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Role of neighborhood context in ovarian cancer survival disparities: current research and future directions.

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Tweetable statement: Neighborhood and environmental context may drive disparities in ovarian cancer survival. This article offers recommendations for advancing research in the role of place on this longstanding cancer disparity.

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Abstract

Ovarian cancer is the fifth leading cause of cancer-associated mortality among US women, with survival disparities seen across race, ethnicity and socioeconomic status, even after accounting for histology, stage, treatment, and other clinical factors. Neighborhood context can play an important role in ovarian cancer survival, and, to the extent that minority racial and ethnic groups and populations of lower socioeconomic status are more likely to be segregated into neighborhoods with lower quality social, built, and physical environment, these contextual factors may be a critical component to ovarian cancer survival disparities. Understanding factors associated with ovarian cancer outcome disparities will allow clinicians to identify patients at risk for worse outcomes and point to measures such as social support programs or transportation aid, to help ameliorate such disparities. However, research on the impact of neighborhood contextual factors in ovarian cancer survival and in disparities in ovarian cancer survival is limited. This commentary focuses on the following neighborhood contextual domains: structural and institutional context, social context, physical context represented by environmental exposures, built environment, rurality, and healthcare access. Research to date is presented, as well as clinical implications and recommendations for future interventions and studies to address disparities in ovarian cancer outcomes are proposed.

Keywords

ovarian cancer; race and ethnicity; social inequities; survival disparities; multilevel framework

Ovarian cancer incidence and survival varies across race and ethnicity (Table 1)[1,2] and is the fifth leading cause of cancer mortality among US women.[2] Compared with women of other races and ethnicities, Black women with ovarian cancer have worse survival,[3]

which may, in part, be due to lower receipt of standard-of-care therapy,[4] and greater chemotherapy dose reduction, even within an equal-access healthcare system.[5] However, inequities in care do not completely explain racial or ethnic survival disparities. Even after accounting for histology, stage, treatment, and other factors, Black women still have 18–29% higher mortality than non-Hispanic White (NHW) women.[6–8] Moreover, little is known regarding survival differences for other groups (e.g., Hispanic/Latino, Asian American, Pacific Islander, American Indian/Alaskan Native (AI/AN) women), with mixed evidence that Hispanic/Latino women may experience more favorable[9] or worse survival than NHW women,[10] and that Asian American/Pacific Islander (AAPI) women, as an aggregated group, experience more favorable survival than other race and ethnicity groups.[11,12]

The understanding that health disparities result from the complex interplay between social and biological factors has gained recognition. A multilevel "cells to society" model proposed by Warnecke and colleagues[13] offers a valuable framework to studying cancer health disparities by recognizing the importance of structural causes and social and physical context alongside individual and biologic factors (Figure 1). This framework identifies three types of determinants: 1) distal factors that include social conditions and policies and institutional context, 2) intermediate factors that include social and physical context and social relationships, and 3) proximal factors that include individual demographics and risk behavior, biological responses, and genetic pathways.[13]

Following the multilevel hierarchy, distal factors, such as structural racism (i.e., "totality of ways in which societies foster racial discrimination through mutually reinforcing systems of housing, education, employment, earnings, benefits, credit, media, health care, and criminal justice"[14]), are considered fundamental causes of health disparities as they determine an individual's access to resources (intermediate and proximal factors) that help mitigate negative health outcomes.[15] Consequently, this theoretical framework suggests that changing individuals' behavior without addressing structural problems would not be optimally effective nor sustainable in ameliorating disparities. To conduct clinically applicable research, it is essential to integrate all three levels of determinants.

Distal and intermediate factors have seldom been examined in the context of ovarian cancer survival disparities. In this commentary, we highlight the current knowledge regarding the influence of these factors on ovarian cancer survival (Supplementary Table 1) and discuss potential ways in which they can impact survival disparities and implications for clinical interventions and future research (Table 2). Moreover, empirical evidence for the role of distal and intermediate factors can motivate broader health system review and mitigation of biases within the system and the level of institutional trustworthiness within the community.

