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JNCI J Natl Cancer Inst (2022) 114(7): djac030

https://doi.org/10.1093/jnci/djac030
First published online February 11, 2022
Review

Rural–Urban Disparities in Cancer Outcomes: Opportunities for Future Research

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Abstract

Cancer care disparities among rural populations are increasingly documented and may be worsening, likely because of the impact of rurality on access to state-of-the-art cancer prevention, diagnosis, and treatment services, as well as higher rates of risk factors such as smoking and obesity. In 2018, the American Society of Clinical Oncology undertook an initiative to understand and address factors contributing to rural cancer care disparities. A key pillar of this initiative was to identify knowledge gaps and promote the research needed to understand the magnitude of difference in outcomes in rural vs nonrural settings, the drivers of those differences, and interventions to address them. The purpose of this review is to describe continued knowledge gaps and areas of priority research to address them. We conducted a comprehensive literature review by searching the PubMed (Medline), Embase, Web of Science, and Cochrane Library databases for studies published in English between 1971 and 2021 and restricted to primary reports from populations in the United States and abstracted data to synthesize current evidence and identify continued gaps in knowledge. Our review identified continuing gaps in the literature regarding the underlying causes of rural–urban disparities in cancer outcomes. Rapid advances in cancer care will worsen existing disparities in outcomes for rural patients without directed effort to understand and address barriers to high-quality care in these areas. Research should be prioritized to address ongoing knowledge gaps about the drivers of rurality-based disparities and preventative and corrective interventions.

REVIEW

According to the 2020 census, approximately 57 million Americans (roughly 17% of the population) live in rural areas. There is increasing evidence for disparities in cancer care among rural populations (1-4). Between 2004 and 2013, trends in annual age-adjusted death rates from cancer fell more slowly in rural areas, leading to a growing survival disparity relative to metropolitan residents, with annual percentage changes of −1.0% and −1.6% for rural vs metro populations, respectively, for all cancer sites (5). The mortality trend disparity is wider for lung cancer (−1.8% vs −2.8%), colorectal cancer (−1.6% vs −2.5%), and breast cancer (−1.0% vs −1.7%), 3 leading causes of cancer mortality. These rurality-associated disparities seem to be worsening (6), likely because of the impact of rurality on access to state-of-the-art cancer prevention, diagnosis, and treatment services, as well as higher rates of risk factors such as smoking and obesity (6). Rural populations tend to be older, have lower educational attainment, and lower median household income compared with nonrural residents (7). The prevalence of poor health, health-related unemployment, smoking, and physical inactivity is statistically significantly higher in rural compared with urban cancer survivors (8). Although closing certain access gaps (eg, to clinical trials) can narrow disparities between rural and nonrural cancer populations (8-12), widespread and equitable access to the entire continuum of cancer care for rural populations remains elusive.

To understand the factors contributing to rural cancer care disparities, the American Society of Clinical Oncology (ASCO) launched a rural cancer care initiative in 2018. As part of this initiative, ASCO conducted a comprehensive scan of the literature to identify existing gaps in the evidence base and inform future research initiatives. This review focused on synthesizing current knowledge of rurality-associated disparities in cancer care and outcomes; identifying the current known drivers of differences in outcomes based on residence; and characterizing

Received: May 10, 2021; **Revised:** July 27, 2021; **Accepted:** February 1, 2022

gaps in knowledge. We summarize the framework for rural–urban disparities in survival in Figure 1 and present the extant literature as well as the current gaps in knowledge below.

Methods

We conducted a comprehensive literature review to provide an overview of the best available evidence regarding rural–urban disparities in cancer outcomes.

Search Strategy for Published Studies

We searched the PubMed (Medline), Embase, Web of Science, and Cochrane Library databases for studies published in English between 1971 and 2021 and restricted to primary reports from populations in the United States. Searches were supplemented by retrieval of any articles meeting eligibility criteria that were cited in reference lists. The search was performed in September 2019 and updated in October 2021. We used the following key terms: "rural," "urban," "disparities," "cancer," and "outcomes" (see Box 1 for detailed search schema). We included observational studies or clinical trials, systematic reviews, and meta-analyses that focused on disparities in between rural and urban populations relating to survival, socioeconomic status, insurance coverage, health-care access, distance and transportation to oncology care, access to specialist care (medical, surgical, radiation oncology), screening, cancer stage at diagnosis, treatment quality, access to clinical trials, health literacy, health behaviors, comorbidities, and oncology infrastructure. We excluded editorial or opinion pieces, case reports, clinical series, and nonsystematic reviews, as well as articles that focused on non-US cohorts. Abstracts identified from searches were screened by 2 independent raters (SB and WL). Both independent raters reviewed full-text versions of the articles, and articles were retained if they met inclusion criteria. In instances where consensus was not achieved between the raters, SB made the final determination regarding inclusion. All data required to answer the study questions were published within the papers, so no contact with authors was necessary. The search identified 630 articles as of October 17, 2021 (201 from PubMed, 278 from Embase, 67 from Web of Science [dates limited to 1990-2021 because of constraints of the database], 25 from Cochrane, and 59 from other sources); we eliminated 128 duplicates. After title, abstract, and full-text assessment, 242 papers were included in this review (see Figure 2; Supplementary Tables 1-3). Over the past 50 years, 172 studies have included a comparative framework when examining rural–urban differences in cancer outcomes. Of these, 56 studies (32.6%) also examined racial differences in cancer outcomes and the rural–urban differences in cancer outcomes. Although reviewed articles varied somewhat in their quality, because of the overall paucity of evidence, we included any studies that were generally sound in their approach and methods.

