Neighbourhood environment and socioeconomic inequalities in cancer admissions: a prospective study using UK Biobank and linked administrative records

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Abstract

Purpose: Neighbourhood environments may influence cancer risk. Average population effect estimates might mask differential effects by socioeconomic position. Improving neighbourhood environments could inadvertently widen health inequalities if important differences are overlooked.

Methods: Using linked records of hospital admissions in UK Biobank, we assessed associations between admission with a primary diagnosis of cancer (any/breast/colorectal), and exposure to neighbourhood greenspace, physical activity facilities, and takeaway food stores, and whether household income and area deprivation modify these associations. We used adjusted Cox proportional hazards models, and estimated relative excess risks due to interaction (RERI) to assess effect modification.

Results: Associations between neighbourhood exposures and cancer-related hospitalisations were weak to null overall, but with some evidence of effect modification. Most notably, more greenspace near home was associated with 16% lower hazard of cancer-related hospital admission in deprived areas (95%CI: 2%-29%). This was further pronounced for people in low-income households in deprived areas, and for breast cancer.

Conclusions: In deprived neighbourhoods, increasing the amount of greenspace may help reduce cancer-related hospitalisations. Examining effect modification by multiple socioeconomic indicators can yield greater insight into how social and environmental factors interact to influence cancer incidence. This may help avoid perpetuating cancer inequalities when designing neighbourhood environment interventions.

Background

Exposure to features of the neighbourhood residential environment has the potential to influence important cancer-related behavioural risks by promoting or hindering physical activity and diet, and exacerbating or mitigating chronic stress. Some environmental exposures, such as greenspace, may also act as a buffer against physical environmental hazards such as air pollution, and boost immune function, potentially offering further protection against cancer[1,2]. The unequal distribution of these environmental exposures by key socio-economic factors may also contribute to inequalities in cancer risk and mortality.

Over the past 25 years, cross-sectional studies have produced inconsistent evidence linking neighbourhood built environment characteristics to chronic disease outcomes[3–5], adiposity and obesity[6], mental health[7], and health behaviours such as PA and diet[8,9]. Recently, findings from longitudinal studies have also contributed to the evidence base (e.g.[10–12]), and these have helped to better elucidate the true causal relationships between neighbourhood environments and these outcomes, by providing greater certainty about the temporal sequence of exposures and outcomes of interest, by eliminating the possibility of reverse causation. The increasing ability to link hospital records and mortality registers to population-based cohorts with geographical data on neighbourhood environments also provides opportunities to examine whether neighbourhood environmental exposures are associated with objectively recorded, prospective health and mortality outcomes.

Numerous features of the neighbourhood built environment have been hypothesised to influence health, mortality and intermediate behaviours and risk factors. These include, the retail food environment (including proximity or density of healthy and unhealthy food stores), accessibility of formal recreation facilities for physical activity (such as public swimming pools, gyms, sports fields), and green spaces such as public parks and private gardens. The potential for food and formal PA environments to influence health via diet and physical activity is straightforward. Greenspace may influence health through a wider range of mechanisms, including facilitating recreational PA, or functional PA such as gardening or active travel, or via other pathways relating to the regulation of stress hormones, improved immune function through exposure to diverse microorganisms, and reduced exposure to air pollution[13], all of which may influence risk of cancer and other chronic diseases. The evidence base for these neighbourhood effects on health is inconsistent, and the relative importance of different neighbourhood exposures is unclear. Causal neighbourhood effects on health are likely to be small, and part of a broader swathe of environmental, social and structural drivers of health behaviours and outcomes, each contributing incrementally to the complex physical and social environments that constrain our ability to make healthy lifestyle choices and mitigate the stresses of modern life.

An important aspect of better understanding these relationships is the possibility that they are not uniform across the population, but that some population subgroups and geographical areas are more sensitive to their neighbourhood environment than others. Important effects concentrated in particular population subgroups or particular places may be masked by average, population-wide estimates. Socioeconomic differences may be one source of such effect heterogeneity. Results of some studies suggest heterogenous neighbourhood health effects according to individual socioeconomic status[14,15] or neighbourhood deprivation[16,17]. These may arise if preferences for particular neighbourhood resources vary according to individual socioeconomic status, regardless of the physical availability of neighbourhood resources, e.g. if low-income households tend to make more use of fast-food/takeaway stores, or if access to gyms and leisure centres is restricted to people from high-income households because of membership fees. Or differences may arise if the quality or accessibility of resources that are present in an area is unevenly distributed spatially, according to area-level deprivation (rather than individual/household socioeconomic position), e.g. if more deprived areas have poorer quality public greenspace. On the other hand, if, for example, greenspace promotes health without an attendant increase in financial costs to the individual, then access to local greenspace may offset inequitable access to formal PA facilities, and therefore have a larger effect in deprived areas or for low-income households. Regardless of the direction of any such heterogeneity of effect, it remains a poorly understood aspect of the relationship between the neighbourhood environment and health. If differential benefits or harms of neighbourhood characteristics are observed by measures of individual socioeconomic status, such as household income, or by neighbourhood deprivation, then any efforts to improve population health by improving neighbourhood built environments (e.g. increasing availability of

PA facilities or reducing the number of fast-food outlets near residential areas) may widen health inequalities if they are blind to socially differential impacts[18].

