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Association of change in the neighborhood obesogenic environment with colorectal cancer risk: The Multiethnic Cohort Study

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ARTICLE INFO

Keywords:

Neighborhood change
Obesogenic environment
Colorectal cancer
Multiethnic Cohort study

ABSTRACT

Background: Neighborhood environment has been associated with health behaviors. Despite the evidence of the influence of neighborhood social and physical factors on cancer risk, no research has evaluated whether changes in the neighborhood obesogenic environment, either by physical moves to different neighborhoods or experiencing neighborhood redevelopment or neglect, affect cancer risk.

Methods: The association of change in neighborhood environment attributes (socioeconomic status, population density, restaurant and retail food environments, numbers of recreational facilities and businesses, commute patterns, traffic density, and street connectivity) with colorectal cancer (CRC) risk was examined among 95,472 Los Angeles, CA, Multiethnic Cohort participants, including 2295 invasive CRC cases diagnosed between 1993 and 2010 using Cox proportional hazards regression, adjusting for age, race/ethnicity, other risk factors including BMI and physical activity, and baseline levels of neighborhood attributes. Stratified analyses were conducted by racial/ethnic group and moving status.

Results: 40% of participants moved (changed physical residence) during follow-up. Across all races/ethnicities, upward change in population density was statistically significantly associated with higher CRC risk among male and female non-movers (HR: 1.35 and 1.41, respectively). The same association was also observed separately among female African American and Japanese American non-movers, male Latino non-movers, female African American and male White movers. Downward change in population density was significantly related to higher CRC risk among female non-movers (HR: 1.33). Downward change in traffic density was associated with lower CRC risk among male non-movers but with higher CRC risk among female movers (HR: 0.66 and 1.43, respectively). Downward changes in street connectivity or the number of recreational facilities were associated with higher CRC risk (HR: 1.34 and 1.54, respectively). Upward change in the number of recreational facilities was associated with lower CRC risk among female non-movers (HR: 0.70). Changes in the other neighborhood attributes did not exhibit significant associations with CRC risk within more than one racial/ethnic group.

Conclusion: Changes over time in neighborhood attributes have an effect on the risk of colorectal cancer, which is separate from the baseline levels of the same attributes and individual-level risk factors, and differs between sexes, movers and non-movers and across racial/ethnic groups.

Introduction

The impact of the neighborhood environment on cancer risk is an area of rapidly increasing interest in epidemiological research (Schule &

Bolte, 2015). There is an established literature demonstrating the influence of neighborhoods on individual health behaviors, such as diet (An & Sturm, 2012; Caspi, Sorensen, Subramanian, & Kawachi, 2012; Mejia, Lightstone, Basurto-Davila, Morales, & Sturm, 2015; Reitzel

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<https://doi.org/10.1016/j.ssmph.2019.100532>

Received 12 October 2019; Received in revised form 11 December 2019; Accepted 19 December 2019

Available online 24 December 2019

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et al., 2016) and physical activity (Keegan et al., 2012; King et al., 2005; Yang, Spears, Zhang, Lee, & Himler, 2012), and a growing body of evidence on its impact on health outcomes, including obesity (Barrientos-Gutierrez et al., 2017; Keegan et al., 2012; Lovasi, Hutson, Guerra, & Neckerman, 2009; Odoms-Young, Zenk, Karpyn, Ayala, & Gittelsohn, 2012; Shariff-Marco et al., 2017), cardiovascular disease (Dragano et al., 2009a, 2009b; Freedman, Grafova, & Rogowski, 2011) and cancer (Gomez et al., 2015), in particular colorectal cancer (CRC) (Doubeni et al., 2012; Kim, Masyn, Kawachi, Laden, & Colditz, 2010). Neighborhood social and built environment can affect the risk of colorectal cancer through a number of pathways (Gomez et al., 2015), one of which is through affecting health behaviors and psychological factors that promote obesity (Berrigan & Berger, 2019). Within the Multiethnic Cohort Study, independent effects of the neighborhood obesogenic environment, defined as neighborhood attributes of the social and built environments that may promote obesity (Conroy, Shariff-Marco, & Yang, 2018), on breast and colorectal cancer risk have been identified (Canchola et al., 2017; Conroy, Clarke, & Yang, 2017).

There are several challenges in studying the neighborhood environment. In particular, many neighborhood attributes are not static over time such as amenities of the built environment that deteriorate or are modernized. Additionally, a change in a person's neighborhood environment can have a separate effect on health outcomes, possibly due to negative factors such as stress related to moving to a new residence and disruption of established social connections or behavioral routines, and positive factors such as moving to a more walkable neighborhood. Thus, accounting for neighborhood change in the analyses would not only help to accurately assess neighborhood exposure, but also answer the question of whether neighborhood change can independently affect health risks with important implications for improving public health. Few studies have examined neighborhood change in its relation to health (Hirsch et al., 2014; Wing et al., 2016). This may be especially salient for chronic diseases such as cancer, which have long latency periods. Additionally, as the patterns of social and physical mobility may differ by race/ethnicity, it is important to study the effects of changing neighborhood environment across racial/ethnic groups.

