Association between adiposity outcomes and residential density: Cross sectional evidence from 419,562 UK Biobank adult participants

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ABSTRACT

BACKGROUND

Obesity is a major health issue and an important public health target for urban design. However, the evidence for identifying the optimal residential density in relation to obesity has been far from compelling. We examined the association of obesity with residential density in a large and diverse population sample drawn from UK Biobank, to identify healthy-weight sustaining density environments.

METHODS

Data from 419,562 adult men and women aged 38-73 years from 22 cities across the UK were used in this cross-sectional study. Residential unit density was objectively assessed within one-kilometer street catchment of participants' residence. Other activity-influencing built environment were measured in terms of density of retail, public transport and street-level movement density modelled from network analyses of through-movement of street links within the defined catchment. Using linear, logistic, and restricted cubic spline (RCS) models as appropriate, adiposity indicators of body-mass index (BMI=Kg/m^2), waist circumference (WC=cm), whole body fat (WBF=Kg) and obesity (World Health Organisation criteria of BMI≥30 Kg/m^2) were regressed on residential density (units/Km^2) adjusting for activity-influencing built environment and individual covariates. We also investigated effect modification by age, sex, employment status and physical activity.

RESULTS

The fitted RCS adiposity-residential density dose-response curve identified a turning point at a residential density of 1,800 residential units/Km^2. Below a residential density of 1,800 units/Km^2, an increment of 1,000 units/Km^2 was positively related with adiposity, being associated with higher BMI (β_{BMI}=0.19, 95% CI: 0.14 to 0.24 Kg/m^2), WC (β_{WC}=0.41, 0.28 to 0.54 cm), WBF (β_{WBF}=0.40, 0.30 to 0.50 Kg) and higher odds of obesity ($OR_{Obesity}$=1.10, 1.07 to 1.14). Beyond 1,800 units/Km^2, residential density had a protective effect on adiposity and was associated with lower BMI (β_{BMI}=-0.22, -0.25 to -0.20 Kg/m^2), WC (β_{WC}=-0.54, -0.61 to -0.48 cm), WBF (β_{WBF}=-0.38, -0.43 to -0.33 Kg) and lower odds of obesity ($OR_{Obesity}$= 0.91, 0.90 to 0.93). Sub-group analyses identified

more pronounced protective effects of residential density among younger, female, those in employment and accumulating higher levels of physical activity, except in case of WBF where the protective effects were stronger among male.

CONCLUSION

Residential density was related to obesity through a curvilinear dose-response curve. Beyond a threshold of 1,800 units/Km^2, residential density consistently had a protective effect on adiposity, suggesting that the relentless thrust towards suburban densification can plausibly be a public health opportunity to be embraced. Housing-level policy related to optimizing healthy density in cities may be potential upstream-level public health intervention towards minimizing/offsetting obesity though further research based on accumulated prospective data is necessary for evidencing specific pathways. It might mean that governments such as in the UK, who are attempting to prevent suburban densification through, for example, prohibiting the subdivision of single lot housing and the conversion of domestic gardens to housing lots, will potentially have the effect of inhibiting the conversion of suburbs into more healthy places to live.

Keywords: Obesity, body mass index, UK Biobank, housing density, sprawl, UKBUMP, built environment, cubic spline model.

Research in context

Evidence before this study

There is now an increasing body of evidence that high urban density, expressed as residential density, retail and service density, street intersection density, land use diversity are all associated with lower body mass index and obesity. Housing is the fundamental component of any city's built environment and residential density is a key parameter around which health-influencing land uses and services are planned and developed. The evidence for identifying the optimum residential density in relation to obesity has been far from compelling. There have been very few studies examining the associations between housing unit density and adiposity. Previous studies have mostly employed aggregate-level census defined data with limited reliability. In some of the studies, residential density only constitutes one component of composite indicators of sprawl and walkability and dose-response relationship can't be established. Most of the studies thus far have been small scale in low density setting within relatively homogeneous environments, generating limited statistical power. As we build and retrofit our cities, there is an increasing necessity to examine the dose-response relationship between residential density and adiposity for identifying healthy-weight sustaining density environments.

Added value of this study

The study employs high quality dataset of unprecedented size (N>419,000 across 22 UK cities) and diversity, both in terms of population characteristics as well as environmental exposures. It employs highly characterized built environment data with objectively measured housing unit density, street-level movement density and density of activity-influencing destinations measured at individual-level. The study uses objective measures of body mass index, waist circumference and whole body fat as indicators of adiposity. These design features enabled analyses with exceptional detail and statistical rigour. Our study is the first to have systematically investigated non-linear associations across the continuum of residential density as well as examine effect modification (by age, sex, employment status and levels of physical activity). The association of residential density and adiposity has been shown to be curvilinear, the dose-response

curve detecting a turning point at 1,800 residential units/Km^2, the findings being consistent across all three measures of adiposity and robust to adjustments. Below 1,800 housing units/Km^2, higher residential density was associated with higher adiposity, while between beyond 1,800 units/Km^2, the associations were protective.

Implications of all the available evidence

Housing unit density is independently associated with adiposity. The curvilinear dose-response curve of residential density and adiposity with identified turning point at a density of 1,800 residential units/Km^2 may have important public health consequences; especially in identifying parameters for residential density associated with lower adiposity and thereby guiding evidence-based policy related to densification as an upstream obesity prevention intervention. Further longitudinal evidence is needed to identify potential pathways and thereby effectively guide policy.

INTRODUCTION

Cities are experiencing rapid urban growth driven by land use changes, demographic shifts and socio-economic development resulting in new public health challenges[1,2]. Obesity has emerged as a global pandemic[3]; excessive adiposity being an important risk factor for morbidity and mortality from type 2 diabetes, for cardiovascular disease and cancer[4-6]. Residential built environment has been associated with obesity[7-9]. A systematic review of 132 articles concluded that neighbourhoods with high residential density, street intersections and services were associated with lower risks of obesity[10].

Housing is the fundamental component of a city's built environment and residential density, expressed as the number of residential units per residential acre, constitutes one of the simplest proxies of urban densification. Specific residential density profiles have carrying capacities to support particular levels of health-influencing land uses and services in their neighbourhood. Thus, optimizing residential density profiles, capable of supporting health-promoting infrastructures and behaviour, via allocation of housing stocks in primal cities and retrofitting in fully-evolved ones is intrinsic to healthy urban living. Higher residential density has been hypothesized to support compact mixed-use urban development, enhancing street-level physical accessibility and connectivity to employment and service destinations. It is also thought to be associated with lower private vehicle-miles travelled, and higher frequency of active travel and physical activity[11-13]. Their protective effects on obesity has been reported in previous studies through direct density metrics[14,15] of as well as more composite indicators of sprawl[16,17].

With the global impact of urban densification, more specifically, the pervasive impact of the built environment on health, the evidence for identifying the optimum residential density in relation to obesity has been far from compelling. There has thus far been no study on the dose-response relationship between residential density and adiposity, adjusting for all other related built environment to identify optimal density levels for guiding healthy housing policy. Furthermore, most studies employ census-defined aggregate data, are relatively small-scale, and conducted in low density setting within relatively homogeneous environments.

