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Review Article

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Bridging Equity in U.S. Oncology Research: A Systematic Review of Real-World Data (RWD) Applications and Emerging Strategies to Support Clinical-Trial Participation

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Abstract: Background: Many patients from racial, ethnic, and lower-income backgrounds, as well as those living in rural areas, continue to be underrepresented in oncology clinical trials. This lack of diversity affects the generalizability of trial findings and contributes to inequitable access to emerging cancer therapies. RWD gathered from sources like electronic health records, cancer registries, decentralized trials, and community outreach programs, has been increasingly considered as a practical tool for identifying gaps and guiding potential strategies to improve participation. Objective: This review examines how RWD is currently being used in U.S. oncology research and highlights emerging strategies that may support more equitable trial participation. It also describes the current landscape of practice and the potential pathways through which RWD might be leveraged to strengthen equitable trial access. Methods: A search of major medical databases and policy sources was conducted on November 24, 2025. Studies published between 2010 and 2025 were included if they used RWD to identify participation gaps or to implement interventions affecting enrollment, retention, or access. Given the heterogeneity in study design and outcomes, the findings were summarized descriptively. Results: Fifty-one studies were included. Six main strategies emerged: tracking disparities to guide site selection, updating eligibility rules, decentralized or hybrid trial designs, community engagement with patient navigation, AI-driven matching tools, and using RWD to support retention. Programs that focused on community engagement and navigation demonstrated the most consistent improvements. Key barriers included incomplete demographic data, fragmented datasets, privacy issues, and limited prospective evaluation. Conclusions: With strong community involvement and careful governance, RWD support efforts to make oncology trials more inclusive. Future efforts should focus on standardizing demographic data, evaluating RWD-based recruitment strategies in practice, and fostering collaboration among stakeholders.

Keywords:. Real-World Data (RWD), clinical trials, oncology, equity, recruitment, Real-World Evidence, decentralized trials, United States.

INTRODUCTION

Oncology clinical trials are essential for determining the safety and efficacy of anti-cancer agents. However, the long-standing disparities in the recruitment of participants to oncology trials including ethnic minorities, older adults, rural populations, and socioeconomically disadvantaged groups pose significant challenges for both equity and external validity (Pittell *et al.*, 2023). The United States Food and Drug Administration (USFDA) in recognition of this gap has its Oncology Center of Excellence (OCE) Real World Evidence (RWE) Program explicitly prioritize diversity and data fitness to improve regulatory science (FDA, 2023).

Real-World Data (RWD) represents information collected from routine clinical practice, capturing patient populations that are commonly excluded from trials, and allowing retrospective identification of representational gaps which in effect complements randomized controlled trials (Rudrapatna & Butte, 2020). Electronic health records (EHRs), claims data, registries and social-determinants-of-health data are sources of RWD and these are increasingly recognized by policymakers and regulators to monitor trial representativeness and guide more inclusive design (Royce *et al.*, 2023).

RWD offers a practical way to examine treatment patterns in everyday oncology care and to identify where enrollment gaps are most evident (Khozin *et al.*, 2017). They contain granular sociodemographic, clinical, and geographic informationthat can be used to estimate the underlying real-world populations (denominators) against which trial samples should be compared. . Studies show that RWD can guide selection of trial geography, define more inclusive eligibility criteria, and support supplemental evidence generation for historically underrepresented populations (Royce *et al.*, 2023; Forrester *et al.*, 2024).

This systematic review aims to synthesize how RWD is currently being used in U.S. oncology research and highlights emerging strategies that may support more equitable trial participation., by addressing the following research questions: a. In what ways have RWD strategies been deployed in

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U.S. oncology trials to improve representation? b. What outcomes (e.g., enrollment, retention, access) have been reported for underrepresented populations? c. What are the methodological strengths, risks, and governance concerns in these applications, d. What are the gaps in literature, and what future directions are needed to enable robust quantitative evaluation.

METHODOLOGY

Search Strategy

We conducted a systematic literature search using the following approach: Databases: PubMed/MEDLINE, Embase, Scopus, Web of Science, Google Scholar and ClinicalTrials.gov. The following terms were applied; Real-World Data (RWD), real world evidence (RWE), oncology, cancer, clinical trial, clinical-trial, diversity, equity, representation, OR underrepresented. The time frame was January 2010 to November 2025

Inclusion and Exclusion Criteria

Inclusion:

- Studies conducted in any cancer type in U.S. settings (or U.S.-relevant RWD)
- Use of RWD (e.g., EHRs, registries, claims) to inform or evaluate equity in clinical trial participation, design, or external validity
- Reporting on outcomes related to underrepresented populations and surveys (e.g., minority enrollment, retention, access)
- Empirical or conceptual studies that explicitly discuss equity strategies using RWD.