The Multiethnic Cohort (MEC) is a large population-based prospective study investigating risk factors for cancer and other chronic diseases among five U.S. racial/ethnic groups: African Americans, Japanese Americans, Native Hawaiians, Latinos, and Whites (Kolonel et al., 2000, 2004) living in Hawaii or California (CA). Prior work has characterized the neighborhood obesogenic environment across a 20 year period for the MEC's CA participants (Conroy et al., 2018). In the present study, we hypothesize that change in the attributes of neighborhood obesogenic environment may have an effect on CRC risk that is separate from that of the baseline levels of these attributes, previously found among the CA MEC participants (Canchola et al., 2017). This study also provides a framework to study change in the neighborhood environment and health outcomes.

Materials and methods

Study subjects

The MEC is a prospective study designed to examine the association of dietary, lifestyle, and genetic factors with the incidence of cancer in a multiethnic population. The study design and implementation have been described previously (Kolonel et al., 2000). Briefly, over 215,000 men and women aged 45–75 years at recruitment and living in Hawaii or CA (largely Los Angeles) were enrolled in 1993–1996. Individuals were identified primarily through driver's license files as well as voter registration lists in Hawaii, and Medicare files in CA. At enrollment, participants completed a self-administered baseline questionnaire on diet, anthropometric measures, medical history, and lifestyle. A shorter repeat questionnaire that included a question on CRC screening was administered in 1998–2002. The study protocol was approved by the

Institutional Review Boards of the University of Hawaii and the University of Southern California.

Address history and neighborhood data

The MEC, through continued active follow-up, has maintained accurate and up-to-date addresses on all participants since its inception. Addresses are updated through participant reports and through linkages, such as with the United States Post Office National Change of Address Service and Medicare. The date of each address change (if known) or the date of notification of change is recorded. Geocoding for all residential addresses of MEC participants (1993–2010) was conducted and is continually updated using geographic information system software (ArcGIS, ESRI) and best available locator data (i.e. tax parcel and centerline reference data) from government agencies and private vendors. Of the total 234,714 residential addresses for 112,003 CA MEC participants from cohort entry to 12/31/2010, 74.9% were geocoded to latitude and longitude coordinates using parcel data and 13.6% to street centerline data. Out of state (7.8%) and P.O. Box addresses (3.1%) were not geocoded and 0.5% addresses failed to geocode; these addresses were excluded from analysis. Addresses were assigned to census periods based on the dates of residence for the purposes of assigning census block group numbers: those dated 1993–1996 were assigned to the 1990 Census, 1997–2005 to the 2000 Census, and 2006–2010 to the 2010 Census. Addresses spanning two or three census periods were split between these census periods, using 1/1/1997 and 1/1/2006 as the cut-off dates. A census block group, an area that includes on average 1500 residents in CA, represented the neighborhood unit in our analysis. For census data, geocodes of baseline addresses were linked to 11,370 unique 1990 Census block groups, 12,387 to 2000 Census block groups and 12,939 to 2010 Census block groups. Due to changes in data collection by the U.S. Census with the discontinuation of the "long" form, many neighborhood attributes for 2010 data were obtained from the American Community Survey (ACS, 2007–2011) for block groups and tracts depending on data availability.

Characterization of the neighborhood obesogenic environment was based on linkage of geocoded addresses to the California Neighborhoods Data System, an integrated data system of small area-level measures of the social and built environments that includes census, business, farmers' market, park, and traffic data (Gomez et al., 2011). For this study, census data included population density (persons per km²); commute patterns; and neighborhood socioeconomic status (nSES), a composite measure created for each census period by principal component analysis of census data on education, housing, employment, occupation, income, and poverty (Yang et al., 2014; Yost, Perkins, Cohen, Morris, & Wright, 2001). The information on the number/type of businesses was based on business listings derived from Walls & Associates' National Establishment Time-Series Database from 1990 to 2008 (Walls & Associates, 2008) and a three-year business activity window (1990–1992, 1999–2001, and 2006–2008 for 1990, 2000, and 2010 Census periods, respectively). In addition to capturing total number of businesses, these data, along with farmers' markets listings from the California Department of Food and Agriculture (California Department of Food and Agriculture, 2010), were used to characterize the recreational facilities and food environment (restaurants and retail food outlets) within block groups. Parks and street connectivity were based on data from NavTeq's NavStreets database (NavTeq, 2010). Street connectivity (Berrigan, Pickle, & Dill, 2010) was measured using the gamma index, a commonly used measure of walkability, and defined as the ratio of actual number of street segments to maximum possible number of intersections. Traffic density, within a 0.5 km radius buffer of a participant's geocoded residence, was based on traffic counts from the California Department of Transportation (California Department of Transportation, 2004) and previously described methods (Gunier, Hertz, Von Behren, & Reynolds, 2003). All data were derived for census block groups (Supplementary Table S1). Whenever the ACS data at the block

group level were sparse or unreliable, data for the corresponding census tract were assigned to this block group.