To establish robust evidence of the links between residential density and obesity, a large and diverse population sample was assessed for residential density and various indicators of adiposity. Objective measures of residential density and activity-influencing built environment were modelled at an individual level of analysis to identify optimal levels of residential density for sustaining healthy weight.

METHODS

Study population

The UK Biobank is a prospective population cohort of 502,649 adults aged 37-73 (99.9% aged between 40-69 years) at recruitment. Participants were selected from the National Health Service patient register and resided within a 25 mile radius of one of the 22 assessment centres. The baseline examination (2006-2010) included extensive questionnaires on socio-demographics, lifestyle, psychosocial factors and medical history; as well as anthropometric measurements; bio-sampling (blood, urine and saliva); imaging; cognitive function and hospital-related outcomes[18]. Details of the UK Biobank study protocol including the scientific rationale and study design can be found elsewhere[19].

UK Biobank received ethical approvals from the North West Multi-centre Research Ethics Committee (MREC), the Community Health Index Advisory Group (CHIAG), the Patient Information Advisory Group (PIAG) and National Health Service National Research Ethics Service.

The present study was a full data cross sectional analyses. Data on adiposity outcomes, socio-demographics and related covariates were collected at baseline (2006-2010), while individual-level built environment exposures were assessed towards the end of the baseline phase (2010). The study analytic sample comprised N=419,562 (83.5%) participants with valid baseline data on BMI, waist circumference, body fat, residential density, other built environment densities.

Obesity indicators

Conventional measures of body mass index (BMI) in Kg/m^2, waist circumference (WC) in cm, and whole body fat (WBF) in Kg constituted the primary indicators of adiposity.

They were assessed as per UK Biobank's standard protocol for anthropometric measurements[19,20]. In addition the World Health Organisation's definition of obesity as BMI ≥30 Kg/m^2 was used. Standing height (cm) was measured using a Seca 202 device and waist circumference (cm) using a Wessex non-stretchable sprung tape. Weight and whole body fat mass (kg) were measured using electrical bio-impedance with the Tanita BC-418 MA body composition analyzer. Body Mass Index (BMI) was derived by dividing weight (kilograms) by square of standing height (square metres).

Exposure assessment – dwelling environment

Built environment data were derived from the UK Biobank Urban Morphometric Platform (UKBUMP). UKBUMP comprises a set of urban objectively assessed metrics of density, design and accessibility to quantify health-influencing environmental exposures within pre-defined catchments of each participant's geocoded dwelling address. In reference to each Biobank participant's dwelling location, multiple health- and activity-influencing built environment metrics were developed through a series of GIS-based spatial and network analyses performed upon the UK Ordnance Survey spatial database and other national-level datasets. The methodology is detailed elsewhere[21]. These built environment metrics of UKBUMP were previously piloted in the Caerphilly Prospective study[22] and has been employed for obesity risk - built environment study within the UK Biobank[23].

Density metrics were modelled from UK-wide AddressBase Premium data of Ordnance Survey comprising approximately 36 million valid address point features of 550 different land use classifications. Residential density (units/Km^2) was defined as the number of housing units including detached, semi-detached, terraced and self-contained flats within one-kilometer street catchment of a participant's geocoded dwelling. We had tested multiple neighbourhoods as a part of prior sensitivity with pilot data and the criterion of 1-Km network catchment for land use density variables corresponding to 10-minute walk from the geocoded dwellings was chosen[22]. It also corresponds well with *priori* evidence on functional neighbourhoods in previous built environment – adiposity studies[14].

Other activity-influencing built environment density variables statistically controlled for included exposure to retail outlets and public transport (bus-stops and train stations), expressed as the density of (number/Km^2) within the 1-km home neighbourhood. A graphical metrics of *betweenness centrality* was used as a proxy of street-level movement density expressed in terms of the underlying morphology and design of street network, modelled through network analyses[24] of the Ordnance Survey Integrated Transport Network database comprising 5 million street links within a 50 Km radius of each of the UK Biobank assessment centres. Movement density within an 800-metre street network catchment of a participant's dwelling was expressed as the simulated counts of movement along each street link, given it's relative position in the network as well as it topological connectivity with all other links in the network[21,22]. Our choice of 800-metres corresponded to a network activity space equivalent to 10-minute walk and was found to be correlated with walking[25] and obesity[23]. Movement density or betweenness of any street link x in a graph of N links may be defined as:

$$Bt\ Wl(x) = \sum_{y \varepsilon N} \sum_{z \varepsilon \boldsymbol{R_y}} L(y)L(z)P(z)OD(y,z,x)$$

where:

y and z are the geodesic end points;

R_y is the set of links within a defined radius (800m in this case) from y;

L(y) and L(z) are length of links y and z respectively;

P_z is the proportion of link z within the defined radius

OD is a function defined as:

$$OD = \begin{cases} 1, & if\ x\ is\ on\ the\ geodesics\ from\ y\ to\ z \\ \frac{1}{2}, & if\ x \equiv y \not\equiv z \\ \frac{1}{2}, & if\ x \equiv z \not\equiv y \\ \frac{1}{2}, & if\ x \equiv z \equiv y \\ 0, & otherwise \end{cases}$$

These built environment variables were categorized into quartiles and modelled as 4-level factors.

Covariates

The addition of study covariates was theoretically informed from *a priori* research evidence on the links between obesity and socio-demographic and lifestyle, and environmental factors. Socio-demographic covariates comprised age, sex, employment status and education. Employment status was expressed as a 3-level factor (employed; retired; and unemployed, home maker, other). Self-report education was coded as a 5-level factor (No qualification, O levels/GCSEs/CSEs, A levels/AS levels, NVQ/HND/HNC/Other professional, and College or University degree). Among the lifestyle-level factors, vehicle ownership was categorized as none, one, two and more than two, while, housing tenure was modelled as a 3-level factor (own outright, own with mortgage, and rented). Processed meat intake was included as a dietary variable expressed as never, up to once, 2-4 times, >4 times a week. In a sub-sample of 60,694 participants, we obtained data on dietary energy intake (in KJ) from the 24-hour diet recall questionnaire[26]. This was calculated from food and beverage consumption yesterday, excluding any supplements. Smoking was coded as a 3-level factor (never, previous, current). Family history of disease was derived from history of mother's illness, coded as 3-level variable (none, heart or cerebrovascular disease, cancer). Self-reported medication use for cholesterol, blood pressure, diabetes, or take exogenous hormones was coded as a four factor variable (none, use of medication for cholesterol, hypertension, insulin-use/others). Neighbourhood deprivation (expressed in terms of Townsend score) was derived from post code of residence and categorized into quintiles. Physical activity behaviour expressed in MET-hours/week was derived from self-reported IPAQ short form and was computed as the sum of weekly walking, moderate and vigorous physical activity components[27]. The physical activity data across all the three activity components were available for 331,814 participants.