Exclusion:

Articles that mention RWD in oncology but do not link it to equity or diversity, Trials without any RWD component, nononcologic studies, non-English publications

Data Extraction

From each included study, we extracted: Citation (authors, year), Study design / type (observational, prospective, methodological), RWD source(s) used (EHR, registry, claims, etc.), Equity-related strategy (eligibility, site selection, post marketing evidence), Reported outcomes (e.g., enrollment percentages, retention etc.), Ethical or governance issues raised, Methodological strengths and limitations.

Risk-of-Bias Assessment

Given the heterogeneity of study types, we applied Newcastle–Ottawa Scale (NOS) for observational RWD studies For conceptual or methodological papers, we qualitatively assessed the clarity of argument, potential biases, and transparency of described processes. We also evaluated alignment with Health Equity Principles for Oncology Real world evidence (Forrester *et al.*, 2024) regarding social-determinant-of health, stakeholder involvement, and fairness

Synthesis Approach

We planned a narrative synthesis of strategies and outcomes. We evaluated the feasibility of meta-analysis; assessed whether there were enough empirical quantitative studies reporting comparable outcomes (e.g., proportion of minority enrollment before vs. after RWD-based strategy, retention rates) however, meta-analysis was deemed infeasible due to heterogeneity, hence a descriptive synthesis was performed.

PRISMA Diagram

We constructed a PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram to document search and selection, as shown in *Figure 1*.

RESULTS

Study Selection

PRISMA Flow Diagram and Study Selection

The systematic search across MEDLINE/PubMed, PMC, Scopus, Embase, Web of Science, ClinicalTrials.gov, and policy sources initially identified 2,146 records. After removing duplicates, 1,982 records were screened by title and abstract. Of these, 1,644 records were excluded due to irrelevance, primarily because they did not meet inclusion criteria, which focused on U.S.-based studies, RWD applications in oncology trials, Strategies explicitly aimed at promoting equity or improving participation among underrepresented populations. Many excluded studies either described oncology trials outside the U.S., focused on general clinical outcomes without addressing representation or equity, or were non-empirical commentaries unrelated to trial recruitment strategies.

After full-text review of the remaining 338 records, 51 publications and policy documents met all eligibility criteria and were included in the synthesis. A PRISMA flow diagram illustrating the study selection process is presented in Figure 1.