As over 95% of CA MEC participants resided in Los Angeles County, neighborhood attributes were categorized based on quintiles or quartiles of their distributions across Los Angeles County block groups using separate cutoff points for each census period. For some attributes, fewer categories were used (e.g. no parks vs. one or more parks). Participants' neighborhood environment may have changed either as a result of physical moves or due to neighborhood redevelopment or deterioration. To distinguish these types of change, we examined neighborhood change based on participants' moving status. Study participants were classified as movers if they had more than one residential address during follow-up or non-movers if they had only one residential address. We examined the differences in the number of residential moves and median time residing at a given address by sex and race/ethnicity. For every participant, change in the exposure to each of the neighborhood environment factors was defined as a shift up or down by at least one category level (e.g., a change from quintile 3 to 4) between the participant's baseline and any subsequent address or between census periods for address durations that included multiple census periods.

Participant inclusion criteria

Of 105,591 African American, Japanese American, Latino, and White MEC participants who lived in California and completed a baseline questionnaire, we excluded participants who had a history of CRC prior to cohort entry ($n = 1305$; identified by self-report on questionnaire or by linkage with cancer registries), had no geocoded residential address (see above) ($n = 2150$), had invalid follow-up data ($n = 8$), had incident CRC with non-adenocarcinoma histologies ($n = 77$ carcinoid tumors, $n = 7$ squamous cell tumors, $n = 24$ other tumors), had missing or invalid body mass index (BMI) ($n = 2247$), or had missing or invalid dietary data ($n = 4281$). Native Hawaiian participants ($n = 171$) were not included due to their small number in the CA cohort. Thus, 95,472 MEC participants ($n = 40,870$ men and $n = 54,602$ women) were eligible for analysis.

Case ascertainment

Incident cases of CRC were identified through linkage of the CA cohort to the California Cancer Registry. Deaths were determined through linkages with CA death certificate files and the National Death Index. Over a median follow-up time of 16.6 years, 2295 incident cases of invasive CRC ($n = 1131$ men and $n = 1164$ women) were identified.

Statistical analysis

The association between change in the neighborhood environment and CRC risk was examined using Cox regression with age as the time metric. Follow-up was calculated as the time between cohort entry and the first diagnosis of invasive CRC, death, or end of follow-up (December 31, 2010). Hazard ratios (HRs) and 95% confidence intervals (CIs) were estimated for upward and downward direction of neighborhood change, using 'no change' (same distribution quintile) as the reference category. Change was treated as a time-dependent covariate, which could take on a new value at the time of move (for movers) or at the start of a new census period (for all participants). The Cox models were fit separately for men and women, for all races/ethnicities combined and adjusted for the following individual-level covariates: age at study entry (years), BMI (kg/m^2 ; <25 , 25 - <30 , ≥ 30), family history of CRC (yes/no), history of intestinal polyps (yes/no), education (8 grades or less; 9-12 grades; vocational school or some college; college or graduate/professional degree), cigarette smoking (never/past/current smoker), multivitamin use at least once a week in the last year (yes/no), use of nonsteroidal anti-inflammatory medication (ever used at least twice a week for one month or longer: yes/no), alcohol consumption during the last year (g/

day), moderate to vigorous physical activity during the last year (hrs/day: <2.5 ; ≥ 2.5), history of diabetes (yes/no), average energy intake during the last year (kcal/day; log-transformed), dietary intake of red and processed meat (g/1000 kcal/day), dietary fiber (g/1000 kcal/day), calcium (mg/1000 kcal/day), folate (mcg/1000 kcal/day), Vitamin D (IU/1000 kcal/day) and use of hormone therapy (women only; never/past/current user). These covariates were selected a priori as they had been previously found to be associated with CRC risk in the literature and/or in our cohort (Nomura et al., 2007; Ollberding, Nomura, Wilkens, Henderson, & Kolonel, 2011; Park et al., 2007). All models were additionally adjusted for the baseline level of the corresponding neighborhood factor. A robust sandwich variance estimate (Lin & Wei, 1989), aggregated over block groups according to the 1990 Census, was used to account for potential correlation within block groups.

Stratified analyses were conducted by race/ethnicity and moving status (non-movers vs. movers) to distinguish the effect of neighborhood environment change due to residential moves from changes in the neighborhood itself. To eliminate the effect of changing neighborhoods from the analysis of movers, we restricted the analysis of movers to a single census period, 1997-2005, linked to the 2000 U.S. Census block groups. Sensitivity analyses were conducted excluding the first 5 years of follow-up, to eliminate a potential effect of neighborhood exposure prior to cohort entry, and with adjustment for CRC screening on the subset of participants with screening data. The proportional hazard assumption for Cox models was verified by plotting scaled Schoenfeld residuals against time to event (Grambsch & Therneau, 1994). All analyses were conducted with SAS version 9.4 (SAS Institute, Inc., Cary NC). All P-values were two-sided, and $P < 0.05$ was defined as statistically significant.