Statistical Analysis

For this cross-sectional analysis a systematic multi-layered analysis protocol was pursued. Separate linear models were fitted for each of the adiposity outcomes using the full data. BMI, waist circumference and whole body fat mass were treated as continuous outcomes and odds of obesity (in reference to non-obese; BMI< 30 Kg/m^2)

was modelled as a binary outcome. Residential density acted as a continuous linear predictor in our models. We estimated average effects of 1,000 units/Km^2 (10 units/hectare) increments in residential density (which is also equivalent to approximately 1 interquartile range) upon adiposity outcomes. Initial model building exercise involved sequential introduction of covariates and assessment of collinearity and fit statistic. Model 1 included socio-demographic and lifestyle level variables of age, sex, income, education, employment status, vehicle ownership, housing tenureship, smoking status, processed meat intake, mother's illness and medication use and health-influencing built environment densities variables of density of retail outlets, public transport and street-level walking density. In model 2 neighbourhood-level deprivation was introduced. Model 3 further controlled for physical activity.

As a second step, we repeated these analyses using restricted cubic spline (RCS) models to examine non-linearity in the associations between residential density and adiposity, with a restricted spline basis for residential density. Harrel's Knots were placed at equal percentiles of the data based in a series of prior iterations with 3, 4, 5, 6, and 7 knots along the residential density spline and comparison of respective goodness-of-fit by Akaike information criteria (AIC) produced the most parsimonious model[28]. The fitted RCS curve showed the variation of adiposity in relation to the residential density continuum. The *mfxrcspline* command in Stata was further employed to generate marginal effect plots of first derivative/slope of the adiposity function with respect to residential density. From these, the *turning point* in the association were determined. Linear models were then fitted piecewise on either side of the identified turning point.

Finally, effect modification was examined by sequentially introducing interaction terms between the residential density spline basis and four variables (age, sex, employment status and physical activity behaviour), adjusting for all other factors.

For each point-estimate, two-tailed 95% confidence intervals estimated by bootstrapping are presented. Stata 14 was used for all analyses.

Results

The analytic sample comprised N=419,562 participants across 22 UK Biobank assessment centres (Table 1). Mean BMI was 27.4 (SD=4.7), mean WC was 90.0 cm (SD=13.4) and mean WBF was 24.8 Kg (SD=9.5), while 23.9% (N=100,411) were categorized as obese. The three markers of adiposity (BMI, WC and WBF) employed as outcome measures in respective models were positively correlated with Pearson's correlation coefficient ranging from 0.65-0.88. This sample had 56% female with an average age of 56.5 years (SD=8.0). The mean weekly physical activity accumulated was 46.5 MET-hr/week (SD=50.3). Outright home owners accounted for 53% of the participants, while 8% didn't own a vehicle. Residential density ranged from 0 to 10,513.2 dwelling units/Km^2 with a mean, median and SD of 1,877.7, 1,755.9, and 1,115.6 respectively (presented in Table 2). Average duration of residence was 17.4 years.

Linear models

Overall, an inverse linear association between residential density and obesity was found. (Table 3). Collinearity remained low with the variance inflation factor lying in the range of 1.2 and 1.9. For the fully controlled model, a 1,000 dwelling units/Km^2 increment within a 1Km dwelling catchment was associated with lower adiposity across the four indicators of BMI (β_{BMI}=-0.14, 95% CI:-0.15 to -0.12 Kg/m^2), WC (β_{WC}=-0.30, 95% CI:-0.35 to -0.26 cm), WBF (β_{WBF}=-0.22, 95% CI:-0.26 to -0.19 Kg) and obesity ($OR_{Obesity}$=0.95, 95% CI: 0.94 to 0.96).

Non-linear models

Goodness-of fit-tests identified models with 3 knots as parsimonious fit for the adiposity outcomes. The best fit statistic for BMI, WC and WBF were AIC_{BMI} = 1918100.6, AIC_{WC} = 2528301.1 and AIC_{WBF} = 2367039.5 respectively. Variance inflation factor remained between 1.2 and 2.2. The fitted RCS models of adiposity-residential density dose-response are shown in Figure 1. A clear obesogenic asymptote corresponding to the turning point (change in direction of the slope) was consistently observed at residential density of approximately 1,800 units/Km^2 for all the three measures of adiposity (point 'a' in the figure). Fully-adjusted piece-wise models developed on either side of the detected turning point are presented in Table 4 (Full results in Supplementary Table 1a-b). Below

a residential density of 1,800 units/Km^2, an increment of 1,000 units/Km^2 was associated with higher BMI (β_{BMI}=0.19, 95% CI: 0.14 to 0.24 Kg/m^2), WC (β_{WC}=0.41, 0.28 to 0.54 cm), WBF (β_{WBF}=0.40, 95% CI: 0.30 to 0.50 Kg) as well as higher odds of obesity ($OR_{Obesity}$=1.10, 95% CI: 1.07 to 1.14). Above 1,800 units/Km^2, residential density had a protective effect across all the markers of adiposity, being beneficially associated with BMI (β_{BMI}=-0.22, 95% CI: -0.25 to -0.20 Kg/m^2), WC (β_{WC}=-0.54, 95% CI: -0.61 to -0.48 cm), WBF (β_{WBF}=-0.38, 95% CI: -0.43 to -0.33 Kg) as well as lower odds of obesity ($OR_{Obesity}$= 0.91, 0.90 to 0.93).

As a sensitivity analysis, we further examined the relationship between physical activity and residential density by re-running the RCS model with log-transformed physical activity (Figure 2) adjusting for all other variables. We also estimated the odds of reporting less than the 7.5 MET-h/week activity (cut-off corresponding to evidenced health benefits[29]) either side of the identified turning point in the adiposity – density relationship. The odds of reporting low PA per 1,000 units/Km^2 increment in residential density were: OR_{Low_PA}=1.14, 95% CI: 1.09 to 1.19 for density ≤1,800 units/ Km^2 and OR_{Low_PA}=0.95, 95% CI: 0.94 to 0.97 for density beyond 1,800 units/ Km^2.

To examine the effects of residential density among participants who are not obese but at risk of obesity, we excluded obese participants from the analyses and modelled the odds of being overweight (BMI≥25 Kg/m^2 and <30 Kg/m^2) in reference to healthy weight (BMI<25 Kg/m^2) category. A slight attenuation in the effects per 1,000 units/Km^2 increment in residential density was observed. The odds ratios for overweight was $OR_{Overweight}$=1.04, 95% CI: 1.01 to 1.07 for residential densities ≤1,800 units/ Km^2 and $OR_{Overweight}$ =0.95, 95% CI: 0.93 to 0.96 for densities beyond 1,800 units/ Km^2.

We also tested the effects of additionally controlling for dietary energy intake in a subsample (n=49,981) for which calorific data was available. Effect estimates remained consistently significant, being slightly modified in the case of WC and WBF (in reference to the models over the full data (Supplementary Table 2).

From a planning perspective, UK policy guideline considers densities below 3,000 units/Km^2 as inefficient use of land and encourages housing development to have densities of 3000-5000 units/Km^2 [30]. As a sensitivity analysis to further interpret our

findings in relation to prevailing residential densification scenario, we created an additional cut-point at 3,200 units/Km^2 (32 unit/hectare) and obtained piecewise effect estimates in the density ranges 1,800-3,200 and >3,200 units/Km^2. This cut-point (point 'b' in Figure 1) represents the average residential density surrounding newly-developed residential units over the period of 2014-16[31]. The associations were protective within the density range 1800-3200 units/ Km^2 for both BMI (β_{BMI}=-0.13, 95% CI: -0.21 to -0.05 Kg/m^2) and obesity ($OR_{Obesity}$= 0.98, 0.94 to 1.02). A more pronounced beneficial effect was however observed beyond the density of 3,200 units/Km^2 for BMI (β_{BMI}=-0.17, 95% CI: -0.21 to -0.12 Kg/m^2) and obesity ($OR_{Obesity}$= 0.92, 0.90 to 0.94). Similar trends were observed in case of WC and WBF (Table 5).