In this paper we use baseline UK Biobank data on neighbourhood exposures to PA facilities, greenspace and fast-food stores, linked to records of subsequent hospital admissions up to January 2016, to examine (1) the relative hazard of being admitted to hospital with a primary diagnosis of cancer, according to exposure to each of the neighbourhood characteristics, and (2) whether there is evidence of effect modification of those associations by household income and/or area deprivation.

Methods

Study design and data collection

We used data from UK Biobank (project 17380), the scientific rationale, study design and survey methods for which have been described elsewhere[19]. More than half a million individuals were recruited to visit one of 22 UK Biobank assessment centres across the UK between 2006 and 2010. All individuals aged 40–69 years living within a 25-mile radius of an assessment centre and listed on National Health Service (NHS) patient registers were invited to participate in the study. The age range was chosen by UK Biobank as an important period for the development of many chronic diseases.

Neighbourhood environment data

Linked to UK Biobank is a high-resolution spatial database of a range of objectively measured characteristics of the physical environment surrounding each participant's exact residential address, known as the UK Biobank Urban Morphometric Platform (UKBUMP). Environmental data in UKBUMP were derived, using automated processes, from multiple pre-existing sources roughly contemporaneous with the individual baseline assessment[20]. Over time, as researchers work with UK Biobank, new linked data are being made available to the research community, including additional environmental measures of greenspace[21] that we have used here in addition to measures from the original UKBUMP.

Linked hospital admissions data

Ongoing prospective linkage of the cohort to administrative health records is a key feature of the UK Biobank resource. At the time of analysis, linked Hospital Episode Statistics were available up to January 2016. These contain information on hospital admissions coded using the International Statistical Classification of Diseases and Related Health Problems, 10th Revision (ICD-10). We used these data to identify incident admissions to hospital for cancer.

Outcomes

Outcomes were any hospital admission for which the primary diagnosis is recorded as cancer (ICD-10 codes C00-C97). In a set of secondary analyses we examine breast cancer and colorectal cancers specifically, as these have some of the strongest links to physical activity[22] and, to a lesser extent, diet[23], two potential mediators of the neighbourhood effects being examined.

Neighbourhood exposures

Three measures of the neighbourhood built environment were examined. To account for skewed distributions and to facilitate a categorical approach to the analysis of effect modification[24], each exposure was split into four categories. The exposures we examined were:

(1) Availability of PA facilities: number of formal PA facilities within a one-kilometre street-network distance of each participant's home address, categorised as 0, 1, 2–3, or 4 or more.

(2) Fast-food proximity: street-network distance in metres from participants' home address to the nearest 'hot/cold fast-food outlet/takeaway', categorised as < 500 m, 500–999 m, 1000–1999 m, 2000 m+.

(3) Greenspace: percentage of 300 m Euclidean buffer around home address classified as 'greenspace' or 'domestic garden' in the Generalised Land Use Database. Combining 'greenspace' and 'gardens' is consistent with previous research using the GLUD to examine relationships with health[10]. A 300 m buffer was chosen to capture greenspace in the immediate vicinity of a person's home. There is some evidence that 300 m is a distance from home beyond which the use of green spaces quickly declines[25,26], and it has been proposed in the UK as a benchmark for greenspace provision[27]. Greenspace was grouped into quartiles.

Exposures (1) and (2) were derived in the UKBUMP from OS AddressBase Premium 2012[20], while (3) was derived by Wheeler et al from the Generalised Land Use Database 2005[21]. We restricted the analyses to people residing in England, because the greenspace data for exposure (3) were not available for UK Biobank participants in Wales and Scotland.

Potential effect modifiers

We examined whether the association between each neighbourhood exposure and cancer admissions was modified by binary indicators for annual, pre-tax household income (<£31,000 or ≥£31,000) and area deprivation (most deprived 40% of UK census output areas vs least deprived 60%, based on the Townsend index). When testing for effect modification, household income and area deprivation were combined with each primary exposure into a categorical variable capturing all combinations of levels of the exposure and potential modifier, with a single reference category (see below for details). We also examined the combined modifying role of income and deprivation. Area-based and individual indicators of socioeconomic disadvantage have been shown to contribute to health outcomes independently of one another, providing a rationale for examining them both in parallel and in combination[28].

Potential confounders

Based on information from previous studies, we identified potential confounders of the primary associations as age (years), sex (binary), ethnicity (White/non-White), educational qualifications (College or University degree; A levels; AS levels or equivalent; O levels or below; other), employment status (paid work; retired; unable to work; unemployed; or other), urban/non-urban, UK Biobank assessment centre, and neighbourhood residential density (count of residential dwellings within a 1-km street-network buffer of home address, log transformed). Annual household income (<£18,000, £18,000–30,999, £31,000–51,999, ≥£52,000) and area deprivation (Townsend score) were also included as possible confounders in any models when not being tested as a potential effect modifier. We also adjusted models for smoking status (current/previous/never), alcohol intake frequency (less than/at least 3 times per week) as these are important risk factors for the outcome and may be correlated with neighbourhood, and number of years living at current (baseline) address to at least partially condition on pre-baseline exposure to neighbourhood environment, which could act as a confounder.