In this commentary, we focus on the following distal and intermediate factors of the multilevel framework for health disparities: structural and institutional context, social context, physical context represented by environmental exposures, built environment, rurality, and healthcare access (a concept that spans across levels of institutional, social, and physical context). While these are interrelated, they present distinct areas from which inequities may arise and hence different opportunities for addressing disparities.

Structural and institutional context

Structural and institutional context encompasses macro-level systems—including housing, education, employment, economic mobility, criminal justice, and healthcare—that interact to reinforce inequities across minoritized populations.[14,16–19] There is growing evidence linking structural racism to cancer outcomes.[20–23] For example, in breast cancer, living in areas with high contemporary redlining (i.e., the denial of mortgage lending based on geographic location), mortgage lending bias (i.e., the denial of mortgage lending based on the applicant's race or ethnicity), or historic redlining are associated with late stage of diagnosis, higher mortality, and lower survival.[20–23] These measures of structural racism impact systemic disinvestment of neighborhoods, contributing to limited healthcare access, inadequate transportation, fewer community resources, and increased exposure to environmental pollutants, which collectively contribute to worse cancer outcomes.[14,24,25] As some studies show, structural racism (distal factor) could also impact individual behavior (proximal factor), such as vaccine hesitancy or general distrust of healthcare system prevalent among racially minoritized individuals.[26,27]

Although disparities in ovarian cancer treatment and survival by race and ethnicity have been documented, few studies have examined the role of structural and institutional context on ovarian cancer outcomes (Supplementary Table 1). Only one recent study, by Westrick et al. (in Florida), has examined the role of racial residential segregation, the geographic separation of marginalized racial and ethnic groups from predominately NHW neighborhoods, on survival among women with ovarian cancer.[9,28] The authors operationalized residential segregation with the Index of Concentration at the Extremes (ICE), which has been used to measure extreme economic and or racial segregation.[29] Adjusting for histology, age at diagnosis, insurance status, tumor stage, and treatment, the study reported that measures of economic and racialized economic residential segregation were more strongly associated with ovarian cancer mortality than was racial and ethnic segregation alone, among both Black and Hispanic/Latino women. Women (of all races and ethnicities) living in more concentrated Black and lower income neighborhoods (lowest quartile of racialized economic segregation) had 1.21-times the hazard of ovarian cancer mortality compared with women living in concentrated NHW and higher income (highest quartile) neighborhoods (95% confidence interval [CI] 1.12, 1.32), and a slightly smaller but statistically significant association was seen for residence in more concentrated Hispanic/Latino neighborhoods.[28] While these findings suggest that individual ovarian cancer outcomes are significantly impacted by structural racism manifested in residential segregation (Figure 1), the applied measures do not capture multilevel (e.g., policies, intergenerational transfer, individual behavior) and multidimensional (e.g., wealth, housing, healthcare, etc.) structural racism.[16,30]

Research that incorporates multidomain measures of structural factors will further our understanding of disparate outcomes among women diagnosed with ovarian cancer and allow interventions at multiple levels to address the negative effects in patients at risk. Interventions at multiple levels may include policies and community-level interventions, as well as efforts to address provider conscious and unconscious bias or build patient trust.[30,31]

Social context

Social attributes of the neighborhood environment refer to the socioeconomic composition of the resident population and the social aspects of neighborhoods, such as crime, community support, collective efficacy, social capital, and disorder.[32] The most commonly assessed construct is neighborhood socioeconomic status (incorporating measures such as income, education, poverty, occupational status, and/or home ownership of residents, denoted as nSES). NSES and social environment can shape the opportunities and resources available to residents. A few ovarian cancer studies using large population-level datasets have reported associations of nSES with being treated at a high-performing hospital,[33] receipt of guideline treatment[34,35], genetic testing,[36] and survival.[6,33,37–40] In the Ovarian Cancer in Women of African American Ancestry Consortium, a mediation analysis showed that when an index of area deprivation is considered as a potential mediator of the survival disparity between African American and White women with ovarian cancer, it explains 21.5% of the observed disparity.[41]

