Geographic disparity in the distribution of cancer clinical trials in the United States and the associated factors

Ningzhou Gu, BS; Zizi Elsisi, BPharm, MS; Ryan Suk, MS, PhD; Meng Li, ScM, PhD

Plain language summary

Studies of new cancer treatments are located very unevenly in the United States with less than half of the country having any phase 1-3 cancer study between 2008 and 2022. Areas that are rural, poor, with less educated people, and fewer cancer doctors are less likely to have these studies. This may be problematic for patients who live in these areas to join studies of potentially life-saving cancer medicines.

Implications for managed care pharmacy

Lack of local availability of cancer trials in disadvantaged areas limits the representativeness of trial population and generalizability of trial results and may later hinder the adoption of new cancer treatments in disadvantaged populations, leading to disparity in health outcomes. Lack of representation of underserved populations in clinical trials creates uncertainty in treatment efficacy in those patients, posing a challenge to value-based formulary decisions.

Author affiliations

Department of Industrial Engineering and Operations Research (IEOR), Columbia University, New York City, NY (Gu); The Comparative Health Outcomes, Policy, and Economics (CHOICE) Institute, School of Pharmacy, University of Washington, Seattle (Elsisi); Department of Pharmaceutical Outcomes and Policy, College of Pharmacy, University of Florida, Gainesville (Suk); Center for the Evaluation of Value and Risk in Health, Institute for Clinical Research and Health Policy Studies, Tufts Medical Center, Boston, MA (Li).

Gu and Elsisi served as co-first authors and contributed equally to the work.

AUTHOR CORRESPONDENCE:
Meng Li, 1.443.831.8152;
meng.li@tuftsmedicine.org, @drmengli

J Manag Care Spec Pharm.
2024;30(4):376-85

ABSTRACT

BACKGROUND: Little is known regarding the geographic disparity in the distribution of phase 1-3 clinical trials of new cancer treatments in the US and the associated factors.

OBJECTIVE: To examine county-level variation in the number of phase 1-3 cancer clinical trials and the associations between county characteristics and having phase 1-3 cancer clinical trials.

METHODS: We identified phase 1-3 cancer clinical trials started in the US between January 2008 and December 2022 from the Aggregate Analysis of ClinicalTrials.gov database. We analyzed the distribution of phase 1-3 cancer clinical trials at the county level. Using a mixed-effects regression with states as random intercepts, we estimated the associations between a county's median age, median household income, percentage of population from racial and ethnic minority groups, proportion of population aged 25 years or older with an educational attainment of bachelor's degree or higher, rurality, cancer incidence rate, and number of medical oncologists per population with having any phase 1-3 cancer clinical trial in a county.

RESULTS: After excluding trials that were suspended, terminated, and withdrawn, a total of 14,977 phase 1-3 cancer clinical trials started in the United States between January 2008 and December 2022 were included in the primary analysis. Only 1,333 out of 3,143 counties (42.4%) had 1 or more trial during this period. Counties that were rural, with lower median household income, a less educated population, fewer medical oncologists per population, and lower cancer incidence rates demonstrated a significantly lower likelihood of having phase 1-3 cancer clinical trials.

CONCLUSIONS: Our study revealed substantial geographic disparities in the distribution of phase 1-3 cancer clinical trials. Limited trial availability in low-income, low-education, low-oncologist, and rural areas can be a significant barrier to patient participation, potentially hindering adoption and worsening outcomes in disadvantaged populations.

Cancer is a significant global public health concern and is the second leading cause of death in the United States.[1] Clinical trials are not only instrumental in generating crucial data on the efficacy of new treatments—for patients with late-stage cancer who have exhausted all other available therapies—clinical trials may also serve as vital treatment options.[2,3] Over the past decade, the number of clinical trials in the United States has shown an upward trend, and there has been a rise in the approval of anticancer drugs.[4,5]

Although significant advancements have been made in cancer clinical trial development, disparities in access to these trials persist. For example, the vast majority of prior research has found that cancer clinical trials enrolled a disproportionately low percentage of racial and ethnic minority patients.[6-12] A recent study by Abbas et al revealed that Black patients with gastrointestinal cancer were 28% less likely to participate in a cancer clinical trial compared with White patients. This disparity further widened when comparing high-income Black patients with high-income White patients, with the former group exhibiting a 33% lower likelihood of participation.[7] In addition to minority race and ethnicity, advanced age[13-15] and lower socioeconomic status[16,17] were also found to be associated with lower participation in clinical trials in previous research.

Underlying the lower participation in clinical trials among disadvantage populations is the deep-seated skepticism toward academic research and the medical establishment,[18,19] which can be traced back to medical research misconduct in history, such as the Tuskegee syphilis experiment.[20] Furthermore, disadvantaged patients may face greater structural barriers for participating in clinical research, such as lack of availability of clinical trials near where they live. The successful conduct and oversight of clinical trials requires substantial investments in health care facilities and personnel, which can be particularly challenging in disadvantaged neighborhoods.[21,22] Furthermore, the 2010 Institute of Medicine report highlighted a concerning trend in which clinical trial sites were often selected based on the locations of investigators rather than the needs of the target patients.[23] This investigator-centric approach to site selection may also create challenges for patients who live far away from trial principal investigators to participate in these clinical trials. A 2015 study found that approximately half of American patients with metastatic breast, prostate, colorectal, and nonsmall cell lung cancer would need to drive more than 60 minutes one way to access a clinical trial site.[24] This long distance to a clinical trial site can create significant burden for both patients and their caregivers.