Statistical analysis

Of the 502,617 participants in UK Biobank for whom some data were available, 502,544 remained after withdrawals were excluded, and 355,691 of these individuals lived in England and had complete data on covariates and data for at least one measure of the neighbourhood environment. Of these, we excluded 29,112 individuals with a previous cancer diagnosis at baseline, leaving a possible N = 326,579 for analysis (Fig. 1). The final analytic sample sizes varied according to availability of the neighbourhood variable under examination. The maximum follow-up time after baseline assessment was 9.8 years, but varied according to the date of an individual's recruitment to the study.

Baseline characteristics were summarised by the mean (and standard deviation) or median (and interquartile range) for continuous variables and number (and percent) for categorical variables. We then examined associations between neighbourhood exposure and incident hospital admission due to cancer following baseline assessment using multivariable Cox proportional hazard models, with adjustment for potential confounders and censoring for death. Results are expressed as hazard ratios (HRs) and 95% confidence intervals (95% CI). The proportional hazards assumption was tested by visual inspection of adjusted log-log plots (Supplementary Figure S3). The reference categories for each neighbourhood exposure are the hypothetically least health-promoting (lowest availability of PA facilities, shortest distance to nearest fast-food store, least greenspace).

We examined whether the primary associations were modified by area deprivation and household income. In line with STROBE recommendations[29] and using the method described by Li and Chambless[30] and VanderWeele[24], the relative excess risk due to interaction (RERI) was estimated to assess effect modification on the additive scale. When dealing with binary and time-to-event outcomes, the decision to examine effect modification on either the multiplicative or the additive scale has implications for interpretation. The additive scale provides important information about the potential public health consequences of intervening on the exposure, in different strata of the effect modifier. This is not information that can usually be estimated directly from an examination of effect modification on the multiplicative scale[24]. The RERI is estimated by first estimating the HR for each combination of the exposure and potential modifier values relative to a single reference category, in this case the least hypothetically health-promoting level of the respective neighbourhood variable (no PA facilities; <500 m from nearest fast-food store; or quartile with least greenspace), and either low income (<£31,000) or more deprived area (home address located in a census output area in the most deprived 40% of all UK areas). In other words, the reference category in each analysis is the group expected to have the highest baseline risk of the outcome. Then, taking the HRs from this model for the least and most exposed groups, the RERI is estimated as:

$$RERI = HR_{11} - HR_{10} - HR_{01} + 1$$

For the model assessing effect modification of PA facility availability by household income, for example, HR_{11} represents the HR (relative to the reference category) for people in high-income households (at least £31,000 per year) and who have the highest level of neighbourhood availability of PA facilities (4 or more within 1000 m of home); HR_{10} represents the HR for people in low-income households with 4 or more PA facilities near home; and HR_{01} is the HR for people in high-income households with no PA facilities near home.

For the models of the other neighbourhood exposures, and models of effect modification by area deprivation, subscript *1* represents those most exposed to the potentially health-promoting neighbourhood exposure and less deprived areas, respectively. As such, a RERI value greater than zero – which implies a positive departure from additivity – suggests that in this case any estimated protective effect of the neighbourhood variable among people in low-income households or in more deprived areas is greater than the estimated protective effect among people from high-income households or less deprived areas. In contrast, a RERI < 0 suggests any protective effect of the neighbourhood variable is greater in the high-income/less deprived group. By contrasting the two extreme categories of exposure we assume this is the most relevant contrast.

Finally, we separately estimated income- and deprivation-stratum specific HRs comparing the groups least and most exposed to each neighbourhood exposure, and HRs for each stratum of income and area deprivation combined.

All analyses were conducted using Stata v14.2 (StataCorp LP, College Station, TX, USA). While the primary analyses for all cancer and colorectal cancer were adjusted for sex, we also repeated these analyses separately for males and females. Analysis of breast cancer admissions was restricted to participants recorded as female.

Sensitivity analyses

The spatial data used in the creation of the UKBUMP to ascertain the neighbourhood food and physical activity exposures were recorded in 2012, just after the baseline data collection period[20]. While it is assumed that neighbourhood exposure will be sufficiently constant over this period, we check this assumption by conducting a sensitivity analysis in which follow-up is restricted to the period from 2012 onwards for all participants, rather than from the baseline assessment date (which could be as early as 2006).

Results

Descriptive

Table 1 summarises the characteristics of the study participants at the baseline assessment. The sample has a mean age of 56 years at baseline and was predominantly of White ethnicity and urban dwelling. Reflecting the age of the sample, just over half were educated to no higher than O levels, and six in every ten were employed at baseline. Participants were evenly distributed across income categories, with roughly half living in households with an annual gross income below £31,000, while 29% lived in the more deprived 40% of areas in the UK.