Another social context attribute is racial and ethnic composition. Ethnically-concentrated neighborhoods, or ethnic enclaves, often result from segregation. Residence in ethnic enclaves has been shown to be associated with both deleterious and beneficial effects on cancer outcomes.[42,43] For example, in breast and prostate cancer, residence in Hispanic ethnic enclaves has been associated with improved survival, and neighborhoods with a higher proportion of Black residents were associated with improved survival among Black women with breast cancer.[42,44,45] Yet, adverse associations with mortality after diagnosis have been observed in neighborhoods with higher concentrations of ethnic minority residents.[43] These conflicting results may be a result of different pathways by which ethnic density or enclaves can impact cancer outcomes. Ethnic enclaves are usually of lower socioeconomic status,[46] but they may confer protective effects through increased co-ethnic social support and collective efficacy and availability of in-language resources. To our knowledge, no studies have investigated the associations between ethnic density or ethnic enclaves and ovarian cancer survival.

Other aspects of social context, such as social capital (i.e., networks of relationships between individuals), social isolation (i.e., lack of social connections), and religious and civic participation, have not been evaluated in ovarian cancer research. Understanding the impact of these social factors will not only help identify interventions that could be effective for individuals with limited resources but also pave the way for improvements at the intermediate level of the multilevel framework (Figure 1). Clinics can also help to bridge patients with these resources at the community level to help address social needs.

Environmental exposures

Environmental exposures are a component of the physical environment that include aspects such as ambient air pollution, diesel emissions, pesticides, contaminated drinking water or proximity to toxic waste sites.[47] Environmental exposures disproportionately impact predominantly Black and Hispanic/Latino[48,49] and low SES neighborhoods.[48]

Only two studies, both using the California Cancer Registry, have evaluated the contribution of environmental exposures to disparities in ovarian cancer survival.[40,50] The first study examined geographic disparities in ovarian cancer survival and overall community disadvantage using a cumulative score that included ozone, fine particulate matter ($PM_{2.5}$), and diesel particulate matter, among other environmental and sociodemographic factors.[40] Neighborhood SES and ozone levels were the strongest contributors to geographic disparities in ovarian cancer survival, and the contribution of $PM_{2.5}$ was suggestive.[40] The second study evaluated exposure to ambient air pollution and ovarian cancer mortality, reporting associations between NO_2 and $PM_{2.5}$ and ovarian cancer mortality after controlling for sociodemographic and treatment factors.[50]

Additional studies have examined environmental exposures and ovarian cancer mortality (as opposed to survival after diagnosis), but these studies cannot distinguish between impacts on incidence versus impacts on survival. More research is needed to better understand the unique effects of physical environmental exposures on survival among women with ovarian cancer. Environmental exposures that have been reported to be associated with increased ovarian cancer mortality include cadmium,[51] water quality,[52–54] asbestos,[55–57] and emissions from industrial plants.[54,58–60] In vitro studies have found that Bisphenol A (BPA) induces ovarian cancer cell proliferation and metastasis,[61,62] as well as resistance to various chemotherapeutics,[63] but no study has examined BPA and ovarian cancer mortality or survival.

Future research should jointly consider geographic, racial and ethnic, and socioeconomic disparities when examining associations between environmental exposures and ovarian cancer survival. Drawing from the multilevel framework that indicates the possibility of biologic-environment interactions, it is also critical to explore the mechanisms through which environmental exposures affect ovarian disease progression.

