REVIEWS

Evidence of Racial Disparities in the Lung Cancer Screening Process: a Systematic Review and Meta-Analysis

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BACKGROUND: Annual lung cancer screening (LCS) with low-dose chest computed tomography for high-risk individuals reduces lung cancer mortality, with greater reduction observed in Black participants in clinical trials. While racial disparities in lung cancer mortality exist, less is known about disparities in LCS participation. We conducted a systematic review to explore LCS participation in Black compared with White patients in the USA.

METHODS: A systematic review was conducted through a search of published studies in MEDLINE, PubMed, EMBASE, Web of Science, and Cumulative Index to Nursing and Allied-Health Literature Database, from database inception through October 2020. We included studies that examined rates of LCS participation and compared rates by race. Studies were pooled using random-effects meta-analysis.

RESULTS: We screened 18,300 titles/abstracts; 229 studies were selected for full-text review, of which nine studies met inclusion criteria. Studies were categorized into 2 groups: studies that reported the screening rate among an LCS-eligible patient population, and studies that reported the screening rate among a patient population referred for LCS. Median LCS participation rates were 14.4% (range 1.7 to 62.6%) for eligible patient studies and 68.5% (range 62.6 to 88.8%) for referred patient studies. The meta-analyses showed screening rates were lower in the Black compared to White population among the LCS-eligible patient studies ([OR]=0.43, [95% CI: 0.25, 0.74]). However, screening rates were the same between Black and White patients in the referred patient studies (OR=0.94, [95% CI: 0.74, 1.19]).

DISCUSSION: Black LCS-eligible patients are being screened at a lower rate than White patients but have similar rates of participation once referred. Differences in referrals by providers may contribute to the racial disparity in LCS participation. More studies are needed to identify barriers to LCS referral and develop interventions to increase provider awareness of the importance of LCS in Black patients.

Trial Registry

PROSPERO; No.: CRD42020214213; URL: http://www.crd.york.ac.uk/PROSPERO

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INTRODUCTION

The burden of lung cancer mortality in the United States (US) is unevenly distributed, with Black males having the highest rate of age-adjusted lung cancer incidence and increased mortality[1]. The Surveillance, Epidemiology, and End Results (SEER) program registry has shown higher standardized lung cancer case-fatality rates for Black compared to White patients with early-stage lung cancer[2]. This is thought to be due to multiple factors including disproportionate excess risk of lung cancer from tobacco use, tumor biology with tendency for more aggressive disease, and, importantly, inequities in healthcare access leading to substandard care in both screening and treatment of lung cancer[3]. Annual lung cancer screening (LCS) with low-dose chest computed tomography (LDCT) in high-risk patients reduces lung cancer mortality[4], with greater mortality reduction observed in Black participants in the National Lung Screening Trial (NLST)[5]. This trial subsequently became the foundation for the original LCS eligibility criteria released in 2013 by the United States Preventive Service Task Force (USPSTF): adults ages 55 to 80 years with at least a 30-pack-year smoking history, who are actively smoking or quit within the last 15 years [6].

However, there was increasing evidence that the 2013 USPSTF criterion of "high-risk patients" did not align with lung cancer risk in the Black population and thus missed a significant cohort of at-risk patients who could benefit from LCS[7,8]. Black patients who developed lung cancer often smoked fewer than the minimum smoking threshold with an overall shorter smoking history compared to White patients[9,10], and presented at a younger age[7]. The recent

decision by the USPSTF to expand LCS eligibility by lowering the age minimum to 50 years and minimum pack-year smoking history to 20 pack-years reflects the ongoing efforts to address this variability in lung cancer risk by race[11]. Thus, while LCS with LDCT has the potential to bring equity to the lung cancer burden in the Black patient population, the expanded screening criteria will only yield a benefit in lung cancer mortality if LCS is adopted by a large and diverse patient population.