Interaction terms were introduced to examine modification by age, sex, employment status and physical activity (Figure 3 and Supplementary Figure 1). Effects on adiposity of increasing residential density were greater in younger age groups, females, those employed and in those with greater physical activity (≥50 MET-h/wk) with $p_{interaction}$ < 0.01 in each case. The results in the case of WBF indicated a more pronounced protective effect in male than in female. The mean WBF for female was also higher at 26.9 Kg (SD=10.0) than in male 22.3 Kg (SD=8.2).

High adiposity may be associated with self-selection and migration to low density areas. As a further sensitivity analyses, adiposity was correlated with density according to high (>10 years), medium (3-10 years) and low (<3 years) duration of residence. No differences in the association were found between these sub-groups.

DISCUSSION

Using objective measures of the built environment, in a large and diverse population sample, the association of residential density and adiposity has been shown to be curvilinear, indicating a turning point at a residential density of 1,800 units/Km^2. This finding was consistent across all three measures of adiposity, with stronger associations being found for younger, female, employed and accumulating higher levels of physical activity. The inference that residential density is a determinant of adiposity in the general population, and that this association can be specified sufficiently precisely to inform policy in support of environments promoting healthy weight is a conclusion of

substantial public health significance requiring careful consideration by urban health planners and policy makers.

Overall, our results indicate that high residential density was significantly and independently associated with lower adiposity outcomes. These are consistent with a few mostly small scale studies on the topic. In a study of 10,878 participants residing a low-density environment in the Atlanta, Georgia[14], significant negative correlation was found between residential density and body mass index and distance walked in males. Density was expressed in persons/acre within census block group. Another largescale Canadian study involving 3.78 and 1.63 million participants of Toronto and Vancouver[15] found a protective association between residential density and body mass index. Their density measure was similar to ours' and the reported effect estimates for BMI were slightly lower than ours for Toronto (at -0.05 Kg/m^2) but higher for Vancouver (at -0.30 Kg/m^2). Another small scale ecological study of 2,375 adolescents of Nanjing, China[32] found that residing in highest density tertile was associated with 2.17 times higher odds of overweight in reference to those in the lowest. This was however an ecological study with a poorer resolution density measure (expressed in terms of number of residents/Km^2 within districts) for children. With respect to physical activity, a recent multi-country study involving 6,822 adults across 14 cities[13] reported a consistent association between net residential density and moderate-to-vigorous-intensity physical activity.

None of the previous residential density – adiposity studies explored non-linearity and associations stratified across density profiles. In this regard, our findings are important in principle and in practice. In principle they demonstrate the value of large high-quality health dataset and detailed environmental metrics to identify environmental determinants of chronic disease. In practice, the curvilinear association of residential density with adiposity identifies turning point with public health consequences; providing a metric for estimating the impact of housing policy and urban planning on adiposity.

In a low residential density setting of ≤1,800 units/Km^2, the positive association between density and adiposity may possibly point to a low density suburban sprawl effect. Typically, the left end of the curve reflects semi-urban neighbourhoods that facilitated

walkability and physical activity via access to private outdoor spaces in the form of larger residential gardens[33], and enhanced exposures to salutogenic green and open amenity[34], however, were not inherently designed to accommodate densification. The density nearing the turning point 'a' of the RCS curve (at 1,800 units/Km^2) may be a proxy of areas experiencing suburban sprawl. The positive associations of suburban sprawl with obesity[16,17] and inadequate physical activity[35] are well established, primarily on account of sedentary lifestyles including higher vehicle-miles travelled to employment centres and lower activity levels. Our physical activity analysis supports this finding with higher odds of reporting <7.5 MET-h/week physical activity. Beyond 1,800 units/Km^2 increasing density had a protective effect on adiposity. This density range corresponds to urban suburbs, compact inner-suburbs and city centres that are well-evolved and designed to accommodate densification with additional supporting infrastructures in the form of retail, employment centres, pedestrian facilities and other attractive destinations. Physical activity model corroborated this with a relatively lower odds of reporting <7.5 MET-h/week physical activity in this density range. The observed associations in these medium-to-high density regions may possibly point to a physical activity-related mechanism with the residential exposures acting as a proxy of the degree of walkability and activity-friendliness of a neighbourhood. Further data based on accumulated longitudinal data is needed to conclusively verify such causal assumption. We also note that fitted RCS curves can be applied with confidence to the UK context and mayn't be valid in other countries. These models, when calibrated in the United States and Australia are likely to lie along the left of our turning point of 1,800 units/Km^2, since apart from the most densely populated parts densities generally tend to be below this figure (US and Australian have average residential densities of 1,200 and 1,000 residential units/Km^2 respectively).

Although current UK housing density averages 2,300 dwellings/Km^2, the average density around dwelling addresses newly allocated in 2013-2014 was 3,100 units/Km and 3,200 units/Km for 2014-2016[31]. From an urban health policy perspective, our models indicate a more pronounced protective effect beyond the range of 3,200 units//Km^2 (compared to 1,800-3,200 units//Km^2), supporting the policy towards healthy suburban densification. As a recommendation for practice, for dense and compact

environments to become active environments, planners need to design them as multi-function urban spaces rather than mono-function suburban spaces[1,36].

Given the potentially significant benefits of healthy density environments on weight outcomes, understanding underlying pathways merits further investigation for effective policy making. Firstly, high residential density is synonymous with compactness, greater access to destinations and walkability, and thus active travel. Recent evidence have reported positive association of walkability[37] as well as active commuting[38] on healthy weight. Physical activity-based pathway is plausible, given the evidenced activity-promoting effects of housing density highlighted previously[13]. Physical activity is related to adiposity via its role in influencing levels of individual energy expenditures[39]. Though we were not able to directly test for mediation, our RCS model for physical activity found higher residential density (beyond 2,000 units/Km^2) had beneficial effects on accumulated weekly activity, while interaction models found that the protective effects of density on adiposity were more pronounced among the highly active participants (>50 MET-h/week). Secondly, a highly compact dense residential environment may act as a proxy for enhanced community social capital and support. The intangible stress-relieving potential of centrality, accessibility and social capital needs to be further examined, given their protective effects on obesity[40]. Thirdly, high residential density after adjusting for all other built environment may also represent a well-designed environments shielding exposures to stressors related to proximity to road as well as having greater provision for recreational activity spaces such as greenspace. The obesogenic potential of air quality and noise pollution[41-43] are well established and so are the protective effects of green access[23].

Limitations originate from the use of cross sectional and observational study design, as indeed prevalent with most studies examining associations between health and environmental exposures. Cross sectional design prevented causal inference. We couldn't take into account the effect of self-selection, with high adiposity attributed to moving into an areas of low residential density. To address this, we examined the association of density with adiposity stratified by duration of residence detected no differences between duration groups; however reverse causation can't be ruled out.