Built environment

The built environment comprises the human-made, physical attributes of neighborhoods, including conditions affecting walkability and recreation, availability of health-promoting resources such as grocery stores and playgrounds, and resources such as fast-food restaurants, liquor stores, and tobacco outlets that can adversely influence individual health behaviors.[32] Eating a healthy diet, engaging in physical activity, maintaining a healthy weight, and not smoking are widely promoted as part of cancer survivorship guidelines, although the evidence is limited for ovarian cancer survivors at this time.[64,65] Individuals' health behaviors (proximal factors) are influenced by the built environment (intermediate factors),[66–68] and underserved communities and marginalized populations are more likely to live in neighborhoods with built environments that place one at risk for adverse health outcomes.[68–70] Thus, neighborhood built environment may play an important role in moderating or mediating racial and ethnic disparities in ovarian cancer survival, yet, to our knowledge no studies have assessed the impact of the built environment in the context of ovarian cancer outcomes.

Rurality

Geographic access to cancer care and, in the case of ovarian cancer, access to gynecologic oncologists, is essential to optimizing ovarian cancer survival, yet residents of rural areas face more barriers to access than those of non-rural regions. In a study of all Medicare patients from five US states, some preferred to go to the nearest hospital to receive care, whereas others preferred to travel farther to receive care at a teaching hospital or a hospital with a wide range of services.[71] Cancer patients in rural areas were found to be less likely to see specialists than generalists[72] and ovarian cancer patients were less likely receive lymph node dissection and debulking surgery.[73] A study using the Pennsylvania Cancer Registry data and Rural-Urban Continuum Codes[74] showed that travel time was significantly higher for ovarian cancer patients living in rural areas than patients in more metropolitan areas (180 minutes versus 49 minutes). In the National Cancer Database, overall ovarian cancer survival was poorer among women living in rural area compared to women living in metropolitan areas as well as for women living farther than 50 miles from a high volume treatment center.[39] Even when receiving their primary treatment in tertiary cancer centers, women with some college or trade school education residing in rural areas had poorer survival and were more likely to have follow-up care locally than urban women with similar education levels.[75,76]

Understanding the effect of residing in a rural area on the receipt of timely, guideline-concordant treatment is important for patients diagnosed with ovarian cancer. Residents living in rural regions may also be exposed to higher levels of environmental contaminants, in addition to poorer social and built environments.[40,77] Worse outcomes among women in rural regions may operate through or interact with these other intermediate-level factors. Technologies such as telemedicine and virtual case conferences, as well as traditional interventions such as transportation aid, would be valuable to help mitigate the negative effects of residing in rural areas.[78,79]

Healthcare access

Healthcare access has been defined by the five A's: availability, accessibility, accommodation, affordability, and acceptability,[80] and spans across levels of institutional, social, and physical context (Figure 1). Using SEER-Medicare data, Akinyemiju et al. assessed the extent to which three healthcare access metrics – affordability (measured using dual enrollment in Medicaid, tract-level SES, and county-level health insurance coverage), accessibility (measured using straight-line distance between patient and hospital zip code centroids), and availability (measured using facility-level metrics including ovarian cancer surgical volume, ownership status, medical school affiliation status, NCI cancer center designation, etc.) – affected ovarian cancer treatment quality (surgery and systemic treatment) between Black and White patients.[81] They found that racial disparities in treatment were partly explained by these healthcare access factors. Additionally, healthcare access has been measured using geographic designations such as Health Professional Shortage Areas and Medically Underserved Areas, capturing availability of healthcare providers and services[82], but these measures have not been applied in ovarian cancer research.

Spatial access to healthcare, including availability (supply) and proximity (travel cost) components[83,84], is considered an integral part of the comprehensive concept of access.[85,86] Several methods have been developed to measure the spatial accessibility of healthcare services, including provider-to-population ratios[87], travel impedance[85], gravity models[88], kernel density[85], floating catchment area[89], two-stage floating catchment area (2SFCA)[83,90], enhanced 2SFCA (E2SFCA)[91], three-stage floating catchment area[92], and Rational Agent Access Model[93], with each method progressively improving upon its predecessor method by more efficiently calculating accessibility costs for accurate modeling of the spatial accessibility to health care.