Results

Results of evidence from our review delineating rural–urban disparities in cancer outcomes, as well as factors contributing to these disparities, are summarized below.

Evidence of Rural–Urban Disparities

Rurality-associated differences have been reported in the quality of screening (13-27), staging (22,28,29), genomic testing (30), treatment selection (31-35), guideline-concordant treatment practices (22,29,31,36-42), and missed appointments (43), with a major impact on survival (1,13,28,44-96) and burden of morbidity (97). Rates of multimodality staging; guideline-concordant treatment, especially curative-intent surgery for early stage cancer; and the quality of surgical resection were different between patients living in rural and metropolitan areas (98). Further, rural and urban residents who received care for non-small cell lung cancer at urban institutions had better quality care and better survival in comparison to rural residents treated at rural institutions (28). Rural residence was associated with a higher rate of stage IV colorectal cancer at presentation, accounting in part for worse outcomes in the rural patients (99). Rural men were more likely than urban men to receive

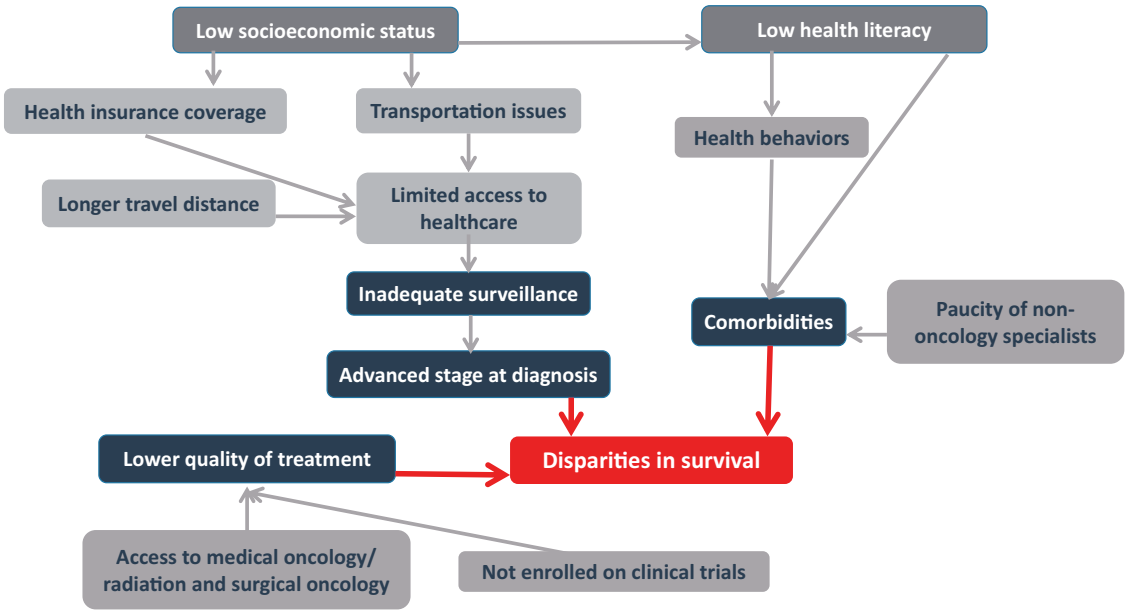

Figure 1. Causes of rural–urban disparities in survival.

Box 1. Database search strategy and inclusion/exclusion criteria

Database search strategy

("rural"[All Fields] OR "ruralities"[All Fields] OR "rurality"[All Fields] OR "rurally"[All Fields] OR "ruralness"[All Fields]) AND ("urban"[All Fields] OR "urbanicity"[All Fields] OR "urbanism"[All Fields] OR "urbanity"[All Fields] OR "urbanization"[MeSH Terms] OR "urbanization"[All Fields] OR "urbanizations"[All Fields] OR "urbanize"[All Fields] OR "urbanized"[All Fields] OR "urbanizes"[All Fields] OR "urbanizing"[All Fields]) AND ("disparate"[All Fields] OR "disparately"[All Fields] OR "disparities"[All Fields] OR "disparity"[All Fields]) AND ("cancer s"[All Fields] OR "cancerous"[All Fields] OR "neoplasms"[MeSH Terms] OR "neoplasms"[All Fields] OR "cancer"[All Fields] OR "cancers"[All Fields]) AND ("outcome"[All Fields] OR "outcomes"[All Fields]) AND "united states"[All Fields] AND ("1971"[Date—Publication] : "2021"[Date—Publication])

