THE INTERPLAY BETWEEN SOCIAL DETERMINANTS OF HEALTH AND CANCER RELATED HEALTH DISPARITIES

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THE INTERPLAY BETWEEN SOCIAL DETERMINANTS OF HEALTH AND CANCER RELATED HEALTH DISPARITIES

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EDITORIAL
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Editorial: The Interplay Between Social Determinants of Health and Cancer Related Health Disparities

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Keywords: cancer, health disparities, social determinants of health, cancer inequalities, cancer prevention and control

Editorial on the Research Topic

The Interplay Between Social Determinants of Health and Cancer Related Health Disparities

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Cancer is the second leading cause of death among adults in the United States. Since the initiation of the "War on Cancer" by Richard Nixon in 1971, advancements in cancer screening modalities and treatment approaches have resulted in marked improvements in cancer-related outcomes. However, not all groups have benefitted equally from advancements in the diagnosis and treatment of cancer. Indeed, we see persistent inequalities across the cancer care continuum, including prevention, screening, diagnosis, treatment, survivorship, and end-of-life care. Population groups at elevated risk for cancer inequalities include socioeconomically disadvantaged populations, underserved rural populations, racial/ethnic, and sexual and gender minorities. Against this backdrop, President Barak Obama signed into legislation the Cancer Moonshot initiative, which aimed to reduce cancer inequalities by making more therapies available to more patients and improving cancer prevention and early detection efforts. In recent years, emphasis has been placed on understanding and addressing the role of social determinants of health (SDOH) on cancer-related health disparities. A better understanding of SDOH can provide researchers and health professionals with effective strategies for reducing cancer-related health disparities and promoting cancer prevention and control.

The World Health Organization's Commission on the Social Determinants of Health has defined SDOH as factors in which people are born, grow, work, live, and age, and the broader set of forces and systems shaping the conditions of daily life that influence health outcomes (1). An extensive body of research has demonstrated that SDOH have an important influence on health inequities (2). Research, guided by multilevel approaches (e.g., the social-ecological model), has started to be conducted which examines the relationships between SDOH (e.g., income, education, health knowledge and behavior, access to health care, housing, poverty, neighborhood safety, economic stability, political conditions) and cancer-related health disparities (3–5). In this Research Topic of Frontiers in Public Health, "*The Interplay Between Social Determinants of Health and Cancer Related* Health Disparities," we solicited articles reviewing and addressing the role of social determinants of health in cancer-related health disparities to give readers an overview of updated health disparities information for their potential use in cancer research and practice. The goal of the Research Topic was to address cancer-related disparities with multilevel approaches, measurable outcomes, and effective solutions focused on innovative and effective strategies to understand the impact of SDOH or improve cancer-related outcomes in diverse populations.

This Research Topic collected 12 studies examining the relationship between SDOH and cancer prevention, treatment, survivorship, and disparities. The majority of research focused on the analyses of individual-level SDOH (e.g., race, gender, marital status, income, insurance, health risk behaviors), followed by community-level (e.g., proximity to care, neighborhood poverty), and interpersonal-level (e.g., social support) SDOH. Several studies incorporated multi-dimensional SDOH at the individual, interpersonal, and community levels in the analysis to better understand cancer-related outcomes and disparities. The findings from the collected articles are summarized as follows.

First, two studies examined the relationship of individual-level SDOH on health outcomes and survivorship among cancer survivors by analyzing national representative datasets. Su et al. analyzed the Behavioral Risk Factor Surveillance System survey data. Results showed that lower family income was associated with cancer survivors' poor mental and physical health. Ishino et al. analyzed survivorship outcomes among colorectal cancer patients using SEER data. Older age at diagnosis, female, widowed, and non-Hispanic White with localized staging were associated with the lowest survivorship class.

Second, two studies examined the influence of individual and community-level SDOH on receipt of cancer-related surgery and treatment. Hu et al. analyzing the Surveillance, Epidemiology, and End Results (SEER) data, found higher rates of refusing recommended surgery among Asian/Pacific Islander and African American patients than white patients. Furthermore, racial disparities in the receipt of timely lung cancer surgery were identified among Louisiana patients by Neroda et al.. Black patients were more likely to have delayed surgery than white patients. Other SDOH (insurance, social support, community poverty level) were also associated with receiving timely surgery.

Third, three studies discussed multilevel SDOH associated with cancer screening utilization. Li et al. found that access to care factors (insurance type, proximity to care) were associated with the uptake of low dose computed tomography (LDCT) among screening eligible patients in an academic medical center. Performing multilevel analysis using Swiss nationwide data, Jolidon et al. found that higher income and married women were significantly associated with higher mammography uptake. Beyond individual factors, Tsui et al. found that the health-related social needs assessment (HRSN) could be conducted at the health care organizational level to improve cancer screening utilization in the Chinese American population.

Fourth, other studies focused on identifying the mechanisms by which SDOH contributes to cancer risks, cancer disparities, and the development of cancer prevention strategies. Zhou et al. analyzed the patterns and trends of disease burden and risk factors attributable to ovarian cancer across age, socio-demographic index, regions, and countries in terms of cancer risks. Tseng T-S. et al. indicated that increased cigarette smoking and other risky behaviors (increased sugary drink consumption, spending more time on screens, decreased physical activity time, and sleeping less) were found among African Americans eligible for LDCT screening during the COVID pandemic. Two articles discussed the barriers and facilitators for accessing smoking cession services and treatments in cancer prevention strategies. Tseng T.S. et al. found that geographical distance was a significant predictor of attendance of smoking cessation counseling classes. Shorter traveling distances were associated with more class attendance. Matthews et al. developed a model for developing and implementing smoking cessation interventions via patient health portals for low-income patients to facilitate patient linkage to receive free telephone-based smoking cessation counseling. Lastly, Gehlert et al. use the Critical Race Theory to address breast cancer disparities at the population level with an emphasis on social factors (e.g., race and discriminatory public policies, attitudes toward healthcare by significant others, training for health providers and professionals, availability of preventive services in communities).

Social determinants of health at various levels (individual, interpersonal, community level) have shown impacts on cancer-related health disparities in existing literature. The Centers for Disease Control and Prevention (CDC) have emphasized the SDOH and promoted SDOH data, research, tools for action, programs, and policy to improve health disparities (https://www.cdc.gov/socialdeterminants/index.htm) (6). President Joe Biden's new national goal for the reignited Cancer Moonshot—is to cut today's age-adjusted cancer mortality rates by at least 50% before 2050 (https://www.whitehouse.gov/briefing-room/statements-releases/2022/02/02/fact-sheet-president-biden-reignites-cancer-moonshot-to-end-cancer-as-we-know-it/) (7). National Institute of Health (NIH) supports research on behavioral, biological, and social determinants of health and structural racism and discrimination (https://www.nih.gov/ending-structural-racism/health-equity-research) (8). National Cancer Institute (NCI) starts to unpack Biden's Moonshot 2.0 goal providing new funding opportunities for cancer research in many areas including studies on cancer disparities. The National Cancer Institute has recognized the need of implementing multilevel cancer intervention research to address health disparities and improve population health (9). Several methodological and data analytic challenges of multilevel interventions have been addressed (10). Researchers, institutes, and governments have recognized the importance of integrating social behavioral and biological sciences to effectively and efficiently prevent, detect, and treat cancers (2, 11). To facilitate the adoption of multilevel interventions, it is important for researcher to gain sufficient knowledge on building a multilevel level conceptual framework based on evidence-based theories and models (e.g., theory of planned behavior, socio-ecological model) and develop appropriate study methods (quantitative, qualitative, and mixed methods) and analytical models (e.g., hierarchical modeling) to measure the impact of multilevel interventions on study outcomes (12, 13).

Despite advancements in cancer screening, diagnosis, and treatment, cancer inequalities remain a persistent public health concern in the United States and globally. The papers presented in this Research Topic contribute to the overall literature on cancer inequalities by describing relationships between SDOH and cancer-related outcomes. Further, the studies presented included novel findings regarding the influence of SDOH at multiple levels, which has implications for future research and intervention development. However, additional research is needed to understand the influence of SDOH on diverse communities experiencing cancer inequalities and to identify the pathways by which SDOH impact cancer outcomes to guide the development of strategies to eliminate or reduce cancer-related disparities.

AUTHOR CONTRIBUTIONS

T-ST and C-CL contributed to the study conception and drafted the first manuscript. AM reviewed the manuscript and did the interpretation of the discussion. All authors contributed to editing and revising the manuscript critically and approved the final version of the article to be published.

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A National Study of Colorectal Cancer Survivorship Disparities: A Latent Class Analysis Using SEER (Surveillance, Epidemiology, and End Results) Registries

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Introduction: Long–standing disparities in colorectal cancer (CRC) outcomes and survival between Whites and Blacks have been observed. A person–centered approach using latent class analysis (LCA) is a novel methodology to assess and address CRC health disparities. LCA can overcome statistical challenges from subgroup analyses that would normally impede variable–centered analyses like regression. Aim was to identify risk profiles and differences in malignant CRC survivorship outcomes.

Methods: We conducted an LCA on the Surveillance, Epidemiology, and End Results data from 1975 to 2016 for adults ≥ 18 ($N = 525{,}245$). Sociodemographics used were age, sex/gender, marital status, race, and ethnicity (Hispanic/Latinos) and stage at diagnosis. To select the best fitting model, we employed a comparative approach comparing sample-size adjusted BIC and entropy; which indicates a good separation of classes.

Results: A four–class solution with an entropy of 0.72 was identified as: lowest survivorship, medium-low, medium-high, and highest survivorship. The lowest survivorship class (26% of sample) with a mean survival rate of 53 months had the highest conditional probabilities of being 76–85 years–old at diagnosis, female, widowed, and non-Hispanic White, with a high likelihood with localized staging. The highest survivorship class (53% of sample) with a mean survival rate of 92 months had the highest likelihood of being married, male with localized staging, and a high likelihood of being non-Hispanic White.

Conclusion: The use of a person–centered measure with population-based cancer registries data can help better detect cancer risk subgroups that may otherwise be overlooked.

Keywords: colorectal (colon) cancer, cancer health disparities, latent class analyses, survivorship (public health), person-centered analysis

INTRODUCTION

Colorectal cancer (CRC) remains the third most diagnosed cancer, and the second leading cause of cancer-related death in both men and women in the United States (US) (1). There are an estimated 147,950 new cases and 53,200 deaths expected in 2020, accounting for 8.4% of all cancer deaths (1, 2). Despite the current estimates, CRC incidence and mortality rates have been decreasing overall since 2000 (1, 3), while incidence rates among adults aged ≤50 years have increased since the mid-1990s (3–5). The reasons for the decline in CRC incidence and mortality rates include advancements in biomedical sciences, leading to early detection and diagnosis, as well as improved treatment, increased screening outreach on a population basis, and adherence to interventions on behavioral lifestyle risk factors like smoking cessation (1, 3).

Regardless of the decline in CRC incidence, mortality, and survival, geographical and racial/ethnic disparities persist (1, 3, 6–12). For instance, between 1995 and 2014 the lowest CRC incidence rate was 29.7/100,000 individuals in Utah while the highest was 49.2/100,000 in Kentucky (1). Similarly, CRC mortality rates range from 11.0/100,000 population in Connecticut to 18.3/100,000 population in Mississippi (1). In terms of race/ethnicity, evidence has shown that non-Hispanic Blacks and American Indians/Alaska Natives experience the highest CRC incidence and mortality rates, compared to non-Hispanic Whites (1). Therefore, there is critical need for research to understand these disparities and to inform the development of interventions to reduce/eliminate them.

The stage of CRC diagnosis is important to treatment, recovery, and survival (3). According to the American Cancer Society, the overall 5-year relative rate for localized stage diagnosis is 90%, regional 71%, distant 14%, and all stages combined 63% (13). Modifiable and non-modifiable risk factors, including age, genetics, sedentary lifestyle, and socioeconomic status (SES) have been known to affect CRC development (7, 14–16). Several studies have examined differences in CRC incidence, mortality, and survival by these factors (12, 16–31). Zhang et al. (31) used the Surveillance, Epidemiology, and End Results (SEER) data from 2007 to 2013 to investigate the impact of SES on overall CRC survival. Results revealed that patients with CRC who were non-Hispanic Black, widowed, on Medicaid, and with the lowest education had relatively poor prognoses. However, studies involving the analysis of overall survivorship of patients with CRC in population subgroups in the US are sparse. As such, this exploratory study aimed to identify profiles and determine disparities in malignant CRC survivorship outcomes using SEER 9 cancer registry program incidence databases from 1975 to 2016. The findings will help identify heterogenous, mutually exclusive profiles and provide important information about how interventions should be tailored to different subpopulations.

MATERIALS AND METHODS

Source and Study Population

This study used data from the SEER database of the National Cancer Institute. The SEER 9 covers ∼10% of the US population with data from nine cancer registries in the states of Georgia (Atlanta), Connecticut, Michigan (Detroit), Hawaii, Iowa, New Mexico, California (San Francisco), Washington (Seattle-Puget Sound), and Utah (32). Patients included in this study were non-Hispanic Blacks and Whites age ≥18 years diagnosed from 1975 through 2016 with malignant, histologically confirmed primary colon and rectal cancer under the International Classification of Diseases for Oncology, Third Edition (ICD-O-3) histology and behavior code. This study was exploratory and not designed to be diagnostic in nature.

Latent Class Analysis

We used latent class analysis (LCA), a person-centered approach, to identify latent or hidden profiles in data. LCA transitions us from variable-centered approaches that examine relationships between variables to a person-centered context in which we can further identify subgroups of risk by profile. We conducted an LCA on SEER 9 data to identify and assess differences in CRC survivorship by observed indicators of sociodemographic factors and derived cancer stage. Observed indicators within the profiles were assessed as conditional probabilities, i.e., likelihood of each indicator being present within the profile with all other indicators present. The distal outcome of survivorship was a continuous measure of survival in total number of months from cancer diagnosis until recorded all-cause death. An automatic Bolck, Croon, and Hagenaars (BCH) method in our LCA was used to account for the distal continuous outcome of survivorship and assess mean differences by profile identified. This approach minimizes bias as algorithms, not the researcher, identify profiles based on observed indicators and survivorship.

Observed indicators from patient sociodemographic characteristics included in our LCA were age, sex/gender, race, Hispanic/Latino origin, and marital status. Age at diagnosis was categorized using the US Preventive Service Task Force screening age recommendation (33) (i.e., 18–49; 50–75; 76–85; 85 and older). Sex/gender was based on dichotomous male or female categories, and race was made into three categories. The first two racial categories included individuals that self-identified as either White or Black. The third racial category, Other race, was a combination of participants that self-identified as American Indian/Alaska Natives and Asian or Pacific Islanders, based on the SEER race recode changes (34). We included Hispanic/Latino as a dichotomous yes or no category based on North American Association of Central Cancer Registries Hispanic Identification Algorithm (35). Marital status was categorized as single/never married; married/common law; divorced/separated; and widow/widower. The derived stage of CRC was categorized as localized, regional, or distant.

Model Fit Assessment for Latent Class Analysis

Multiple models were created based on number of classes (i.e., 1-, 2-, 3-, 4-, 5-class solutions) and compared using the following criteria: (1) entropy [i.e., the acceptable quality of classification and indication of good separation of classes]; (2) Bayesian information criterion (BIC) and sample-size-adjusted BIC (ssa-BIC); and (3) theoretical implications (36). This comparative approach allowed us to select our final model for interpretation based on high entropy, as well as parsimony assessed *via* BIC, ssa-BIC, and practical application. All statistical analyses were conducted using Mplus 8.4 (Muthén and Muthén).

RESULTS

Sociodemographic Characteristics

A total of 525,245 patients with malignant CRC were included. Of these patients, a little over half were males (50.4%), aged 50–75 years (57%), and married (57%) at the time of CRC diagnosis. Most of the patients were non-Hispanic White (83.5%) with localized stage disease (41%). The mean survival time from CRC diagnosis was 77.3 ± SE months [SE = 0.123, 95% CI: 77.1–77.6] (**Table 1**).

Patients' risk profiles/survival subgroups were identified using LCA model fit assessment (**Table 2**). The best model fit selected was a four-class solution that had a low ssa-BIC (4,662,336.8) and an entropy of 0.72, which indicated a clear separation of classes or profiles. The classes were named by relative survival in months from CRC diagnosis until death from all-cause mortality.

Latent Class Analysis Subgroups/Profiles of Survivorship

Class 1, or the lowest survivorship group (26% of sample), had ∼53 months of survival from diagnosis. The lowest survival group had the highest conditional probabilities of being 76–85 years old at time of diagnosis (43.8%), female (78.9%), and widowed (85.2%) and had a high likelihood of being White

TABLE 2 | Latent class analysis model fit assessment (*N* = 525,245).

Class	BIC	SSA-BIC	Entropy
1-Class Solution	4831811.6	4831773.4	–
2-Class Solution	4687966.2	4687886.7	0.88
3-Class Solution	4667251.0	4667130.3	0.65
4-Class Solution	4662498.8	4662336.8	0.72
5-Class Solution	4659145.0	4658941.6	0.68

AIC, Akaike Information Criterion; BIC, Bayesian Information Criterion; SSA-BIC, Sample-Size Adjusted Bayesian Information Criterion.

TABLE 1 | Sample demographic characteristics (*N* = 525,245).

	N	%
Age at diagnosis		
18–49	41,926	8.0
50–75	298,295	56.8
76–85	134,292	25.6
≥86	50,493	9.6
Sex		
Male	264,853	50.4
Female	260,392	49.6
Race		
White	436,947	83.5
Black	47,912	9.1
Other	38,708	7.4
Hispanic/latino		
No	502,892	95.7
Yes	22,353	4.3
Marital status		
Single/never married	54,264	10.8
Married/common law	286,518	57.0
Separated/divorce	44,127	8.8
Widow/widower	117,898	23.4
Derived staging		
Localized	199,057	41.5
Regional	182,007	37.9
Distant	98,854	20.6

	M	SE	95% CI	
			Lower	Upper
Survival in months	77.3	0.123	77.1	77.6

M, Months; SE, Standard Error; CI, Confidence Interval.

(86.8%). This subgroup had the highest conditional probability of having malignant localized stage disease (40.8%).

Class 2, or the medium-low survivorship group (3% of sample), had 71.7 months of survival from diagnosis until death (**Table 3**). This subgroup had the highest conditional probabilities of being White (99%), Hispanic/Latino (100%) and male (58.2%) or female (41.8%). The medium-low survivorship group had high probabilities of being 50–75 years old at the time of diagnosis (66.8%), married (63.3%), and of localized stage CRC (39.3%). In addition, this subgroup had the second highest probability of regional stage malignant CRC diagnosis (38%).

The Class 3, or medium-high survivorship group represents 17% of the study sample (**Table 3**). The Class 3 group also had 73.5 months of survival since diagnosis with the highest conditional probabilities of being 50–75 (71.0%) years at diagnosis, single/never married (31.1%), divorced/separated (22.3%), and Black (25.7%). This group also had an almost equal probability of being male (52.3%) or female (48.7%) with distant stage disease (28.1%).

The last risk profile subgroup identified in our LCA is Class 4, or the highest survivorship group (53% of sample), with 91.7 months of survival from diagnosis (**Table 3**). This subgroup had the highest conditional probabilities of being male (65.1%), married/common law marriage (91.7%), and localized stage CRC diagnosis (44.3%). Class 4 had high probabilities of being between 50 and 75 years old (64.6%) and non-Hispanic White (88.1%). The highest survivorship group also had the lowest conditional probability of distant stage disease (17.9%). See **Table 3** for detailed mean survivorship and conditional probabilities.

Equity test of survivorship means across classes using the automatic BCH procedure with 3 degrees of freedom for overall test was found significant ($x^2 = 17587.5$, $p < 0.001$; see **Table 4**). That is, mean survivorship was significantly different between profiles.

DISCUSSION

This study used LCA, a person-centered method, to identify profiles of survivorship among patients with malignant CRC in a large population-based SEER cancer registry. This analysis of more than 525,000 patients with CRC diagnosed between 1975 and 2016 found heterogenous profiles by survivorship, age at diagnosis, sex/gender, race, ethnicity, marital status, and cancer derived staging. Four profiles of CRC survivorship were identified: lowest survivorship (53.0 months), medium-low survivorship (71.7 months), medium-high survivorship (73.5 months), and highest survivorship (91.7 months).

We identified that the highest survivorship profile (91.7 months; Class 4) had the highest conditional likelihoods of being married and diagnosed with localized disease, followed by a high likelihood of being 50–75 years of age, White, and male. The lowest survivorship profile (Class 1) with 53.0 months from diagnosis to death had the highest likelihoods of being female, widowed, older (i.e., 76–85 years of age), and with regional disease. The lowest survivorship profile also had the second highest likelihood of localized disease when compared to the highest survivorship profile. As such, marital status and sex/gender had the greatest disparity in survivorship. These findings were consistent with Aizer et al. (37), Jin et al. (38), Johansen et al. (39), Li et al. (40), and Wang et al. (41) who reported that married patients with cancer were less likely to present with CRC metastasis and survived significantly longer, compared to unmarried and widowed patients.

The profile identified with medium-low survivorship was found to be exclusively Hispanic/Latino and had the second highest likelihoods of being diagnosed at a distant stage and of being between 50 and 75 years. While the medium-low profile also had the second highest likelihood of being married (63%) when compared to all other profiles, it also had the second highest likelihoods of being single/never married and divorced/separated. The medium-high survivorship profile had the highest likelihood of being Black when compared to all other profiles. This profile also had the highest likelihoods of being single/never married and divorced/separated. Our findings revealed that disparities in CRC survival outcomes may not be attributable to race/ethnicity alone, but to other factors related to marital status for both males and females. Studying the impact of marriage on CRC stage at diagnosis and survival using SEER dataset, Li et al. (40) found that CRC cause specific survival among the married group was almost 70% compared to the never married (59%), divorced/separated/widowed groups (60%). The reason for these disparities are attributed to higher rates of depression, anxiety, medication non-adherence, and negative emotions among widowed patients (42–44).

Overall, while disparities in CRC mortality and survivorship have been found in prior studies, our study has expanded the limited literature concerning CRC disparities using a person-centered approach. We have identified four heterogenous survivorship profiles that are affected by multiple interacting factors, not just by racial/ethnic categories. While prior studies have found associations in CRC incidence and survival by race/ethnicity and age group (5, 20, 21, 45–48), these associations have been found to vary by database. For instance, Gabriel et al. (20) used the National Cancer Data Base (NCDB) from 2006 to 2012 to analyze CRC differences in demographic and pathologic factors with age related rates and overall survival. Results indicated disparities in overall survival, but African American and Hispanic/Latino patients aged ≤50 years experienced increased morality (20). In contrast, Murphy et al. (5) investigated CRC incidence and relative survival using SEER 13 registries data (1992–2014) among younger adults, aged ≤50, and found that while absolute CRC incidence was higher for Blacks than Whites, Blacks experienced a slightly higher 5-year relative survivorship improvement with colon cancer, and increased survival with rectal cancer (i.e., from 55.5 to 70.8%) (5).

Racial and ethnic health disparities have long been associated with CRC disparities, with many persisting if not worsening and shifting the burden of morbidity and mortality to other medically underserved and underrepresented groups. Our exploratory, person-centered study identified racial/ethnic CRC disparities in survivorship among CRC patients. By identifying the unique and inextricable context of racial/ethnic groups that may play a critical role in disease progression may also play a role

TABLE 3 | Latent class analysis of survivability rates among invasive CRC patients ($N = 525{,}245$).

	Class 1	**Class 2**	**Class 3**	**Class 4**
	Lowest survivorship	**Medium-low survivorship**	**Medium-high survivorship**	**Highest survivorship**
	138,458	**17,438**	**89,547**	**279,802**
	26%	**3%**	**17%**	**53%**
Age at diagnosis				
18 - 49	0.000	0.204	0.220	0.0610
50 - 75	0.305	0.668	0.710	0.646
76 - 85	0.438	0.110	0.067	0.241
≥ 86	0.257	0.018	0.003	0.052
Sex/Gender				
Male	0.211	0.582	0.513	0.651
Female	0.789	0.418	0.487	0.349
Marital Status				
Single/Never Married	0.074	0.203	0.311	0.043
Married/Common Law	0.000	0.633	0.436	0.917
Divorced/Separated	0.075	0.137	0.223	0.040
Widow/Widower	0.852	0.030	0.030	0.000
Race				
White	0.868	0.990	0.647	0.881
Black	0.082	0.000	0.257	0.038
Other	0.05	0.010	0.096	0.081
Hispanic				
No	0.972	0.000	0.993	0.986
Yes	0.028	1.0000	0.007	0.014
Derived Staging				
Localized	0.408	0.393	0.353	0.443
Regional	0.390	0.380	0.366	0.379
Distant	0.202	0.227	0.281	0.179
Survival in Months	52.959 (0.196)	71.741 (0.859)	73.497 (0.475)	91.700 (0.236)

**Color gradient indicates the conditional probabilities ranging from 0 in green to 30% in orange to 60% in lavender to 100% in violet. SE, Standard Error.*

in efficiently and efficaciously addressing CRC disparities. For instance, we found that the medium-low and medium-high survivorship profiles had the highest likelihoods to belonging to an ethnic/racial minority (Hispanic or non-Hispanic Black, respectively). We observed, however, that in these profiles there were increased likelihoods of being single/never married or divorced/separated. Additionally, these profiles had a decreased likelihood of being diagnosed at a localized stage; especially, when compared to the lowest and highest survivorship profiles that were primarily racially White and non-Hispanic. Epidemiological studies have previously found that minority and underserved populations, like that of US Blacks, have worse CRC prognoses compared to Whites (1, 3–5, 7), with only few studies reporting no significant difference (49, 50).

Our findings revealed that racial/ethnic disparities in the context of available sociodemographic characteristics have heterogenous profiles of survivorship based on race/ethnicity but nuanced by marital status. While cancer registries are expanding data collection to discern risk factors for cancer incidence, prevalence, and outcomes, marital status may be a more reliable indicator for survivorship in the absence of available contextual risk factors. For instance, in a Tennessee cancer registry study by Montiel Ishino et al. (51), among patients with malignant CRC, White widowed women were found to have the greatest likelihood of delay for CRC surgical treatment followed by Blacks regardless of health insurance status when compared to White married men, i.e., the profile with the lowest likelihood of surgical treatment delay. Black patients were also more likely to be single/never married or divorced/separated, with a lower likelihood of delayed surgical treatment, than White widowed women. However, they had a higher likelihood of delay when compared to White married men (51).

Our LCA study is among the first to differentiate between profiles using the distal continuous outcome of survivorship. Policy-level and public health recommendations, as well as clinical implications, can be garnered from our exploratory, person-centered analysis and findings. Considerations should be given to improved data collection at cancer registries to

TABLE 4 | Equity test survivorship means across classes using BCH procedure with 3 degrees of freedom for overall test ($N = 525,245$).

	Chi-square	*p*-value
Overall test	17587.5	0.000
Class 1 vs. 2	449.3	0.000
Class 1 vs. 3	1477.5	0.000
Class 1 vs. 4	15946.4	0.000
Class 2 vs. 3	3.2	0.000
Class 2 vs. 4	486.4	0.000
Class 3 vs. 4	861.9	0.000

BCH, Bolck, Croon, and Hagenaars; DF, Degrees of Freedom.

enhance risk assessments. In this manner, CRC interventional studies can be designed by leveraging large datasets such as SEER that are publicly available to better tailor interventions and prevention programs. Using person-centered methods, we can move beyond associations between variables to examine the context of variables among subpopulations. By using these person-centered approaches, we can better approximate CRC patient profiles to identify the most salient factors within profiles and prioritize care and access at a clinical level. In this manner we can better promote and tailor screenings and intervene upon factors related to decreased survivorship among CRC patient subpopulations. For instance, while CRC screening interventions are in place, the role of marital status must be further examined within the scope of these interventions to understand the direct and indirect effects it has on survivorship. Furthermore, indicators such as SES, access to quality care and provider expertise must also be assessed to truly capture a person-centered, multilevel context. However, these factors were not available in the SEER 9 database. Geographic and ecological data would have made the person-centered context much richer by including socioeconomic status (e.g., family income; education) and environmental exposures (e.g., tobacco smoke; pollutants).

Our findings indicated that derived stage of CRC alone may not be sufficient to predict CRC survival outcomes, but rather it is a constellation of social determinants. It is, therefore, crucial that while we focus on the social determinants of health in understanding cancer disparities that we contextually examine risk factors that interact at the person-level to mitigate subpopulation disparities and promote health equity. The relationship between race and cancer survival is a complex one (52, 53). Several interacting factors including tumor type, grade, stage, comorbidities, access to healthcare/quality services, provider expertise, and SES are known to confound this relationship and contribute to these disparities (1, 3, 15, 46). Regardless, our LCA, using a distal continuous outcome of survivorship, provides a proof of concept to identify the complex context of CRC associated variables to account for multiple complex interactions on possible risk profiles. Future research directions would explore the effects of race/ethnicity, social support, and cancer staging to understand the complex and dynamic interaction of multiple determinants of health and cancer health disparities. We would then examine the protective and risk factors that may be associated with marital status, in addition to how psychological characteristics correlate with survivorship.

Limitations

This study adds to the current literature by identifying how CRC survival outcome disparities exist using a large population-based SEER database, as well as differentiating between profiles to demarcate the extent of the disparity. Nonetheless, a number of limitations should be addressed. The first is the level of representativeness to generalize findings to the US population, although the sample is very large. SEER datasets primarily include data from White individuals in urban metro areas. Second, SEER registries do not collect SES variables such as income, education, employment, health insurance status, as well as quality of healthcare patients received. In addition, some sociodemographic variables reported may be inaccurate. For example, marital status is only collected at the time of diagnosis. Individuals whose status changed are never updated and other environmental factors are also not available. Despite these limitations, the SEER program has a reputation of reporting long-term, high quality incidence, prevalence, and survival data (3). Currently, the program covers over 28% of the US population, which serves as a major data source for cancer stage distribution, stage-specific survival, and lifetime incidence of developing cancer (54).

Conclusions

The use of a person–centered measures such as LCA with population-based cancer registry data can help better detect cancer risk subgroups that may otherwise be overlooked. This study identified four risk subgroups: lowest, medium-low, medium-high, and highest survivorship subgroups. Of interest is the fact that racial or sociodemographic disparities alone do not account for differences in invasive CRC survival. Hence, this study revealed that Whites have almost equal chances of both good and poor CRC prognosis while Blacks continue to experience worse outcomes. Females, Hispanics, and widowed patients have poorer survival outcomes among the risk profiles/subgroup identified in this study. Thus, in developing tailored interventions for CRC, these high-risk subgroup populations should be considered in order to improve malignant CRC survivorship.

DATA AVAILABILITY STATEMENT

Publicly available datasets were analyzed in this study. These data can be found at: https://seer.cancer.gov/data-software/.

AUTHOR CONTRIBUTIONS

FM: conceptualization, methodology, software, formal analysis, writing-original draft preparation, and visualization. EO: writing-original draft preparation and writing-review and editing. KV: writing-review and editing, software, and validation. XL: software, data curation, and validation. BS:

data curation and writing-review and editing. HM: supervision and writing-reviewing and editing. FW: project administration, supervision, resources, and writing-reviewing and editing. All authors: contributed to the article and approved the submitted version.

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A Critical Theoretical Approach to Cancer Disparities: Breast Cancer and the Social Determinants of Health

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Breast cancer is the most commonly experienced cancer among women. Its high rates of incidence and survival mean that a number of women will live it for periods of their lifetimes. Group differences in breast cancer incidence and mortality occur by race and ethnicity. For example, while white women are slightly more likely to be diagnosed with breast cancer, Black women are 40% more likely to die from the disease. In this article, rather than focusing the discussion on individual-level factors like health behaviors that have the potential to blame Black women and those living in poverty for their conditions, we view breast cancer disparities through the lens of Critical Race Theory, taking a historical perspective. This allows us to delve beyond individual risk factors to explore social determinants of breast cancer disparities at the population level, paying special attention to the myriad ways in which social factors, notably views of race and discriminatory public policies, over time have contributed to the disproportionate breast cancer mortality experienced by Black women. We suggest ways of addressing breast cancer disparities, including methods of training healthcare professionals and public policy directions, that include rather than marginalize Black and lower socioeconomic status women.

Keywords: cancer, breast, social determinants, poverty, race, health disparities

INTRODUCTION

The term "cancer" refers to a group of diseases sharing significant characteristics such as the rapid proliferation of cells. Yet this group of diseases, referred to as cancer types, varies in a number of ways that affect their impact on individuals experiencing them and their social networks and communities. Because cancer types vary by site of origin (e.g., prostate, breast, colon, pancreas, and blood), require more or less demanding and costly treatment approaches, and have markedly different incidence, mortality, and survival rates, it is problematical to consider cancer as a single entity in determining how it affects, and is affected by, an individual's social circumstances. In the following manuscript, we focus on breast cancer, the most commonly experienced cancer among women worldwide. According to the National Cancer Institute, 279,100 women were diagnosed with breast cancer in the United States in 2020, making it an area worthy of attention (1).

Prevention and treatment of cancer depend on knowledge of its determinants and their interplay. Arguably, social determinants have received less attention than have genetics and individual health behaviors. After briefly outlining what is known about the social determinants of breast cancer disparities and drawing on salient theory, we provide our perspective on the social contributors to disparities. We suggest new directions for the training of healthcare professionals and new approaches to public policy to reduce breast cancer disparities.

BACKGROUND

Breast cancer is the most common cancer and the second highest cause of cancer death among women, exceeded only by lung cancer. Although it has among the highest 5-year rates of survival among cancers (90%, compared to 47% for ovarian cancer and 10% for cancer of the pancreas), it nonetheless affects a very high percentage of women. According to the National Cancer Institute, one in eight women, or 12.9% of all women, will develop breast cancer at some point in their lifetimes (2). The combination of high rates of survival and high rates of incidence means that a number of women will live with breast cancer for significant periods of their lives.

Differences in incidence, mortality, and survival occur by race and ethnicity. The National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) program and the Centers for Disease Control and Prevention's National Program of Cancer Registries have followed incidence and survival trends by Black and white race since 1975, with data on Asian/Pacific Islander, Hispanic/Latina, and American Indian/Alaska Native subpopulations added in 1990. Yet, studies of incidence and mortality have principally focused on race alone (i.e., without also considering ethnicity), and have found marked differences in both incidence and mortality.

DeSantis et al. analyzed SEER incidence data on breast cancer from 2012 to 2016 and SEER mortality data from 2013 to 2017 (3). They found that incidence rates were highest among white women (130.8 per 100,000), followed closely by Black women (126.7 per 100,000). Incidence was lowest among Asian/Pacific Islander women at 93.2 per 100,000. The picture differs for breast cancer mortality, in which the rates for Black women are 40% higher than those of white women (28.4 per 100,000 and 20.3 per 100,000, respectively), and both higher than other groups. The rates for Asian/Pacific Islander women, for example, were lower than those of either white or Black women (11.5 per 100,000).

When age is considered, additional differences between Black and white women emerge. Black and white differences in breast cancer mortality are most pronounced at younger ages and begin to converge later in life. Black women 50 years of age and younger, for example, are 1.9–2.6 times more likely to die from breast cancer than white women of the same age, yet they are only 1.1–1.2 times more likely to die from the disease at 70 years of age or older (3).

Mortality differences by age have in part been attributed to differences in the proportions of breast cancer molecular subtypes experienced (4). This is because mortality rates differ across breast cancer subtypes. For example, HR-positive/HER2 negative (hormone receptor-positive and human epidermal growth factor receptor 2) breast cancers, which have the most favorable outcomes, are 23% higher in white women over the age of 20 years than Black women of the same ages, and 45% higher than in Hispanic and American Indian/Alaska Native women of those ages. The triple-negative breast cancer (ER-negative, PR-negative, and HER2-negative) subtype, for which outcomes are the least favorable, is more common among Black women 50 years of age and younger. Thus, there is an interplay between race, age, and breast cancer subtype. Yet, this does not explain the mortality differences between Black and white women.

More recent efforts that have considered both ethnicity and race have yielded a more nuanced picture that may shed some additional light on disparities. Davis-Lynn and colleagues used SEER data to examine trends for non-Hispanic women vs. Hispanic women (5). The authors found that while Black and white women's incidence rates began to converge in 2012, the picture differs somewhat when ethnicity is added to analyses. In their study, incidence rates were highest for non-Hispanic white women and lowest for Hispanic white women, with non-Hispanic Black women's rates in between the two. This split between non-Hispanic and Hispanic white women, with non-Hispanic Black women between the two, provides additional nuance to our understanding of how race and ethnicity contribute to breast cancer disparities.

SOCIAL DETERMINANTS AND BREAST CANCER

In addition to the effects of age and molecular effects, it is now widely recognized that social determinants of health such as racism, racial residential segregation, economic hardship, and housing insecurity, drive the production of racial/ethnic health inequities in the United States (6). Further, the United States does not provide universal health insurance to its citizens and residents. Uninsurance and underinsurance have been associated with poorer health outcomes including later disease detection, poor medication adherence and management of chronic illnesses (7). Specifically, lack of health insurance is associated with later stage of breast cancer diagnosis among Black, Indigenous, and Latinx women compared to white women (8). Other structural features of the United States including the implementation of racist policies and practices, such as redlining, contribute to the country remaining deeply segregated by race. Most health-promoting resources, such as access to healthful food options, safe places to recreate, and healthcare, are patterned by race. While an in-depth discussion of the policies and practices that led to the extraordinarily high, deeply entrenched racial residential segregation throughout the country is beyond the scope of this paper, it is important to note that segregation did not occur naturally. Rather, segregation was "by design" (9).

However, the highly impactful, insidious nature of segregation must be underscored (10). Most of the health-promoting resources, both directly and indirectly related to health, are afforded by context. Therefore, many Black Americans reside in neighborhoods that prohibit them from achieving their optimal level of health, including obtaining breast cancer screening and treatment (11). These context inequities are linked to poorer breast cancer outcomes among Black women.

Socioeconomic status (SES), including vital resources such as education, income, and wealth, is another key social determinant of health. For example, researchers have highlighted the overall importance of education, not only health literacy and communicating effectively with providers, but providing access to the higher levels of income and stable employment with benefits. Income is critical in helping individuals to afford their day-to-day needs such as food, housing, and services. More income allows individuals to purchase homes in more desirable, better-resourced neighborhoods. In this way, researchers have described SES as a fundamental cause—allowing individuals to avoid health risks. Employment is also important, especially since most Americans obtain their health insurance through their employer (12). In addition to healthcare insurance, paid time off, and the flexibility in work schedules to take the time to obtain screening or adhere to treatment plans are other critical benefits associated with the types of jobs individuals can access. Because Black women develop breast cancer at a younger age than white women, they are more likely to be diagnosed prior to retirement than white women, and thus to rely on employer-provided health insurance. Otis Brawley tells the poignant story of a young Black woman diagnosed with breast cancer who was the sole provider for her small children (13). She died because although she had health insurance through her employer, she lacked sufficient sick days to accommodate the treatment regimen recommended by her oncologist. Her difficult choice to keep her job to provide for her children cost her life.

In support of the contribution of health insurance to breast cancer mortality, is recent evidence of the effect of Medicaid expansion on rates of screening mammography. Screening mammography is important because if breast cancer is diagnosed early, treatment can begin before cancer cells have proliferated. Toyoda et al. found that mammography screening rates were significantly higher in states that expanded Medicaid than states that did not (14). Le Blanc et al. examined breast cancer stage, race/ethnicity, age, and insurance status using SEER data from 2007 to 2016. This allowed a comparison before and after the 2010 passage of the Affordable Care Act, which gave states the option of expanding Medicaid (15). The authors found that Medicaid expansion was associated with reduced incidence of advanced breast cancer, with Black women and women under 50 years of age achieving the greatest benefit. The incidence rates of Black women in expansion states decreased from 24.6 to 21.6%, compared to 27.4–27.5% in states that did not expand Medicaid (15).

There are policies and practices beyond healthcare that have influenced breast cancer inequities. The cleavages of Jim Crow policies, state and local laws that were adopted to oppress Black Americans and enforce segregation, continue to manifest today, including in breast cancer outcomes. For example, Krieger et al. examined whether breast cancer outcomes differed by birth in a Jim Crow state. They found that Black women who were born in Jim Crow states had poorer breast cancer outcomes, including more aggressive forms of cancer, compared to white women, regardless of their state of birth (16).

Health inequities, such as racial differences in breast cancer mortality, are strongly influenced by neighborhood context, including access to health promotive resources such as full-service grocery stores and safe places to recreate, in addition to preventative healthcare (10). Social environmental stressors, especially chronic exposure to these stressors, play a critical role in racial/ethnic breast cancer inequities. Researchers have documented the extent to which chronic stressors are deleterious to human health through their activation of a cascade of physiological reactions such as the release of hormones. Yet, the same adaptive mechanisms that allow individuals to escape life-threatening situations, such as increased blood pressure, are associated with poor health outcomes when activated chronically. Chronic activation of the physiological stress response system is associated with poor immune system functioning, which could contribute to negative cancer outcomes (17–20).

As technology and analysis tools are refined, researchers are better able to delineate the effects of the social environment on cancer incidence and the social patterning of cancer. For example, scholars have demonstrated the role of epigenetics in the occurrence of cancer and differential vulnerability to cancer across race/ethnicity (21). Epigenetic changes, or those that occur through changes in how genes are expressed rather than through changes in underlying gene sequence, represent a potential route through which the social environment affects physiological responses. Linnenbringer et al. link this to breast cancer mortality disparities by suggesting that weathering (i.e., wearing down over time) of the body's stress response system may contribute to the expression of breast cancer subtypes with less favorable outcomes (22).

It is clear that without addressing the barriers imposed by social determinants of health such as racism, housing stability, and access to quality education, it is highly likely that observed racial disparities in breast cancer will persist, even as screening and treatment improve [(23, 24); see **Figure 1**].

HEALTHCARE INEQUITIES

In addition to the aforementioned social determinants of health, the United States health system presents unique barriers to care as well as deeply entrenched biases based on race, gender, immigration status, among other factors. A seminal study on racial bias in healthcare, *Unequal Treatment: Confronting Racial and Ethnic Disparities in Health Care*, found that racial and ethnic minorities received less than the standard of care across many health conditions, including heart and kidney care and health services including intensive care (25). Racial inequities were found even after controlling for income, insurance status, and age (25). The authors also concluded that provider-side bias and patient mistrust contribute to differences in treatment (25).

More recent studies have found that Black people continue to experience inequities in healthcare treatment, above and beyond those that come from barriers to access. For example, a large body of evidence indicates that Black people are systematically

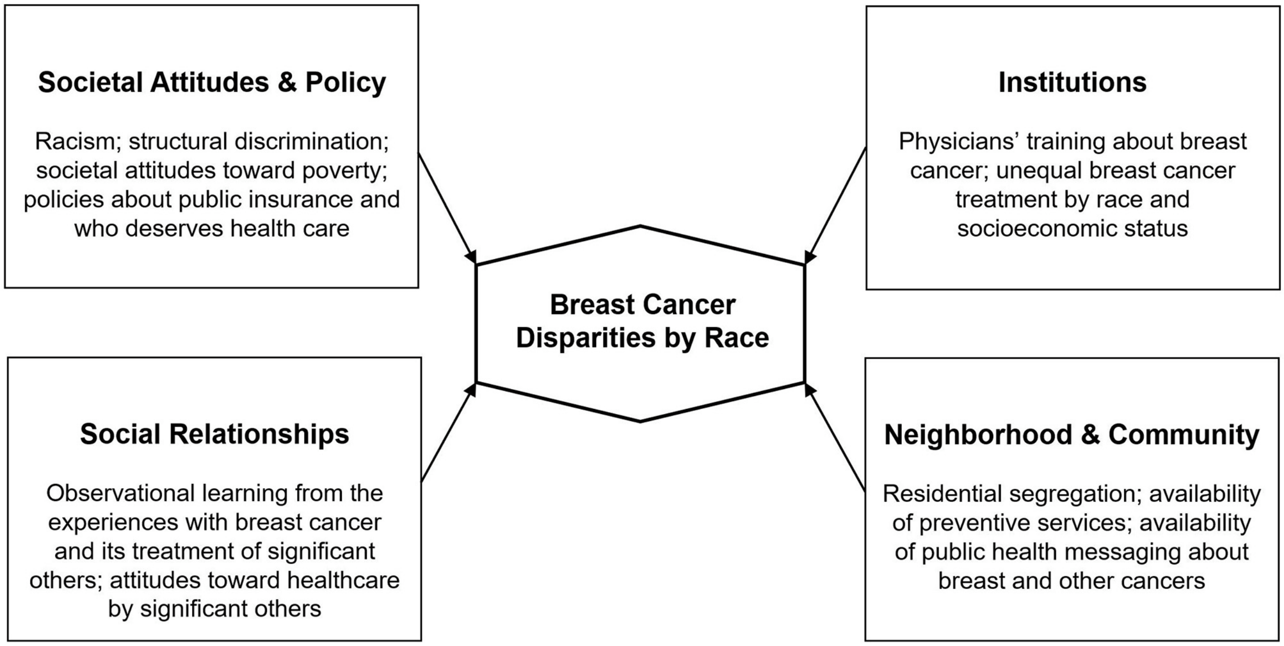

FIGURE 1 | Social factors that influence differential breast cancer disparities by race.

undertreated for pain compared to white people (26, 27). Further, a study of over 400 medical students and residents found that differences in pain management could be explained by the fact that some providers believe Black people are different biologically than white people (26). Hoffman et al. found that a large number of white laypeople, medical students, and residents believe a constellation of erroneous beliefs about Black people's biology including that Black people have thicker skin, fewer nerve endings, and smaller brains. Importantly, these erroneous beliefs predict the accuracy of the providers' pain management recommendations. The study is among the first to demonstrate that false beliefs about biological differences between racial groups directly affect treatment.

Racial and ethnic differences in post-mastectomy pain management have also been found. A study of over 80,000 women who had undergone mastectomies reported Black, Latinx, and Asian women were less likely to receive regional anesthetic techniques, i.e., focused pain relief at the surgical site, than white women (28). This is in spite of the fact that regional anesthetic techniques are increasingly favored for the management of post-mastectomy pain. Pain from treatments, either experienced personally or described by trusted others, may act as a deterrent to participation in screening and treatment.

Breast cancer screening is effective in detecting breast cancer early, thus allowing for earlier treatment to prevent progression (29). Recent evidence using SEER data demonstrates that when factors other than race are controlled for, no significant Black and white differences in screening mammography rates are found (30). The Centers for Disease Control and Prevention (CDC) instead found lower screening rates to be associated with lower educational attainment and income, not having a usual source of care, and being uninsured or having only public health coverage (30). Thus, it seems that Black women being diagnosed later than their white counterparts has more to do with social determinants than with anything inherent in race.

All told, racial and ethnic minorities in general, and Black women in particular, continue to face discrimination and inequities in treatment. Despite findings that indicate that Black women have similar rates of breast cancer screening as white women are more compliant with breast cancer screening recommendations, they are still more likely to experience more aggressive, rapidly advancing cancer compared to white women (31). As a result, mistrust of healthcare providers and medical institutions may be understood as a rational adaptation to a healthcare system that is often implicitly and explicitly hostile to Black people. The research literature suggests Black and Latinx people, including Black women, are less likely than white people to trust their physician, even after controlling for socioeconomic status, health status, and healthcare access (32).

KEY GAPS IN KNOWLEDGE AND ACTION

(Mis)conceptualizing Race

To reduce disparities in breast cancer mortality, cancer researchers and practitioners may benefit from the application of Critical Race Theory (CRT). One tenet of CRT is to examine race as a social factor rather than an immutable biological factor (16, 33, 34). As the aforementioned study by Hoffman notes, erroneous beliefs about innate biological differences between Black and white people contribute to differences in treatment (26). Historians and sociologists of science have demonstrated that much of medical practice rests on long-held, debunked beliefs about the fundamental differences between Black and white bodies. Steven Jay Gould, for example, wrote of the fundamental errors inherent in Morton's 1839 *Crania Americana*, in which Morton filled the crania of skulls with pepper seeds and equated cranial-capacity with intellectual ability. Morton interpreted differences across groups as evidence of the mental superiority of Caucasians (35, 36). In a second example, Lundy Braun relates that during slavery, Black people were believed to have poorer lung capacity compared to white people (37). Importantly, doctors did not consider the profoundly deleterious physical and psychological effects of slavery. Instead, they attributed health problems to the innate biological inferiority of Black people. Based on these false beliefs, modern spirometry meters were created to "correct for race" when no innate biological lung differences actually exist. Racial differences are, however, based on the social determinants of health, not innate physiological differences. However, Chowkwanyun and Reed argue that in spite of a well-documented cross-disciplinary critique of biological explanations of socially determined racial differences, this type of thinking persists in contemporary medical treatment (38).

To address the negative consequences of relying on biological definitions of race, some American medical students have organized to change the nature of medical training. In their report, *Toward the Abolition of Biological Race in Medicine*, Chadha et al. argue that racism, not race, causes health disparities (39). Further, because clinical training relies on biological explanations of racial differences, patients of color are systematically misdiagnosed and undertreated. In this manner, Chadha et al. point out that biological explanations of racial disparities in health fail to address structural discrimination. Brown University medical students have also noted that "preclinical medical curricula inaccurately employ race as a definitive medical category without context, which may perpetuate misunderstanding of race as a bioscientific datum, increase bias among student–doctors, and ultimately contribute to worse patient outcomes" [(40), p. 1]. Importantly, Tsai and colleagues reported that in response to the students' concerns, the medical school changed the curriculum to include a longitudinal race-in-medicine component (40). As such, to improve health and health care outcomes, we must refine medical training to root out both racial bias and the over-reliance on race over racism as a risk factor for illness.

To that end, researchers have begun to reconsider how race and racism should be factored into health disparities research. Increasingly, some scholars emphasize the need to move away from the idea of race as a risk factor for disease, which reifies the notion of race as a matter of biology, while turning to more structural explanations that center the ways racism harms human health (41). Boyd et al. argue that "racism kills. Whether through force, deprivation, or discrimination, it is a fundamental cause of disease and the strange but familiar root of racial health inequities" (41). They also note that despite recent calls to actively acknowledge structural racism as a determinant of health, the majority of health disparities research often defaults to genetic and/or biological explanations of racial differences in health outcomes (41).