Another limitation of cross-sectional data is that they may not reflect the long-term impact of an exposure. However, an average duration of residence of 17.5 years indicates a cohort with relatively stable residential histories. However, future studies should employ accumulated longitudinal data to model changes in health in relation to changes in built environment. Similarly as accumulated follow-up data becomes available in the UK Biobank, other designs such as the effect of migration from one density environment to another may also be considered for a small sub-sample of participants moving houses.

Large-scale data also pose some challenges. Temporal mismatch between assessment of outcomes and covariates and measurement of exposures was inevitable. The model outcomes and covariates were assessed during the study's baseline period (2006-2010), while the built environment was measured in 2010. This was less likely to have significantly affected our findings as the built environment typically change slowly in UK. The issue of inferring small effects (often encountered in environment – health studies) with caution in big data statistical analyses must be stated. Our data also deciphered significant differences among population sub-groups. We followed a detailed multilayered statistical modelling framework. In addition to preliminary analyses employing the full data, subsequent models were developed by stratifying the data by density profiles and meaningful population characteristics, thereby obtaining a range of reliable estimates with respect to different chunks of data.

The risk of residual confounding exists as in all observational data. Apart from built environment, the study didn't consider other environmental attributes including land use heterogeneity, quality of transit services, green quality and their recreation potential. We couldn't study how these effects might have moderated the associations. The study didn't have data on weight-influencing intestinal microbiota, while the calorific intake data was available for a subset of participants. There is also a need to control for intangible effects of prevailing urban and environmental policy and demographic contexts to enhance generalizability.

The range of residential density available to the analysis was representative of UK semi-urban and urban environments. The findings should not however be extrapolated

beyond this range for other socially and culturally different contexts. The UK and most European cities does not have the very high-density developments as commonly encountered in Asian population centres such as in Hong Kong and many cities of Mainland China and India and it's likely that other turning points would be encountered, endemic to such density extremes. We emphasize that comparable country-specific evidence from other countries (with different contexts) need to be reproduced by others, is likely to produce different curves, but help us gain insights for global healthy densification policies.

The UK Biobank is an adult cohort (in the age range of 38-73 years) and the reported findings are not generalizable to young adults and children. Additionally, the sampling is associated with a healthy volunteer selection bias and thus may not be representative with respect to the prevalence of obesity and related comorbidities. However, given the sufficiently diverse population and heterogeneity of environmental exposures, sample selection is unlikely to lead to have a material effect on the associations reported[44,45].

Notwithstanding the mentioned limitations, this is the first systematic large scale analysis examining the trajectory of adiposity along the residential density continuum after adjusting for other built environment and covariates as well as testing for non-linearity and effect modification. Strengths of the study originates from the use of high quality dataset of unprecedented size (N>419,000) and diversity (22 cities). The UK Biobank data underwent considerable centralized quality control. Standardized measurement protocol ensured uniformity and reliability of the markers of adiposity. The use of multiple markers[46] provided a more holistic measure of adiposity. A distinctive feature was the use of UKBUMP built environment data which were characterized using objective indicators[46]. Reliance on the UK-wide Ordnance Survey data meant the density data could be measured at the building unit level within street network catchment as functional neighbourhoods, rather than parcel level data within census-defined neighbourhoods used in all prior studies. Data were analyzed at the individual level to avoid the modifiable unit area problem and the ecological fallacy. These design features have provided analyses of exceptional detail and statistical power enabling a multi-layered analysis to detect non-linear associations across the density continuum,

and informative subgroup analyses. Although longitudinal data are required to confirm these findings, they are not dissimilar to previous reports. The inverse relationships between residential density and obesity in sprawling suburbs has been shown elsewhere[16,17], as have differential effects according to gender[47] and age[48] on adiposity.

Conclusion

With increasing demand for urban housing, alongside controlling sprawl and enhancing infrastructure, sustaining healthy communities is a major planning challenge. This large scale study provides evidence that informs the planning equation in terms of identifying parameters for residential density that may sustain healthy weight. Our study consistently found that beyond a threshold of 1,800 units/Km^2, residential density had a protective effect on adiposity outcomes suggesting that the relentless trend towards suburban densification can plausibly be a public health opportunity to be embraced. Further longitudinal studies based on accumulated data are needed to measure changes in adiposity in relation to changes in density, infer causality and thereby characterize obesogenic environments, given the enduring public health value of reducing obesity.

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Author contributions

CS, CW and JG had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of data analysis. CS, CW and JG conceived the study. CS designed the study, developed the built environment metrics and performed the formal analysis. CS drafted the report. CW and JG commented on the draft and contributed to redrafting. CS produced the final submitted draft.

Conflict of interest

None.

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Tables:

Table 1. Summary of individual characteristics by obesity for 419,562 participants of UK Biobank.

Participant characteristics	Not obese (BMI<30 Kg/m^2)	Obese (BMI≥30 kg/m^2)	Overall
N	319,151	100,411	419,562
Mean (SD)			
BMI (Kg/m^2)	25.31 (2.7)	33.92 (3.8)	27.37 (4.7)
Waist circumference (cm)	85.33 (10.3)	104.73 (11.0)	89.97 (13.4)
Whole body fat mass (Kg)	21.12 (6.0)	36.61 (9.1)	24.83 (9.5)
Physical activity (MET-h/wk)*	48.23 (50.6)	40.70 (48.7)	46.51 (50.3)
Age (years)	56.37 (8.1)	56.76 (7.8)	56.46 (8.0)
N (%)			
Gender: Female	179,710 (56.3)	53,953 (53.7)	233,663 (55.7)
Male	139,441 (43.7)	46,458 (46.3)	185,899 (44.3)
Education: None	46,307 (14.5)	20,897 (20.8)	67,204 (16.0)
College or University degree	114,516 (35.9)	25,588 (25.5)	140,104 (33.4)
O levels/GCSEs/CSEs	85,185 (26.7)	29,427 (29.3)	114,612 (27.3)
A levels/AS levels	37,424 (11.7)	10,735 (10.7)	48,159 (11.5)
NVQ/HND/HNC/Other professional	35,719 (11.2)	13,764 (13.7)	49,483 (11.8)
Employment status: Employed	190,147 (59.6)	56,831 (56.6)	246,978 (58.9)
Retired	106,396 (33.3)	33,578 (33.4)	139,974 (33.3)
Unemployed, home maker, others	22,608 (7.1)	10,002 (10.0)	32,610 (7.8)
Vehicle ownership: None	22,173 (6.9)	9,365 (9.3)	31,538 (7.5)
One	130,946 (41)	42,936 (42.8)	173,882 (41.4)
Two	128,681 (40.3)	36,093 (35.9)	164,774 (39.3)
> Two	37,351 (11.7)	12,017 (12)	49,368 (11.8)
Tenureship: Own outright	174,728 (54.7)	48,589 (48.4)	223,317 (53.2)
Mortgage	120,477 (37.7)	39,074 (38.9)	159,551 (38.0)
Rent	23,946 (7.5)	12,748 (12.7)	36,694 (8.8)
Smoking status: Nonsmoker	180,969 (56.7)	51,715 (51.5)	232,684 (55.5)
Previous smoker	105,859 (33.2)	39,446 (39.3)	145,305 (34.6)
Current smoker	32,323 (10.1)	9,250 (9.2)	41,573 (9.9)
Processed meat intake: Never	32,325 (10.1)	5,999 (6)	38,324 (9.1)
Up to once/week	194,449 (60.9)	57,951 (57.7)	252,400 (60.2)
2-4 times/week	80,999 (25.4)	31,863 (31.7)	112,862 (26.9)
>4 times/week	11,378 (3.6)	4,598 (4.6)	15,976 (3.8)
Calorific energy intake (KJ)^^; Mean (SD)	8,794.42 (3,100.9)	8,943.34 (3,416.5)	8,827.86 (3175.1)
Medication use: None	231,974 (72.7)	55,014 (54.8)	286,988 (68.4)