As a relatively new cancer screening practice in the US, the process of LCS with LDCT has not yet become as ubiquitous or streamlined as a preventive care measure compared to colonoscopy for colorectal cancer screening or mammography for breast cancer screening. Overall, there has been low uptake of LCS in the US, with nationwide screening rates of only 2.0 to 3.9% among eligible adults[12]. Low participation may in part be related to the complexity of cancer screening. All cancer screening is a multi-step process which requires (1) identification of eligible patients, (2) shared decision making about the screening process between the provider and patient, (3) referral for the screening test by a provider, (4) completion of the screening test by the patient, and (5) ongoing participation in subsequent follow-up studies. Each step presents with unique challenges driven by provider or patient factors, which may serve as potential targets for intervention.

Little is known about racial disparities in LCS participation and behaviors in clinical practice, in part due to low rates of racial and ethnic minorities in the large clinical trials. In the NLST, Black individuals constituted only 4.5% of the study cohort despite making up 14% of the US population[13,14]. While there is increasing recognition that Black patients have lower participation in LCS[15], it is not yet clear where in the cancer screening process the disparities become manifest. Given the greater potential for LCS to reduce lung cancer mortality in Black patients, it is important to understand racial disparities in LCS participation, as well as where in the cancer screening process this occurs. We performed a systematic review to explore LCS participation among Black compared with White patients in the US.

METHODS

Protocol

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines[16]. The protocol was published (PROSPERO: CRD42020214213) prior to commencing the review.

Eligibility Criteria

The Patient-Intervention-Comparator-Outcome-Study Design (PICO) criteria were used to determine eligibility of the articles based on the type of study design, type of population, type of exposure, and outcome. All observational and randomized clinical trials were eligible. Articles not from a clinical study (editorials, narrative reviews) were excluded. We focused our review on studies which examined rates of LDCT acquisition for LCS and included race as a demographic factor. Given the limited availability of literature including race beyond White and Black or African American race, analysis was restricted to studies which included Black race identified as follows: Black, African American, Non-Hispanic Black, and Non-White/Caucasian (majority of the Non-White population were Black).

Data Sources and Searches

The literature search was conducted in collaboration with a clinical librarian (AB) using a combination of free text and index terms focusing on three concepts: lung cancer, screening with low-dose CT scan, and uptake (receipt of screening CT). We searched the following databases from their inception until October 13, 2020: MEDLINE (Ovid), PubMed, EMBASE (Ovid), Center Register of Controlled Trials (Cochrane CENTRAL), CINAHL (ebsco), and Web of Science-Core Collection. No restrictions on publication language were applied and search strategies were piloted prior to use. Search strategies for all databases are presented in Appendix Table 1. We also searched the reference lists of included or relevant articles to identify additional references.

Study Selection

The initial screening of titles and abstracts was conducted independently by two investigators (Y.K., L.B.). Abstracts included by either reviewer underwent full-text review. Full texts of selected studies were reviewed based on the selection criteria (Y.K., L.B., B. B, K.A.). Disagreements were resolved by consensus.

Data Extraction and Quality Assessment

To minimize error, two reviewers used a data collection form to extract information (patient and study characteristics, patient eligibility criteria for lung cancer screening, and meta-analysis outcomes (defined as LDCT performed)) from included studies. The restrictions on the study populations were based on eligibility for LCS which includes age and smoking history. For studies with missing or incomplete data on eligibility criteria, race, or LDCT referral or participation, we attempted to contact authors to retrieve those data. The Newcastle-Ottawa Scale (NOS) for cohort and case-control studies[17] was used for quality assessment of the selected observational studies by two investigators (Y.K., L.B.) using a numerical score out of 9 points, with higher scores indicating higher quality of the study.

Data Synthesis and Meta-analysis

When at least two studies were available with comparable outcomes for the purposes of our meta-analysis (LDCT performed), we performed random-effects meta-analyses and estimated pooled odds ratios (ORs) with 95% CI using the restricted maximum likelihood method[18]. We evaluated heterogeneity visually and with the I^2 statistic. I^2 values of 25%, 50%, and 75% were considered low, medium, and high heterogeneity, respectively[19]. Meta-regression and tests for publication bias were not performed due to the limited number of included studies[20]. Heterogeneity was explored by sensitivity analysis by removing individual studies sequentially (Appendix Table 2). Statistical analysis was performed using Stata/IC, version 16.1 (StataCorp, College Station, Texas).