Policy Perspectives on Reducing Breast Cancer Disparities

CRT encourages scholars to move beyond the consideration of individual risk factors in the production of disease. Rather, an accurate sociohistorical perspective is necessary to fully understand inequities. Another tenet of CRT is to privilege the voices of marginalized people (16, 33, 34). This is critical in the development of policies that are capable of improving the environmental and social factors that Black women face and fuel inequities in breast cancer outcomes.

Metzl and Hansen have called for extending a structural lens to medical training and practice (42). They define structural competency as "the trained ability to discern how a host of issues defined clinically as symptoms, attitudes, or diseases (e.g., depression, hypertension, obesity, smoking, medication adherence, trauma, and psychosis) also represent the downstream implications of a number of upstream decisions about such matters as health care and food delivery systems, zoning laws, urban and rural infrastructures, medicalization, or even about the very definitions of illness and health" [(42), p. 128]. They also outline five key tenets of training medical providers: (1) recognizing the structures that shape clinical interactions; (2) developing an extra-clinical language of structure; (3) rearticulating "cultural" formulations in structural terms; (4) observing and imagining structural interventions; and, (5) developing structural humility. The authors advocate for helping medical practitioners to understand the ways in which socioeconomic forces contribute to epigenetic changes. This should be integrated with existing medical models to foster pedagogical change.

Given the body of research on weathering and critical periods in the potential development of breast cancer later in life, medical practice and social policy must be aligned to address the temporal, social-emotional, and physical needs of women, particularly ethno-racial minorities. Further, addressing systematic racism must be central to any strategy to reduce racial health disparities including breast cancer. Policy strategies may include: (1) expanding social safety net policies to improve social determinants of health and (2) addressing medical training to include structural competency, which emphasizes structural discrimination as opposed to biological explanations of socially patterned racial differences in health (36).

Based on state-level comparisons on social service expenditures (including cash transfers, food stamp benefits), Bradley and colleagues found that states that spent more on social services had better health outcomes (e.g., adult obesity, lung cancer mortality, mentally unhealthy days, type 2 diabetes) than states that spent less (43). Studies that evaluate the relationship between social spending and health outcomes in OECD (Organization for Economic Cooperation and Development) countries compared to the United States find similar patterns (44).

The above studies suggest that investing in social safety net programs may improve health outcomes overall, particularly for racial and ethnic minorities who are disproportionately represented among people living in poverty. To that end, Newman et al. outline several policy recommendations to mitigate inequities in health that are germane both to cancer disparities and those that have emerged from the current COVID-19 pandemic (45). They argue that a combination of community collaboration, increased racial diversity in clinical trials, expanding health insurance, and increased funding for safety-net hospitals, would go a long way toward mitigating both cancer and COVID-19 racial health inequities.

All told, recent scholarship suggests a move away from individual-level interventions toward more macro-level policy solutions. Conceptualizing cancer disparities at the structural level provides an important framework for moving forward in this vein. It is not until this occurs that we can begin to see health equity.

Dissemination and Implementation

CRT guides scholars to affirm the knowledge of Black people, privileging the voices of those who have experiential knowledge of being marginalized in order to highlight to where interventions should be directed (33). This calls for an intentional consideration of the experiences Black women in order to craft appropriate strategies to redress breast cancer disparities.

One way to facilitate the dissemination of information about breast cancer is to use storytelling and narrative. Qualitative research is a powerful tool to elucidate the barriers that Black women face related to breast cancer screening and treatment seeking (46, 47). Narratives aid in advocacy efforts in a way that is often more powerful than simply displaying data. A broader application of this aspect of CRT is through meaningful community engagement. The principles of community engagement can aid in privileging historically marginalized voices to address racial health inequities (48, 49). For example, by building the capacity of organic social networks that exist within communities and providing linkages between communities and other sectors, such as business and government, communities can gain greater collective efficacy, setting the agendas and goals needed to advocate for needed resources (50).

DISCUSSION

Black-White inequities in breast cancer are well-established. These observed racial inequities are driven more by social, environmental, and economic factors than by biological factors (51, 52). As scholars and practitioners consider ways to narrow Black-white inequities, it is critical to examine the structural factors that are both determinants of breast cancer as well as barriers to screening and care (53). We implore the field to delve deeper, beyond rudimentary "racial" explanations and individual risk factors to consider the broader ecology in which people are embedded. This requires an understanding of the key factors that have shaped their environments, both to reduce victim-blaming and to motivate new solutions to the barriers faced by historically marginalized communities. It is critical that more robust health promotion efforts are developed to promote cancer screening and navigate complex treatment environments. Engaging with a range of communities will help to ensure that health communication messaging and promotion efforts are calibrated to the needs of Black women. Effectively building that knowledge base and crafting appropriate solutions will require amplifying, validating, and incorporating the voices of these communities, all of which are critical to any effective policy or practice change efforts (54).

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author/s.

AUTHOR CONTRIBUTIONS

SG, DH, and TS: conceptualization and writing. All authors contributed to the article and approved the submitted version.

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Health Related Social Needs Among Chinese American Primary Care Patients During the COVID-19 Pandemic: Implications for Cancer Screening and Primary Care

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Research Objective: Initiatives to address social determinants of health (SDOH) and measure health-related social needs (HRSN) within clinic settings are increasing. However, few have focused on the specific needs of Asian Americans (AA). We examine the prevalence of HRSN during a period spanning the COVID-19 pandemic to inform strategies to improve cancer screening and primary care among AA patients.

Methods: We implemented a self-administered HRSN screening tool in English and Chinese, traditional (T) or simplified (S) text, within a hospital-affiliated, outpatient primary care practice predominantly serving AA in New Jersey. HRSN items included food insecurity, transportation barriers, utility needs, interpersonal violence, housing instability, immigration history, and neighborhood perceptions on cohesion and trust. We conducted medical chart reviews for a subset of participants to explore the relationship between HRSN and history of cancer screening.

Results: Among 236 participants, most were Asian (74%), non-US born (79%), and privately insured (57%). One-third responded in Chinese (37%). Half reported having ≥1 HRSN. Interpersonal violence was high across all participants. Transportation needs were highest among Chinese-T participants, while food insecurity and housing instability were highest among Chinese-S participants. Lower-income patients had higher odds of having ≥2 HRSN (OR:2.53, 95% CI: 1.12, 5.98). Older age and public insurance/uninsured were significantly associated with low neighborhood perceptions.

Conclusions: We observed higher than anticipated reports of HRSN among primary care patients in a suburban, hospital-affiliated practice serving AA. Low neighborhood perceptions, particularly among Chinese-S participants, highlight the importance of addressing broader SDOH among insured, suburban AA patients.

These study findings inform the need to augment HRSN identification to adequately address social needs that impact health outcomes and life course experiences for Asian patients. As HRSN measuring efforts continue, and COVID-19's impact on the health of minority communities emerge, it will be critical to develop community-specific referral pathways to connect AA to resources for HRSN and continue to address more upstream social determinants of health for those who are disproportionately impacted.

Keywords: social determinants, social needs, cancer screening, Asian American (AA), primary care, COVID-19

INTRODUCTION

The recognition that social determinants of health and structural barriers drive inequities in health and heath care has long been a central tenet in public health (1–6). However, there is recent focus to address social determinants of health within health care settings (7–17) as a way to reduce higher rates of chronic disease and poorer outcomes among vulnerable patients (18–20). Health related social needs (HRSN), including transportation, food insecurity, housing stability and interpersonal violence which are more downstream factors that impact health care, also result directly in both poorer outcomes and weaker health system performance (17, 21–23). Thus, efforts to systematically collect information on HRSN in clinical settings and develop solutions to address HRSN are on the rise (12, 13, 16, 23–32). Few clinic-based HRSN studies to date, however, have focused on measuring HRSN in languages other than English or Spanish or in diverse immigrant populations, including Asian Americans (AA), where cultural factors and immigration experiences can pose additional barriers to accessing care and routine preventive services (33). Furthermore, AA patients as a group are often masked by small or aggregated numbers and a lack of linguistically appropriate measurement tools within larger health system settings (34–36).

AAs are among the fastest growing populations in the United States (US) and New Jersey ranks third among states having the largest proportion of AA residents (>10%), following California and Hawaii (37, 38). Chinese Americans are the largest AA subgroup and nearly two-thirds of Chinese-Americans are born outside of the US (39). Within New Jersey, Chinese Americans are the second largest AA ethnic group and the majority reside in Northern and Central New Jersey counties (38). Prior data indicate specific AA populations experience higher rates of chronic disease and poorer mental well-being compared to non-minorities (40–44). Many—particularly the elderly – may experience significant emotional or psychosocial distress, lower levels of social engagement (45), and low health literacy (46). Additional socioeconomic and cultural barriers unique to Asian immigrants further contribute to disparities in access to health care, uptake of preventive screenings, and adherence to chronic disease management for AA populations (45, 47, 48). Factors related to trauma and immigration experiences, as well as resilience that is developed through the coping of these life events, can negatively and positively impact their health outcomes (16, 49–53). Perceptions of neighborhood, including social cohesion and trust can also impact health care utilization and outcomes (54, 55). Thus, focusing on improving the measurement of HRSN within clinic settings for AA populations, and providing in-language screening tools for larger population groups, such as Chinese patients, can inform broader health system strategies to address population level unmet social needs.

Cancer inequities among AAs are a prime example of the influence of HRSN on health disparities. Cancer is the first leading cause of death in the US for AAs and the second leading cause of death among other racial/ethnic groups. Breast cancer mortality rates in immigrant AA women are higher compared to US-born counterparts (56). Socioeconomic factors, income, and transportation-related barriers have all been implicated in cancer screening disparities among AA immigrants. Lower rates of cancer screening have been observed in AAs (57), but also specifically in Chinese Americans (46). For example, Chinese Americans have some of the lowest rates of breast and cervical cancer screening among all AA subgroups (58). In New Jersey, rates of colorectal cancer screening were lowest among Asians in 2012–2016 compared to all other racial/ethnic groups (59). Unless targeted efforts are made to develop appropriate HRSN screening tools for AAs within clinic settings, newly implemented tools to address population health and health care disparities, including for cancer, will be limited for AA populations.

This study aims to understand and more accurately assess the prevalence of HSRN and neighborhood perceptions among AA primary care patients, using an adapted HRSN screening tool among patients in a suburban primary care practice in New Jersey. At study initiation, which occurred ∼6 months prior to the COVID-19 pandemic, we hypothesized that a higher proportion of lower-income and more recently immigrated patients would report having HRSN and lower neighborhood perceptions. We examined the relationship between HRSN and neighborhood perceptions on history of prior breast or colorectal cancer screening among age-eligible study participants as an exploratory assessment of the impact of HRSN on preventive care utilization. Given that our study period intersected with the COVID-19 pandemic and associated discrimination against AA communities, we further compared reports of HRSN and neighborhood perceptions between participants recruited before and during the pandemic.

MATERIALS AND METHODS

Study Setting and Target Population

We assessed HRSN, neighborhood perceptions (social cohesion, trust), and immigration characteristics (time since immigration, birthplace) through a cross-sectional survey among established patients at the Center for Asian Health (CAH), an outpatient primary care practice of Saint Barnabas Medical Center, a community hospital in suburban New Jersey belonging to the RWJBarnabas Health system. The Center for Asian Health was started in 2013 with the goal of meeting the healthcare needs of the growing Chinese American population in Northern New Jersey. CAH sees 5,000 patient visits per year with a mix of primary care providers and specialists. In March 2020 when COVID-19 stay-at-home orders began, patients were exclusively seen via telehealth until restrictions eased in June 2020. In-person office visits increased by late July but then were scaled back in Fall 2020 when community COVID-19 transmissions increased again regionally.

Recruitment

This study was approved by the Rutgers Biomedical Health Sciences Institutional Review Board and the Saint Barnabas Medical Center Institutional Review Board. Adult patients age 18 and over who could complete the survey in English or Chinese were approached to participate in the study. New patients and those who could not complete a survey in English or Chinese were excluded. Recruitment occurred between September 2019 and November 2020. Prior to the COVID-19 pandemic (September 2019-March 2020), research team members, including bilingual Mandarin/Cantonese speaking CAH clinic volunteer staff, approached patients in the waiting room to introduce the study components and assess interest in participation. Interested patients were then screened for study eligibility and asked to review and sign a written informed consent form.

Following COVID-19 stay-at-home orders (May 2020-August 2020), CAH patients with telehealth visits were invited to participate in the study through the CAH patient portal or via email. If they agreed, the eligibility screener, consent, and survey were then completed online via REDCap. When in-person primary care visits resumed more broadly during the COVID-19 pandemic (September 2020-November 2020), recruitment via in-person visits was reinitiated, with an additional option of completing the eligibility screener, consent form, and survey at home, either online or via paper/pencil to be mailed back to the clinic.

Survey Administration

The 38-item survey instrument, which took participants ∼10–15 min to complete, was available electronically on iPads in English and Chinese [Chinese-Traditional (T), Chinese-Simplified (S)], for study participants to complete in the waiting room or in the clinic exam room following the in-person enrollment procedures described above. Both Chinese-T and Chinese-S survey language text were made available based on clinic staff and provider input about language needs of the CAH patient population. Paper surveys were available for in-person participants upon request. During the COVID-19 pandemic, participants were provided a survey link via email or the patient portal to complete online at home. Participants who completed the survey received a $10 gift card which was given either in person (if completed in person) or mailed to them (if completed online or via mail).

Survey Measures

The 38-item survey instrument included: health-related social needs screening items, a neighborhood perception scale, and measures used in prior studies to assess immigration experiences, trauma, and sociodemographic factors (60).

Health Related Social Needs

Our HRSN measures were based on the 2016 Centers for Medicare and Medicaid Services (CMS) screening tool for HRSN through CMS Accountable Health Communities (61), which comprised of a ten-item (27, 36, 62–65) HRSN Screening Tool covering the following social needs: housing instability (*"What is your living situation today?"*), food insecurity (2 questions: *"Within the past 12 months, you worried that your food would run out before you got money to buy more;" "Within the past 12 months, the food you bought just didn't last and you didn't have money to get more."*), transportation (*"In the past 12 months, has lack of reliable transportation kept you from medical appointments, meetings, work or from getting to things needed for daily living?"*), utility needs (*"In the past 12 months has the electric, gas, oil, or water company threatened to shut off services in your home?"*), and interpersonal violence (4 questions: *"How often does anyone, including family and friends, physically hurt you?" "How often does anyone, including family and friends, insult or talk down to you?" "How often does anyone, including family and friends, threaten you with harm?" "How often does anyone, including family and friends, scream or curse at you?"*)

We created composite measures for each domain that had more than one question with yes (at least one reported need within the domain) and no (answer no to all questions in the domain). We also created an HRSN composite measure by aggregating the number of unmet HRSN reported and then categorized overall HRSN as none vs. 1 or more, and none/one vs. 2 or more. We compared frequency distributions of HRSN reported by study participants with frequencies reported from the 2019 New Jersey statewide Health and Well-Being Poll (66). The Health and Well-Being Poll was developed by the Rutgers Center for State Health Policy with funding from the Robert Wood Johnson foundation. Abt Associates, under contract to Rutgers, drew a statewide random digit dialed telephone (landline and cell) sample and conducted interviews in English and Spanish, from January to February 2019 with adults living in New Jersey.

Neighborhood Perceptions

We measured neighborhood perceptions related to connectedness, belonging, and trust using a 12-item scale, previously implemented in other studies (67–70), including studies focused on elderly Chinese Americans (71). For each item, participants were asked to respond to a five-point scale (strongly disagree, disagree, neutral, agree or strongly agree). A composite score was constructed using the sum of all 12 items and then dichotomized to low (unfavorable) neighborhood perceptions (total score ≤ 36) and high (favorable) neighborhood perceptions (total score >36). Participants with missing data for any single item were still included in the final analysis, and were included within the "disagree" category for those items.

Other Sociodemographic Factors

We examined the following sociodemographic variables from the survey: gender, age (18–49, 50–65, >65 years), survey language (English, Chinese-Traditional (T), Chinese-Simplified (S)), race/ethnicity (Non-Hispanic-Asian, Other race/ethnicity), household income (<\$75,000; \$75, 000 or more; unknown/missing), education level (less than college, college or beyond), and insurance status (private insurance, Medicaid/Medicare, uninsured/unknown). Participants reported whether they were born in the US or born outside of the US, as well as indicating country of birth. We calculated percent of life spent in the US using current age and age at time of immigration among those born outside of the US and constructed the following mutually exclusive categories: US-born, <25% of life spent in US, ≥25% of life spent in the US.

Medical Record Chart Abstraction

We abstracted data from CAH's electronic medical records (Cerner PowerChart) for patients age-eligible (51–75 years) for routine breast (females only) and colorectal (females and males) cancer screening based on current US Preventive Services Task Force (USPSTF) guidelines (72, 73). Records were reviewed retrospectively until the timing of the last screening service was able to be identified or up until 10 years from the survey date. For patients who did not have a complete 10-year look-back period, we reviewed all records that were retrospectively available.

Cancer Screening

We examined ever-screened vs. never-screened and receipt of guideline-concordant screening (yes/no) for both breast and colorectal cancer among eligible survey participants. Receipt of guideline-concordant breast cancer screening was determined as whether a mammogram was received within the last 2 years from the time of survey completion. We excluded women who had undergone bilateral mastectomies ($n = 2$). Receipt of guideline-concordant colorectal cancer screening was determined as either receiving a colonoscopy within the last 10 years, or completing a multi-target stool DNA test within the last 12 months (72). We recorded whether screening was ever received, as well as the year they were last received. Regardless of whether the participants completed the survey in 2019 or 2020, we used 2019 as the year to start the look-back period for retrospective chart review for all participants to employ a more inclusive approach of whether screening occurred within guideline recommendations.

Statistical Analysis

Descriptive statistics were used to summarize the demographic characteristics, HRSN variables, neighborhood perception, and enrollment pre-COVID-19 vs. during COVID-19 among eligible study participants age 18 and over in the final analytic sample, and compared across survey language using Chi-square test and Fisher's exact test. We used survey language (English, Chinese-T, Chinese-S) as a primary comparison based on observed demographic differences across the Chinese language groups in our study sample as well as input and feedback from CAH clinic staff and community partners from the Asian Health Initiative at the Rutgers Institute for Health, Healthcare Policy & Aging Research.

A total of 12 participants were excluded due to incomplete or duplicate responses or surveys completed in Korean ($n = 1$). While a Korean survey instrument was available at the start of our study, study recruitment for Korean participants was limited due to staff availability and appointments with the Korean speaking provider were only available 1 day a week. For surveys that were missing information on age ($n = 24$), we used the medical record to determine the missing ages of these participants. We were able to identify missing ages for 23 participants. An additional 8 participants were excluded due to missing data for other variables of interest. The final analytic sample for the primary analysis included 236 participants (**Figure 1**). In univariate analyses we compared reports of having ≥2 HRSN compared to reporting ≤1 HRSN, as well as low neighborhood perceptions (score <36) compared to high neighborhood perceptions (score ≥ 36) using logistic regression models. We ran separate multivariable models to determine sociodemographic factors associated with reporting ≥2 HRSN and low neighborhood perceptions. Independent variables in the final models were based on significant univariate associations, prior literature, and the overall analytic sample size. We report odds ratios (OR) and 95% confidence intervals (CIs).

We also compared receipt of cancer screening (ever vs. never; guideline-concordant vs. non-guideline-concordant) by report of HRSN and neighborhood perceptions using Chi-square test and Fisher's exact test among study participants who completed the survey and age-eligible for cancer screening. Participants were excluded from the analysis who were not age-eligible for screening at the time of survey, unable to be matched in the medical record based on the recorded survey name, or had no name on the survey (**Figure 1**). Only descriptive analyses were examined for cancer screening because the primary study sample was not powered to examine the association between HRSN or neighborhood perceptions and receipt of screening, as well as the limited frequency distribution in cancer screening measures within the study population. All analyses were conducted in R version 4.0.3 (74).

RESULTS

Characteristics of the study participants ($n = 236$) are shown in **Table 1**. The majority of participants were recruited in-person and completed the survey via tablet with the exception of 21 participants. A large proportion of participants self-identified as being a woman (64%) and non-Hispanic Asian (75%), having a college degree (68%), and having an annual income of more than \$75,000 (52%). The mean age at the time of the survey was 52.6 years.

Over three quarters of participants were born outside of the U.S. ($n = 187$, 79%). All participants who completed the survey in Chinese-T (19%) and Chinese-S (18%) were non-US born,

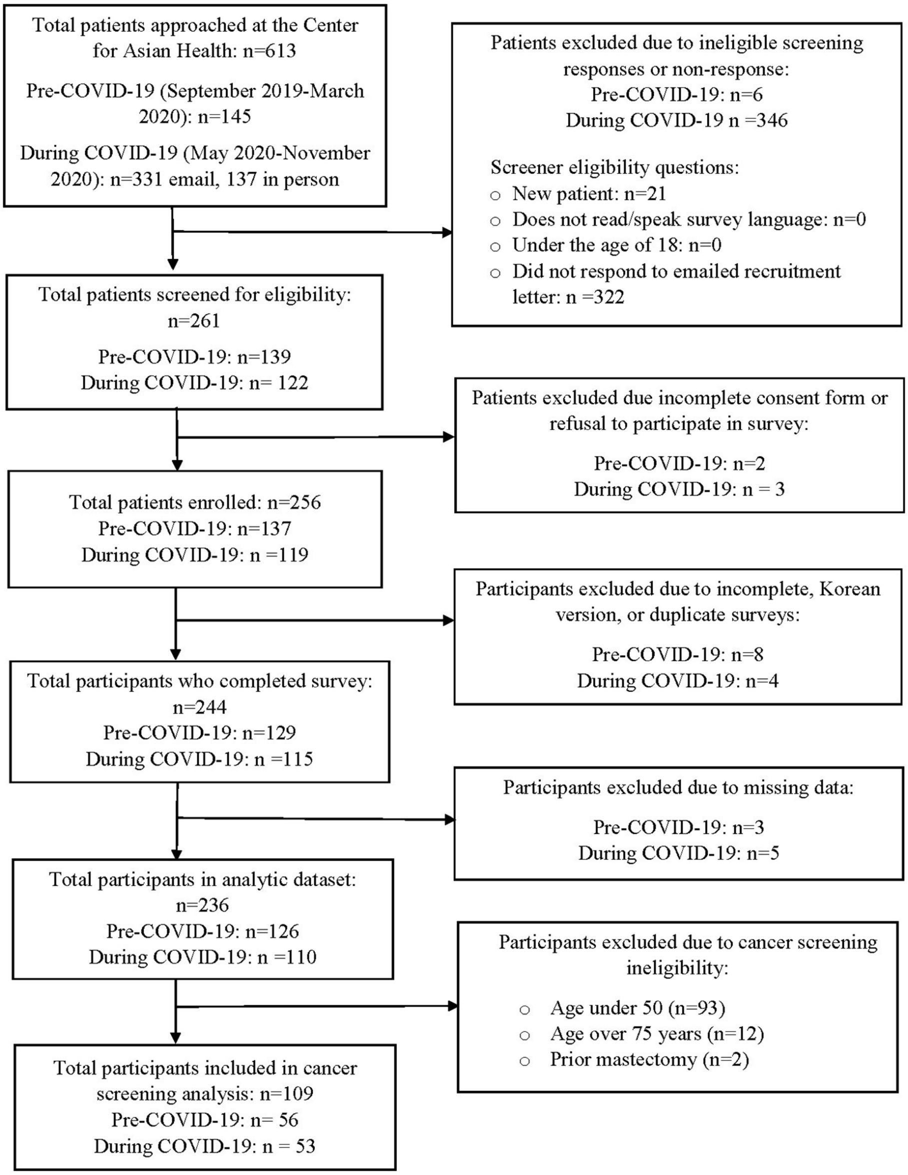

FIGURE 1 | Recruitment and study enrollment (September 2019 to November 2020).

with the most common location of birth being China (*n* = 70) or Taiwan (*n* = 45). There were observed differences in demographic characteristics across the three survey language groups and in immigration characteristics between Chinese-T and Chinese-S survey participants. Compared to Chinese-T respondents, higher proportions of Chinese-S respondents reported having incomes less than $75K (52% vs. 26%), residing in the US for <25% of their lifetime (34% vs. 12%), and having less than a college degree (48% vs. 28%). Overall, a lower proportion of Chinese-S respondents were recruited during the COVID-19 pandemic period (34%) compared to Chinese traditional (44%) and English (51%) respondents.

Health Related Social Needs

Half of all participants (50%) reported having at least one HRSN, with minimal differences across language groups (English: 48%, Chinese-T: 56%, Chinese-S: 55%; *p*-value: 0.533). While a smaller proportion of overall participants reported having ≥2 HRSN (14%), larger differences were observed across survey language. Compared to 14% of Chinese-T and 11% of English respondents, a quarter of Chinese-S respondents reported having ≥2 HRSN (**Table 1**).

Higher proportions of Chinese-S respondents reported housing instability (23%) compared to both English (12%) and Chinese-T respondents (5%) (*p*-value: 0.038) (**Figure 2**).

TABLE 1 | Characteristics of study participants by survey language.

	Total *N* = 236		English *N* = 149		Chinese traditional *N* = 43		Chinese simplified *N* = 44		
Characteristic	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	***p*-value**[a]
Race/ethnicity									<0.001
NH-Asian	175	74.2	94	63.0	41	95.0	40	91.0	
Other race/ethnicity	61	25.8	55	37.0	2	4.7	4	9.1	
Gender									0.19
Female	154	65.3	103	69.0	27	63.0	24	55.0	
Male	82	34.7	46	31.0	16	37.0	20	45.0	
Age									0.112
18–49	93	39.4	65	44.0	11	26.0	17	39.0	
50–65	92	39.0	58	39.0	17	40.0	17	39.0	
>65	51	21.6	26	17.0	15	35.0	10	23.0	
Education									0.022
Less than college	70	30.0	38	26.0	12	28.0	20	48.0	
College or beyond	163	70.0	110	74.0	31	72.0	22	52.0	
Health insurance									0.008
Private	135	57.2	98	66.0	21	49.0	16	36.0	
Medicaid/Medicare	73	30.9	36	24.0	16	37.0	21	48.0	
Uninsured/unknown	28	11.9	15	10.0	6	14.0	7	16.0	
Income									0.044
Less than $75K	95	40.3	61	41.0	11	26.0	23	52.0	
$75K or more	122	51.7	79	53.0	27	63.0	16	36.0	
Unknown/missing	19	8.1	9	6.0	5	12.0	5	11.0	
Percent life spent in US									<0.001
US-born	49	20.8	49	37.0	0	0.0	0	0.0	
<25 in the US	23	9.7	6	4.5	5	12.0	12	34.0	
25–99 in the US	138	58.5	79	59.0	36	88.0	23	66.0	
Health-related social needs									0.533
None	117	49.6	78	52.0	19	44.0	20	45.0	
At least 1	119	50.4	71	48.0	24	56.0	24	55.0	
Health-related social needs									0.078
1 or fewer	202	85.6	132	89.0	37	86.0	33	75.0	
At least 2	34	14.4	17	11.0	6	14.0	11	25.0	
Neighborhood perceptions score									0.002
Low (36 or lower)	47	19.9	25	17.0	5	12.0	17	39.0	
High (>36)	189	80.1	124	83.0	38	88.0	27	61.0	
Recruitment period									0.133
Pre-COVID-19	126	53.4	73	49.0	24	56.0	29	66.0	
During COVID-19	110	46.6	76	51.0	19	44.0	15	34.0	

[a] *Statistical tests performed: chi-square test of independence; Fisher's exact test.*

Similarly, though not statistically significant, higher proportions of Chinese-S respondents reported food insecurity (16%) compared to both English (9%) and Chinese-T respondents (7%) (*p*-value: 0.317) (**Figure 2**). While Chinese-T respondents were the least likely to report experiencing utility needs (5%), they were more likely to report having transportation needs (16%) than either English (5%) or Chinese-S (7%) respondents (*p*-value: 0.039). More than one-third of all respondents reported experiencing at least one interpersonal violence measure across all three survey languages.

When comparing these findings to statewide data from the New Jersey Health & Well-Being Poll (**Table 2**), transportation needs were higher in our sample of Chinese-T participants (16%) compared to New Jersey residents overall (6%). Food insecurity was also higher among our sample of Chinese-S participants (23%) compared to New Jersey residents (11%).

In the univariate analysis, Chinese-S participants (OR: 2.59; 95% CI: 1.08, 6.01) had higher odds of having $\geq$2 HRSNs compared to English survey respondents (**Table 3**). Similarly, participants with lower income (<$75,000) had higher odds (OR:

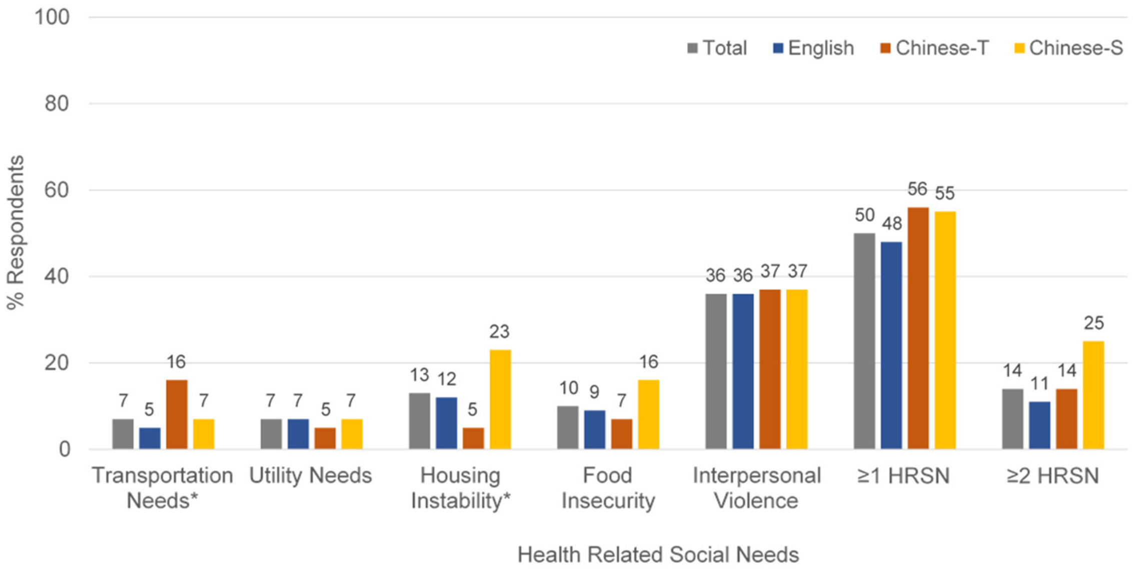

FIGURE 2 | Health related social needs by survey language among all study participants ($n = 236$). $^*p < 0.05$.

TABLE 2 | Comparison of study participants reporting HRSN to state data.

	% Transportation needs	% Utility needs	% Housing instability*	% Food insecurity	% Interpersonal violence**
Study participants					
English	4.7	7.4	3.3	9.4	26.4
Chinese-T	16.0	4.8	0.0	7.0	34.9
Chinese-S	6.8	6.8	6.8	16.0	27.9
New Jersey Health & Well-Being Poll	6.5	5.9	6.9	11.2	13.0

Housing instability based on comparable survey item only (current living situation), not composite measure shown in **Figure 1.*

*** Interpersonal violence measure also based on comparable survey item only (screamed or cursed at by loved one), not composite measure shown in **Figure 1**.*

2.52, 95% CI: 1.15, 5.77) of having ≥2 HRSNs compared to higher income participants. After adjusting for gender, age, and recruitment period, participants with incomes <$75,000 still had higher odds of reporting ≥2 HRSNs (OR: 2.53; 95% CI: 1.12, 5.98) compared to higher income participants.

Neighborhood Perceptions

Neighborhood perceptions among study participants are shown in **Figure 3**. Significant differences in neighborhood perceptions were observed across survey language. A larger proportion of Chinese-S survey respondents (39%) had low neighborhood perceptions (score ≤ 36) compared to 12% Chinese-T respondents and 17% English respondents ($p = 0.002$). For individual neighborhood perception items, no Chinese (simplified or traditional) respondents disagreed with the fact that their neighborhood was a good place to live, although nearly one-fifth of Chinese-S respondents felt "neutral" ($p = 0.029$). More Chinese-S (42%) and Chinese-T (35%) respondents did not feel they could recognize their neighbors compared to English respondents (25%), suggesting differences in neighborhood belonging and familiarity. Lower proportions of Chinese survey respondents agree that they feel at home in their neighborhood (Chinese-S 45%, Chinese-T 64%, English 89%; $p < 0.001$). Chinese-T respondents (86%) were much more likely to expect to live in their neighborhood for a long time than either English (67%) or Chinese-S (63%) respondents.

In the univariate analysis (**Table 3**), Chinese-S respondents, participants with lower incomes, and patients with Medicaid/Medicare had significantly higher odds for reporting low overall neighborhood perceptions. In the adjusted model including participants in all languages and after adjusting for gender, age, health insurance, and recruitment period, older participants (age > 65 years) had lower odds of having low neighborhood perceptions (OR: 0.34; 95% CI: 0.11, 0.98) compared to younger participants, whereas those with Medicaid/Medicare (OR: 3.87; 95% CI: 1.50, 10.3) had higher odds of having low neighborhood perceptions compared to privately insured participants. A similar relationship was observed for participants who were uninsured or had unknown insurance compared to privately insured participants (OR: 3.01; 95% CI: 1.00, 8.77). In our sensitivity analysis of

TABLE 3 | Factors associated with reporting ≥ 2 HRSN and low neighborhood cohesion (n = 236).

	≥2 HRSN				Low neighborhood perceptions			
	Univariate models		Multivariable model		Univariate models		Multivariable model	
	OR[a]	95% CI[a]	OR	95% CI	OR	95% CI	OR	95% CI
Gender								
Male	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Female	0.97	0.46, 2.14	1.00	0.45, 2.28	1.50	0.76, 3.13	1.74	0.81, 3.94
Age								
18–49	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
50–65	0.61	0.26, 1.36	0.56	0.23, 1.30	1.01	0.49, 2.08	0.97	0.43, 2.17
>65	0.60	0.20, 1.55	0.46	0.15, 1.28	0.83	0.33, 1.97	**0.34**	**0.11, 0.98**
Survey language								
English	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Chinese simplified	**2.59**	**1.08, 6.01**	2.40	0.96, 5.87	**3.12**	**1.48, 6.58**	2.26	0.95, 5.29
Chinese traditional	1.26	0.43, 3.27	1.66	0.54, 4.64	0.65	0.21, 1.70	0.59	0.17, 1.70
Income								
$75K or more	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Less than $75K	**2.52**	**1.15, 5.77**	**2.53**	**1.12, 5.98**	**3.33**	**1.64, 7.08**	1.93	0.85, 4.47
Unknown/missing	2.69	0.68, 9.06	2.68	0.65, 9.42	**4.89**	**1.59, 14.6**	**3.78**	**1.12, 12.2**
Health insurance								
Private	Ref	Ref			Ref	Ref	Ref	Ref
Medicaid/Medicare	2.07	0.94, 4.55			**3.42**	**1.68, 7.13**	**3.87**	**1.50, 10.3**
Uninsured/unknown	1.33	0.36, 4.06			**2.97**	**1.09, 7.75**	**3.01**	**1.00, 8.77**
Recruitment period								
Pre-COVID-19	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
During COVID-19	0.77	0.36, 1.60	0.89	0.41, 1.93	0.81	0.42, 1.55	0.93	0.44, 1.92

[a] *OR, Odds Ratio; CI, Confidence Interval. Bolded items represent significant associations at the* $p < 0.05$ *level.*

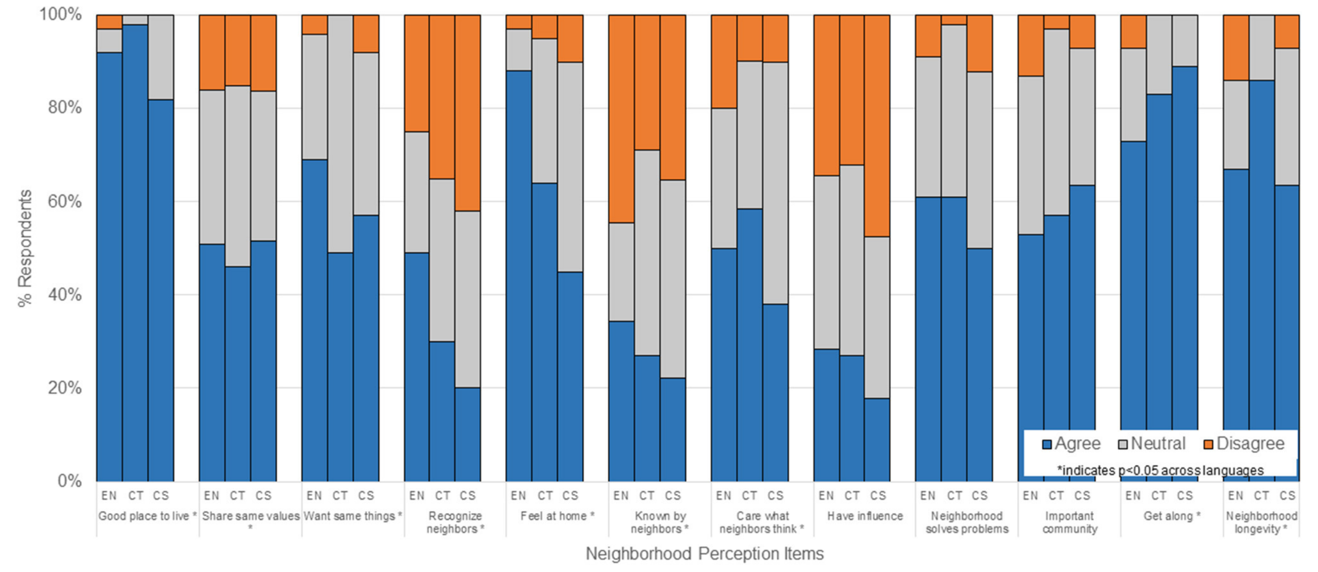

FIGURE 3 | Neighborhood perceptions among study participants by survey language.

participants who were missing responses for 6 or more of the 12 neighborhood perception items (n = 6), associations between uninsured/unknown insurance and low neighborhood perceptions and low income/unknown income and low neighborhood perceptions were no longer significant (data not shown).

Relationship Between HRSN & Low Neighborhood Perception on Cancer Screening

Our exploratory analysis of cancer screening history and health-related social needs included 67 women age-eligible for breast cancer (BC) screening and 109 men and women eligible for colorectal cancer (CRC) screening. Ever receiving a prior BC screening (87%) or CRC screening (81%) as well as having a guideline concordant screening history (BC: 72%, CRC: 76%) were high among patients who participated in our HRSN screening assessment (**Table 4**). We did not observe significant differences in ever receiving a previous BC or CRC screening, or receipt of guideline-concordant BC or CRC screening, by HRSN status or neighborhood perceptions. For BC screening, although not statistically significant, we observed a slightly higher proportion of those with fewer (≤1) HRSN who did not receive guideline-concordant screening (29%), compared to those with ≥2 HRSN (22%). A similar percentage of patients reporting ≥2 HRSN did not receive guideline-concordant CRC screening (23%), compared to those with ≤1 HRSN (24%). For BC screening, a similar percentage of patients reporting low neighborhood cohesion had never been screened (13%), compared to those reporting high neighborhood cohesion (13%).

DISCUSSION

This is one of the few clinic-based studies to implement a HRSN screening tool in languages other than English and Spanish and assess the prevalence of social needs among patients in an Asian American focused primary care clinic. We found similar, and in some cases higher, reports of health-related social needs within our study population of primarily privately-insured, higher educated, suburban non-Hispanic Asian patients compared to statewide New Jersey data.

We observed alarmingly higher than anticipated reports of interpersonal violence across all survey languages. While these reports did not significantly increase among participants recruited during the COVID-19 pandemic compared to those recruited prior to the start of the COVID-19 pandemic, we observed higher rates of interpersonal violence needs across participants in both time periods and all three survey languages when compared to similar measures in the state level data. These findings warrant focused efforts for developing clinic strategies in increasing clinician awareness, follow-up and referral processes, and longer-term interventions to address interpersonal violence as a health-related social need among AA primary care patients. These data also substantiate the need to address the "Invisible Minority" status of Asian Americans, as interpersonal violence risks are just as prevalent in our sample as state reported rates. The wave of recent hate crimes directed toward Asian Americans during the COVID-19 pandemic (75), unfortunately indicate interpersonal violence is increasing. A March 2021 Pew survey found that nearly three-quarters of people (71%) feel that AAs experience "a lot" or "some" discrimination (76). Other reports have cited up to a tenfold increase in the number of reports of anti-Asian sentiment, including verbal harassment and physical assault in the larger New York City region in February-March 2021 compared to the same period in 2020 (76). The anti-Asian hate and violence will not only increase the mental health care needs of AAs going forward, but also impact long-term access, utilization and adherence to health services overall, leading to downstream effects of increased chronic conditions (77).

Housing instability and food insecurity needs were also notably high among participants who completed the survey in simplified Chinese text, which comprise of participants who are younger and immigrated to the US in more recent years. Although food insecurity has decreased since 2011, the COVID-19 pandemic has caused rates to double (78). Similarly, homelessness has decreased overall since 2007, but has increased annually between 2017 and 2019 (79). Efforts to address social needs within health care settings as a strategy to improve overall health among AA specifically has been limited, despite the emphasis on measuring and addressing HRSN among low-income and other racial/ethnic minority patients (12, 27, 80). Our findings indicate vulnerability to HRSN among patients in a clinic setting serving AA who are higher-income and privately insured. These findings are consistent with other work that challenge the Model Minority Myth (45, 60, 81) for AA and further support the need to adapt and tailor existing clinic-based HRSN assessment and intervention/referral strategies to address the social needs and life course experiences of heterogeneous AA populations (82). At a minimum, broader efforts to screen HRSN within clinic populations need to be linguistically appropriate for AA patients.

Our findings also point to higher transportation needs among Chinese American patients who completed the survey in traditional Chinese, which consist of participants who are older overall compared to English and simplified Chinese survey participants. Access to transportation has been identified in prior studies among elderly AA and other racial/ethnic minority populations as logistical barriers to accessing health care (8, 48). For elderly AA patients in suburban areas, such as New Jersey, where public transportation options are limited and social services support programs for those who have limited English proficiency are more disperse, overcoming transportation needs to health care may be a greater obstacle compared to AA patients in more urban centers. The majority of CAH patients reside across three counties in Northern New Jersey, however, a number of patients live outside of these immediate areas and seek care from CAH, often citing the in-language care as the reason for traveling further. A recent report on the State of AA in New Jersey, indicated that Chinese Americans are the second largest Asian American ethnic group in the state following Indian Americans, with a large proportion residing in Northern and Central New Jersey counties (38). In-language healthcare is often not geographically close for residents of suburbs and access becomes an issue, especially for those who cannot drive. It is important to monitor and address these needs for suburban AA communities living outside of densely populated ethnic enclaves, such Chinatowns in Manhattan and Brooklyn, as they can contribute to health disparities and poorer outcomes. Linguistic and geographic challenges to health care are often not detected in aggregated data and similar to the bimodal distribution of income

TABLE 4 | Breast or colorectal cancer screening history among age-eligible participants by HRSN and neighborhood perceptions.

	Breast Cancer (*n* = 58)				**Colorectal Cancer (*n* = 109)**			
	Ever screened	**Never screened**	**Guideline concordant**	**Non-guideline concordant**	**Ever screened**	**Never screened**	**Guideline concordant**	**Non-guideline concordant**
Total	86.6%	13.4%	71.6%	28.4%	80.7%	19.3%	76.1%	23.9%
HRSN								
None	80.0%	20.0%	62.9%	37.1%	82.1%	17.9%	76.8%	23.2%
1 or more	93.8%	6.0%	81.3%	18.8%	79.2%	20.8%	75.5%	24.5%
HRSN								
None or 1	86.2%	14.0%	70.7%	29.3%	80.2%	19.8%	76.0%	24.0%
2 or more	88.9%	11.0%	77.8%	22.2%	84.6%	15.4%	76.9%	23.1%
Transportation needs								
None	85.0%	15.0%	70.0%	30.0%	81.0%	19.0%	77.0%	23.0%
Yes	100.0%	0.0%	85.7%	14.3%	77.8%	22.2%	66.7%	33.3%
Utility needs								
None	86.2%	14.0%	70.8%	29.2%	81.7%	18.3%	76.9%	23.1%
Yes	100.0%	0.0%	100.0%	0.0%	60.0%	40.0%	60.0%	40.0%
Living situation needs								
None	86.2%	14.0%	70.7%	29.3%	81.4%	18.6%	78.4%	21.6%
Yes	88.9%	11.0%	77.8%	22.2%	75.0%	25.0%	58.3%	41.7%
Food insecurity								
None	88.5%	11.0%	72.1%	27.9%	79.8%	20.2%	75.8%	24.2%
Yes	66.7%	33.0%	66.7%	33.3%	90.0%	10.0%	80.0%	20.0%
Interpersonal violence								
None	80.0%	20.0%	66.7%	33.3%	80.6%	19.4%	75.0%	25.0%
Yes	100.0%	0.0%	85.0%	15.0%	82.9%	17.1%	80.0%	20.0%
Neighborhood perception								
Low (36 or lower)	86.7%	13.3%	73.3%	26.7%	70.0%	30.0%	65.0%	35.0%
High (>36)	86.5%	13.5%	71.2%	28.9%	83.1%	16.9%	78.7%	21.4%
Recruitment period								
Pre-COVID-19	88.6%	11.0%	77.1%	22.9%	82.1%	17.9%	76.8%	23.2%
During COVID-19	84.0%	16.0%	65.6%	34.4%	79.2%	20.8%	75.5%	24.5%

in AA, which is often masked in population data within suburban areas (55).

In our assessment of neighborhood perceptions, we also observed notable differences across survey language groups. Chinese participants responding in simplified text reported more negative perceptions about their neighborhood compared to English and traditional Chinese text respondents, including fewer Chinese-S participants "feeling at home" or "knowing their neighbors." We did observe slight increases in specific measures between the pre-COVID-19 vs. during COVID-19 periods, including "feeling at home" (from 49% to 51%) and "caring about what neighbors think" (from 46% to 54%). Similar to our findings for interpersonal violence described above, we did not observe significant differences in overall low neighborhood perceptions between participants recruited during the COVID-19 pandemic compared to those recruited before the COVID-19 pandemic began. We may not have observed significant differences in HRSN, specifically interpersonal violence, or neighborhood perceptions between COVID-19 periods because of a bias in the patients who were seeking and able to receive health care during the COVID-19 pandemic period. Patients who make it to a primary care encounter either in-person or through telehealth, may be less likely to have lost health insurance, be less vulnerable to having HRSN, less likely to have experienced fear or trauma from COVID-19 and related social impacts, or more chronically ill and requiring primary care follow-up. Prior research on neighborhood cohesion have highlighted how AA communities may mitigate disparities and cultural stress for AA patients, showcasing the potential protective effects of community interactions (19). On the other hand, AA living in more suburban and less densely AA populated areas may face isolation or lack of belonging (53). Further investigation is needed to understand the complex relationships between neighborhood connectedness on health care utilization and health outcomes among diverse AA patients.

Recent studies have shown a positive relationship between screening for and addressing HRSN and health care utilization, including cancer screening and treatment (82–85). In addition, lower rate of colorectal cancer screen are observed in other educated AA populations elsewhere, which we did not observe in our study. We did not observe significant differences in reported HRSN or neighborhood perceptions by cancer screening history in our exploratory analysis based on medical chart review. Some possible reasons for lack of significant associations include the high proportion of patients ever receiving and routinely receiving cancer screening at CAH, the temporality of HRSN and our cancer screening measures, and the smaller sample size of participants over age 50. The CAH has partnered with national and state level initiatives to focus on Hepatitis B screening (86) and colorectal cancer screening (ScreenNJ www.screennj.org), thus already high rates of cancer screening observed in our study may be a result of ongoing patient, provider, and clinic efforts. It will be important to monitor the impact of the COVID-19 pandemic on increased HRSN, delays in routine primary care visits, and delays in routine cancer screening moving forward, as recent data have shown large decreases in patient visits both nationally and within CAH between April and November 2020 (87–89). Furthermore, more research is needed on how HRSN may differentially impact disparities across stages of the cancer care continuum from screening to survivorship.

There are some limitations to our study that should be noted. First, we focus on a single primary care clinic that serves a high proportion of Chinese patients in a large suburban hospital system, contributing to a modest sample size. While our study population of largely immigrant, Chinese American patients may not be representative of the broad diversity of Chinese Americans or heterogeneous AAPI populations in New Jersey, it does provide important insight on HRSNs experienced by suburban Asian patients who are otherwise understudied but experience disparities in health and health care. In addition, our data are cross-sectional, precluding analyses of causality. We make numerous statistical comparisons, raising the possibility of finding significance by chance. We combined response categories in some HRSN measures due to small cell sizes and were not able to assess whether these edits impact the validity of the measures. Nevertheless, this study highlights the important need to focus on suburban AA patients, a largely understudied group, who may have social needs and access to support services distinct from their urban counterparts. Second, it is important to note, while these findings highlight the need to implement language appropriate health-related social needs screening tools for AA patients who otherwise would be omitted from clinic-based screening assessments, there is a need to address the heterogeneity of groups within Asian Americans and the community-specific factors that may impact health care utilization and outcomes. While we did find differences between Chinese-S and Chinese-T immigrant participants, we did not specifically compare acculturation using validated measures between these groups. The decision to compare across survey languages was informed by clinic providers and community partners. Per their experiences with the community, Chinese-T immigrants in NJ had largely immigrated earlier (many from Taiwan & Hong Kong) than many who were Chinese-S immigrants (mainland China) and thus many had more years in the US and might be more established and have fewer HSRN. This was seen in many of the measures but it did not hold true for transportation, highlighting vulnerabilities that come with older age and across groups. Third, although we made every effort to continue study recruitment using the same methods during the pandemic. Patients recruited during the pandemic (April 2020 and beyond) are likely those who could more likely overcome barriers and who felt safe from COVID exposure to access primary care again. Thus, the lack of change in HRSNs and neighborhood perceptions between pre-COVID-19 and during COVID-19 recruitment may be due to a bias from the differences in enabling factors among patients who were seen during the COVID-19 pandemic.