Table 1
Descriptive characteristics of sample (n = 326,579)

Variable	Participants (n = 326,579)
Female (n, %)	168,663 (51.65%)
Age (years) (mean, SD)	55.96 (8.09)
Non-White ethnicity (n, %)	16,850 (5.16%)
Urban (n, %)	279,786 (85.67%)
Education (n, %)	
College or University degree	112,131 (34.34%)
A levels/AS levels or equivalent	38,051 (11.65%)
O levels or below/other	176,397 (54.01%)
Employment status (n, %)	
Paid work	201,696 (61.76%)
Retired	98,978 (30.31%)
Unable to work	8,948 (2.74%)
Unemployed	5,140 (1.57%)
Other	11,817 (3.62%)
Residential density (residential sites per 1000m buffer) (median, IQR)	1921 (1109–3130)
Years at current address (median, IQR)	15 (7–25)
Area deprivation (mean Townsend score, SD)	-1.42 (2.97)
Area deprivation (n, % in two most deprived quintiles of the UK)	95,818 (29.34%)
Household income (n, %)	
<£18,000	72,429 (22.18%)
£18 000–30 999	82,854 (25.37%)
£31 000–51 999	85,845 (26.29%)
£52 000 or more	85,451 (26.17%)
Smoking status (n, %)	
Current	33,789 (10.35%)
Previous	113,722 (34.82%)
Never	179,068 (54.83%)

Variable	Participants (n = 326,579)
Frequency of alcohol consumption (n, % ≥3 times per week)	147,838 (45.27%)

The mean follow-up time for participants was 6.8 years. Over the follow-up period, 13,935 individuals (4.27%) were admitted to hospital with cancer (Table 2). Proportionally, there were more hospital admissions among people from low-income households, whereas admissions were similar across levels of area deprivation.

Table 2
Hospital admissions by household income and area deprivation

	N	Number of cancer admissions (%)
Total	326,579	13,935 (4.27)
Household income (annual pre-tax)		
<£31,000	155,283	8126 (5.23)
£31,000 or more	171,296	5809 (3.39)
Area deprivation		
More deprived	95,818	4043 (4.22)
Less deprived	230,761	9892 (4.29)
* Self-reported average total household income before tax		
** 'More deprived' refers to people living in areas in the top two most deprived quintiles of the UK, based on the Townsend index.		

Associations between neighbourhood characteristics and admissions for all cancer types

Figure 2 summarises the hazard ratios for hospital admissions due to cancer associated with each of the three neighbourhood environment measures, across the sample as a whole. While 95% CIs for all associations include 1, there was some indication of a slightly lower hazard of cancer-related hospital admission among those people with at least four PA facilities within one kilometre of their home, compared to people with no nearby formal PA facilities (HR = 0.96; 95%CI: 0.91–1.01), but no evidence that one, two or three facilities offers a benefit compared to the reference. For fast-food proximity and neighbourhood greenspace, we observed no association with risk of cancer-related admission when averaging across the study population as a whole.

Modification of associations between neighbourhood characteristics and cancer-related hospital admissions, by

income and area deprivation

The association between PA facilities and all cancer admissions does not appear to be modified by income or by area deprivation. Stratum-specific HRs were similar across socioeconomic groups, and RERIs were close to zero for both potential effect modifiers (Table 3).

Table 3
Modification of the association between built environment variables and hospital admissions due to cancer, by household income and area deprivation

Cancer-related admissions	*Annual household income**		*Area deprivation***	
	< £31,000	**At least £31,000**	**More deprived**	**Less deprived**
	HR (95% CI)	*HR (95% CI)*	*HR (95% CI)*	*HR (95% CI)*
Number of PA facilities				
None (ref)	1.00	0.96 (0.90, 1.02) P = 0.209	1.00	1.02 (0.94, 1.11) P = 0.605
One	0.98 (0.92, 1.05) P = 0.588	0.98 (0.91, 1.06) P = 0.608	1.07 (0.97, 1.19) P = 0.175	1.00 (0.92, 1.09) P = 0.961
2–3	1.00 (0.94, 1.06) P = 0.918	0.94 (0.87, 1.00) P = 0.066	1.06 (0.96, 1.16) P = 0.249	0.99 (0.91, 1.08) P = 0.844
4 or more	0.99 (0.93, 1.05) P = 0.676	0.89 (0.83, 0.96) P = 0.001	1.01 (0.92, 1.11) P = 0.846	0.98 (0.90, 1.06) P = 0.581
Stratum-specific HRs (4 + facilities vs 0)	0.97 (0.91, 1.04) P = 0.395	0.95 (0.87, 1.03) P = 0.184	1.02 (0.92, 1.13) P = 0.673	0.95 (0.89, 1.01) P = 0.110
Relative excess risk due to interaction (RERI)	-0.058 (-0.145, 0.030) P = 0.197		-0.055 (-0.163, 0.053) P = 0.320	
Fast-food proximity				
Closer than 500m (ref)	1.00	0.89 (0.82, 0.97) P = 0.006	1.00	0.92 (0.85, 0.99) P = 0.029
500-999m	0.94 (0.88, 1.00) P = 0.053	0.93 (0.86, 1.00) P = 0.039	0.90 (0.83, 0.97) P = 0.009	0.94 (0.88, 1.01) P = 0.083
1000-1999m	0.98 (0.92, 1.04) P = 0.472	0.90 (0.84, 0.97) P = 0.008	0.99 (0.91, 1.08) P = 0.843	0.92 (0.85, 0.98) P = 0.017
At least 2000m	0.94 (0.88, 1.01) P = 0.098	0.91 (0.84, 0.99) P = 0.021	0.93 (0.84, 1.03) P = 0.165	0.92 (0.85, 0.99) P = 0.024
Stratum-specific HRs (≥ 2000m vs < 500m)	0.97 (0.90, 1.05) P = 0.451	0.97 (0.89, 1.07) P = 0.591	0.93 (0.83, 1.04) P = 0.187	1.00 (0.93, 1.07) P = 0.966