Local availability of clinical trials is critical to ensuring equitable participation by patients from diverse backgrounds. Therefore, there is a pressing need to understand the geographic disparity in the distribution of cancer clinical trials and factors associated with local availability of cancer trials to inform strategies for site selection to facilitate greater and more equitable participation in clinical trials. This is especially relevant today because the Food and Drug Omnibus Reform Act was passed in 2022, mandating increased diversity in clinical trials.[25]

With this objective in mind, our study pursued 2 specific aims. First, we aimed to characterize geographic disparity in the distribution of cancer clinical trials in the United States. Second, we aimed to assess whether county-level characteristics, including the county population's median age, education level, household income level, proportion of population from racial and ethnic minority groups, rurality, cancer incidence rate, and health care resources (ie, number of medical oncologists per population), were associated with having cancer clinical trials in a county.

Methods

DATA AND VARIABLES

We identified all phase 1-3 cancer clinical trials registered between January 2008 and December 2022 from the Aggregate Analysis of ClinicalTrials.gov (AACT) database,[26] using medical terms "Cancer," "Neoplasm," "Carcinoma," "Tumor," "Leukemia," and "Lymphoma." The AACT is a publicly available relational database that contains all information (protocol and result data elements) on every study registered in ClinicalTrials.gov.[27] The Food and Drug Administration Amendments Act of 2007 mandated registration of studies that were controlled clinical investigations (other than phase 1 investigations) of any US Food and Drug Administration (FDA)–regulated drug or biological product for any disease or condition, as well as certain studies of FDA-regulated medical devices, excluding small clinical trials to determine feasibility and certain clinical trials to test prototype devices.[28] We extracted information on cancer types, registration year, start year, study phase, sponsorship, zip codes of each clinical trial's locations, and trial status from AACT. We defined sponsorship based on the lead sponsor and the presence of the following collaborators: industry only, federal agencies (including the National Institutes of Health, the FDA, and the Centers for Disease Control and Prevention) only, other groups (universities, individual sponsors, and community-based organizations) only, or more than 1 sponsor. We used the National Clinical Trial (NCT) numbers to identify unique trials. The 2010 United States Postal Service ZIP Code Crosswalk file was used to map zip codes to counties.[29] It is important to note

that a trial with a unique NCT number may have multiple sites within the same county, and we treated them as 1 unique trial for that county in this study.

We used the Agency for Healthcare Research and Quality Social Determinants of Health Database in the year 2010 for county-level characteristics.[30] County-level characteristics in this study included median age, median household income, percentage of population from minority racial and ethnic groups, and proportion of population 25 years or older with an educational attainment of bachelor's degree or higher. We used the 2013 Rural-Urban Continuum Codes to categorize counties into rural vs nonrural.[31] The 2013 Rural-Urban Continuum Codes segment US counties into 9 distinct categories based on criteria such as metropolitan status, population size, and degree of urbanization. Specifically, codes 8 and 9 are designated for completely rural, nonmetropolitan counties, whereas codes 1 to 7 are used to identify various levels of urban counties. We obtained the number of medical oncologists per 100,000 persons in each county from a previous study.[32] In this study, physicians who self-reported as providing oncologic care were identified using the health care provider taxonomy code in the National Provider Identifier data, and these figures were then aggregated on a county level.[32] County-level age-adjusted cancer incidence data were taken directly from State Cancer Profile.[33] The incidence data were the average of the latest 5 years (2018-2023). Because all data sources for this study were aggregated at a county level and were publicly available, our study was exempted by the institutional review board at University of Texas MD Anderson Cancer Center.

STATISTICAL ANALYSIS

We first examined the temporal trend of unique cancer clinical trials started in the United States between 2008 and 2022. We then compared county-level characteristics between counties that had at least 1 phase 1-3 clinical trial to those who did not have any. We used two-sided t-tests to test for significant differences in continuous variables and two-sided chi-square tests for categorical variables. We also counted the number of unique phase 1-3 cancer trials in a county and plotted a map.

We ran regression analyses to determine if having at least 1 phase 1-3 cancer clinical trial in a county between 2008 and 2022 was associated with the county's population age, household income, education level, size of minority population, rurality, and density of medical oncologists. Our data were hierarchical in nature with counties nested in states, and to account for this structure, we ran a generalized linear mixed model, treating state as a random effect. In hierarchical models, random effects are variables that are not the focus of a study but may impact the outcome and therefore need to be included. Fixed effects are key predictors of the study, and in our study, are the county-level characteristics. In the primary analysis, we excluded clinical trials that were suspended, withdrawn, or terminated. In sensitivity analysis, we included all trials that started between 2008 and 2022. All tests were at the 5% significance level and the analyses were conducted using RStudio Version 4.3.1. using packages "dplyr," "ggplot2," "usmap," and "lme4."[34-38]