CONCLUSIONS

This is one of few studies examining HRSN and related factors within AA populations in a health care setting. We observed higher than anticipated reports of HRSN, including high reports of interpersonal violence and housing needs among all Chinese participants, and low neighborhood perceptions among Chinese-S participants, suggesting the need to assess HRSN and the broader context of social determinants even among higher educated, suburban AA patients with health insurance. These study findings inform the need to adapt and augment HRSN data collection strategies to adequately address social needs and life course experience for Asian language speaking patients within clinic settings. As efforts to address HRSN within clinical settings continue, including establishing systematic screening measures, implementation across settings, and policies to incentivize providers, it will be important to accurately measure the needs of all diverse racial/ethnic groups. It is also important to recognize and address the more upstream impacts of SDOH, including discrimination and structural racism, while efforts to focus on more downstream impacts of unmet health related social needs are ongoing (90). Institutional efforts to address implicit bias, structural racism and the other contributors to SDOH, as has been undertaken by the larger hospital system of CAH (91), are critical for confronting the many root issues and creating larger-scale change. As the impact of the COVID-19 pandemic on physical and mental health for racial/ethnic minority communities emerge, aspects of addressing unmet social needs will become even more important. Effectively addressing community-specific HRSN referral needs as well as more upstream social determinants of health that contribute to health and health disparities for Asian Americans will require multilevel strategies at the community, health system, and policy levels.

DATA AVAILABILITY STATEMENT

The datasets presented in this article are not readily available because Data cannot be shared publicly because of sensitive information collected from participants and the current protocol approved by the Saint Barnabas Medical Center Institutional Review Board. Requests to access the datasets should be directed to tsuijenn@usc.edu.

ETHICS STATEMENT

This study was approved by the Rutgers Biomedical Health Sciences Institutional Review Board and the Saint Barnabas Medical Center Institutional Review Board. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

JT and SW planned the study. JT obtained funding, directed the data collection, analysis and interpretation, and led the manuscript writing. SW, RB, and JCa contributed to the study planning, funding acquisition, design and interpretation of study findings. AY, BA, and BX conducted the data collection and data acquisition. JCh conducted the data analysis and data revisions for the manuscript. AY, BA, and JCh contributed to the manuscript preparation. All authors contributed to the manuscript revisions, reviewed, and approved the final submitted manuscript.

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Racial Disparity and Social Determinants in Receiving Timely Surgery Among Stage I–IIIA Non-small Cell Lung Cancer Patients in a U.S. Southern State

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Delayed surgery is associated with worse lung cancer outcomes. Social determinants can influence health disparities. This study aimed to examine the potential racial disparity and the effects from social determinants on receipt of timely surgery among lung cancer patients in Louisiana, a southern state in the U.S. White and black stage I–IIIA non-small cell lung cancer patients diagnosed in Louisiana between 2004 and 2016, receiving surgical lobectomy or a more extensive surgery, were selected. Diagnosis-to-surgery interval >6 weeks were considered as delayed surgery. Social determinants included marital status, insurance, census tract level poverty, and census tract level urbanicity. Multivariable logistic regression and generalized multiple mediation analysis were conducted. A total of 3,616 white (78.9%) and black (21.1%) patients were identified. The median time interval from diagnosis to surgery was 27 days in whites and 42 days in blacks ($P < 0.0001$). About 28.7% of white and 48.4% of black patients received delayed surgery ($P < 0.0001$). Black patients had almost two-fold odds of receiving delayed surgery than white patients (adjusted odds ratio: 1.91; 95% confidence interval: 1.59–2.30). Social determinants explained about 26% of the racial disparity in receiving delayed surgery. Having social support, private insurance, and living in census tracts with lower poverty level were associated with improved access to timely surgery. The census tract level poverty level a stronger effect on delayed surgery in black patients than in white patients. Tailored interventions to improve the timely treatment in NSCLC patients, especially black patients, are needed in the future.

Keywords: non-small cell lung cancer, timely surgery, racial disparity, social determinants, cancer registry

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INTRODUCTION

Lung cancer is the leading cause of cancer death in the United States (U.S.), accounting for 24% of all cancer deaths (1). In 2020, it is estimated that up to 228,820 new cases and 135,720 deaths from lung cancer occurred in the U.S (2). Non-small cell lung cancer (NSCLC) represents about 85% of all lung cancer cases (3). Survival of NSCLC patients has improved with the advancement of early detection and treatment (4). Surgical resection is the primary recommended treatment for patients with stage I-IIIA NSCLC (5). Timely care is an important indicator of the quality of care recommended by the Institute of Medicine (5). Delayed surgery is associated with tumor upstaging and worse survival (4, 6). Patients who receive surgery tend to have a longer wait time than those not receiving surgery, because of the multiple staging studies and preoperative examinations that are required (7, 8). It is of public health importance to examine the timeliness of NSCLC surgery.

Racial disparities exist in NSCLC diagnosis, treatment, and outcomes. Black patients are 16% less likely to be diagnosed at an early stage, 57% less likely to receive guideline concordant treatment, and 19% less likely to receive surgical treatment, when compared to their white counterparts. The survival rate is also lower in black patients than in white patients (9–11). From 2010 to 2015, Louisiana ranked 7th among states in the U.S. for lung cancer incidence and mortality rate (12). Blacks make up approximately 1/3 of the population in Louisiana, and have worse health status than other racial groups (10). Black residents in Louisiana have a higher lung cancer incidence (68.9 vs. 61.1 per 100,000) and poorer survival compared to black people in the U.S. on average (13, 14). Additionally, 17.9% of black NSCLC patients in Louisiana received early diagnosis while 21.4% of whites received early diagnosis (10). Thus, Louisiana NSCLC patients are the appropriate population to investigate the racial disparity in timely surgery of NSCLC.

Social determinants of health are societal factors that contribute to one's overall health or the health of the community (15). It has been argued throughout history that racial health disparities are not caused by biological difference; rather they are influenced by societal factors (16). Previous studies have found that social and economic factors influence disparities in lung cancer incidence and survival, even more than biological differences. Several social determinants, including income, insurance status, marital status, and rural residence, are associated with the receipt of standard care for NSCLC (17). This study had three objectives: (1) to investigate whether there is a racial disparity in receipt of timely surgery among stage I–IIIA NSCLC patients; (2) if the racial disparity exists, to examine whether the disparity can be explained by multiple social determinants; and 3) to explore whether the social determinants have a differential effect on timely surgery in each racial group.

METHODS

Data Source and Study Population

The Louisiana Tumor Registry (LTR) is a population-based state cancer registry and a participant of the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) program and the National Program of Cancer Registries of the Centers for Disease Control and Prevention. LTR routinely collects data on the characteristics, diagnosis, and the first course treatment of newly diagnosed cancers among Louisiana residents. This study identified white and black patients who were diagnosed with stage I-IIIA NSCLC between 2004 and 2016 from the LTR database. Only patients who received surgery of lobectomy or more extensive surgery were included. Patients who received neoadjuvant treatment, or who had unknown timing of treatment initiation were excluded.

Variables

The main exposure variable was race (white, black). The outcome variable was timely receipt of surgery. As we included stage I–IIIA patients to whom the recommended first definitive treatment was surgery, and excluded the patients who received neoadjuvant treatment and those whose timing of treatment initiation was unclear, we considered that surgery was the first treatment for the selected patients. The main guidelines for the timing of treatment initiation of NSCLC patients is to receive surgery within 6 weeks, as specified by the RAND corporation (18), within 8 weeks by the British Thoracic Society (19), and within 4–8 weeks by the American College of Chest Physicians (20). Thus, we used $\leq$6 weeks as a middle representation across these guidelines ($\leq$6 weeks, >6 weeks).

Social determinants examined in this study included type of insurance (private, Medicare, Medicaid, no insurance, unknown), marital status (married, single or divorced or widowed or other, unknown), census tract level population under the federal poverty level (<10%, 10–19.9%, $\geq$20%), and census tract level urbanicity (urban, rural). Census tract level urbanicity was determined based on the Census Bureau's identification of urban and rural areas. Other covariates included age at diagnosis (<54, 55–64, 65–74, $\geq$75), sex, tumor histology (adenocarcinoma, other), tumor size (<3 cm, 3–7 cm, >7 cm), American Joint Committee on Cancer (AJCC) stage (I, II, IIIA), grade (well-differentiated, moderately differentiated, poorly differentiated/undifferentiated, unknown), lymph node involvement status (negative, positive), surgery type (resection of lob, resection extended), and comorbidity (Charlson Comorbidity Index score of 0, 1, 2+) (21).

Statistical Analysis

We used Chi-square test to compare the categorical variables. Students' t-test and Wilcoxon-Mann-Whitney test were applied to compare the mean and median time interval between tumor diagnosis and surgical resection by race. We applied three logistic regression models to examine the racial difference in receiving timely surgery. In Model 1, we employed a crude model to examine the racial disparity for delayed surgery. In Model 2, we controlled for clinical factors, including age, sex, comorbidity, histology type, tumor size, AJCC stage, tumor grade, lymph node involvement status, and surgery type, to examine whether the adjusted odds ratio (OR) of delayed surgery remained significant for race. As a final step, social determinants were adjusted in Model 3 to examine

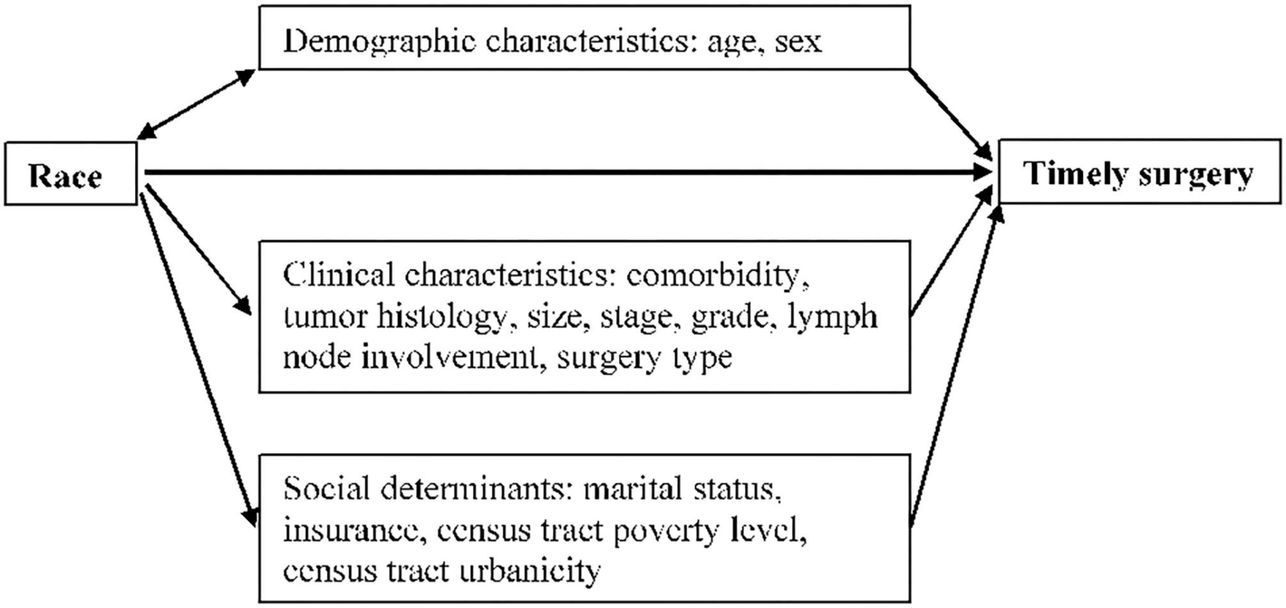

FIGURE 1 | Conceptual diagram of racial disparity in receiving timely surgery for non-small cell lung cancer patients.

whether the racial disparity could be explained. To examine the effect of social determinants on delayed surgery in each racial group, a stratified analysis was conducted among white and black patients. These analyses were performed using SAS 9.4 (SAS Institute Inc.), and statistical tests of significance were based on a 2-sided test with significance levels of 0.05.

To examine the percentage of racial differences in receiving timely surgery which was explained by the social determinants, we conducted general multiple mediation analysis (MMA) to evaluate the mediating effects. MMA evaluates the mediating effects under the counterfactual framework, which can report joint mediation effects through multiple selected mediators simultaneously, considering the correlation among these mediators (22). As shown in the conceptual diagram in **Figure 1**, race was treated as exposure variable and timely surgery as outcome variable. Demographic characteristics (age, sex) were deemed as potential confounders. Clinical factors (comorbidity, tumor histology, size, stage, grade, lymph node involvement, and surgery type) and social determinants (marital status, insurance, census tract poverty level, and census tract urbanicity) were considered as groups of mediators in the pathway between race and timely surgery. The total effect of race on timely surgery was the sum of the direct effect from race and the indirect effect through each group of mediators (total effect = direct effect + indirect effect) (22). The percentage of the total effect explained by each group of mediators was calculated as the ratio of the indirect effect divided by the total effect. We used R version 4.0.0 with mma package to conduct the mediation analysis. The 95% confidence interval was obtained by bootstrap with 500 repetitions.

RESULTS

A total of 3,616 patients, including 2,854 (78.9%) white and 762 (21.1%) black patients were included in our study (**Table 1**). White patients were more likely to be older than 65 years, married, have stage I or lymph node negative disease, while black patients were more likely to be covered by Medicaid, live in a census tract with higher urbanicity and poverty level. For both racial groups, over half of patients were male, without comorbid conditions, diagnosed with adenocarcinoma and <3 cm tumors, or receiving lobectomy. The median time interval from diagnosis to surgery was 27 days for whites and 42 days for blacks ($P < 0.0001$). About 28.7% of white patients and 48.4% of black patients received surgery after 6 weeks from diagnosis ($P < 0.0001$).

Compared to white patients, the OR of receiving surgery more than 6 weeks after diagnosis for black patients was 2.33 (95% confidence interval [CI]: 2.00-2.74) in the crude model, which decreased to 2.19 (95% CI: 1.84–2.60) after controlling demographic and tumor characteristics. With additional adjustment of social determinants, the OR remained significant at 1.91 (95% CI: 1.59–2.30) (**Table 2**). Being unmarried (OR: 1.27, 95% CI: 1.08–1.48), having Medicare or other public insurance (OR:1.20, 95% CI: 1.01–1.44), having Medicaid insurance (OR:1.67, 95% CI: 1.31–2.14), no insurance (OR:3.03, 95% CI: 1.98–4.65), and living in high poverty level area (OR 1.43, 95% CI: 1.08–1.48) were associated with a significantly higher likelihood of delayed surgery. After stratification by race, living in a high poverty census tract was significantly associated with delayed surgery in both racial groups, but with a higher OR in blacks (OR: 1.91, 95% CI: 1.09–3.35) than in whites (OR: 1.37, 95% CI: 1.10–1.71) (**Table 3**). Among white patients, the

TABLE 1 | Characteristics of Louisiana stage I–IIIA non-small cell lung cancer patients by race, 2004–2016, *n* (%).

	Total	White	Black	*P*-value
N	3,616	2,854 (78.9)	762 (21.1)	
Demographic factors				
Age				<0.0001
<54	496 (13.7)	353 (12.4)	143 (18.8)	
55–64	980 (27.1)	722 (25.3)	258 (33.9)	
65–74	1463 (40.5)	1176 (41.2)	287 (37.7)	
75+	677 (18.7)	603 (21.1)	74 (9.7)	
Sex				0.47
Female	1,913 (52.9)	1,501 (52.6)	412 (54.1)	
Male	1,703 (47.1)	1,353 (47.4)	350 (45.9)	
Clinical factors				
Tumor histology				0.09
Adenocarcinoma	2,186 (60.5)	1,705 (59.7)	481 (63.1)	
Non-adenocarcinoma	1,430 (39.5)	1,149 (40.3)	281 (36.9)	
Tumor size				0.84
<3 cm	2,149 (59.4)	1,702 (59.6)	447 (58.7)	
3–7 cm	1,289 (35.6)	1,014 (35.5)	275 (36.1)	
>7 cm	178 (4.9)	138 (4.9)	40 (5.3)	
AJCC stage				0.02
Stage I	2,447 (67.7)	1,964 (68.8)	483 (63.4)	
Stage II	750 (20.7)	568 (19.9)	182 (23.9)	
Stage IIIA	419 (11.6)	322 (11.3)	97 (12.7)	
Lymph node involvement				0.02
Negative	2,758 (76.3)	2,202 (77.2)	556 (73.0)	
Positive	858 (23.7)	652 (22.9)	206 (27.0)	
Grade				0.64
Well-differentiated	420 (11.6)	335 (11.7)	85 (11.2)	
Moderately differentiated	1,467 (40.6)	1,170 (41.0)	297 (39.0)	
Poorly/undifferentiated	1,449 (40.1)	1,129 (39.6)	320 (42.0)	
Unknown	280 (7.7)	220 (7.7)	60 (7.9)	
Surgery type				0.67
Resection of lobe	3,200 (88.5)	2,529 (88.6)	671 (88.1)	
Resection extended	416 (11.5)	325 (11.4)	91 (11.9)	
Comorbidity score				0.05
0	2,000 (55.3)	1,587 (55.6)	413 (54.2)	
1	1,053 (29.1)	844 (29.6)	209 (27.4)	
2+	563 (15.6)	423 (14.8)	140 (18.4)	
Social determinants				
Marital status				<0.0001
Married	2,111 (58.4)	1,798 (63.0)	313 (41.1)	
Single/divorced/widowed/other	1,395 (38.6)	968 (33.9)	427 (56.0)	
Unknown	110 (3.0)	88 (3.1)	22 (2.9)	
Insurance				<0.0001
Private	1,347 (37.3)	1,100 (38.5)	247 (32.4)	
Medicare/other public	1,682 (46.5)	1,390 (48.7)	292 (38.3)	
Medicaid	409 (11.3)	245 (8.6)	164 (21.5)	
No insurance	104 (2.9)	67 (2.4)	37 (4.9)	
Unknown	74 (2.0)	52 (1.8)	22 (2.9)	
Census tract level poverty				<0.0001
<10%	902 (24.9)	839 (29.4)	63 (8.3)	
10–19.9%	1,407 (38.9)	1,225 (42.9)	182 (23.9)	

(Continued)

TABLE 1 | Continued

	Total	White	Black	*P*-value
≥20%	1,307 (36.2)	790 (27.7)	517 (67.9)	
Census tract level urbanicity				<0.0001
Urban	2,597 (71.8)	1,953 (68.4)	644 (84.5)	
Rural	1,019 (28.2)	901 (31.6)	118 (15.5)	
Time interval from diagnosis to surgery, mean (std)	40.8 (44.8)	32.7 (35.6)	47.1 (43.0)	<0.0001
Time interval from diagnosis to surgery, median (Q1–Q3)	29 (6–50)	27 (3–46)	42 (14–70)	<.0001
Receiving surgery >6 weeks from diagnosis	32.9	28.7	48.4	<0.0001

AJCC, American Joint Committee on Cancer; std, standard deviation; Q1, the first quartile; Q3, the third quartile.

OR of receiving surgery more than 6 weeks after diagnosis was significant for those with Medicare coverage (OR: 2.11, 95% CI: 1.56–2.85) and no insurance coverage (OR: 4.15, 95% CI: 2.46–7.04), compared to those with private insurance coverage. Among black patients, those with Medicaid coverage had a significantly higher risk of delayed surgery (OR: 1.48, 95% CI: 1.01-2.16) (**Table 3**).

From the mediation analysis, the total effect of race on timely surgery was 0.905 (95% CI; 0.735–1.091), the direct effect was 0.652 (95% CI: 0.470–0.854), and the indirect effect through clinical factors and social determinants were 0.009 (95% CI: −0.013–0.028), and 0.235 (95% CI: 0.151–0.321). The percentage of racial disparities transmitted through social determinants was 25.97%.

DISCUSSION

With population-based data collected by the state cancer registry, we found that black stage I-IIIA NSCLC patients had almost two-fold odds of receiving delayed surgery, compared to their white counterparts. Multiple social determinants, including insurance, marital status, and poverty level in the census tract, were significant predictors of delayed surgery, but these factors did not fully explain the racial disparity in delayed NSCLC surgery in a U.S. southern state.

Our findings of a higher risk of delayed surgery among black patients are consistent with a few studies using nationwide databases. However, the magnitude of the racial disparity was more profound in Louisiana than in U.S. on average. One recent study using 2008–2013 National Cancer Data Base (NCDB) reported a median time from diagnosis to surgical resection of 26 days for whites and 31 days for blacks ($p < 0.0001$) (9). White patients in Louisiana had a similar median wait time for surgery compared to white patients in the U.S. (27 days vs. 26 days), but black patients in Louisiana experienced a 30% longer wait time compared to black patients in the U.S. (42 days vs. 31 days). The larger difference in diagnosis-to-surgery interval between black and white patients in Louisiana is also reflected in the higher OR found in our study. One study using SEER-Medicare data reported that black NSCLC patients had 1.18 times the odds of receiving delayed treatment compared to white patients (23). Another study using NCDB data reported an adjusted OR of 1.48 of delayed surgery in blacks than in whites. In Louisiana, black patients had 1.92 times the odds of having delay in NSCLC surgery compared to white patients, after adjusting for clinical factors and social determinants.

We examined the impact from several social determinants on timely surgery and whether the examined social determinants could explain the observed racial disparity. Unsurprisingly, private insurance was a significant predictor of the receipt of timely surgery or guideline-concordant care in lung cancer patients (17). Medicaid insured patients tended to experience the largest delay in receiving treatment (17). In a national study, compared to NSCLC patients with private insurance, the diagnosis-to-surgery interval was 2.3 days longer for Medicare patients, 10.8 days longer for Medicaid patients, and 7.8 days for longer for patients who were uninsured or whose insurance status was unknown (9). Another study found that patients covered by both Medicare and Medicaid were less likely to receive timely surgical treatment than patients with only Medicare (23). Insurance was also a significant predictor of delayed surgery in our study, however, we additionally found different effects of insurance coverage on timely treatment in two racial groups. Among white patients, Medicaid covered patients had two times the odds and patients without insurance had four times the odds of having delayed surgery compared to their privately insured counterparts. Compared to black patients with private insurance, the odds of receiving surgery more than 6 weeks after diagnosis was 1.5 times for the Medicare group, but no significant differences were observed for those with Medicaid or those without insurance. The small sample size of black patients may be a reason for a lack of finding significant ORs. However, the point estimates of the ORs in these two groups were also lower in black patients than in white patients. Another possible reason is the availability of charity hospitals in Louisiana, which provide medical services to uninsured residents. As the majority of patients receiving care through charity hospitals are black, the black uninsured patients may have had more healthcare access benefits through the charity hospitals than white uninsured patients. This could be a possible explanation of the insignificant odds ratios of receiving delayed surgery for black Medicaid covered or uninsured patients compared to black privately insured patients (in contrast with the highly significant odds ratios observed in white patients). The adoption of public policies, such as the

TABLE 2 | Odds ratio (95% confidence interval) of receiving surgery 6 weeks or later after diagnosis for non-small cell lung cancer patients.

	Model 1*	Model 2†	Model 3¶
Race			
White	1	1	1
Black	2.33 (2.00, 2.74)	2.19 (1.84, 2.60)	1.91 (1.59, 2.30)
Age, %			
<54		1	1
55–64		1.24 (0.98, 1.58)	1.40 (1.09, 1.80)
65–74		1.14 (0.90,1.43	1.27 (0.98, 1.64)
75+		1.34 (1.03,1.74)	1.48 (1.11, 1.97)
Sex, %			
Female		1	1
Male		0.99 (0.86,1.16)	0.93 (0.80, 1.08)
Tumor histology, %			
Adenocarcinoma		1	1
Non-adenocarcinoma		1.06 (0.90,1.23)	1.02 (0.87, 1.20)
Tumor size, %			
<3 cm		1	1
3–7 cm		1.27 (1.09, 1.49)	1.27 (1.08, 1.49)
>7 cm		0.90 (0.62, 1.29)	0.93 (0.64, 1.34)
AJCC stage, %			
Stage I		1	1
Stage II		1.16 (0.89, 1.51)	1.09 (0.84, 1.42)
Stage IIIA		1.46 (1.03, 2.10)	1.43 (0.99, 2.05)
Lymph node involvement, %			
Negative		1	1
Positive		0.90 (0.67, 1.20)	0.93 (0.69, 1.25)
Grade, %			
Well-differentiated		1	1
Moderately differentiated		1.02 (0.80, 1.31)	0.97 (0.76, 1.25)
Poorly/undifferentiated		1.49 (1.10, 2.10)	1.08 (0.84, 1.40)
Surgery type, %			
Resection of lobe		1	1
Resection extended		0.87 (0.69, 1.10)	0.85 (0.67, 1.08)
Charlson comorbidity index, %			
0		1	1
1		1.15 (0.98, 1.36)	1.11 (0.94, 1.31)
2+		1.39 (1.14, 1.70)	1.32 (1.08, 1.62)
Marital status, %			
Married			1
Single/divorced/widowed/other			1.27 (1.08, 1.48)
Unknown			0.67 (0.41, 1.09)
Insurance, %			
Private			1
Medicare/other public			1.20 (1.01, 1.44)
Medicaid			1.67 (1.31, 2.14)
No insurance			3.04 (1.98, 4.65)
Unknown			0.66 (0.34, 1.20)
Census tract poverty, %			
<10%			1
10–19.9%			1.17 (0.96, 1.43)
≥20%			1.43 (1.17, 1.76)
Census tract urbanicity, %			
Urban			1
Rural			1.02 (0.86, 1.21)

(Continued)

TABLE 2 | Continued

**Crude model; †Adjusted age at diagnosis, sex, marital status, histology, tumor size, AJCC stage, tumor grade, lymph node involvement status, surgery type, and comorbidity. ¶Additionally adjusted for insurance, marital status, census tract level poverty and urbanicity.*

Affordable Care Act (ACA) can improve access to high quality healthcare for marginalized populations receiving disparate care. Previous studies have shown that cancer survivors in Medicaid expansion states were more likely to be insured, to have access to care, and to be diagnosed at an early stage of disease than those in non-expansion states (17, 24). Louisiana was one of the states with earliest initiation of ACA expansion in the country (23).

Our findings indicate that those who are single, widowed or divorced are more likely to receive delayed surgical treatment for NSCLC. Being married or living with a partner is an indication of social support. Social support has been found to be a protective factor for the prevention and maintenance of many diseases (25). Previous studies reported that being married is a predictor of receiving standard care and better outcomes (26–28), while experiencing social isolation or loneliness has a negative influence on lung cancer patients (29). In our study, being married showed a similar protective effect for receiving timely surgery in both white and black patients, while the insignificance of the OR among black patients may be due to the smaller sample size of black patients in our study.

Our study revealed that living in census tracts with a higher proportion of the population living above the national poverty level was associated with higher risk of receiving delayed surgery, and the relationship showed a dose-response effect. This finding is consistent with previous research that evaluated both individual level household income and census-tract level income (9, 30). Even among Medicare covered NSCLC patients who have equal health care access, income level is positively associated with timely treatment (23). After stratification by race, we found that the impact from income was even stronger among black patients, while the strength of the association among white patients was similar to findings from national data (23). Although urban residence was associated with lower lung cancer incidence and better outcomes (31, 32), similar to another study (23), living in urban census tracts was not a significant predictor of timely surgery in our study.

Unsurprisingly, social determinants of health are important contributing factors of racial disparities in cancer prognosis and outcomes (33–35). It has also been found that social determinants account for racial disparities in receiving guideline-recommended curative treatment for NSCLC, breast, and prostate cancer, specifically with insurance status, geographical access, and SES factors having been identified as contributors (36–39). Although black NSCLC patients are less likely to receive guideline concordant surgical treatment than whites, the literature on the role of social determinants in the receipt of timely cancer was limited (27, 40, 41). Black women are less likely on average to receive hormone therapy, chemotherapy, radiotherapy and surgical treatment for breast cancer in a timely manner as compared to white women (42). Additionally, both high and low-risk black prostate cancer patients experienced longer wait times from diagnosis to definitive treatment compared to white patients (43). One study reported that the differences in social determinants explained about 26% of racial disparities, while in our study, the majority of the racial disparity was not explained by the measured mediators. The remaining unexplained racial disparity indicates that there are other social-cultural differences between the two racial groups that influence the timeliness of surgical receipt for NSCLC. One limitation of our study is the lack of information on patients' perceptions and attitudes toward cancer treatment. Black patients may be reluctant to seek care due to stigma, distrust in physicians, and negative perceptions about surgery. Previous research indicates that black, at-risk NSCLC patients commonly seek a second opinion or are skeptical of information provided to them by a physician with whom they had no previous relationship with (44). Black patients also tend to have negative perceptions about surgical treatment, and believe it to be riskier than radiation or chemotherapy treatment (45). Future research could examine whether these risk factors can explain racial disparity in timely NSCLC surgery and design tailored intervention to improve the timely treatment in both racial groups. Another limitation of this study is that we did not have data on several individual-level social determinants, such as household income, education, and employment. Lower educational level is associated with decreased odds of having surgery and poorer survival rates (32). Population-based administrative data or cancer registry data usually do not have information on such individual-level variables. Surveys or additional medical record data extraction are needed to address this gap. Despite these limitations, our study is the first to investigate the impact of social determinants of health on receipt of timely NSCLC surgical treatment by race. Our findings can provide important evidence for future intervention.

TABLE 3 | Adjusted odds ratios (95% confidence interval) of receiving surgery 6 weeks or later after non-small cell lung cancer diagnosis, stratified by race.

	White	Black
Age		
<54	1	1
55–64	1.43 (1.05, 1.94)	1.26 (0.81, 1.96)
65–74	1.22 (0.90, 1.66)	1.39 (0.87, 2.21)
75+	1.64 (1.17, 2.28)	0.92 (0.49, 1.70)
Sex		
Female	1	1
Male	0.99 (0.83, 1.18)	0.76 (0.55, 1.05)
Tumor histology		
Adenocarcinoma	1	1
Non-adenocarcinoma	1.12 (0.94, 1.34)	0.74 (0.53, 1.03)
AJCC Stage		
Stage I	1	1
Stage II	1.16 (0.85, 1.59)	0.90 (0.53, 1.03)
Stage IIIA	1.43 (0.93, 2.19)	1.36 (0.69, 2.71)
Tumor size		
<3cm	1	1
3–7cm	1.26 (1.05, 1.52)	1.30 (0.93, 1.81)
>7cm	0.96 (0.63, 1.47)	0.80 (0.39, 1.66)
Lymph node involvement		
Negative	1	1
Positive	0.96 (0.68, 1.35)	0.82 (0.47, 1.44)
Grade		
Well-differentiated	1	1
Moderately differentiated	0.99 (0.74, 1.33)	0.84 (0.50, 1.40)
Poorly/undifferentiated	1.10 (0.80, 1.47)	0.98 (0.57, 1.66)
Surgery type		
Resection of lobe	1	1
Resection extended	0.90 (0.68, 1.18)	0.72 (0.44, 1.17)
Comorbidity index		
0	1	1
1	1.11 (0.91, 1.34)	1.13 (0.80, 1.61)
2+	1.33 (1.05, 1.70)	1.29 (0.86, 1.94)
Marital status		
Married	1	1
Single/divorced/widowed/other	1.26 (1.05, 1.52)	1.21 (0.87, 1.68)
Insurance		
Private	1	1
Medicare/other public	1.123 (0.92, 1.38)	1.47 (1.01, 2.15)
Medicaid	2.13 (1.57,2.88)	1.16 (0.75, 1.79)
No insurance	4.10 (2.42, 6.95)	1.55 (0.75, 3.21)
Unknown	0.67 (0.31,1.44)	0.74 (0.28, 1.94)
Census tract poverty		
<10%	1	1
10–19.9%	1.14 (0.92, 1.40)	1.49 (0.80, 2.75)
≥20%	1.37 (1.10, 1.72)	1.90 (1.08, 3.34)
Census tract urbanicity		
Urban	1	1
Rural	0.97 (0.81, 1.17)	1.33 (0.87, 2.02)

In summary, while timely surgery is an important predictor of the prognosis of curable NSCLC, we found a significant racial disparity among Louisiana patients. Black patients had almost twice the odds of receiving delayed surgery than white patients, after adjusting for demographic, clinical, and social factors. Having social support, private insurance, and living in census tracts with higher income level was associated with improved access to timely surgery, but these factors explained only about 26% of the observed racial disparity. Majority of racial disparity remained unexplained. As the state of Louisiana has high proportion of black population and high lung cancer incidence, the findings from this study provide evidence for tailored interventions to improve timely treatment. Black patients living in census tracts with a higher poverty level should be particularly targeted, as they experienced a higher risk of delayed surgery. Future studies are needed to examine the effects of other individual level social determinants to decipher the racial disparity in NSCLC timely treatment.

DATA AVAILABILITY STATEMENT

The data analyzed in this study is subject to the following licenses/restrictions: The de-identified dataset can be requested through the Louisiana Tumor Registry. Requests to access these datasets should be directed to mhsieh@lsuhsc.edu.

AUTHOR CONTRIBUTIONS

M-CH and X-CW provided data. M-CH and LZ ran the analyses. PN and LZ wrote the first draft of the paper, which was reviewed by all authors. All authors conceptualized, initiated the study and provided advice.

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Use of Geographic Information System Technology to Evaluate Health Disparities in Smoking Cessation Class Accessibility for Patients in Louisiana Public Hospitals

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Research has shown cigarette smoking is a major risk factors for many type of cancer or cancer prognosis. Tobacco related health disparities were addressed continually in cancer screening, diagnosis, treatment, prevention and control. The present study evaluated the health disparities in attendance of smoking cessation counseling classes for 4,826 patients scheduled to attend between 2005 and 2007. Of 3,781 (78.4%) patients with records to calculate the distance from their home domicile to counseling sites using Geographic Information System technology, 1,435 (38%) of smokers who attended counseling had shorter travel distances to counseling sites (11.6 miles, SD = 11.29) compared to non-attendees (13.4 miles, SD = 16.72). When the travel distance was >20 miles, the estimated odds of attending decreased with greater travel distance. Smokers who actually attended were more likely to be older, female, White, living in urban areas, and receiving free healthcare. After controlling for other socio-demographic factors, shorter distances were associated with greater class attendance, and individuals more likely to attend included those that lived closer to the counseling site and in urban settings, were female, White, commercially insured, and older than their counterparts. These findings have the potential to provide important insights for reducing health disparities for cancer prevention and control, and to improve shared decision making between providers and smokers.

Keywords: tobacco control, smoking cessation, geographic information system, distance, cancer control

INTRODUCTION

Despite improvements in smoking cessation interventions, cigarette smoking continues to be the most preventable cause of morbidity and mortality in the United States (1). The 2019 United Health Foundation's report, *America's Health Rankings*, places Louisiana 49th in overall health, with smoking having the greatest negative impact on health (2). Tobacco use increases the risk of multiple cancers, such as lung, pancreas, bladder, stomach, and colon. In addition, continued tobacco use following a cancer diagnosis increases the risk of cancer recurrence, poor prognosis and adverse treatment-related outcomes (3). In Louisiana, males, ethnic minorities, persons aged 25 to 64, and those over 20 years old with less than a high school education smoke more than their counterparts (4). Between 2005 and 2009, more than 7,200 adults in Louisiana died annually due to smoking, resulting in more than 1.8 billion dollars of attributable health care expenditures in 2009 (4). Based on this data, public health advocates should identify barriers to accessing smoking cessation programs, to decrease the prevalence of smoking and smoking-related deaths in Louisiana.

Tobacco related health disparities were addressed continually in cancer screening, diagnosis, treatment, prevention and control. These health disparities often reflect a greater burden among vulnerable populations (5). A 2014 review identified three major barriers to smoking cessation amongst vulnerable populations (defined as disadvantaged populations facing lower income, cultural differences, and/or social exclusion): the use of smoking as stress management, high acceptability and prevalence of smoking within the community, and lack of support and access to smoking cessation programs (6). Such vulnerable populations are overrepresented in Louisiana. For example, in the 2010 population census, Louisiana had a greater percentages of persons living in poverty (19.7%) compared to the United States general population (12.3%) (7).

There are various types of smoking cessation interventions, including self-help materials, medication, telephone quit lines, and behavioral counseling (8). Behavioral counseling increases smoking quit attempts and rates of long-term smoking abstinence (9). A 2009 meta-analysis found that intensive interventions such as behavioral group counseling were more likely to promote smoking cessation compared to controls (10). A recent study has showed that telephone counseling would be effective under more real-world conditions (11). However, studies examining attendance of behavioral counseling have found low rates of participation due to factors such as low health literacy (12), high costs of attending counseling (13), and being a racial/ethnic minority (14).

Geographic Information System (GIS) technology has been utilized in a variety of health applications, such as modeling and mapping of disease location, monitoring disease spread, and assessing utilization of healthcare services (15). In the context of smoking, GIS has been employed in various applications, including analyzing demographic predictors of tobacco outlet density (16), assessing which neighborhoods were more likely to sell tobacco to minors (17), and monitoring tobacco industry billboard advertisements (18). However, few studies have utilized GIS to assess outcomes related to smoking cessation. In 2010, GIS analysis was employed to track the distribution and impact of a smoking cessation program in New York City (19). In this study, GIS was used to provide real-time visualization of participation in the cessation program. Findings showed that enrollment within the cessation program was higher in low-income, high-smoking prevalence neighborhoods, compared to high-income, high-smoking neighborhoods. Furthermore, GIS analysis was applied to assess the effectiveness of a message card campaign on compliance with the University of Kentucky's tobacco-free campus policy (20). GIS mapping software was used to display the location of cigarette butts, which were used as a measure of compliance. Additionally, GIS mapping has been utilized to demonstrate that tobacco outlet density is associated with knowledge of cigarette brand names (21).

These studies demonstrate the promising potential of GIS for assessing the effect of traveling distance on attendance of tobacco cessation counseling and smoking quit rates. Health outcomes related to distance can be analyzed via GIS in three main ways: travel time, road distance (distance between 2 points if traveling via roads), and map distance (direct distance on a map between 2 points) (22). A major assumption underlying studies of this type is that patients are more likely to use the health facility nearest to them; however, this may not always be the case in urban areas where there is a greater density of healthcare facilities (23). Conversely, in rural areas, patients are more likely to utilize the nearest health facility. Patients who reside in rural areas are less likely to quit smoking, in part due to a lack of local cessation programs (24). Furthermore, travel distance affects utilization of treatment, as demonstrated in regard to cancer treatments such as chemotherapy and radiation (25, 26). For example, a 2015 study used GIS to calculate the road distance between patients' residence and the nearest radiotherapy department and found less radiotherapy utilization with longer road distance from the patients' residence (26). Nevertheless, although people living in rural areas are more likely to travel longer distances to access smoking cessation programs, no studies have yet examined the effect of traveling distance on attendance of tobacco cessation counseling and smoking quit rates in urban and rural settings.

The Louisiana Tobacco Control Initiative (LA-TCI) is a statewide program that integrates evidence-based treatments into routine clinical practice within state hospitals of the LSU Health Care Services Division (LSU HCSD). Patients in these hospitals represent Louisiana's most medically vulnerable, with 49% being uninsured, and 77% being African-American (27). The LA-TCI provides free group behavioral counseling, which includes four consecutive 1-h sessions facilitated by certified tobacco treatment specialists (28). The initiative uses various methods, including GIS, to evaluate and improve cessation programs, visualize smoking prevalence, examine at-risk populations, and analyze trends. Previous LA-TCI studies include integrating evidence-based treatment of tobacco use into patient care practices (29) and demonstrating the utility of a health informatics system to optimize efforts to control tobacco use (30). The present investigation involved use of GIS to examine the effect of distance on attendance of smoking cessation class in a patient population with access to free counseling services provided by the LA-TCI.

METHODS

Study Population

The study population included 4,824 LSU HCSD patients scheduled to attend counseling classes between 2005 and 2007. Of these, 3,910 (81.06%) had data available to calculate the distance between their residence and the referring hospital. Patients were excluded if (1) race reported was "Other," (2) insurance status was missing, or (3) if they were listed as a "Prisoner." Altogether, 3,781 patients were included. The LSU Health Sciences Center Institutional Review Board approved this research.

Data Collection

The LA-TCI collects and reports data in the Cessation Management and Evaluation Database (CMED), a customized relational database developed to evaluate program delivery. At all facilities, CMED is used by TCI staff to identify opportunities for process improvements and to track program processes, such as patients referred, patients contacted, patients who participated in behavioral counseling, and prescription receipts for cessation medication.

Measures

The outcome measure was class attendance, defined as scheduled patients who attended at least one 1-h group counseling session over the course of 4 weeks. The primary predictor variable was geographic distance, defined as the distance measured along the surface of the Earth. In other words, distances are defined by geographic coordinates in terms of latitude and longitude. With AreGIS software, patients' home addresses and counseling location were geocoded using geographical coordinates. Geocoding allows us to transform an address to a location on the earth's surface. We linked a table with patients' addresses, then we used Geocode to generate locations with geographic features, including attributes, and finally, we exported the data using R package for analysis. Covariates included age, gender (female, male), race (African American, White, Other), insurance status (Medicare, Medicaid, commercial, free care, and self-pay), and location (urban vs. rural hospital). We categorized hospitals as urban or rural based on population size according to the 2010 census. Urban hospitals included the Earl K. Long Medical Center (EKL) in Baton Rouge, the Walter O. Moss Medical Center (WOM) in Lake Charles, the Medical Center of Louisiana (MCL) in New Orleans, the University Medical Center (UMC) in Lafayette, and the Leonard J. Chabert Medical Center (LJC) in Houma, Louisiana (**Figure 1**). Rural hospitals included the Lallie Kemp Medical Center (LAK) in Independence and the Bogalusa Medical Center (BMC) in Bogalusa, Louisiana (**Figure 1**).

Data Analysis

Spearman's correlation, chi-square, and ANOVA determined the relationships between class attendance and distance and other risk factors individually. Multivariate logistic regressions jointly considered all risk factors and identified those associated with class attendance. Multiple Additive Regression Trees (MART) (31) illustrated the potential non-linear relationship and complex interactions of risk factors to explain the class attendance rate. All analyses were performed using R (4.0), except for geographic distance between the home address and counseling site for each patient, which was calculated using SAS and Excel. The MART analysis was performed using the R package gbm. When fitting the model, we use the out-of-bag samples to control the overfitting and set the shrinkage parameter at 0.001, and the total number of trees at 10,000. The maximum depth of variable interactions is set at 3 to avoid very complicated interactions.

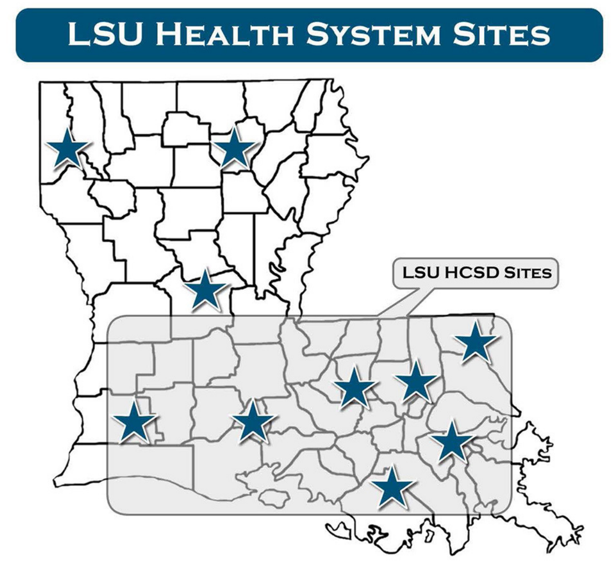

FIGURE 1 | Louisiana Public Hospital system.

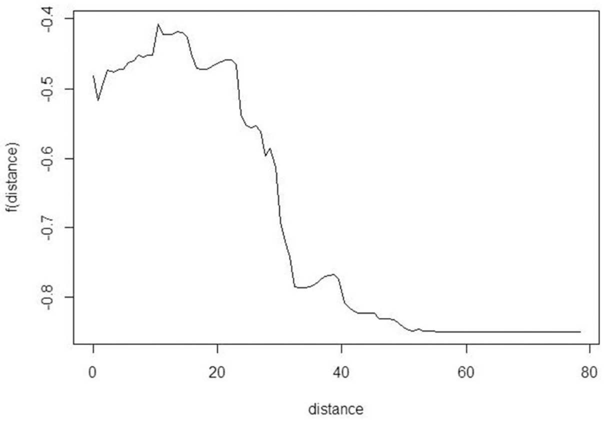

FIGURE 2 | Partial dependence plot to explore the relationship between class attendance and distance to facility. The y-axis is the log odds of attending the smoking cessation class.

Partial dependence plots derived from the MART analysis were used to depict the relationships among variables. The partial dependence plot graphs the functional relationship between a small number of input variables and the outcome. In this paper, the outcome is the predicted log odds of attending the smoking cessation class. The plots show how the log odds (of attending class) changes with the distance to facilities (**Figure 2**), adjusting for other variables (**Figures 3**, **4**).

RESULTS

Overall, 3,781 smokers who scheduled a group counseling class were included in this study. Of these, 38% (1,435) attended class. **Table 1** provides demographic characteristics and class

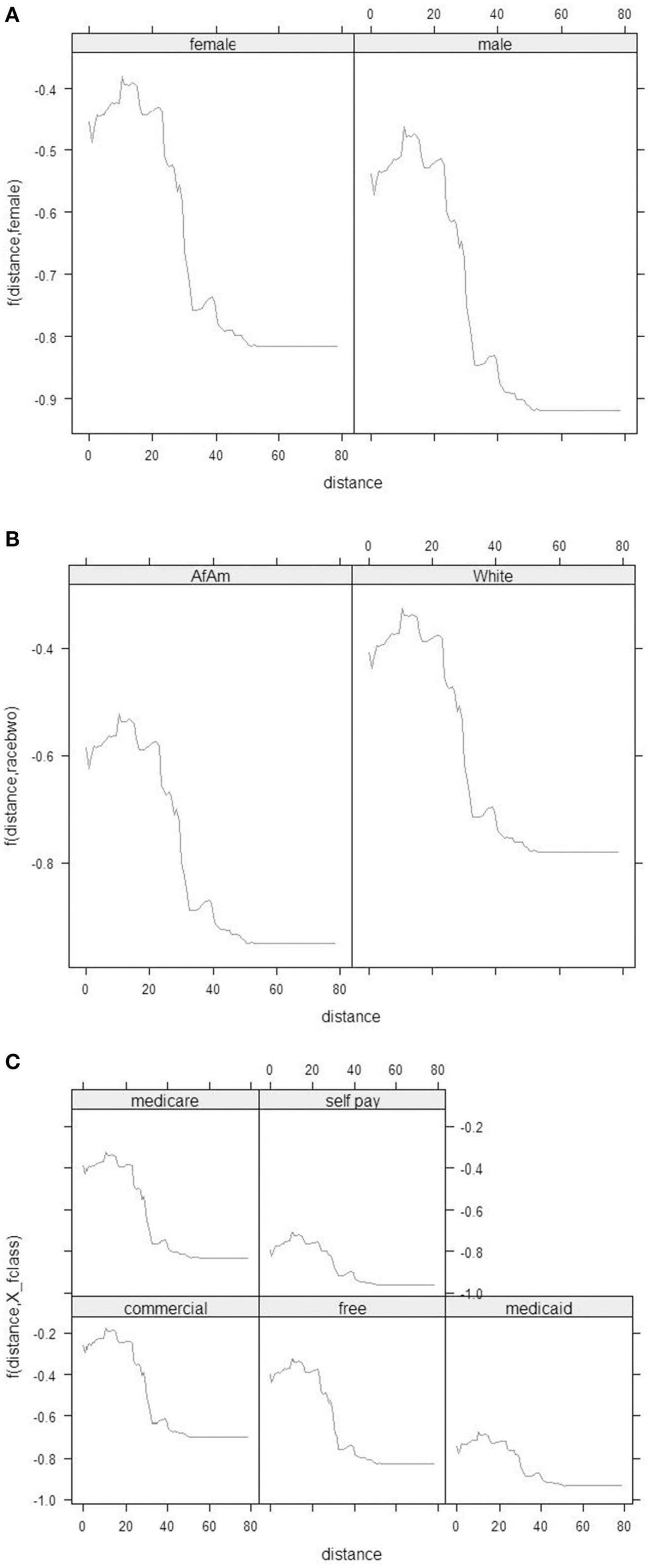

FIGURE 3 | (A) Partial dependence plots between the distance (x-axis) and the log odds of attending the smoking cessation class by females and males separately. **(B)** Partial dependence plots between the distance (x-axis) and the log odds of attending the smoking cessation class by races. **(C)** Partial dependence plots between the distance (x-axis) and the log odds of attending the smoking cessation class by Payment Method.

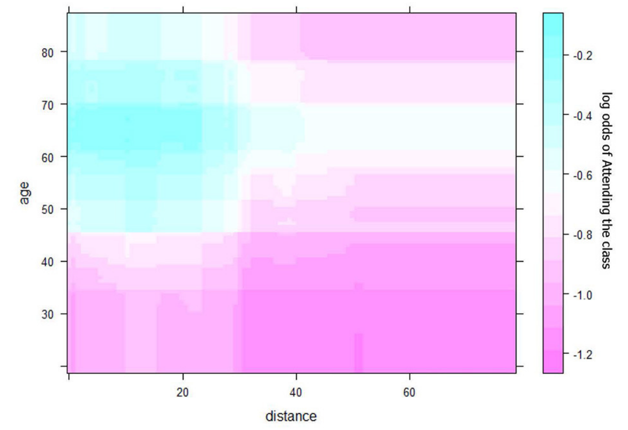

FIGURE 4 | Joint effect of age and distance on class attendance.

TABLE 1 | Summary statistics classified by smoking cessation class attendance.

Variables	Number of patients (%)		*p*-value**
	Scheduled only (*n* = 2,346)	**Attended class (*n* = 1,435)**	
Age*	51.7 (11.35)	54.6 (10.5)	<0.001
Gender			0.002
Female	1,524 (64.96)	1,004 (69.97)	
Male	822 (35.04)	431 (30.03)	
Race			<0.001
African-American	986 (42.03)	514 (35.82)	
White	1,360 (57.97)	921 (64.18)	
Location			<0.001
Rural	1,539 (65.60)	841 (58.61)	
Urban	807 (34.34)	594 (41.39)	
Payer			<0.001
Medicaid	342 (14.58)	144 (10.03)	
Medicare	282 (12.02)	212 (14.77)	
Commercial	111 (4.73)	102 (7.11)	
Free care	1,274 (54.31)	857 (59.72)	
Self-pay	337 (14.36)	120 (8.36)	
Distance*	13.4 (16.72)	11.6 (11.29)	<0.001

**Mean (SD) for continuous variables age and distances. **To test the associations between each variable and the outcome (class attendance), we used ANOVA for the continuous variables and Chi-squared tests for the categorical variables.*

TABLE 2 | Logistic regression results on smoking cessation class attendance.