Inclusion/Exclusion criteria

Inclusion criteria

- Article type
  - Data-based observational study or clinical trial
  - Systematic review
  - Meta-analysis
- Focus on rural vs urban disparities cancer relating to the following:
  - Survival
  - Socioeconomic status
  - Insurance
  - Transportation
  - Distance to care
  - Limited health-care access
  - Inadequate surveillance
  - Advanced stage at diagnosis
  - Lower quality of treatment
  - Access to medical, radiation, and surgical oncology
  - Access to clinical trials
  - Health literacy
  - Health behaviors
  - Comorbidities
  - Paucity of nononcology specialists

Exclusion criteria

- Article type
  - Opinion
  - Editorial
  - Case report
  - Clinical series
  - Review (nonsystematic)
- Non-US cohort

nondefinitive surgical treatment or no treatment for early stage prostate cancer (100). Treatment in a rural hospital was associated with higher odds of in-hospital mortality for patients with multiple myeloma (45). There is emerging evidence that socioeconomic status may predicate these differences (101-116). Further, numerous barriers to the delivery of high-quality oncologic care for rural populations have been identified, including limited availability of supportive services, limited patient resources, burden of patient decision making and care coordination, and lack of adequate patient–provider communication (117). There remains much to do to understand the underlying reasons for rurality-associated disparities to eliminate them.

Factors Contributing to Rural–Urban Disparities

Oncology Infrastructure

The availability of infrastructure and human resources for optimal care delivery varies substantially between rural and urban communities (118). Certain diagnostic and staging procedures as well as treatments carry high facility establishment and maintenance costs and aggregate in densely populated communities (119,120). For example, the mean density of gastroenterologists and general surgeons was higher in urban compared with rural counties (46,121), adversely impacting colorectal cancer screening services and colorectal cancer outcomes in rural areas. Clinicians with difficult-to-acquire skillsets such as advanced surgical techniques also cluster in population-dense communities (122-128). The ASCO Workforce Information System examined geographic distribution of medical oncologists and hematologists (129). Of 11 664 oncologists, only 3.1% practiced in rural areas. The dearth of rural providers was most apparent in Nevada, Oklahoma, North Dakota, South Dakota, and Wyoming. A Medicare study revealed that almost all urban zip codes had access to home hospice care, whereas 24% of rural zip codes not adjacent to an urban area did not (130).

Such clusters of services in metropolitan areas and their paucity in rural populations may be viewed superficially as maldistribution of resources, but they are driven by pragmatic

reasons such as market forces and the need for high-volume repetition to avoid obsolescence of perishable resources, including skillsets. Some clustering patterns will be relatively immutable. Others, for example procedure suites for low-risk diagnostics such as colonoscopy, infusion centers for systemic therapy, and home hospice care services, are less difficult to provide within rural communities. Indeed, there is also some evidence that concentrated, collaborative efforts to develop outreach activities are successful in delivering cancer screening and early detection services in remote rural areas (131).

Health Insurance Coverage

Health care in the United States relies on employment-based insurance for most individuals younger than 65 years, supplemented by Medicaid for poorer individuals who meet program eligibility criteria. Unfortunately, Medicaid coverage for the poor with cancer is often only obtained emergently as a result of a cancer diagnosis, which itself is often delayed by prior lack of insurance coverage, resulting in more advanced disease at treatment onset and, consequently, poorer prognosis. Rurality is associated with lower rates of commercial insurance and higher rates of Medicaid and noninsurance compared with urban areas (132). With the Affordable Care Act (ACA), Medicaid expansion states have observed a greater reduction in the uninsured rate when compared with nonexpansion states (133). The ACA was associated with statistically significant reductions in rural–urban disparities in colonoscopies (134), suggesting that out-of-pocket costs are an important barrier for screening among rural residents. In addition, Medicaid expansion associated with ACA was associated with a shift to early stage cancer at diagnosis and a narrowing of rural–urban disparities in young adult cancer patients (135). However, Medicaid expansion states also observed a corresponding shift from non-Medicaid to Medicaid insurance, which may paradoxically exacerbate disparities in access to care and cancer outcomes (133).