Results

The 40,870 male and 54,602 female CA MEC participants included in the analyses were followed for an average of 16.6 years (Table 1). Latinos represented the largest racial/ethnic group, comprising 48.4% of men and 38.5% of women, followed by African Americans (26.2% of men and 34.9% of women); Japanese Americans and Whites each comprised $<16\%$ of participants. The average age at cohort entry was 61.7 years among men and 60.8 years among women. At baseline, 6.0% men and 7.6% women reported a family history of CRC; 18.7% men and 27.9% women were obese; and 19.4% men and 14.2% women were current tobacco smokers. The distribution of baseline characteristics was similar among movers and non-movers (Supplementary Table S2).

A majority of the participants (61.5% of men and 58.7% of women) were non-movers (Table 2). Of the five racial/ethnic groups, Japanese Americans had the highest proportion of non-movers (72.7% of men and 71.8% of women). Among the movers, 55% had one move and $<3\%$ had 4 or more moves during the follow-up period. The median length of residence at one address among movers ranged from 5.4 years among African American women to 7.4 years among Japanese American women.

Apart from the moderate correlations of nSES with population density and percent commute (Spearman's $\rho = -0.61$ and 0.51 , respectively), correlation among neighborhood attributes was low ($\rho < 0.5$, data not shown). For most of the neighborhood attributes, 35-47% of address changes resulted in the new address being in the same distribution quintile as the previous address (Table 3). For the number of fast food restaurants and recreational facilities, a higher proportion of moves (64-68%) was to an address within the same quintile. The moves that resulted in a shift in quintile were more likely to be into neighborhoods with higher nSES (31% vs. 25% into lower nSES), percent commuters by car/motorcycle (35% vs. 30% into lower percent commuters), numbers of fast food restaurants (17% vs. 15%), total businesses (34% vs. 29%) and recreational facilities (21% vs. 15%); and lower population density (33% vs. 23% moves into higher population density), traffic density (30% vs. 26%) and street connectivity (32% vs. 28%). Changes in the

Table 1
Baseline study sample characteristics, CA Multiethnic Cohort, 1993–2010.

Baseline characteristics	Males	Females
	N = 40,870	N = 54,602
Age at cohort entry (years) ^a	61.7 ± 8.2	60.8 ± 8.4
Race/ethnicity (%)		
African American	26.2	34.9
Japanese American	13.9	10.9
Latino	48.4	38.5
White	11.5	15.7
Family history of colorectal cancer (%)	6.0	7.6
Body mass index (kg/m ² , %)		
<25.0	31.6	36.4
25.0–<30.0	49.7	35.7
≥30.0	18.7	27.9
Education completed (%)		
less than high school	28.4	26.4
high school	21.7	26.7
some college	28.6	29.0
college or higher	21.3	17.9
Smoking status (%)		
Never smoker	30.2	56.6
Past smoker	50.5	29.2
Current smoker	19.4	14.2
Pack-years of cigarette smoking ^{a,b}	17.7 ± 15.6	13.9 ± 13.6
History of intestinal polyps (%)	4.5	3.6
History of diabetes (%)	15.0	13.0
Physical activity >2.5 hrs/wk (%)	11.3	8.0
Nonsteroidal anti-inflammatory use (%) ^d	54.0	60.1
Current use of hormone replacement therapy (%)	–	23.0
Multivitamin use (%) ^e	48.2	53.6
Energy intake (kcal/day) ^{a,f}	2390 ± 1223	1968 ± 1021
Alcohol intake (g/day) ^a	13.5 ± 33.6	3.7 ± 14.1
Red & processed meat (g/1000 kcal/day) ^a	22.2 ± 14.5	18.3 ± 13.4
Fiber (g/1000 kcal/day) ^a	11.8 ± 4.2	13.3 ± 4.4
Calcium (mg/1000 kcal/day) ^a	376.1 ± 120.4	411.9 ± 136.6
Folacin (mcg/1000 kcal/day) ^a	181.6 ± 78.5	196.7 ± 82.4
Vitamin D (IU/1000 kcal/day) ^a	154.8 ± 189.0	188.3 ± 229.1

^aMean ± standard deviation.^bFor current and former smokers only.^cHours per day of vigorous activity.^dEver used at least 2 times per week for 1 month or longer.^eRegular use (at least once a week) in the last year.^fAverage energy intake during the last year.

neighborhoods themselves between census periods were less drastic and most likely to be within the same quintile for all attributes except percent commuters, while most quintile shifts amounted to one quintile up or down (Supplementary Fig. 1). Neighborhood changes accompanied by a quintile shift were somewhat more likely to be into a higher quintile of street connectivity and the numbers of fast food restaurants, supermarkets/farmers' markets, businesses and recreational facilities;

Table 2
Distribution (%) of the number of moves and median time at address among Multiethnic Cohort participants residing in California, 1993–2010.