* Self-reported average total household income before tax

** 'More deprived' refers to people living in areas in the top two most deprived quintiles of the UK, based on the Townsend index.

Q = quartile

Cancer-related admissions	*Annual household income**		*Area deprivation***	
	< £31,000	**At least £31,000**	**More deprived**	**Less deprived**
	HR (95% CI)	*HR (95% CI)*	*HR (95% CI)*	*HR (95% CI)*
Relative excess risk due to interaction (RERI)	0.082 (-0.012, 0.176) P = 0.088		0.070 (-0.042, 0.182) P = 0.218	
Greenspace				
Q1 (least greenspace) (ref)	1.00	0.86 (0.80, 0.93) P = 0.000	1.00	0.93 (0.87, 1.01) P = 0.070
Q2	0.98 (0.92, 1.05) P = 0.595	0.91 (0.84, 0.98) P = 0.012	0.99 (0.92, 1.07) P = 0.764	0.95 (0.89, 1.01) P = 0.129
Q3	0.96 (0.90, 1.03) P = 0.249	0.94 (0.87, 1.01) P = 0.112	1.00 (0.91, 1.10) P = 0.976	0.95 (0.89, 1.01) P = 0.094
Q4 (most greenspace)	0.95 (0.87, 1.02) P = 0.166	0.96 (0.88, 1.04) P = 0.287	0.86 (0.75, 0.98) P = 0.024	0.96 (0.89, 1.04) P = 0.325
Stratum-specific HRs (Q4 vs Q1)	0.97 (0.89, 1.06) P = 0.490	1.05 (0.95, 1.17) P = 0.336	0.84 (0.71, 0.98) P = 0.027	1.04 (0.96, 1.13) P = 0.332
Relative excess risk due to interaction (RERI)	0.149 (0.060, 0.238) P = 0.001		0.170 (0.045, 0.296) P = 0.008	
* Self-reported average total household income before tax				
** 'More deprived' refers to people living in areas in the top two most deprived quintiles of the UK, based on the Townsend index.				
Q = quartile				

In contrast, there was some evidence of effect modification by socioeconomic conditions for the associations between the other neighbourhood exposures and cancer. The most marked evidence was for a modifying effect of area deprivation on the association between greenspace and cancer-related admissions. In that case, the positive departure from additivity indicated by the RERI of 0.170 suggests the reductions in admissions due to increased exposure to neighbourhood greenspace may be greater in more deprived areas (Table 3). In more deprived areas, the stratum-specific HRs estimate a 16% lower hazard of cancer-related hospitalisation among those in the most green quartile compared with those from the least green quartile (HR = 0.84; 95% CI: 0.71–0.98), while no association was observed among people living in more affluent areas. A similar pattern was observed for fast-food proximity and cancer-related admissions, albeit with a smaller and non-significant departure from additivity (RERI = 0.070) and a smaller estimated reduction in hazard among the more deprived areas (HR = 0.93; 95% CI: 0.83–1.04). For household income, although the RERIs for both fast-food proximity and greenspace did indicate some departure from additivity, the stratum-specific HRs suggested there was no meaningful association between these neighbourhood exposures and cancer-related admissions in either income group (Table 3).

Combining area deprivation and household income, a beneficial association of having greater exposure to greenspace within 300 m of home was observed among low-income households in deprived areas, where the hazard of cancer-related hospital admission was 24% lower among people living in the greenest quartile than among people living in the least green quartile (HR = 0.76, 95% CI: 0.63–0.92, Table 4). Intermediate quartiles showed no significant difference from the least green quartile, but all HRs were less than one.

Table 4
Association between neighbourhood characteristics and cancer-related hospital admissions, stratified by household income and area deprivation in combination