The older age of rural dwellers results in greater reliance on Medicare coverage. Because oral medications are covered under Medicare Part D, the increasing use of oral therapy for cancer brings the extra burden of greater out-of-pocket costs in the form of co-pays. The required additional payment for prescription drug coverage under Medicare Part D may place an undue burden on low-income rural populations and may contribute to poor adherence to oral cancer therapy. Further, dual Medicaid- and Medicare-eligible patients have worse cancer care and outcomes than Medicare-enrolled patients (133). In contrast, childhood and adolescent cancer survival does not vary by rural–urban residence. The widespread availability of public health insurance for children and adolescents and a nationwide network of pediatric cancer providers may explain this finding (136).

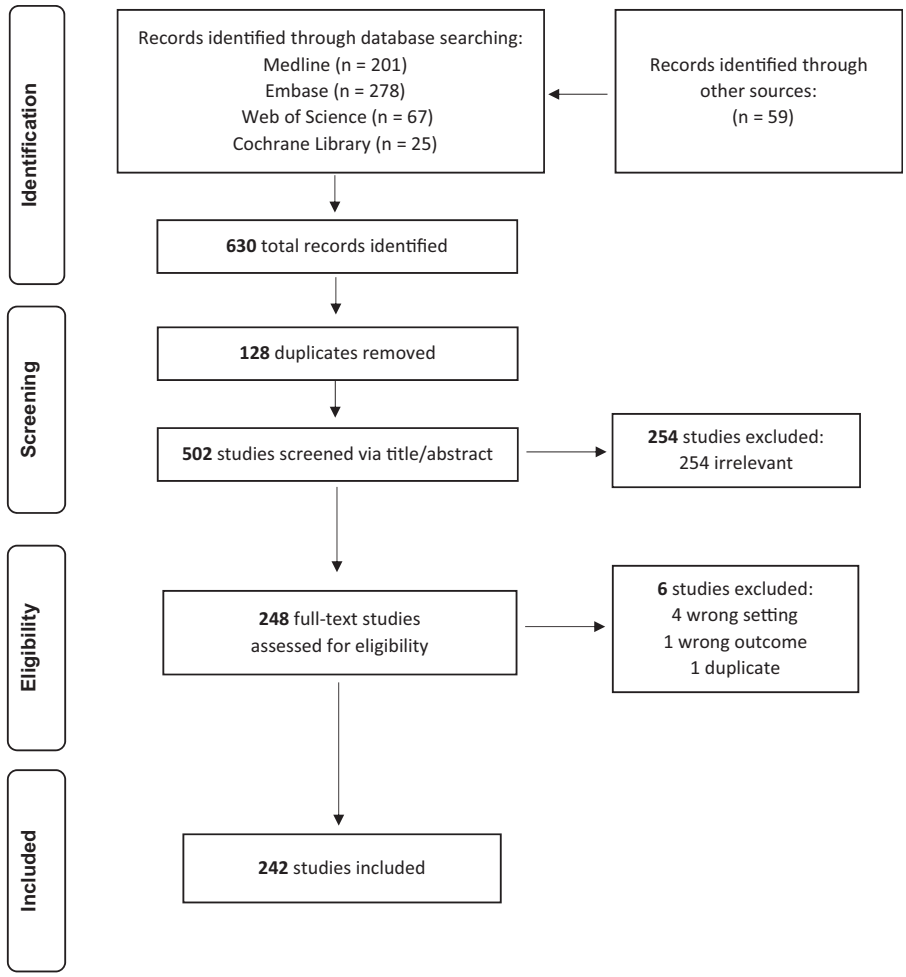

Figure 2. PRISMA diagram of database search.

Geographic Access to Care and Challenges With Transportation

Physical distance from their oncology providers and treatment facilities is a challenge for rural cancer patients. This challenge manifests itself in many ways, including lack of resources to pay for transportation to oncology facilities, public options for transportation, and time or resources to allow for long periods of travel to health-care facilities (117).

Rural patients who need screening procedures for cancers often require transportation to larger diagnostic centers. Research shows that low screening rates, increased time to diagnosis and treatment, later stage presentation, and poorer outcomes for rural patients with esophageal, colorectal, lung, breast, cervical, and endometrial cancers are related in part to the distance to health care and transportation challenges (83,137-174). Compared with residents within 12.5 miles of their treatment facility, the use of adjuvant chemotherapy for stage III colon cancer and radiation therapy for stage II and III rectal cancer was statistically significantly lower in patients with a driving distance more than 50 miles to their treatment facility (175,176).