Sex/ethnicity	N	Number of moves (address changes)						Median time at address (y) ^a
		0	1	2	3	4	5+	
		Participants (%)						
Men	40870	61.5	21.5	10.1	4.2	1.7	1.0	6.4
African American	10720	61.0	21.5	10.2	4.3	1.9	1.2	6.1
Japanese American	5659	72.7	18.7	5.9	1.7	0.7	0.3	7.2
Latino	19797	59.1	21.5	11.3	5.0	2.0	1.2	6.3
White	4694	59.4	25.2	9.8	3.6	1.4	0.6	6.6
Women	54602	58.7	22.8	10.8	4.7	1.9	1.1	5.6
African American	19062	57.9	22.4	11.2	5.1	2.1	1.3	5.4
Japanese American	5964	71.8	19.8	5.9	1.7	0.5	0.2	7.4
Latino	21030	56.0	22.9	12.0	5.4	2.4	1.3	5.5
White	8546	58.0	25.6	10.4	4.0	1.3	0.8	5.6

^a Among participants who had 1 or more address changes.

and into a lower quintile of population density and traffic density. Neighborhood SES was nearly equally likely to increase (22%) or decrease (23%) between census periods.

Among the 10 neighborhood obesogenic attributes, upward change in population density was most consistently associated with the increased risk of CRC across sex, race/ethnicity, and moving status (Table 4; Supplementary Table S3). For non-movers of all races/ethnicities, upward change in population density was statistically significantly associated with higher CRC risk among men (HR: 1.35, 95% CI: 1.03–1.77) and women (HR: 1.41, 95% CI: 1.06–1.88). The association among men remained significant after Bonferroni correction ($p < 0.005$). For movers, the association was borderline significant among men (HR: 1.42, 95% CI: 0.97–2.06) but not among women (HR: 1.24, 95% CI: 0.87–1.78). In race/ethnicity-stratified analyses, the same statistically significant association was observed among female African American and Japanese American non-movers, male Latino non-movers, as well as female African American and male White movers, with HRs ranging between 1.42 and 3.07. Downward change in population density was significantly related to higher CRC risk among female non-movers of all races/ethnicities (HR: 1.33; 95% CI: 1.06–1.67) and within White female non-movers (HR: 2.54; 95% CI: 1.52–4.26).

Among male non-movers of any race/ethnicity, upward changes in

Table 3
Distribution (% shifts) of quintile change in neighborhood attributes, CA Multiethnic Cohort.

Neighborhood attribute	Same address (neighborhood change, N = 118,619)			Address changes (physical moves, N = 97,744)		
	Down ^a	Same Q ^b	Up ^c	Down ^a	Same Q ^b	Up ^c
nSES	22.8	55.1	22.1	25.3	44.2	30.5
Population density	22.4	65.4	12.2	32.7	43.8	23.4
Fast food	9.1	75.9	15.0	14.6	68.8	16.7
Restaurants ^d	19.5	50.3	30.2	28.4	39.5	32.1
Supermarkets	17.7	55.8	26.5	26.1	47.0	26.9
Percent commute	31.6	36.3	32.1	29.6	35.5	34.9
Total businesses	21.2	56.1	22.7	28.8	37.7	33.5
Traffic density	14.6	71.7	13.7	30.4	43.2	26.4
Street connectivity (Gamma)	21.0	52.9	26.2	31.7	40.3	28.0
Recreational facilities	10.2	67.2	22.5	15.1	63.9	21.0

NOTE: Percentage of shifts in the indicated direction of change throughout the study period. Change is measured relative to the preceding residential address or census period for each participant.

^a A shift down by 1 or more distribution quintiles.^b Same distribution quintile.^c A shift up by 1 or more distribution quintiles.^d Other than fast food restaurants.

Table 4
Association between neighborhood change and colorectal cancer incidence, CA Multiethnic Cohort, 1993–2010.