	Comparison	Odds ratio (95% CI)	*p*-value
(Intercept)			<0.001
Distance	1 mile	0.99 (0.98, 0.99)	<0.001
Urban	Rural	1.51 (1.30, 1.75)	<0.001
Male	Female	0.78 (0.67, 0.90)	<0.001
White	Black	1.66 (1.40, 1.89)	<0.001
Age	1 year younger	1.03 (1.03, 1.08)	<0.001
Free	Commercial insurance	0.69 (0.52, 0.93)	0.013
Medicaid	Commercial insurance	0.46 (0.33, 0.64)	<0.001
Medicare	Commercial insurance	0.65 (0.46, 0.91)	0.012
Self-pay	Commercial insurance	0.41 (0.29, 0.58)	<0.001

*In the analysis, we included all variables that we analyzed to be significantly related with the outcome (class attendance, see **Table 1**).*

attendance for this sample. The probability of a smoker attending class was associated with the distance needed to travel to the counseling site. Smokers who attended class had shorter travel distances to counseling sites (11.6 miles, SD = 11.29) compared to those who scheduled but did not attend class (13.4 miles, SD = 16.72). When the travel distance was more than 15 miles (24 km), the estimated odds of attending class decreased with greater travel distance (**Figure 2**). Compared with patients who only scheduled class, smokers who actually attended class were more likely to be older (54.6 vs. 51.7%), female (69.9 vs. 64.9%), White (64.1 vs. 57.9%), living in urban areas (41.3 vs. 34.3%), and receiving free care (59.7 vs. 54.3%).

Results from logistic regression analyses revealed that shorter distances between home residence and counseling site were associated with higher class attendance rates, even after controlling for other socio-demographic factors (**Table 2**). Individuals more likely to attend counseling included those that lived closer to the counseling site (OR = 1.01, 95% CI = 1.01–1.02), lived in urban settings (OR = 1.51, 95%CI = 1.30–1.75), or were female (OR = 1.28, 95%CI = 1.11–1.49), White (OR = 1.66, 95% CI = 1.40–1.89), commercially insured (OR = 2.41, 95% CI = 1.72–3.44), or older (see OR = 1.03, 95% CI = 1.03–1.08) than their counterparts. There was no evidence for interactions between exposures (sex, race, insurance, and age) and outcome (class attendance).

Partial dependence plots (**Figures 2**, **3**) show the visual relationship between class attendance and distance to facility. **Figure 2** shows that the odds of attending class decreased dramatically if the smoker lived more than 15 miles (24 km) away. Similar patterns were observed for gender, age, and insurance type.

Figure 3 describes how distance from residence to hospital was related with class attendance. For distances within 20 miles (32 km), class attendance rates did not change regularly with greater distance. However, when the distance was >20 miles (32 km), the attendance rate decreased with greater distance. The distance-class attendance relationship changed by gender (**Figure 3A**), race (**Figure 3B**), and payment method (**Figure 3C**). The relationship was not changed significantly by the three variables as indicated by the almost parallel lines depicting the distance-class attendance relationship. Generally, at the same distance, males, African Americans, and patients with Medicaid or self-pay had lower class attendance rates compared with their counterparts.

Figure 4 shows the joint relationship of age and distance on class attendance. Smokers who were older and lived closer to counseling facilities were more likely to attend class. Although older smokers were more likely to attend class than younger smokers, age did not influence this relationship; hence, there was no interaction between age and distance on class attendance. In the analysis, age was considered a continuous variable. In general, people older than 60 had a higher average attendance rate when compared with younger smokers. Specifically, the attendance rate increased with age until about 65, and then decreased slightly.

DISCUSSION

For a patient population with access to free cessation counseling, this analysis examined the effect of distance between residence and counseling site on attendance of cessation counseling classes. Patients who were older, female, White, commercially insured, and with residences in urban areas were more likely to attend cessation counseling class than their counterparts. In addition, for those within a distance of 20 miles (32 km), class attendance rates did not change consistently with greater distance. However, as the distance increased beyond 20 miles (32 km), attendance rates decreased with greater distance. Although previous studies suggest that transportation difficulties and distance between residence and counseling site are associated with attendance for health education counseling (32), little is known about the relationship between distance and attendance of classes for smoking cessation counseling. Specifically, no studies have identified a cutoff point for how far is "too far" for smokers to utilize smoking cessation services. In addition, accessibility to health care service or smoking cessation class is a particular concern to reduce/eliminate health care disparities. A studies in South Africa also showed that distance plays a complex role in mediating health care utilization behavior. To reduce the distance that poor South Africans must travel to obtain health care in poorer areas will reduce inequality. Another study also showed that driving distance from the centroid of each census tract to the nearest CT facility in CT facility access has implications for lung cancer screening (LCS) implementation. Individuals in densely populated areas have relatively greater spatial access to CT facilities than those in sparsely populated tracts (33).

The results for age were consistent with previous reports showing that older patients may be more motivated to quit smoking and attend cessation counseling (34). Older patients are more likely to develop age-related medical illnesses that are exacerbated by smoking, and thus may be more likely to quit smoking in order to improve their health and/or longevity (35).

For this present population, class attendance was associated with gender and race. Females are more likely than males to participate in counseling-based smoking cessation activities (36, 37). Consistent with the present results, in a population of pediatric patients attending a weight management clinic, female patients were more likely to attend (38).

Black smokers are at greater risk for smoking cessation failure compared to their White counterparts (39). However, the factors that contribute to this disparity remain unclear. The present study found that White smokers were more likely to attend smoking cessation counseling classes compared to their Black counterparts, providing a possible explanation for why Black smokers are less likely than White smokers to quit.

Patients living in urban areas may not utilize the nearest health facility, as there may be multiple healthcare facilities within a reasonable distance (23). However, patients living in rural areas are indeed more likely to utilize the nearest health facilities. Patients living in rural areas are less likely to quit smoking in part due to a lack of local cessation programs (24). These results offer a potential explanation for our findings, which showed that smokers residing in rural areas were less likely to attend cessation classes than smokers residing in urban areas. Although rural cancer patients encounter substantial barriers to care, they more often report receiving timely care than urban patients. Recent studies also showed that Geographic distance differentially influences the initiation and completion of treatment among urban and rural cervical cancer patients (40).

Knowing the distance at which attendance of smoking cessation classes substantially decreases is important for inferring how far is "too far" for smokers to utilize smoking cessation services. The present study showed that, within 20 miles (32 km), class attendance rates did not change consistently with greater distance. However, as distance increased to more than 20 miles (32 km), attendance rates decreased sharply with increased distance. To our knowledge, this is the first study to identify a distance cutoff point for attendance of smoking cessation classes. The finding of a distance of 20 miles (32 km) is consistent with other studies. For example, in California, living within 20 miles (32 km) of receiving care was protective against mortality for patients with advanced-stage ovarian cancer (41). Also consistent with our results, another study found that racial and ethnic minorities residing within 20 miles (32 km) were less likely to receive care compared to Whites, and patients with low socioeconomic status (SES) were more likely to live farther away from treatment hospitals than their counterparts (42). Also similar to our results, colorectal cancer surgery patients living 30 km (18.6 miles) from a hospital possessed poorer survival prospects compared to patients who lived close by (43).

Identified distance points beyond which attendance significantly decreases show variations, depending on the main transportation type, type of treatment, and urban or rural location. For example, studies on hospital attendance in rural areas where patients generally reach health facilities by walking have found 3.0–3.5 km (1.9–2.2 miles) to be the distance where 50% of potential attendances are lost (44, 45). Although our finding of 20 miles (32 km) likely represents a driving distance, we cannot be certain what mode of transportation patients took to attend classes.

In the present population, the cost of attending class may have been problematic for smokers of lower SES. Using insurance status as a proxy for SES, we found that, compared to smokers of higher SES (commercial insurance), smokers of lower SES (self-pay, Medicaid, Medicare, or free care), were less likely to attend class. A previous study also found that privately insured patients were more likely to attend weight management class, and Gender and insurance status were the most significant predictors of class attendance (32), consistent with our results.

Results from the present study have limitations. First, since the study utilized a retrospective design, only associations could be determined. Further research is warranted to investigate the underlying etiology of these results. The study was also limited by selection bias, as we assessed only those smokers who were scheduled for and attended cessation counseling classes. Smokers who were not screened by hospital providers for smoking status, or were unable to access cessation services, may not be represented. In other words, the study focused only on smokers who were screened and scheduled for group counseling services. Moreover, since most smokers came from a low SES group, findings may not be translatable to the general population. Additionally, we measured geographic distance along the surface of the earth. With GIS technology, we geocoded patients' home address and class location using geographical coordinates. Thus, the distances measured may not reflect actual traveling time, due to traffic and road environments such as highways, mountains, and speed limits. However, previous studies suggest that distances estimated with GIS technology correlate with driving distances, and mean errors between the two are relatively small (46). Therefore, future studies should confirm the effect of travel time on class attendance in this population. Another limitation of this study is the time frame (2005–2007). However, with the exception of one clinic, the location of all clinics included in this study have remained the same since 2005–2007. The one clinic that changed location is less than half a mile away from the previous location, within the same zip code (previously LSU Interim Hospital, currently University Medical Center). Thus, the results of the current study may still reflect the current traveling distance for patients attending our group counseling classes.

CONCLUSION

Among patients in Louisiana public hospitals, utilization of cessation counseling classes inversely related to the distance from residences to hospitals. Patients who were older, female, White, commercially insured, and with residences in urban areas were more likely to attend cessation counseling classes than their counterparts. To our knowledge, the present study is the first to identify a specific distance where smoking cessation class attendance significantly decreases. This study examined the effect of distance between residence and counseling site on attendance of cessation counseling classes, in a patient population with access to free classes for counseling. Patients who were older, female, White, commercially insured, and with residences in urban areas were more likely to attend cessation counseling classes than their counterparts. Therefore, smokers who live within 20 miles (32 km) of a smoking cessation class site should be considered a priority population for class recruitment. Further, when referring patients to smoking cessation classes, providers should take into account factors that limit patient participation, and consider offering alternative methods of obtaining smoking cessation resources. A distance of 20 miles (32 km) can be used to optimize locations for new smoking cessation programs. Using GIS tool is an efficient way to develop targeted interventions aimed at eliminating disparities in health for racial and ethnic minorities as well as other at-risk populations.

FUTURE RESEARCH

Future research should develop approaches for improving attendance of smoking cessation classes. Greater communication between patients and providers relating to barriers that patients face in obtaining smoking cessation resources is needed. Smoking cessation programs should consider providing more accessible smoking cessation counseling, such as mobile counseling in the community and telemedicine. Furthermore, studies should examine transportation methods and real driving times to smoking cessation resources. Further work is needed to identify access disparities of smoking cessation class to optimize smoking cessation service among eligible smokers for reducing health disparities for cancer prevention and control. Research in this field has the potential to guide tobacco control policies and to improve shared decision making between providers and smokers.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/supplementary files, further inquiries can be directed to the corresponding author.

ETHICS STATEMENT

The present study was reviewed and approved by the Institutional Review Board of Louisiana State University Health Sciences Center New Orleans. Written informed consent for participation was not required for this study in accordance with the national legislation and the institutional requirements.

AUTHOR CONTRIBUTIONS

TT and MC: conceptualization and data collection. TT and QY: methodology and data analysis. TT, MC, and ML: writing—original draft preparation. TL, ML, and SM-T: writing—review and editing. All authors have read and agreed to the published version of the manuscript.

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Examination of the Association Between Access to Care and Lung Cancer Screening Among High-Risk Smokers

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Objective: The purpose of this study was to examine the influence of access to care on the uptake of low-dose computed tomography (LDCT) lung cancer screening among a diverse sample of screening-eligible patients.

Methods: We utilized a cross-sectional study design. Our sample included patients evaluated for lung cancer screening at a large academic medical center (AMC) between 2015 and 2017 who met 2013 USPSTF guidelines for LDCT screening eligibility. The completion of LDCT screening (yes, no) was the primary dependent variable. The independent variable was access to care (insurance type, living within the AMC service area). We utilized binary logistic regression analyses to examine the influence of access to care on screening completion after adjusting for demographic factors (age, sex, race) and smoking history (current smoking status, smoking pack-year history).

Results: A total of 1,355 individuals met LDCT eligibility criteria, and of those, 29.8% ($n = 404$) completed screening. Regression analysis results showed individuals with Medicaid insurance (OR, 1.51; 95% CI, 1.03-2.22), individuals living within the AMC service area (OR, 1.71; 95% CI, 1.21–2.40), and those aged 65–74 years (OR, 1.49; 95% CI, 1.12–1.98) had higher odds of receiving LDCT lung cancer screening. Lower odds of screening were associated with having Medicare insurance (OR, 0.30; 95% CI, 0.22–0.41) and out-of-pocket (OR, 0.27; 95% CI, 0.15–0.47).

Conclusion: Access to care was independently associated with lowered screening rates. Study results are consistent with prior research identifying the importance of access factors on uptake of cancer early detection screening behaviors.

Keywords: racial disparities, lung cancer screening, low-dose computed tomography, social determinants of health, access to care

INTRODUCTION

Chronic high-frequency cigarette smoking is the leading preventable cause of lung cancer worldwide (1). Lung cancer is the second most common cancer diagnosis and the leading cause of cancer-related mortality in the United States (2). In 2020, there were an estimated 228,820 new cases of lung cancer diagnosed (3). The overall 5-year survival rate for lung cancer is 18.6%, with more than half of all lung cancer patients dying within 1 year of diagnosis (4). In 2013, the National Lung Screening Trial (NLST) demonstrated low-dose computed tomography (LDCT) lung cancer screening in older smokers reduced lung cancer mortality by 15–20% due to the early detection of treatable lesions (5). Based on the results from the NLST trial, the United States Preventive Services Task Force (USPSTF) recommended annual screening with LDCT in older adults aged 55–80 years who have a 30 pack-year smoking history and currently smoke or who have quit within the past 15 years (6). In addition, the Centers for Medicare and Medicaid Services (CMS) and private insurers cover annual LDCT screening among people at high risk for lung cancer (7, 8).

Early detection of cancer through screening is an effective way of reducing cancer deaths. Healthy People 2030 sets a national objective for increasing the proportion of adults get lung cancer screened to be 7.5% (9). Despite the benefits of LDCT and increasing coverage by health care insurers, the uptake of lung cancer early detection among eligible smokers remains limited (10). The estimated percentage of qualified individuals who reported completion of LDCT screening ranged from 3.8% in the 2015 National Health Interview Survey (11) to 14.4% in the 2017 Behavioral Risk Factor Surveillance System (BRFSS) survey (12). To date, the factors contribute to the low uptake of LDCT screening among high-risk patients are not well-understood, additional research to identify the provider and patient-level barriers to engagement in screening among high-risk and eligible patients is needed (13–15). Researchers have identified provider-level barriers to patient screening, including poor clinician knowledge (e.g., lack of knowledge about screening guidelines) (16–19), concerns about screening (e.g., skepticism about evidence base and potential harms) (20–22), and time constraints prohibiting appropriate counseling and shared decision making (17, 18). Patient or individual-level barriers to lung cancer screening include fear related to lung cancer (20, 23), lack of knowledge (24), and negative attitudes and inaccurate beliefs about lung cancer screening (25). Furthermore, a range of individual-level demographics is associated with lung cancer screening. For example, older participants, single, insured, or diagnosed with cancer, were more likely to undergo LDCT screening (26). Although individual-level factors contribute to poor health-related outcomes, it has become increasingly clear factors outside of the individual are instrumental to the development and persistence of cancer health inequalities (27).

For the past decade, research to examine the influence of social determinants of health (SDOH) on a myriad of health inequalities, including cancer, has been conducted (28, 29). Social determinants of health are the environmental conditions, both social and physical, affect a wide range of risk exposures, health behaviors, and health-related outcomes (30, 31). In general, the SDOH includes five interconnected domains: economic stability, education, neighborhood, built environment, social and community context, and access to care and health care quality (18, 19). The National Institutes of Health has adopted the SDOH framework to guide research associated with health inequalities and has encouraged additional research to understand better the associations between the SDOH and health-related inequalities and the mechanistic pathways associated with these relationships (32).

Access to care represents a significant yet highly modifiable SDOH. Beyond the SDOH framework, access to health care is central to several theoretical models of health promotion. For example, Andersen's behavioral model of health services utilization has defined access to care (e.g., health insurance, proximity to healthcare facility) as one of the enabling factors related to health services utilization, including cancer screening (33). Prior research has shown poor access to health care is associated with disparities in breast, cervical, and colorectal cancer screening across various patient populations (34–36). However, limited research exists related to the influence of access to care on lung cancer screening after controlling for patient demographic characteristics (e.g., age, race, sex) and smoking behaviors (current smoking status and frequency and length of time smoked). To address this gap in the lung cancer screening literature, we examined the influence of access to care (health insurance type, proximity to healthcare facility) on the completion of LDCT lung cancer screening among patients who met the 2013 USPSTF screening eligibility guidelines. We hypothesized access to health care may be associated with LDCT lung cancer screening uptake after controlling for individual demographic and smoking variables.

METHODS

Study Design

The study utilized a cross-sectional study design using data (2015–2017) from a prominent mid-western academic medical center (AMC). The AMC is located close to the west side of Chicago which are largely racially segregated neighborhoods of concentrated poverty and have a significant proportion of premature deaths attributed by chronic diseases and cancer (37). These neighborhoods comprise more than 500,000 individuals within the AMC's primary service area (38).

First, we identified potentially eligible patients for LDCT lung cancer screening at the AMC. Next, we determine which patients met the 2013 USPSTF guideline for LDCT screening (6). Eligibility criteria were: (i) aged 55–80 years, (ii) no diagnosis of lung cancer or lung-related symptoms, (iii) either a current or former smoker, and (iv) reporting a 30+ pack-year smoking history. We were unable to identity smokers who quit smoking within 15 years due to limited data collection. Therefore, we eliminated 313 patients (18.7%) who did not meet screening criteria. The final analytical dataset included $N = 1,355$ patients (see **Figure 1**). The Institutional Review Boards (IRB) of the Rush University Medical Center approved the study.

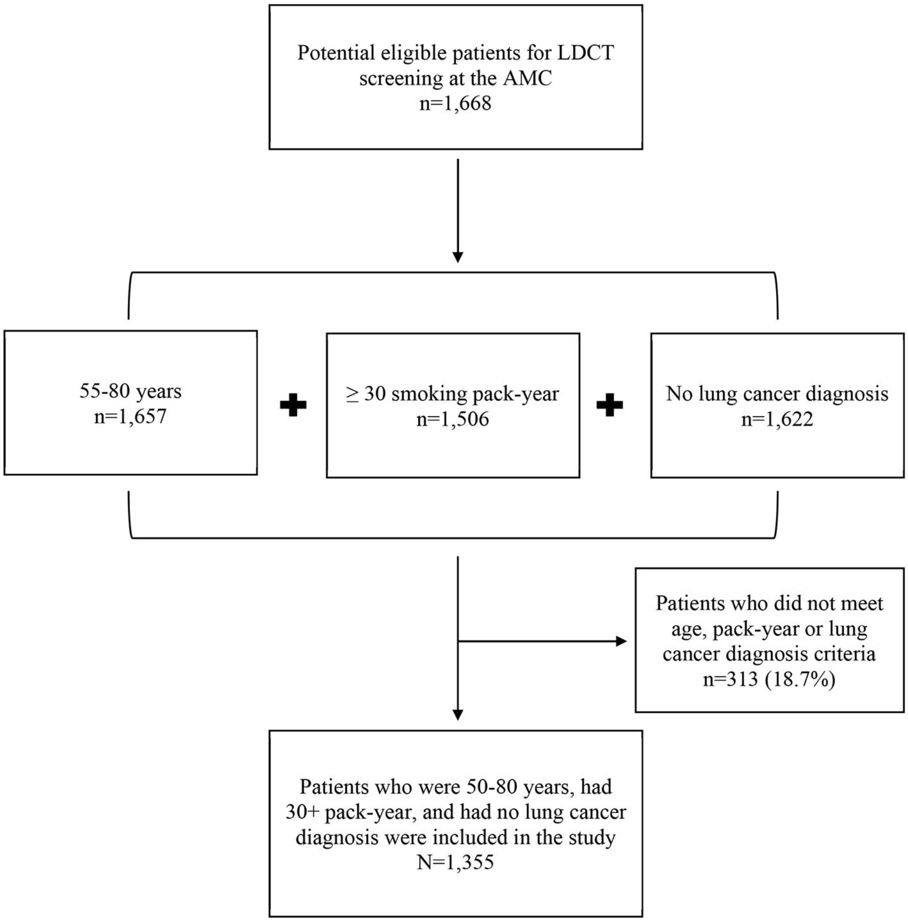

FIGURE 1 | Study sample flow chart.

Lung Cancer Screening Program

Rush University launched its lung cancer screening program in 2015. The program aimed to increase primary care physicians and other providers assess lung cancer screening eligibility among their active patients who smoke. Providers were trained to determine their patients' eligibility for LDCT screening based on USPSTF guidelines, complete shared decision-making about LDCT with the patient, and place an order for LDCT screening. In the program, two registered nurse navigators provide administrative oversight. They review patient eligibility, track results, address patient questions, and coordinate care for patients requiring additional imaging or procedures.

Measures

Independent Variable

Access to health care (a critical social determinant of health) was the primary independent variable. In the current study, we measured two indicators of health care access: primary insurance type (Medicare, Medicaid, private insurance, out-of-pocket) and whether the patient lived within the AMC service area (yes, no). The AMC service area (39) included patients residing in the following residential zip codes 60607, 60608, 60612, 60622, 60623, 60624, 60639, 60644, 60647, and 60651. Proximity to healthcare settings is an established indicator of access to care (40).

Dependent Variable

Patient completion of LDCT lung cancer screening (yes, no) following the determination of eligibility was the primary outcome measure. We verified lung cancer screening completion via chart review.

Control Variables

Demographic factors and smoking behaviors which are known to be associated with cancer screening behaviors, were study control variables. Demographic factors included age (in years), race/ethnicity (African American, White, Other race/ethnicity), and sex (male or female). Smoking history included current smoking status (former smoker, current smoker) and the number of smoking pack-years. We calculated the number of smoking pack-years by multiplying the average number of cigarettes smoked per day by the number of years smoked (6).

Statistical Analysis

Descriptive statistics, including frequency, percentage, mean, and standard deviation (S.D.), were used to describe the characteristics of the study sample. We conducted bivariate tests to examine the associations between LDCT screening completion and independent and control variables. Further, we stratified analysis by race/ethnicity to identify any different variables associated with LDCT screening completion between Whites, African Americans, and Other race/ethnicity. Finally, we conducted binary logistic regression analyses to examine the influence of access to care on LDCT screening completion in three regression models. The first model examined the influence of access to care on LDCT screening completion (model 1) without adjusting for covariates. In the second model, demographic factors were adjusted in the model to examine the association between access to care on LDCT screening completing (model 2). Lastly, demographics and smoking variables were adjusted together in the model to examine the extent to which access to care affects screening completion (model 3).

We performed all statistical analyses and data management using SAS software version 9.4 (SAS Institute, Cary, NC).

RESULTS

Characteristics of Study Participants

Table 1 displays the characteristics of study participants. A total of 1,355 patients were eligible for LDCT screening between 2015

TABLE 1 | Characteristics of the study sample (*N* = 1,355).

	Overall (*n* = 1,355)	**LDCT completion**		***p*-Value**
		Yes (*n* = 404, 29.8%)	**No (*n* = 951, 70.2%)**	
		***N* (%)**	***N* (%)**	
DEMOGRAPHIC FACTORS				
Age (Years) [Mean ± SD]	66.3 ± 6.2	65.8 ± 6.2	66.5 ± 6.3	0.049*
Age				0.291
55–64	583 (43.0)	186 (31.9)	397 (68.1)	
65–74	591 (43.6)	170 (28.8)	421 (71.2)	
75–80	181 (13.4)	48 (26.5)	133 (73.5)	
Sex				0.593
Male	683 (50.4)	199 (29.1)	484 (70.9)	
Female	672 (49.6)	205 (30.5)	467 (69.5)	
Race/Ethnicity				0.005**
White	894 (66.0)	248 (27.7)	646 (72.3)	
African American	350 (25.8)	128 (36.6)	222 (63.4)	
Others	111 (8.2)	28 (25.2)	83 (74.8)	
ACCESS TO HEALTHCARE FACTORS				
Insurance type				<0.001***
Medicare	454 (33.5)	78 (17.2)	376 (82.8)	
Medicaid	142 (10.5)	70 (49.3)	72 (50.7)	
Private	645 (47.6)	241 (37.4)	404 (62.6)	
Out-of-Pocket	114 (8.4)	15 (13.2)	99 (86.8)	
Lives within the AMC service area			<0.001***	
Yes	222 (16.4)	92 (41.4)	130 (58.6)	
No	1133 (83.6)	312 (27.5)	821 (72.5)	
SMOKING HISTORY				
Smoking status				0.002**
Former	766 (56.5)	202 (26.4)	564 (73.6)	
Current	589 (43.5)	202 (34.3)	387 (65.7)	
Smoking pack-years [Mean ± SD]	*51.5 ± 42.3*	*46.9 ± 21.7*	*53.4 ± 48.4*	<0.001***
Smoking pack-years				0.017*
30–39	417 (30.8)	139 (33.3)	278 (66.7)	
40–49	478 (35.3)	150 (31.4)	328 (68.6)	
50+	460 (33.9)	115 (25.0)	345 (75.0)	

SD, standard deviation.
**p < 0.05, **p < 0.01, ***p < 0.001.*

and 2017. Eligible patients were on average 66.3 years of age (SD = 6.2), male (50.4%), Caucasian (66.0%), former smokers (56.5%), and reported a mean smoking pack-year history of 51.5 years (SD = 42.3).

Bivariate Analyses

Less than a third of all eligible participants (29.8%, $n = 404$) completed LDCT lung cancer screening. As shown in **Table 1**, patients who received screening were younger (65.8 ± 6.2) than those who did receive screening (66.5 ± 6.3). African American ethnicity (36.6%), Medicaid insurance (49.3%), who lived within the AMC service area (41.4%), current smoker (34.3%), and patients who reported a 30–39 pack-year smoking history (33.3%) were correlates of lung cancer screening completion. **Table 2** presents LDCT screening completion rates stratified by racial/ethnic group. Variations in correlates of screening uptake were observed based on race/ethnicity. Among African Americans, a higher percentage of patients with Medicaid (50.8%), who lived within the AMC service area (43.5%), and who were current smokers (42.6%) received screening. For Whites, patients with Medicaid (49.2%) were more likely to complete screening. None of the demographic, access to care factors, or smoking variables was associated with LDCT completion among individuals from the combined other race category. Regardless of racial/ethnic, patients who received screening had a lower smoking pack-year than those who did not receive screening.

Multivariate Analyses

Table 3 displays the results of hierarchical logistic regression models. In Model 1, we examined the influence of access to care (insurance type and living within the AMC service area) on LDCT screening completion. Compared to patients with private

TABLE 2 | LDCT screening completion rates stratified by race/ethnicity.

	White ($N = 894$)			**African American ($N = 350$)**			**Other Race/Ethnicity (N=111)**		
	LDCT completion			**LDCT completion**			**LDCT completion**		
	Yes ($n = 248$)	**No ($n = 646$)**		**Yes ($n = 128$)**	**No ($n = 222$)**		**Yes ($n = 28$)**	**No ($n = 83$)**	
	***N* (%)**	***N* (%)**	***p*-Value**	***N* (%)**	***N* (%)**	***p*-Value**	***N* (%)**	***N* (%)**	***p*-Value**
DEMOGRAPHIC FACTORS									
Age (years) [Mean ± SD]	65.9 ± 6.2	66.6 ± 6.2	0.162	65.6 ± 6.4	66.5 ± 6.5	0.195	65.8 ± 5.3	66.3 ± 6.3	0.664
Age			0.719			0.184			0.709
55–64	106 (28.2)	270 (71.8)		66 (41.8)	92 (58.2)		14 (28.6)	35 (71.4)	
65–74	114 (28.2)	290 (71.8)		45 (31.9)	96 (68.1)		11 (23.9)	35 (76.1)	
75–80	28 (24.6)	86 (75.4)		17 (33.3)	34 (66.7)		3 (18.8)	13 (81.3)	
Sex			0.550			1.000			0.247
Male	124 (26.8)	338 (73.2)		53 (36.8)	91 (63.2)		22 (28.6)	55 (71.4)	
Female	124 (28.7)	308 (71.3)		75 (36.4)	131 (63.6)		6 (17.7)	28 (82.4)	
ACCESS TO HEALTHCARE FACTORS									
Insurance type			<0.001***			<0.001***			0.053
Medicare	49 (16.2)	254 (83.8)		26 (21.1)	97 (78.9)		3 (10.7)	25 (89.3)	
Medicaid	30 (49.2)	31 (50.8)		34 (50.8)	33 (49.3)		6 (42.9)	8 (57.1)	
Private	157 (35.7)	283 (64.3)		67 (44.4)	84 (55.6)		17 (31.5)	37 (68.5)	
Out-of-Pocket	12 (13.3)	78 (86.7)		1 (11.1)	8 (88.9)		2 (13.3)	13 (86.7)	
Living within AMC's service area		0.060			0.032*			0.247	
Yes	25 (38.5)	40 (61.5)		60 (43.5)	78 (56.5)		7 (36.8)	12 (63.2)	
No	223 (26.9)	606 (73.1)		68 (32.1)	144 (67.9)		21 (22.8)	71 (77.2)	
SMOKING HISTORY									
Smoking Status			0.069			0.020*			0.816
Former	131 (25.3)	386 (74.7)		53 (30.5)	121 (69.5)		18 (24.0)	57 (76.0)	
Current	117 (31.0)	260 (69.0)		75 (42.6)	101 (57.4)		10 (27.8)	26 (72.2)	
Smoking pack-years [Mean±SD]	48.1 ± 20.9	52.1 ± 31.2	0.026*	45.0 ± 22.2	57.2 ± 82.6	0.039*	45.8 ± 26.3	53.7 ± 32.6	0.251
Smoking pack-years			0.127			0.119			0.311
30–39	81 (32.0)	172 (68.0)		46 (35.7)	83 (64.3)		12 (34.3)	23 (65.7)	
40–49	88 (27.8)	229 (72.2)		54 (42.9)	72 (57.1)		8 (22.9)	27 (77.1)	
50+	79 (24.4)	245 (75.6)		28 (29.5)	67 (70.5)		8 (19.5)	33 (80.5)	

SD, standard deviation.
$^*p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$.

TABLE 3 | Influence of access to healthcare, smoking history, and demographic factors on LDCT screening completion.

	Model 1		**Model 2**		**Model 3**	
	Adjusted OR (95% C.I.)	***P*-value**	**Adjusted OR (95% C.I.)**	***P*-value**	**Adjusted OR (95% C.I.)**	***P*-value**
ACCESS TO HEALTHCARE FACTORS						
Insurance type						
Private	Ref.		Ref.		Ref.	
Medicaid	1.48 (1.02–2.15)	0.038*	1.47 (1.01–2.14)	0.043*	1.51 (1.03–2.22)	0.033*
Medicare	0.34 (0.25–0.45)	<0.001***	0.35 (0.26–0.48)	<0.001***	0.30 (0.22–0.41)	<0.001***
Out-of-pocket	0.26 (0.15–0.45)	<0.001***	0.27 (0.15–0.48)	<0.001***	0.27 (0.15–0.47)	<0.001***
Living within AMC service area						
No	Ref.		Ref.		Ref.	
Yes	1.79 (1.31–2.45)	<0.001***	1.78 (1.30–2.44)	<0.001***	1.71 (1.21–2.40)	0.002**
SMOKING HISTORY						
Current smoking status						
Former			Ref.		Ref.	
Current			1.25 (0.98–1.60)	0.077	1.28 (1.00–1.64)	0.054
Smoking pack-year						
30–39			Ref.		Ref.	
40–49			0.98 (0.73–1.32)	0.915	0.96 (0.72–1.29)	0.802
50+			0.82 (0.60–1.11)	0.200	0.76 (0.55–1.04)	0.089
DEMOGRAPHIC FACTORS						
Age						
55–64					Ref.	
65–74					1.49 (1.12–1.98)	0.006**
75–80					1.48 (0.97–2.25)	0.069
Race/Ethnicity						
White					Ref.	
African American					1.10 (0.81–1.49)	0.548
Others					0.78 (0.49–1.26)	0.312
Sex						
Female					Ref.	
Male					0.97 (0.76–1.25)	0.817

*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$.

insurance, Medicaid patients were more likely to complete screening (adjusted OR = 1.48; 95% CI = 1.02–2.15), while Medicare patients (adjusted OR = 0.34; 95% CI = 0.25–0.45) and out-of-pocket patients (adjusted OR = 0.26; 95% CI = 0.15–0.45) were less likely to complete screening. Patients living within the AMC service area were more likely to complete screening (adjusted OR = 1.79; 95% CI = 1.31–2.45) than those living outside the AMC service area. Model 2 shows the influence of smoking variables (current smoking status and smoking pack-year history) and access to care on LDCT screening. After adjusting for smoking status and smoking pack-year history, access to health care variables, including insurance coverage, and living within the AMC service area remained significantly associated with screening completion. In model 3, we entered demographic variables (age, race, and sex) along with smoking and access to care factors. The influence of insurance type and living within the AMC service area variables on screening completion were consistent with the results of Models 1 and 2 (Nagelkerke's R-square = 0.125; Hosmer and Lemeshow Goodness-of-Fit Test, $p = 0.372$). Among demographic variables, age was the only statistically significant predictor of screening completion. Specifically, people aged 65–74 (adjusted OR = 1.49; 95% CI = 1.12–1.98) were more likely to receive screening than those aged 55–64.

DISCUSSION

The study analyzed data obtained from a large mid-west AMC serves a diverse patient population to examine the influences of access to care on completion of LDCT lung cancer screening. In particular, study results showed insurance type and proximity to healthcare were significantly associated with LDCT lung cancer screening uptake. Furthermore, access to care had a more significant impact on screening completion than individual demographics and smoking history.

In the current study, LDCT completion rates among eligible patients were low, with less than one-third of eligible patients receiving a screening test. The low uptake of screening is notable because all patients were at elevated risk of lung cancer based on their chronic and high-frequency smoking history. In addition, low screening uptake among eligible smokers is particularly concerning given a quarter of the sample was African American, a population with known lung cancer disparities. For example, in Cook County, where Chicago is, the 5-year lung cancer incidence rates among African Americans are elevated compared to whites (41), especially in communities characterized by concentrated disadvantage, racial segregation, and poor access to health care. Further, the all-cause morbidity and mortality due to smoking are higher among low-income and African American smokers due to a high prevalence of illnesses exacerbated by smoking (e.g., diabetes) (42). Thus, persistent smoking-related inequalities underscore the importance of identifying and reducing barriers to lung cancer screening among diverse patient populations.

Prior research has shown access to health care is an essential social determinant of health. In particular, proximity to a screening facility seems to influence cancer screening behaviors (43, 44). In the current study, access to health care was associated with LDCT lung cancer early detection screening after controlling other demographic and smoking variables. Specifically, patients who reported living within the AMC service area were more likely to engage in lung cancer screening than those outside these boundary areas (41.0 vs. 27.5%). These study results are consistent with previous study findings proximity to the screening center was one of the most critical factors associated with adherence to cancer early detection screenings (45–47).

Type of insurance coverage was another important indicator of healthcare access. In this study, patients reporting Medicaid insurance coverage had a higher likelihood of completing LDCT lung cancer screening than privately insured individuals. In 2014, Medicaid expansion was enacted under the Patient Protection and Affordable Care Act. Medicaid expansion provides coverage for eligible low-income individuals who do not have health care insurance (48). Medicaid expansion has improved access to care among low-income individuals (49, 50). More specifically, studies have found Medicaid expansion was associated with increased cancer screenings among low-income adults (51–54). Illinois is one of the states with early implementation of Medicaid expansion (55). According to the U.S. Census Statistics, 18.4% of Chicago city residents live at or below the poverty rate (56). Additional research is needed to understand better the role of Medicaid coverage in increasing LDCT completion rates.

In addition, we found individuals with Medicare were less like to complete LDCT screening. There are several explanations for this association. A large proportion of Medicare beneficiaries are people aged 65 years and older. This older population might have more severe comorbidities or have a short life expectancy. Therefore, healthcare provider might not recommend this group of older people to be screened, given potential risks may outweigh the benefits of screening in this population (57). Furthermore, CMS requires a mandated shared decision-making visit between the provider and Medicare beneficiary before the screening can be ordered and performed (7). Shared decision-making can improve patients' knowledge of the benefits and potential harms of LDCT screening and help in making patient-centered decision through patient-provider communication (20). However, a recent study showed only about 7% of patients who underwent LDCT screening had a shared decision-making visit (58). As such, the requirement for a separate shared decision-making visit may be a barrier (59, 60) to the uptake of LDCT screening among Medicare beneficiaries. Additional research is needed to evaluate whether the mandated shared decision-making appointment represents an unanticipated barrier to screening and identify other factors associated with potentially lower LDCT engagement among Medicare beneficiaries.

Disparities in the utilization of preventive healthcare services persist based on demographic factors. In the present study, participant age was a statistically significant correlate of screening among eligible patients. Our results were consistent with prior research showing older participants (aged 65–69) were most likely to be screened for lung cancer compared to younger participants (aged 55–59 or 55–64) (26, 61). In addition, our study found no difference in LDCT screening among people aged 75–80. One potential explanation is older adults with an anticipated life expectancy of fewer than 10 years may not be recommended for cancer screening by providers (62). Counter to prior research findings related to the influence of race/ethnicity on engagement in cancer screening (63–65), in the current study, a higher percentage of African Americans completed LDCT screening compared to white and members of other racial/ethnic groups. The AMC's lung cancer program aims to increase health screening and to improve health outcomes among people living in underserved communities (66–68). The medical center is immediately adjacent to a predominately low-income and African American community on the west side of Chicago. As an anchor institution on the West Side of Chicago, the medical center continuously works with the low-income communities to help residents address the causes of poor health and achieve better health (69, 70). These targeted initiatives may have resulted in increased interest and willingness to receive screenings among eligible patients. The observed racial differences in LDCT screening were no longer present after controlling whether patients lived within the AMC's serving areas. These findings suggest the importance of community-level outreach and engagement efforts for increasing screening behaviors among underserved communities.

LIMITATIONS

We acknowledge several limitations within our study. First, smoking behaviors used to determine an individual's eligibility for LDCT screening were self-reported. However, all official eligibility assessments for LDCT lung cancer screening are self-reported. As such, any recall bias is likely equally distributed across all study participants. Second, the study sample size of eligible individuals for LDCT screening among former smokers might be slightly over or under-estimated due to an absence of verifiable information on how long it has been since participants quit smoking. Third, the study sample included patients seen in a large AMC located in a Midwestern state. As a result, our study results may not generalize to patients who receive services in other types of health care settings. Further, reported screening completion rates may be inaccurate due to other comorbidities (e.g., heart diseases, other cancers or severe lung diseases like asthma or chronic obstructive pulmonary disease) would exclude eligible patients from screening (71), or patients may have completed LDCT screening at another healthcare facility. Further study can examine the influence of comorbidities on screening behavior. Finally, other factors influencing cancer screening behavior such as having a usual source of care (72), access to transportation (73, 74), health literacy (75, 76), doctor's recommendation (77, 78), and other socioeconomic factors (e.g., marital status, education, income, poverty level, home rental, etc.) (79–81) were not measured due to data limitation and can be controlled in future studies.

CONCLUSIONS

Our study highlights the influence of a critical social determinant of health, healthcare access, and lung cancer screening uptake among eligible patients. These results are consistent with prior research suggesting the relative importance of access on engagement with a range of cancer screening behaviors (34–36). Therefore, additional efforts to identify which health care coverage serves as a barrier to obtaining lung cancer screening among eligible patients are needed. Further, offering high-quality screening in different locations may reduce barriers to cancer screening.

DATA AVAILABILITY STATEMENT

The data analyzed in this study is subject to the following licenses/restrictions: Rush IRB will not allow the dataset to be shared with people outside of study team.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Rush University Institution of Review Board. Written informed consent for participation was not required for this study in accordance with the national legislation and the institutional requirements.

AUTHOR CONTRIBUTIONS

C-CL and AM: study concept and design, interpretation of study results, and manuscript write-up. Y-HK and W-TL: data analysis and interpretation of study results. JB and LD: acquisition of data and critical revision of the manuscript. All authors contributed to the article and approved the submitted version.

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Disease Burden and Attributable Risk Factors of Ovarian Cancer From 1990 to 2017: Findings From the Global Burden of Disease Study 2017

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Aim: We aimed to estimate the disease burden and risk factors attributable to ovarian cancer, and epidemiological trends at global, regional, and national levels.

Methods: We described ovarian cancer data on incidence, mortality, and disability-adjusted life-years as well as age-standardized rates from 1990 to 2017 from the Global Health Data Exchange database. We also estimated the risk factors attributable to ovarian cancer deaths and disability-adjusted life-years. Measures were stratified by region, country, age, and socio-demographic index. The estimated annual percentage changes and age-standardized rates were calculated to evaluate temporal trends.

Results: Globally, ovarian cancer incident, death cases, and disability-adjusted life-years increased by 88.01, 84.20, and 78.00%, respectively. However, all the corresponding age-standardized rates showed downward trends with an estimated annual percentage change of −0.10 (−0.03 to 0.16), −0.33 (−0.38 to −0.27), and −0.38 (−0.32 to 0.25), respectively. South and East Asia and Western Europe carried the heaviest disease burden. The highest incidence, deaths, and disability-adjusted life-years were mainly in people aged 50–69 years from 1990 to 2017. High fasting plasma glucose level was the greatest contributor in age-standardized disability-adjusted life-years rate globally as well as in all socio-demographic index quintiles and most Global Disease Burden regions. Other important factors were high body mass index and occupational exposure to asbestos.

Conclusion: Our study provides valuable information on patterns and trends of disease burden and risk factors attributable to ovarian cancer across age, socio-demographic index, region, and country, which may help improve the rational allocation of health resources as well as inform health policies.

Keywords: ovarian cancer, Global Burden of Disease (GBD), incidence, death, disability adjusted life-years

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INTRODUCTION

Ovarian cancer (OC) is the most common cancer in females worldwide and has a high mortality rate (1–3). Around 290,000 new OC cases (3.4% of all new cancer cases in females) have been diagnosed annually (3). Based on the latest global cancer statistics published in 2018, the age-standardized incidence rate (ASIR) and death rate (ASDR) of OC were 6.6 and 3.9 per 100,000 people, respectively. Epidemiological data from Saudi Arabia (4), China (5), and India (6) showed a remarkable OC burden with associated incidence and mortality. The Global Burden of Disease (GBD) studies provide global, regional, and country-specific epidemiological data of diseases and injuries showing the burden, distribution, and trends in different countries and regions (7–9). At present, there are no comprehensive and comparable assessments of incidence, mortality, disability, and epidemiological trends of OC at the global scale or in most regions.

Aside from family history, genetic factors, such as BRCA mutations as well as non-genetic factors, such as diabetes mellitus, high body mass index (BMI), tobacco, and alcohol use are the main risk factors for OC (10). Various single-institute studies have demonstrated the correlations between OC and these risk factors (11–13). Patients with risk factors such as diabetes mellitus are reportedly at a notably high risk for OC, and interventions such as metformin use dramatically reduce OC incidence (14). A systematic review suggested that OC risk was inversely associated with intake of black tea or calcium, and positively associated with intake of skim/low-fat milk or lactose (15). Such findings imply the necessity of comprehensive and comparable assessments of risk factors attributable to OC, which could then help in the development of prevention and treatment strategies.

In this study, we evaluated the burden and risk factors attributable to OC by location, social-development index (SDI), and age, providing valuable information on the distribution and trends of incident cases, deaths, disability-adjusted-life-years (DALYs), and risk factors, which could be beneficial to the improvement of health resources allocation and in the informed formulation of policies.

MATERIALS AND METHODS

Data Acquisition

Annual data (inclusive dates: 1990–2017) on incidence, death, DALYs, and the corresponding age-standardized rates (ASRs) as well as risk factors attributable to OC were searched in the Global Health Data Exchange (GHDx) database (http://ghdx.healthdata.org/). All data are computed for direct inquiry and download through the GBD Results Tool. Details of methodology were described in the database help page and previous publications (16). These data were segmented by SDI quintiles, regions, countries, and territories. SDI reflects the degree of social development and correlates with total fertility, per capita income, and average years of education (17). All countries and territories were sorted into five quintiles based on SDI (http://ghdx.healthdata.org/record/ihme-data/gbd-2017-socio-demographic-index-sdi-1950%E2%80%932017). GBD regions are not actual geopolitical units; rather, these are groupings of countries created for analytical purposes alone (http://www.healthdata.org/sites/default/files/files/Data_viz/GBD_2017_Tools_Overview.pdf). Risk is defined as exposure, behavior, or other factors that are causally related to an increased (or decreased) probability of OC. If the probability decreased, the risk was considered a protective factor. In this GBD database, all of these risks were organized in four Levels, where Level 1 represents the overarching categories (behavioral, environmental and occupational, and metabolic) nested within Level 1 risks; Level 2 contains both single risks and risk clusters (such as the high fasting plasma glucose level); Level 3 contains the disaggregated single risks from within Level 2 risk clusters (such as low birthweight and short gestation); and Level 4 details risks with the most granular disaggregation, such as for specific occupational carcinogens, the subcomponents of child growth failure, and suboptimal breastfeeding (18). GBD risk hierarchy with levels were shown in the **Supplementary Table 2** of Supplementary Appendix 1 in this paper (18). Data of all level risks were extracted to evaluate their variation tendency and effect on OC.

This study followed the Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER) for cross-sectional studies (19).

Statistical Analyses

ASRs were analyzed to compare the OC incidence and mortality trends between different cohorts. DALYs refer to the years lived with disability and years of life lost (20). Estimated annual percentage changes (EAPCs) indicate ASR trends during a defined period. The specific EAPC algorithm has been described in our previous works (7, 9, 21, 22).

World maps and graphs were generated to display the distribution and change trends of global, regional, and national disease burden and risk factors attributable to OC. All calculations and figures were performed and made using EXCEL 2013 (Microsoft Corporation) and R software (version 4.0.0) with “openxlsx,” “ggplot2,” “RColorBrewer,” “maptools,” and other packages.

RESULTS

Global OC Incidence

The incident cases of OC increased from 152,090 (95% UI: 145,450–162,170) to 286,130 (95% UI: 278.08 to 295.31) globally, with a total increase of 88.01% from 1990 to 2017. The ASIR values demonstrated a downtrend (EAPC: −0.10, 95% UI: −0.03 to 0.16) (**Table 1**). In 2017, the prevalence case number of OC was 1,353,050. Most of these cases were distributed in East, South, and Southeast Asia (**Supplementary Figure 1**). In all SDI quintiles, the prevalence of OC in the high SDI quintile (410,127) ranked first, followed by the middle SDI quintile (335,709).

OC incident cases increased in a total of 184 countries and territories. The incident cases in Venezuela increased most from 106.25 to 1178.45 (**Figure 1** and **Supplementary Table 1**). Compared with other countries and territories, higher number

TABLE 1 | The incidence of ovarian cancer, and its temporal trends from 1990 to 2017.