RESULTS

Study Selection

The medical database search yielded 18,300 studies, of which 229 studies were selected for full-text review. Nine studies[21–29] were identified for inclusion in the systematic review (Fig. 1).

Common reasons for exclusion after full-text review included different outcome of interest from the meta-analyses, missing race as a patient characteristic, abstracts with inadequate information, duplicate publications, and review articles without original data.

Study Characteristics

The included studies were composed of 1 prospective cohort study[29], 3 retrospective cohort studies[21,22,28], 1 retrospective case-control study[24], and 4 cross-sectional studies[23,25–27]. All studies were conducted in the US at single healthcare centers[22,24,25,28], regional healthcare networks[21,26], community-based recruitment[29], or utilized databases including Medicare[27] and the Behavioral Risk Factor Surveillance System (BRFSS) data from 10 states[23]. No clinical trial met criteria for inclusion into the systematic review or meta-analysis.

Main characteristics and findings of the 9 included studies are summarized in Table 1.

The studies were subdivided into those which examined rates of LCS in a baseline population of (a) LCS-eligible patients[22,23,25,27,29] (5 *eligible* studies), or (b) patients referred for LCS by a provider[21,24,26,28] (4 *referred* studies). The *eligible* versus *referred* studies were separated because they used a different denominator of a screening eligible population versus a population both eligible and referred for screening. Therefore, these rates of screening were not comparable. For the *eligible* studies, the method of determining an eligible patient cohort varied by study. Three studies[23,25,29] applied the 2013 USPSTF LCS criteria to their study population cohort which included (a) recruited patients from the community in the state of Indiana (n=438 eligible patients, 62.2% screening rate)[29], (b) a random patient sample from a healthcare organization electronic medical record (EMR; n=134, 23% screening rate)[25], or (c) BRFSS reported data where smoking history was provided (n=4373, 14.4% screening rate)[23]. Two studies estimated the LCS-eligible population using a combination of census data, county or state level smoking data, and either 2013 USPSTF criteria (n=2,531,725, 13.5% screening rate)[27] or an age threshold of 55 years or above with any smoking history (n=15,566, 1.6% screening rate)[22]. The eligible patients who completed LDCTs were identified through self-report[23,25,29], EMR review[22], or Medicare claims data[27].

For the *referred* studies, all patients in the referred patient population met the 2013 USPSTF LCS criteria and had a referral placed by a provider in the EMR (total n=2117). The referred patients who completed LDCTs were identified through EMR review.

Among the *eligible* studies, the number of participants ranged from 134 to 4373; two studies[22,27] used an estimated total cohort population. The median number of participants for the *referred* studies was 564 (range 171 to 818). Basic demographics were similar for *eligible* and *referred* studies with average age of 65.2 years and 64.0 years, respectively, and average proportion of male participants 50% and 52% respectively. When comparing the *eligible* versus *referred* studies, the median screening rates were 14.4% (range 1.7 to 62.6%) and 68.5% (range 62.6 to 88.8%), respectively.

Additional demographics, comorbidities, clinical variables, and socioeconomic variables reported in each study are summarized in Appendix Table 3. Six studies[21,23,24,26,28,29] reported socioeconomic variables (insurance category, education level, neighborhood level) but did not adjust for these factors in LCS participation rates.

Quality Appraisal

Study quality was based on three main elements: selection, comparability, and outcome. Overall, the studies had a median NOS score of 5 (range 2–8) out of a possible 9 points (Table 2). Studies lost points primarily due to being single-center studies or lack of adjustment for a comprehensive set of potential confounders. Specifically for the *eligible* studies, use of self-reported data or use of estimates to calculate the number of eligible patients in the study cohort resulted in lower quality appraisals.