Parameter	Direction of change ^a	Men			Women		
		All	Nonmovers	Movers (1997-2005)	All	Nonmovers	Movers (1997-2005)
		HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
nSES	down	1.02 (0.85–1.22)	1.13 (0.91–1.41)	0.88 (0.58–1.33)	1.01 (0.84–1.22)	0.88 (0.68–1.14)	1.20 (0.84–1.70)
	up	1.01 (0.86–1.19)	1.11 (0.91–1.37)	0.86 (0.63–1.17)	1.06 (0.92–1.24)	1.05 (0.85–1.29)	1.04 (0.76–1.42)
Population density	down	1.07 (0.91–1.27)	1.06 (0.86–1.31)	1.18 (0.85–1.64)	1.08 (0.91–1.28)	1.33 (1.06–1.67)	1.14 (0.80–1.61)
	up	1.37 (1.12–1.67)	1.35 (1.03–1.77)	1.42 (0.97–2.06)	1.23 (0.99–1.52)	1.41 (1.06–1.88)	1.24 (0.87–1.78)
Fast food	down	1.03 (0.76–1.38)	0.87 (0.62–1.22)	1.20 (0.65–2.21)	1.09 (0.84–1.42)	0.87 (0.64–1.18)	1.37 (0.75–2.51)
	up	1.19 (0.97–1.45)	1.14 (0.86–1.50)	1.10 (0.76–1.59)	0.96 (0.79–1.17)	0.95 (0.73–1.25)	0.99 (0.68–1.44)
Restaurants ^b	down	0.89 (0.74–1.09)	0.92 (0.73–1.17)	0.87 (0.59–1.29)	1.06 (0.88–1.27)	1.09 (0.86–1.37)	1.16 (0.85–1.60)
	up	0.94 (0.81–1.10)	0.85 (0.69–1.04)	1.14 (0.82–1.57)	1.07 (0.89–1.29)	1.06 (0.87–1.30)	1.27 (0.91–1.77)
Supermarkets	down	1.14 (0.96–1.36)	1.15 (0.92–1.44)	1.08 (0.79–1.48)	0.95 (0.79–1.15)	1.05 (0.81–1.37)	0.77 (0.54–1.09)
	up	0.95 (0.80–1.13)	0.96 (0.77–1.19)	0.84 (0.59–1.19)	1.12 (0.96–1.30)	1.04 (0.84–1.28)	1.06 (0.77–1.44)
Percent commute	down	0.87 (0.74–1.02)	0.88 (0.72–1.07)	0.80 (0.57–1.13)	0.99 (0.85–1.16)	0.96 (0.79–1.17)	1.00 (0.71–1.40)
	up	1.08 (0.93–1.27)	1.03 (0.85–1.26)	1.00 (0.74–1.36)	1.10 (0.94–1.30)	1.14 (0.92–1.41)	1.02 (0.74–1.40)
Total businesses	down	0.89 (0.74–1.07)	0.83 (0.65–1.06)	1.10 (0.78–1.54)	0.93 (0.79–1.10)	0.98 (0.78–1.23)	0.79 (0.57–1.09)
	up	0.87 (0.73–1.03)	0.76 (0.60–0.95)	1.07 (0.77–1.50)	0.92 (0.77–1.10)	1.06 (0.84–1.33)	0.74 (0.52–1.07)
Traffic density	down	0.80 (0.63–1.01)	0.66 (0.46–0.96)	0.90 (0.60–1.34)	1.18 (0.94–1.47)	1.18 (0.83–1.70)	1.43 (1.02–2.00)
	up	0.84 (0.70–1.01)	0.91 (0.70–1.17)	0.83 (0.56–1.22)	1.09 (0.88–1.36)	0.99 (0.74–1.32)	0.99 (0.65–1.52)
Street Connectivity (Gamma)	down	1.17 (0.96–1.42)	1.34 (1.03–1.73)	1.25 (0.88–1.78)	0.95 (0.78–1.16)	0.91 (0.68–1.21)	0.96 (0.65–1.44)
	up	1.03 (0.87–1.22)	1.02 (0.81–1.29)	1.03 (0.72–1.46)	0.99 (0.85–1.16)	1.06 (0.85–1.32)	0.86 (0.60–1.23)
Recreational facilities	down	1.18 (0.93–1.50)	1.54 (1.14–2.06)	0.69 (0.40–1.20)	0.80 (0.57–1.13)	0.75 (0.48–1.17)	0.90 (0.45–1.78)
	up	1.07 (0.91–1.27)	1.09 (0.88–1.35)	1.09 (0.78–1.52)	0.83 (0.70–0.98)	0.70 (0.55–0.89)	1.12 (0.83–1.51)

NOTE: All models are adjusted for the following covariates measured at baseline: age at study entry, body mass index, family history of CRC, history of intestinal polyps, education, cigarette smoking, multivitamin use at least once a week in the last year, use of nonsteroidal anti-inflammatory medication, alcohol consumption during the last year, moderate to vigorous physical activity during the last year, history of diabetes, average energy intake during the last year; dietary intake of red and processed meat, dietary fiber, calcium, folate, and Vitamin D; use of hormone therapy (women only), and baseline level of the corresponding neighborhood factor. HR: hazard ratio; CI: confidence interval. Asterisk (*) indicates associations statistically significant after Bonferroni correction for multiple comparisons.

^a A shift up or down by 1 or more distribution quintiles.

^b Other than fast food restaurants.

the number of businesses and downward change in traffic density were associated with lower CRC risk (HR: 0.76; 95% CI: 0.60–0.95 and HR: 0.66; 95% CI: 0.46–0.96; respectively), while downward changes in street connectivity or the number of recreational facilities were associated with higher CRC risk (HR: 1.34; 95% CI: 1.03–1.73 and HR: 1.54; 95% CI: 1.14–2.06; respectively). The latter association was also observed among Japanese American and White male non-movers. On the other hand, upward change in the number of recreational facilities was associated with lower CRC risk among female non-movers (HR: 0.70; 95% CI: 0.55–0.89); this association was significant after Bonferroni correction and was also present among African American and White female non-movers. The above associations were also observed in the sensitivity analyses with 5-year lag, although some were no longer statistically significant. Estimates from models additionally adjusted for CRC screening were within 1–3% of those from the main models. Changes in the other neighborhood attributes did not exhibit significant associations with CRC risk in more than one racial/ethnic group.