Characteristics	1990		2017		1990–2017	
	Incident cases No. ×10^3 (95% UI)	**ASIR per 100,000 No. (95% UI)**	**Incident cases No. ×10^3 (95% UI)**	**ASIR per 100,000 No. (95% UI)**	**Change in Incidence No. (%)**	**EAPC No. (95% CI)**
Global	152.09 (145.45–162.17)	6.71 (6.43–7.14)	286.13 (278.08–295.31)	6.83 (6.63–7.05)	88.01	−0.10 (−0.03 to 0.16)
SDI						
High SDI	74.91 (73.80–76.06)	11.28 (11.11–11.45)	91.49 (88.39–94.67)	9.20 (8.89–9.52)	22.13	−0.92 (−1.03 to −0.81)
High-middle SDI	34.04 (32.08–35.82)	6.31 (5.96–6.64)	59.26 (57.22–61.32)	6.38 (6.15–6.60)	74.08	−0.19 (−0.31 to 0.07)
Middle SDI	21.88 (20.50–24.62)	3.68 (3.46–4.13)	67.61 (64.75–70.72)	5.69 (5.46–5.95)	209.00	1.55 (1.48–1.62)
Low-middle SDI	14.17 (12.30–17.81)	4.17 (3.64–5.21)	47.69 (42.75–56.05)	6.74 (6.07–7.82)	236.56	1.81 (1.76–1.86)
Low SDI	6.76 (5.12–10.04)	3.49 (2.69–5.09)	19.20 (17.00–22.32)	4.58 (4.06–5.34)	184.02	0.91 (0.73–1.09)
Regions						
Andean Latin America	0.31 (0.27–0.35)	2.36 (2.10–2.65)	1.88 (1.64–2.16)	6.42 (5.60–7.37)	506.45	4.19 (3.38–4.19)
Australasia	1.31 (1.27–1.36)	10.69 (10.29–11.09)	1.89 (1.65–2.16)	8.37 (7.31–9.63)	44.27	−1.06 (−1.16 to −0.97)
Caribbean	0.30 (0.27–0.34)	2.03 (1.84–2.32)	1.67 (1.50–1.91)	6.34 (5.69–7.27)	456.67	4.18 (3.26–5.11)
Central Asia	1.42 (1.24–1.69)	4.85 (4.24–5.75)	2.83 (2.65–3.01)	6.16 (5.79–6.54)	99.30	0.95 (0.80–1.11)
Central Europe	8.66 (8.43–8.90)	11.02 (10.71–11.32)	10.87 (10.35–11.39)	11.06 (10.53–11.61)	25.52	−0.03 (−0.09 to 0.15)
Central Latin America	2.59 (2.51–2.66)	4.66 (4.53–4.79)	9.50 (9.02–9.99)	7.25 (6.89–7.62)	266.80	1.66 (1.47–1.85)
Central Sub-Saharan Africa	0.55 (0.39–0.74)	3.71 (2.76–4.73)	1.44 (1.11–1.83)	4.30 (3.31–5.43)	161.82	0.36 (0.21–0.50)
East Asia	16.19 (14.92–18.47)	2.92 (2.70–3.34)	43.75 (41.18–46.25)	4.22 (3.96–4.46)	170.23	1.18 (0.91–1.46)
Eastern Europe	16.06 (14.74–18.01)	10.00 (9.11–11.29)	17.39 (16.52–18.25)	9.84 (9.29–10.41)	8.21	−0.30 (−0.30 to 0.01)
Eastern Sub-Saharan Africa	3.16 (2.54–4.22)	6.56 (5.38–8.53)	7.02 (5.87–8.03)	6.72 (5.67–7.62)	122.15	−0.25 (−0.43 to −0.06)
High-income Asia Pacific	6.39 (6.26–6.52)	5.87 (5.74–5.99)	12.10 (11.34–12.80)	7.12 (6.65–7.60)	89.36	0.90 (0.62–1.19)
High-income North America	21.81 (21.33–22.40)	11.77 (11.52–12.11)	27.68 (26.20–29.12)	9.54 (8.96–10.10)	26.91	−1.09 (−1.26 to −0.92)
North Africa and Middle East	4.00 (3.41–5.36)	3.89 (3.36–5.14)	12.77 (12.01–13.63)	5.22 (4.91–5.55)	219.25	1.18 (1.11–1.25)
Oceania	0.09 (0.06–0.12)	4.34 (3.29–5.81)	0.31 (0.23–0.43)	7.05 (5.54–9.17)	244.44	1.99 (1.87–2.10)
South Asia	12.74 (10.91–16.48)	3.70 (3.19–4.79)	48.75 (43.90–56.10)	6.34 (5.76–7.20)	282.65	1.95 (1.79–2.12)
Southeast Asia	9.93 (8.49–12.83)	5.80 (5.01–7.42)	27.41 (24.13–31.86)	7.93 (7.00–9.19)	176.03	1.19 (1.11–1.27)
Southern Latin America	1.78 (1.64–1.92)	6.93 (6.38–7.48)	3.10 (2.75–3.51)	7.46 (6.62–8.48)	74.16	0.20 (0.02–0.38)
Southern Sub-Saharan Africa	0.91 (0.83–1.00)	4.97 (4.51–5.42)	2.10 (1.89–2.27)	6.04 (5.45–6.54)	130.77	0.75 (0.16–1.34)
Tropical Latin America	3.10 (2.97–3.25)	5.35 (5.15–5.60)	7.96 (7.60–8.32)	6.24 (5.96–6.53)	156.77	0.34 (0.18–0.49)
Western Europe	39.11 (38.40–39.86)	13.22 (12.96–13.49)	40.41 (38.33–42.59)	10.04 (9.49–10.56)	3.32	−1.22 (−1.31 to −1.14)
Western Sub-Saharan Africa	1.69 (1.34–2.32)	3.34 (2.66–4.59)	5.30 (4.18–6.69)	4.47 (3.54–5.59)	213.61	1.10 (1.09–1.12)

ASIR, age standardized incidence rate; EAPC, estimated annual percentage change; CI, confidence interval; UI, uncertainty interval; SDI, socio-demographic index.

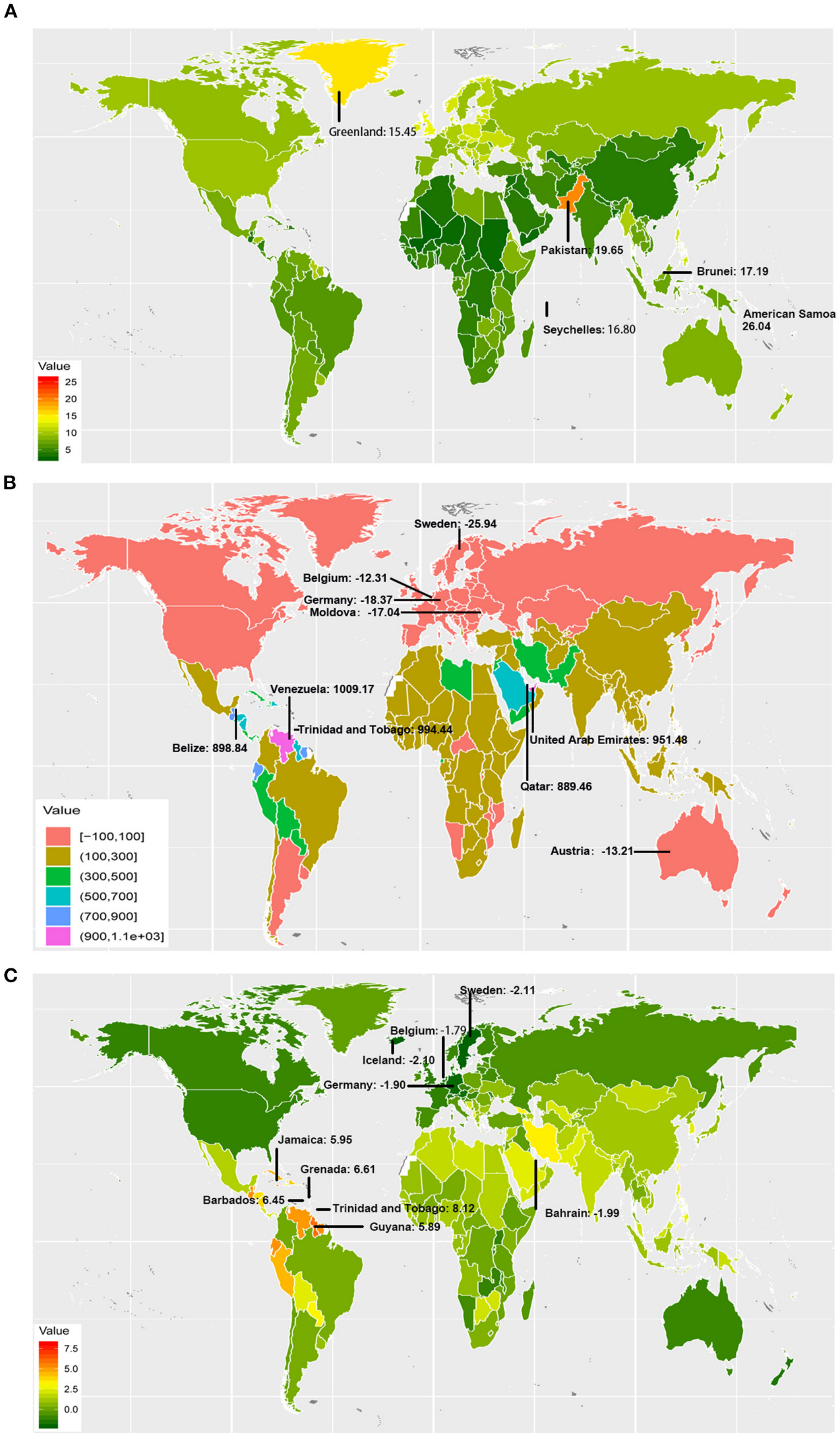

FIGURE 1 | The incidence burden of ovarian cancer in 195 countries and territories. **(A)** The ASIR (per 100,000 people) of ovarian cancer globally in 2017; American Samoa, Pakistan, Brunei, Seychelles, and Greenland had the top 5 ASIR in 2017. **(B)** The relative change (%) in incident cases of ovarian cancer between 1990 and 2017; the greatest changes were exhibited in Venezuela and Sweden. **(C)** The EAPC of ovarian cancer ASIR from 1990 to 2017; the greatest EAPC were exhibited in Trinidad and Tobago, and Sweden. ASIR, age-standardized incidence rate; EAPC, estimated annual percentage change.

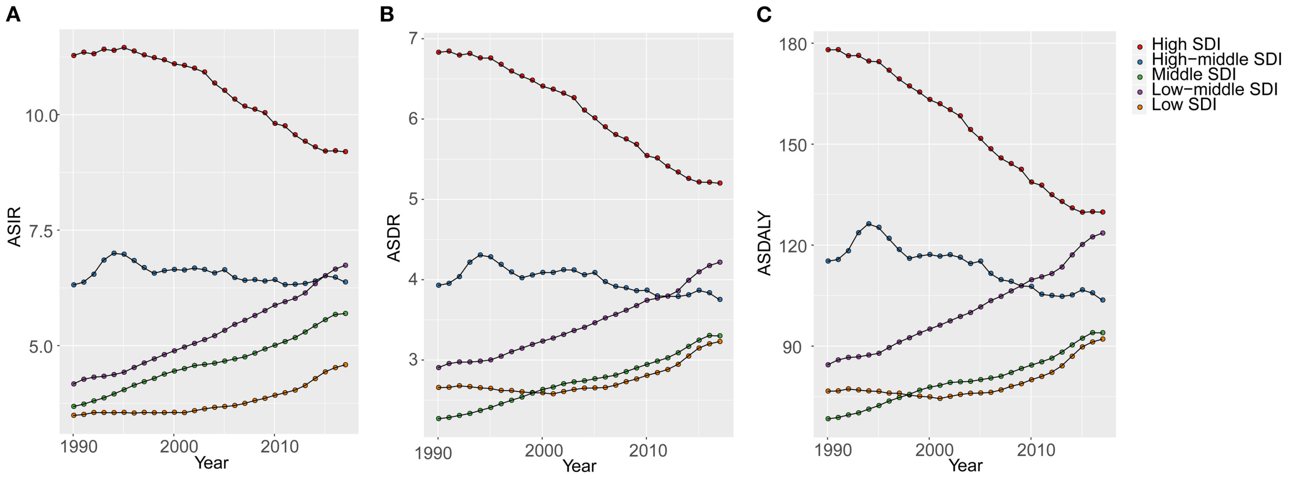

FIGURE 2 | The changes of age-standardized rates of different SDI quintiles from 1990 to 2017 (per 100,000). **(A)** ASIR, age standardized incidence rate; **(B)** ASDR, age standardized death rate; **(C)** DALY, disability adjusted life-year. SDI, socio-demographic index; GBD, global burden of diseases.

of incident cases were observed in China (40646.50, 95% UI: 38111.86–43093.19) and India (31441.05, 95% UI: 27725.81–36329.42), whereas fewer cases were observed in Kiribati (1.42, 95% UI: 0.96–1.95) and Northern Mariana Islands (1.89, 95% UI: 1.54–2.30) (**Supplementary Figure 2** and **Supplementary Tables 2**, **3**). On the other hand, American Samoa had the highest ASIR (26.04 per 100,000 people), whereas Mali had the lowest (2.33 per 100,000 people) in 2017 (**Figure 1** and **Supplementary Figure 3**). The video shows the dynamic changes of countries with the top 10 ASIR of OC from 1990 to 2017 (**Supplementary Video 1**).

OC incident cases increased in 16 GBD regions from 1990 to 2017 (**Table 1**). The greatest increase was observed in Andean Latin America (506.45%). In the high and high-middle SDI quintiles, incident cases increased whereas the corresponding ASIRs decreased (EAPC: −0.92 and −0.19, respectively) (**Table 1**). The highest (EAPC: 1.81) and lowest (EAPC: 0.91) increase in OC incidence were observed in the low-middle and low SDI quintiles, respectively. The ASIRs trended upwards in the low, low-middle, and middle SDI quintiles over 28 years from 1990 to 2017 (**Figure 2**). On the other hand, ASIRs demonstrated a temporary increase in 1995 and 1996 in the high-middle and high SDI quintiles, respectively.

In addition, the EAPC of ASIR of 195 countries and territories was correlated with SDI ($\rho = -0.169$, 95% CI: −0.303 to −0.029, $P = 0.018$), but not correlated with ASIR itself ($\rho = -0.009$, 95% CI: −0.149 to 0.132, $P = 0.905$; **Figures 3A,B**).

Global OC Mortality

The OC death cases increased globally by 84.20%, from 95,540 (95% UI: 91,780–101,190) to 175,980 (95% UI: 171,380–181,200) between 1990 and 2017. By contrast, the corresponding ASDR decreased worldwide (EAPC: −0.33, 95% UI: −0.38 to −0.27) (**Table 2**).

From 1990 to 2017, OC death cases decreased in 11 countries, and the corresponding ASDRs decreased in 60 countries (**Supplementary Table 4**). The highest number of death cases were observed in China (25040.26, 95% UI: 23558.50–26505.37) and India (20621.80, 95% UI: 18228.44–23704.20). The countries with the lowest number of death cases were Kiribati (0.76, 95% UI: 0.53–1.02) and Northern Mariana Islands (0.91, 95% UI: 0.77–1.09) (**Supplementary Figure 2** and **Supplementary Tables 2**, **3**). On the other hand, American Samoa had the highest ASDR (12.85 per 100,000 people), whereas Mali had the lowest (1.64 per 100,000 people) in 2017 (**Supplementary Figures 3**, **4**). The video shows the dynamic changes of countries with the top 10 OC ASDRs from 1990 to 2017 (**Supplementary Video 2**).

OC death cases increased in all regions whereas the ASDRs decreased in 8 regions (**Table 2**). Compared with data from 1990, OC death cases in 2017 increased in all SDI quintiles. ASDRs decreased in the high and high-middle SDI quintiles (−1.17 and −0.36, respectively). The ASDRs trended upwards in the middle and low-middle SDI quintiles before 2017, and the opposite trend was observed in the high SDI quintiles after the rise and fall from 1990 to 1993 (**Figure 2**). Moreover, ASDRs demonstrated a decrease after two peaks in 1994 (4.31) and 2002–2003 (4.12) in the high-middle SDI quintiles, whereas ASDRs in the low SDI quintiles demonstrated an increase after a low peak in 2001 (2.58) (**Figure 2**).

Additionally, the EAPC of ASDR of 195 countries and territories was correlated with SDI ($\rho = -0.182$, 95% CI: −0.315 to −0.043, $P = 0.011$), but not correlated with ASDR itself ($\rho = -0.065$, 95% CI: −0.204 to 0.077, $P = 0.371$; **Figures 3C,D**).

Global OC-Related DALYs

OC-related DALYs increased from 2,625,250 (95% UI: 2,493,770–2,829,950) to 4,673,030 (95% UI: 4,528,650–4,828,610) in the past 28 years. However, the DALY ASR decreased globally (EAPC: −0.38, 95% UI: −0.32 to −0.25) (**Table 3**).

Decreases in OC-related DALYs were observed in 21 countries, and the DALY ASRs decreased in 66 countries as well

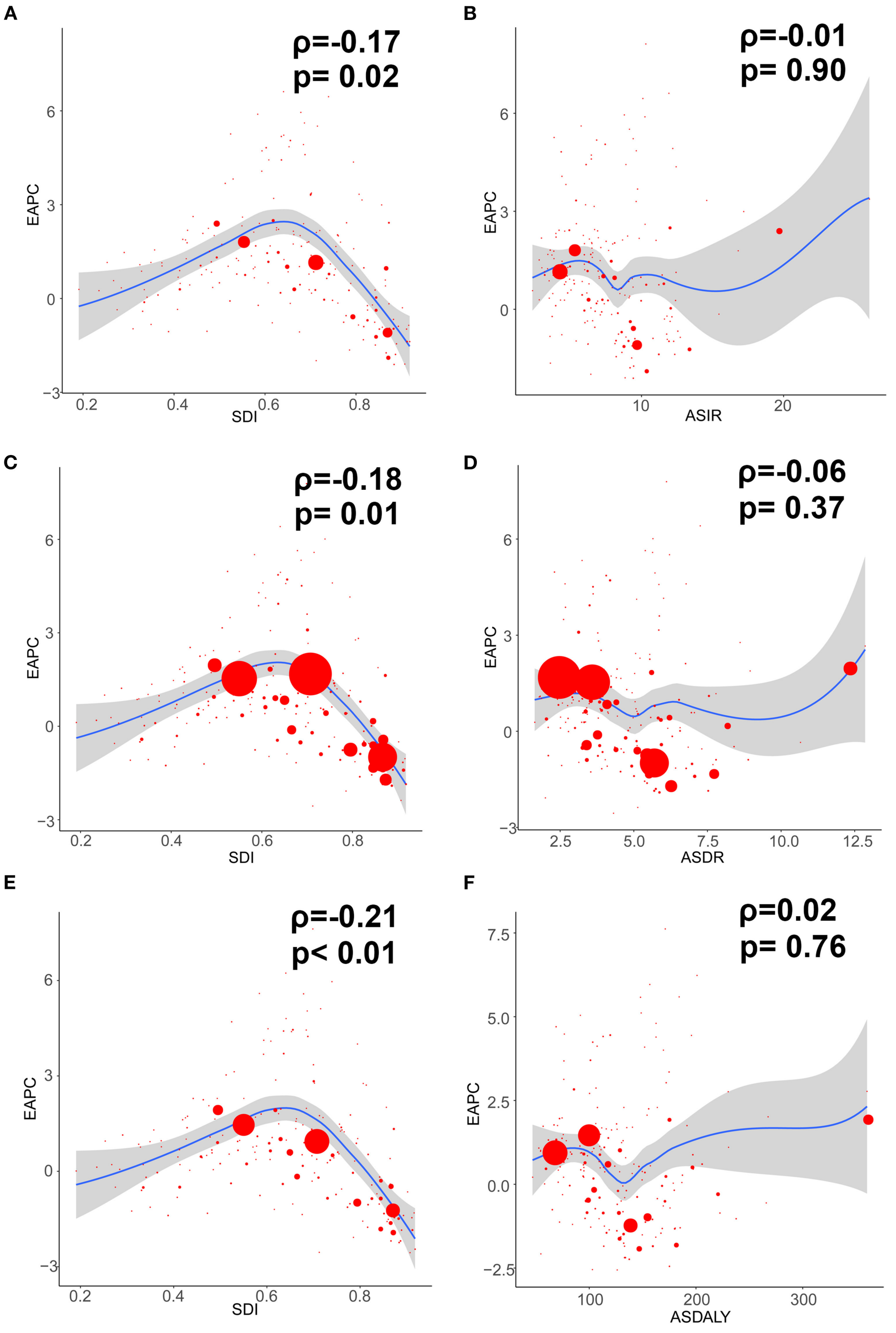

FIGURE 3 | The correlation between EAPC and ovarian cancer ASR (per 100,000) in 1990 as well as SDI in 2017. The circles represent countries and territories that were available on SDI data. The size of circle is increased with the cases of ovarian cancer. The *R* and *P*-values presented were derived from Pearson correlation analysis. **(A)** EAPC and SDI in incidence; **(B)** EAPC and ASIR; **(C)** EAPC and SDI in death; **(D)** EAPC and ASDR; **(E)** EAPC and SDI in DALYs; **(F)** EAPC and age-standardized DALY rate. ASIR, age standardized incidence rate; ASDR, age standardized death rate; EAPC, estimated annual percentage change; SDI, socio-demographic index; DALY, disability adjusted life-year.

TABLE 2 | The death of ovarian cancer, and its temporal trends from 1990 to 2017.

Characteristics	**1990**		**2017**		**1990–2017**	
	Deaths No. ×10^3 (95% UI)	**ASDR per 100,000 No. (95% UI)**	**Deaths No. ×10^3 (95% UI)**	**ASDR per 100,000 No. (95% UI)**	**Change in Death No. (%)**	**EAPC No. (95% CI)**
Global	95.54 (91.78–101.19)	4.36 (4.19–4.61)	175.98 (171.38–181.20)	4.14 (4.03–4.26)	84.20	−0.33 (−0.38 to −0.27)
SDI						
High SDI	49.14 (48.49–49.86)	6.83 (6.74–6.93)	60.86 (58.83–62.87)	5.20 (5.03–5.37)	23.85	−1.17 (−1.25 to −1.09)
High-middle SDI	20.88 (19.89–21.88)	3.93 (3.74–4.12)	36.37 (35.22–37.50)	3.75 (3.63–3.87)	74.19	−0.36 (−0.48 to −0.23)
Middle SDI	11.78 (11.27–13.39)	2.27 (2.14–2.53)	38.84 (37.31–40.48)	3.30 (3.17–3.44)	229.71	1.40 (1.35–1.45)
Low-middle SDI	8.77 (7.67–10.96)	2.90 (2.55–3.61)	27.25 (24.68–31.11)	4.22 (3.83–4.79)	210.72	1.40 (1.33–1.47)
Low SDI	4.59 (3.56–6.65)	2.66 (2.09–3.79)	12.13 (10.79–24.09)	3.23 (2.88–3.75)	164.27	0.65 (0.45–0.85)
Regions						
Andean Latin America	0.18 (0.16–0.21)	1.58 (1.41–1.75)	1.07 (0.94–1.22)	3.80 (3.33–4.31)	494.44	3.71 (2.95–4.48)
Australasia	0.85 (0.82–0.88)	6.58 (6.37–6.82)	1.26 (1.11–1.44)	4.99 (4.41–5.69)	48.24	−1.18 (−1.25 to −1.11)
Caribbean	0.18 (0.17–0.21)	1.30 (1.18–1.49)	1.04 (0.94–1.17)	3.86 (3.50–4.35)	477.78	4.01 (3.11–4.93)
Central Asia	0.86 (0.75–1.03)	3.03 (2.63–3.59)	1.65 (1.57–1.75)	3.78 (3.58–3.99)	91.86	0.93 (0.77–1.09)
Central Europe	5.70 (5.55–5.84)	6.83 (6.66–6.99)	7.78 (7.43–8.18)	6.89 (6.57–7.23)	36.49	0.10 (−0.02 to 0.22)
Central Latin America	1.47 (1.43–1.51)	3.05 (2.97–3.13)	5.20 (4.94–5.46)	4.09 (3.89–4.28)	253.74	1.11 (0.96–1.26)
Central Sub-Saharan Africa	0.38 (0.28–0.49)	2.87 (2.20–3.55)	0.94 (0.72–1.18)	3.20 (2.43–4.09)	147.37	0.26 (0.11–0.40)
East Asia	8.03 (7.42–9.23)	1.62 (1.49–1.86)	26.53 (25.04–28.06)	2.48 (2.35–2.63)	230.39	1.66 (1.45–1.87)
Eastern Europe	10.65 (9.91–11.73)	6.06 (5.63–6.70)	11.27 (10.85–11.72)	5.64 (5.42–5.87)	5.82	−0.51 (−0.83 to −0.20)
Eastern Sub-Saharan Africa	2.14 (1.76–2.78)	5.04 (4.18–6.41)	4.30 (3.62–4.88)	4.82 (4.08–5.46)	100.93	−0.46 (−0.64 to −0.29)
High-income Asia Pacific	3.80 (3.73–3.87)	3.36 (3.30–3.42)	6.55 (6.23–6.88)	3.12 (2.96–3.29)	72.37	−0.34 (−0.49 to −0.20)
High-income North America	13.98 (13.70–14.33)	6.97 (6.84–7.15)	18.62 (17.80–19.46)	5.67 (5.39–5.94)	33.19	−1.01 (−0.48 to −0.23)
North Africa and Middle East	2.47 (2.14–3.25)	2.69 (2.35–3.50)	6.81 (6.42–7.23)	3.10 (2.93–3.30)	175.71	0.59 (0.52–0.65)
Oceania	0.04 (0.03–0.06)	2.53 (1.98–3.23)	0.14 (0.11–0.18)	3.92 (3.29–4.85)	250.00	1.86 (1.76–1.96)
South Asia	8.29 (7.12–10.83)	2.72 (2.35–3.53)	29.55 (27.07–32.61)	4.15 (3.81–4.56)	256.45	1.48 (1.30–1.66)
Southeast Asia	5.17 (4.45–6.57)	3.45 (2.99–4.34)	13.56 (12.03–15.64)	4.09 (3.65–4.70)	162.28	0.68 (0.62–0.75)
Southern Latin America	1.27 (1.17–1.37)	4.86 (4.49–5.26)	2.03 (1.81–2.29)	4.54 (4.05–5.14)	59.84	−0.31 (−0.47 to 0.15)
Southern Sub-Saharan Africa	0.56 (0.50–0.62)	3.41 (2.98–3.77)	1.35 (1.22–1.46)	4.14 (3.75–4.49)	141.07	0.92 (0.46–1.39)
Tropical Latin America	1.86 (1.80–1.93)	3.58 (3.47–3.71)	4.78 (4.60–5.00)	3.73 (3.59–3.90)	156.99	−0.06 (−0.21 to 0.09)
Western Europe	26.48 (26.05–26.92)	7.99 (7.87–8.12)	28.33 (26.80–29.81)	5.86 (5.53–6.16)	6.99	−1.31 (−1.37 to −1.25)
Western Sub-Saharan Africa	1.18 (0.94–1.62)	2.58 (2.06–3.53)	3.22 (2.57–4.01)	3.19 (2.55–3.97)	172.88	0.79 (0.75–0.83)

ASDR, age standardized death rate; EAPC, estimated annual percentage change; CI, confidence interval; UI, uncertainty interval; SDI, socio-demographic index.

TABLE 3 | The DALYs of ovarian cancer, and its temporal trends from 1990 to 2017.

Characteristics	1990		2017		1990–2017	
	DALYs No. $\times 10^3$ (95% UI)	Age standardized DALY rate (per 100,000) (95% UI)	DALYs No. $\times 10^3$ (95% UI)	Age standardized DALY rate (per 100,000) (95% UI)	Change in DALYs No. (%)	EAPC No. (95% CI)
Global	2625.25 (2493.77–2829.95)	115.97 (110.29–124.73)	4673.03 (4528.65–4828.61)	110.94 (107.51–114.64)	78.00	−0.38 (−0.32 to −0.25)
SDI						
High SDI	1165.76 (1145.94–1185.90)	178.01 (175.02–181.12)	1286.70 (1243.45–1329.61)	129.78 (125.52–134.12)	10.37	−1.42 (−1.35 to −1.28)
High-middle SDI	619.01 (584.87–650.41)	115.22 (98.00–102.08)	986.76 (952.27–1019.77)	103.65 (99.98–107.15)	59.41	−0.63 (−0.76 to −0.50)
Middle SDI	398.06 (372.24–448.21)	68.37 (64.00–76.82)	1136.41 (1089.47–1187.13)	93.93 (90.10–98.14)	185.49	1.13 (1.07–1.20)
Low-middle SDI	285.87 (248.30–359.55)	84.40 (73.52–105.68)	865.01 (778.22–1001.88)	123.55 (111.45–142.26)	202.59	1.42 (1.37–1.48)
Low SDI	150.70 (114.44–223.63)	76.59 (58.92–111.58)	383.56 (339.68–445.46)	92.06 (81.68–106.87)	154.52	0.38 (0.58–0.78)
Regions						
Andean Latin America	6.17 (6.93–5.47)	48.10 (42.56–53.84)	31.36 (27.28–35.98)	108.38 (94.20–124.08)	408.27	3.45 (2.73–4.18)
Australasia	20.68 (19.97–21.49)	171.47 (165.44–178.21)	26.57 (23.38–30.47)	118.78 (104.23–136.21)	28.48	−1.53 (−1.60 to −1.46)
Caribbean	5.59 (4.99–6.57)	38.30 (34.20–44.87)	26.91 (25.57–32.90)	107.98 (96.55–124.64)	381.40	3.83 (2.97−4.70)
Central Asia	26.91 (23.54–31.76)	93.11 (81.37–110.03)	51.43 (48.38–54.70)	111.15 (104.61–118.13)	91.12	0.54 (0.72–0.89)
Central Europe	160.77 (156.34–164.85)	201.83 (196.37–206.75)	187.24 (178.37–196.50)	188.57 (179.79–197.81)	16.46	−0.22 (−0.32 to −0.12)
Central Latin America	47.50 (46.20–48.84)	88.15 (85.74–90.59)	155.32 (147.47–163.15)	118.61 (112.62–124.54)	227.00	1.16 (1.03–1.29)
Central Sub-Saharan Africa	12.39 (8.98–16.59)	80.77 (59.66.41–104.33)	29.85 (22.91–38.23)	88.14 (68.24–111.90)	140.92	0.15 (0.00–0.30)
East Asia	279.83 (257.75–319.49)	51.68 (47.72–59.14)	735.86 (692.70–779.50)	68.62 (64.57–72.74)	162.97	0.95 (0.71–1.18)
Eastern Europe	297.05 (274.68–329.81)	181.51 (167.37–202.60)	295.74 (283.21–309.03)	164.36 (157.04–172.69)	−0.44	−0.67 (−1.00 to −0.33)
Eastern Sub-Saharan Africa	70.94 (57.05–94.27)	146.17 (119.01–190.79)	141.10 (118.32–161.45)	137.51 (116.21–156.12)	98.90	−0.56 (−0.75 to −0.37)
High-income Asia Pacific	110.19 (107.97–112.44)	100.02 (98.00–102.08)	146.36 (138.57–155.16)	89.81 (84.81–95.70)	32.83	−0.42 (−0.56 to −0.28)
High-income North America	322.94 (315.58–332.21)	178.80 (174.68–184.13)	401.40 (380.99–421.83)	136.49 (128.84–144.04)	24.30	−1.27 (−1.40 to −1.13)
North Africa and Middle East	79.12 (67.42–106.24)	77.46 (66.35–103.03)	213.12 (200.76–226.90)	88.49 (83.42–93.94)	169.36	0.55 (0.49–0.61)
Oceania	1.51 (1.12–2.05)	78.05 (58.89–103.58)	5.10 (3.91–6.84)	116.84 (92.79–150.95)	237.75	1.63 (1.72–1.81)
South Asia	268.96 (230.29–350.55)	77.09 (66.23–100.47)	914.75 (831.99–1021.95)	119.33 (108.88–132.59)	240.11	1.54 (1.36–1.72)
Southeast Asia	172.75 (146.62–224.15)	103.43 (88.42–132.80)	423.82 (372.40–494.86)	121.20 (106.63–141.00)	145.34	0.63 (0.56–0.70)
Southern Latin America	33.43 (30.88–36.20)	130.72 (120.78–141.33)	50.53 (44.83–57.41)	121.97 (107.97–138.61)	51.15	−0.32 (−0.47 to −0.17)
Southern Sub-Saharan Africa	17.59 (15.89–19.26)	97.78 (87.95–106.83)	38.58 (35.00–41.98)	111.47 (101.11–121.05)	119.33	0.56 (−0.02 to 1.14)
Tropical Latin America	57.85 (55.67–60.30)	100.79 (97.30–104.77)	133.77 (128.31–139.95)	103.94 (99.71–108.70)	131.24	−0.05 (−0.25 to 0.01)
Western Europe	597.25 (586.96–608.43)	204.71 (201.13–208.51)	559.91 (528.82–590.19)	140.59 (133.04–148.17)	−6.25	−1.58 (−1.65 to −1.52)
Western Sub-Saharan Africa	35.84 (28.58–49.00)	71.19 (56.93–97.25)	102.69 (81.41–129.01)	87.76 (69.81–110.20)	186.52	0.34 (−0.04 to 0.85)

DALY, disability adjusted life-year; EAPC, estimated annual percentage change; CI, confidence interval; UI, uncertainty interval; SDI, socio-demographic index.

(**Supplementary Table 5**). The OC-related DALYs of Trinidad and Tobago increased by ∼9-fold. China (692806.34, 95% UI: 649947.79–734597.46) had the highest DALYs, followed by India (609130.85, 95% UI: 536743.45–702242.28). On the other hand, the DALYs were low in Kiribati (25.86, 95% UI: 17.66–35.50) and Northern Mariana Islands (27.48, 95% UI: 22.63–33.17) (**Supplementary Figure 2** and **Supplementary Tables 2**, **3**). Furthermore, Pakistan had the highest DALY ASR (360.24 per 100,000 people), whereas Mali had the lowest (46.92 per 100,000 people) in 2017 (**Supplementary Figures 3**, **5**). The video shows the dynamic changes of countries with the top 10 OC DALY ASRs from 1990 to 2017 (**Supplementary Video 3**).

Compared with data from 1990, the OC-related DALYs in 2017 decreased only in Eastern and Western Europe (−0.44 and −6.25%, respectively) (**Table 3**). DALY ASR decreases were observed in 9 GBD regions, of which Western Europe had the greatest decrease (−1.58). Most of the OC-related DALYs were distributed in South (914,750) and East Asia (735,860) in 2017 (**Table 3**). DALY ASRs had the highest increase in the Caribbean (3.83), whereas the lowest increase was observed in Central Sub-Saharan Africa (0.15) (**Table 3**). OC-related DALYs increased in all SDI quintiles, whereas the OC DALY ASRs decreased in the high-middle and high SDI quintiles (EAPC: −0.63 and −1.42, respectively). Additionally, the EAPC of DALY ASRs of 195 countries and territories was correlated with SDI ($\rho = -0.209$, 95% CI: −0.340 to −0.070, $P = 0.003$), but not correlated with DALY ASRs itself ($\rho = 0.022$, 95% CI: −0.119 to 0.162, $P = 0.760$; **Figures 3E,F**).

Age Distribution of OC Incidence, Deaths, and DALYs

From 1990 to 2017, global OC incidence and DALYs were mainly distributed in populations aged 50–69 years followed by those aged 15–49 years (**Supplementary Figure 6**). Although OC death cases occurred mainly in populations aged 50–69 years, the number of OC death cases is higher in those aged >70 years compared to those aged 15–49 years. Additionally, no huge difference was observed in OC incidence, deaths, and DALYs with respect to age between 1990 and 2017. However, the proportion of patients aged 50–69 years decreased and became the lowest population among the considered age groups around year 2000.

Risk Factors for OC Burden

Global OC DALY ASRs attributable to all risks increased from 12.16 (95% UI: 5.59–20.95) to 12.56 (95% UI: 5.42–22.53) per 100,000 between 1990 and 2017 (**Figure 4**). Among the all risks, the high fasting plasma glucose level was the greatest contributor in DALY ASRs globally, as well as in all SDI quintiles in 1990 and 2017 (**Figure 4**). Another important contributor was high body mass index (BMI), which was the secondary contributor to DALY ASRs globally and in all SDI quintiles in 2017 (**Figure 4**). The third distributor in DALY ASRs in 2017 was the occupational exposure to asbestos, which contributed more to DALY ASRs globally and in most SDI quintiles in 1990.

As shown in **Figure 5**, OC DALY ASRs attributable to all risks increased mainly in the low, low-middle, and middle SDI quintiles, while it decreased in the high, high-middle SDI quintiles. Global OC DALY ASRs attributable to high fasting plasma glucose level maintained an upward trend from 1990 (6.27 per 100,000) to 2017 (7.22 per 100,000) but varied by SDI quintiles in 2017. Of the 534,059 (95% UI: 230,578–958,755) global OC DALYs attributable to all risks, 307,210 (95% UI: 61,032–717,907) was attributable to high fasting plasma glucose level. High fasting plasma glucose-related OC DALYs in 2017 increased globally when compared with data in 1990 (data not shown). Moreover, high fasting plasma glucose-related OC DALY ASRs increased in the low, low middle, and middle SDI quintiles, whereas in the high, high-middle SDI quintiles (**Figure 5B**), the values decreased.

Global OC DALY ASRs attributable to high BMI increased in 2017 (3.53 per 100,000) when compared with data in 1990 (2.99 per 100,000). The proportion of high BMI-attributed DALY ASRs decreased in the high SDI quintile, but increased in the other quintiles, especially in the middle and low-middle SDI quintiles (**Figure 5C**).

Global OC DALY ASRs attributable to occupational exposure to asbestos was 2.35 per 100,000 in 2017, which was a great decrease compared with data in 1990 (3.42 per 100,000) globally. The attributed DALY ASRs in the high and high-middle SDI quintiles decreased from 1990 to 2017, but were still higher than those in the other three SDI quintiles. Meanwhile, the attributed DALY ASRs showed a decrease in low and low-middle SDI quintiles and a increase in the middle SDI quintiles from 1990 to 2017 (**Figure 5D**).

The OC ASDRs attributable to these risk factors displayed patterns similar to the DALY ASRs (**Figures 5E–H**). While, OC ASDRs attributable to all risks decreased slightly from 0.571 per 100,000 in 1990 to 0.570 per 100,000 in 2017. In a comparison of data between 1990 and 2017, OC ASDRs attributable to high fasting plasma glucose level and high BMI increased, whereas OC ASDRs attributable to occupational exposure to asbestos decreased.

DISCUSSION

Our analysis showed the latest global patterns and trends on disease burden and risk factors attributable to OC. The incidence, deaths, and DALYs increased globally from 1990 to 2017 and has been in a continuous upward trend (**Supplementary Figure 7**). The corresponding ASRs of OC all showed general downward trends with a peak and trough around 1994 and 2014 (**Supplementary Figure 8**). Previous paper about the incidence and mortality burden of ovarian cancer confirmed our findings (23). Besides, the latest research about the global disease burden of women cancer revealed that the incidence, deaths, and DALYs of ovarian cancer were 294,420, 198,410, and 5,359,740, respectively in 2019 globally which showed increases from 2017 (24). These findings could be helpful to the allocation of the limited health service resources as well as the evaluation of interventions or programs. According to a global cancer burden study (from 1990 to 2016) (25), increases in OC incidence were mainly attributable to population growth (12.4%) and changes in

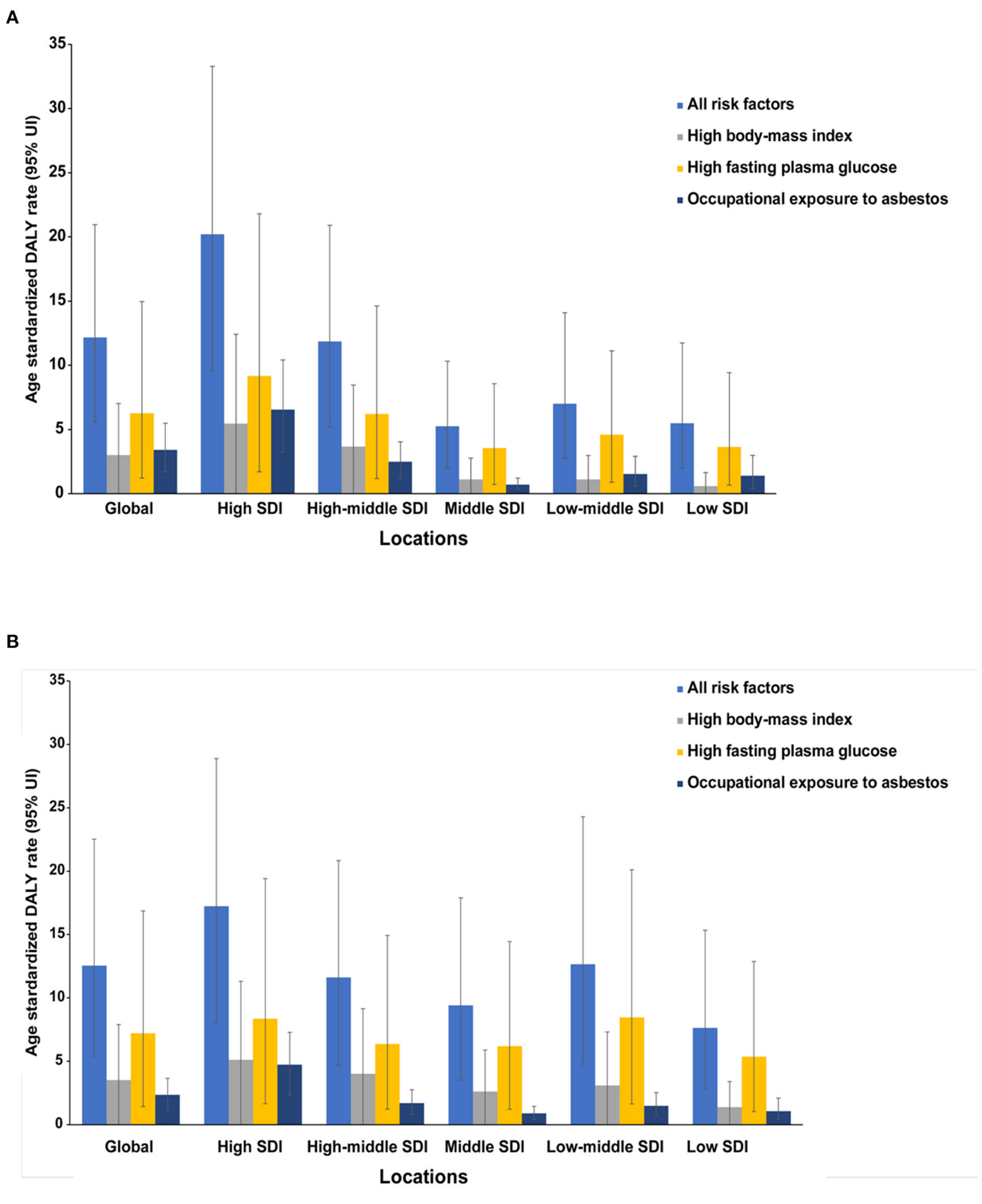

FIGURE 4 | The ovarian cancer DALYs attributable to risk factors compared in 1990 **(A)** and 2017 **(B)** by SDI quintiles. DALY, disability-adjusted life year.

age structure (14.9%) over the last decade, whereas the reverse contributed a 3.2% decrease. Specifically, in the high, high-middle, and middle SDI quintiles, changes in age structure were the main factor that contributed to changes in incidence (13.1, 14.6, and 20%, respectively). Furthermore, negative changes in ASIRs in the high (−9.4%) and high-middle (−8.4%) SDI quintiles were attributable to decreases in incidence. Population growth was the greatest contributor in the incidence changes in the low-middle (16.6%) and low SDI (32.3%) quintiles. Generally, population growth and aging are continuing and may still be the main factors contributing to the increase in OC incidence. China, India, the United States, Pakistan, and the Russian Federation were the top 5 countries with the highest incidence, mortality, and DALYs in not only 2017 but also a few years prior (26).

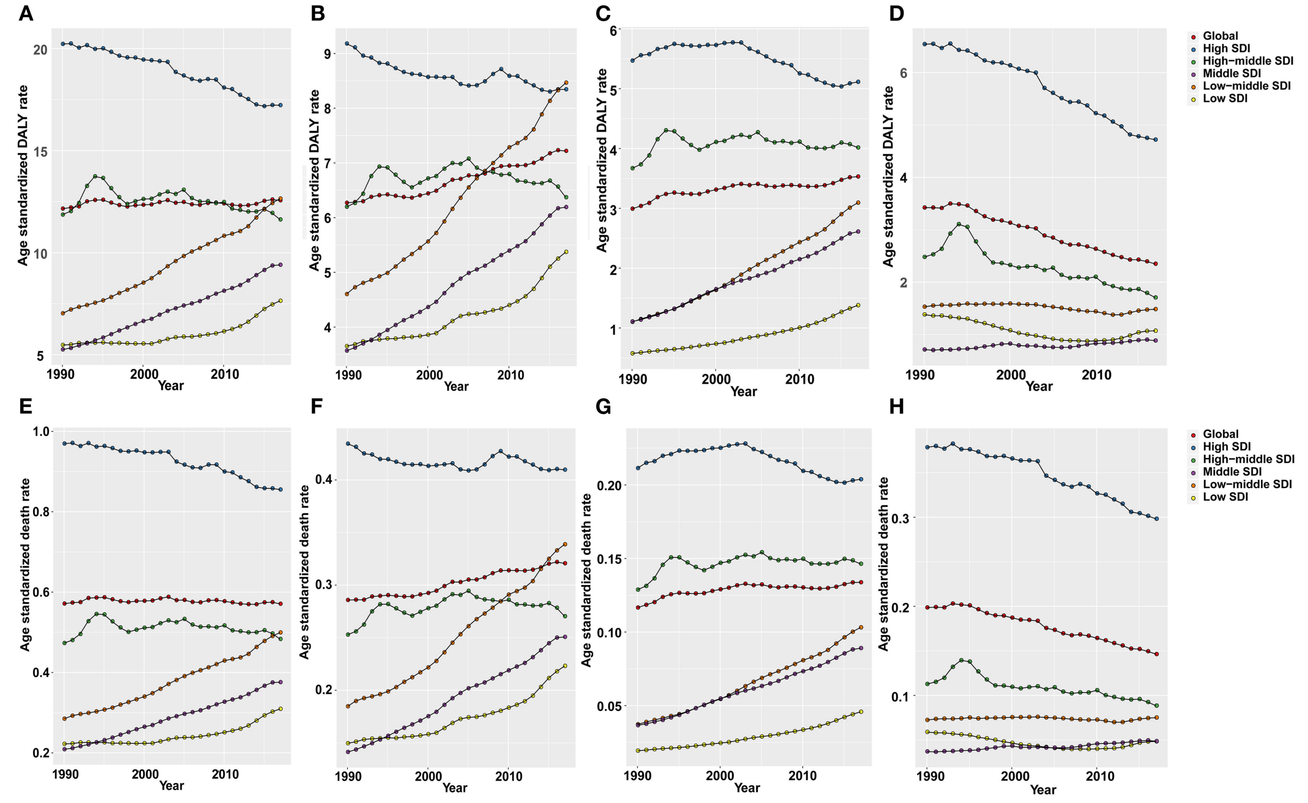

FIGURE 5 | The age-standardized rates of DALYs and deaths (per 100,000) attributable to all risks **(A,E)**, high fasting plasma glucose **(B,F)**, high body mass index (BMI) **(C,G)**, and occupational exposure to asbestos **(D,H)** globally and in all SDI quintiles from 1990 to 2017.

European and North American regions had the highest ASRs in recent years, as described in published reports (10, 26, 27). Therefore, in the coming decades, the number of OC patients who need specialist treatment will also continue to increase.

High fasting plasma glucose level is the most important risk factor for OC deaths and DALYs globally. A previous case-control study in China showed that fasting plasma glucose and high BMI were significantly prevalent in OC (28). By searching the GHDx database, we also found that in China, DALYs and mortality attributable to high fasting plasma glucose levels decreased in 2017 after a long-term upward trend in 1990 to 2016 (data not shown). Moreover, various studies from other institutes have also reported the high risk for OC in patients with diabetes mellitus (29, 30). Mechanistic studies indicate that glucose in diabetes mellitus patients provides energy not only to normal cells but also to tumor cells, hence promoting tumor growth (31). Additionally, hyperinsulinemia caused by insulin resistance could promote cancer cell mitosis through molecules such as insulin receptor-A and insulin-like growth factor-1, or through activation of the insulin-like growth factor-1 receptor signaling pathway (32–34). Other studies have demonstrated that diabetes mellitus also promoted carcinogenesis through regulation of programmed cell death and immune system surveillance (35, 36). Moreover, some studies have investigated the effect of anti-diabetes medications or other treatments on OC risk. Several studies report that metformin and breastfeeding reduce OC risk in diabetes mellitus patients (14, 37, 38).

Although asbestos use is banned in most countries, there are millions of people still working in factories with asbestos exposure, and at least 90,000 people die from asbestos-related diseases or cancer diseases every year (39). Based on mortality data from the World Health Organization Health Statistics database for the year 2009, Argentina, Brazil, Colombia, and Mexico reflected the greatest numbers of estimated OC deaths attributable to occupational asbestos exposure in 5 years (40). Asbestos use has decreased for many years; nevertheless, governments should increase efforts to limit asbestos production and use and look for alternatives to reduce asbestos exposure. Occupational disease screening and routine physical examination of workers could also help improve the early detection rate of diseases. The association between high BMI and OC risk has been addressed in various studies (28, 41, 42). Obesity has always been a health topic of great concern. It is associated with many diseases, and people should control obesity through a reasonable diet, healthy work and rest, and exercise.

Studies of global cancer incidence, mortality, and DALYs based on the GHDx program provide high-quality estimates of cancer burden. However, these studies rely on the quality of actual raw data, which are unavailable in the GBD database. More accurate estimates of disease burden could be easily obtained in developed countries because they have timely and accurate disease registration data. Nevertheless, these estimates may be influenced by data reliability and poor enrollment rate biases, which could manifest in mathematical modeling errors. Moreover, heterogeneity in data acquisition and processing, including disease detection, diagnosis, and coding, may lead to results deviations. Our research is no exception to these limitations.

CONCLUSION

OC disease burden increased worldwide, and the heaviest burden was distributed in South and East Asia and Western Europe. High fasting plasma glucose level was the greatest contributor in DALY ASRs globally. Our study provides valuable information on the patterns and trends of disease burden and risk factors attributable to OC across age, SDI, regions, and countries, which may help improve the rational allocation of health resources as well as inform policy formulation.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/**Supplementary Material**, further inquiries can be directed to the corresponding author/s.

ETHICS STATEMENT

The Ethics Committee of the Second Affiliated Hospital of Xi'an Jiaotong University determined that this study did not need ethical approval because it used publicly available data.

AUTHOR CONTRIBUTIONS

HK designed the research. ZZ, XW, and NW collected and arranged the data. ZZ, LZ, and NW performed the statistical analysis and made the figures and tables. ZZ, XR, XW, and HK wrote and revised the manuscript. All authors read, critically reviewed, and approved the final manuscript.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2021.619581/full#supplementary-material

Supplementary Figure 1 | The crude prevalence cases (×1,000) of ovarian cancer in different GBD regions and SDI quintiles in 2017.

Supplementary Figure 2 | The incidence, mortality and DALYs cases (×1,000) of ovarian cancer in 195 countries and territories in 2017. DALY, disability adjusted life-year.

Supplementary Figure 3 | The countries with top 10 age-standardized rates (per 100,000 people) in 2017. **(A)** ASIR, age standardized incidence rate; **(B)** ASDR, age standardized death rate; **(C)** age-standardized DALY rate. DALY, disability adjusted life-year.

Supplementary Figure 4 | The global death burden of ovarian cancer in 195 countries and territories in 2017. **(A)** The age-standardized death rate (per 100,000 people) of ovarian cancer in 2017; **(B)** the relative change in death cases between 1990 and 2017; **(C)** the EAPC of ovarian cancer ASDR. EAPC, estimated annual percentage change.

Supplementary Figure 5 | The global DALY burden of ovarian cancer in 195 countries and territories in 2017. **(A)** The age-standardized DALY rate (per 100,000 people) of ovarian cancer in 2017; **(B)** the relative change in DALYs between 1990 and 2017; **(C)** the EAPC of the age-standardized DALY rate. ASDR, age-standardized death rate; EAPC, estimated annual percentage change.

Supplementary Figure 6 | The proportion of different age groups in ovarian cancer by years. **(A)** Incidence. **(B)** Death. **(C)** DALY disability adjusted life-year.

Supplementary Figure 7 | The global change in ovarian cancer incidence, death and DALYs from 1990 to 2017. DALY, disability-adjusted life year.