However, geographic distance is not consistently associated with treatment receipt in expected or consistent ways (177). For example, the disparity is mitigated for rural patients traveling to high-volume centers for treatment (80). Socioeconomic considerations are essential in examining the problem of rurality and travel distance. Gainful employment and the ability to pay influence access to transportation. A survey of Vermont cancer survivors demonstrated that more rural patients retired after their cancer diagnosis and were less likely to receive disability payments compared with those who resided in metropolitan areas (178). Such income shifts could impair access to transportation during cancer treatment. The interaction between socioeconomic status, length of travel, and cancer survival is exemplified in a study of prostate cancer patients, which revealed worse outcomes among Medicaid patients who traveled longer distances for medical attention (179). A recent study of the National Cancer Institute (NIH) Surveillance, Epidemiology, and End Results and the Centers for Medicare and Medicaid Services' Medicare Consumer Assessment of Healthcare Providers and Systems database suggested that timeliness of diagnostic procedures is improving for rural patients (180). These findings suggest that diverse and differential barriers are encountered by urban and rural residents in accessing high-quality cancer care (181). There is a need for additional research to clarify which aspects of transportation serve as barriers to health-care access, measure the impact of transportation barriers on clinically meaningful outcomes, and measure the impact of transportation barrier interventions and transportation policy changes on outcome disparities.

The COVID-19 pandemic has provided a catalyst for rapid adoption of telehealth. For example, a recent study found that telemedicine is acceptable to the majority of patients with gynecologic cancer and may offer financial and logistical advantages for patients who live far from gynecologic oncology care (182). Overall, patients had high rates of internet use and expressed comfort with using technology for their health care. A regional cancer center used a hybrid model of on-site visits and telehealth to increase access to advanced oncology care for patients in rural communities. The model provided the patient with timely access to specialty cancer care in their local community, reducing patient travel time and travel costs (183). Telemedicine could be incorporated into standard practice to reduce health-care disparities related to care access. Furthermore, a study found that providing nurse practitioners autonomy reduces disparities in timely cervical cancer screening (184). Another study found that telehealth, education, and collaboration with local oncology practices may be beneficial (185). In contrast, a large, single center study during the COVID-19 pandemic found that video use was less common among rural residents (186). These findings underscore disparities in telehealth use for cancer care across historically underserved populations.

Health Behaviors

Cancer-related outcomes are often intertwined with the prevalence of risky behaviors that influence cancer risk, treatment effectiveness, and survivorship (187). Here we describe the rural–urban differences in the use of tobacco products, diet, physical activity, and obesity.

Rurality is associated with higher cigarette smoking prevalence, higher age-adjusted smoking-associated cancer incidence, higher smoking-associated cancer mortality, and higher proportion of smoking-attributable cancer deaths (188). Overall use of cigarettes and smokeless tobacco products (chew and snuff) as well as dual or polytobacco use of traditional products are higher in rural areas, compared with urban areas (8). Conversely, cigarillo and hookah use and dual or polytobacco use of emerging products (eg, e-cigarettes) are higher in urban areas (189). Across all tobacco products, urban–rural differences are particularly pronounced in certain geographic regions (eg, the southeast) (190-192). Examination of cigarette smoking trends in rural vs urban areas using annual cross-sectional data from the National Survey on Drug Use and Health from 2007 through 2014 reveals a divergence over the 8-year study period (193). The growing disparities appear related to unequal application or enforcement of tobacco control policy and regulation. For example, regulatory factors that disproportionately benefit urban areas such as enforcement of regulations around the sale and marketing of tobacco products and treatment availability may contribute to the relatively lower rates of smoking-related health behaviors in nonrural areas (188-193).

Rural residents are less likely to report leisure-time physical activity (8). Data from the 1999-2006 National Health and Nutrition Examination Survey, which included 14 039 participants aged 20 years or older, revealed greater prevalence of obesity in rural residents (35.6% vs 30.4%; $P < .01$), among men (37.7% vs 32.5%; $P < .01$) and women (33.4% vs 28.2%; $P < .01$). Compared with urban adults, more rural adults reported no leisure-time physical activity (38.8% vs 31.8%; $P < .01$), and fewer rural adults met or exceeded physical activity recommendations (41.5% vs 47.2%; $P < .01$). Home and neighborhood environments influence physical activity in cancer survivors, informing the need for interventions to meet the unique built environment needs of rural cancer survivors to improve cancer survivorship outcomes and reduce cancer health disparities (194). Rural adults had lower intake of fiber and fruits and higher intake of sweetened beverages. After adjusting for sociodemographics, health, diet, sedentary behaviors, and physical activity, the odds of being obese among rural adults were higher than that among urban adults (195).

Access to Primary Care Services and Nononcology Specialists

The poorer health observed in rural residents could be partly due to poor access to primary care services. In a study of 51 920 adults from the 2014-2016 Medical Expenditure Panel Survey, compared with metropolitan county residents, residents of the most rural counties were more likely to have a usual source of care (81% to 74%), but their providers were less likely to be

physicians (22% to 35%) (196). Despite having to travel longer to reach their usual care providers, residents of the most rural counties were less likely than metropolitan residents to have care providers with office hours on nights and weekends (27% vs 39%) (196).