Cancer-related admissions	***Combined household income and area deprivation***			
	Less than £31,000 & more deprived	**At least £31,000 & more deprived**	**Less than £31,000 & less deprived**	**At least £31,000 & less deprived**
	HR (95% CI)	*HR (95% CI)*	*HR (95% CI)*	*HR (95% CI)*
Number of PA facilities				
None	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
One	1.05 (0.93, 1.18) P = 0.452	1.14 (0.93, 1.40) P = 0.212	0.95 (0.88, 1.03) P = 0.203	1.02 (0.94, 1.10) P = 0.694
2–3	1.07 (0.95, 1.19) P = 0.256	1.05 (0.87, 1.28) P = 0.598	0.96 (0.89, 1.03) P = 0.258	0.98 (0.90, 1.07) P = 0.656
4 or more	1.05 (0.93, 1.18) P = 0.434	0.98 (0.81, 1.19) P = 0.850	0.94 (0.86, 1.02) P = 0.152	0.96 (0.87, 1.05) P = 0.324
Fast-food proximity				
Closer than 500m	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
500-999m	0.89 (0.81, 0.98) P = 0.015	0.93 (0.80, 1.08) P = 0.347	1.00 (0.92, 1.10) P = 0.945	1.06 (0.96, 1.18) P = 0.254
1000-1999m	0.97 (0.87, 1.08) P = 0.569	1.01 (0.86, 1.20) P = 0.899	1.03 (0.94, 1.12) P = 0.572	0.98 (0.88, 1.09) P = 0.733
At least 2000m	0.88 (0.77, 1.01) P = 0.063	1.06 (0.85, 1.32) P = 0.607	1.02 (0.93, 1.13) P = 0.655	0.98 (0.88, 1.10) P = 0.743
Greenspace				
Q1 (least greenspace)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Q2	0.98 (0.90, 1.08) P = 0.720	0.97 (0.83, 1.13) P = 0.654	1.02 (0.93, 1.13) P = 0.612	1.03 (0.93, 1.15) P = 0.566
Q3	0.96 (0.85, 1.08) P = 0.456	1.03 (0.84, 1.26) P = 0.768	1.01 (0.92, 1.12) P = 0.803	1.05 (0.94, 1.18) P = 0.357

* Self-reported average total household income before tax
** 'More deprived' refers to people living in areas in the top two most deprived quintiles of the UK, based on the Townsend index.
Q = quartile

Cancer-related admissions	*Combined household income and area deprivation*			
	Less than £31,000 & more deprived	**At least £31,000 & more deprived**	**Less than £31,000 & less deprived**	**At least £31,000 & less deprived**
Q4 (most greenspace)	0.76 (0.63, 0.92) P = 0.005	1.05 (0.78, 1.40) P = 0.752	1.04 (0.93, 1.16) P = 0.543	1.08 (0.95, 1.22) P = 0.233
* Self-reported average total household income before tax				
** 'More deprived' refers to people living in areas in the top two most deprived quintiles of the UK, based on the Townsend index.				
Q = quartile				

People from low-income households in deprived areas were also the group where living at least 2 km from a fast-food store had the strongest association with cancer-related admissions (HR = 0.88, 95% CI: 0.77–1.01), but there was no clear trend of decreasing hazard with decreasing proximity (Table 4).

No income/deprivation combined subgroup appeared to experience a cancer-related benefit of having more PA facilities near home, although there was some evidence that those in low-income households in more affluent areas had a somewhat reduced hazard (6%) if they had at least four PA facilities with a kilometre of home, compared with no facilities (HR = 0.94, 95% CI: 0.86–1.02, Table 4).

Sex differences

For the relationships between all three neighbourhood exposures and admissions for any cancer, the findings were generally consistent for females and males (Supplementary Figure S1 and Tables S1-S3).

Secondary outcomes: Breast and colorectal cancer

When we explored whether the results for cancer hospitalisations were driven by either of the two cancers most strongly linked to some of the plausible pathways by which neighbourhood characteristics might influence cancer risk (namely breast and colorectal cancer) we found that the evidence of effect modification by area deprivation of the association between greenspace and cancer was magnified for breast cancer (RERI = 0.316, Supplementary Table S5) and the same was true for effect modification by household income (RERI = 0.307). In deprived areas, the hazard of being admitted to hospital with a primary diagnosis of breast cancer was reduced by 31% among females with the greatest exposure to neighbourhood greenspace, compared with females who had the least greenspace near home (HR = 0.69, 95% CI: 0.47–0.99, Supplementary Table S5). No such association was observed for females living in less deprived areas, and no association was observed between greenspace and breast cancer for the sample as a whole. For females from lower-income households who also lived in deprived areas, risk of a breast cancer-related admission was reduced by 39% among those with the greatest exposure to greenspace, compared with those who had the least exposure (HR = 0.61, 95% CI: 0.38–0.97, Supplementary Table S6)

For formal PA facilities, no overall association was observed with either cancer subtype (Supplementary Figure S2), just as was the case for all cancers combined. However, reduced colorectal cancer risk appeared to associated with greater availability of PA facilities among people living in more affluent areas, and in particular among people from lower-income households within more affluent areas (Supplementary Tables S7 and S8).Contrasting this, there was some indication of effect modification by income for breast cancer, such that females from higher income households may benefit from some protection against breast cancer if they have at least four PA facilities near home (Supplementary Table S5).

For fast-food proximity, neither cancer type showed an association with this neighbourhood exposure and there was limited evidence of any effect modification by either income or deprivation (Supplementary Figure S2 and Table S7).

Sensitivity analyses

In general, restricting follow-up to the period from 2012 onwards for all participants, rather than from the baseline assessment date, reduced precision around point estimates, but made minimal difference to the overall direction and magnitude of most coefficients and RERI estimates (Supplementary Tables S10 and S11). Results were also robust to adjustment for additional risk factors for cancer (Supplementary Tables S12 and S13).