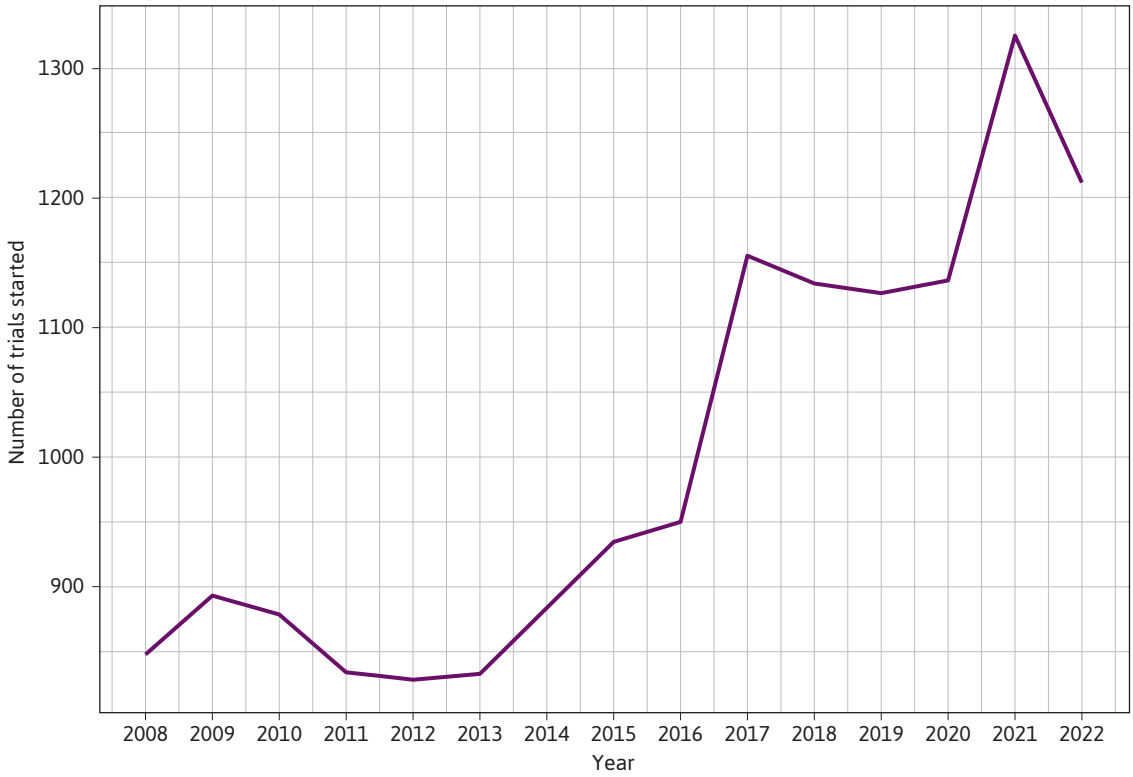
Results

Between January 2008 and December 2022, there were a total of 19,097 unique phase 1-3 cancer clinical trials that started in the United States, 4,120 of which were suspended, terminated, or withdrawn, leaving 14,977 active or completed trials. Overall, there has been an increase in the number of trials annually over the last 15 years, from 848 started in 2008 to 1,214 in 2022 (Figure 1). Industry-sponsored trials accounted for roughly 30% of all phase 1-3 cancer trials, whereas trials sponsored by the National Institute of Health and other federal agencies accounted for less 10% and demonstrated a declining trend to just 4.6% in 2022 (Supplementary Figure 1, available in online article). Nearly half of trials had more than 1 type of sponsor (eg, industry, federal agency, university, community, etc).

Our descriptive analysis revealed significant geographic variation in the distribution of phase 1-3 cancer clinical trials across the nation. Less than half of the counties in the United States (n = 1,333, 42.4%) had 1 or more cancer clinical trial between 2008 and 2022. Figure 2 highlights the uneven distribution. Counties with a higher number of phase 1-3 cancer clinical trials were primarily in the Great Lakes Region and the Northeast, as well as in parts of California and Washington.

Table 1 summarizes and compares the characteristics of US counties with and without phase 1-3 cancer clinical trials between 2008 and 2022. Counties with cancer clinical trials had significantly lower median age (38.7 vs 40.7, $P < 0.001$), higher median household income ($47,561 vs $39,891, $P < 0.001$), and greater percentage of people 25 years or older with a bachelor's degree or higher (23.3% vs 15.9%, $P < 0.001$). These counties also had, on average, a significantly higher number of medical oncologists per 100,000 population (3.8 vs 0.4, $P < 0.001$) and higher mean age-adjusted cancer incidence per 100,000 population (456.7 vs 442.2, $P < 0.001$). Furthermore, counties with phase 1-3 cancer clinical trials were considerably less likely to be rural (6.0% vs 31.2%, $P < 0.001$). There was no statistically significant difference between counties in terms of mean percentage of population