Meta-analysis of LCS Participation by Race

The meta-analyses were performed separately for the 5 *eligible* studies and the 4 *referred* studies (Fig. 2). For the 5 *eligible* studies, the meta-analysis showed lower LCS participation by Black compared to White patients eligible for LCS ([OR]=0.43, [95% CI: 0.25, 0.74]). However, there was no significant difference in LCS participation between Black and White patients among the 4 studies of patients referred for LCS (OR=0.94, [95% CI: 0.74, 1.19]). Heterogeneity was

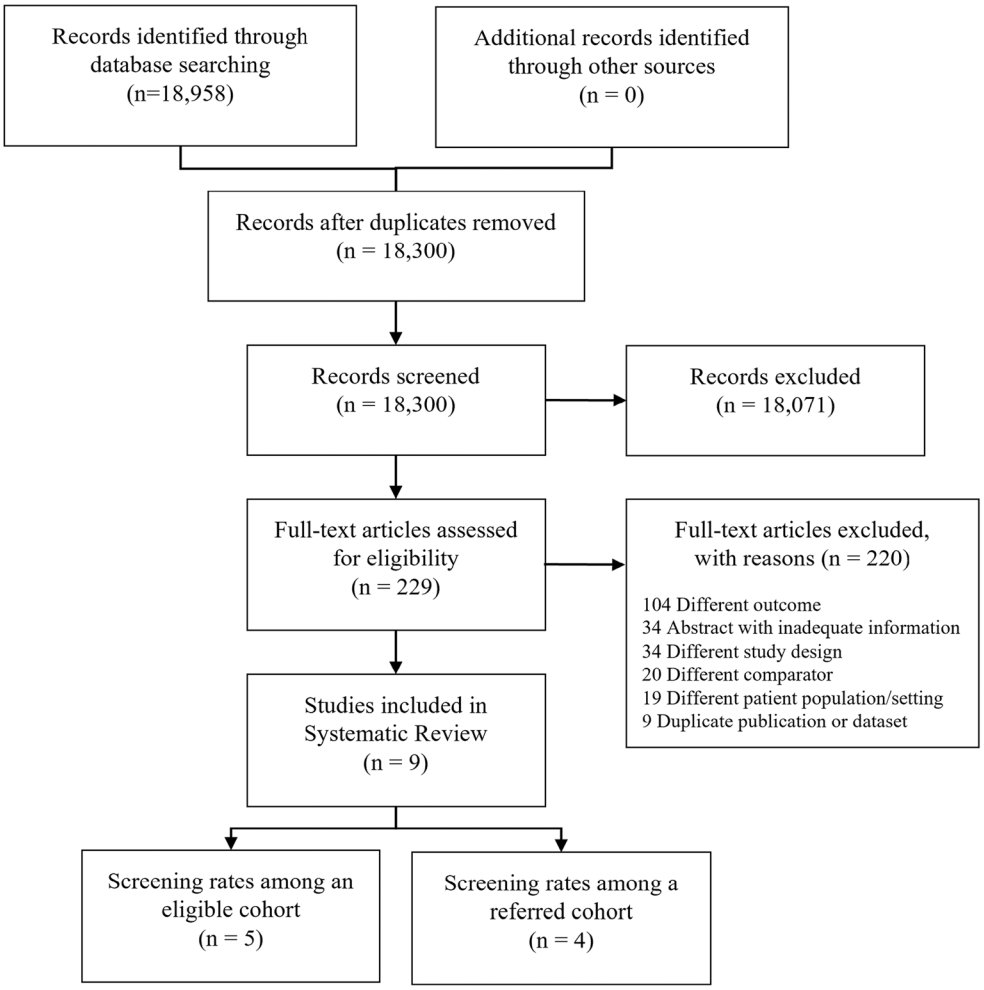

Figure 1. Evidence search and selection.

high for studies reporting eligible patients screened (I^2=93%) and low for studies of referred patients screened (I^2=0%). The high heterogeneity for studies of eligible patients screened was explored using sensitivity analysis but no substantial difference was seen on heterogeneity or pooled effect by sequentially removing individual studies (Appendix Table 2).