Collaboration between oncologists, primary care providers, and nononcology specialists (such as endocrinologists) is important to optimize cancer care. This need is greater in rural areas, where the population has a higher prevalence of comorbid conditions, in conjunction with higher risk factors (eg, tobacco use, obesity, and less access to care) (197,198). There are fewer primary care providers and specialists in rural areas (39.8 per 100 000 and 30 per 100 000) compared with urban areas (53.3 per 100 000 and 263 per 100 000) (196,199,200); this is accompanied by higher physician turnover in rural areas. Poor access to specialists could partly explain the inferior outcomes of rural populations. In a nationally representative survey of Medicare beneficiaries with 1 or more complex chronic conditions, which represented 61% of rural and 57% of urban Medicare beneficiaries, rural residence was associated with a 40% higher preventable hospitalization rate and a 23% higher mortality rate. One or more specialist visits during the previous year was associated with a 15.9% lower preventable hospitalization rate and a 16.6% lower mortality rate for people with chronic conditions, after controlling for primary care provider visits. Access to specialists accounted for 55% and 40% of the rural–urban difference in preventable hospitalizations and mortality, respectively (201). This has implications for survivorship care as well; with fewer primary care physicians, there will be fewer opportunities to transfer survivorship care out of resource-stretched rural oncology practices. Access to palliative and end-of-life care is an additional area of concern for rural patients with cancer (202-204), and although the relevant literature is sparse, research points to the value of developing end-of-life resources in rural communities and strategies to accomplish this (140,205).

Rural cancer survivors have poor vitality, physical, social, and emotional functioning when compared with their urban counterparts (206). Lung cancer survivors who live in rural areas are at statistically significantly greater risk for experiencing poorer mental health outcomes 12 to 15 months postdiagnosis (207,208). Ovarian cancer patients living in rural areas are more likely to experience poor sleep and depression following treatment than their urban counterparts (209). This is likely due to poorer access to resources for coping with mental stressors associated with the cancer experience (210). Suicide risk is statistically significantly higher for patients with head and neck cancer residing in rural areas (211); access to social workers and mental health providers is lower (212,213). In 2015, one-quarter of metropolitan counties lacked a psychiatrist, compared with nearly two-thirds of nonmetropolitan counties, and about 50% of nonmetropolitan counties lacked a psychologist, compared with 20% of metropolitan counties (214).

Access to Clinical Trials

Rural patients enrolled into NCI-sponsored clinical trials have similar overall, progression-free, and cancer-specific survival as urban patients enrolled in the same trials. However, rural patients are less likely to be invited (215-217) as well as less likely to participate in clinical trials (1,197,218,219). In response to this fact, the NCI created Minority-Underserved Community Oncology Research Programs to provide access to clinical trials for cancer patients in 23 states with large rural populations. Rural cancer patients face many barriers that directly or indirectly impact accrual to clinical trials. The Accrual to Clinical Trials Framework (220) categorizes barriers into 4 levels of influence: community, system, providers, and patients. Community barriers include isolation, greater travel times to receive care (221), and fewer public and private transportation options (47). System barriers include access to clinics and cancer specialists, access to clinical trials and protocols, and electronic medical record systems that can remind providers to ask about trial participation (129,200,222). Research infrastructure remains underfunded in rural institutions, which often operate on very thin margins, impacting the ability to hire and retain support staff and maintain a viable clinical research program in many rural areas. At the provider level, barriers can include lack of training, including how best to inform patients about a trial; peer influence (223); inadequate time to discuss trials during clinic visits; and lack of incentives (224,225). Patient-level barriers include economic, health, and personal and influential family or friends' information and beliefs about trials (226,227).

The same framework can be used to categorize strategies to improve enrollment of rural patients in clinical trials. At the community level, strategies include clinical trial awareness campaigns, addressing social determinants of health, improving access to cancer specialists, and transportation. At the system level, strategies include opening clinical trials relevant to the catchment area's cancer burden, using electronic medical record processes to identify and manage patients, regularly reviewing accrual data, training staff to ask about the social determinants of health, expanding hours, and employing patient navigators. Education about clinical trials, issues facing rural residents, how to use navigators, prioritize (and incentivize) clinical trial enrollment, how to address barriers, and schedule adequate time to talk to patients about clinical trials can address provider barriers. Patient education, identification, and resolution of identified barriers to participation, using navigators, inclusion of family and friends in discussions, and provision of resources to address needs such as transportation, lodging, and financial assistance represent patient-level opportunities for intervention.

Information Needs and Health Literacy

Unmet information needs may impede patient education in cancer care, especially for rural patients. In a cancer information needs survey of 36 rural Kansas primary care practices, 23% of 801 patients reported a cancer information need. Of these, 184 patients (45%) reported either not discussing cancer or having insufficient discussion time with their physicians; 44% needed more information after consulting their physician. Patients more likely to report a cancer information need were young, female, internet users, persons with a prior cancer diagnosis, and persons seeing male physicians or physicians in group or multispecialty practices. Patients and physicians were unfamiliar with the relevant services provided by national cancer organizations (228).