Discussion

Across this very large sample of mid-aged adults in the UK, we examined the relationship between three characteristics of the neighbourhood built environment and hospital admissions due to cancer, over almost 10 years of follow up. We examined whether these associations were modified by area deprivation and household income, with the aim of identifying which neighbourhood characteristics might best be intervened on to improve health without widening existing health inequalities.

We observed very little evidence that any of the three neighbourhood exposures were associated with overall hospitalisations due to cancer. However, investigation of effect modification by household income and area deprivation uncovered interesting patterns that may help to illuminate important elements of the links between the neighbourhood built environment and health. The largely null overall associations appeared to mask potentially important variation in the strength and magnitude of some of those associations by sex, individual socio-economic conditions and area deprivation.

For neighbourhood greenspace and cancer-related hospital admissions – and particularly for women admitted for breast cancer – we found evidence of effect modification by area deprivation, suggesting a greater protective influence of greenspace against cancer in more deprived areas than in less deprived areas. This finding is consistent with some other studies that have previously found relationships between greenspace and health to be stronger in more deprived communities[1], including in the UK[31,32]. In contrast, there did not appear to be any association between formal PA facilities and cancer within any income or area deprivation subgroup, and conflicting patterns of effect modification by income for breast and colorectal cancer specifically.

One pathway through which greenspace is hypothesised to influence health is via physical activity. However, the fact we observed no association between PA facilities and cancer, including in deprived areas, combined with other, not yet published findings in which we found no relationship between greenspace and CVD, suggests that greenspace might influence health generally through pathways unrelated to PA. This contrasts, to some extent, with a 2016 study in the US in which PA was estimated to explained a small proportion (2.1%) of an observed association between greenspace and cancer mortality[12], but is consistent with a recent study from Spain that reported an association between urban greenspace and breast cancer unlikely to be mediated by physical activity[33]. While formal PA facilities are unlikely to influence health via pathways other than through physical activity itself, there is emerging evidence that greenspace may influence health via multiple pathways, including mental wellbeing, immune function, and respiratory health[13], as well as PA. Several studies have concluded that greenspace-health relationships, if causal, are mediated by pathways other than PA, most notably psychosocial ones[12,34,35]. One of the principal mechanisms by which greenspace is thought to influence health is the regulation of cortisol secretion[36]. Cortisol secretion is an indicator of stress and its dysregulation is associated with various health outcomes including cancer[37]. A recent study in a deprived setting in Scotland found that the presence of more greenspace near the home was associated with lower levels of stress across objective cortisol secretion measures and subjective measures of stress, but this relationship did not appear to be mediated by physical activity[36]. Access to greenspace near home may also plausibly mitigate other biological pathways through which chronic psychological stress (more prevalent in deprived populations) influences cancer risk, such as oxidative stress-induced DNA damage and telomere shortening[38,39]. Similarly, greenspace may mitigate some of the effects on cancer risk of air and noise pollution (also often higher in deprived areas), operating though these and related inflammatory and oxidative stress pathways[40,41].

For fast-food proximity and cancer, there was no evidence of an interaction with income, and only very weak evidence that area deprivation modifies the effect of fast-food proximity. The measure of fast-food proximity we have used is somewhat problematic, however, and these results may not be reliable. There is likely to be some systematic misclassification, random error, and geographical inconsistency in quality in the proximity measure we have used, due to our reliance on an off-the shelf measure based on local authority data sources collected for non-research purposes. This highlights some of the trade-offs made in the use of big data and administrative data for the purposes of epidemiological research. Further research repeating this UK-wide analysis using improved measures of the fast-food environment may clarify this relationship.

An important *a priori* rationale for examining effect modification by factors such as income and area deprivation, when a study is sufficiently powered to do so, is that it is plausible that some groups of people will be more sensitive to their neighbourhood environment than others, and that some may be almost completely insensitive for various reasons. Population-wide, average effect estimates smooth out these differences and potentially lead to erroneous conclusions about the importance of neighbourhood environments for some people in some places. Indeed, in this study, we found very little evidence of association between these neighbourhood exposures and cancer across the study population overall, but stronger evidence for associations were observed within more deprived subgroups. We would only expect small effect sizes overall, given the complexity and multitude of causes of cancer, and how distal the outcome is from the exposures, but nonetheless, in some cases these population-average null findings contradict what we might expect based on previous research. In particular, evidence from food environment research in the UK has been mounting of a detrimental effect of excessive exposure to unhealthy food outlets[15,42–44]. Limitations of the fast-food proximity measure are described above, and are also likely to have led to conservative estimates. Similarly, the greenspace measure may not adequately capture the full extent of relevant greenness of one's neighbourhood, as it does not include smaller parcels of greenspace such a street trees, or reflect 'quality' of greenspace.