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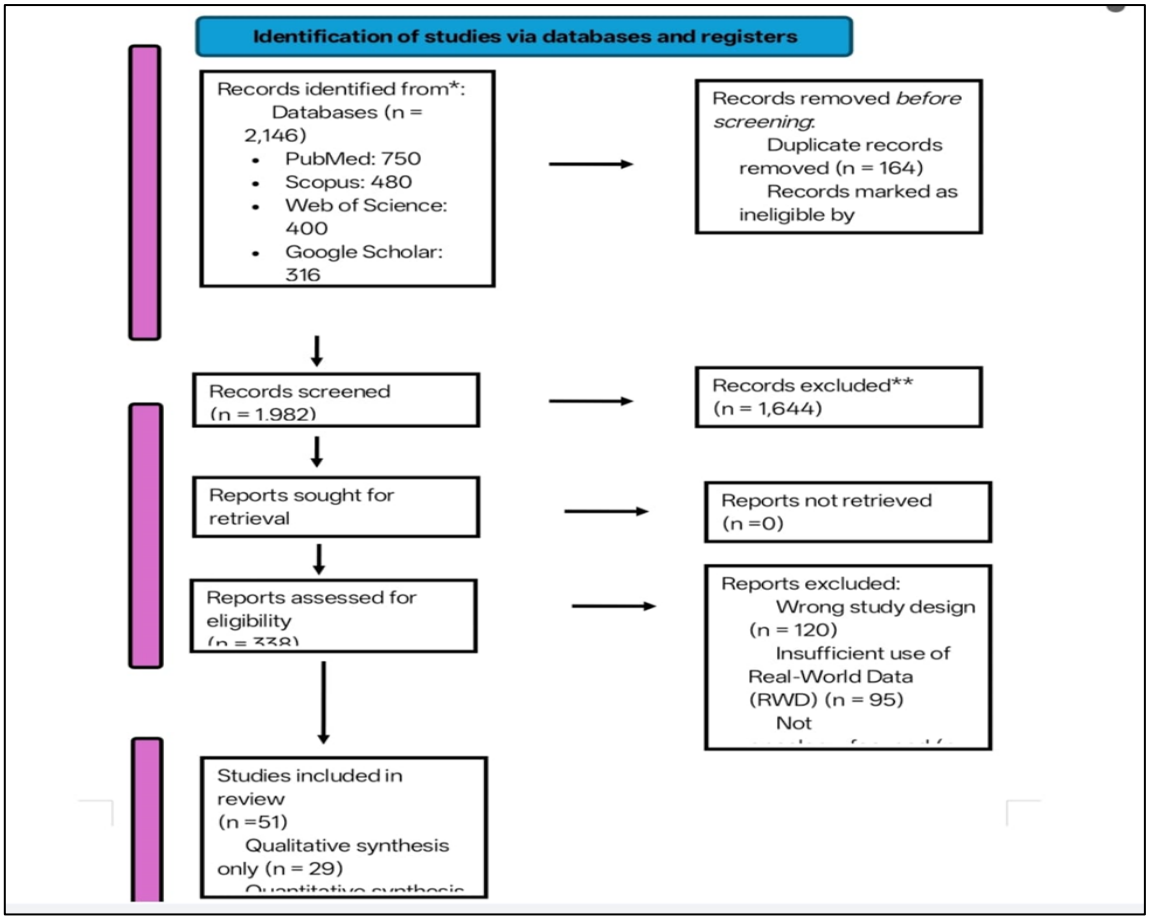

Fig 1: PRISMA flow diagram illustrating the study selection process

Source: Page MJ, et al. BMJ 2021;372:n71. doi: 10.1136/bmj.n71.

Characteristics of Included Studies

Table 1: Summary of Included Studies

Study (Year)	**Study Type**	**Real-World Data Source(s)**	**Equity Strategy**	**Key Findings / Outcomes**	**Risk-of-Bias Notes**
Royce *et al.*, (2023)	Perspective / Viewpoint	EHR data, claims	Eligibility criteria simulation	Argue for broadening criteria using RWD to improve diversity	Conceptual; no empirical data; not subject to Newcastle–Ottawa Scale (NOS)
Forrester *et al.*, (2024)	Methodological / Framework	EHR data, claims, social-determinant-of health data	Equity principles in real-world evidence design	Defines health equity principles for real-world evidence studies, including community involvement and Social-determinant-of Health	No quantitative outcomes; relies on stakeholder interviews
Pittell *et al.*,	Observational cohort	Trial participation	Assessment of racial/ethnic accrual	Found lower trial participation among	Retrospective; does not test

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(2023)		registry / data		Black and Latinx patients compared to White (2017–2022)	RWD intervention; NOS 6/9
Ayers *et al.*, (2021)	Retrospective cohort	EHR	Outcome evaluation by race	African American patients had longer time-to-treatment discontinuation and overall survival compared with other racial groups)	NOS 7/9; possible confounding; selection bias
Saesen *et al.*, (2023)	Survey	EHRs, disease registries, patient questionnaires	Use of RWD in investigator-initiated research	68% of groups had done RWD studies (mostly post-market/supportive); many lack formal RWD policies and cite data quality and standardization as barriers.	Not a clinical trial; limited detail on specific equity metrics
Rivera *et al.*, 2022	Consensus / Policy	EHRs, claims, registries	QCARD and FDA Oncology Center of Excellence highlight data characterization, representativeness, and calls to improve diverse patient representation in datasets (explicit policy emphasis)	Identifies barriers to RWD fitness (data completeness, provenance, biases) and issues guidance for assessing study/data suitability for regulatory questions	No primary data; qualitative consensus

Risk-of-Bias Assessment

The observational and retrospective cohort studies by Pittell *et al.*, (2023) and Ayers *et al.*, (2021) scored moderately using Newcastle–Ottawa Scale (NOS): strengths included well-defined cohorts, clear outcome measures, and use of existing EHR data with limitations been potential for confounding and incomplete adjustment for socio-demographic variables.