Cholesterol lowering	44,197 (13.8)	26,713 (26.6)	70,910 (16.9)
Blood pressure medication	26,527 (8.3)	15,604 (15.5)	42,131 (10)
Insulin and others	16,453 (5.2)	3,080 (3.1)	19,533 (4.7)
Mother's illness: None	229,414 (71.9)	66,913 (66.6)	296,327 (70.6)
Heart/cerobro-vascular disease	74,471 (23.3)	28,241 (28.1)	102,712 (24.5)
Cancer	15,266 (4.8)	5,257 (5.2)	20,523 (4.9)

*****N=331,814 with valid METs data across the three physical activity categories.
**N=60,694 with valid METs data on energy intake.

Table 2. Descriptive statistics of environmental exposure variables.

Environmental exposure	Mean ± SD	Minimum	P_{25}	P_{50}	P_{75}	Maximum
Residential density (units/Km^2)	1877.65 ± 1115.62	0	1235.94	1755.89	2267.88	10513.24
Retail density (units/Km^2)	43.22 ± 64.70	0	7.32	21.09	52.85	1752.07
Public transport density (units/Km^2)	22.61 ± 10.86	0	15.51	21.72	28.45	207.23
Street-level movement density (unitless)	$4.58 \times 10^6 \pm 5.46 \times 10^6$	5076.23	8.48×10^5	2.63×10^6	6.38×10^6	8.75×10^7
Townsend deprivation index (unitless)	-1.50 ± 2.95	-6.26	-3.71	-2.28	0.20	11.0

P_{25}, P_{50} and P_{50} represent the 25^{th}, 50^{th} and 75^{th} data percentiles.

Table 3. Linear models of association of adiposity with residential density among N=419,562 participants of UK Biobank.

Residential density (per 1,000 units/Km^2)	Body mass index (kg/m^2)	Waist circumference (cm)	Whole body fat (Kg)	Obesity (BMI>30 Kg/m^2)
	β (95% CI)	β (95% CI)	β (95% CI)	OR (95% CI)
Linear models:				
Model 1**	-0.05* (-0.07 to -0.03)	-0.11* (-0.15 to 0.07)	-0.08* (-0.11 to -0.05)	0.99* (0.98 to 1.00)
Model 2†	-0.13* (-0.15 to -0.11)	-0.29* (-0.33 to -0.24)	-0.21* (-0.24 to -0.18)	0.96* (0.95 to 0.97)
Model 3‡	-0.14* (-0.15 to -0.12)	-0.30* (-0.35 to -0.26)	-0.22* (-0.26 to -0.19)	0.95* (0.94 to 0.96)

**Effect estimates after controlling for age, sex, education, employment, car ownership, housing tenureship, smoking status, processed meat intake, mother's illness and medication use and health-influencing built environment densities variables of density of retail outlets, public transport and street-level movement density.
†Effect estimates after further controlling for neighbourhood-level deprivation.
‡Fully-adjusted effect estimates after additionally controlling for physical activity (MET-hours/week); N=331,814.
*Statistically significant effect estimates.

Table 4. Fully adjusted models fitted on either side of the detected turning point in the density – adiposity RCS curves at 1,800 residential units/Km^2.

Residential density (per 1,000 units/Km^2)	Body mass index (kg/m^2) β (95% CI)	Waist circumference (cm) β (95% CI)	Whole body fat (Kg) β (95% CI)	Obesity (BMI>30 Kg/m^2) OR (95% CI)
Piece-wise linear models †:				
≤ 1,800 units/Km^2	0.19* (0.14 to 0.24)	0.41* (0.28 to 0.54)	0.40* (0.30 to 0.50)	1.10* (1.07 to 1.14)
> 1,800 units/Km^2	-0.22* (-0.25 to -0.20)	-0.54* (-0.61 to -0.48)	-0.38* (-0.43 to -0.33)	0.91* (0.90 to 0.93)

†Fully-adjusted effect estimates controlling for age, sex, education, employment, car ownership, housing tenureship, smoking, processed meat intake, mother's illness and medication use, physical activity, retail density, public transport, street-level movement density and neighbourhood deprivation.
*Statistically significant effect estimates.

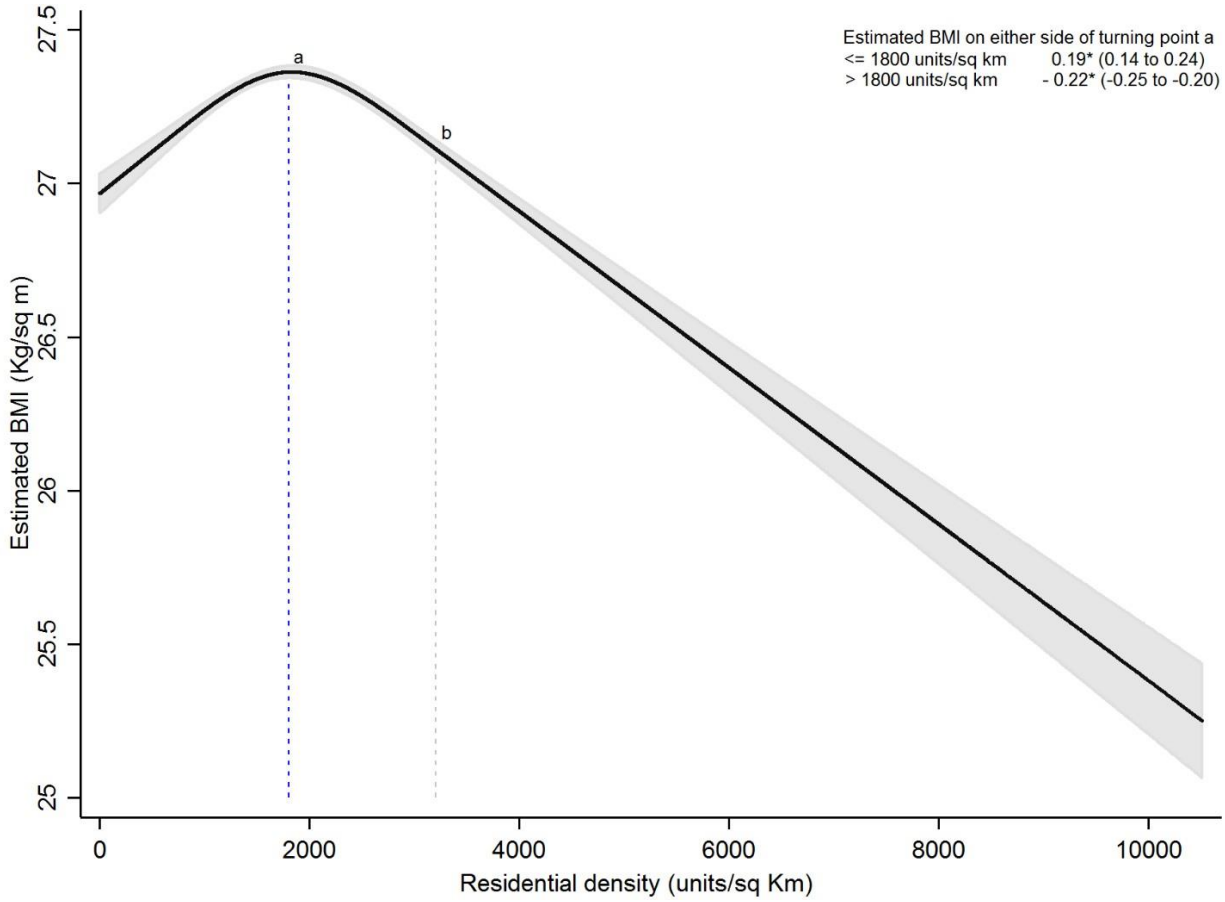
Table 5. Sensitivity analyses beyond the detected turning point of 1,800 units/Km^2 with linear models fitted on either side of the cut-point of 3,200 units/Km^2 corresponding to current density surrounding newly developed residential units in UK.

