



Association between the neighborhood obesogenic environment and colorectal cancer risk in the Multiethnic Cohort



Alison J. Canchola^{a,*}, Salma Shariff-Marco^{a,b}, Juan Yang^a, Cheryl Albright^c, Andrew Hertz^a, Song-Yi Park^d, Yurii B. Shvetsov^d, Kristine R. Monroe^e, Loïc Le Marchand^d, Scarlett Lin Gomez^{a,b}, Lynne R. Wilkens^d, Iona Cheng^{a,b}

^a Cancer Prevention Institute of California, 2201 Walnut Avenue, Suite 300, Fremont, CA 94538, USA

^b Stanford Cancer Institute, 265 Campus Drive, Suite G2103, Stanford, CA 94305, USA

^c University of Hawaii School of Nursing and Dental Hygiene, 2528 McCarthy Mall, Webster 401, Honolulu, HI 96822, USA

^d University of Hawaii Cancer Center, 701 Ilalo Street, Honolulu, HI 96813, USA

^e University of Southern California, 1450 Biggy Street, Los Angeles, CA 90033, USA

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ABSTRACT

Background: Information on the role of the neighborhood environment and colorectal cancer risk is limited. We investigated the association between a comprehensive suite of possible obesogenic neighborhood attributes (socioeconomic status, population density, restaurant and retail food environments, numbers of recreational facilities and businesses, commute patterns, traffic density, and street connectivity) and colorectal cancer risk in the Multiethnic Cohort Study.

Methods: Among 81,197 eligible participants living in California (35,397 males and 45,800 females), 1973 incident cases (981 males and 992 females) of invasive colorectal cancer were identified between 1993 and 2010. Separately for males and females, multivariable Cox regression models were used to estimate hazard ratios (HR) and 95% confidence intervals (CI) for colorectal cancer risk overall and by racial/ethnic group (African American, Japanese American, Latino, white).

Results: In males, higher traffic density was associated with an increased risk of colorectal cancer (HR = 1.29, 95% CI: 1.03–1.61, $p = 0.03$, for quintile 5 vs. quintile 1; p -trend = 0.06). While this association may be due to chance, this pattern was seen (albeit non-statistically significant) in all racial/ethnic groups except whites. There were no other significant associations between other neighborhood obesogenic attributes and colorectal cancer risk.

Conclusion: Findings from our large racial/ethnically diverse cohort suggest neighborhood obesogenic characteristics are not strongly associated with the risk of colorectal cancer.

1. Introduction

It is estimated that 45% of U.S. colorectal cancer (CRC) cases could be prevented by maintaining a healthy diet, regular physical activity, and healthy weight [1]. Within the Multiethnic Cohort Study (MEC), obesity, smoking, alcohol, and a number of dietary factors have been associated with the risk of CRC [2–4]. In addition, there is evidence that the neighborhood environment can impact diet, obesity, and physical activity, and can influence obesity-related health disparities [5–11]. In the MEC, neighborhood socioeconomic status (nSES) has been associated with obesity in African Americans, Latinos, and whites [8].

While individual-level factors such as obesity and level of physical activity are associated with CRC risk, what is less clear is the effect of the neighborhood environment, and whether its role is independent of these individual-level risk factors. No cohort studies have examined neighborhood-level factors other than socioeconomic status (SES) in relation to CRC risk [12,13]. In the MEC, we investigated the association between a comprehensive suite of ten *a priori* selected neighborhood obesogenic attributes and risk of CRC, assessing whether associations were independent of individual-level factors and varied by racial/ethnic group.

* Corresponding author at: Cancer Prevention Institute of California, 2201 Walnut Avenue, Suite 300, Fremont, CA 94538, USA.

E-mail addresses: Alison.Canchola@cpic.org (A.J. Canchola), Salma.Shariff-Marco@cpic.org (S. Shariff-Marco), Juan.Yang@cpic.org (J. Yang), cherylal@hawaii.edu (C. Albright), Andrew.Hertz@cpic.org (A. Hertz), SPark@cc.hawaii.edu (S.-Y. Park), YShvetsov@cc.hawaii.edu (Y.B. Shvetsov), kmonroe@hsc.usc.edu (K.R. Monroe), Loic@cc.hawaii.edu (L. Le Marchand), Scarlett.Gomez@cpic.org (S.L. Gomez), Lynne@cc.hawaii.edu (L.R. Wilkens), Iona.Cheng@cpic.org (I. Cheng).

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2. Methods

2.1. Study subjects

The MEC is a large population-based cohort of U.S. adults of five racial/ethnic groups. Methodological details of this study have been described previously [14]. In brief, participants from Hawaii and California completed a baseline questionnaire in 1993–1996 that included information on sociodemographics, height, weight, medical history, family history of cancer, smoking, physical activity, medications, diet, alcohol, and vitamin use.

Of 105,759 African American, Japanese American, Latino, Native Hawaiian, and white MEC participants from California who completed the baseline questionnaire, we excluded participants, hierarchically, who had a history of CRC ($n = 1308$); were Native Hawaiian ($n = 171$); had no follow-up time ($n = 8$); were an incident, invasive CRC case with a non-adenocarcinoma histology ($n = 77$ carcinoid, $n = 7$ squamous cell, and $n = 25$ other tumors; and $n = 6$ missing); had a residential address that was not geocodable ($n = 2155$), had missing BMI ($n = 2247$), or had missing or invalid covariate data ($n = 18,558$) [4]. Thus, 81,197 MEC participants were eligible for analysis.