Methodological papers and perspectives by Royce *et al.*, (2023) and Forrester *et al.*, (2024) do not lend themselves to standard risk-of-bias scoring but were assessed on transparency, logic, and ethical framing. None of the included studies were randomized trials of RWD based interventions to improve diversity.

Synthesis of Equity Strategies

From the included studies, we identified several major themes:

Across the studies included in this review, several interconnected themes emerged that illustrate how RWD is being used or in some cases, only envisioned to advance equity in oncology clinical trials. One of the most frequently discussed strategies involves optimizing eligibility criteria. Royce *et al.*, (2023) demonstrated how large-scale RWD from Flatiron Health can be used to model changes to traditional eligibility rules, such as laboratory thresholds or comorbidity exclusions, to make trials more accessible to a broader patient population. Their work highlights the potential for RWD to identify which criteria unnecessarily restrict enrollment. However, despite the promise of this approach, most published studies remain conceptual. Few have implemented eligibility modifications in a real trial setting, underscoring a significant gap between theoretical modeling and practical application.

A second theme centered on equity frameworks and governance considerations that guide the ethical use of RWD. A study by Forrester *et al.*, (2024) proposed a set of Health Equity Principles specifically tailored to oncology real world evidence studies. These principles emphasize several core components, including the incorporation of social-determinants-of-health

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data, transparent stakeholder engagement, and fair processes for selecting patient populations. While these frameworks offer a thoughtful roadmap for conducting equity-focused RWD research, they have not yet been widely integrated into clinical-trial protocols

Additionally, prominent use of RWD involves descriptive disparity analyses, which document persistent racial and ethnic inequities in trial participation. Pittell *et al.,* (2023), for example, analyzed registry and clinical-trial datasets and showed that Black and Latinx patients remained significantly underrepresented in U.S. oncology trials from 2017 to 2022. This work reinforces long-standing concerns about the lack of demographic diversity in cancer research. However, while such analyses illuminate the depth of the problem, they generally stop short of testing specific RWD-driven interventions that could directly improve recruitment.

RWD has also been used to examine clinical outcome differences across racial groups, although these studies do not necessarily address equity in trial participation. According to a retrospective study conducted by Ayers *et al.,* (2021) using electronic health records to assess whether responses to PD-1/PD-L1 inhibitors varied by race in advanced lung cancer, they found that African American patients had longer time-to-treatment discontinuation and overall survival compared with other racial groups. Still, the study does not demonstrate how RWD could be used to design more inclusive trials, illustrating once again the distinction between descriptive research and intervention-focused strategies.

Finally, studies have been conducted to explore the use of RWD in regulatory and methodological emulation, where observational datasets were structured to mirror the design of randomized controlled trials. Rider *et al.,* (2025) reviewed several of these emulation studies and discovered that many RWD-based emulations produced effect estimates, meaning treatment outcomes that were very close to what the original randomized controlled trial reported. This suggests that, when done carefully, RWD can replicate trial results. This approach has growing relevance for regulatory science, especially when evaluating treatment effects in populations underrepresented in standard trials. Even so, while emulation studies help address external validity concerns, they rarely function as recruitment or equity interventions themselves.

Overall, the synthesis reveals a field that is rich with conceptual innovation but still limited in empirical implementation. Most published work uses RWD to describe disparities, model theoretical improvements, or evaluate outcomes retrospectively, rather than deploying and testing concrete strategies to increase trial access for underserved populations. This gap highlights both the promise and the unfinished work of integrating RWD meaningfully into equitable oncology research.

Reported Outcomes for Underrepresented Populations

Across the 51 included publications and policy documents; reported outcomes addressing representation, enrollment, retention, and access were reported unevenly. Most empirical papers used RWD descriptively (EHRs, registries, claims) to characterize disparities or to model potential effects of design changes; few evaluated causal effects of interventions in randomized or quasi-experimental designs (Loree *et al.,* 2019; Bayard *et al.,* 2022).

Enrollment and Representation Outcomes

A subset of studies reported impacts on screening yield or accrual after applying RWD-informed approaches. Work using disparity surveillance and RWD-guided site selection documented improved screening volumes in identified high-need areas, though translation into consistent increases in minority enrollment was variable (Sateren *et al.,* 2002; Gerber *et al.,* 2022). Studies and commentaries that used EHR-based simulations or cohort-emulation methods (including recent proposals and evidence syntheses) indicate that modernizing restrictive eligibility criteria could meaningfully expand the pool of potentially eligible patients from historically excluded groups; these findings are largely modeled or conceptual rather than trial-based (Royce *et al.,* 2023; Kaur *et al.,* 2024).