Even when information needs are addressed, low health literacy may remain an obstacle to patient education. Health literacy refers to an individual's ability to understand and act on basic health information and services. Lower health literacy is a predictor of poor overall health and end-of-life care as well as mortality among older adults (229,230). Another survey-based study found that rural cancer patients had a 33% higher odds of having lower levels of health literacy; this association was mediated in part by socioeconomic status (231). Statistically significant rural–urban disparities are observed in awareness of healthy diet (232), genetic testing (233), and cancer prevention (234). In addition, there are statistically significant rural health

disparities in knowledge and awareness of human papillomavirus and its vaccine compared with urban counterparts (235) as well as mouth and throat cancer awareness (236). Rural patients have poorer perception of care coordination than urban patients related to communication and operational challenges (237). Rural patients are less likely to adopt health information technology for self-management, presenting a need to understand the underlying reasons for this digital divide and develop appropriate interventions (238,239). Written patient–provider communication improves timely follow-up care for rural cancer survivors (240).

A mixed methods evaluation of health literacy and patient navigation needs among 53 rural cancer patients and 41 staff from 5 oncology clinics in rural Wisconsin uncovered multiple unmet navigation needs, health literacy limitations, and barriers to quality cancer care. The study concluded that system-level implementation of patient navigation and health literacy best practices could improve cancer care and patient outcomes among rural populations (241). All these findings underscore the need for efforts to reach the rural community with plain-language materials appropriate for persons with limited health literacy and appropriate cancer prevention messages.

Discussion: Gaps in Knowledge

Our review identified continuing gaps in the literature regarding the underlying causes of rural–urban disparities in cancer outcomes. Understanding and addressing the challenge of rurality in cancer care delivery will remain an area of productive research for many years. Such research should focus on solutions beyond the usual source-of-care provider as an overall indicator and instead investigate disparities using multiple indicators of access based on theoretically distinct domains (242). Specific areas of research are described below to provide needed evidence to answer the key questions articulated in Table 1.

The intersections between rurality and insurance coverage, co-insurance (the percentage of costs paid by the insured after meeting the set deductible amount), co-pays (the set rate paid by the insured for prescriptions, doctor visits, and other types of care), and cancer care delivery is worthy of further investigation. For example, rurality was a statistically significant predictor of lower commercial insurer participation in a county's Medicare Advantage market (243). The impact of ACA on rural cancer care delivery is another area of great policy-level interest.

Research is needed to understand how best to overcome the distance gap and transportation challenges for rural patients. There are gaps in knowledge regarding how best to leverage and access technology, for example, with telehealth programs such as telecolposcopy (244,245), telehealth genetic cancer risk assessment (246), and teledermatology for skin cancers (244,247). The rapid adoption of telemedicine due to the COVID-19 pandemic provides an opportunity to study this issue; however, this remains a key gap in knowledge about care outcomes in rural areas. Future research should evaluate potential underlying contributors to disparities in technology access, internet capability, and video vs phone visits and their impact on cancer outcomes. The impact of alternative strategies to bring providers to rural communities using technology-based options and home-based programs also needs to be studied. Visiting oncology provider clinics are used in rural areas (248,249), but how they improve outcomes requires more study. Home-based programs, such as the Reach-out to ENhancE Wellness trial (250), which tested intervention on diet and exercise for breast, prostate, and colorectal cancer survivors and demonstrated improved outcomes in functioning and physical health for rural cancer survivors, need to be further implemented and tested.

Table 1. Identified research gaps

Problem area	Research questions
Oncology infrastructure and care delivery	Why is guideline-concordant care less likely for rural patients? How much of the problem is access to key skillsets and expertise, especially surgery?
	Is nonsurgical treatment more frequently used because patients are too high risk or because providers are insufficiently proficient or unavailable for surgical treatment of early stage cancer?
	What are the causes of higher nontreatment rates? To what extent is nontreatment an appropriate reaction to greater rates of comorbidities/poor performance status vs an indication of barriers to accessing care?
	Why is deployed treatment less effective? How much of the lack of efficacy is influenced by lower quality care? How much of the lower quality care is due to provider vs institutional factors?
	How can we most efficiently extend access to multidisciplinary decision making; determine optimal models of multidisciplinary care; benchmark and oversee care delivery?
Causes of disparities	How do each of the following types of factors drive rurality-associated disparities: patient (health literacy, health behaviors, sociodemographics, insurance); caregiver or influencer; provider (eg, availability, knowledge, proficiency, beliefs); institutional (eg, availability and quality of services or institutional culture, access to clinical trials); community (eg, support services)?
	Why are disparities greatest at the curative-intent end of the disease spectrum?
Health policy	What are the most effective (and efficient) policy-level incentives to overcome barriers to optimal treatment and proper oversight of care?
	How can investment in technology narrow or eliminate rurality-based disparities in access, quality, and outcomes? How can technology help to eliminate distance barriers to care; improve patient and provider convenience; reduce cost; measure, oversee quality; improve provider availability, knowledge, interaction, performance and oversight; reduce the cost of care delivery at the institutional and community levels?
	Will transportation and lodging support improve access to distant services such as radiation therapy (adjuvant and other radiation treatments) and surgical resection?
	How will regionalization of care, much advocated by volume-outcome proponents, impact on access, quality, and outcomes of care for rural residents?