Research suggests that better spatial access to cancer care services ensures timely care and improves outcomes for patients.[94] Similarly, several studies that included cancers of the ovary,[81,95] rectum,[94] gastrointestinal, genitourinary tract[96] and breast[96,97] reported that those living a farther distance from cancer care services was associated with greater likelihood of an advanced-stage cancer diagnosis.[81,94,97,98] In ovarian cancer, access to specialists is especially critical, as outcomes are more favorable when individuals are treated at high-volume facilities and by high-volume providers or specialized gynecologic oncologists.[33,34,38,81,99–104] Differential geographic availability of and access to specialty centers may also exacerbate disparities to the extent that specialty centers are typically more likely to adopt new advances in cancer treatment and management that can enhance survival.

An Australian study reported that the farther women lived from a hospital with a gynecologic oncologist, the less likely they were to receive treatment from a specialist and that led to less favorable outcomes.[105] Geographical differences in receipt of surgery and chemotherapy and survival have also been reported among women with ovarian cancer.[106–109] A single US study reported that farther travel distance to a high-volume facility was associated with care non-concordant with National Comprehensive Cancer Network (NCCN) guidelines, and this disproportionately affected minority women and those of lower socioeconomic status.[99] However, a study using data from the California Cancer Registry reported that access to the closest high-quality hospital and distance traveled did not improve ovarian cancer survival after adjusting for receipt of NCCN treatment guideline-concordant care.[110] A study in Georgia that used the E2SFCA approach combined spatial accessibility with area-based sociodemographic variables, like income, poverty, race, and education level, to derive an overall measure of “geosocial vulnerability”,[111] and demonstrated an association of this indicator with ovarian cancer mortality.

Recognizing the multidimensional nature of healthcare access (Figure 1), it is also important to examine how its effect varies by factors of social and physical context such as public transit access, automobile access, neighborhood disorder, and nSES. However, there is a lack of research investigating how these intermediate factors interact and affect healthcare access for individuals with ovarian cancer. With increasing availability of technology that has potential to make aspects of healthcare accessible regardless of physical distance, it will be especially beneficial to understand the detailed effects of disparate healthcare accessibility on ovarian cancer outcomes.

Recommendations for interventions and future research

Social inequities in cancer survival are persistent, and ovarian cancer is no exception. While research increasingly demonstrates the relevance of different domains of structural, social, and physical context in cancer survival, and in disparities in cancer survival,[20,21,32,112] research on the impact of these factors on survival of women with ovarian cancer is limited. As summarized above, to date, only a handful of studies have evaluated distal and intermediate level factors in ovarian cancer survival, including racialized segregation, nSES, air pollution, rurality, and different domains of healthcare access.

Given the limited research conducted to date on the impact of distal and intermediate level factors and disparities in ovarian cancer survival, we offer recommendations for future research studies. These recommendations are outlined in Table 2 and discussed below.

Accurate measurement of complex constructs related to structural, social, and physical context, is important for achieving reliable estimates. Given the multilevel nature of these exposures, it is valuable to use measures assessed objectively through geospatial data as well as perceived neighborhood measures assessed through self-report. For example, the PhenX toolkit[113] provides an expert-panel recommended set of tools for assessing structural, social, and physical context.

An analytical approach that can accommodate the multilevel nature of health disparities is important. We propose a hierarchical modeling approach with fixed and random effects whereby different levels of health determinants are accommodated within a single model.[114–116] For example, the proximal level can include, but is not limited to, individual characteristics (e.g., genetic, demographic, etc.), while the intermediate level could include population-level “neighborhood” effects, such as census tract unemployment status or neighborhood disorder. The distal level could involve city, county, or state-level policy as a factor that impacts individuals, where inter-city, county, or state comparisons are a focus. Furthermore, drawing from the multilevel framework, distal factors, such as structural racism, need to be recognized and examined as fundamental causes of health disparities. Accordingly, intermediate and proximal factors should be examined as consequences of the fundamental causes and can be analyzed as mediators of health disparities.