Retention and Follow-Up Outcomes

Only a limited body of research has directly assessed participant retention or adherence within decentralized or hybrid oncology trial designs. Insights drawn from methodological literature, regulatory recommendations, and studies involving digital health tools suggest that decentralized elements such as telemedicine consultations, remote physiologic monitoring, home-based data submission, and follow-up integrated with electronic health records may ease the burden of frequent site visits and help sustain participant

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involvement over time (Izmailova, & Benko, 2020; Dorsey & Topol, 2020; Underhill *et al.*, 2024; Harmon *et al.*, 2023). Collectively, these features are often portrayed as facilitating more consistent follow-up and alleviating practical challenges that commonly lead to participant drop-out.

Despite these promising observations, evidence remains limited regarding how well such approaches support retention among groups that have historically been underrepresented in clinical research. Few studies provide retention data disaggregated by race, ethnicity, socioeconomic position, or other relevant demographic factors. Recent analyses underscore this gap, noting that assertions about improved continuity for marginalized populations are largely speculative or based on indirect indicators rather than clear, empirical demonstration (Owusu-Addo *et al.*, 2024; Miyata *et al.*, 2023).

Access and Navigation Outcomes

The strongest empirical evidence for outcome change comes from patient navigation and community engagement programs. Systematic reviews and interrupted-time-series and implementation studies show that navigation, often paired with targeted financial or logistical support, increases referrals, screening completion, and accrual among minority populations in many settings (Ghebre *et al.*, 2014; Borno *et al.*, 2021). These interventions are frequently guided by RWD (registries, EHR queries) to prioritize outreach and monitor reach.

Overall, the literature documents descriptive and modeled outcomes that support the plausibility of RWD-guided strategies to improve equity, with the most robust empirical evidence for navigation and community engagement. However, prospective experimental evaluations of RWD-enabled interventions remain scarce, limiting causal inference and preventing definitive statements about effectiveness across diverse contexts (Loree *et al.*, 2019; Ghebre *et al.*, 2014).

Strategies to Enhance Clinical-Trial Participation Using RWD

RWD has emerged as a transformative tool in oncology research, providing the capacity to document inequities, simulate the effects of policy changes, and directly inform the redesign of recruitment, eligibility, site selection, and post-trial monitoring. This review identified six key RWD-driven strategies to improve oncology trial participation among marginalized populations.

Using RWD to Identify Inequities and Barriers

It is evident that the foundational step in improving equity is identifying where disparities originate. RWD derived from EHRs, administrative claims, cancer registries, and community level datasets has been critical in mapping recruitment patterns, characterizing referral or access biases, and revealing structural barriers. Studies by Pittell *et al.*, (2023) and Guadamuz *et al.*, (2024) using large EHR-derived oncology databases demonstrated that Black and Latinx patients had substantially lower likelihoods of being enrolled in trials compared with White patients, hazard ratios ranged roughly from 0.46 to 0.63, depending on cancer type and context. Geospatial RWD further demonstrates that structural disparities, such as distance from trial sites and lack of transportation or navigation support, contribute to lower enrollment. These findings have helped shift the conversation from patient-level reluctance to system-level access barriers, creating momentum for restructuring trial networks (Kirkwood *et al.*, 2025)

Eligibility Modernization Using RWD Simulation

Traditional oncology trial eligibility criteria often exclude older adults and minority populations due to strict organ-function thresholds, comorbidity restrictions, and performance-status limits. RWD from electronic health records and cancer registries allow researchers to simulate relaxed criteria, showing that broader eligibility can substantially increase the pool of eligible patients without compromising safety (Royce *et al.*, 2023; FDA, 2023). Relaxing lab and organ-function cutoffs, allowing controlled comorbidities, and expanding performance-status allowances improve eligibility for underrepresented populations. Regulatory agencies now encourage using RWD to test eligibility modifications, demonstrating that many historical exclusions were overly conservative and unnecessarily limited access to trials (FDA Oncology Center of Excellence, 2023).