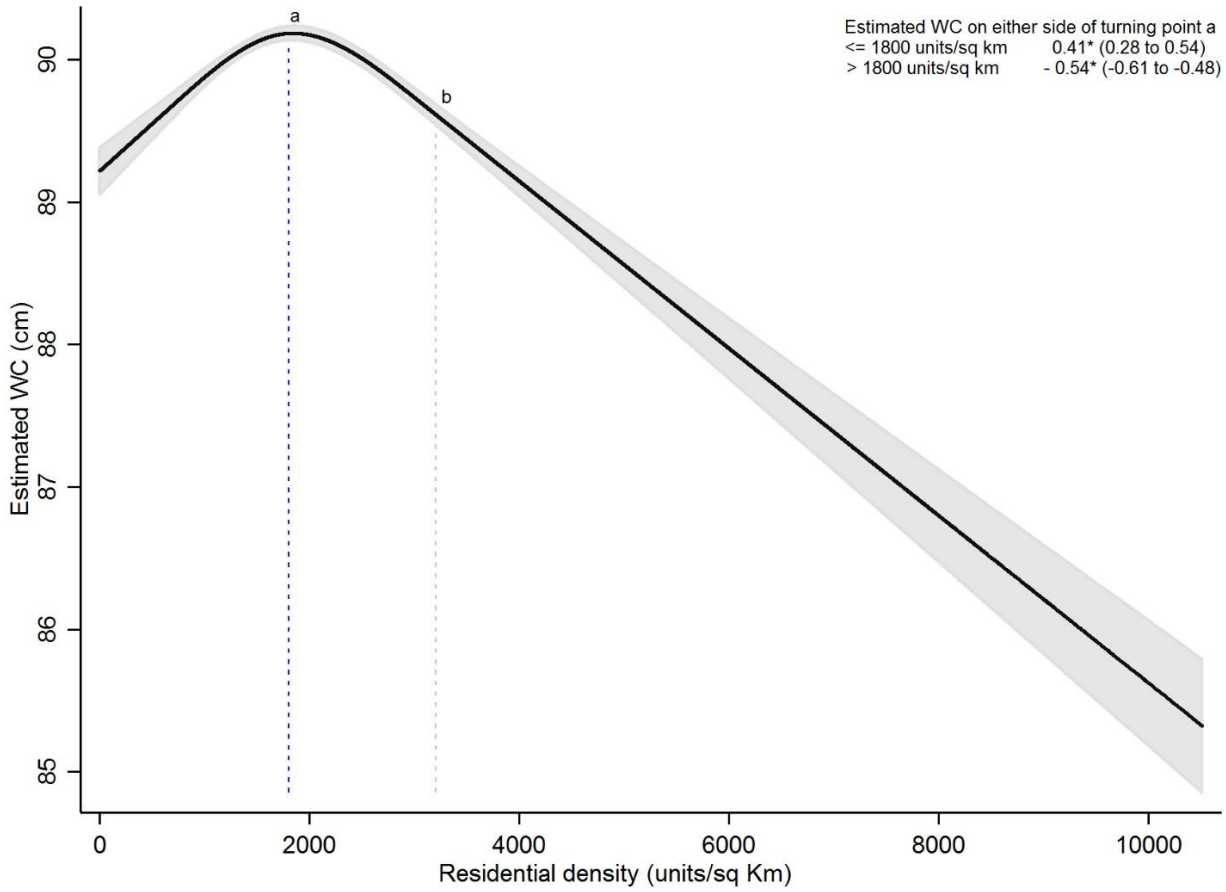
Residential density (per 1,000 units/Km^2)	Body mass index (kg/m^2) β (95% CI)	Waist circumference (cm) β (95% CI)	Whole body fat (Kg) β (95% CI)	Obesity (BMI>30 Kg/m^2) OR (95% CI)
Piece-wise linear models †:				
1,800 – 3,200 units/Km^2	-0.13* (-0.21 to -0.05)	-0.19* (-0.38 to -0.00)	-0.14 (-0.29 to 0.02)	0.98 (0.94 to 1.02)
> 3,200 units/Km^2	-0.17* (-0.21 to -0.12)	-0.53* (-0.64 to -0.43)	-0.31* (-0.39 to -0.22)	0.92* (0.90 to 0.94)

†Fully-adjusted effect estimates controlling for age, sex, education, employment, car ownership, housing tenureship, smoking, processed meat intake, mother's illness and medication use, physical activity, retail density, public transport, street-level movement density and neighbourhood deprivation.
*Statistically significant effect estimates.

Figure

Figures:




Estimated WC on either side of turning point a
<= 1800 units/sq km 0.41* (0.28 to 0.54)
> 1800 units/sq km - 0.54* (-0.61 to -0.48)
a
b
Estimated WC (cm)
85
86
87
88
89
90
0
2000
4000
6000
8000
10000
Residential density (units/sq Km)