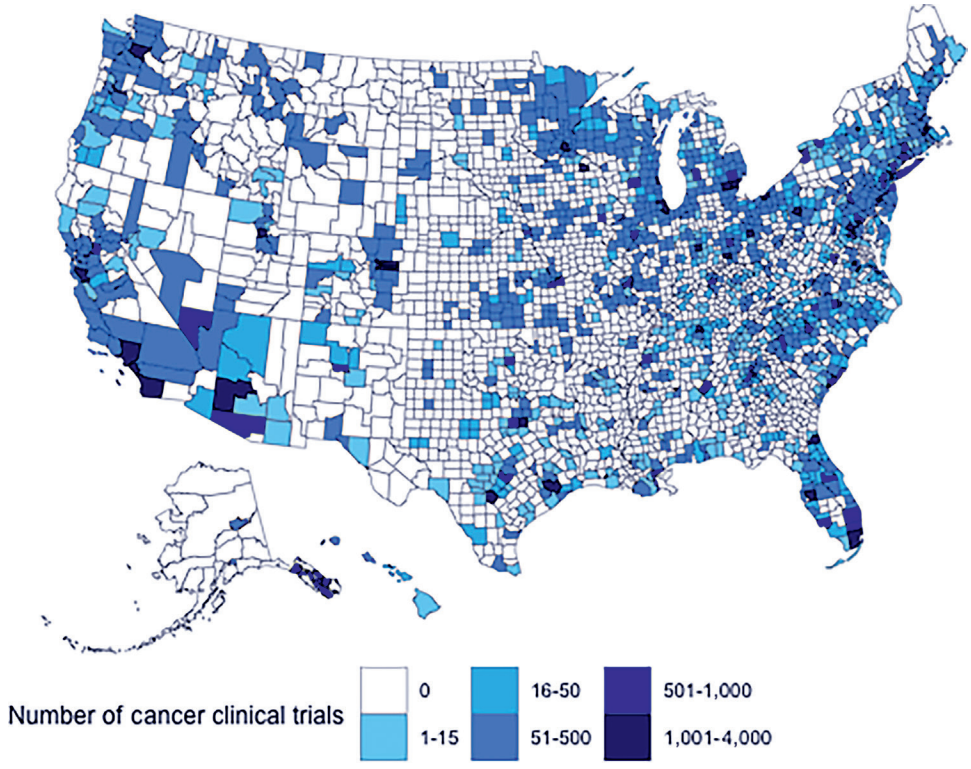
FIGURE 1 Number of Phase 1-3 Cancer Clinical Trials Started in the United States Over Time, Excluding Those That Were Withdrawn, Terminated, or Suspended



that are from racial and ethnic minority groups (16.6% vs 15.9%, $P = 0.25$). Our examination of county characteristics by clinical trial phase revealed generally consistent patterns across various phases. However, counties with early phase 1 trials had higher density of medical oncologists, higher educational level, and a smaller proportion of rural counties (Supplementary Table 1).

Our generalized linear mixed model with state random effect revealed significant associations between several factors and having phase 1-3 cancer clinical trials (Table 2). Our results indicated that the odds of having a cancer clinical trial were significantly higher in counties with higher median household income, with greater percentage of population with a bachelor's degree or higher, with greater number of medical oncologists per population, with higher cancer incidence, and are nonrural. Compared with counties in the lowest quintile of median household income, the odds ratio of having phase 1-3 cancer clinical trials in counties in the second, third, fourth, and the highest quantile were 1.84 (95% CI = 1.29-2.64, $P = 0.001$), 2.30 (95% CI = 1.56-3.40, $P < 0.001$), 3.18 (95% CI = 2.09-4.84, $P < 0.001$), and 5.08 (95% CI = 3.19-8.07, $P < 0.001$), respectively. Compared with counties in the lowest quintile of percentage of population 25 years and older with a bachelor's degree or higher, the odds of having cancer clinical trials in the third, fourth, and fifth quintiles were 1.51 (95% CI = 1.04-2.18, $P < 0.001$), 2.74 (95% CI = 1.84-4.09, $P < 0.001$), and 6.08 (95% CI = 3.81-9.71, $P < 0.001$), respectively. When compared with counties in the lowest quintile of cancer incidence rates, the odds of having a cancer trial in counties in the second, third, fourth, and the highest quintile were 1.78 (95% CI = 1.24-2.58, $P = 0.002$), 1.72 (95% CI = 1.17-2.52), 2.43 (95% CI = 1.64-2.61), and 2.63 (95% CI = 1.74-3.97), respectively. The odds of having a cancer clinical trial also rose with number of medical oncologists per population; the odds ratio for each additional medical oncologist per 100,000 population was 1.41 (95% CI = 1.34-1.49, $P < 0.001$). Rural counties were significantly less likely to have phase 1-3 cancer clinical trials compared with nonrural counties, with an odds ratio of 0.56 (95% CI = 0.40-0.79, $P = 0.03$). Intraclass correlation was 19%, suggesting that approximately 19% of the county-level variability in the likelihood of having cancer clinical trials was attributable to differences between states.

FIGURE 2 Geographic Distribution of Phase 1-3 Cancer Clinical Trials Across US Counties From 2008 to 2022



Different sites of the same trials (same NCT) in the same county were counted as 1 in this map.

TABLE 1 Descriptive Summary of County Characteristics by Availability of Phase 1-3 Cancer Clinical Trials

	Counties with no trial (n = 1,810)	Counties with at least one trial (n = 1,333)	*P* value
Median age, mean (SD)	40.7 (5.0)	38.7 (4.6)	**<0.001**
Number of medical oncologists per 100,000 population, mean (SD)	0.40 (1.5)	3.8 (6.3)	**<0.001**
Median household income, mean (SD)	$39,890.5 (8,246.5)	$47,561.4 (11,909.4)	**<0.001**
Age-adjusted cancer incidence per 100,000 population, mean (SD)	4,42.2 (68.0)	456.7 (47.5)	**<0.001**
Percentage of population from racial and ethnic minority groups, mean (SD)	15.9 (18.2)	16.6 (14.6)	0.245
Percentage of population having bachelor's degree or higher, mean (SD)	15.9 (6.1)	23.3 (9.7)	**<0.001**
Rural, n (%)	564 (31.2)	80 (6.0)	**<0.001**
Region, n (%)			
Midwest	618 (58.6)	437 (41.4)	**<0.001**
Northeast	51 (23.5)	166 (76.5)	
South	865 (60.7)	558 (39.2)	
West	275 (61.4)	173 (38.6)	

In sensitivity analysis, when trials that were suspended, withdrawn, or terminated were included along with active and completed trials, results were robust (Table 3).

