tumorous"[All Fields] OR "Tumour"[All Fields] OR "Neoplasms"[MeSH Terms] OR "Neoplasms"[All Fields] OR "Tumor"[All Fields] OR "tumour s"[All Fields] OR "tumoural"[All Fields] OR "tumourous"[All Fields] OR "Tumours"[All Fields] OR "Tumor"[All Fields]) AND ("malign"[All Fields] OR "malignance"[All Fields] OR "malignances"[All Fields] OR "Malignant"[All Fields] OR "malignants"[All Fields] OR "malignities"[All Fields] OR "malignity"[All Fields] OR "malignization"[All Fields] OR "malignized"[All Fields] OR "maligns"[All Fields] OR "Neoplasms"[MeSH Terms] OR "Neoplasms"[All Fields] OR "Malignancies"[All Fields] OR "Malignancy"[All Fields])) OR "Oncology"[All Fields] OR "Medical oncology"[MeSH Terms]) AND "humans"[MeSH Terms]) AND (humans[Filter])	3,920,224

#2	Genetics and/or genomics research (humans)	(("genetic research"[MeSH Terms] OR "research genetic"[All Fields] OR "genomic research"[All Fields] OR "genetics research"[All Fields] OR "genomics research"[All Fields] OR "genetic testing"[MeSH Terms] OR "genetics testing"[All Fields] OR "genetic profiling"[All Fields] OR "genomic profiling"[All Fields] OR "genomics profiling"[All Fields] OR "genome testing"[All Fields] OR "genomic testing"[All Fields] OR "genomics testing"[All Fields] OR "Whole-genome sequencing"[All Fields] OR "exome sequencing"[All Fields] OR "exomic sequencing"[All Fields] OR "sequence analysis dna"[All Fields] OR "genome sequencing"[All Fields] OR "genomic sequencing"[All Fields] OR "genomic sequencing"[All Fields] OR "genomic sequence"[All Fields] OR "genetic sequencing"[All Fields] OR "genetics sequencing"[All Fields] OR "genetic sequence"[All Fields] OR "clinical sequencing"[All Fields] OR "genetic carrier screening"[All Fields] OR "carrier screening"[All Fields] OR "genetic screening"[All Fields] OR "genetic susceptibility testing"[All Fields] OR "genomic risk profiling"[All Fields] OR "genome-based testing"[All Fields] OR "genomic medicine"[All Fields] OR "genetic counseling"[All Fields] OR "genetic information"[All Fields] OR "genetic diagnosis"[All Fields] OR "genomic diagnosis"[All Fields] OR "genetic diagnoses"[All Fields] OR "genomic diagnoses"[All Fields] OR "precision medicine"[All Fields] OR "individual genetic"[All Fields] OR "individual genomic"[All Fields] OR "individual genomics"[All Fields] OR "individual genome"[All Fields]) AND "humans"[MeSH Terms]) AND (humans[Filter])	280,114

#3	Declination/refusal to participate (humans)	(("patient participation"[MeSH Terms] OR "refusal to participate"[MeSH Terms] OR "decision making"[MeSH Terms] OR "patient decision making"[All Fields] OR "patients decision making"[All Fields] OR "participant decision making"[All Fields] OR "participants decision making"[All Fields] OR "participation factors"[All Fields] OR (("reason"[All Fields] OR "reasonable"[All Fields] OR "reasonably"[All Fields] OR "reasons"[All Fields]) AND ("decline"[All Fields] OR "declined"[All Fields] OR "decliner"[All Fields] OR "decliners"[All Fields] OR "declines"[All Fields] OR "declining"[All Fields])) OR "reasons for participation"[All Fields] OR "enrollment barriers"[All Fields] OR "enrollment"[All Fields] OR "participate"[All Fields] OR "decline"[All Fields] OR "declining"[All Fields] OR "declining to participate"[All Fields] OR "risk perception"[All Fields] OR "participation factors"[All Fields] OR "decisional preferences"[All Fields] OR "participant preferences"[All Fields] OR "concern"[All Fields] OR "concerns"[All Fields] OR "barriers"[All Fields] OR "cancer worry"[All Fields] OR "genetic discrimination"[All Fields] OR "trial participation"[All Fields] OR "recruitment"[All Fields] OR "facilitators"[All Fields] OR "return of results"[All Fields]) AND "humans"[MeSH Terms]) AND (humans[Filter])	1,108,448
#4		#1 AND #2 AND #3	4,656
Search developed for MEDLINE (Pubmed), conducted on July 19th, 2024. Filters: Species, Humans			

Supplementary Table 2. Data extraction instrument.

Publication Details	Study characteristics	Study Methods	Study participants sociodemographic characteristics	Study participants clinical characteristics	Study Results
1.- Paper ID (Covidence ID) 2.- Publication source (database) 3.-Year of publication. 4.- First author (last name, name) 5.- Senior author (last name, name) 6.- Academic affiliation first author (industry, academic, foundation, government). 7.- Academic affiliation corresponding author (industry, academic, foundation, government)	1- Study design (cross-sectional, cohort study, case-control, clinical trial, review, qualitative, mix methods). 2.- Study aims. 3.-Study setting/location. 4.-Study sponsor/funding source (industry, academia, foundation, government). 5.- Period under study.	1.- Sampling method (i.e., method of participant identification/inclusion). 2.- Incentive of participation. 3.- Inclusion criteria. 4.- Exclusion criteria. 5.- Primary vs. secondary data analysis. 6.- Sequencing platform/technology. 7.- Time commitment. 8.- Study activities (surveys, interviews, specimen donation). 9.- Method of recruitment (electronic/digital, phone, phase-to-phase contact, mail, etc).	1.- Sample size. 2.- Racial and ethnic composition. 3.- Gender distribution. 4.- Age and/or age range. 5.- Socioeconomic status. 6.- Income level. 7.- Nativity (US-born vs. non-US-born). 8.- Region of origin. 9.- Insurance. 10.- Marital status. 11.- Level of education.	1.- Tumor site. 2.-Tumor type. 3.- Tumor stage at diagnosis. 4.- Tumor grade at diagnosis. 5.- Primary vs. secondary recurrence. 6.- Treatment phase (pre-, during, post-treatment). 7.- Family history of cancer (positive vs. negative first degree relative). 8.- Time since diagnosis to treatment. 9.- Time since diagnosis to study recruitment.	1.- Decline participation (i.e., participation rate). 2.- Reasons for declining participation. 3.- Characteristics of decliners (i.e., sociodemographic and clinical characteristics) 4.- Strategies to increase participation (i.e., enhance participation rate).