DISCUSSION

Here, we present the first systematic review to focus on the relationship between race and LCS participation in the US. The meta-analyses revealed that Black LCS eligible patients are being screened at a lower rate than White patients [Summary OR=0.43 (0.25–0.74)]. However, once referred for LCS by a provider, the difference in LCS participation between Black and White patients was almost negligible [Summary OR=0.94 (0.74–1.19)]. This result demonstrates that racial disparity is present in LCS participation. Importantly, racial disparity in LCS participation is attenuated once patients are referred for screening by a provider. This indicates that racial disparities in LCS participation for the higher-risk Black population may be reduced by more equitable provider referral practices.

Currently, little is known about LCS referral practices in the US. The complexity of the LCS eligibility criteria poses a challenge for conducting large-scale research on LCS participation because screening eligibility cannot be easily extracted from an EMR. This was exhibited in the literature search for this systematic review, where only one abstract specifically examined rates of referral among an eligible population as a primary outcome. This abstract by Kats and colleagues reported that Black race and higher age were associated with lower rates of referral[30]. This is consistent with prior systematic reviews which have summarized how implicit bias towards racial and ethnic minorities by healthcare providers can negatively affect healthcare outcomes[31,32].

The patient-provider relationship is crucial in cancer screening, including LCS, where shared-decision making is a required step. Establishing a strong patient-provider relationship may be particularly challenging for Black patients because of underlying discrimination or by the lack of a regular primary care provider (PCP). Nonetheless, the relationship between perceived racism or medical discrimination and cancer screening participation is not straightforward. Crawley and

Table 1. Characteristics of Included Studies

Author, year	Study type	Data source/ setting	Study period	State	Eligibility criteria	Outcome assessment	*N*	% Black	Screening rate (%)
Studies of patient population eligible for screening									
Carter-Harris, 2018	Prospective cohort	Community-based recruitment	Jan–Feb, 2017	IN	USPSTF	Self-reported*	438	42	62.2
Japuntich, 2018	Cross-sectional	Single center/ health org.	2016	RI	USPSTF	Self-reported	134	49	23.0
Richmond, 2020	Retrospective cohort	Community based cancer center	Jan–June, 2016	NC	Current smokers >55y	EMR	15,566‡	27	1.6
Tailor, 2020	Cross-sectional	Medicare	2016	N/A	USPSTF, 65–79y	Medicare claims data	2,531,725‡	13.5	4.1
Zgodic, 2020	Cross-sectional	BRFSS	2017	Mult†	USPSTF	Self-reported	4373	13.4§	14.4
Studies of patient population referred for screening									
Gerber, 2020	Case-control	Parkland Health and Hospital System	2017–2019	TX	USPSTF/ NLST	EMR	453	52.1	61.6
Lake, 2020	Retrospective cohort	Single academic center	2015–2017	PA	USPSTF	EMR	675	46.7	70.7
Raju, 2020	Retrospective case-control	Single academic center	2015–2016	OH	USPSTF	EMR	818	14.6	66.3
Rennert, 2020	Cross-sectional	Prisma Health System	2016–2017	SC	USPSTF	EMR	171	13.5§	88.8

**Includes intent to screen in addition to screened*
†10 states (including FL, GA, KS, ME, MD, MO, NV, OK, VT, WY)
‡Estimated
§Non-White
USPSTF criteria (2013): adults ages 55 to 80 years with at least a 30-pack-year smoking history, who are actively smoking or quit within the last 15 years
Abbreviations: USPSTF, United States Preventive Task Force; EMR, electronic medical record; Mult, multiple; NLST, National Lung Cancer Screening Trial; BRFSS, Behavioral Risk Factor Surveillance System

colleagues found lower rates of colorectal cancer screening among patients who had experienced medical discrimination compared to those who had not[33]. However, other studies observed weak or no correlation between perceived discrimination or racism and use of preventive health services, including cancer screening, after adjusting for socioeconomic status (SES)[34,35]. As many of these studies were limited to single institutions without a standardized method to evaluate racism or discrimination, it is difficult to draw conclusions.