Discussion

We analyzed phase 1-3 cancer clinical trials started in the United States between January 2008 and December 2022 and found that less than half of US counties have ever had any phase 1-3 cancer clinical trial during this 15-year period. Our results also showed that nonrural counties, counties with higher cancer incidence rates, counties with more medical oncologists per population, counties with higher education level, and counties with higher household income were more likely to have cancer clinical trials.

There have been ongoing efforts from different stakeholders to improve diversity and inclusion in clinical trials. The 2022 Food and Drug Omnibus Reform Act legislation requires trial sponsors to submit a diversity plan for phase 3 or pivotal clinical studies.[25] In October 2023, the White House Office of Science and Technology Policy's Clinical Trials Readiness Initiative also aims to build a stronger and more diverse clinical trial infrastructure in the United States and make clinical trials "faster, more inclusive, simpler, and more efficient" across a wide range of communities and clinical settings.[39] Understanding the barriers to clinical trial participation is the first step to improving diversity of clinical trials' patient populations. Existing research has identified several factors that can influence clinical trial participation, which include individual patient's sex, age, race and ethnicity, socioeconomic status, and education level, as well as locations of clinical trial sites and infrastructure support.[7-18,24,40,41]

TABLE 2 Generalized Linear Mixed Model Assessing the Associations Between County-Level Characteristics and Odds of Having at Least 1 Cancer Clinical Trial Between 2008 and 2022 With State Random Effects, Excluding Trials That Were Suspended, Terminated, and Withdrawn

County-level characteristics	Odds ratio (95% CI)	*P* value
Median age, years		
Quintile 1 (<36.3)	Ref	Ref
Quintile 2 (36.3-38.9)	0.98 (0.70-1.38)	0.902
Quintile 3 (38.9-40.9)	0.77 (0.54-1.10)	0.147
Quintile 4 (40.9-43.6)	0.86 (0.59-1.27)	0.458
Quintile 5 (43.6-62.5)	0.67 (0.44-1.02)	0.059
Median household income		
Quintile 1 (<$34.998.0)	Ref	Ref
Quintile 2 ($34,998.0-$39,259.8)	1.84 (1.29-2.64)	**0.001**
Quintile 3 ($39,359.8-$43,503.0)	2.30 (1.56-3.40)	**<0.001**
Quintile 4 ($43,503.0-$49,691.6)	3.18 (2.09-4.84)	**<0.001**
Quintile 5 ($49,691.6-$119,075.0)	5.08 (3.19-8.07)	**<0.001**
Percentage of population with bachelor's degree or higher		
Quintile 1 (<19.58%)	Ref	Ref
Quintile 2 (19.58%-25.74%)	1.37 (0.97-1.93)	0.056
Quintile 3 (25.74%-30.06%)	1.51 (1.04-2.18)	**<0.001**
Quintile 4 (30.06%-38.43%)	2.74 (1.84-4.09)	**<0.001**
Quintile 5 (38.43%-70.95%)	6.08 (3.81-9.71)	**0.003**
Number of medical oncologists per 100,000 population	1.41 (1.34-1.49)	**<0.001**
Age-adjusted cancer incidence of per 100,000 population		
Quintile 1 (<410.5)	Ref	Ref
Quintile 2 (410.5-438.7)	1.78 (1.24-2.58)	**0.002**
Quintile 3 (438.7-461.1)	1.72 (1.17-2.52)	**0.006**
Quintile 4 (461.1-482.5)	2.43 (1.64-3.61)	**<0.001**
Quintile 5 (482.5-1,237.4)	2.63 (1.74-3.97)	**<0.001**
Percentage of population from racial and ethnic minority groups		
Quintile 1 (<7.03%)	Ref	Ref
Quintile 2 (7.03%-14.65%)	1.12 (0.79-1.58)	0.515
Quintile 3 (14.65%-25.03%)	1.37 (0.94-2.00)	0.097
Quintile 4 (25.03%-38.57%)	1.49 (0.96-2.30)	0.074
Quintile 5 (38.57%-96.67%)	1.37 (0.97-1.93)	0.212
Rural	0.59 (0.42-0.83)	**0.003**

Ref = reference category.

The results of our study added new evidence on the disparity in the distribution of cancer clinical trial sites across the nation and the characteristics of those pockets of "clinical trial deserts."

Lack of access to clinical trials of new cancer drugs may affect health

TABLE 3 Generalized Linear Mixed Model Assessing the Associations Between County-Level Characteristics and Odds of Having at Least 1 Cancer Clinical Trial Between 2008 and 2022 With State Random Effects, All Trials