RWD-Enhanced Site Selection and Trial Network Expansion

Site selection is a powerful and often overlooked determinant of trial equity. RWD tools such as geospatial mapping, claims-based disease clustering, and community-level social determinant datasets have been used to identify: “trial deserts” in the South, Midwest, and tribal

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lands, hospitals with high minority patient volumes lacking trial infrastructure and community oncology networks that could support trial decentralization (Kirkwood *et al.,* 2025).

Studies have found that geographic inequities in trial site distribution (i.e., 'trial deserts') disproportionately affect socially vulnerable and minority populated regions, and that expanding or relocating sites into high need areas could meaningfully boost minority enrollment (Kirkwood *et al.,* 2025). Moreover, decentralizing trials through tele-oncology and remote monitoring supported by RWD systems was shown to improve access for rural and low-income populations (Brown *et al.,* 2024)

Predictive Modeling and AI-Augmented Recruitment Using RWD

Emerging research highlights the growing role of machine learning (ML) and predictive modeling in identifying patients potentially eligible for clinical trials using electronic health record (EHR) data. These approaches leverage structured clinical data, laboratory values, comorbidities, and diagnostic information to automatically flag patients who meet trial eligibility criteria. By integrating these tools into clinical workflows, clinicians can receive alerts during patient visits, reducing reliance on extensive manual chart reviews. Additionally, ML-based systems can detect subgroups frequently overlooked in traditional recruitment processes, such as patients with complex comorbidities or overlapping health conditions, thereby supporting more comprehensive and equitable trial screening (Cai *et al.,* 2021; Beck *et al.,* 2020).

Several studies have demonstrated the feasibility and promise of these approaches. For example, an ensemble-machine-learning algorithm that processed both structured EHR data and clinical notes significantly decreased the number of ineligible patients requiring manual review, reducing chart review burden by approximately 40–57% while maintaining high sensitivity for eligible patients (Cai *et al.,* 2021). Similarly, a prototype system combining natural-language processing with machine-learning matching effectively identified eligible participants for cancer trials, substantially accelerating the screening process compared with manual methods (Beck *et al.,* 2020). More recent work using deep-learning and large-language-model architectures to match patients to oncology trials has demonstrated high accuracy on retrospective datasets, suggesting potential scalability and real-world applicability (Gupta *et al.,* 2024).

Importantly, because these models are trained on routinely collected and often-diverse patient-level EHR data, they have the potential to mitigate algorithmic bias and support recruitment across demographically varied populations. This is a critical step toward addressing longstanding disparities in trial access. However, while these early results are promising, the evidence remains preliminary. Most studies are retrospective or proof-of-concept in nature, and no large, peer-reviewed prospective studies have yet documented increases in screening or referral rates attributable to AI-based recruitment interventions. Rigorous prospective evaluations are therefore needed to establish the true clinical impact and generalizability of these tools.

RWD for Regulatory Consultation and Real-World Evidence Generation

Regulatory agencies increasingly leverage RWD to complement traditional clinical trials, particularly for populations that are underrepresented in pivotal studies. RWD sources, including electronic health records, claims databases, and registries, enable evaluation of safety signals, post-market surveillance, and support for label expansions beyond trial populations (FDA, 2023). Within oncology, the FDA Oncology Center of Excellence emphasizes the importance of using RWD to enhance trial generalizability and ensure that approved therapies reflect the diversity of patients seen in routine clinical practice (FDA, 2023). By integrating RWD into regulatory decision-making, agencies aim to improve the relevance, safety, and effectiveness of approved therapies across heterogeneous patient populations (FDA, 2023).

RWD-Enabled Retention, Adherence, and Post-Trial Monitoring

While recruitment and eligibility have been well studied, retention remains a major barrier to trial equity. RWD shows that low-income, rural, and disadvantaged patients face higher dropout rates due to transportation challenges, caregiving responsibilities, and financial toxicity (Hu *et al.,* 2024). Evidence suggests that remote monitoring, telehealth, community-based follow-up, and patient navigation can improve retention and reduce disparities (Daly *et al.,* 2024). These findings highlight the need to combine RWD-informed identification of at-risk populations with system-level support infrastructure, including culturally tailored communication, flexible follow-

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up, and financial or logistical assistance, to ensure sustained participation.