It will be beneficial to leverage current approaches in geospatial sciences, including using measures at appropriate geographic scales (e.g., census block groups or tracts when measuring neighborhoods), applying geospatial regression modeling, applying mixture modeling approaches to account for joint effects of multiple environmental exposures, and using the most current spatial accessibility measures that account jointly for availability and proximity. Specific to ovarian cancer outcomes, spatial accessibility measures need to account for access to gynecologic oncology specialists.

Given how factors across multiple levels are interconnected, it is important to assess interactions of patient-level sociodemographic factors and intermediate factors, in addition to interactions among, and effect modification by, intermediate factors (e.g., rurality, nSES, and spatial accessibility). To address the heterogeneity of rural areas, it is valuable to

examine particular attributes of these areas that are associated with access to care, receipt of guideline treatment, and survival.

Data on physical context (e.g., environmental exposures, built environment) and ovarian cancer are scarce. It will be important to evaluate associations of environmental exposures and community disadvantage with survival. Additionally, studies that examine characteristics of physical context such as neighborhood stability, transit, food, and social services access, will bridge the research gap on the impact of the built environment on ovarian cancer outcomes.

Clinically, these data can identify patients with adverse social context and social needs who may be at risk of poor outcomes to allow early and meaningful interventions to mitigate the risk through the course of their cancer care. Such interventions can be individual-level, such as addressing provider conscious and unconscious bias, and system-level, such as providing transportation aid or options for telemedicine visits to those with limited spatial access to healthcare.

Recognizing the principal role of structural, social, and physical context in cancer health inequities, multilevel studies are needed to comprehensively evaluate the joint roles of distal, intermediate, and proximal factors on disparities in ovarian cancer outcomes, to inform clinical interventions toward improving outcomes for vulnerable patients.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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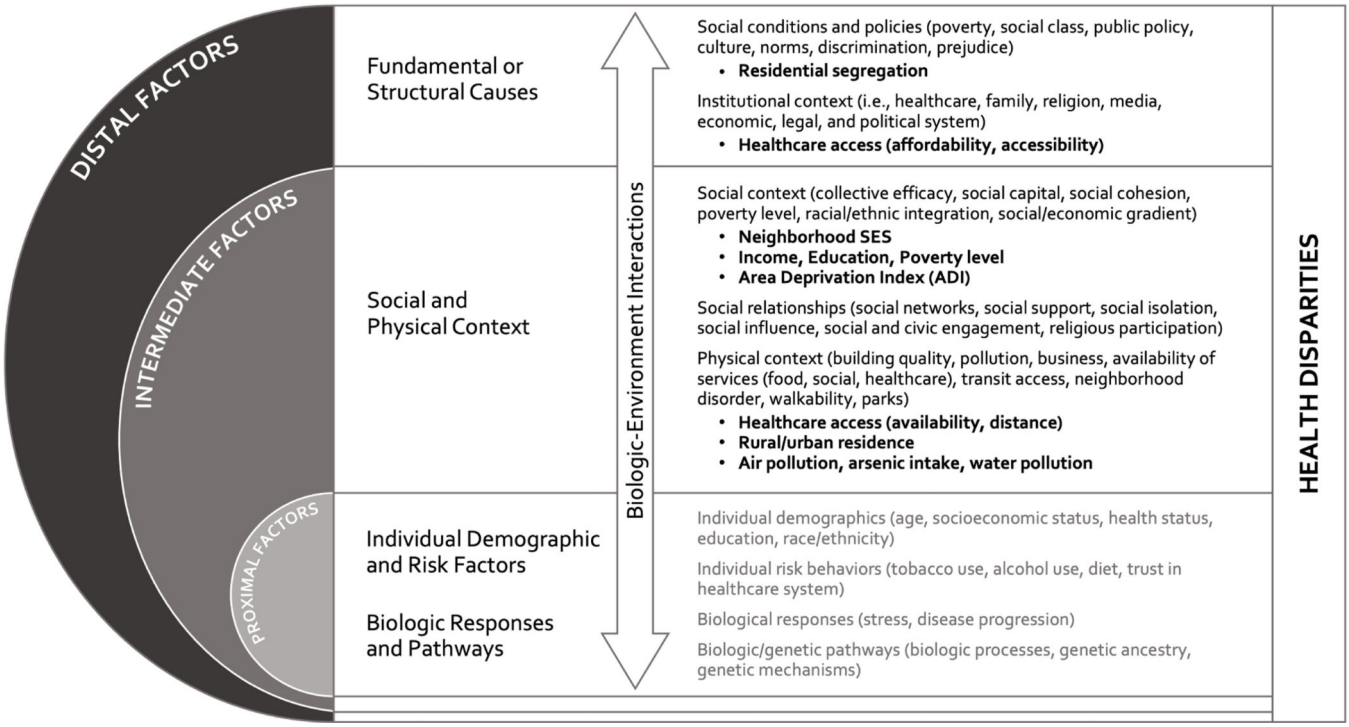