County-level characteristics	Odds ratio (95% CI)	*P* value
Median age, years		
Quintile 1 (<36.3)	Ref	Ref
Quintile 2 (36.3-38.9)	0.93 (0.66-1.31)	0.688
Quintile 3 (38.9-40.9)	0.76 (0.53-1.08)	0.129
Quintile 4 (40.9-43.6)	0.85 (0.58-1.26)	0.424
Quintile 5 (43.6-62.5)	0.69 (0.46-1.06)	0.090
Median household income		
Quintile 1 (<$34,998.0)	Ref	Ref
Quintile 2 ($34,998.0-$39,259.8)	1.72 (1.21-2.46)	**0.003**
Quintile 3 ($39,359.8-$43,503.0)	2.13 (1.45-3.14)	**<0.001**
Quintile 4 ($43,503.0-$49,691.6)	2.98 (1.97-4.53)	**<0.001**
Quintile 5 ($49,691.6-$119,075.0)	4.69 (2.95-7.44)	**<0.001**
Percentage of population with bachelor's degree or higher		
Quintile 1 (<19.58%)	Ref	Ref
Quintile 2 (19.58%-25.74%)	1.40 (0.99-1.97)	0.056
Quintile 3 (25.74%-30.06%)	1.61 (1.11-2.33)	**0.012**
Quintile 4 (30.06%-38.43%)	2.87 (1.93-4.28)	**<0.001**
Quintile 5 (38.43%-70.95%)	6.41 (4.01-10.24)	**<0.001**
Number of medical oncologists per 100,000 population	1.42 (1.34-1.50)	**<0.001**
Age-adjusted incidence of cancer per 100,000 population		
Quintile 1 (<410.5)	Ref	Ref
Quintile 2 (410.5-438.7)	1.73 (1.20-2.49)	**0.003**
Quintile 3 (438.7-461.1)	1.70 (1.16-2.50)	**0.007**
Quintile 4 (461.1-482.5)	2.31 (1.56-3.42)	**<0.001**
Quintile 5 (482.5-1,237.4)	2.55 (1.69-3.85)	**<0.001**
Percentage of population from racial and ethnic minority groups		
Quintile 1 (<7.03%)	Ref	Ref
Quintile 2 (7.03%-14.65%)	1.09 (0.77-1.54)	0.621
Quintile 3 (14.65%-25.03%)	1.35 (0.93-1.97)	0.112
Quintile 4 (25.03%-8.57%)	1.49 (0.96-2.30)	0.074
Quintile 5 (38.57%-96.67%)	1.31 (0.80-2.14)	0.284
Rural	0.56 (0.40-0.79)	**0.001**

Ref = reference category.

equity in multiple ways. First, clinical trials of experimental treatments are an important treatment option for many patients with cancer, especially those who have failed all available therapies.[3] Several studies have shown that enrollment in clinical trials may be associated with improved survival for some cancer types.[42-46] Even in trials that did not meet their endpoints and for those randomized to the control arm, trial participation may still be beneficial because of strict adherence to treatment and supportive care required by study protocols. Although many trials may fail because of a flawed study design, an inappropriate statistical endpoint, or insufficient enrollment, the experimental treatment might still be efficacious.[47] Research has found that nearly 50% of phase 3 trials of novel therapeutics failed because of reasons other than inadequate efficacy.[48]

In addition to directly benefiting the participants, clinical trials can also provide critical, early information on the experimental new drugs, and such early exposure may lead to faster adoption at the trial sites after the new drugs receive approval.[49] The decision to adopt by the trial principal investigators—the influential members of the system—may then be communicated to other providers nearby, who will then follow the lead, according to the classic diffusion of innovations theory.[50] This may lead to geographic disparity in adoption of new cancer medicines by proximity to their clinical trials, which may lead to disparity in health outcomes of patients. In fact, 1 recent study that examined the adoption of 21 newly introduced cancer medicines found that patients in the vicinity of the leading trial investigators have an initial 36% higher probability of being treated with these new drugs, with the rates evening out across regions after 4 years.[51] The slower adoption of effective new medicines in regions where there is a lack of clinical trials may further worsen health disparity. Finally, the low enrollment of disadvantaged and underserved patients due to the lack of accessibility of clinical trials in their neighborhood can result in the lack of representativeness of the trial population. This may increase the uncertainty of

efficacy in those patient subgroups, which in turn may result in slower and lower adoption, worse outcomes, and greater disparity in health.

To increase diversity in clinical trial enrollment, our results also pointed out possible paths forward. Creating a network of clinical trial sites in underserved communities requires establishing long-term relationships and investing in the community. This includes moving clinical trials beyond academic medical centers and establishing research sites in locations where potential participants receive care, such as community health centers and rural health centers. It also includes developing a diverse pool of investigators and staff and raising awareness of available research opportunities among health care providers in community settings. Moreover, sustainable community building efforts also requires engaging in conversations about the importance of volunteer participation in trials, commitment to transparent engagement throughout the process, and seeking input from community members.

LIMITATIONS

This study has several limitations. First, we cannot draw any causal links between the county-level characteristics and having cancer clinical trials. Therefore, the results of our analysis should be interpreted as associations. Second, our analysis did not account for the varying sizes of counties and the distance that patients would have to travel to participate in a clinical trial if there is no trial in their county of residence. Therefore, our results should not be interpreted as measuring the accessibility to cancer clinical trials by patients. Third, there are other factors, such as presence of academic medical centers and leading investigators in the area, that may be associated with having cancer clinical trials, but we were not able to account for them in our analysis. As a result, there may be some residual confounding. Finally, we examined county-level factors that were associated with having any cancer clinical trial between 2008 and 2022. We did not consider the number of unique trials, the number of trial sites, or the total enrollment of patients in a county.

Conclusions

There is substantial geographic disparity in the distribution of phase 1-3 clinical trials. Limited availability of cancer clinical trials in low-income, low-education, and rural areas with few medical oncologists presents a barrier for patients in those areas to participate in clinical trials, limiting the generalizability of the trial finding, as well as potentially contributing to the worse outcomes of patients with cancer in those disadvantaged neighborhoods.