There is limited information regarding health literacy in cancer patients, in general. The existing literature is limited by the use of small samples from geographically limited areas and a lack of comparison between rural and urban populations. Understanding the sociodemographic factors associated with low health literacy, and its downstream effects on health behaviors such as screening practices, is a research imperative.

Contemporary mapping of rural oncology specialists vs the rural cancer population, with the 2020 Census figures, will be needed. We also need more knowledge about the impact of provider density on screening, treatment, and outcomes disparities for all cancer types. Existing observational studies demonstrating urban–rural differences are unable to determine causality; therefore, uncertainty remains about their solutions, which may be at the patient, provider, institutional, or community levels. Because the intensity, pattern, and location of survivorship care are ideally risk-based and related to the stage of disease at treatment, these challenges are also relevant to survivorship care. Studies are needed to understand how nononcology specialists located in urban or rural areas influence the outcomes of rural cancer patients, from diagnosis through survivorship and to end of life.

Given the links between health behaviors such as smoking and exercise, an important knowledge gap includes the impact of sociodemographic factors associated with tobacco use, physical activity, and obesity. Important areas for further research include patterns of tobacco use, the age of initiation, diet and physical activity levels, association with lack of health literacy, mediators and moderators of the association between rurality and high use of tobacco and obesity, the association between tobacco use and downstream effects on development of comorbidities, and the ultimate impact on the inferior cancer outcomes experienced by rural dwellers. It will also be essential to examine the rural–urban differences in prevalence of other health behaviors (eg, alcohol consumption, illicit drug use, physical activity, and diet).

More information on barriers and facilitators to enrollment on clinical trials is needed, particularly examining different rural settings (eg, frontier, tribal lands, Appalachia, the rural Mississippi Delta) as compared with other rural areas and by the multiple levels of influence—patient and family, provider, and system. The creation and oversight of sustainable research infrastructure, engagement and training of the organizations, clinicians, and staff in rural areas are potentially fruitful lines of inquiry.

Rapid advances in cancer care, including early detection, noninvasive diagnostics, minimally invasive procedures, and biomarker-driven treatment will worsen existing disparities, in the absence of a concerted effort to reverse this course. Research focused on causal factors and corrective interventions is critical. Modifying the structure and processes of care delivery can overcome institutional and provider-level disparities in providing high-quality care. For example, the Project Extension for Community Healthcare Outcomes model of training local care providers, initially deployed to expand access to hepatitis care in rural New Mexico, is being adapted for cancer care delivery (251). By extending multidisciplinary decision making into rural care delivery environments, this model can potentially overcome institutional and provider-level knowledge disparities driving guideline-discordant treatment and poor outcomes (28,252). Deploying structure- and process-focused interventions across rural health-care systems, with support from more resource-replete health-care systems, can overcome rurality-associated cancer care delivery disparities.

Funding

Not applicable.

Notes

Role of the funder: Not applicable.

Disclosures: RUO has stock and other ownership interests in Lilly, Pfizer, and Gilead, has received honoraria from Biodesix, serves in a consulting or advisory role for the Association of Community Cancer Center, AstraZeneca, the American Cancer Society, the GO2 Foundation, the Lungevity Foundation, and Triptych Health Partners, holds patents, royalties, or other intellectual property, and has a relationship with Oncobox Device Inc. EDP has stock and other ownership interests in Pfizer and Meridian Bioscience Inc and has received research funding from Merck and Pfizer. KBP has served in a consulting or advisory role for Agios and Bayer and has received research funding from Agios, Abbvie, BioMimtex, and Novocure. WL has received research funding from Merck paid to institution. SB, JKM, and JP have no disclosures.

Author contributions: Conceptualization: SB, WL, EDP, KBP, JKM, JP, and RUO. Methodology: SB, WL, EDP, KBP, JKM, JP, and RUO. Formal analysis and Investigation: SB, WL, EDP, KBP, JKM, JP, and RUO. Validation: SB, WL. Visualization: SB, WL. Writing—original draft: SB, WL, EDP, KBP, JKM, JP, and RUO. Writing—review and editing: SB, WL, EDP, KBP, JKM, JP, and RUO. Project administration: JKM, MP. Supervision: SB.

Acknowledgements: The authors would like to thank and acknowledge the contributions of the members of the ASCO Rural Cancer Care Task Force.

Data Availability

The data underlying this article are available in the article and in its online supplementary material.

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