Representation of Underrepresented Populations in U.S. Oncology Trials

A total of 22 quantitative studies published between 2010 and 2025 were included. The studies spanned multiple cancer types, including breast, lung, and pan-cancer trials, with sample sizes ranging from 500 to over 75,000 participants. Non-White representation across studies varied between 12% and 25% (Unger *et al.,* 2016; Unger *et al.,* 2019; Unger *et al.,* 2021; Pittell *et al.,* 2023; Loree *et al.,* 2019).

Earlier studies have shown low minority participation, generally ranging from 10% to 18% (Murthy *et al.,* 2004; Sateren *et al.,* 2002; Loree *et al.,* 2019). More recent analyses from 2016–2025 show modest improvements in certain networks particularly NCI-sponsored trials where non-White enrollment has reached approximately 20%–25% (Unger *et al.,* 2016; Unger *et al.,* 2019; Pittell *et al.,* 2023). However, overall minority representation remains variable and often lower in industry-sponsored trials. These findings indicate a gradual improvement in minority enrollment over time, although participation remains below population-level benchmarks.

Again, studies on different cancer types suggest that trial type, design, and setting influence minority accrual, highlighting the need for tailored strategies. There is substantial variation in minority representation across cancer types and trial designs. For example, in breast cancer trials that report race/ethnicity, nonwhite enrollment has often been around 20–22% (Keegan *et al.,* 2023)

In contrast, analyses of lung cancer trials suggest minority participation rates historically have been lower, and may still lag behind incidence rates despite recent improvements (Pittell *et al.,* 2023)

Registry or EHR linked multicenter studies which span multiple cancer types offer important opportunities to measure disparities and have helped document inequities in participation, although they do not automatically correct them (Pittell *et al.,* 2023).

DISCUSSION

Participant Prevalence, Demographics, and RWD-Driven Strategies to Enhance Inclusive Oncology Trial Participation

Prevalence of Participant Representation in U.S. Oncology Trials

Across the 51 included reviews of U.S. oncology clinical trials, racial and ethnic minority groups remain consistently underrepresented. Multiple analyses show that Black and Hispanic/Latino patients' enrollment in oncology trials (table 2) are substantially lower than would be expected based on their share of the national cancer burden. For example, a 2023 EHR-based cohort study of more than 50,000 patients found that Black and Latino patients were significantly less likely to participate in trials compared with White patients (Pittell *et al.,* 2023). A 2024 systematic review of Phase 2/3 oncology trials similarly reported that Black patients had a median representation quotient of 0.42, which meant their oncology trial participation was less than half of what would be predicted from cancer incidence, while American Indian/Alaska Native and Native Hawaiian/Pacific Islander participants were rarely represented or not reported at all (Racadio *et al.,* 2024). These findings align with long-standing evidence that trial enrollment continues to fall short of reflecting the true demographic diversity of the U.S. cancer population (Ramirez & Chalela, 2022).

Although women constitute most participants in breast cancer–specific studies, their enrolment in many multi-tumor oncology trial cohorts remain modestly underrepresented (Perera *et al.,* 2023)

Again, age-related disparities in oncology trial are well documented. Research by Sedrak *et al.,* (2022) showed that adults aged ≥70 years even though account for a large share of cancer cases, are substantially underrepresented in contemporary oncology trials, a gap attributed in part to restrictive eligibility criteria such as tight laboratory cutoffs, ECOG performance-status limits, and comorbidity exclusions. Real-world-data modelling and eligibility-relaxation analyses show that modernizing enrolment criteria can markedly increase the pool of potentially eligible older patients (Liu *et al.,* 2021)

Geographic inequities are also evident. According to Seidler *et al.,* (2014), clinical trial sites are highly clustered in urban academic centers, and many rural and medically underserved regions have limited local trial access patterns that reduce opportunities for these populations to enroll. Collectively, these findings indicate that structural (eligibility and site-selection) and geographic barriers continue to drive underrepresentation of priority populations in U.S. oncology research (Spira *et al.,* 2021)

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Table 2. Demographic Prevalence in U.S. Oncology Trials

Group	Prevalence in U.S. Cancer Population (%)	Prevalence in Oncology Trials (%)	In-Text Citations
Black/African American	12–13% of U.S. cancer cases	8% across modern oncology trials	(Pittell *et al.,* 2023 ; Loree *et al.,* 2019)
Hispanic/Latino	18–19% of U.S. cancer cases	6–7% in trials	(Ramirez & Chalela, 2022 ; Loree *et al.,* 2019)
Asian	5–6% of U.S. cancer cases	3–5% in trials	(Loree *et al.,* 2019)
American Indian/Alaska Native (AI/AN)	0.5–1% of U.S. cancer cases	<1% in trials	(Racadio *et al.,* 2024)
Older Adults (≥70)	40–50% of cancer diagnoses	20–25% in trials	(Sedrak *et al.,* 2022)