REFERENCES

1. American Cancer Society. 2022 cancer facts & figures cancer | Cancer death rate drops. Accessed May 2, 2023. https://www.cancer.org/latest-news/facts-and-figures-2022.html

2. National Cancer Institute. Choices for care with advanced cancer - NCI. Accessed November 12, 2023. https://www.cancer.gov/about-cancer/advanced-cancer/care-choices

3. Novitzke JM. The significance of clinical trials. *J Vasc Interv Neurol*. 2008;1(1):31.

4. Olivier T, Haslam A, Prasad V. Anticancer drugs approved by the US Food and Drug Administration from 2009 to 2020 according to their mechanism of action. *JAMA Netw Open*. 2021;4(12):e2138793. doi:10.1001/jamanetworkopen.2021.38793

5. IQVIA. Global oncology trends. 2022. Accessed May 2, 2023. https://www.iqvia.com/insights/the-iqvia-institute/reports/global-oncology-trends-2022

6. Habr D, Ferdinand R. Addressing racial/ethnic disparities in cancer clinical trials: Everyone has a role to play. *Cancer*. 2021;127(18):3282-9. doi:10.1002/cncr.33600

7. Abbas A, Diaz A, Obeng-Gyasi S, et al. Disparity in clinical trial participation among patients with gastrointestinal cancer. *J Am Coll Surg*. 2022;234(4):589-98. doi:10.1097/XCS.0000000000000129

8. Loree JM, Anand S, Dasari A, et al. Disparity of race reporting and representation in clinical trials leading to cancer drug approvals from 2008 to 2018. *JAMA Oncol*. 2019;5(10):e191870. doi:10.1001/jamaoncol.2019.1870

9. Kwiatkowski K, Coe K, Bailar JC, Swanson GM. Inclusion of minorities and women in cancer clinical trials, a decade later: Have we improved? *Cancer*. 2013;119(16):2956-63. doi:10.1002/cncr.28168

10. Balakrishnan AS, Palmer NR, Fergus KB, et al. Minority recruitment trends in phase III prostate cancer clinical trials (2003 to 2014): Progress and critical areas for improvement. *J Urol*. 2019;201(2):259-67. doi:10.1016/j.juro.2018.09.029

11. Awidi M, Al Hadidi S. Participation of Black Americans in cancer clinical trials: Current challenges and proposed solutions. *JCO Oncol Pract*. 2021;17(5):265-71. doi:10.1200/OP.21.00001

12. Pittell H, Calip GS, Pierre A, et al. Racial and ethnic inequities in US Oncology Clinical Trial participation from 2017 to 2022. *JAMA Netw Open*. 2023;6(7):e2322515. doi:10.1001/jamanetworkopen.2023.22515

13. Ludmir EB, Mainwaring W, Lin TA, et al. Factors associated with age disparities among cancer clinical trial participants. *JAMA Oncol*. 2019;5(12):1769-73. doi:10.1001/jamaoncol.2019.2055

14. Sedrak MS, Freedman RA, Cohen HJ, et al; Cancer and Aging Research Group (CARG). Older adult participation in cancer clinical trials: A systematic review of barriers and interventions. *CA Cancer J Clin*. 2021;71(1):78-92. doi:10.3322/caac.21638

15. Lau SW, Huang Y, Hsieh J, et al. Participation of older adults in clinical trials for new drug applications and biologics license applications from 2010 through 2019. *JAMA Netw Open*. 2022;5(10):e2236149. doi:10.1001/jamanetworkopen.2022.36149

16. Mohd Noor A, Sarker D, Vizor S, et al. Effect of patient socioeconomic status on access to early-phase cancer trials. *J Clin Oncol*. 2013;31(2):224-30. doi:10.1200/JCO.2012.45.0999

17. Sharrocks K, Spicer J, Camidge DR, Papa S. The impact of socioeconomic status on access to cancer clinical trials. *Br J Cancer*. 2014;111(9):1684-7. doi:10.1038/bjc.2014.108

18. Corbie-Smith G, Thomas SB, St George DM. Distrust, race, and research. *Arch Intern Med*. 2002;162(21):2458-63. doi:10.1001/archinte.162.21.2458

19. Scharff DP, Mathews KJ, Jackson P, Hoffsuemmer J, Martin E, Edwards D. More than Tuskegee: Understanding mistrust about research participation. *J Health Care Poor Underserved*. 2010;21(3):879-97. doi:10.1353/hpu.0.0323

20. Alsan M, Wanamaker M. Tuskegee and the health of Black men. *Q J Econ*. 2018;133(1):407-55. doi:10.1093/qje/qjx029

21. Chan KS, Gaskin DJ, McCleary RR, Thorpe RJ. Availability of health care provider offices and facilities in minority and integrated communities in the U.S. *J Health Care Poor Underserved*. 2019;30(3):986-1000. doi:10.1353/hpu.2019.0069

22. Freeman Anderson K. Racial residential segregation and the distribution of health-related organizations in urban neighborhoods. *Soc Probl*. 2017;64(2):256-76. doi:10.1093/socpro/spw058

23. Institute of Medicine (US) Forum on Drug Discovery, Development, and Translation. *Transforming clinical Research in the United States: Challenges and opportunities: Workshop summary*. National Academies Press (US); 2010. Accessed May 2, 2023. http://www.ncbi.nlm.nih.gov/books/NBK50892/

24. Galsky MD, Stensland KD, McBride RB, et al. Geographic accessibility to clinical trials for advanced cancer in the United States. *JAMA Intern Med*. 2015;175(2):293-5. doi:10.1001/jamainternmed.2014.6300

25. Food and Drug Omnibus Reform Act, as included in the Consolidated Appropriations Act of 2023, Pub. Law 117-328. Accessed December 1, 2023. https://www.congress.gov/117/bills/hr2617/BILLS-117hr2617enr.pdf