In conjunction with the interpersonal racism that may manifest as provider racial bias in cancer screening referral practices, structural racism creates barriers to healthcare access and thus equitable LCS participation in the US. For patients to participate in LCS, they must have access to a PCP who can inform them of the LCS process and place a referral. Studies have shown that contact with a regular PCP is an important factor determining cancer screening referral and participation[36]. Residential racial segregation in the US has had long standing effects including perpetuation of inequities in wealth, education, and access to healthcare, which have also manifested through cancer disparities[37]. Greater residential segregation is associated with later stage of lung cancer diagnosis, lower likelihood of undergoing surgery for early stage lung cancer, and higher lung cancer–specific mortality[38,39].

Thus, the relationship between residential segregation, SES, the social/political construct of race in the US, and cancer outcomes is complex. The literature used in this systematic review did not consistently include or adjust for socioeconomic variables which would have allowed us to better distinguish between interpersonal and structural racism that may be affecting LCS participation. Historically, studies on breast cancer screening or colorectal cancer screening have shown that

Table 2 Study Quality Assessment Using Newcastle-Ottawa Quality Assessment Scale

Author, year	Selection	Comparability	Outcome	NOS score	Limitations
Carter-Harris, 2018	0*00	00	0*0	2/9	Community recruitment, self-reported outcome, no adjustment
Japuntich, 2018	**00	*0	0*0	4/9	1 site, self-reported outcome, adjustment for age only
Richmond, 2020	00**	00	**0	4/9	Estimated eligible, no adjustment
Tailor, 2020	0***	**	***	8/9	Estimated eligible
Zgodic, 2020	**00	**	0*0	5/9	Self-reported outcome
Gerber, 2020	00**	00	***	5/9	Part of a clinical trial, no adjustment
Lake, 2020	0***	**	***	8/9	1 site
Raju, 2020	0***	00	***	6/9	1 site, no adjustment
Rennert, 2020	0***	00	***	6/9	1 site, no adjustment

NOS, Newcastle Ottawa Scale
**Asterisk indicates item achieves 1 point, 0 indicates 0 points in the NOS category*

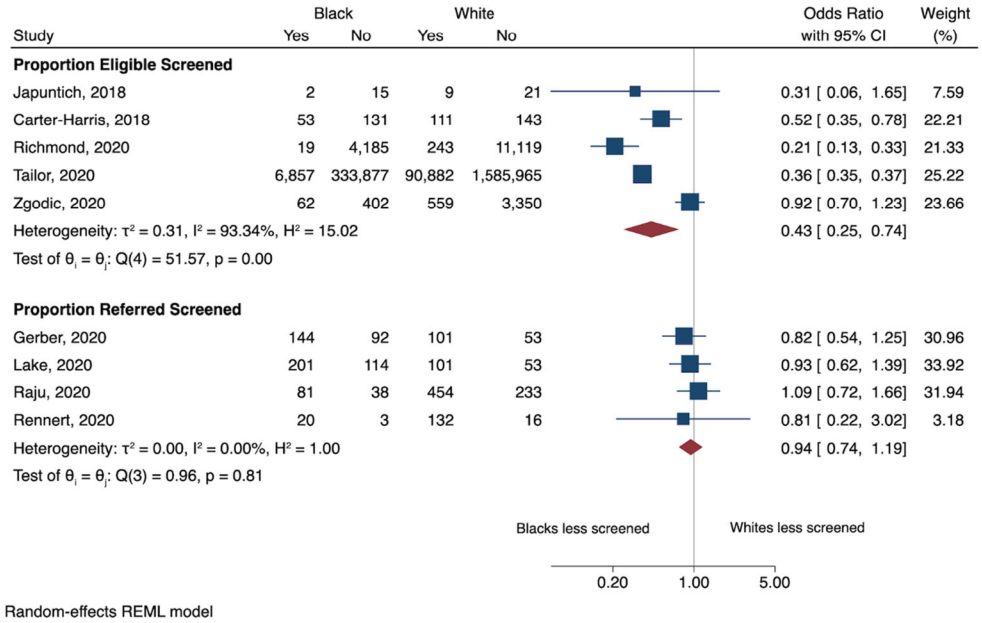

Figure 2. Meta-analysis of lung cancer screening utilization by race.

even after adjusting for SES, racial disparities in rates of screening persist between Black and White patients[40,41]. Similarly, in our systematic review, Tailor and colleagues who used Medicare data (indicating equal insurance status) still demonstrated 64% lower odds of LCS participation among Black patients[27]. In addition, a recent systematic review by Sosa and colleagues provided examples of studies where SES variables such as household income or education were associated with lower LCS participation[42]. Thus, while there is evidence that racial disparities exist in cancer screening after accounting for SES, targeted work in clarifying the interaction between SES and race in LCS participation is needed.