Supplementary Figure 8 | The global change in age-standardized incidence, death, and DALYs rates of ovarian cancer from 1990 to 2017. DALY, disability-adjusted life year.

Supplementary Table 1 | The incidence of ovarian cancer among 195 countries and territories, and its temporal trends from 1990 to 2017.

Supplementary Table 2 | The top five countries and territories of ovarian cancer incidence, death, or DALYs in 2017.

Supplementary Table 3 | The bottom five countries and territories of ovarian cancer incidence, death, or DALYs in 2017.

Supplementary Table 4 | The deaths of ovarian cancer among 195 countries and territories, and their temporal trends from 1990 to 2017.

Supplementary Table 5 | The DALYs of ovarian cancer among 195 countries and territories, and their temporal trends from 1990 to 2017.

Supplementary Video 1 | The dynamic changes of countries with top 10 ASIR (per 100,000) of OC from 1990 to 2017 (MP4). This video shows the dynamic change of the top 10 countries with highest ASIR of OC annually from 1990 to 2017.

Supplementary Video 2 | The dynamic changes of countries with top 10 ASDR (per 100,000) of OC from 1990 to 2017 (MP4). This video shows the dynamic change of the top 10 countries with highest ASDR of OC annually from 1990 to 2017.

Supplementary Video 3 | The dynamic changes of countries with top 10 DALY ASR (per 100,000) of OC from 1990 to 2017 (MP4). This video shows the dynamic change of the top 10 countries with highest DALY ASR of OC annually from 1990 to 2017.

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STUDY PROTOCOL
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A Study Protocol for Increasing Access to Smoking Cessation Treatments for Low-Income Minority Smokers

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Background: Smoking rates among low-income patients are double those of the general population. Access to health care is an essential social determinant of health. Federally qualified health care centers (FQHC) are government-supported and community-based centers to increase access to health care for non-insured and underinsured patients. However, barriers to implementation impact adherence and sustainability of evidence-based smoking cessation within FQHC settings. To address this implementation barrier, our multi-disciplinary team proposes Mi QUIT CARE (Mile Square QUIT Community-Access-Referral-Expansion) to establish the acceptability, feasibility, and capacity of an FQHC system to deliver an evidence-based and multi-level intervention to increase patient engagement with a state tobacco quitline.

Methods: A mixed-method approach, rooted in an implementation science framework of RE-AIM (Reach, Effectiveness, Adoption, Implementation, and Maintenance), will be used in this hybrid effectiveness-implementation design. We aim to evaluate the efficacy of a novel delivery system (patient portal) for increasing access to smoking cessation treatment. In preparation for a future randomized clinical trial of Mi QUIT CARE, we will conduct the following developmental research: (1) Examine the burden of tobacco among patient populations served by our partner FQHC, (2) Evaluate among FQHC patients and health care providers, knowledge, attitudes, barriers, and facilitators related to smoking cessation and our intervention components, (3) Evaluate the use of tailored communication strategies and patient navigation to increase patient portal uptake among patients, and (4) To test the acceptability, feasibility, and capacity of the partner FQHC to deliver Mi QUIT CARE.

Discussion: This study provides a model for developing and implementing smoking and other health promotion interventions for low-income patients delivered via patient health portals**.** If successful, the intervention has important implications for addressing a critical social determinant of cancer and other tobacco-related morbidities.

Trial Registration: U.S. National Institutes of Health Clinical Trials, NCT04827420, https://clinicaltrials.gov/ct2/show/NCT04827420.

Keywords: smoking cessation, access to care, social determinants, patient portals, federally qualified health center (FQHC), health disparities

INTRODUCTION

Smoking rates among adults in the United States are at a 50-year low (14.1%) (1). Despite overall declines in prevalence rates, smoking remains elevated among multiple underserved communities. For example, in Chicago, smoking rates among Blacks are significantly higher compared to whites (25.2 vs. 13.2%, respectively) (2). In urban areas like Chicago, smoking rates are also more pronounced among individuals living at or below the federal poverty level (26.8%) (2). Due to historical and current practices of structural racism, including redlining and community divestment, many Blacks in Chicago reside in neighborhoods characterized by concentrated disadvantage, racial segregation, and poor access to health care (3). Indeed, smoking rates in Chicago community areas with the highest poverty and racial segregation range from 22 to 35% of community residents (2). The negative consequences of smoking are well-established, with smoking contributing to a range of life-limiting conditions, including lung cancer, chronic obstructive pulmonary disease, and emphysema (1). In Cook County, where Chicago is located, lung cancer rates among Blacks are substantially higher than whites (116.9 vs. 81.1 per 100,000 for men and 63.3 vs. 54.7 per 10,000 for women) (2). Further, the all-cause morbidity and mortality due to smoking are higher among low-income and Black smokers due to a high prevalence of illnesses exacerbated by smoking (e.g., diabetes) (4). Combined, these inequalities underscore tobacco use as an urgent public health priority for Chicago and similar urban areas across the United States.

Reduced access to smoking cessation treatments, a key social determinant of health, is a persistent driver of smoking-related health inequalities among lower-income and racial/ethnic minority groups. Federally Qualified Health Care Centers (FQHCs) are safety-net clinics that serve low-income and uninsured patients. A recent study found that the overall proportion of tobacco use in FHQCs across multiple states was 25.8% compared to 20.6% in the general population (5). Mile Square Health Center (MSHC) is a network of FQHCs located in the greater Chicago metropolitan area, including Chicago, Rockford, and Cicero, Illinois. MSHC clinics are located in high-poverty neighborhoods with documented inequalities in lung cancer and other smoking-related health inequalities (i.e., asthma). Given the high levels of tobacco use observed among FQHC patients, health system-wide tobacco cessation interventions can potentially improve health inequalities at the patient's level and the surrounding community areas.

Tobacco Cessation Treatments

In 2000, the U.S. Public Health Service clinical practice guideline, Treating Tobacco Use and Dependence, recommended that providers consistently identify and document patients' tobacco use status and treat tobacco users via the "5As" framework (Ask-Advise-Assess-Assist-Arrange) (6). Although effective, the 5As model is time-consuming and can be challenging to implement in high-volume clinical settings (7). A simplified version of the framework (Ask-Advise-Refer, [AAR]) was subsequently developed (8). When implemented in clinical settings, AAR has demonstrated effectiveness for increasing patient engagement with recommended treatment approaches such as state tobacco quitlines (9–12). State-run tobacco quitlines offer free telephone counseling and nicotine replacement for low-income smokers. The average quit rates among quitline users are 12.7%, increasing to 28.1% when counseling is combined with nicotine replacement (6). Despite the efficacy of provider interventions such as AAR for linking smokers to treatment, these interventions are underutilized in clinical settings.

FQHCs are required to report annually on their implementation and dissemination of evidence-based tobacco cessation per their Uniform Data Set (UDS) guidelines for FQHCs (5). The Centers for Disease Control and Prevention reports that, although 62.7% of outpatient visits included tobacco screening, only 20.9% of current tobacco users received counseling and 7.6% received a prescription for pharmacotherapy during their visit (13). Barriers to provider adherence to AAR practice guidelines are well-documented (i.e., time restraints) (7). As such, innovation in implementing AAR clinical practice guidelines is needed to facilitate the delivery of evidence-based smoking cessation treatments, especially in clinical populations disproportionately burdened by tobacco use.

Advances in electronic health records (EHR) have allowed the delivery of population health interventions in clinical settings. EHRs are a means for systematically obtaining and electronically storing details about a patient's health history, including demographic characteristics, clinical diagnoses, and treatment histories. A key feature of EHR is that they increase the safety and quality of health care services by allowing for the sharing of information among health care providers both within and across health institutions. Using patient health portals is an innovative strategy for proactively offering health promotion information and guidance at the health system level. Patient portals are tied to EHR and are secure online tools specifically designed to help patients access and manage their health history, including communicating with their providers (14). Patient portals allow

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Abbreviations: AA, African Americans; AAR, Ask-Advise-Refer; ALA, American Lung Association; HER, electric health records; FQHC, Federally Qualified Health Care Centers; ITQL, Illinois Tobacco Quitline; LHL, low-health literacy; Mi QUIT CARE, Mile Square QUIT Community-Access-Referral-Expansion; MSHC, Mile Square Health Center; PN, patient navigation; SEM, socio-ecological model; UI, University of Illinois; UI Health, The University of Illinois Hospital and Health Sciences System.

patients to view a subset of the more extensive health-related information contained in their EHR (e.g., diagnoses, medication lists, appointments). In addition, specific information can be provided to patients via their patient portals outside of a traditional health care visit. Patient health portals can be accessed via computers or internet-enabled smartphones (15, 16). According to the American Hospital Association, 93% of hospitals provide patients access to electric health records (EHRs) *via* patient portals (17). Data from the National Cancer Institute found that 52% of patients reported being offered access to their patient portals by their providers (18). Enrolling in newly available patient portal systems has demonstrated effectiveness in increasing patient-provider communication access to health information and delivering evidence-based preventive services (14, 18).

To date, a small number of randomized controlled trials have used the EHR to identify an entire population of smokers and proactively engage them in treatment (14, 18–21). Proactive engagement can be defined as the systematic targeting of all smokers in a population (e.g., health care system). Proactively calling smokers in the general population to offer free quitline counseling increases quit attempts and cessation rates (22). Several trials have demonstrated the benefit of population-based outreach efforts compared to standard clinical practice on receipt of smoking cessation counseling or medications (range 12.8–14.5 vs. 5.1–7.3%, respectively), and abstinence rates (range 5.3–13.5 vs. 1.1–10.9%, respectively) (20). A few studies have evaluated the reach and feasibility of delivering health promotion interventions *via* patient portals (14, 23). However, few have tested the use of patient portals to offer population-level smoking cessation treatments consistent with the AAR framework that directly links smokers to a state tobacco quitline and does not require trained clinical staff to implement.

Despite the early promise, the potential of patient portals as a health intervention delivery system will be limited by patient enrollment, especially among patients impacted by the digital divide (24). Integrating the promotion of patient portal use into routine primary care practices and offering assistance in enrollment may increase the use of patient portals (25). Patient navigation (PN) is a recognized and evidence-based approach for reducing health inequalities (26) and has been shown to increase patient access to health care services (27). The primary role of the PN is to address patients' informational, emotional, and practical needs associated with accessing health care. A recent meta-analysis of randomized clinical trials of PN interventions demonstrated that, compared to usual care, patients who received PN were significantly more likely to access health screening (OR 2.48, $p < 0.00001$) and to attend a recommended care event (OR 2.55, $p < 0.01$) (27). However, more research is needed to evaluate whether PN can increase patient portal access among patients with low health literacy, racial/ethnic minorities, and patients with limited computer skills; thereby, helping to realize the potential of patient portals for widespread delivery of smoking cessation interventions.

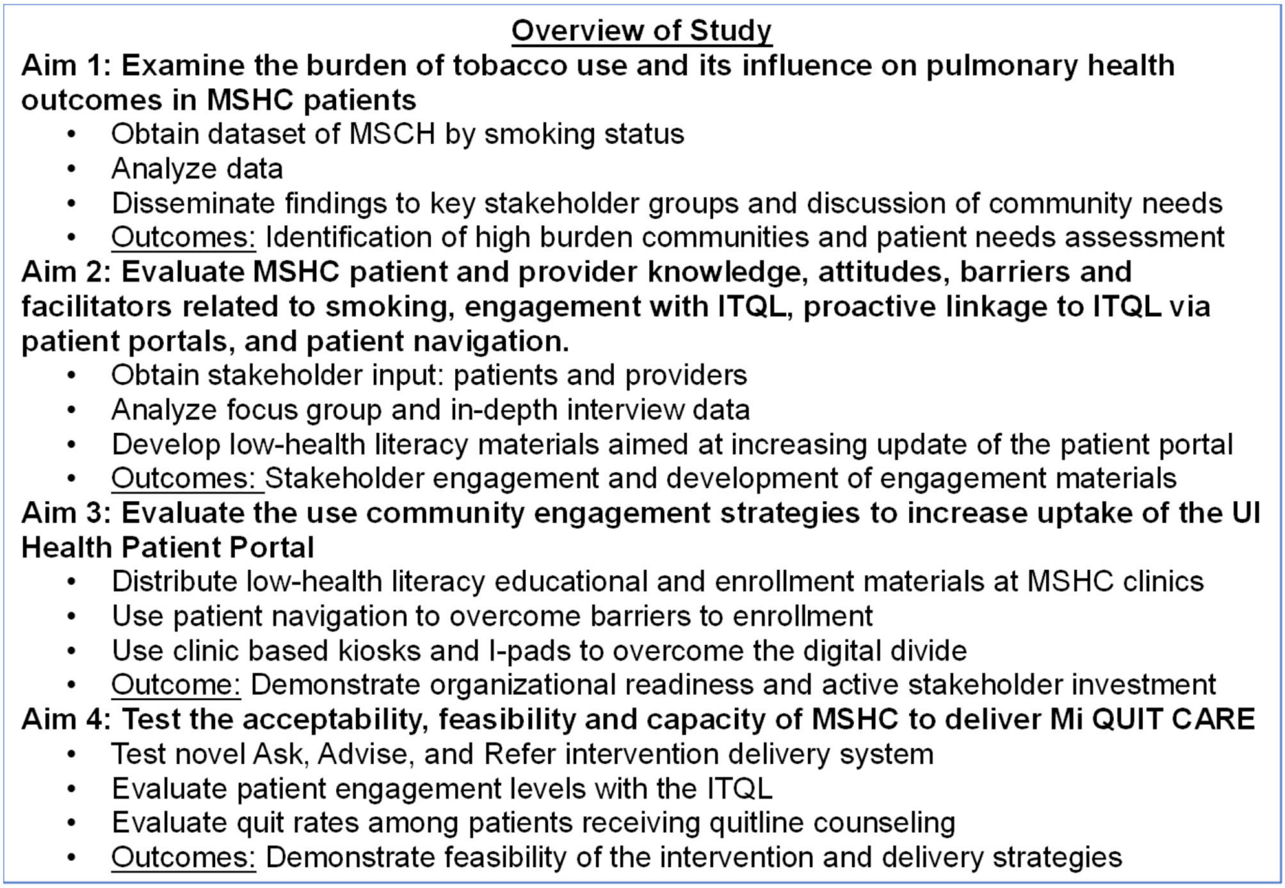
There is strong evidence that health care providers offering screening, brief counseling, and pharmacotherapy reduces tobacco use (6). However, consistent delivery of provider-led tobacco cessation treatments in clinical settings is challenging (28). Our multi-disciplinary team proposes Mi QUIT CARE, an innovative implementation strategy for providing guideline-concordant tobacco treatment in an urban FQHC system to address this implementation barrier. Informed by the socioecological framework (29), my Mi Quit Care includes electronically delivering the AAR brief smoking cessation intervention via the patient portal (8–12). This approach will allow for proactively linking all identified smokers to the state tobacco quitline (30). Further, we will provide patient navigation to reduce barriers to engagement with the patient portal and the state tobacco quitline (26, 27). Patient portals represent a promising strategy for enhancing access to smoking cessation treatments among low-income smokers. However, developmental work is necessary before a full implementation trial to increase this approach's feasibility, acceptability, and cultural appropriateness. As such, the specific aims of this formative study are to:

1. Examine the burden of tobacco use (smoking prevalence) and its influence on pulmonary health inequalities (lung cancer, COPD, and asthma) in the patient populations served by MSHC.
2. To evaluate among MSHC patients and health care providers, knowledge, attitudes, barriers, and facilitators related to smoking cessation, engagement with the tobacco quitline, linkage to the tobacco quitline via a patient health portal, and receipt of patient navigation to facilitate access to the tobacco quitline.
3. To evaluate the use of tailored communication strategies and patient navigation to increase patient portal uptake among patients receiving care at MSHC.
4. To test the acceptability, feasibility, and capacity of a federally qualified health care system to deliver Mi QUIT CARE, an evidence-based and multi-level intervention to increase engagement with the quitline via the patient portal.

MATERIALS AND METHODS

Study Design

Study design and procedures are described below according to study-specific aims (see **Figure 1**). Qualitative (examining implementation) and quantitative methods (following a randomized controlled trial design) will be used in this hybrid effectiveness-implementation pilot design (31) to evaluate the feasibility and acceptability of a novel delivery system (patient portal) in increasing access to effective smoking cessation treatments. To ensure the scientific rigor and reproducibility of the study, we will use an established evaluation framework, RE-AIM (32). RE-AIM is a planning and evaluation model that addresses five dimensions of the individual- and setting-level outcomes critical to program impact and sustainability: Reach, Effectiveness, Adoption, Implementation, and Maintenance (32). RE-AIM was selected because it is a valuable framework



Overview of Study

Aim 1: Examine the burden of tobacco use and its influence on pulmonary health outcomes in MSHC patients

- Obtain dataset of MSCH by smoking status
- Analyze data
- Disseminate findings to key stakeholder groups and discussion of community needs
- Outcomes: Identification of high burden communities and patient needs assessment

Aim 2: Evaluate MSHC patient and provider knowledge, attitudes, barriers and facilitators related to smoking, engagement with ITQL, proactive linkage to ITQL via patient portals, and patient navigation.

- Obtain stakeholder input: patients and providers
- Analyze focus group and in-depth interview data
- Develop low-health literacy materials aimed at increasing update of the patient portal
- Outcomes: Stakeholder engagement and development of engagement materials

Aim 3: Evaluate the use community engagement strategies to increase uptake of the UI Health Patient Portal

- Distribute low-health literacy educational and enrollment materials at MSHC clinics
- Use patient navigation to overcome barriers to enrollment
- Use clinic based kiosks and I-pads to overcome the digital divide
- Outcome: Demonstrate organizational readiness and active stakeholder investment

Aim 4: Test the acceptability, feasibility and capacity of MSHC to deliver Mi QUIT CARE

- Test novel Ask, Advise, and Refer intervention delivery system
- Evaluate patient engagement levels with the ITQL
- Evaluate quit rates among patients receiving quitline counseling
- Outcomes: Demonstrate feasibility of the intervention and delivery strategies

FIGURE 1 | Overview of study design.

for planning, implementing, and evaluating practice-based interventions to improve external validity.

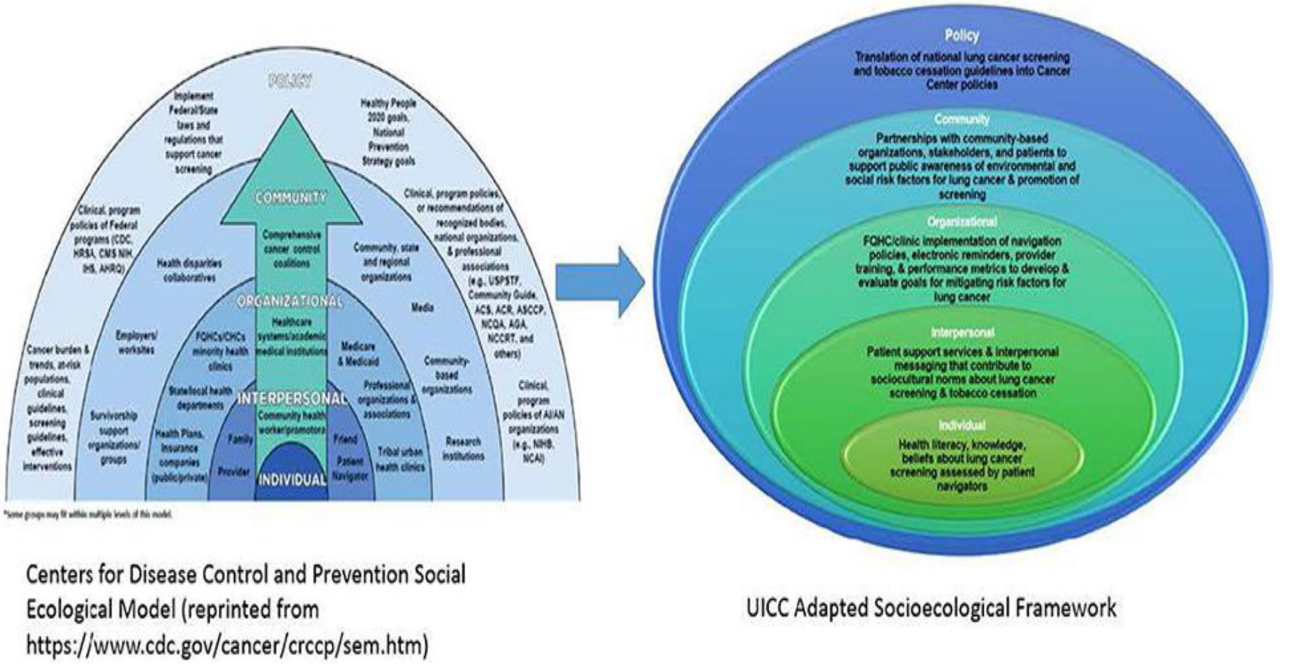
Further, we will use well-tested data collection methods, training, and supervision to ensure intervention fidelity and biochemical verification of smoking status. The overall study protocol has been approved by the University of Illinois at Chicago Institutional Review Board (Protocol # 2020-0532). Aim 1 of the study was determined to be exempt due to the lack of human subject involvement (Protocol #2020-1621). Aim 2 was determined to be exempt from IRB approval due to minimal risk (Protocol #2021-0578). However, informed consent will be obtained from all study participants in this aim. Each aim of the study will be reviewed and approved by the IRB committee and informed consent obtained from participants in each of the aims determined by the IRB to represent human subjects research. The study funding period and study timeline will take place between June 2020-May 2023.

Theoretical Model

Mi QUIT CARE is informed by the Centers for Disease Control's Socioecological Model (SEM) (29) and cognitive-behavioral theories (33). The University of Illinois (UI) Cancer Center and MSHC have experience conducting multi-level interventions to reduce cancer-related disparities (34). Guided by the SEM (29), the UI Cancer Center has proposed a new pathway in reducing pulmonary health inequalities. At the *individual level* and consistent with prior research, cognitive-behavioral models of behavior change (i.e., Theory of Planned Behavior) (33) will be used to understand attitudes toward smoking cessation among patients at FQHCs. *Interpersonal interventions* will include patient navigators to support patient uptake of the patient portals and address barriers to receiving evidence-based tobacco cessation treatments. We will evaluate a system-wide smoking cessation intervention delivered via a patient health portal at the organizational level. *Community-level support* is fostered through ongoing partnerships with organizations like the American Lung Association and the Illinois Tobacco Quitline. Lastly, at the *policy level*, the UI Cancer Center acknowledges the role of policy in improving pulmonary health outcomes, such as the regulation of flavored tobacco products, including mentholated brands (35, 36) (see **Figure 2**).

Setting

This multi-level intervention will be delivered via the University of Illinois Hospital and Health Sciences System (UI Health) Patient Portal, a cost-effective and sustainable intervention



Centers for Disease Control and Prevention Social Ecological Model (reprinted from https://www.cdc.gov/cancer/crccp/sem.htm)

UICC Adapted Socioecological Framework

FIGURE 2 | UICC adapted socioecological framework.

delivery system. Mi QUIT CARE will be conducted in six Mile Square Health Center (MSHC) clinics, a network of 13 community-located FQHCs, including school-based health centers. MSHC is co-owned and operated by UI Health. MSHC serves communities experiencing a high burden of pulmonary health morbidity and mortality associated with tobacco use. The majority of MSHC patients are Black (74%), live at or below the federal poverty level (98%), and are insured through Medicaid (55%, 10% are uninsured). MSHC has the infrastructure to complete the study and monitor the impact of the intervention on their patients' smoking and pulmonary health status over time. Metrics demonstrating implementation readiness include: (1) consistent assessment and documentation of smoking status in the electronic health record by providers; (2) current availability of a system-wide patient portal that can be used to communicate with patients regarding their care; (3) an established collaboration with the Illinois Tobacco Quitline as part of an existing smoking cessation program at MSHC, and (4) an existing patient navigation program for smoking cessation and lung cancer screening.

TABLE 1 | Mi CARE QUIT community advisory board.

Level of engagement	Stakeholder name or entity
Policy	American Lung Association Illinois Tobacco Quitline Chicago Department of Public Health American Cancer Society
Community	American Lung Association Illinois Tobacco Quitline Chicago Department of Public Health
Organizational	Providers at MSHC American Lung Association Illinois Tobacco Quitline Chicago Department of Public Health American Cancer Society
Interpersonal	Patient Navigators Implementation and Dissemination Specialist Providers
Individual	Current and former smokers who are patients at MSCH

Stakeholder Engagement

Community engagement is essential to the development of effective interventions. As shown in **Table 1**, we have assembled a diverse community advisory board representing multiple engagement levels across the socioecological model (29). Engaging community stakeholders is essential to developing tailored tobacco cessation interventions for at-risk populations (37). Specifically, community engagement will help to ensure: (a) the smoking cessation intervention is informed by and responsive to stakeholder needs; (b) the implementation of evidence-based interventions that align with patient preference and clinic culture; (c) the sustainability and scalability due to iterative stakeholder input; and (d) broad dissemination of findings to local, regional and national organizations (37). The community advisory board will meet quarterly throughout the project and will help to ensure the appropriateness of methods used.

Study Procedures

Below is a description of study procedures, separated by study aims.

Aim 1: Examine the burden of tobacco use (smoking prevalence) and its influence on pulmonary health inequalities (lung cancer, COPD, and asthma) in the patient populations served by MSHC.

Patient-level data from the electronic health records (EHR) of all six MSHC locations will be analyzed to evaluate the burden of tobacco use in our patient population. MSHC utilizes the epic platform for their EHR and can extract de-identified patient-level data. Eligibility criteria for inclusion in the analyses include (1) age 18 years and older, (2) a patient at one of the six participating MSHC clinics, and (3) having received care at MSHC within the past 2 years. Patient-level demographic data include age, gender, race/ethnicity, education, income status, relationship status, insurance type, and zip code. Smoking data include current smoking status (current, former, never). Smoking-related lung conditions to be examined include a diagnosis of lung cancer, COPD, and asthma. Chronic health conditions are exacerbated by smoking, including HIV infection, high blood pressure, cardiovascular disease, stroke, asthma, and diabetes. The data manager will prepare a request for the data sets, and the study biostatistician will analyze data to characterize the burden of tobacco use on pulmonary health outcomes. Prevalence, comparisons across clinic locations, and associations (e.g., race/ethnicity, gender, age) will be examined. Data from this aim of the study will allow us to establish a baseline level of smoking among the patient population and the presence of smoking-related comorbidities among patients who smoke. These data will serve as secondary endpoints in tracking the progress of our tobacco cessation intervention. No human subjects are involved in this aim.

Aim 2: Evaluate among MSHC patients and providers, knowledge, attitudes, barriers, and facilitators related to smoking cessation, engagement with the tobacco quitline, linkage to the tobacco quitline via a patient health portal, and receipt of patient navigation to facilitate access to the tobacco quitline.

A qualitative design will obtain stakeholder input on the interventions to test Mi QUIT CARE. Five focus groups ($N = 50$) will be conducted with current smokers, and in-depth interviews will be conducted with providers at MSHC ($N = 24$). The goals of the qualitative interviews will be to understand knowledge, attitudes, beliefs, and barriers related to (1) smoking cessation, (2) engagement with the quitline, (3) linkage to the quitline via the UI Health Patient Portal, and (4) the acceptability of patient navigation to facilitate enrollment in the patient portal and address barriers to engaging with the quitline. Eligibility criteria for focus groups include: (1) aged 18 years and older, (2) current smoker, (3) English speaking, and (4) ability to provide informed consent. Eligibility criteria for providers include: (1) employed at MSHC and (2) providing primary care for adults. All study participants will be recruited from MSHC via posted flyers and clinic-based recruitment activities conducted by trained research assistants.

Focus groups (90 min) and individual interviews (45 min) will be conducted according to standardized methodology, including using trained moderators, a moderator's guide, post-session debriefings, and a review of transcribed audiotapes (38). The moderator's guide for the focus groups and in-depth interviews will be developed based on cognitive-behavioral models of health behavior change. Questions will include knowledge, attitudes, perceived social norms, perceived risks and benefits, self-efficacy, and barriers and facilitators regarding receipt of smoking cessation treatment and the use of the patient portal. Focus group participants will also complete a brief demographic survey. Interviews will be analyzed according to the methods of framework analysis (39). We expect to reach saturation with the proposed sample sizes based on our prior experience (40–43). NVivo will be used for qualitative data management and analyses. First, focus groups and in-depth interviews will be analyzed based on study questions and additional sub-themes identified. These design and analytic approaches are appropriate for applied research (39). The information obtained from patients and providers will help us understand initial attitudes and opinions about the intervention approaches and help refine intervention-related strategies.

Based on focus group data, we will partner with health literacy experts to tailor project informational materials to the needs of patients with low levels of health and technology literacy. Informational materials will include information about enrollment and use of the patient portal, communication from MSHC providers advising all current smokers to make a quit attempt, smoking cessation educational pamphlets, and a description of the tobacco quitline. Materials will be tailored to the needs of low-income patients in terms of language, health literacy, and health beliefs. In addition, tailoring of patient educational materials will be on Kreuter's methods for cultural tailoring (38) and will include (a) peripheral (images, etc. salient to smokers); (b) evidential (cancer rates specific to smoking); (c) linguistic (language and terms used by group); (d) constituent-involving (involving diverse populations of smokers); and (e) sociocultural tailoring (including cultural beliefs). After tailoring materials, a new sample of smokers ($N = 25$) and providers ($N = 10$) will be recruited based on the above eligibility criteria. In-depth interviews will collect data on the usability, acceptability, and comprehension of tailored educational materials. A trained research assistant will review materials with individual participants (30 min). The talk-aloud approach (44) will be used to obtain users' feedback. All sessions will be audiotaped, and information reviewed to make suggested changes and to finalize educational materials. All participants will receive a stipend. This aim was deemed exempt from IRB approval due to the low potential risk for participant harm. However, standard information materials will be provided and informed consent obtained before data collection. The information obtained from patients and providers will support the development of the patient portal strategies to increase the intervention's usability, acceptability, and cultural appropriateness.

Aim 3: Evaluate the use of community engagement strategies to increase uptake of the Patient Portal.

The utility of patient health portals as a health promotion delivery system will be limited if uptake is low among patients in FQHC who may have issues with general literacy, health literacy, and technology-based literacy levels. In this aim, we will evaluate a tailored multi-modal educational campaign to increase the enrollment of MSHC patients in the UI Health Patient Portal. Currently, only 1% of MSHC patients are enrolled in the patient portal. The goal is to increase enrollment to 40% across the 3 years of the developmental trial to demonstrate the feasibility of delivering Mi QUIT CARE *via* the patient portal. The educational campaign will occur in three MSHC locations (Main, South Shore, and Englewood). The remaining three locations (Back-of-the-Yards, Cicero, and Humboldt Park) will serve as waitlist controls. The following strategies will be used to increase enrollment: (1) branding of the outreach initiative, *"My UI Health"*; (2) conducting a clinic campaign using materials tailored to low health literacy populations; (3) offering written provider recommendation and enrollment information during all clinical encounters; (4) mailing informational letters to all MSHC patients that includes enrollment instructions; and (5) offering onsite enrollment assistance provided by patient navigators. Trained patient navigators will assist clinic patients in enrolling in the patient portal *via* kiosks and secure iPads. After the data collection phase, the patient enrollment campaign will be conducted at the three waitlist control clinics.

Study investigators will first evaluate patient portal enrollment considering all patients aged 18 and older who have had an office visit during the previous 24-month period to establish a baseline comparator. During the campaign, enrollment rates will be examined for each clinic to monitor increases in enrollment in the patient portal during the campaign period. We will compare enrollment rates for the intervention clinics vs. the control clinics. Further, we will evaluate whether additional targeted outreach efforts are needed for some patient groups by analyzing whether demographic factors (age, education, gender, race/ethnicity, last provider visit) are associated with portal enrollment. In addition, we will collect reasons for refusal among patients approached in the clinics by patient navigators. Data on enrollment will establish the feasibility of population-based engagement of health promotion interventions via the patient portal. Informed consent will not be required as this aim is part of a quality improvement project at the clinic to increase access to the patient portal. All analysis of portal uptake will be based on de-identified data.

Aim 4: Test the acceptability, feasibility, and capacity of MSHC FQHC to deliver Mi QUIT CARE.

We propose a Hybrid Type I effectiveness-implementation design grounded in RE-AIM (32). Hybrid I types are appropriate for evaluating outcomes associated with clinical intervention and implementation strategies (45). Led by our informatics team, our web application development will be spread across three phases: design, production, and testing/deployment. During the design phase of the study, our technical teams will work closely to refine and document all system specifications and requirements. System logic/rules will be generated. Wireframes, storyboards, interface mock-ups, schematics, and database designs will be produced. In the production phase, the technical team will build the application's site and database. The process will conclude with the testing and deployment phase in which the study and technical teams pass through multiple cycles of quality assurance. After the system is deployed to the live environment, the study and technical teams will stay engaged over the project's lifespan.

All English-speaking adult patients at three MSHC locations (Main, South Shore, and Englewood) who smoke and are enrolled in the UI Health Patient Portal will be eligible for this pilot test. An equal number of patients (total $N = 100$) will be randomly selected from each location for the feasibility trial using a software program developed by programmers at the University of Illinois at Chicago. Human subject approval will be obtained before data collection, and formal informed consent obtained from participants.

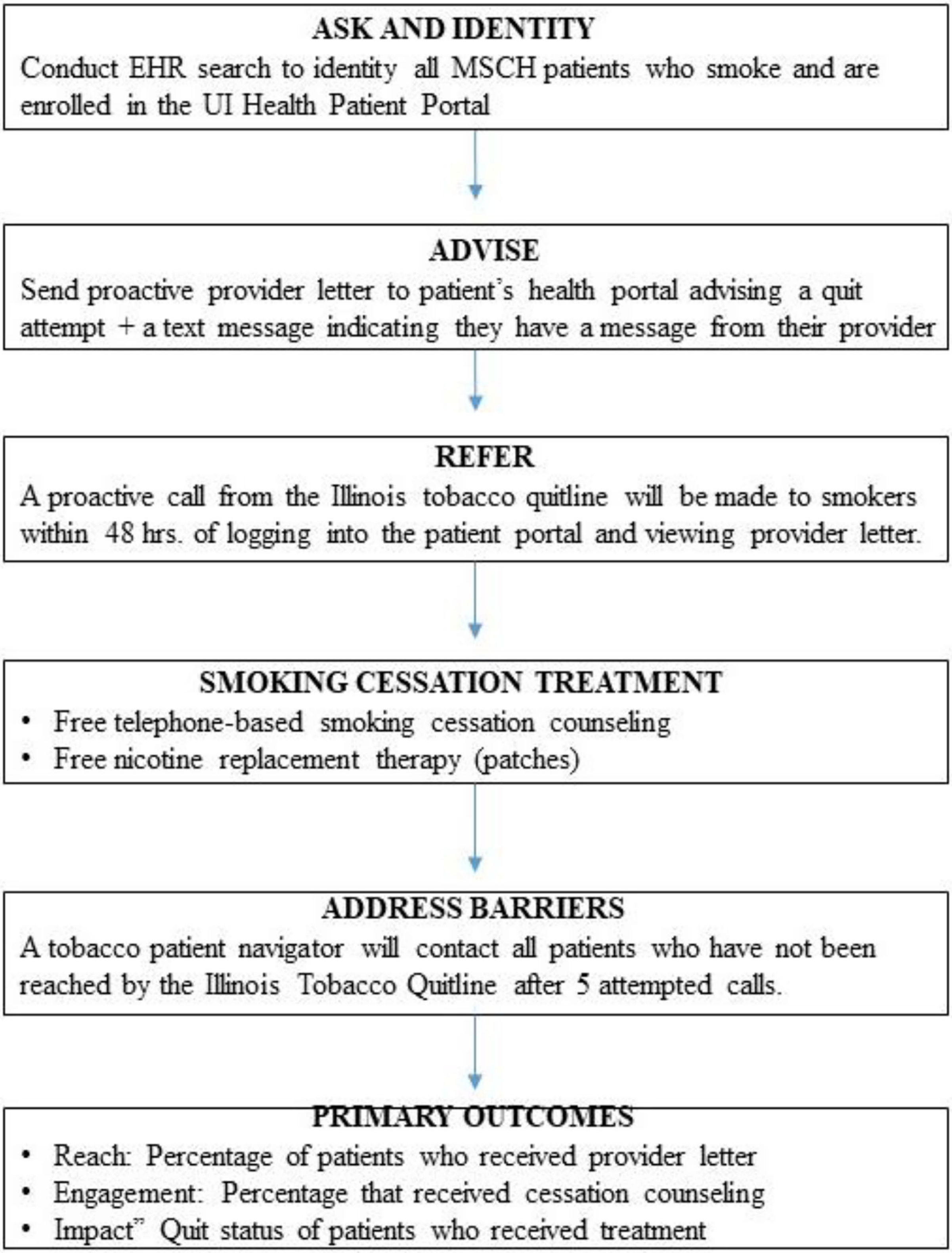
Figure 3 displays an overview of the activities to be conducted in Aim 4 of the study. The intervention will be based on the 3 A's framework (Ask-Advise-Refer, [AAR]) (9, 11, 12). In the first phase of this aim, we will *Ask and Identity, All Smokers.* Project staff will review the electronic health record of the six participating clinic locations to identify all current smokers. Any patient without documented smoking status will be flagged for input during the subsequent clinical encounter. Next, we will *Advise a Quit Attempt.* A random selection of all smokers enrolled in the patient portal will be sent a signed letter from their provider via the portal. The letter will describe health risks associated with smoking, explain the availability of free treatments, strongly encourage the patient to make a quit attempt, and inform them that they will be receiving a call from the Illinois Tobacco Quitline. Patients will be informed that the ITQL will provide free smoking cessation counseling and nicotine replacement therapy (nicotine patches). An automated text or email message with a hyperlink to the portal login page will be generated and sent to patients to alert them of the message from their providers.

Refer

The provider letter will describe the benefits of smoking cessation, advise the patient to quit smoking, and notify them they will receive a call from the ITQL within the next 48 h. Once the patient views the electronic provider letter via the patient portal, an automated referral will be sent to the ITQL with the patient's name, phone number, and unique ID number. Patients will also be allowed to opt-out of the treatment engagement call.

Treatment

A trained tobacco quitline counselor will call patients. Once reached, quitline counselors will assess the patient's readiness to quit smoking and provide an appropriate treatment plan. If interested in making a quit attempt, quitline counselors will provide smokers with an overview of the program, obtain cessation goals, recommend a treatment approach (counseling only or counseling + nicotine replacement therapy), and schedule the next session. The ITQL counseling program is based on the Freedom from Smoking (46, 47) program. It offers up to 6 weeks of free nicotine replacement (patches) to those 18 and older, medically eligible, and uninsured or on Medicaid. The American Lung Association operates the Illinois Tobacco Quit



ASK AND IDENTITY

Conduct EHR search to identity all MSCH patients who smoke and are enrolled in the UI Health Patient Portal

ADVISE

Send proactive provider letter to patient's health portal advising a quit attempt + a text message indicating they have a message from their provider

REFER

A proactive call from the Illinois tobacco quitline will be made to smokers within 48 hrs. of logging into the patient portal and viewing provider letter.

SMOKING CESSATION TREATMENT

- Free telephone-based smoking cessation counseling
- Free nicotine replacement therapy (patches)

ADDRESS BARRIERS

A tobacco patient navigator will contact all patients who have not been reached by the Illinois Tobacco Quitline after 5 attempted calls.

PRIMARY OUTCOMES

- Reach: Percentage of patients who received provider letter
- Engagement: Percentage that received cessation counseling
- Impact" Quit status of patients who received treatment

FIGURE 3 | Overview of the brief smoking cessation intervention.

Line. Certified counselors speak both English and Spanish and have expertise in the treatment of diverse smokers.

Address Barriers

Quitline counselors will make 5 attempts to reach the patient before referring the case to the MiQuit Care patient navigator. Trained patient navigators will call non-responders to encourage them to make a quit attempt and engage with the tobacco quitline. A standardized assessment of the patient's interest in smoking cessation and barriers to engagement with the quitline will be conducted. Smokers who are not interested in quitting will receive brief motivational counseling and be advised to make a quit attempt soon. Smokers interested in quitting smoking will be referred to the quitline by the patient navigator using the patient portal. MSHC has an existing lung health navigation program for smoking cessation and lung cancer screening. Study investigators will oversee the training and ongoing supervision of existing lung health patient navigators to ensure fidelity to the treatment protocol.

Data Analysis

Consistent with RE-AIM (32), our primary outcomes will include Reach and Impact (Reach x Efficacy). We will obtain feasibility data from the patient portal. First, we will assess which patients received (opened) an electronically generated message from their providers advising them to make a quit attempt, describing free stop smoking services from the ITQL, and informing them about an upcoming call from the ITQL. All patients will be allowed to opt into the proactive ITQL counselor call. We will evaluate what percentage of patients opt-in to treatment and the demographic factors associated with the decision to accept linkage to the ITQL. Next, we will assess the percentage of patients who opted-in to treatment and were subsequently reached by the ITQL. Finally, we will evaluate the percentage of patients who engaged in stop smoking treatment (participated in more than 1 counseling call) and their quit outcomes. Patient receipt of treatment and self-reported quit rates will be obtained from the ITQL. The ITQL will provide a monthly report on patient engagement and quit rates. Statistical analyses (multivariable logistic regression models) will be conducted to determine demographic factors (age, race, gender, clinic) associated with receipt of the provider message and advice to quit smoking, receipt of treatment by the ITQL, and quit rates. One of our smoking cessation patient navigators will contact patients who opted-in to linkage to the ITQL and who were not reached by an ITQL counselor. Patient navigators will record barriers to quitline engagement that will be qualitatively analyzed. Data from this aim will refine implementation strategies and procedures in preparation for a fully powered randomized controlled trial.

DISCUSSION

The purpose of this paper is to describe the engagement and developmental protocol for an NIH-funded research study aimed at increasing access to smoking cessation treatments for FQHC patients. Specifically, we aim to determine the feasibility, acceptability, and capacity of an FQHC system to deliver evidence-based smoking cessation treatments to smokers using a patient health portal. Increasing access to evidence-based and cost-effective smoking cessation treatments is a national priority for reducing pulmonary health inequalities among highly vulnerable patients. Federally qualified health care systems represent a mechanism for addressing the health care needs of low-income and under-insured individuals and communities. However, given the complexity of patient healthcare needs, time for health promotion counseling within the confines of the typical clinical appointment is limited. As such, innovations are needed to provide cost-effective and system-wide approaches to supporting patients in making health-related behavioral changes. Additionally, per their uniform data system requirements, FQHCs are required to report annually on their implementation and uptake of evidence-based tobacco cessation interventions.

Patient portals are increasingly available across various health care systems and are being used to improve patient-provider communication and health-related information. Furthermore, researchers are investigating the use of patient portals to deliver evidence-based health promotion interventions across a range of health promotion behaviors (i.e., diabetes self-management). As has been the case with a variety of health care innovations, low-income, and other marginalized patient populations may not have access to the accompanying benefits of patient health portals due to access barriers, including low literacy levels. Patient engagement approaches in the forms of advisory boards, qualitative studies with patients and providers, further tailoring health information to the needs of patients with low health literacy, and the identification of groups in need of additional assistance in the form of patient navigation and other supportive resources can help to overcome access barriers associated with health-related technologies. Equally important is implementing/dissemination approaches to expand provider and system-level bandwidth to provide patients with needed health promotion interventions, including smoking cessation.

Limitations

While this study has several strengths and contributes to existing gaps in the literature, we also acknowledge several limitations. First, the sample is drawn from a single FQHC system in a single geographical location. As such, additional research should be conducted with FQHC systems in other geographic areas. Although the percentage of FQHC with access to patient portals is growing, not all locations have the capacity currently, which could lower the impact of the intervention. Finally, patient navigators play an essential role in reducing health disparities. However, not all locations may have them as a part of the established clinic workforce.

CONCLUSIONS

Guided by the RE-AIM framework (32), our proposed study aims to conduct the developmental work necessary to evaluate Mi Quit Care's efficacy and implementation endpoints fully. Study findings from our developmental aims will provide initial data on Reach and Effectiveness. Following completion of this current study, we will conduct a fully-powered randomized clinical trial in which we will confirm the research and efficacy of the study as well as implementation outcomes (Adoption, Implementation, and Maintenance). Further, this study has the potential to develop and deploy evidence-based interventions for FQHCs that are required per their UDE mandates to implement evidence-based tobacco cessation interventions. Combined, the current and proposed future study have the potential to shape knowledge and future research on the feasibility of using patient health portals to deliver smoking cessation to high-risk patient populations receiving treatments in safety-net health centers.

ETHICS STATEMENT

The overall study protocol has been approved by the University of Illinois at Chicago Institutional Review Board (Protocol # 2020-0532) as a Center Grant. No human subjects may be recruited or enrolled, or their records, data, or biospecimens accessed or analyzed, under this protocol. Any human subject research supported by this Center Grant will require a separate application to the UIC IRB. Aim 1 of the study was determined to be exempt due to the lack of human subject involvement (Protocol #2020-1621). Aim 2 was determined to be exempt from IRB approval due to minimal risk (Protocol #2021-0578). However, standardized procedures for obtaining informed verbal consent will be obtained from all study participants in Aim 2. Research activities associated with Aims 3 and 4 have not just been started. However, prior to the initiation of research related to these two aims, the study protocols will be reviewed and approved by the IRB committee and informed written consent obtained from participants in each of the aims determined by the IRB to represent human subjects research.

AUTHOR CONTRIBUTIONS

AM, KW, and RW are the multiple principal investigators and designed and drafted the study protocol. AS contributed to the study design and analytic plan. CD contributed to the description of the study protocols and intervention components. All authors contributed to the overall design of the study and the preparation of the protocol manuscript, read, and approved the final manuscript.

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Association Between Household Income and Self-Perceived Health Status and Poor Mental and Physical Health Among Cancer Survivors

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Background: Health-related quality of life (HRQoL) is multidimensional and is composed of, at a minimum, self-perceived health status, physical functioning, and psychological well-being. HRQoL measures reflect the extent of disability and dysfunction associated with a chronic disease such as cancer. The objective of this study is to examine factors associated with HRQoL among cancer survivors.

Methods: Data from the 2009 Behavioral Risk Factor Surveillance System survey was used to examine factors associated with HRQoL among participants who reported having ever been diagnosed with cancer. Four questions associated with HRQoL included self-perceived health status, number of bad physical health days, and number of bad mental health days per month. Least square regression and logistic regression models, adjusted for confounding variables, were used for an ordinal and dichotomous [5 (bad) vs. 1–4 (excellent, very good, good, fair)] scale of HRQoL, respectively.

Results: Fifty nine thousand one hundred seventy three participants reported having ever been diagnosed with cancer. Adjusted mean self-perceived health status (5-point scale) among survivors of thyroid, colon, lung, cervical, breast, prostate, and ovarian cancer was 3.83 (0.05), 4.02 (0.04), 4.36 (0.06), 3.77 (0.03), 3.88 (0.03), 3.78 (0.04), and 3.96 (0.05), respectively. After adjusting for confounders, a positive dose-response effect was observed between income range and all three HRQoL measures across all seven cancer sites. Income was consistently and inversely associated with a higher chance for reporting poorer HRQoL [OR: 0.64, 95% CI: 0.57–0.71], [OR: 0.63, 95% CI: 0.48–0.82], [OR: 0.67, 95% CI: 0.56–0.80], [OR: 0.69, 95% CI: 0.56–0.86], [OR: 0.55, 95% CI: 0.49–0.62], [OR:0.55, 95% CI: 0.44–0.69], [OR: 0.75, 95% CI: 0.62–0.91] among those with thyroid, colon, lung, cervical, breast, prostate, and ovarian cancer, respectively.

Discussion: This study found that income range was associated with HRQoL among cancer survivors. It is plausible that financial resources may lessen the overall burden of cancer survivors, which could improve health-related quality of life among cancer survivors.

Keywords: health-related quality of life (HRQL), cancer survivorship, household income, mental health, physical health

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INTRODUCTION

When the quality of life is considered in the context of disease and health, it is commonly referred to as health-related quality of life (HRQoL). Health-related quality of life is multidimensional and is composed of, at a minimum, self-perceived health status, physical functioning, and psychological well-being (1). According to the Centers for Disease Control and Prevention (CDC), HRQoL is defined as "an individual's or group's perceived physical and mental health over time" (2). Despite the potentially subjective nature of self-reporting, HRQoL measures tend to reflect the true extent of disability and dysfunction associated with a chronic disease like cancer (3, 4). Due to the significance in both clinical and survivorship contexts, it is of interest to examine potential associations of HRQoL with various sociodemographic and clinical factors.

Thanks to the early diagnosis of cancer and the advancements in technologies and treatments for cancer, the number of cancer survivors has increased significantly over the past decade. However, there are associated negative consequences associated with longer survival time. For example, because of the high cost associated with advanced treatment, patients with cancer can face serious financial challenges (5). Many cancer survivors will return to the workforce while they will encounter higher insurance premiums or co-payment due to "pre-existing conditions" (6, 7). Evidence indicates that cancer survivors carry a greater burden of medically-related financial responsibility, generally known as "financial toxicity," compared with individuals without a history of cancer (8).

The current study utilized nationally representative data to examine demographic and socioeconomic characteristics and three domains of HRQoL among cancer survivors in the United States (US). We hypothesized that cancer survivors with lesser economic opportunity and thus experienced more financial toxicity, irrespective of cancer site, are more likely to experience poorer HRQoL compared to survivor counterparts with greater economic opportunity.

MATERIALS AND METHODS

Design and Participants

Data were from the 2009 Behavioral Risk Factor Surveillance System (BRFSS) cross-sectional survey conducted by the CDC (9). BRFSS is a population-based, random-digit-dialed telephone survey of the non-institutionalized United States (US) adult population aged ≥18. Standard questions asked by all states query participants on current health-related perceptions (i.e., self-perceived health status), conditions (e.g., diabetes, cardiovascular disease), and behaviors (e.g., tobacco use), as well as demographic characteristics (9). Typically, the "Cancer Survivorship" module is an optional component of the survey. However, in 2009, the module was administered as a standard or required component of the survey (9). Data were analyzed to examine factors associated with reporting multiple measures of HRQoL among all participants who reported having ever been diagnosed with one of seven selected cancer sites. Seven cancer sites were selected based on group sample size, prevalence, and to capture various prognoses. A total of 26,391 survivors were included and grouped according to their reported cancer site. This study was determined as non-human subject research by the University of Arkansas for Medical Sciences Institutional Review Board because we used the de-identified public use data for our analysis.