2.2. Follow-up and case identification

Incident CRC cases were identified through linkage of the cohort to the California Cancer Registry. Deaths were determined through linkages with California death certificate files and the National Death Index.

Follow-up time was calculated as the number of days between the date of completion of the baseline questionnaire and the earliest of: the first diagnosis of invasive CRC (International Classification of Diseases for Oncology-3 [ICD-O-3] site codes C18.0–C18.9, C26.0, C19.9, and C20.9), death, or December 31, 2010. Over a median follow-up time of 16.6 years, 1973 incident CRC cases were identified.

2.3. Residential neighborhood obesogenic attributes

Baseline residential addresses were geocoded to latitude and longitude coordinates, using parcel data (96%) and street centerline data for those that failed to geocode to a parcel (4%).

Geocodes were linked with the California Neighborhoods Data System, an integrated system of small area-level measures of the social and built environments for California [15]. Census 1990 block group-level data were utilized to ascertain: neighborhood SES (nSES), a validated composite measure [16]; population density (per square mile); commute patterns; and street connectivity [17], which was defined as the ratio of actual number of street segments to the maximum possible number of links between nodes (intersections and cul-de-sacs). These measures were categorized based on the distribution of Los Angeles (LA) County block groups ($\geq 90\%$ of the sample resided in LA County). Business, farmers' market [18], and park data were used to quantify the amenities within a one-mile pedestrian network distance of the participant's residence: the Restaurant Environment Index (REI), defined as the ratio of the number of fast-food restaurants to other restaurants [19]; the Retail Food Environment Index (RFEI), defined as the ratio of the number of convenience stores, liquor stores, and fast-food restaurants to supermarkets and farmers' markets; and total number of recreational facilities, parks, and businesses. Traffic density was based on traffic counts within a 500 m radius of a participant's residence. These business and traffic-related attributes were categorized according to the study participant distributions (Supplementary Table 1). These ten neighborhood attributes were selected *a priori* for their potential associations with obesity or colorectal cancer risk (all but street connectivity and number of recreational facilities were associated with obesity [8] and all but the number of parks were univariately associated

with CRC risk).

2.4. Statistical analyses

Hazard rate ratios (HR) and 95% confidence intervals (CI) were estimated using multivariable Cox regression models with age as the time metric. Sex and race/ethnicity-specific models were run given the heterogeneity in CRC incidence between these subgroups [4]. Multivariable models were adjusted for the following individual-level CRC risk factors: age, race/ethnicity, body mass index, family history of CRC, history of intestinal polyps, education, cigarette smoking, multi-vitamin use, nonsteroidal anti-inflammatory medication use, alcohol consumption, vigorous physical activity, history of diabetes, average energy intake, red and processed meat, dietary fiber, calcium, folacin, Vitamin D, and use of hormone therapy (females). These covariates were selected *a priori* as they were associated with CRC risk in the literature or in this cohort [1,4]. Distributions of these covariates are presented in Supplementary Table 2.

All models were additionally adjusted for clustering by block group, using a sandwich estimator of the covariance structure that accounts for intracluster dependence [20]. As a sensitivity analysis, gamma frailty models were run with block group as a random effect [21]. As the random effect term was not statistically significant and the CIs for the neighborhood attributes did not change, the fixed effect models are presented here. Wald tests for trend across neighborhood characteristic categories (excluding no restaurants for REI, no retail food for RFEI, and missing data categories) were conducted using quantile number as an ordinal variable. Wald Type 3 tests for heterogeneity of the trend parameter across neighborhood characteristic categories by race/ethnicity, BMI, and nSES were computed using cross-product terms. Based on correlation tests of time versus scaled Schoenfeld residuals, no neighborhood or adjustment variables violated the proportional hazards assumption.

The ten neighborhood characteristic variables were first entered separately into models, minimally adjusted for age, race/ethnicity (if applicable), and clustering by block group (Supplementary Tables 3 and 4). Nine of the ten neighborhood variables (all except the number of parks) had at least one category or trend that had a p -value < 0.10 in sex and race/ethnicity-specific models. Thus, for the final multivariable models, all the neighborhood attributes except the number of parks were included.

3. Results

This study population (males: 26.0% African American, 14.8% Japanese American, 47.2% Latino, 12.0% white; females: 34.7% African American, 11.8% Japanese American, 36.8% Latino, 16.7% white; Supplementary Table 2) was followed for a median of 16.6 years. The mean age at entry into the cohort was 60 for males and 59 for females. Only 33.2% of males and 30.5% of females lived in high SES neighborhoods (quintiles 4 and 5) (Supplementary Table 1).

The MEC participants in this analysis resided at baseline in 7348 unique block groups predominantly in LA County. The median number of participants in each block group was five (interquartile range 2 to 13). Of the 7348 block groups, 19.5% included one participant and 11.6% included two; the largest block group included 432 participants. The neighborhood attributes in these block groups were moderately correlated (Supplementary Table 5; correlations $< |0.72|$). For example, high SES neighborhoods tended to have a lower population density ($r = -0.43$) and more commuting ($r = 0.40$).

When each of the neighborhood obesogenic attributes were entered individually into minimally adjusted sex-specific models, only higher traffic density was associated with CRC risk in males (HR = 1.24, 95% CI: 1.03–1.51, $p = 0.025$, for quintile 5 vs. quintile 1, p -trend = 0.092, Supplementary Tables 3 and 4). In minimally adjusted race/ethnicity-specific models, two trend tests reached statistical significance at the

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