Figure 1. Multilevel framework for studying ovarian cancer disparities.

Adopted from Warnecke et al. 2008.[13] The figure reflects the underlying hierarchy of factors, i.e., distal factors impact disparate health outcomes by various pathways via intermediate and proximal factors. Bulleted points refer to the concepts/measures examined in ovarian cancer research to date. Proximal factors are not the focus of this commentary.

Table 1.

Ovarian cancer age-adjusted incidence (95% CIs) per 100,000 and 1-, 3- and 5-year ovarian cancer survival, overall and by race and ethnicity, SEER 2015–2019[a]

Race and ethnicity	Incidence Rate	Ovarian Cancer Survival		
		1-yr	3-yr	5-yr
Overall	10.6 (10.5–10.7)	79.3 (78.7–79.9)	61.2 (60.4–62.0)	47.7 (49.0–50.4)
Non-Hispanic White	11.0 (10.9–11.1)	78.5 (77.8–79.2)	60.3 (59.3–61.3)	48.5 (47.6–49.4)
Non-Hispanic Black	9.1 (8.8–9.4)	73.5 (71.4–75.5)	52.8 (50.5–55.6)	41.2 (39.0–43.5)
Hispanic (all races)	10.3 (10.1–10.5)	81.5 (80.1–82.8)	65.5 (63.5–67.4)	53.8 (52.1–55.6)
Non-Hispanic Asian/Pacific Islander	9.4 (9.1–9.7)	85.1 (83.5–86.6)	66.7 (64.1–69.1)	58.0 (55.9–60.1)
Non-Hispanic American Indian/Alaska Native	11.4 (9.7–13.3)	80.1 (72.5–85.8)	63.2 (52.5–72.2)	43.5 (33.6–53.0)

[a]. Surveillance Research Program, National Cancer Institute,[1] and SEER*Stat software version 8.4.0.

Table 2.

Measures of distal and intermediate factors examined in studies of disparities in ovarian cancer, clinical implications, and recommendations for interventions and future research.