The discordance in the meta-analysis results between the two study groups, *eligible* patients and *referred* patients, illustrates the important role of providers and their referral practices in creating disparities in LCS participation. Therefore, interventions should target providers, especially PCPs, in several domains to motivate conversations between PCPs and patients. First, increased education on LCS in general is necessary, as qualitative studies on physician perspectives on LCS have shown that only 47–58% of providers are well-informed on the 2013 USPSTF guidelines[43,44]. Second, we must raise awareness among PCPs of the greater benefits of LCS in Black patients and how the updated USPSTF LCS eligibility guidelines better align with lung cancer risk in the Black population. Third, continued emphasis is needed on the importance of trust and PCP engagement in the shared decision making process for cancer screening, and the potential provider biases contributing to racial disparities in referral patterns[44,45].

In general, identifying who is eligible for LCS complicates the referral process because of the need to assess the patient's smoking history[46]. Unlike other cancer screening criteria which are predominantly based on gender and age, LCS eligibility also relies on the following: total pack-year smoking history and, among former smokers, time since last use. As there is no standardized method of incorporating smoking histories into the EMR, this information cannot be easily or reliably located in a patient's chart or developed into EMR advisories. The discordance rate between the smoking history within a patient's EMR and the history obtained during a shared decision-making discussion has been reported to be as high as 90%[47]. On a more systemic level, considering ways to have more accurate and updated smoking history data or simplified LCS criteria to generate EMR reminders for providers may facilitate the referral process[48].

Limitations

The present study has several limitations. First, publication bias likely affected inferences from this systematic review. Given that it has been less than a decade since the formal implementation of LCS by the USPSTF, many LCS programs are still in their nascency with inadequate data. Second, two studies in the *eligible* group relied on estimates of a LCS-eligible population and three studies used patient self-report of LCS completion. This, in addition to the significant heterogeneity between the studies, may impact the reliability of the meta-analysis estimates. One study by Richmond and colleagues used a different eligibility criterion of current smokers >55 years without a total pack-year cutoff. With a broader eligibility criterion, the percentage of screened patients may be lower than what would have been observed if USPSTF criteria had been used instead. Finally, several factors limited the potential to extrapolate the results to the general US population. Most studies represented only one medical center or hospital system, with only two[23,27] using a cohort across multiple states. Academic centers may have a higher LCS participation rate due to their ability to establish centralized

LCS referral programs. While geographic locations varied by study, not all US regions were represented equally and there is heterogeneity in prevalence of smokers in each state.

CONCLUSION

In summary, we demonstrate racial disparities exist in LCS participation in the US. Eligible Black patients are less likely to participate in LCS compared to eligible White patients despite the higher burden of lung cancer in the Black population. However, the racial disparity is attenuated among patients referred to LCS, suggesting the importance of the referral step in the LCS process as a target to reduce disparities. There is a need to promote LCS referral among providers with particular emphasis on the significant benefits of LCS in the Black patient population. More studies are needed to identify barriers to LCS referral and better understand both the provider and patient characteristics that may influence LCS participation.

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Author Contribution: *Y.K. and L.B. screened articles, extracted data, and performed the analyses. B.B. and K.A. contributed to study review for selection and disagreements were resolved in consensus by Y.K., L.B., B.B., K.A., and A.B. conducted the literature search and C.G. conducted the statistical analysis for the meta-analyses. All authors have contributed substantially to the manuscript. Y.K. and L.B. had full access to all data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.*

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Declarations:

Conflict of Interest: *The authors declare that they do not have a conflict of interest.*

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