There are several other limitations of the current study. First, the hospital admissions data only captures inpatient care, so any early detection of cancer that occurs in primary care settings after baseline and is then effectively treated without admission to hospital will not be counted. Such cases are probably more likely to occur in higher income or less deprived subgroups[45], and this may have contributed to lower risk of hospital admission in those groups, potentially distorting the magnitude of effect modification on the additive scale. In the future, when GP records are fully linked to the UK Biobank cohort, it will be possible to examine this potential source of bias. Related to this, if some types of health care have shifted to outpatient settings over the course of the follow-up period, it may result in some dilution of the true association overall and between subgroups. We have not distinguished between elective and emergency admissions, and differences in these may also be socially patterned.

Second, it is unclear what period of follow-up is likely to be necessary to capture the effect of interest, given that people will have been exposed to their baseline neighbourhood conditions for varying lengths of time depending on how long they have lived at that address, and whether relevant changes had occurred in their neighbourhood during that time, and the nature of previous neighbourhood exposures. We adjusted our analyses for years living at baseline address to attempt to deal with this, and are reassured by the long average time people have lived at the address we are using (median = 15 years), but there may be remaining imprecision, and potential bias of estimates in either direction, that we cannot overcome using observational data of this kind. Longer follow up may prove to be more revealing, and that will become possible in future years, but ideally future work would also account for changes in the built environment over that period. UK Biobank would be made richer by the addition of measurement of neighbourhood exposures at one or more post-baseline time points. Our sensitivity analyses using a shorter follow-up period to account for the timing of the exposure ascertainment showed that most point estimates were robust to this specification, but there was a loss of precision presumably driven by the substantial reduction in the number of hospital admissions occurring during the shortened follow-up period (Supplementary Table S9).

Finally, we cannot rule out self-selection into more health promoting neighbourhoods by people more disposed to healthy behaviours. We can, however, by the longitudinal nature of the study and exclusion of people with prevalent disease at baseline, rule out active self-selection prior to baseline into neighbourhoods on the basis of prevalent disease (e.g. following a cancer diagnosis earlier in life, deciding to relocate to a neighbourhood more supportive of a healthy lifestyle). This means that we likely minimise masking of the true effect via this avenue, but may still have some residual positive confounding that could bias the association away from the null, despite our comprehensive adjustment for observed potential confounders. However, UK Biobank is a residentially very stable sample, and most of our strongest findings were within more deprived subgroups, where financial resources enabling relocation for health purposes are presumably the least. In additional robustness checks (not shown) we also confirmed that further model adjustment for baseline hypertension, BMI, and medications for hypertension or cholesterol, made no material difference to our findings (these were not included in the main analysis because of ambiguity regarding temporal precedence i.e. they may be on the causal pathways from neighbourhood environment to cancer if neighbourhood exposure predates them, rather than being confounders).

Overall, despite no estimated protective effect of greenspace on cancer across the mid-aged English population taken as a whole, subgroup effects were observed. Living in a neighbourhood with a greater percentage of greenspace is associated with lower risk of cancer-related hospitalisation among people living in more deprived areas. There is some evidence of the same being true for reduced fast-food proximity and cancer. Greater availability of PA facilities close to home is not associated with lower risk of cancer for any of the analysed groups. Improving deprived neighbourhoods by increasing the amount of public and private greenspace and limiting the proximity of fast-food outlets to residential areas, may improve health outcomes in the population.

Taken together, these results suggest that improving access to greenspace may have a greater public health impact in more deprived areas, but the pathway(s) by which these benefits might arise require further elucidation and should not be assumed to be restricted to the promotion and facilitation of physical activity. We also show that by examining effect modification by multiple socioeconomic indicators in parallel, potentially important insights can be gained that may be missed when we focus only on a single measure of either household or area-level socioeconomic conditions. Understanding the potentially different ways in which different aspects of the socioeconomic conditions of people's lives influence their relationship with the built environment and its effects on cancer risk may help to avoid intervention-generated inequalities when neighbourhood-based built environment interventions are designed.

Declarations

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Competing interests

The authors have no relevant financial or non-financial interests to disclose.

Author contributions

KM and SC conceived of the study, and KM, SC and NP designed the analysis. KM led the data management, statistical analysis, and writing of the manuscript. SC and NP contributed to the interpretation of results, and all authors contributed to and approved of the final manuscript.

Data availability

All data used in this study are available to approved researchers on application to UK Biobank https://www.ukbiobank.ac.uk/

Ethics approval and consent to participate

UK Biobank has ethical approval from the North West Multi-centre Research Ethics Committee (reference 16/NW/0274), the Patient Information Advisory Group (PIAG), and the Community Health Index Advisory Group (CHIAG). Additional ethical approval for the specific study was obtained from the London School of Hygiene and Tropical Medicine’s Research Ethics Committee in September 2016 (reference 11897), and the study was performed in accordance with the Declaration of Helsinki. Informed consent was obtained from all individual participants included in UK Biobank.

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Figures

Figure 1

UK Biobank sample for analyses

Figure 2

Adjusted hazard ratios for hospital admission due to cancer, by availability of formal PA facilities, proximity to nearest fast-food/takeaway store, and neighbourhood greenspace

Note: Models are adjusted for age, sex, ethnicity, education, household income, employment status, urban/non-urban, assessment area, residential density, smoking status, alcohol intake, and number of years living at home address. For plots from sex-stratified models, see Supplementary Material Figure S1.

Supplementary Files

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