Discussion

With the multilevel, prospective data in the MEC, we are able to not only investigate the potential impact of neighborhood obesogenic environments on cancer risk at the onset of the study, but also to examine the dynamic changes of the participants’ neighborhoods over time. Thus, accounting for the neighborhood environment and its change can inform longitudinal studies of cancer etiology since such changes may more accurately capture neighborhood exposure over time. The assessment and quantification of temporal change in neighborhood exposures involves a number of challenges. If geographic units (e.g. census block groups) differ between time points, conversion of data between units may introduce additional measurement error. It has been recognized that combining data from multiple spatial scales has the potential to

influence findings and must be done carefully, accounting for data variability at different spatial scales and for the loss of information due to aggregation (Gotway & Young, 2002). Second, the neighborhood units often do not exactly match across multiple time periods, which makes it difficult to measure temporal change on the scale of neighborhood units and may introduce additional measurement error. Finally, some neighborhood characteristics, especially composite measures, such as neighborhood SES, have a data driven scale dependent on the time point of reference. When such characteristics are computed separately for each time period (census) and/or with different data sources (e.g., Census long form and ACS), the computed values may not be compatible across time periods (e.g. 1990 and 2000 U.S. Census), which prevents the use of quantitative measures of change such as arithmetic differences or cumulative averages. Time-invariant measures of neighborhood SES have been proposed in a recent study (Miles et al., 2016), but their applicability to other studies has not been determined.

Due to the above considerations, in our assessment of neighborhood change we focused on study participants and their neighborhood exposure, rather than characterizing neighborhood attributes for neighborhood units and using them as spatial variables in the analysis. Thus, change was measured for each individual through their follow-up period. This approach overcomes the first two of the above challenges. To address the third challenge, we assessed change in neighborhood attributes using census period specific quintiles of the attribute’s distribution. In other words, our measure of change represents a shift in the relative standing of a neighborhood in terms of a specific attribute, compared to all other neighborhoods from that time period that were examined in this study. Since there is no established threshold for impact for many of these attributes, we believe that our strategy was a reasonable approach.

In the analysis of neighborhood change and CRC risk, we have found that across all races/ethnicities, a relative increase in population density

was statistically significantly associated with higher CRC risk among movers and non-movers. A possible reason for this finding could be that high-density neighborhoods often have lower nSES and more inequity in resources. In our study, population density was negatively correlated with nSES ($\rho = -0.61$), which supports this hypothesis. At the same time, a relative decrease in population density was also associated with higher risk of CRC among female non-movers across all races/ethnicities. This observation illustrates that a change regardless of the direction (upward/downward) can be detrimental to health, possibly due to disruption of established behavioral routines or stress associated with changing neighborhood obesogenic environment, which may contribute to the accumulation of excess body fat (Kyrou, Chrousos, & Tsigos, 2006) and thus affect CRC risk (Ma et al., 2013).

The above findings are consistent with our earlier analysis of baseline neighborhood attributes in the MEC, reported by Canchola et al. (Canchola et al., 2017), where lower population density was associated with lower CRC risk, nonsignificantly among African American and Japanese American men and significantly among Latino women. Considering the negative correlation between population density and nSES, our findings also agree with the recent report by Zhang et al. (Zhang, Matthews, Powell-Wiley, & Xiao, 2019), which examined trajectories of nSES in relation to CRC incidence among participants of the NIH-AARP Diet and Health Study and found consistently low or decreasing nSES associated with higher CRC risk.

The number of recreational facilities exhibited consistent associations across racial/ethnic groups and in the entire study sample, but its association with CRC risk was statistically significant only among non-movers (i.e., upward change was associated with decreased risk among women). A possible reason may be that slow, gradual changes in the neighborhood composition that result in more or fewer recreational facilities tend to affect residents' health behaviors, whereas those who move to a neighborhood with fewer facilities may continue to adhere to their established health routines by using facilities outside of their new residential neighborhood. The observed protective effect of an upward change in the number of recreational facilities is also consistent with prior evidence that physical activity is protective against CRC risk (Shaw et al., 2018). A number of statistically significant associations were only observed within a single racial/ethnic group. While this suggests racial/ethnic differences in the effect of neighborhood environment on health and underscores the need to examine the effects of neighborhood change by racial/ethnic group, we cannot discount the possibility that some of these associations could be chance findings.

Neighborhoods, through material deprivation, psychosocial mechanisms and access to resources, can influence residents' health behaviors, which in turn affect their health outcomes such as cancer incidence (Gomez et al., 2015). A person's exposure to neighborhood factors can change due to moving to another neighborhood or due to changes in the neighborhood itself, such as redevelopment or neglect. It has been hypothesized that changes in the built environment may be associated with neighborhood sociodemographic characteristics and thus can either reduce or magnify existing inequalities (Hirsch et al., 2016). Additionally, individual perception of changes in the neighborhood environment can differ by social status (e.g., race/ethnicity, sex, SES, immigration) and between the two types of change.

In this analysis, a majority of the participants did not physically change residence throughout the follow-up period. Among those who did move, a vast majority had 1-2 moves, and on average resided at the same address for 5-7 years. Therefore, to properly assess the effect of neighborhood environment change due to physical moves, one needs a reasonably long follow-up to observe a sufficient number of physical moves. A more mobile population with several physical moves over many years (perhaps military families) could also be investigated.