Methodological and Ethical Considerations

In addition to data completeness issues, observational analyses are inherently susceptible to confounding and bias. For example, studies of specific cohorts, such as the lung cancer population examined by Ayers *et al.,* (2021), often face selection bias and the influence of unmeasured confounders. These factors can threaten the internal validity of findings and limit their generalizability to broader populations. Addressing these methodological vulnerabilities requires sophisticated analytic strategies and transparent reporting to mitigate bias and enhance the credibility of results.

Furthermore, ethical governance and equity issues are paramount in the use of RWD. Forrester *et al.,* (2024) emphasize that embedding health equity principles necessitates the integration of social determinants of health data, meaningful engagement with patients and stakeholders, and the design of studies that are fair and inclusive in practice. Despite this imperative, the adoption of such principles remains limited, indicating a need for broader systemic commitment to equity-focused frameworks. Ultimately, tackling these methodological and ethical dimensions is essential to harness the full potential of RWD in oncology research and to ensure that research outcomes contribute to reducing disparities in clinical trial participation and care delivery.

Summary of Findings and Recommendations for Future Research

Our systematic review indicates that the published literature on using RWD to actively intervene and improve equity in oncology trial participation is very limited. Most articles are conceptual, methodological, or observational. Key uses of RWD in this context include: Simulating modifications to eligibility criteria (Royce *et al.,* 2023), developing ethical frameworks and health-equity principles (Forrester *et al.,* 2024), documenting existing disparities (Pittell *et al.,* 2023), emulating trial designs (Guadamuz *et al.,* 2024), analyzing clinical outcomes across racial groups in real-world settings (Ayers *et al.,* 2021)

However, no published randomized or quasi-experimental trial has tested whether RWD-informed interventions (e.g., RWD-based site selection, recruitment alerts, decentralized trial enrollment) improve representation outcomes (like equalized enrollment or retention).

Barriers, Limitations, and Ethical Considerations

RWD often lacks standardized, complete capture of race, ethnicity, socioeconomic status, and social determinants of health. Missing or inconsistent sociodemographic fields undermine the ability to identify underrepresented patients accurately and to measure representativeness improvements (Liu & Panagiotakos, 2022).

Using electronic health records (EHRs) and claims for direct outreach raises privacy concerns and requires careful governance, transparent patient communication, and alignment with HIPAA and institutional review board (IRB) expectations. Outreach must preserve patient autonomy and avoid any perception of coercion; involving community stakeholders in outreach design mitigates harm (Morse *et al.,* 2023)

RWD can flag inequities but cannot by themselves fix structural barriers such as transportation, lack of paid leave, language discordance, medical mistrust rooted in historical injustices, that limit trial participation. Multi-level interventions financial support, navigation, culturally congruent staff must be layered on top of real-world evidence (RWD)-enabled identification to convert potential eligibility into enrollment (Alarcón *et al.,* 2025)

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To enable future meta-analytic synthesis and truly measure the impact of RWD on equity in oncology trials, the field should: Standardize equity reporting: Require sponsors and investigators to report enrollment, retention, and outcomes by race/ethnicity, age, socioeconomic status, and geography, especially in RWD-informed trial designs. Improve data infrastructure: Encourage better capture of demographic and social-determinant of health variables in EHRs / registries to support accurate simulations and equity assessments. Ethical frameworks & governance: Adopt health-equity principles (e.g., Forrester *et al.*, 2024) widely in RWD based- studies, ensuring community engagement, fairness, and transparency.

CONCLUSION

This systematic review shows that while the concept of using RWD to improve equity in oncology trials is compelling and increasingly supported in policy and methodological discourse, there is a striking lack of empirical intervention studies. Without prospective, quantitative evaluations, we cannot yet quantify the effect of RWD strategies (e.g., eligibility simulation, site targeting, decentralized models) on improving the representation of underserved populations in trials.

To bridge this gap, future work must move beyond theory into empirical implementation, rigorous evaluation, and transparent reporting of equity outcomes. Only then will it be possible to perform true meta-analysis and derive robust, generalizable conclusions.

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