26. Clinical Trials Transformation Initiative. AACT Database | Accessed May 2, 2023. https://aact.ctti-clinicaltrials.org/

27. National Library of Medicine. ClinicalTrials.gov. Accessed May 3, 2023. https://clinicaltrials.gov/

28. U.S. Food and Drug Administration (FDA). FDA's role: ClinicalTrials.gov information. Accessed November 13, 2023. https://www.fda.gov/science-research/clinical-trials-and-human-subject-protection/fdas-role-clinicaltrialsgov-information

29. Office of Policy Development and Research. HUD USPS ZIP code crosswalk files. Accessed November 13, 2023. https://www.huduser.gov/portal/datasets/usps_crosswalk.html

30. Health Resources & Services Administration. Area health resources files. Accessed May 2, 2023. https://data.hrsa.gov/topics/health-workforce/ahrf

31. USDA ERS. Rural-urban continuum codes. Accessed June 16, 2023. https://www.ers.usda.gov/data-products/rural-urban-continuum-codes/

32. Shih YT, Kim B, Halpern MT. State of physician and pharmacist oncology workforce in the United States in 2019. *JCO Oncol Pract*. 2021;17(1):e1-10. doi:10.1200/OP.20.00600

33. National Cancer Institute. State cancer profiles. Accessed May 2, 2023. https://statecancerprofiles.cancer.gov/

34. R Core Team. (2023). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. https://www.R-project.org/

35. Lorenzo PD. usmap: US Maps including Alaska and Hawaii. Published online October 21, 2023. Accessed November 13, 2023. https://cran.r-project.org/web/packages/usmap/index.html

36. Bates D, Mächler M, Bolker B, Walker S. Fitting linear mixed-effects models using lme4. *J Stat Softw*. 2015;67(1):1-48. doi:10.18637/jss.v067.i01

37. Wickham H. *Create elegant data visualisations using the grammar of graphics*. Springer-Verlag New York; 2016. Accessed November 17, 2023. https://ggplot2.tidyverse.org/

38. Wickham H, François R, Henry L, et al. dplyr: A grammar of data manipulation. Accessed November 17, 2023. https://cran.r-project.org/web/packages/dplyr/index.html

39. A stronger clinical trial infrastructure for better health outcomes | OSTP. The White House. Accessed November 21, 2023. https://www.whitehouse.gov/ostp/news-updates/2023/10/26/a-stronger-clinical-trial-infrastructure-for-better-health-outcomes/

40. Unger JM, Vaidya R, Hershman DL, Minasian LM, Fleury ME. Systematic review and meta-analysis of the magnitude of structural, clinical, and physician and patient barriers to cancer clinical trial participation. *J Natl Cancer Inst*. 2019;111(3):245-55. doi:10.1093/jnci/djy221

41. Duma N, Vera Aguilera J, Paludo J, et al. Representation of minorities and women in oncology clinical trials: Review of the past 14 years. *J Oncol Pract*. 2018;14(1):e1-10. doi:10.1200/JOP.2017.025288

42. Braunholtz DA, Edwards SJ, Lilford RJ. Are randomized clinical trials good for us (in the short term)? Evidence for a "trial effect". *J Clin Epidemiol*. 2001;54(3):217-24. doi:10.1016/S0895-4356(00)00305-X

43. Shahar T, Nossek E, Steinberg DM, et al. The impact of enrollment in clinical trials on survival of patients with glioblastoma. *J Clin Neurosci*. 2012;19(11):1530-4. doi:10.1016/j.jocn.2012.04.005

44. Field KM, Drummond KJ, Yilmaz M, et al. Clinical trial participation and outcome for patients with glioblastoma: Multivariate analysis from a comprehensive dataset. *J Clin Neurosci*. 2013;20(6):783-9. doi:10.1016/j.jocn.2012.09.013

45. Engelbak Nielsen Z, Eriksson S, Schram Harsløf LB, et al. Are cancer patients better off if they participate in clinical trials? A mixed methods study. *BMC Cancer*. 2020;20(1):401. doi:10.1186/s12885-020-06916-z

46. Bleyer A, Montello M, Budd T, Saxman S. National survival trends of young adults with sarcoma: Lack of progress is associated with lack of clinical trial participation. *Cancer*. 2005;103(9):1891-7. doi:10.1002/cncr.20995

47. Fogel DB. Factors associated with clinical trials that fail and opportunities for improving the likelihood of success: A review. *Contemp Clin Trials Commun*. 2018;11:156-64. doi:10.1016/j.conctc.2018.08.001

48. Hwang TJ, Carpenter D, Lauffenburger JC, Wang B, Franklin JM, Kesselheim AS. Failure of investigational drugs in late-stage clinical development and publication of trial results. *JAMA Intern Med*. 2016;176(12):1826-33. doi:10.1001/jamainternmed.2016.6008

49. Denig P, Haaijer-Ruskamp FM, Wesseling H, Versluis A. Impact of clinical trials on the adoption of new drugs within a university hospital. *Eur J Clin Pharmacol*. 1991;41(4):325-8. doi:10.1007/BF00314961

50. Dearing JW, Cox JG. Diffusion of innovations theory, principles, and practice. *Health Aff (Millwood)*. 2018;37(2):183-90. doi:10.1377/hlthaff.2017.1104

51. Agha L, Molitor D. The local influence of pioneer investigators on technology adoption: Evidence from new cancer drugs. *Rev Econ Stat*. 2018;100(1):29-44. doi:10.1162/REST_a_00670