Measures

In this survey, HRQoL was measured across the following domains: self-perceived health status, the quantity of poor physical health days per month, and poor mental health days per month. All participants who reported having ever been diagnosed with cancer were asked the following questions:

> "*Would you say that in general your health is…?*"
> *"Would you say that in general your health is; excellent, very good, good, fair, or poor?"*,
> *"Now thinking about your physical health, which includes physical illness and injury, for how many days during the past 30 days was your physical health not good?"* and
> *"Now thinking about your mental health, which includes stress, depression, and problems with emotions, for how many days during the past 30 days was your mental health not good?"* (3)

Responses to the first question were reported as a nominal response (i.e., "excellent" = 1, "very good" = 2, "good" = 3, "fair" = 4, and "poor" = 5). Responses to the second and third questions were reported as a quantity ranging from "0" to "30" (days per month). Dichotomous poor physical and mental health status was defined as having 14 or more days of poor health days (Zhao G, Okoro CA, Hsia J, Town M 2018) (Measuring Health Days CDC 2000).

Statistical Analysis

Univariate analyses yielded frequencies of sociodemographic characteristics (e.g., sex, race and ethnicity, marital status, educational attainment, annual household income, and health care coverage status) of survivors by cancer site. Group sample size, mean age at the time of the survey, and respective standard deviation was reported by the cancer site. Multivariate analyses yielded the mean self-perceived health status of survivors by site, adjusted for confounders, and calculated with the ordinal 5-point scale of general health using the least square regression method. Confounding variables for all multivariate analyses included age, sex, race and ethnicity, marital status, educational attainment, annual household income, health care coverage, and a history of myocardial infarction, stroke, and/or diabetes. Multivariate logistic regression modeling yielded the odds of reporting "poor" self-perceived health status, more than 14 days or 2 weeks per month of bad physical health days and more than 2 weeks per month of bad mental health days among survivors of the seven selected cancer sites according to income range. Odds ratios and respective 95% confidence intervals (CIs) were reported. If 95% CIs did not contain the null hypothesis value of 1.0, the results were considered to be statistically significant. All statistical analyses were performed using SAS software, version 9.4 (SAS Institute, Inc., Cary, NC). BRFSS utilizes an iterative proportional fitting method in determining the appropriate weights. Therefore, sampling weights from BRFSS were used

TABLE 1 | Sociodemographic characteristics of survivors of various cancers.

	Thyroid	Colon	Lung	Cervical	Breast	Prostate	Ovarian
N (%)	1,195 (2.0)	3,074 (5.2)	1,252 (2.1)	3,512 (6.0)	10,314 (17.6)	5,713 (9.8)	1,304 (2.2)
Age (mean, SD)	59.1 (13.9)	70.5 (12.8)	68.9 (11.7)	53.7 (15.2)	67.4 (13.2)	72.2 (9.6)	60.2 (15.5)
Sex							
Female	979 (81.9)	1,810 (58.9)	772 (61.7)	3,512 (99.6)	10,248 (99.4)		1,304 (99.8)
Male	216 (18.1)	1,264 (41.1)	480 (38.3)		66 (0.6)	5,713 (99.8)	
Race, ethnicity							
White only, non-hispanic	1,018 (85.2)	2,597 (84.5)	1,073 (85.7)	2,867 (81.3)	8,801 (85.3)	4,713 (82.4)	1,067 (81.6)
Black only, non-hispanic	55 (4.6)	210 (6.8)	86 (6.9)	202 (5.7)	638 (6.2)	523 (9.1)	80 (6.1)
Hispanic	62 (5.2)	109 (3.6)	26 (2.1)	194 (5.5)	355 (3.4)	193 (3.4)	62 (4.7)
Other race only, non-hispanic	41 (3.4)	66 (2.2)	33 (2.6)	138 (3.9)	275 (2.7)	148 (2.6)	43 (3.3)
Multi-racial, non-hispanic	12 (1.0)	49 (1.6)	20 (1.6)	106 (3.0)	160 (1.6)	72 (1.3)	46 (3.5)
Marital status							
Married	715 (59.8)	1,479 (48.1)	560 (44.7)	1,510 (42.8)	4,642 (45)	3,877 (67.7)	558 (42.7)
Other	480 (40.2)	1,595 (51.9)	692 (55.3)	2,016 (57.2)	5,672 (55)	1,846 (32.3)	749 (57.3)
Education							
Less than high school	66 (5.5)	405 (13.2)	212 (16.9)	424 (12.0)	832 (8.1)	646 (11.3)	159 (12.2)
High school	336 (28.1)	1,057 (34.4)	468 (37.4)	1,164 (33.0)	3,248 (31.5)	1,566 (27.4)	429 (32.8)
Some college	356 (29.8)	816 (26.6)	326 (26.0)	1,169 (33.2)	2,962 (28.7)	1,241 (21.7)	375 (28.7)
College	432 (36.2)	786 (25.6)	242 (19.3)	764 (21.7)	3,258 (31.6)	2,263 (39.5)	341 (26.1)
Income							
<$15,000	114 (9.5)	403 (13.1)	190 (15.2)	666 (18.9)	1,159 (11.2)	397 (6.9)	227 (17.4)
$15,000 to <25,000	173 (14.5)	666 (21.7)	279 (22.3)	743 (21.1)	1,946 (18.9)	917 (16.0)	295 (22.6)
$25,000 to <35,000	112 (9.4)	401 (13.0)	189 (15.1)	400 (11.3)	1,287 (12.5)	754 (13.2)	132 (10.1)
$35,000 to <50,000	144 (12.1)	408 (13.3)	151 (12.1)	449 (12.7)	1,392 (13.5)	959 (16.8)	173 (13.2)
$50,000 or more	502 (42.0)	709 (23.1)	223 (17.8)	890 (25.2)	2,755 (26.7)	2,091 (36.5)	293 (22.4)
Health care coverage							
Have health care coverage	700 (58.6)	796 (25.9)	359 (28.7)	2,147 (60.9)	3,605 (35.0)	1,060 (18.5)	640 (49.0)
Do not have health care coverage	54 (4.5)	75 (2.4)	28 (2.2)	506 (14.4)	332 (3.2)	84 (1.5)	138 (10.6)
Don't know/not sure/refused	441 (36.9)	2,203 (71.7)	865 (69.1)	873 (24.8)	6,377 (61.8)	4,579 (80.0)	529 (40.4)

to calculate the estimated population size and 95% confidence interval (CI).

RESULTS

Univariate Analyses

With the consideration of sampling weights from BRFSS, 59,173 were considered having ever been diagnosed with cancer out of the 432,607 participants who completed the survey (**Table 1**: Sociodemographic Characteristics by Cancer Site). Of the 59,173 survivors, 1,195 had been diagnosed with thyroid cancer, 3,074 with colon cancer, 3,526 with cervical cancer, 10,314 with breast cancer, 5,723 with prostate cancer, and 1,307 with ovarian cancer. The mean age was 59, 71, 69, 54, 67, 72, and 60 years for survivors of thyroid, colon, lung, cervical, breast, prostate, and ovarian cancer, respectively (**Table 1**). Excluding the sex-specific cancer sites, the majority of participants were female (82, 59, 62%) among thyroid, colon, and lung cancer survivors, respectively. Non-Hispanic Whites were the majority race-ethnicity across all seven cancer sites. Level of educational attainment among survivors varied by cancer site, although most had at least graduated high school. An annual household income of <$50,000 was most common among survivors across all seven cancer sites. Participants widely "refused" or responded as "unsure" when asked if they had health care coverage (**Table 1**).

Multivariate Analyses

Adjusted mean self-perceived health status among survivors of thyroid, colon, lung, cervical, breast, prostate, and ovarian cancer was 3.83 ± 0.05, 4.02 ± 0.04, 4.36 ± 0.06, 3.77 ± 0.03, 3.88 ± 0.03, 3.78 ± 0.04, and 3.96 ± 0.05, respectively (**Figure 1**: Adjusted Mean Self-Perceived Health Status). A positive dose-response effect was observed between the income range and all three HRQoL measures across all seven cancer sites (**Table 2**: Odds of Reporting Poor HRQoL).

Self-Perceived Health Status

Univariate analysis was conducted to examine the relationship between socioedemographic charcateristics and self-perceived general health, poor physical health, and poor mental health among cancer survivors of seven cancer sites included. We found statistically significant association in every factors (**Supplementary Table 1**). However, income was consistently

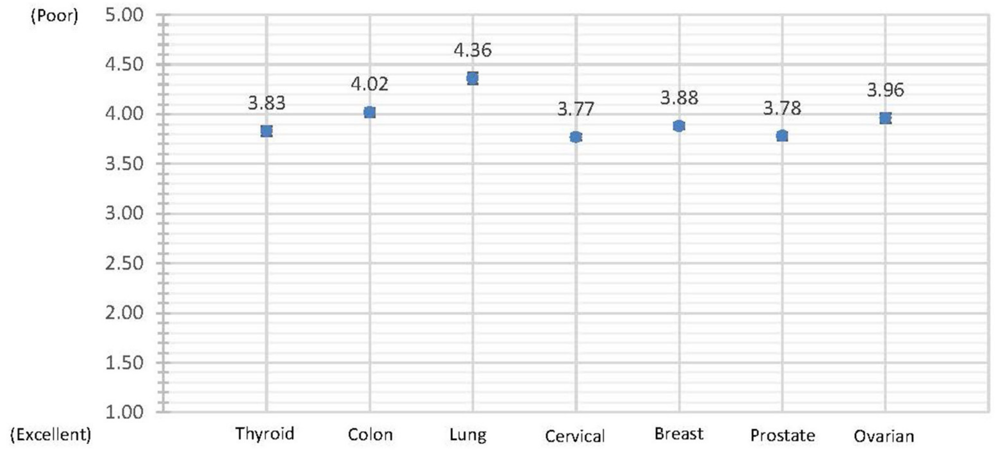

FIGURE 1 | Adjusted mean self-perceived health status. Self-Perceived Health is reported as a whole value on a 5-point scale where "Excellent" = 1; "Very Good" = 2; "Good" = 3; "Fair" = 4; and "Poor" = 5.

and inversely associated with a higher chance of reporting poorer self-perceived health status. Among survivors of cervical, breast, and ovarian cancers, odds ratio estimates demonstrated a consistent positive-dose response effect, and respective 95% CIs were statistically significant for every range of income.

Cervical

Among cervical cancer survivors, the odds of reporting poorer self-perceived health status decreased as income increased [OR: 0.44, 95% CI: 0.31, 0.63], [OR: 0.21, 95% CI: 0.13, 0.35], [OR: 0.18, 95% CI: 0.11, 0.30], [OR: 0.09, 95% CI: 0.06, 0.16] among those with an annual household income range of <\$15,000 (ref), \$15,000 to <25,000, \$25,000 to <35,000, \$35,000 to <50,000, and \$50,000 or more, respectively (**Table 2**).

Breast

Among breast cancer survivors, the odds of reporting poorer self-perceived health status decreased as income increased [OR: 0.49, 95% CI: 0.34, 0.70], [OR: 0.28, 95% CI: 0.18, 0.44], [OR: 0.21, 95% CI: 0.13, 0.33], [OR: 0.16, 95% CI: 0.10, 0.25] among those with an annual household income range of <\$15,000 (ref), \$15,000 to <25,000, \$25,000 to <35,000, \$35,000 to <50,000, and \$50,000 or more, respectively (**Table 2**).

Ovarian

Among ovarian cancer survivors, the odds of reporting poorer self-perceived health status decreased as income increased [OR: 0.33, 95% CI: 0.17, 0.64], [OR: 0.38, 95% CI: 0.16, 0.89], [OR: 0.33, 95% CI: 0.14, 0.75], [OR: 0.27, 95% CI: 0.13, 0.60] among those with an annual household income range of <\$15,000 (ref), \$15,000 to <25,000, \$25,000 to <35,000, \$35,000 to <50,000, and \$50,000 or more, respectively (**Table 2**).

Physical Health

Income was inversely associated with a higher chance for reporting two or more weeks of bad physical health days per month. A positive-dose response was observed, albeit, less consistently across cancer sites compared to self-perceived health status. Among survivors of cervical and breast cancers, odds ratio estimates demonstrated a consistent positive-dose response effect, and respective 95% CIs were statistically significant for every range of income.

Cervical

Among cervical cancer survivors, the odds of reporting two or more weeks per month of bad physical health days decreased as income increased [OR: 0.33, 95% CI: 0.17, 0.64], [OR: 0.38, 95% CI: 0.16, 0.89], [OR: 0.33, 95% CI: 0.14, 0.75], [OR: 0.27, 95% CI: 0.13, 0.60] among those with an annual household income range of <\$15,000 (ref), \$15,000 to <25,000, \$25,000 to <35,000, \$35,000 to <50,000, and \$50,000 or more, respectively (**Table 2**).

Breast

Among breast cancer survivors, the odds of reporting two or more weeks per month of bad physical health days decreased as income increased [OR: 0.33, 95% CI: 0.17, 0.64], [OR: 0.38, 95% CI: 0.16, 0.89], [OR: 0.33, 95% CI: 0.14, 0.75], [OR: 0.27, 95% CI: 0.13, 0.60] among those with an annual household income range of <\$15,000 (ref), \$15,000 to <25,000, \$25,000 to <35,000, \$35,000 to <50,000, and \$50,000 or more, respectively (**Table 2**).

Mental Health

Income was often inversely associated with a higher chance for reporting two or more weeks of bad mental health days per month. A positive dose-response effect between income and poor mental health days was observed among survivors of lung, cervical, and breast cancers. However, CIs were not consistently statistically significant for all ranges of income.

Lung

Among lung cancer survivors, the odds of reporting two or more weeks per month of bad mental health days decreased as income increased [OR: 0.33, 95% CI: 0.17, 0.64], [OR: 0.38, 95% CI: 0.16, 0.89], [OR: 0.33, 95% CI: 0.14, 0.75], [OR: 0.27, 95% CI: 0.13,

TABLE 2 | Odds of reporting poor health-related quality of life among cancer survivors.

Cancer Site	Income	OR^1 [95% CI^^{1}]	OR^2 [95% CI^^{2}]	OR^3 [95% CI^^{3}]
Thyroid	<$15,000*	Ref	Ref	Ref
n = 1,195	$15,000 to <25,000	0.30 [0.11, 0.81]	0.56 [0.22, 1.42]	0.61 [0.22, 1.70]
	$25,000 to <35,000	0.30 [0.09, 1.06]	0.53 [0.16, 1.73]	0.37 [0.11, 1.26]
	$35,000 to <50,000	0.14 [0.04, 0.51]	0.45 [0.16, 1.24]	0.50 [0.16, 1.53]
	$50,000 or more	0.13 [0.04, 0.40]	0.21 [0.08, 0.57]	0.51 [0.18, 1.46]
Colon	<$15,000	Ref	Ref	Ref
n = 3,074	$15,000 to <25,000	0.64 [0.35, 1.17]	0.64 [0.32, 1.28]	0.85 [0.39, 1.85]
	$25,000 to <35,000	0.39 [0.18, 0.86]	0.59 [0.25, 1.40]	0.36 [0.13, 1.02]
	$35,000 to <50,000	0.33 [0.15, 0.69]	0.54 [0.25, 1.19]	0.58 [0.24, 1.37]
	$50,000 or more	0.19 [0.09, 0.40]	0.20 [0.09, 0.42]	0.43 [0.18, 1.01]
Lung	<$15,000	Ref	Ref	Ref
n = 1,252	$15,000 to <25,000	0.48 [0.22, 1.03]	0.40 [0.15, 1.07]	0.54 [0.15, 1.90]
	$25,000 to <35,000	0.36 [0.14, 0.89]	1.7 [0.46, 5.95]	0.58 [0.14, 2.33]
	$35,000 to <50,000	0.30 [0.11, 0.78]	0.22 [0.06, 0.72]	0.09 [0.02, 0.55]
	$50,000 or more	0.20 [0.08, 0.50]	0.41 [0.13, 1.24]	0.05 [0.01, 0.34]
Cervical	<$15,000	Ref	Ref	Ref
n = 3,512	$15,000 to <25,000	0.44 [0.31, 0.63]	0.53 [0.38, 0.74]	0.74 [0.53, 1.03]
	$25,000 to <35,000	0.21 [0.13, 0.35]	0.36 [0.23, 0.55]	0.40 [0.26, 0.60]
	$35,000 to <50,000	0.18 [0.11, 0.30]	0.22 [0.14, 0.34]	0.28 [0.18, 0.43]
	$50,000 or more	0.09 [0.06, 0.16]	0.19 [0.12, 0.28]	0.27 [0.18, 0.39]
Breast	<$15,000	Ref	Ref	Ref
n = 10,314	$15,000 to <25,000	0.49 [0.34, 0.70]	0.52 [0.36, 0.75]	0.69 [0.47, 1.02]
	$25,000 to <35,000	0.28 [0.18, 0.44]	0.35 [0.23, 0.54]	0.31 [0.20, 0.50]
	$35,000 to <50,000	0.21 [0.13, 0.33]	0.29 [0.19, 0.43]	0.30 [0.19, 0.46]
	$50,000 or more	0.16 [0.10, 0.25]	0.20 [0.13, 0.30]	0.23 [0.15, 0.35]
Prostate	<$15,000	Ref	Ref	Ref
n = 5,713	$15,000 to <25,000	1.70 [0.70, 4.10]	0.99 [0.40, 2.48]	0.41 [0.12, 1.34]
	$25,000 to <35,000	0.54 [0.20, 1.52]	0.52 [0.20, 1.41]	0.14 [0.04, 0.53]
	$35,000 to <50,000	0.41 [0.15, 1.13]	0.40 [0.16, 0.99]	0.32 [0.11, 0.95]
	$50,000 or more	0.14 [0.05, 0.39]	0.36 [0.15, 0.88]	0.19 [0.06, 0.57]
Ovarian	<$15,000	Ref	Ref	Ref
n = 1,304	$15,000 to <25,000	0.33 [0.17, 0.64]	0.67 [0.36, 1.25]	0.40 [0.20, 0.81]
	$25,000 to <35,000	0.38 [0.16, 0.89]	0.42 [0.19, 0.95]	0.47 [0.20, 1.13]
	$35,000 to <50,000	0.33 [0.14, 0.75]	0.30 [0.14, 0.68]	0.14 [0.06, 0.35]
	$50,000 or more	0.27 [0.13, 0.60]	0.39 [0.19, 0.81]	0.20 [0.09, 0.45]

^{1,2,3}*Adjusted odds ratio.*

^95% Confidence Interval.

**Reference Group.*

OR^1 and 95% CI^^{1}: Odds of reporting "poor" self-perceived health status.

OR^2 and 95% CI^^{2}: Odds of reporting more than 2 weeks per month of bad physical health days.

OR^3 and 95% CI^^{3}: Odds of reporting more than 2 weeks per month of bad mental health days.

0.60] among those with an annual household income range of <$15,000 (ref), $15,000 to <25,000, $25,000 to <35,000, $35,000 to <50,000 and $50,000 or more, respectively (**Table 2**).

Cervical

Among cervical cancer survivors, the odds of reporting two or more weeks per month of bad mental health days decreased as income increased [OR: 0.33, 95% CI: 0.17, 0.64], [OR: 0.38, 95% CI: 0.16, 0.89], [OR: 0.33, 95% CI: 0.14, 0.75], [OR: 0.27, 95% CI: 0.13, 0.60] among those with an annual household income range of <$15,000 (ref), $15,000 to <25,000, $25,000 to <35,000, $35,000 to <50,000, and $50,000 or more, respectively (**Table 2**).

Breast

Among breast cancer survivors, the odds of reporting two or more weeks per month of bad mental health days decreased as income increased [OR: 0.33, 95% CI: 0.17, 0.64], [OR: 0.38, 95% CI: 0.16, 0.89], [OR: 0.33, 95% CI: 0.14, 0.75], [OR: 0.27, 95% CI: 0.13, 0.60] among those with an annual household income range of <\$15,000 (ref), \$15,000 to <25,000, \$25,000 to <35,000, \$35,000 to <50,000, and \$50,000 or more, respectively (**Table 2**).

DISCUSSION

This study utilized the latest national representative survey data to examine factors associated with HRQoL. We found that lower family income is the primary factor associated with both poorer mental and physical health among cancer survivors, regardless of the cancer site. Our finding is consistent with the analysis of the BRFSS survey from 2000 to 2002 (10). Another study used a more recent BRFSS examined the HRQoL among cancer survivors utilized the cancer survivor module as our study (11). However, the study of the 2016 BRFSS survey 2016 only included nine states in the US. Although the authors did not have household income levels in their models, they found non-employment status is significantly associated with all measures of HRQoL, which is related to the financial well-being of the cancer survivor. Female and marital status of divorced/widowed/separated/never married are the only other factors associated with all measures of HRQoL. Our analysis did not find a statistically significant association of gender and marital status after adjusting for confounders.

Very few studies evaluated sociodemographic characteristics for cancer survivors on HRQoL across various cancer sites. The publication by Applewhite summarized published studies of the quality of life among survivors of the thyroid, colon, glioma, breast, and gynecologic cancer. The authors suggested that breast cancer survivors had a better overall quality of life than all other cancers compared. The overall quality of life was similar among patients with colon cancer, glioma, gynecologic cancer, and thyroid cancer (12). Our study, however, found that. regardless of cancer site, income level was inversely associated with HRQoL among cancer survivors. We do not see a significant racial difference among different racial groups either. It is plausible that financial resources may lessen the overall burden of cancer survivors, which could improve self-perceived health-related quality of life, psychological well-being, and physical function among cancer survivors. We believe the current study's findings add to a growing body of literature demonstrating that survivorship is associated with financial hardship (8, 13–21).

Cancer survivors are living longer with their cancer as a chronic illness, thanks to early diagnosis and advancements in medical technologies and treatment (22). Cancer survivors have to be monitored for an extensive period of time (23). Therefore, there is an increased reliance on patients to make larger co-payments and financial contributions to their healthcare. It will result in financial toxicity results when medical expenditures with associated out-of-pocket costs are high relative to family income. Research has demonstrated that financial toxicities appear to constitute part of the pathway that ultimately leads to adverse health outcomes and poorer HRQoL (24–26). Even in countries where there is universal healthcare or when individuals have health insurance, additional patient out-of-pocket expenses are expected (22, 27). Chen et al. reported that an income gradient in avoidable mortality rates persisted throughout a 40-year study period from 1971 to 2008 using national data of all deaths reported in Taiwan (28). Universal guaranteed access to medical care in 1995 may have helped reduce, but did not eliminate, the income gradient in mortality disparities. Income vulnerability also adversely impacts the utilization of healthcare services (29).

Studies found that younger and minority cancer patients are disproportionately affected by financial toxicity as they may have fewer savings, more educational debts, and fewer assets than older cancer patients (30, 31). Because these younger cancer patients are likely still active in the workforce. Doctor visits, appointments for exams and treatments, the time needed to recover from treatment, and follow-up visits can all make it difficult to take time away from their careers (32). Psychological stress for an extended period could have a toll on both their physical and mental well-being (33, 34). We found that increased family income level was significantly associated with fewer bad physical days among cancer survivors of six sites after adjusting for confounders, including age, other than lung cancer, with a clear dose-response relationship. Higher family income was associated with fewer bad mental days among survivors of lung, cervical, breast, prostate, and ovarian cancers. The financial ability to access resources to address both mental and physical stress appeared to play a significant role in the well-being of cancer survivors, regardless of the type of cancer. We did not find a significant association between the age of participants and HRQoL in any cancer.

Mental and physical health among people living with and beyond cancer has been identified as a growing clinical and research priority (35, 36). This study provides a cross-sectional examination of the factors associated with HRQoL, which including both mental and physical health, among cancer survivors using a national representative sample. However, like many others, this study has its limitations such that the results should be interpreted with consideration of its design. First, the cross-sectional nature of this survey yields the possibility of survivorship bias. The length of time that has passed since their last treatment is unknown for each survivor. Cancer survivors in the survey were likely diagnosed at an earlier stage and were healthy enough to complete the survey. Additionally, the selection of seven pathologically heterogeneous cancer sites might introduce questions concerning disparities in treatment toxicity (e.g., surgery vs. chemotherapy and radiation), economic burden (e.g., duration and extent of treatment), and lifetime prognoses (e.g., survival times differ markedly).

CONCLUSION

The survey was conducted prior to the enactment of the Affordable Care Act (ACA). Ideally, the health care reform would have eased the contribution of family income to the HRQoL among cancer survivors. However, the study conducted in Taiwan did not observe reversing the trend for the relationship between the financial burden for cancer survivors and HRQoL after the implementation of universal guaranteed access to medical care in Taiwan (28). It has been more than 10 years since BRFSS has included the module of HRQoL among cancer survivors in all 50 states and Washington, DC. Public health researchers and policymakers need the information to assess the impact of the ACA on the HRQoL among cancer survivors regarding financial well-being. We hope the CDC will consider implementing the cancer survivor module in all states in the coming BRFSS survey.

DATA AVAILABILITY STATEMENT

Publicly available datasets were analyzed in this study. This data can be found here: https://www.cdc.gov/brfss/annual_data/annual_2009.htm.

AUTHOR CONTRIBUTIONS

LS initiated the research concept, participated in the data analysis, and completed the draft of manuscript. SO'C conducted the statistical analysis and initiated the manuscript. T-CC contributed in the draft and organization of the manuscript. All authors participated in the review and revision of the manuscript.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2021.752868/full#supplementary-material

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BRIEF RESEARCH REPORT
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The Impact of COVID-19 on Risky Behaviors and Health Changes in African-American Smokers Who Are Eligible for LDCT Screening

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The COVID-19 pandemic has disrupted much of day-to-day life in the US and around the world. Smokers have a higher risk of adverse outcomes due to COVID-19. This study investigated the impact of COVID-19 on risky behaviors and health changes in lower income African-American smokers eligible for Low dose computed tomography (LDCT) screening, who may be more adversely impacted by the COVID-19 pandemic. A total of 22 African-American daily smokers who were eligible for LDCT screening participated in this study. The mean age of participants was 61.2 years old (SD = 4.7), 77.3% of the smokers were female, all participants had an income below $20,000, and 63.6% were on Medicaid. Descriptive statistics were used to provide summary information on demographics, COVID-19, and health status. Results showed that participants increased cigarette smoking, spent more time on screens, increased sugary drink consumption, consumed more vegetables and fruits, and engaged in more gardening activities during the COVID-19 pandemic. However, participants also decreased physical activity time and slept less during the pandemic. In general, more than one-third of participants gained more body weight and reported increased stress and anxiety. Our results suggest that African-American smokers who qualify for LDCT screening should be encouraged to consider strategies not only for smoking cessation, but also risky behavior control and management.

Keywords: smoking, risky behavior, LDCT lung cancer screening, COVID-19, African American (AA), healthy behavior

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INTRODUCTION

The COVID-19 pandemic has disrupted much of day-to-day life in the US and around the world (1). The first case of COVID-19 was identified in the US on January 20, 2020, and has resulted in ~32 million cases and 600,000 deaths in the US, as of May 2021 (2). Smoking has been associated with a greater risk of adverse outcomes in COVID-19, with current and former smokers being 1.4 times more likely to suffer severe symptoms of COVID 19, and 2.4 times more likely to need ICU support, mechanical ventilation, or die, compared to non-smokers (3). However, some studies have shown that smokers tend to increase the frequency of smoking behaviors during quarantine, which further increases the negative health risks associated with smoking (4). In a study on a predominantly African-American population of patients with COVID-19, those who were smokers showed an increased need of ICU admission and higher mortality (5). Furthermore, African-Americans are more likely to have comorbid conditions such as hypertension, diabetes, and obesity, all of which may exacerbate COVID-19 outcomes (6). During the COVID-19 pandemic, African-Americans in a US national survey were more likely than White Americans to leave their homes, possibly due to social circumstances or lower access to accurate knowledge of how the disease is spread (7).

African-Americans and White Americans smoke at comparable rates; however, when compared to White smokers, African-American smokers smoke fewer cigarettes per day, and initiate smoking at a later age (8). Despite this, African-American smokers bear a disproportionate burden of smoking-related diseases (8). African-American smokers are also more likely than White smokers to want to quit and attempt to quit, but are less likely to quit successfully than White smokers (9). This may be due to lower access and utilization of smoking cessation services (9). Despite knowledge about the increased risk of COVID-19 on smokers and the health disparities facing African-American smokers, smoking behaviors during the COVID-19 pandemic have not been well-investigated in this population. Currently, the smoking behaviors of African-American smokers during COVID-19 are unclear.

In addition to smoking, changes in other health behaviors due to COVID-19 are also of concern. Previous studies have demonstrated increased weight gain, decreased physical activity, decreased consumption of fruit and vegetables, increased screen time, decreased sleep, and increased alcohol consumption during quarantine (4, 10–13). Risky behaviors, such as smoking, are likely to cluster with other risky behaviors, such as alcohol use (14). In a separate nationally representative survey of 604 African-Americans, fewer than 80% of participants reported adhering to the four COVID-19 public health recommendations of frequently washing hands for at least 20 s, staying 6 or more feet apart from others in public, avoiding touching the face, and wearing a mask when in contact with others (15). In Louisiana, African-Americans represent 32.2% of the state population, but 70.5% of COVID-19 deaths are African-American (16). This disparity may be due to several risk factors facing the African-American population in Louisiana, such as higher prevalence of chronic disease, lower access to knowledge about COVID-19, increased shelter insecurity, and other factors (7). Because of this stark disparity, it is important to understand the behavioral changes of African-American smokers during COVID-19. The objective of this study was to investigate the impact of COVID-19 on risky behaviors and health changes in lower income African-American smokers eligible for Low dose computed tomography (LDCT) screening, who may be more adversely impacted by the COVID-19 pandemic.

METHODS

Study Design and Population

This study applied a cross-sectional design via phone survey in 2020. Eligible participants were African Americans smokers ages 55–77 years old have who had either had 30+ pack-years of smoking or had received an LDCT exam in the past year, who were eligible for LDCT screening in primary care clinics at a large hospital in New Orleans, LA. A total of 22 African-American daily smokers agreed to participate in the survey via phone. Enrollees were asked to give verbal consent to confirm that they understood the rights and privacy protection disclaimer before the survey. After completing the survey, an e-informed consent document was distributed to all participants for their records. The survey was an anonymous questionnaire that collected demographic information, COVID-19 and health status, and behavior related information. This study protocol was reviewed and approved by the Institutional Review Board of LSUHSC-NO (approval #10104).

Subject Demographics

Participant demographics included age, gender, income, education, marriage status, and insurance type. Gender was classified as female or male. Income level included two categories (<\$20,000, and equal to, or higher than \$20,000). Education level was classified into four groups (Grades 1 through 8, Grades 9 through 11, Grade 12 or GED, and College 1–3 years). Marital status was classified into four categories [married, divorced, widowed, and single (i.e., never married and not now living with a partner)]. Insurance type included health insurance (private health insurance, Blue Cross and Blue Shield, and HMOs), Medicaid, Medicare, paid with cash, and others.

COVID-19 and Health Status

There were three questions pertaining to COVID-19, including "Have you been diagnosed positive for COVID-19 in the recent months?"(Yes/No), "If Yes, did you stay at a hospital to treat COVID-19?"(Yes/No), and "How likely do you think it is that you will get COVID-19 in the future?" (very low to very high, using a 5-point Likert scale). Health status included body mass index (BMI) and chronic disease history. BMI was classified into normal weight (<25 kg/m^2), overweight (25–29.9 kg/m^2), and obese (≥ 30 kg/m^2). Participants were asked the question "Have you been diagnosed with any of the following chronic diseases?" to identify their chronic disease history [responses included hypertension, diabetes, asthma, chronic obstructive pulmonary disease (COPD), mental health disorder, coronary heart disease, arthritis, kidney disease, liver disease, and cancer].

Behavioral Changes During the COVID-19 Pandemic

We assessed behavioral changes via the question "Did you change the following behaviors during the COVID-19 pandemic?" Responses included twelve behaviors: cigarette smoking, alcohol consumption, vegetable and fruit consumption, sugary drink consumption, exercise times, sleep hours, screen time, vitamin intake, gardening, body weight, stress, and anxiety. Each question had five levels of response (decrease, slightly decrease, no change, slight increase, and increase).

Statistical Analyses

Descriptive statistics were used to provide summary information on demographics, COVID-19, and health status. All analyses

TABLE 1 | Participant demographics ($n = 22$).

Variables	*n* (%)
Age, Mean (SD)	61.2 (4.7)
Gender	
Female	17 (77.3)
Male	5 (22.7)
Annual income	
<$20,000	22 (100.0)
Education level	
Grades 1 through 8	1 (4.6)
Grades 9 through 11	10 (45.5)
Grade 12 or GED	8 (36.4)
College 1–3 years	3 (13.6)
Marital status	
Married	2 (9.1)
Divorced	7 (31.8)
Widowed	2 (9.1)
Single#	11 (50.0)
Insurance	
Paid with cash	4 (18.2)
Health insurance$	2 (9.1)
Medicaid	14 (63.6)
Medicare	8 (36.4)
Others	1 (4.6)

#*Never married and not now living with a partner.*

$*Private health insurance, Blue Cross and Blue Shield, HMOs.*

TABLE 2 | COVID-19 and Health Status ($n = 22$).

Variables	*n* (%)
COVID-19	
Have you been diagnosed positive for COVID-19 in the recent months?	
No	19 (90.5)
Yes	2 (9.5)
If YES, did you stay at a hospital to treat COVID-19?	
No	1 (50.0)
Yes	1 (50.0)
How likely do you think it is that you will get COVID-19 in the future?	
Very low	13 (65.0)
Somewhat low	5 (25.0)
Moderate	1 (5.0)
Somewhat high	0 (0.0)
Very high	1 (5.0)
Health Status	
Body Mass Index	
Normal (18.5–24.9 kg/m^2)	6 (27.3)
Overweight (25–29.9 kg/m^2)	7 (31.8)
Obese (≧30 kg/m^2)	9 (40.9)
Have you been diagnosed with the following chronic diseases?	
Hypertension	10 (47.6)
Diabetes	11 (52.4)
Asthma	5 (23.8)
COPD	6 (28.6)
Mental health disorder	2 (9.5)
Coronary heart disease	4 (19.1)
Arthritis	12 (57.1)
Kidney diseases	1 (4.8)
Liver disease	3 (14.3)
Cancer	1 (4.8)

were performed using SAS version 9.4 (SAS Institute, Cary, NC, USA).

RESULTS

The demographic characteristics of all participants are shown in **Table 1**. The mean age of participants was 61.2 years old (SD = 4.7). As shown in **Table 1**, 77.3% of participants were female, and all participants reported an income below $20,000. Half of participants reported an education of high school or below, half reported being single (i.e., never married and not now living with a partner), and 63.6% were on Medicaid.

Table 2 shows COVID-19 and health status. Two smokers (10%) had been diagnosed positive for COVID-19, and one of them was treated in a hospital. Eighteen smokers (90%) felt that they had a very low or low risk of getting COVID-19 in the future. In terms of health status, 72.7% of participants were overweight or obese. More than half of smokers mentioned that they had been diagnosed with hypertension, diabetes, or arthritis. About one-third had asthma or COPD.

Behavioral changes during the COVID-19 pandemic are shown in **Table 3**. Regarding smoking behavior, 42.9% of participants reported increased cigarette smoking and 28.6% of participants reported decreased cigarette smoking during the COVID-19 pandemic. For alcohol intake, only 19% of participants reported that they consumed more alcohol during the pandemic. Additionally, 38.1% of participants consumed more vegetables and fruits, and around 40% of participants reported that they engaged in more gardening activities. However, 33.3% of participants increased sugary drink intake, 23.8% of participants decreased physical activity time, and 42.9% of participants spent more time on screens (including TVs, smartphones, tablets, and computers). Over 30% of participants gained more body weight, slept less, and felt increased stress and anxiety during the pandemic.

DISCUSSION

Most African-American smokers eligible for LDCT screening reported increased cigarette smoking during the COVID-19 pandemic, although about one-third reported decreasing cigarette smoking. This finding is consistent with some previous studies that also reported decreases in cigarette consumption during COVID-19 quarantine periods (17, 18). One previous study reported that smoking was associated with a greater risk of adverse outcomes in COVID-19, with current and former smokers being 2.4 times as likely to need ICU support or die,

TABLE 3 | Behavior and health changes ($n = 22$).

Variable	***n* (%)**
DID YOU CHANGE THE FOLLOWING BEHAVIORS DURING THE COVID-19 PANDEMIC?	
Cigarette smoking	
Decrease	2 (9.5)
Slightly decrease	4 (19.1)
No change	6 (28.6)
Slightly increase	5 (23.8)
Increase	4 (19.1)
Alcohol consumption	
Decrease	0 (0.0)
Slightly decrease	1 (4.8)
No change	15 (71.4)
Slightly increase	2 (9.5)
Increase	2 (9.5)
NA	1
Vegetable and fruit consumption	
Decrease	2 (9.5)
Slightly decrease	1 (4.8)
No change	10 (47.6)
Slightly increase	3 (14.3)
Increase	5 (23.8)
Sugary drink consumption	
Decrease	1 (4.8)
Slightly decrease	0 (0.0)
No change	13 (61.9)
Slightly increase	5 (23.8)
Increase	2 (9.5)
Exercise time	
Decrease	3 (14.3)
Slightly decrease	2 (9.5)
No change	13 (61.9)
Slightly increase	2 (9.5)
Increase	1 (4.8)
Sleep hours	
Decrease	2 (9.5)
Slightly decrease	4 (19.1)
No change	11 (52.4)
Slightly increase	2 (9.5)
Increase	2 (9.5)
Screen time (i.e., TV, phone, PC, tablet)	
Decrease	1 (4.8)
Slightly decrease	0 (0.0)
No change	11 (52.4)
Slightly increase	4 (19.1)
Increase	5 (23.8)
Vitamin intake	
Decrease	3 (14.3)
Slightly decrease	0 (0.0)
No change	16 (76.2)
Slightly increase	1 (4.8)
Increase	0 (0.0)
NA	1 (4.8)
Gardening	
Decrease	0 (0.0)
Slightly decrease	1 (4.8)
No change	12 (57.1)
Slightly increase	4 (19.1)
Increase	4 (19.1)
Body weight	
Decrease	0 (0.0)
Slightly decrease	1 (4.8)
No change	12 (57.1)
Slightly increase	4 (19.1)
Increase	4 (19.1)
Stress	
Decrease	1 (4.8)
Slightly decrease	0 (0.0)
No change	11 (52.4)
Slightly increase	5 (23.8)
Increase	4 (19.1)
Anxiety	
Decrease	1 (4.8)
Slightly decrease	1 (4.8)
No change	12 (57.1)
Slightly increase	3 (14.3)
Increase	4 (19.1)

compared to non-smokers (3). Although this study focused on smoking and other risky behavioral changes during the pandemic, it should be noted that African-American smokers may be more adversely impacted by the COVID-19 pandemic. A recent study showed that African-Americans are more likely to have comorbid conditions such as hypertension, diabetes, and obesity, all of which may exacerbate COVID-19 outcomes (6). Our results also showed that 72.7% of African-American smokers in this study were overweight or obese. Furthermore, more than half of participants mentioned that they have been diagnosed with hypertension, diabetes, or arthritis, which may lead to more adverse COVID-19 related outcomes.

Our results also showed that 38% of participants experienced an increase in bodyweight during the COVID-19 pandemic. This may have resulted from increased sugary drink intake, increased screen time, and decreased physical activity. Compared to pre-pandemic, screen time increased (42%) and exercise time decreased (23.8%) during the pandemic. Previous studies have shown that individuals reported higher levels of screen time during the pandemic, which was associated with poorer mental health (19). Additionally, another study demonstrated that COVID-19 home lockdown was associated with a decrease in physical activity levels, as well as unhealthier eating patterns (20). However, African-American smokers in this study consumed more vegetables and fruits during the pandemic, and around

40% of participants reported they engaged in more gardening activities. Home gardening has been shown to increase food security and the intake of nutritious foods, and has been suggested as a potential strategy to combat food insecurity in areas affected by COVID-19 labor shortages (21). These results suggest that the COVID-19 pandemic can influence smokers' eating, home gardening and food consumption behaviors.

Another important finding in this study is that participants reported sleeping less and feeling more stress and anxiety during the pandemic. These mental health changes could be due to the perception of potential illness and life challenges exacerbated by the COVID-19 pandemic. A recent systematic review demonstrated that the COVID-19 pandemic has resulted in significant negative psychological impacts, and contributed to a concurrent mental health epidemic (22). Consistent with our findings, several studies have also shown changes in sleep, stress, and anxiety as a result of the pandemic (23–25).

It is important to note that there are some limitations inherent to this study. First, this is a pilot study using self-reported data, which tends to give narrow estimated associations. Second, the small sample size from a single hospital targeting lower income African-American smokers limits the generalizability and reliability of results. Third, the behavioral changes were only collected at one time point during the pandemic, and may have changed as the pandemic progressed. Despite these limitations, this study focuses on lower income, higher risk African-American smokers who may be more adversely impacted by the COVID-19 pandemic during the time of data collection.

CONCLUSION

This study found that African-American smokers who were eligible for LDCT screening increased cigarette smoking, spent more time on screens, increased sugary drink consumption, consumed more vegetables and fruits, and engaged in more gardening activities during the COVID-19 pandemic. However, participants also decreased time spent pursuing physical activities and slept less. In general, more than one-third of participants gained more body weight and felt increased stress and anxiety. Our results suggest that African-American smokers who qualify for LDCT screening should be encouraged to consider strategies not only for smoking cessation, but also risky behavior control and management.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article and supplementary material. Further inquiries can be directed to the corresponding author(s).

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the Institutional Review Board of LSUHSC-NO (approval #10104). The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

T-ST contributed to the study conception and drafted the first manuscript. ML reviewed the manuscript and conducted the literature review. H-YL checked quality and results. T-ST, Y-HK, and L-SC contributed to the data analysis and the interpretation of the study. All authors contributed to editing and revising the manuscript critically and approved the final version of the article to be published.

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frontiers in Public Health

BRIEF RESEARCH REPORT
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Factors Associated With Patient's Refusal of Recommended Cancer Surgery: Based on Surveillance, Epidemiology, and End Results

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Objectives: Most non-metastatic cancer patients can harvest a preferable survival after surgical treatment, however, patients sometimes refuse the recommended cancer-directed surgery. It is necessary to uncover the factors associated with patent's decision in taking cancer surgery and explore racial/ethnic disparities in surgery refusal.

Methods: Based on the Surveillance, Epidemiology and End Results (SEER)-18 program, we extracted data of non-metastatic cancer patients who didn't undergo surgery. Ten common solid cancers were selected. Four racial/ethnic categories were included: White, black, Hispanic, and Asian/Pacific Islander (API). Primary outcome was patient's refusal of surgery. Multivariable logistic regression models were used, with reported odds ratio (OR) and 95% confidence interval (CI).

Results: Among 318,318 patients, the incidence of surgery refusal was 3.5%. Advanced age, female patients, earlier cancer stage, uninsured/Medicaid and unmarried patients were significantly associated with higher odds of surgery refusal. Black and API patients were more likely to refuse recommended surgery than white patients in overall cancer (black-white: adjusted OR, 1.18; 95% CI, 1.11–1.26; API-white: adjusted OR, 1.56; 95% CI, 1.41–1.72); those racial/ethnic disparities narrowed down after additionally adjusting for insurance type and marital status. In subgroup analysis, API-white disparities in surgery refusal widely existed in prostate, lung/bronchus, liver, and stomach cancers.

Conclusions: Patient's socioeconomic conditions reflected by insurance type and marital status may play a key role in racial/ethnic disparities in surgery refusal. Oncological surgeons should fully consider the barriers behind patient's refusal of recommended surgery, thus promoting patient-doctor shared decision-making and guiding patients to the most appropriate therapy.

Keywords: cancer, surgery, refusal, racial disparities, marital status, insurance type

INTRODUCTION

Although patients with non-metastatic cancers have an opportunity to receive surgery and subsequently harvest a preferable survival, there is always no cancer-directed surgery available to them. It remains unknown which and how many reasons for non-cancer-directed surgery exist in various non-metastatic cancers. The patient's refusal of recommended surgery is one of the modifiable reasons that should be addressed. It has been found that black patients are more likely to refuse recommended surgery than white patients in several cancers (1–3). However, it is unclear whether black-white disparities in refusal are largely mediated by patient's socioeconomic status, such as insurance type and marital status. Therefore, this study seeks to explore the factors that associate with the patent's decision in taking recommended cancer surgery. This study also seeks to explore whether that racial/ethnic disparity in refusal could be narrowed down by controlling the factors such as insurance type and marital status.

METHODS

Study Population

This population-based cohort study was based on the Surveillance, Epidemiology and End Results (SEER)-18 Registries (Nov 2018 Sub). SEER program covers 28% of US population and collects data on different cancers from population-based cancer registries (https://seer.cancer.gov/). SEER*Stat software 8.3.8 was used to retrieve data (https://seer.cancer.gov/seerstat/). Ten common solid cancers were selected: Prostate, lung/bronchus, liver/IBD, pancreas, breast, colorectal, oral cavity/pharynx, stomach, kidney/renal pelvis, and uterus. The inclusion criteria were as follows: (1) Adult patients diagnosed from 2007 to 2015 (2) Non-metastatic cancer patients with the American Joint Committee on Cancer (AJCC) stage I-III; (3) Patients who didn't receive cancer surgery; and (4) Patients with completed data on age, sex, marital status, and insurance type. Patients missing racial/ethnic information were excluded. American Indian/Alaska Native patients were also excluded for limited numbers. A flow diagram was shown in **Supplementary Figure 1**. Ultimately, 318,318 patients were included.

Variables

Patient age, sex, race/ethnicity, cancer primary site, AJCC stage, marital status and insurance coverage type were retrieved. Patient survival status and cancer specific survival (CSS) were also retrieved. Four racial/ethnic categories were included: white (non-Hispanic), black (non-Hispanic), Hispanic, and Asian/Pacific Islander (API) (4). Reasons for no cancer-directed surgery were retrieved (5), including: (1) recommended but unperformed surgery, patient refused; (2) recommended but unperformed surgery, unknown reason; (3) patient died before recommended surgery; and (4) not recommended for cancer surgery. Patients with recommended but unperformed surgery due to refusal were compared with patients with recommended but unperformed surgery due to other reason. The primary outcome was patient's refusal.

Statistical Analysis

Frequencies of different reasons for no-cancer-directed surgery were depicted by cancer type and race/ethnicity. Association of race/ethnicity with surgery refusal was measured using multivariable logistic regression model by stepwise adjustment of insurance and marital status. In multivariable model A, racial association with surgery refusal was assessed by adjusting for age, sex, cancer site, and AJCC stage. In multivariable model B, racial association with surgery refusal was assessed by additionally adjusting for insurance status. In multivariable model C, racial association with surgery refusal was assessed by additionally adjusting for insurance and marital status. In subgroup analysis, racial association with surgery refusal was also assessed in every selected cancer type. Adjusted odds ratios (OR) and 95% confidence intervals (CI) were reported. Association of surgery refusal with cancer specific survival (CSS) was measured using multivariable Cox regression. Adjusted hazard ratio (HR) with 95% confidence interval (CI) was reported. $P < 0.05$ was statistically significant. Statistics and graphics were conducted using SPSS 24.0 and Graph-pad Prism 7.0.

RESULTS

Descriptives of the Four Reasons for No Cancer-Direct Surgery

There were 318,318 stage I-III cancer patients who didn't receive surgery (mean age, 68.1 years; 243,646 [76.5%] male; 217,154 [68.2%] white, 50,370 [15.8%] black, 30,134 [9.5%] Hispanic and 20,660 [6.5%] Asian/Pacific Islander [API]; 85,069 [26.7%] stage I, 154,882 [48.7%] stage II and 78,367 [24.6%] stage III; 162,768 [51.13%] prostate, 76,290 [23.97%] lung/bronchus, 21,982 [6.91%] liver/IBD, 15,762 [4.95%] pancreas, 13,095 [4.11%] breast, 8,251 [2.59%]colorectal, 7,498 [2.36%] oral cavity/pharynx, 5,310 [1.67%] stomach, 4,779 [1.50%] kidney/renal pelvis, and 2,583 [0.81%] uterus). Overall, the incidence of recommended but unperformed surgery was 9.4% (29,932/318,318); it was more prevalent in breast (33.6%), colorectal (25.0%), uterus (19.2%), and kidney/renal pelvis (18.4%) cancers. Overall, the incidence of patient's refusal of recommended surgery was 3.5% (11,221/318,318); it was more prevalent in breast (12.6%), colorectal (12.2%), uterus (10.3%), and kidney/renal pelvis (9.1%) cancers (**Figure 1**).

Factors Associated With Patient's Refusal

Among the 29,932 patients with recommended but unperformed surgery, 11,221 (37.49%) patients were due to refusal and 18,711 (62.51%) patients were due to other unspecific reason. The demographic and clinical characteristics of the 29,932 patients were presented in **Table 1**.