Compared to physical moves, changes in the neighborhood environment attributes due to redevelopment or neglect were less drastic, with most neighborhoods remaining in the same distribution quintile of an attribute. Physical moves tended to result in more dramatic change in

the neighborhood attributes. As such, the impact of any changes in a neighborhood's physical characteristics on CRC risk was different from that of physical moves, for example, changes in street connectivity, the number of businesses and recreational facilities affected CRC risk among non-movers for all racial/ethnic groups but not among movers. In terms of population density, both types of change (upward and downward) were associated with CRC risk. Thus, our results provide evidence that the effect of changes in the neighborhood social and built environments on CRC risk is different from that of physically moving to another neighborhood. This further underscores the differences between the two types of neighborhood environment change and the need to properly distinguish them in studies of neighborhood environment change over time.

Strengths of this investigation include its large sample size, long follow-up period, and multiethnic composition, that allowed the assessment of neighborhood changes over long (>15 y) periods of time and examining their effect across sexes and racial/ethnic groups. A limitation of the analysis was that the geographic location of participants was largely one county, Los Angeles County, which may limit generalizability of our results to other geographic locations. Second, due to the limited temporal resolution of our data (three points in time corresponding to U.S. Census years or, for some neighborhood attributes, a measurement window of 1-3 years), we were unable to capture neighborhood changes that occurred in shorter time intervals or to examine more precise timing of change. However, these may not be relevant for diseases with long latency periods. Third, conversion of 2010 U.S. Census tract data to block group scale may have inflated the measurement error, and the results may have been influenced by the choice of geographic unit, which is known as the "Modifiable Areal Unit Problem" (Flowerdew, Manley, & Sabel, 2008; Haynes, Daras, Reading, & Jones, 2007; Houston, 2014); however, this was likely to be limited given this was done only for one variable over one time period. Fourth, while we accounted for the correlation within block groups, our analysis did not account for potential spatial correlation between neighborhoods in close proximity to one another. We have also adjusted our models for the baseline levels of neighborhood attributes. Although baseline adjustment is not recommended under some conditions, such as change measured before baseline and unreliable or unstable outcome measure (Glymour, Weuve, Berkman, Kawachi, & Robins, 2005), these conditions do not apply to our study. Fifth, it is unclear whether block groups are the best scale to represent residents' perceptions of neighborhood environment change. Haynes et al. (Haynes et al., 2007) observed that residents' perception of neighborhoods typically refers to a very small distance around their residence and thus does not cover a predefined areal unit such as a block group; however, Diez-Roux et al. (Diez-Roux, 2007) pointed to good correlation between census block boundaries and perceived neighborhoods. Besides, using census boundaries allows one to efficiently examine a number of social and built environment factors across a large number of geographic units that would have been costly to obtain through other sources. Lastly, we only considered residential neighborhood environment, although it has been recognized that work environment may play a greater role in health outcomes than residential environment (Burgoine & Monsivais, 2013). Few studies have collected neighborhood information beyond residential, and devising reliable methods to collect it would be a promising area of future research. Future efforts could also examine different types of moves (forced move, move by choice, change in employment or family situation, etc.) and their impact on health risks.

In summary, this study provides a framework for examining neighborhood change in relation to cancer risk. We observed that changes in the neighborhood obesogenic environment, both due to change of residence and due to change in the neighborhood itself, are associated with CRC risk across several racial/ethnic groups. Further studies are needed to continue method development and refinement in this area, to better delineate the effects of changing neighborhood environment exposure among different racial/ethnic groups and to examine possible

mechanisms of the influence of neighborhood environment change on health behaviors and outcomes.

Ethical approval

The Multiethnic Cohort study protocol was approved by the Institutional Review Boards of the University of Hawaii and the University of Southern California.

Declaration of competing interest

None.

CRediT authorship contribution statement

Yurii B. Shvetsov: Methodology, Software, Formal analysis, Writing - original draft. **Salma Shariff-Marco:** Conceptualization, Methodology, Resources, Writing - review & editing. **Juan Yang:** Software, Data curation. **Shannon M. Conroy:** Writing - review & editing. **Alison J. Canchola:** Software, Formal analysis, Writing - review & editing. **Cheryl L. Albright:** Conceptualization, Writing - review & editing. **Song-Yi Park:** Writing - review & editing. **Kristine R. Monroe:** Writing - review & editing. **Loïc Le Marchand:** Resources, Writing - review & editing, Supervision, Funding acquisition. **Scarlett Lin Gomez:** Conceptualization, Methodology, Resources, Writing - review & editing. **Lynne R. Wilkens:** Methodology, Resources, Writing - review & editing, Funding acquisition. **Iona Cheng:** Conceptualization, Methodology, Resources, Writing - review & editing, Supervision, Project administration, Funding acquisition.

Acknowledgements

We thank all participants in the Multiethnic Cohort Study. We also thank Andrew Hertz for collecting, visualizing and recoding the GIS neighborhood data. This work was supported by National Cancer Institute grant R01 CA154644. The Multiethnic Cohort Study was supported by National Cancer Institute grant U01 CA164973. The development of the California Neighborhoods Data System was supported by National Cancer Institute grant (R03 CA117324) and by a Rapid Response Surveillance Study from the SEER program under a modification to contract N01-PC-35136.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ssmph.2019.100532>.

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