Measure	Clinical implications	Recommendations for interventions and future research
DISTAL FACTORS		
Structural and institutional context		
Economic and racial residential segregation measured by the Index of Concentration at the Extremes (ICE)[28]	• Structural barriers to accessing appropriate medical information, resources, and facilities. • Structural factors are upstream impacts on patient social needs (e.g., housing and food insecurity).	• Incorporate comprehensive measures of structural and institutional racism, covering multiple levels (e.g., policies, individual behavior, internalized racism) and dimensions (e.g., wealth, housing, healthcare) of structural racism. • Recognizing and examining structural racism as a fundamental cause of health disparities.[15] • In clinical settings, address conscious and unconscious bias.
INTERMEDIATE FACTORS		
Social context		
Neighborhood Socioeconomic Status (nSES) measured by Yost and Yang scores[33–35,40] Area Deprivation Index (ADI)[41]	• Deleterious effects: limited economic and social opportunities and resources for accessing adequate treatment.	• Besides socioeconomic status, examine other aspects of social context like racial and ethnic composition, social capital, social isolation, religious and civic participation.
Median household income[6,37,38] Education level[39] Residential poverty[36]	• Beneficial effects: community support, self-efficacy, ethnicspecific and in-language resources.	• Assess interactions of patient-level sociodemographic factors and contextual factors (e.g., in-dividual SES and nSES). • In clinical settings, support models of care that consider social risk.[117]
Physical context		
Environmental exposure to ozone, diesel, $PM_{2.5}$, NO_2, cadmium, arsenic, water pollutant emissions, asbestos, emissions from industrial plants[40,50–52,54–60] Environmental Quality Index (EQI), air, water, land, built environment and sociodemographic domains[53] Rural-Urban Continuum Codes (RUCC) and Rural Urban Commuting Area codes (RUCA)[12,74,75,107] Urban/rural designation[39]	• Environmental exposures may lead to carcinogenesis. • Treatment access, effectiveness, and survival may be impacted by community disadvantage or environmental quality • Limited opportunities and resources in rural areas for accessing adequate treatment and follow-up. • Barriers to cancer treatment due to longer travel times.	• Collect data to evaluate suggestive associations of community disadvantage, air pollution, and other markers of poor environmental quality with ovarian cancer survival. • Collect data on environmental exposures (e.g., cadmium, water quality, asbestos, and emissions from industrial plants) that have not been studied in relation to ovarian cancer survival. • Explore the mechanisms through which environmental exposures affect ovarian cancer progression. • Leverage current approaches in geospatial sciences like mixture modeling approaches to account for joint effects of multiple environmental exposures. • Examine particular attributes of rural areas that are associated with access to care, receipt of guideline treatment, and survival. • Jointly consider geographic, racial and ethnic, and socioeconomic disparities when looking at the association between environmental exposures and ovarian cancer survival. • In clinical settings, partner with disadvantaged communities and improve navigation to services,[117] utilize telemedicine where appropriate.
DISTAL & INTERMEDIATE FACTORS		
Healthcare context		
Affordability (dual enrollment in Medicaid, tract-level SES, and county-level health insurance coverage),	• Low availability and access to specialized cancer facilities and gynecologic oncologists	• Leverage current approaches in geospatial sciences, including using measures at appropriate geographic scales (e.g., census block groups or tracts when measuring

Measure	Clinical implications	Recommendations for interventions and future research
accessibility (straight-line distance between patient and hospital ZIP Code centroids), availability (facility-level metrics)[81] Distance to a hospital with gynecologic oncologist[105], to high-volume facility[118], to treatment center[39], to closest high-quality-of-care hospitals[110] Geographic variation by state and gynecologist to population ratio in a county[107], by SEER region[109], by Hospital Referral Regions (HRR)[106] Health system characteristics of the Hospital Referral Regions (HRR)[108] Geosocial vulnerability defined by geospatial access to gynecologic oncologist clinics and sociodemographic characteristics (% residents 65 and older, poverty level, absence of a high school diploma)[86]	can result in non-guideline concordant treatment.	neighborhoods), applying geospatial regression modeling, and using the most current geographic accessibility measures that account jointly for availability and proximity. • Examine other contributing factors (e.g., built and social environment) exacerbating or mitigating deleterious effects of low availability and access of ovarian cancer specialists. • In clinical settings, same measures as above can be applied: partnering with disadvantaged communities, improving navigation to services,[117] utilizing telemedicine where appropriate.