As shown in **Table 2**, in patients with recommended but unperformed surgery, black patients were more likely to refuse recommended surgery than white patients (adjusted

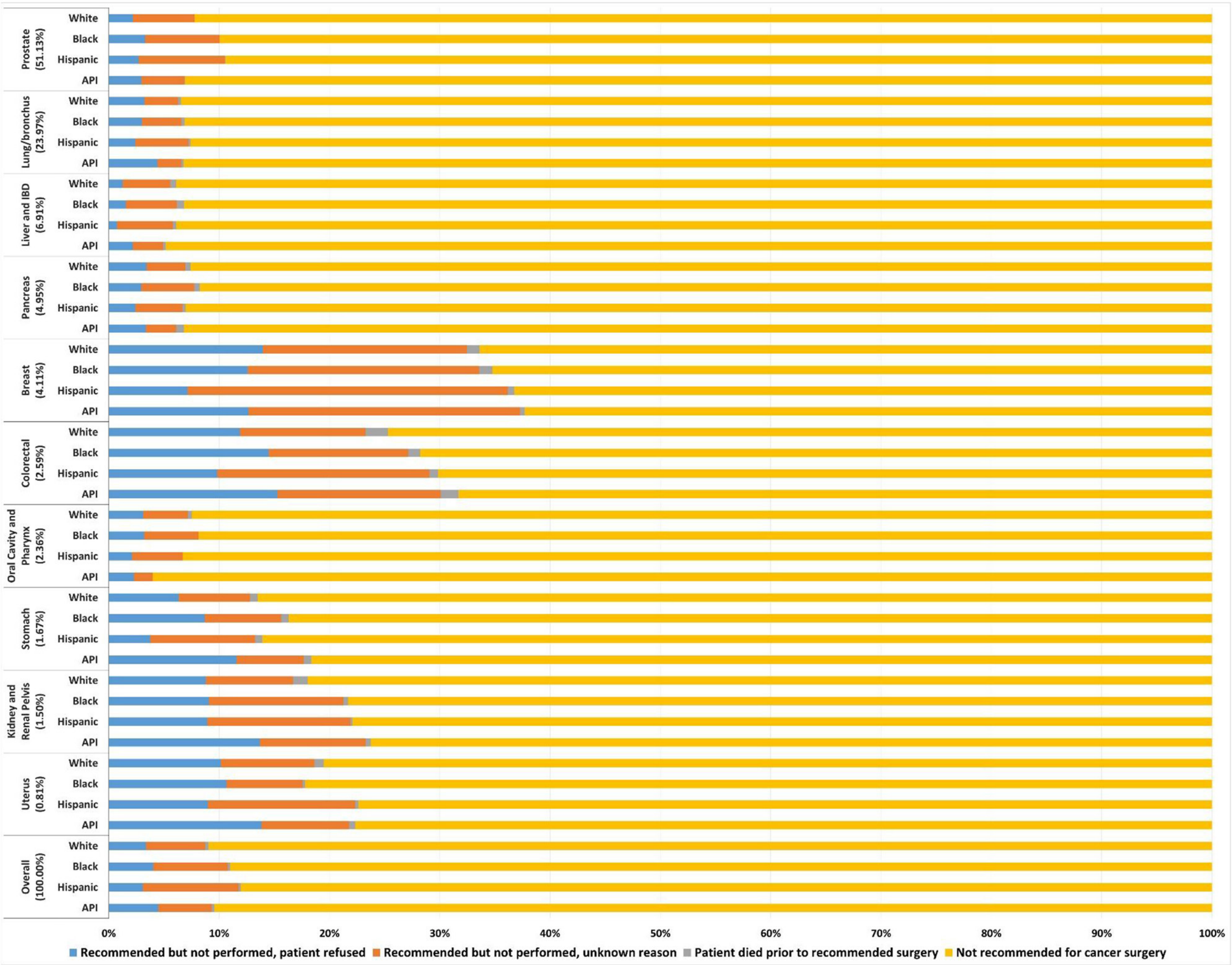

FIGURE 1 | Frequency of the four reasons for no cancer-directed surgery for non-metastatic cancers. Each reason proportion is presented by the four racial and ethnic categories in 10 primary cancers. API, Asian/Pacific Islander; IBD, liver/intrahepatic bile duct.

OR, 1.18; 95% CI, 1.11–1.26). API patients were more likely to refuse recommended surgery than white patients (adjusted OR, 1.56; 95% CI, 1.41–1.72). Those black-white and API-white disparities in surgery refusal narrowed after additionally adjusting for insurance type and marital status. Patients who refused recommended surgery were more likely to have worse CSS than those who unperformed recommended surgery due to other unspecific reason (adjusted HR, 1.15; 95% CI, 1.10–1.21). In addition, surgery refusal probability significantly increased along with age increase. Female patients were more likely to refuse surgery than male patients (adjusted OR, 1.21; 95% CI, 1.12–1.31). Patients with high cancer stage were less likely to refuse surgery than those with early cancer stage (adjusted OR, 0.55; 95% CI, 0.51–0.59). Uninsured/Medicaid patients were more likely to refuse surgery than insured patients (adjusted OR, 1.41; 95% CI, 1.31–1.52). Unmarried patients were more likely to refuse surgery than married patients (adjusted OR, 1.23; 95% CI, 1.17–1.30).

Racial/Ethnic Disparity in Refusal in Every Selected Cancer Type

As shown in **Table 3**, in subgroup analysis, black patients were more likely to refuse surgery than white patients in prostate (adjusted OR, 1.15; 95% CI, 1.05–1.26) and colorectal cancers (adjusted OR, 1.39; 95% CI, 1.06–1.83); API patients were more likely to refuse surgery than white patients in prostate (adjusted OR, 1.97; 95% CI, 1.65–2.35), lung/bronchus (adjusted OR, 1.93; 95% CI, 1.46–2.54), liver/IBD (adjusted OR, 2.77; 95% CI, 1.90–4.04), and stomach (adjusted OR, 1.97; 95% CI, 1.23–3.15) cancers. Those black-white and API-white disparities in surgery refusal narrowed after additionally adjusting for insurance type and marital status in those specific cancer types.

DISCUSSION

Nowadays, racial and ethnic inequality in healthcare has garnered widespread attention in the United States. Sometimes it's even

TABLE 1 | Demographic and clinical characteristics of patients with recommended but unperformed cancer surgery.

	Overall (*n* = 29,932)	Prostate (*n* = 13,647)	Lung/bronchus (*n* = 4,872)	Liver/IBD (*n* = 1,234)	Pancreas (*n* = 1,092)	Breast (*n* = 4,403)	Colorectal (*n* = 2,066)	Oral cavity and pharynx (*n* = 511)	Stomach (*n* = 734)	Kidney and renal pelvis (*n* = 877)	Uterus (*n* = 496)
Age (years)											
<60	7,660 (25.6)	3,007 (22.0)	689 (14.1)	481 (39.0)	195 (17.9)	2,053 (46.6)	515 (24.9)	188 (36.8)	144 (19.6)	194 (22.1)	194 (39.1)
60-69	9,644 (32.2)	5,909 (43.3)	1,159 (23.8)	436 (35.3)	237 (21.7)	848 (19.3)	463 (22.4)	155 (30.3)	152 (20.7)	169 (19.3)	116 (23.4)
70-79	7,488 (25.0)	3,860 (28.3)	1,600 (32.8)	186 (15.1)	326 (29.9)	564 (12.8)	385 (18.6)	89 (17.4)	193 (26.3)	218 (24.9)	67 (13.5)
≥80	5,140 (17.2)	871 (6.4)	1,424 (29.2)	131 (10.6)	334 (30.6)	938 (21.3)	703 (34.0)	79 (15.5)	245 (33.4)	296 (33.8)	119 (24.0)
Sex											
Male	20,234 (67.6)	13,647 (100.0)	2,531 (51.9)	978 (79.3)	511 (46.8)	28 (0.6)	1,155 (55.9)	387 (75.7)	467 (63.6)	530 (60.4)	0
Female	9,698 (32.4)	0	2,341 (48.1)	256 (20.7)	581 (53.2)	4,375 (99.4)	911 (44.1)	124 (24.3)	267 (36.4)	347 (39.6)	496 (100.0)
Race/ethnicity											
White	19,019 (63.5)	8,618 (63.1)	3,674 (75.4)	599 (48.5)	750 (68.7)	2,506 (56.9)	1274 (61.7)	376 (73.6)	392 (53.4)	541 (61.7)	289 (58.3)
Black	5,435 (18.2)	2,975 (21.8)	634 (13.0)	188 (15.2)	153 (14.0)	777 (17.6)	298 (14.4)	61 (11.9)	115 (15.7)	150 (17.1)	84 (16.9)
Hispanic	3,550 (11.9)	1,501 (11.0)	291 (6.0)	280 (22.7)	111 (10.2)	690 (15.7)	305 (14.8)	35 (6.8)	120 (16.3)	135 (15.4)	82 (16.5)
API	1,928 (6.4)	553 (4.1)	273 (5.6)	167 (13.5)	78 (7.1)	430 (9.8)	189 (9.1)	39 (7.6)	107 (14.6)	51 (5.8)	41 (8.3)
AJCC stage											
I	9,364 (31.3)	2,944 (21.6)	1,900 (39.0)	673 (54.5)	429 (39.3)	1,008 (22.9)	804 (38.9)	101 (19.8)	407 (55.4)	702 (80.0)	396 (79.8)
II	15,379 (51.4)	10,476 (76.8)	657 (13.5)	305 (24.7)	495 (45.3)	2,326 (52.8)	645 (31.2)	150 (29.4)	180 (24.5)	104 (11.9)	41 (8.3)
III	5,189 (17.3)	227 (1.7)	2,315 (47.5)	256 (20.7)	168 (15.4)	1,069 (24.3)	617 (29.9)	260 (50.9)	147 (20.0)	71 (8.1)	59 (11.9)
Insurance status											
Insured	25,599 (85.5)	12,697 (93.0)	4,071 (83.6)	933 (75.6)	928 (85.0)	3,304 (75.0)	1,627 (78.8)	412 (80.6)	579 (78.9)	686 (78.2)	362 (73.0)
Uninsured/Medicaid	4,333 (14.5)	950 (7.0)	801 (16.4)	301 (24.4)	164 (15.0)	1,099 (25.0)	439 (21.2)	99 (19.4)	155 (21.1)	191 (21.8)	134 (27.0)
Marital status											
Married	15,871 (53.0)	8,882 (65.1)	2,041 (41.9)	543 (44.0)	538 (49.3)	1,849 (42.0)	932 (45.1)	232 (45.4)	361 (49.2)	335 (38.2)	158 (31.9)
Unmarried	14,061 (47.0)	4,765 (34.9)	2,831 (58.1)	691 (56.0)	554 (50.7)	2,554 (58.0)	1,134 (54.9)	279 (54.6)	373 (50.8)	542 (61.8)	338 (68.1)

API, Asian/Pacific Islander; IBD, liver/intrahepatic bile duct; AJCC, American Joint Committee on Cancer.
Data are presented by number (%).

TABLE 2 | Factors associated with patient's refusal of recommended cancer surgery (the outcome is patient's refusal).

Characteristics	**Recommended but not performed cancer surgery**		**Crude model**		**Adjusted model**					
	Other reason (%)	**Patient refused (%)**			**Multivariable model A**		**Multivariable model B (multivariable model A + insurance status)**		**Multivariable model C (multivariable model A + insurance + marital status)**	
	***n* = 18,711**	***n* = 1,1221**	**OR (95% CI)**	***P***	**OR (95% CI)**	***P***	**OR (95% CI)**	***P***	**OR (95% CI)**	***P***
Age (years)										
<60	5,447 (71.1)	2,213 (28.9)	1.00		1.00		1.00		1.00	
60–69	6,587 (68.3)	3,057 (31.7)	1.14 (1.07–1.22)	<0.001	1.21 (1.13–1.29)	<0.001	1.24 (1.16–1.33)	<0.001	1.23 (1.15–1.32)	<0.001
70–79	4,666 (62.3)	2,822 (37.7)	1.49 (1.39–1.59)	<0.001	1.45 (1.35–1.56)	<0.001	1.52 (1.41–1.63)	<0.001	1.51 (1.41–1.63)	<0.001
≥80	2,011 (39.1)	3,129 (60.9)	3.83 (3.55–4.13)	<0.001	3.04 (2.81–3.29)	<0.001	3.22 (2.97–3.49)	<0.001	3.13 (2.88–3.39)	<0.001
Sex										
Male	13,503 (66.7)	6,731 (33.3)	1.00		1.00		1.00		1.00	
Female	5,208 (53.7)	4,490 (46.3)	1.73 (1.65–1.82)	<0.001	1.27 (1.17–1.38)	<0.001	1.26 (1.16–1.36)	<0.001	1.21 (1.12–1.31)	<0.001
Race/ethnicity										
White	11,680 (61.4)	7,339 (38.6)	1.00		1.00		1.00		1.00	
Black	3,409 (62.7)	2,026 (37.3)	0.95 (0.89–1.01)	0.080	1.18 (1.11–1.26)	<0.001	1.14 (1.07–1.22)	<0.001	1.10 (1.03–1.18)	0.005
Hispanic	2,622 (73.9)	928 (26.1)	0.56 (0.52–0.61)	<0.001	0.65 (0.59–0.70)	<0.001	0.60 (0.55–0.66)	<0.001	0.60 (0.55–0.66)	<0.001
API	1,000 (51.9)	928 (48.1)	1.48 (1.34–1.62)	<0.001	1.56 (1.41–1.72)	<0.001	1.49 (1.35–1.64)	<0.001	1.54 (1.39–1.70)	<0.001
Cancer site										
Prostate	9,628 (70.6)	4,019 (29.4)	1.00		1.00		1.00		1.00	
Lung/bronchus	2,417 (49.6)	2,455 (50.4)	2.43 (2.28–2.60)	<0.001	2.00 (1.82–2.19)	<0.001	1.91 (1.74–2.09)	<0.001	1.86 (1.70–2.04)	<0.001
Liver/IBD	943 (76.4)	291 (23.6)	0.74 (0.65–0.85)	<0.001	0.70 (0.61–0.81)	<0.001	0.66 (0.57–0.77)	<0.001	0.64 (0.55–0.74)	<0.001
Pancreas	579 (53.0)	513 (47.0)	2.12 (1.87–2.40)	<0.001	1.51 (1.32–1.74)	<0.001	1.46 (1.27–1.68)	<0.001	1.45 (1.26–1.67)	<0.001
Breast	2,753 (62.5)	1,650 (37.5)	1.44 (1.34–1.54)	<0.001	1.15 (1.02–1.28)	<0.001	1.09 (0.97–1.22)	0.134	1.08 (0.97–1.21)	0.161
Colorectal	1,057 (51.2)	1,009 (48.8)	2.29 (2.08–2.51)	<0.001	1.80 (1.61–2.00)	<0.001	1.70 (1.53–1.90)	<0.001	1.68 (1.50–1.87)	<0.001
Oral cavity and pharynx	290 (56.8)	221 (43.2)	1.83 (1.53–2.18)	<0.001	2.00 (1.66–2.42)	<0.001	1.91 (1.58–2.31)	<0.001	1.86 (1.53–2.25)	<0.001
Stomach	372 (50.7)	362 (49.3)	2.33 (2.01–2.71)	<0.001	1.68 (1.42–1.97)	<0.001	1.59 (1.35–1.88)	<0.001	1.57 (1.34–1.85)	<0.001
Kidney and renal pelvis	443 (50.5)	434 (49.5)	2.35 (2.05–2.69)	<0.001	1.57 (1.35–1.83)	<0.001	1.48 (1.27–1.73)	<0.001	1.44 (1.24–1.68)	<0.001
Uterus	229 (46.2)	267 (53.8)	2.79 (2.33–3.35)	<0.001	1.92 (1.56–2.36)	<0.001	1.81 (1.47–2.22)	<0.001	1.77 (1.44–2.18)	<0.001
AJCC stage										
I	5,124 (54.7)	4,240 (45.3)	1.00		1.00		1.00		1.00	
II	10,265 (66.7)	5,114 (33.3)	0.60 (0.57–0.64)	<0.001	0.81 (0.76–0.86)	<0.001	0.81 (0.76–0.86)	<0.001	0.81 (0.76–0.86)	<0.001
III	3,322 (64.0)	1,867 (36.0)	0.68 (0.63–0.73)	<0.001	0.55 (0.51–0.60)	<0.001	0.55 (0.51–0.59)	<0.001	0.55 (0.51–0.59)	<0.001
Insurance status										
Insured	16269 (63.6)	9330 (36.4)	1.00		–	–	1.00		1.00	
Uninsured/medicaid	2442 (56.4)	1891 (43.6)	1.35 (1.27–1.44)	<0.001	–	–	1.47 (1.37–1.58)	<0.001	1.41 (1.31–1.52)	<0.001
Marital status										
Married	1,0665 (67.2)	5,206 (32.8)	1.00		–	–	–	–	1.00	
Unmarried	8,046 (57.2)	6,015 (42.8)	1.53 (1.46–1.61)	<0.001	–	–	–	–	1.23 (1.17–1.30)	<0.001

API, Asian/Pacific Islander; IBD, liver/intrahepatic bile duct; AJCC, American Joint Committee on Cancer.
Multivariable model A adjusted for age, sex, cancer site, and AJCC stage.
Multivariable model B additionally adjusted for insurance status.
Multivariable model C additionally adjusted for insurance and marital status.

described as a serious and shameful public health crisis. Different from other disparities in healthcare, racial and ethnic disparity is rooted in history and modern times, involving multiple elements, such as medical systems, infrastructures, administrative processes, healthcare providers, and individualized patients (6). Occasionally, the term "structural racism" is used to describe racial and ethnic disparities in cancer surgical treatment (7, 8). It remains a key question whether racial and ethnic disparities in cancer surgery utilization are due to structural racism or just socioeconomic status.

Unlike previous studies (1–3), our study compared patients with recommended but unperformed surgery due to refusal to those with recommended but unperformed surgery due to other reason. We found that racial and ethnic disparity in

TABLE 3 | Adjusted OR (95% CI) for patient's refusal of surgery in every selected cancer type.

	Prostate (*n* = 13,647)	**Lung/bronchus (*n* = 4,872)**	**Liver/IBD (*n* = 1,234)**	**Pancreas (*n* = 1,092)**	**Breast (*n* = 4,403)**	**Colorectal (*n* = 2,066)**	**Oral cavity and pharynx (*n* = 511)**	**Stomach (*n* = 734)**	**Kidney and renal pelvis (*n* = 877)**	**Uterus (*n* = 496)**
Race/ethnicity	Multivariable model 1 (adjusted for age, sex, and AJCC stage)									
White	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Black	**1.15** **(1.05–1.26)**	0.96 (0.80–1.15)	1.39 (0.94–2.07)	0.84 (0.56–1.25)	1.16 (0.97–1.40)	**1.39** **(1.06–1.83)**	1.01 (0.56–1.80)	1.45 (0.93–2.27)	0.84 (0.57–1.24)	1.46 (0.87–2.43)
Hispanic	**0.86** **(0.76–0.97)**	**0.46** **(0.35–0.60)**	**0.49** **(0.33–0.75)**	0.64 (0.41–1.02)	**0.49** **(0.39–0.61)**	**0.67** **(0.51–0.89)**	0.57 (0.26–1.24)	**0.45** **(0.28–0.72)**	0.75 (0.50–1.13)	0.68 (0.40–1.16)
API	**1.97** **(1.65–2.35)**	**1.93** **(1.46–2.54)**	**2.77** **(1.90–4.04)**	1.15 (0.69–1.91)	1.17 (0.93–1.47)	1.24 (0.89–1.72)	1.88 (0.93–3.79)	**1.97** **(1.23–3.15)**	1.33 (0.72–2.46)	1.62 (0.80–3.26)
	Multivariable model 2 (additionally adjusted for insurance type and marital status based on multivariable model 1)									
White	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Black	**1.14** **(1.04–1.25)**	0.84 (0.70–1.02)	1.18 (0.78–1.77)	0.74 (0.50–1.11)	1.03 (0.86–1.25)	1.32 (1.00–1.74)	0.94 (0.52–1.70)	1.24 (0.78–1.98)	0.81 (0.54–1.19)	1.42 (0.84–2.39)
Hispanic	**0.82** **(0.73–0.94)**	**0.40** **(0.30–0.52)**	**0.45** **(0.30–0.69)**	**0.57** **(0.36–0.92)**	**0.45** **(0.35–0.56)**	0.66 (0.49–0.87)	0.47 (0.21–1.05)	**0.39** **(0.24–0.64)**	0.68 (0.45–1.04)	0.69 (0.40–1.18)
API	**1.92** **(1.61–2.29)**	**1.87** **(1.41–2.48)**	**2.52** **(1.70–3.74)**	1.05 (0.62–1.77)	1.16 (0.92–1.47)	1.26 (0.90–1.75)	2.01 (0.97–4.15)	**1.85** **(1.13–3.00)**	1.23 (0.66–2.28)	1.63 (0.81–3.30)

API, Asian/Pacific Islander; IBD, liver/intrahepatic bile duct; AJCC, American Joint Committee on Cancer.

Data are presented by adjusted OR (95% CI).

Bold values indicate statistical significance.

surgery refusal, particularly between black and white patients, was largely mediated by socioeconomic status, like insurance type and marital status. It is well established that cancer patients who refuse surgery have worse survival than those undergoing surgery (9–11). Our study revealed that even when surgery is recommended but unperformed, the patient with refusal would suffer a worse CSS. This might be because patients refusing recommended surgery might also be negative to other alternative recommended treatments.

For prostate cancer patients, Islam et al. (12) found that ∼3.9% patients refuse the suggested surgery; black, single, Medicaid/Medicare-covered, or early-stage prostate cancer patients are more likely to refuse the surgery. Those results are consistent with our present findings in prostate cancer. In our study, about 2.47% (4,019/162,768) prostate cancer patients refused recommended surgery. In addition, we identified that API patient was also a population with high odds of refusing recommended surgery. A latest study by Dee et al. (13) found that black and Asian patients are more likely to refuse locoregional treatment (radiotherapy and surgery) than white patients in prostate cancer; locoregional treatment refusal rate for prostate adenocarcinoma has increased over time. For Lung/bronchus cancer patients, Mehta et al. (14) found that blacks and "other" races are more likely to refuse recommended surgery than whites; refusal of surgery is influenced by county variations. In addition, refusal of surgery is influenced by low educational status in lung cancer (15). In recent years, stereotactic body radiotherapy (SBRT) is considered as an alternative proposal for early stage non-small cell lung cancer patients who refuse surgery (16). Nonetheless, a systematic review suggested that SBRT has an inferior effect on survival and long-term distant control compared with surgery for early stage non-small cell lung cancer (17). To date, only a few study explored refusal of surgery in liver/IBD cancer (18). Our study indicated that API-white disparity in surgery refusal significantly existed in liver/IBD cancer. Tohme et al. (2) and Coffman et al. (19) explored the factors associated with surgery refusal in early-stage and non-metastatic pancreatic cancer, respectively, based on the National Cancer Database (NCDB); both of them identified that treatment at a non-academic/research medical center leads to higher odds of refusing pancreatic cancer-directed surgery. Those results suggested that hospital level is a key factor influencing patient's trust and decision in taking surgery. Much attention has been paid to surgery refusal in colorectal cancer patients (1, 9–11, 20). Surgery refusal rate for non-metastatic colorectal cancer is increasing over time, which increases colorectal cancer-specific mortality (adjusted HR: 5.10, 95% CI: 4.62-5.62) (20). Our study indicated that there was a significant black-white disparity in surgery refusal in non-metastatic colorectal cancer, which was largely mediated by patient's socioeconomic status. Surgery refusal has been also well investigated in breast cancer patients (21–23). Compared to refusals of chemotherapy and endocrine therapy, refusal of surgery causes the highest mortality risk for patients with invasive breast cancer (23). To date, other cancer types such as stomach, oral cavity/pharynx, kidney/renal pelvis and uterus cancers, are relatively less reported in surgery refusal, which warrants reinforced studied in the future.

Some limitations should be noticed in this SEER-based population study. First, this study is retrospective, it is intriguing to know whether and which complementary therapy that the patients would choose after refusing the recommended surgery. Secondly, in this pan-cancer analysis, prostate, lung and breast cancer patients account for the majority. The main findings apply to overall cancer population and must be prudently extended to every selected cancer type for potential selection bias. Thirdly, patient's decision in taking recommended surgery involves various influencing factors. It is a patient-doctor mutual participation result. Besides patient's socioeconomic conditions, more factors such as surgeon's conversation skills are warranted to be noticed in the future.

CONCLUSION

As early as 2009, the American Society of Clinical Oncology (ASCO) has recognized racial and ethnic disparity as a major obstacle to achieving cancer health equity and listed it in cancer care as a critical issue to conquer. ASCO has issued a series of policies and recommendations to promote cancer health equity, such as ensuring equitable access to high-quality care and research, removing structural barriers, and increasing awareness and action (6). Patient's socioeconomic conditions reflected by insurance type and marital status may play a key role in racial/ethnic disparities in surgery refusal. According to our findings, in the future, oncological surgeons should fully consider the hindrances behind patient's refusal of recommended surgery, thus promoting patient-doctor shared decision-making and guiding patients to the most appropriate therapy.

DATA AVAILABILITY STATEMENT

Publicly available datasets were analyzed in this study. This data can be found at: https://seer.cancer.gov/.

ETHICS STATEMENT

Ethical review and approval was not required for the study on human participants in accordance with the local legislation and institutional requirements. Written informed consent for participation was not required for this study in accordance with the national legislation and the institutional requirements.

AUTHOR CONTRIBUTIONS

WY, HY, and YS contributed to the study conception and revised the manuscript. XH contributed to the data analysis and interpretation and draft the manuscript. All authors contributed to the article and approved the submitted version.

SUPPLEMENTARY MATERIAL

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frontiers in Public Health

BRIEF RESEARCH REPORT
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Revisiting the Effects of Organized Mammography Programs on Inequalities in Breast Screening Uptake: A Multilevel Analysis of Nationwide Data From 1997 to 2017

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This study revisits the effects of mammography screening programs on inequalities in breast screening uptake in Switzerland. The progressive introduction of regional mammography programs by 12 out of the 26 Swiss cantons (regions) since 1999 offers an opportunity to perform an ecological quasi-experimental study. We examine absolute income and marital status inequalities in mammography uptake, and whether the cantons' implementation of mammography programs moderate these inequalities, as previous research has devoted little attention to this. We use five waves of the Swiss Health Interview Survey covering the 1997–2017 period and comprising data on 14,267 women aged 50–70. Both up-to-date and ever-screening outcomes are analyzed with multilevel models which assess the mammography programs' within-canton effect. Findings show that higher income women and married women (compared to unmarried women) had significantly higher mammography uptake probabilities. Mammography programs did not moderate absolute income differences in up-to-date screening; however, they were associated with smaller absolute income differences in ever-screening uptake. Mammography programs related to higher screening uptake for married women, more than for unmarried women. In conclusion, we showed absolute income inequalities in mammography uptake which were not revealed by previous studies using relative inequality measures. Mammography programs may have contributed to reducing income inequalities in ever-screening, yet this was not observed for up-to-date screening. This study has implication for preventive health interventions—e.g., cancer screening promotion should pay attention to women's marital status since screening programs may widen the screening gap between married and unmarried women.

Keywords: socioeconomic inequalities, Switzerland, breast cancer screening, marital status, multilevel analysis, organized population-based screening programs

INTRODUCTION

Socioeconomic inequalities in breast cancer screening uptake have been shown to be higher in countries which do not have a nationwide population-based screening program (1, 2). However, country-specific studies have brought mixed evidence on screening programs' potential to reduce inequalities in mammography uptake (3–8). This is the case of Switzerland where regional mammography programs were not found to importantly moderate socioeconomic inequalities in screening uptake (9).

In Switzerland, 12 out of the 26 cantons (regions) have implemented organized mammography programs at different timepoints from 1999 to present. There is no nationwide mammography program since the cantons autonomously manage their own healthcare system and prevention. In cantons where a program is implemented, eligible women are systematically invited for a mammography every 2 years; while in cantons without a program, screening uptake is "opportunistic", i.e., it depends on women's individual initiative to undergo mammography and on doctors' recommendation to patients. The Swiss context provides an opportunity to study screening uptake inequalities across organized and opportunistic screening contexts (cantons), in an "ecological quasi-experimental" setting (9). That is, in opportunistic screening contexts, individual factors carry more weight and differences in socioeconomic status may lead to larger screening inequalities, while screening programs may reduce the role of individual economic or social support resources in screening uptake (1).

Inequalities in cancer screening uptake persist since people who possess more resources, such as knowledge, money and social networks, are able to deploy these to adopt available protective strategies and enhance their access to healthcare, while more disadvantaged individuals with less resources face more barriers in accessing healthcare (10). Income level was shown to be an essential determinant of (preventive) health services use across European countries (11, 12). Lower income households are deterred from healthcare uptake by healthcare direct costs, by indirect costs, such as transportation and medication co-payment, as well as opportunity costs from time off work. As a socioeconomic status indicator, income level not only captures individuals' ability to access healthcare, it also accounts for individuals' broader material circumstances which, in turn, impact their psychosocial resources and ability to adopt health-enhancing lifestyles and choices.

It is particularly relevant to assess income-based inequalities in mammography screening uptake in Switzerland, and whether mammography programs moderate these inequalities, since the Swiss health insurance system involves considerable patient out-of-pocket payments which were shown to cause inequalities in healthcare access, as well as healthcare forgoing among lower income populations (13). This context may have contributed to shaping income-inequalities which were documented in cervical and colorectal cancer screening uptake (14–16). Concerning mammography, it is important to note that mammograms conducted within a screening program framework are reimbursed by the national health insurance system, while in cantons without a mammography program reimbursement is subject to doctor's prescription and insurance deductibles involving out-of-pocket expenses. Previous studies focused on relative measurements of screening inequalities in Switzerland, e.g., by comparing income quintiles (9), similarly to the health inequalities literature which has predominantly focused on relative health inequalities (17). However, research suggests that socioeconomic inequalities should also be assessed with absolute measurements, particularly since relative measures do not capture information on absolute variation of prevalence within groups, and can be sensitive to an outcome's overall prevalence (3, 4, 18).

Additionally, we examine how mammography programs moderate the association between marital status and screening uptake. Supportive ties and close relationships are essential determinants of health behaviors and preventive health services uptake (19). Social relations can provide tangible support to access healthcare, as well as encouragement to undergo screening. In particular, a (marital) relationship can have direct positive effects on health status and healthcare uptake. Such health benefit was widely documented and related, in part, to the health-related social control provided by a (marital) partner (20). Thus, the presence of a spouse or a partner is a key social support resource for preventive health behaviors. Marital status was commonly used as a proxy for the support provided by an intimate relationship and being married was found to be associated with higher mammography uptake (21, 22). Nevertheless, little attention was devoted to the effect of marital status on screening uptake in Switzerland, and to how mammography programs may modify this effect.

This study covers a 20-year period from 1997 to 2017. It is the first to analyze the most recent 2017 wave of the Swiss Health Interview Survey in relation to mammography screening, and the most recent mammography programs implemented by three cantons in the 2012–2017 period. We use multilevel modeling to account for the mammography programs' progressive implementation by the Swiss cantons over time. These models allow to assess a context-level variable, such as cantons' mammography program, and how it moderates individual-level variables with cross-level interactions. However, previous studies did not use multilevel models to analyze the mammography programs' moderation effect on screening inequalities across the Swiss cantons.

DATA AND METHODS

We used data from the Swiss Health Interview Survey (SHIS), a cross-sectional nationally representative survey implemented every 5 years and based on a stratified random selection of residents older than 14 years of age. We pooled the 5 most recent survey waves (from 1997 to 2017) and restricted the sample to 50–70 year-old women ($N = 17{,}038$). The final sample contained 14,267 women after excluding missing data.

We computed two binary outcomes: "ever-screening" (1 = ever did a mammography, 0 = never did a mammography) and "up-to-date screening" (1 = did a mammography in the past 2 years, 0 = more than 2 years ago). We measured the implementation of mammography screening programs across cantons and time with a variable coded as: (1) "program," if a canton had implemented a mammography program before a SHIS survey year, and (0) "no program," if no program was implemented (**Supplementary Table S1**). Individual-level predictors are monthly household income and marital status,[1] and control variables are education level, employment status, urban/rural area of residence, linguistic region of residence, age, self-rated health, and general practitioner or gynecologist visits in the last 12 months. We also included dummy variables for survey years and cantons to control for country-wide temporal trends and between-canton unobserved heterogeneity (23). In order to assess absolute income inequalities in screening uptake, we used a continuous measure of monthly household income, as provided by the SHIS. The household income variable is weighted according to the OECD-modified scale and logged. The OECD-modified scale assigns a weight to each household member in order to take into account differences in household size and composition (24): 1.0 to the first adult of the household, 0.5 to each additional household member aged 14 and over, and 0.3 to children under 14 years old. Total household income is divide by the sum of the weights. Descriptive statistics are reported in **Supplementary Table S2**.

We performed multilevel logistic models with individuals (level-1) nested in canton-year clusters (level-2), i.e., each level-2 cluster combines a specific canton and survey year. The 5 pooled survey waves provided 130 canton-year clusters (26 cantons × 5 survey waves) (**Supplementary Table S3**). By including a random intercept for canton-year, the multilevel design accounts for similarities between women who belong to the same canton-year cluster and the fact that cantons implemented mammography programs at different timepoints between 1997 and 2017. It also takes into account cluster-level heteroscedasticity and error correlation in data affected by hierarchies, which is not accounted for in standard regression models (25).

First, we used a likelihood ratio test to assess whether models with a random intercept for canton-year performed better than models without random intercepts. Second, we analyzed the effect of household income, marital status and mammography programs on screening uptake (model 1), controlling for all individual-level covariates, and for time and canton fixed effects (dummy variables) to account for country-wide temporal trends and within-canton clustering. Third, we performed cross-level interactions between mammography program and individual-level variables in separate models (models 2a and 2b) to examine whether these programs moderated individual-level differences in screening uptake. The data is analyzed with Stata 16.

RESULTS

The models with a random intercept for canton-year performed better than equivalent single-level models [up-to-date screening: $\chi^2_{(1)} = 1{,}447.52$, $p < 0.001$; ever-screening: $\chi^2_{(1)} = 1931.53$, $p < 0.001$], revealing significant differences in up-to-date and ever-screening uptake between canton-year clusters. As expected, women with higher household income and married women (compared to unmarried women) had significantly higher up-to-date screening and ever-screening probabilities (**Table 1**; **Supplementary Table S4**). Cantons with a mammography program had higher up-to-date screening uptake than cantons without programs, but did not have higher ever-screening uptake.

As shown in **Table 2**, mammography programs were associated with smaller income differences in ever-screening, as pointed out by the cross-level interaction term significant at a 95% confidence level (**Supplementary Table S5**). This effect is graphed in **Figure 1** which shows that women with lower household income had higher ever-screening probabilities in cantons with a mammography program, than in cantons without a program. It was significant for women with monthly household income from the first to the fifth decile, i.e., for women with monthly household income lower than 4,000 CHF,[2] and the lower the income the stronger the effect was, as analyses presented in **Supplementary Material** revealed (**Supplementary Table S6**). For up-to-date screening, no interaction effect was observed. Finally, a cross-level interaction also revealed that, in cantons with a mammography program, married women had higher screening uptake than their unmarried counterparts, compared to cantons without a program (**Table 2**). **Figure 2** depicts this effect for both up-to-date and ever-screening uptake.

DISCUSSION

We found evidence of absolute income inequalities in mammography uptake in Switzerland over the 1997–2017 period. The fact that mammograms are reimbursed by the health insurance system in cantons with screening programs, while more constraints (e.g., doctor's prescription) and out-of-pocket expenses apply in cantons without programs, might be driving these income-based inequalities. These absolute inequalities were not evidenced by Cullati et al. (9) who examined relative income inequalities. While relative measures focus on the magnitude of inequalities between groups, our results showed that absolute screening inequalities persisted across the entire range of income levels. Thus, it is recommended to consider both absolute and relative measures to accurately monitor screening inequalities and inform policymakers (3, 4, 17).

The cantons' implementation of mammography programs was associated with higher up-to-date screening uptake; however, we found no evidence that these programs moderated income inequalities in up-to-date screening. This confirms the findings

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[1] We used the marital status since information on respondents' partnership and co-habitation status was not available across the 5 survey waves of the SHIS, but only in the 3 most recent waves (2007–2017 period). Analysis of those 3 waves using the partnership status variable (whether or not a respondent is "living with a partner") instead of marital status produced substantively similar results.

[2] Monthly household income was weighted using the OECD-modified scale, as detailed in the methods section. 1 CHF was approximately equivalent to 0.79 USD in average over the period considered by this study (1997–2017).

TABLE 1 | Association of up-to-date and ever-screening mammography uptake with individual-level and mammography program variables, results of logistic multilevel analysis, odds ratios and confidence intervals ($n_{\text{individual}} = 14{,}267$; $n_{\text{canton-year}} = 130$).

	Up-to-date screening OR (95% CI)	Ever-screening OR (95% CI)
Model 1[a]		
Individual level		
Household income (logged)	1.222*** (1.130–1.321)	1.225*** (1.128–1.331)
Marital status (ref: single, divorced, widow) married	1.364*** (1.261–1.475)	1.428*** (1.305–1.562)
Canton-year level		
Mammography program (ref: no program) program	1.737*** (1.463–2.062)	1.170 (0.961–1.424)
Level-2 variance		
Canton-year[b]	0.015	0.015

*Significance levels: *p ≤ 0.05, **p ≤ 0.01, ***p ≤ 0.001.*

[a] *Model adjusted for level-1 (individual) covariates (including education level, employment status, age, linguistic region, area of residence, self-rated health, GP or gynecologist visits in the past 12 months), and time (survey year dummies) and canton-level heterogeneity (canton dummies) at the model's level-2.*

[b] *The inclusion of a level-2 (canton-year) variance in the models was assessed with likelihood ratio tests. The tests showed significant differences between canton-year clusters in up-to-date [$\chi^2_{(1)} = 7.44$, $p = 0.006$] and ever-screening [$\chi^2_{(1)} = 3.92$, $p = 0.05$] uptake.*

Between 1997 and 2017, 12 out of 26 cantons implemented mammography programs.

Source: SHIS 1997–2017.

TABLE 2 | Cross-level interactions between mammography program and individual-level variables in their effect on mammography uptake, results of logistic multilevel analysis, odds ratios and confidence intervals ($n_{\text{individual}} = 14{,}267$; $n_{\text{canton-year}} = 130$).

	Model 2a		Model 2b	
	Up-to-date screening OR (95% CI)	Ever-screening OR (95% CI)	Up-to-date screening OR (95% CI)	Ever-screening OR (95% CI)
Individual level				
Household income	1.233*** (1.116–1.363)	1.302*** (1.175–1.443)	1.223*** (1.131–1.322)	1.228*** (1.130–1.334)
Marital status (ref: single, divorced, widow)	1.363*** (1.261–1.475)	1.426*** (1.303–1.560)	1.283*** (1.169–1.409)	1.357*** (1.229–1.498)
Canton-year level				
Mammography program (ref: no program) program	2.092 (0.626–6.994)	4.716* (1.189–18.702)	1.551*** (1.275–1.887)	1.012 (0.806–1.272)
Cross-level interaction				
Household income (logged) × program	0.978 (0.846–1.130)	0.844* (0.715–0.996)		
Married × program			1.214* (1.033–1.426)	1.299* (1.047–1.612)
Level-2 variance				
Canton-year[a]	0.015	0.015	0.015	0.015

*Significance levels: *p ≤ 0.05, **p ≤ 0.01, ***p ≤ 0.001.*

[a] *The inclusion of a level-2 (canton-year) variance in the models was assessed with likelihood ratio tests. The tests showed significant differences between canton-year clusters in Model 2a for up-to-date [$\chi^2_{(1)} = 7.37$, $p = 0.007$] and ever-screening [$\chi^2_{(1)} = 3.86$, $p = 0.05$] uptake, and in Model 2b for up-to-date [$\chi^2_{(1)} = 7.09$, $p = 0.008$] and ever-screening [$\chi^2_{(1)} = 3.92$, $p = 0.05$] uptake.*

Models are adjusted for all level-1 (individual) covariates, and time (survey year dummies) and canton-level heterogeneity (canton dummies) at the model's level-2.

Source: SHIS 1997–2017.

of Cullati et al. (9) who did not observe a reduction of up-to-date income-based screening inequalities associated with mammography programs over the 1992–2012 period. In contrast, European cross-national research evidenced that screening programs contributed to reducing inequalities in screening uptake (2). This was explained by the screening programs' systematic invitation of all eligible women which offers equal access to screening and reduces the information gap between individuals with different socioeconomic status and health literacy levels.

Persistence of the observed screening inequalities in Switzerland might be explained, partly, by the fact that not all women undergo mammography through the program in cantons with organized screening, and opportunistic screening uptake may still persist. Furthermore, inequalities in screening knowledge and negative attitudes toward mammography may persist, and particularly affects lower socioeconomic groups' screening uptake (26, 27). While research showed that screening programs successfully increase overall screening participation, and that invitation letters importantly contribute to this increase, they may not necessarily reduce inequalities in screening uptake (28, 29). Program invitation mechanisms and invitation letter features may affect participation. For example, long and detailed letters can discourage lower socioeconomic status individuals to

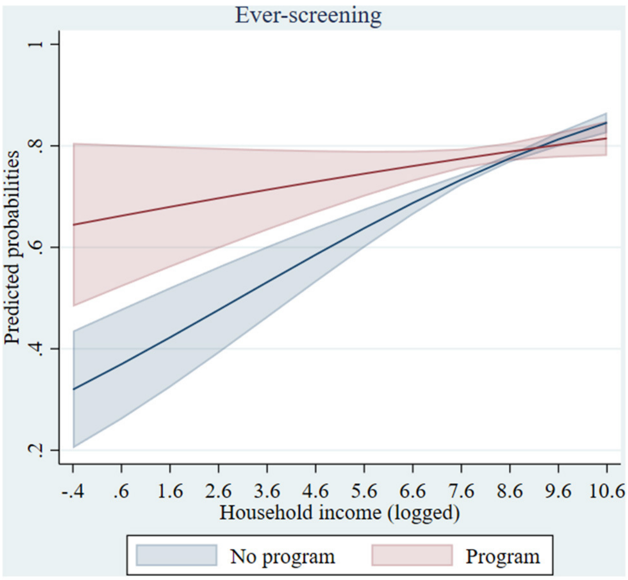

FIGURE 1 | Predicted probabilities of mammography ever-screening by household income in cantons with/without a mammography program (based on model 2a). Confidence intervals were calculated using a multiplier of 1.39 standard errors since two parameters are compared rather than a parameter and a single (fixed) point (Goldstein H, Healy MJR. The graphical presentation of a collection of means. *J R Statist Soc*. (1995) 158:175–7).

participate, and whether a scheduled appointment is included in the letter was also shown to have an impact on screening participation (30). Information on the features and specific content of invitation letters sent by the cantons' programs should be collected (for example, by Swiss Cancer Screening in the monitoring report of the mammography programs) so future research may assess their effects in order to inform interventions. Finally, we should note that the majority of the mammography programs were implemented recently, in the last 10 years of the 20-year period considered in this study. More time might be necessary to be able to observe an inequality-reducing effect, particularly since higher socioeconomic status individuals are usually quicker than more disadvantaged individuals in adopting the offer of new preventive health services (31).

Mammography program implementation was not associated with significantly higher ever-screening uptake. However, it was associated with smaller income inequalities in ever-screening. As depicted in **Figure 1**, ever-screening was higher among lower income women in cantons with organized screening. Previous studies suggested that the reduction of financial barriers and awareness-raising brought by the Swiss mammography programs may have played a role in promoting uptake among lower income women who had never screened (without necessarily increasing overall ever-screening uptake) (5, 32). Our results highlighted that not only "up-to-date screeners" but also "ever- and never-screeners" should be taken into account, as different determinants may shape their screening uptake. Notably, never-screeners were shown to face greater socioeconomic barriers to cervical cancer screening uptake (16) and to be more strongly affected by a lack of screening knowledge in their mammography uptake (33, 34). Cognitive, emotional, structural and communication barriers might differ between never-screeners and those who have already screened but are off-schedule (33). Thus, further studies are needed to investigate the specific reasons for non-attendance in different groups and tailor interventions according to screening status (35). Otherwise, standard invitations and reminder letters may fail to trigger participation among participants with specific profiles.

Married women had a higher mammography uptake than unmarried women and some evidence indicated that this gap increased in cantons with organized programs, compared to cantons without programs. Spouses can encourage each other's health-enhancing behaviors, and a couple's shared psychosocial and economic resources may also facilitate healthcare use (22, 36). Oppositely, those who do not have a partner are more at risk of delaying contacts with healthcare services. Having a marital partner may help mitigate well-known barriers to cancer screening, such as fear or embarrassment, and may provide the practical support facilitating healthcare access and screening program utilization. This finding is important to physicians who should pay more attention to the screening uptake of women living alone or without a (marital) partner.

This study has strengths and limitations. Our statistical models preclude causal inference. However, controlling for relevant confounders of mammography uptake provides support to a causal interpretation of the mammography programs' effect. Moreover, by using a multilevel model which controlled for country-wide temporal trends and canton-level unobserved heterogeneity, we extend previous studies and assessed the mammography programs' within-canton, between-canton-year effect. We used marital status as a proxy for the social support provided by an intimate relationship since information on respondents' partnership and cohabitation status was not available across the 5 waves of the SHIS. The marital status variable does not capture the social support provided by non-married and homosexual relationships and may involve some misclassification bias. Finally, survey data are susceptible to errors in self-reporting, and confounding from unmeasured variables cannot be excluded.

To conclude, this study reported evidence of absolute income inequalities in mammography uptake in Switzerland. Mammography programs may have contributed to reducing these income inequalities in ever-screening uptake; however, programs have not modified inequalities in up-to-date screening, and may have potentially increased inequalities in screening uptake between married and unmarried women. Hence, more specific and targeted public health interventions might be required to complement mammography programs and better reach women with lower income and those who do not live with a (marital) partner, and support their screening uptake. That is, the cost-reducing intervention of screening programs may not suffice to engage specific groups of non-participants in mammography screening and further strategies should be considered (28).

Interventions focusing on behavioral change can be successful. For example, text message reminders can be a cost-effective

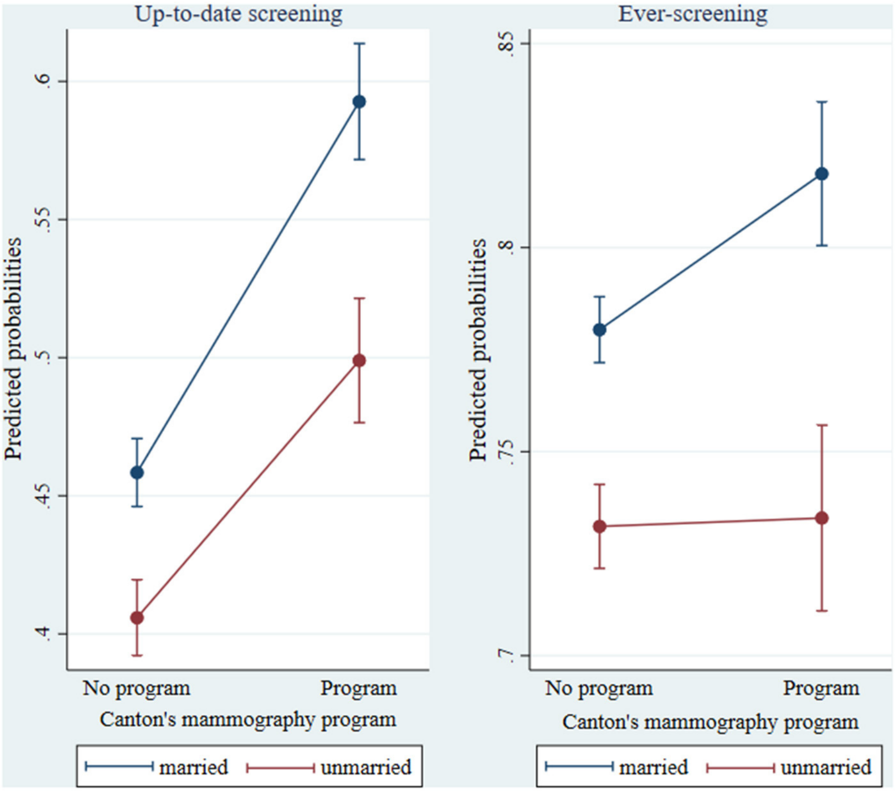

FIGURE 2 | Predicted probabilities of mammography up-to-date and ever-screening by marital status in cantons with/without a mammography program (based on model 2b). Confidence intervals were calculated using a multiplier of 1.39 standard errors since two parameters are compared rather than a parameter and a single (fixed) point (Goldstein H, Healy MJR. The graphical presentation of a collection of means. *J R Statist Soc*. (1995) 158:175–7).

solution which was shown to increase mammography uptake among women who never had a mammography and hard-to-reach populations (37). Providing a phone number in the invitation letter to a call center with patient navigators who schedule appointments and are able to give information and tackle (structural and psychological) barriers to screening was also shown to improve mammography uptake among socioeconomically disadvantaged women (38). Provision of information through invitation letters and their effect on screening uptake may reach a limit when program coverage is high (39). However, combining postal letters with other invitation strategies, such as phone calls or text messages, in a "multiple-component intervention", was shown to be effective to increase uptake among low income women (40). Finally, there is overwhelming evidence that recommendation from primary care physician to patient improves screening uptake (41). Their involvement in screening programs should thus be promoted. Beyond the mere recommendation to undergo screening, patient-provider communication is fundamental. As studies showed, physician enthusiasm and encouragement perceived by patients is a key determinant of screening adherence (41), and a more comprehensive patient-provider communication on broader topics including sexual health can improve breast and cervical screening uptake among unmarried women (42).

Breast cancer is a leading cause of women's amenable mortality in Switzerland, where both geographic and socioeconomic inequalities in breast cancer care and stage at diagnosis were documented (43). Switzerland's healthcare system weakness in tackling health inequalities, implementing health prevention and producing nationwide health data and quality of care indicators was linked to its high decentralization (due to the cantons' autonomy to manage healthcare) (44, 45). Regional mammography programs may thus risk reproducing socioeconomic and geographic inequalities in breast cancer outcomes. For these reasons, we join previous research in stressing the need for more and better nationwide coordination of quality-controlled prevention and cancer screening programs in Switzerland to reduce disparities in early detection (46).

DATA AVAILABILITY STATEMENT

This study used data from the Swiss Health Interview Survey. The data is available for a fee (1600 Swiss Francs, plus 7.7% tax) and users must request permission from the Swiss Federal Statistical Office (sgb@bfs.admin.ch). Data must be destroyed after five years. Requests to access these datasets should be directed to Swiss Federal Statistical Office (sgb@bfs.admin.ch).

ETHICS STATEMENT

The research uses anonymized survey data from the Swiss Health Interview Survey (SHIS). Access to the data was granted by the Swiss Federal Statistical Office upon application and contract signing. Compliance with Swiss National Guidelines and Legal Basis (Swiss statistical law) were stated in the data delivery contract signed with the Swiss Federal Statistical Office.

AUTHOR CONTRIBUTIONS

VJ: conceptualization, methodology, formal analysis, writing—original draft, and writing—review and editing. VD and AB: conceptualization and writing—review and editing. PB, CB-J, and SC: conceptualization, writing—review and editing, supervision, funding acquisition, and project administration. All authors approved the final version of the manuscript.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2022.812776/full#supplementary-material

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