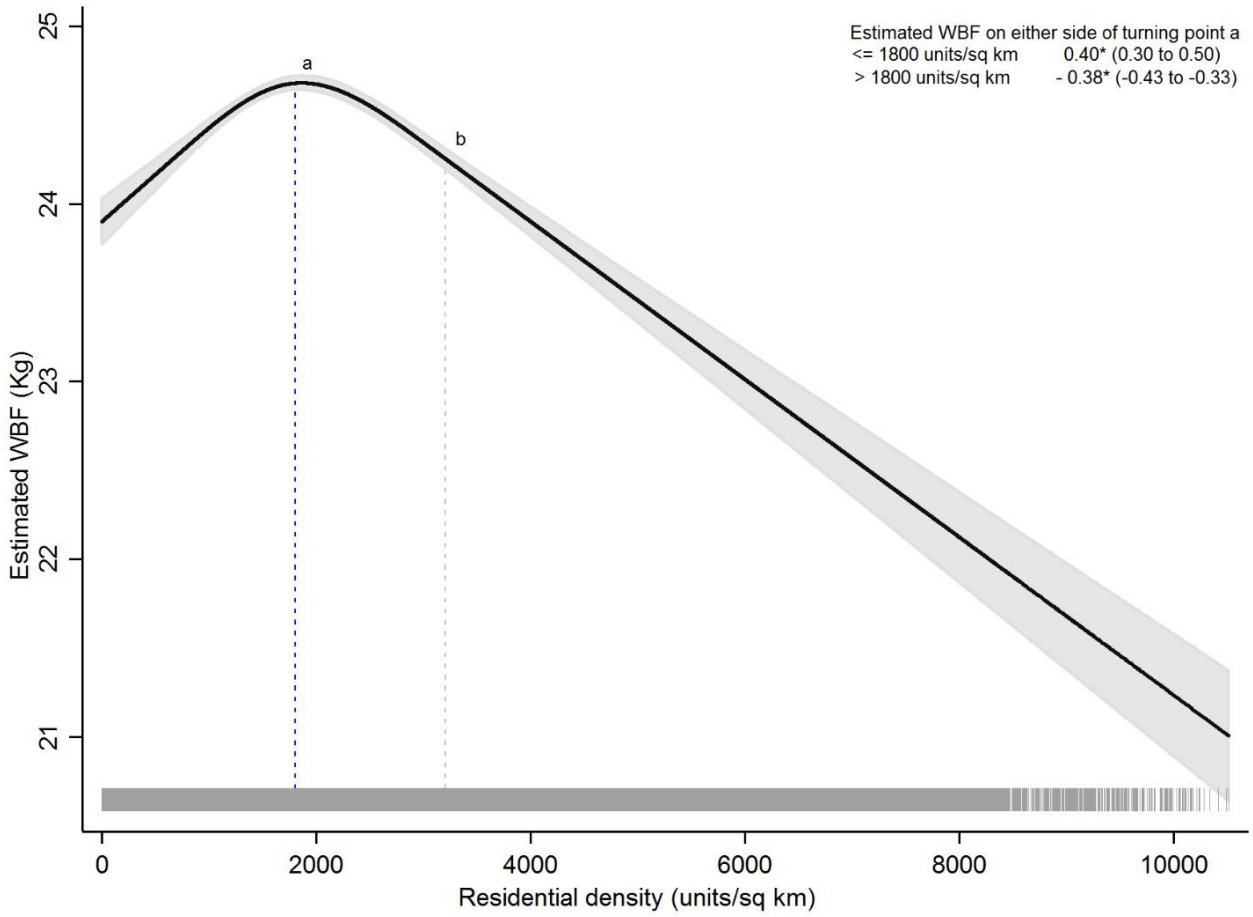


Figure 1: Association between adiposity and housing density, allowing for non-linear effects, with 95% CIs.

The continuous line represents the estimated mean adiposity outcome.

Separate models were fitted for body mass index, waist circumference and whole body fat with restricted cubic splines with Harrell's knots adjusting for age, sex, education, employment, car ownership, housing tenureship, smoking, processed meat intake, mother's illness and medication use, physical activity, retail, public transport, street-level movement density and neighbourhood deprivation.

Point 'a' indicates the detected turning point of the curve (at which the first derivative/slope changes sign), observed at a density of 1,800 units/Km^2. Point 'b' represents the point in the curve corresponding to the residential density of 3,200 units/ Km^2, which is the density of newly developed housing in the UK over the past 2 years.

Effect estimates (β) were measured per 1,000 units/Km^2 increase in residential density from piecewise linear model fitted on either side of the turning point 'a' of the best fitting restricted cubic spline (chosen on the basis of goodness-of-fit parameter; Akaike information criterion).

*Statistically significant effect estimates.

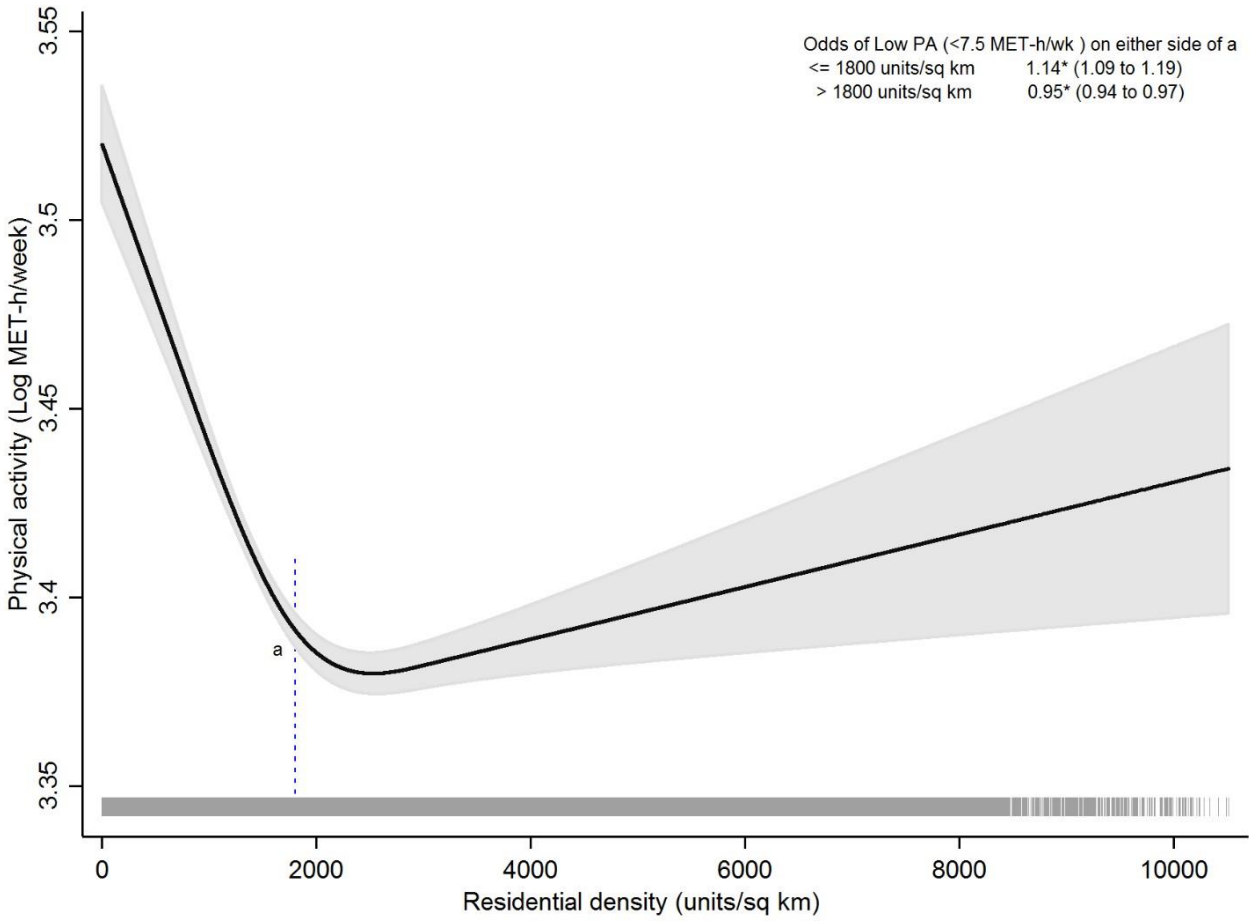
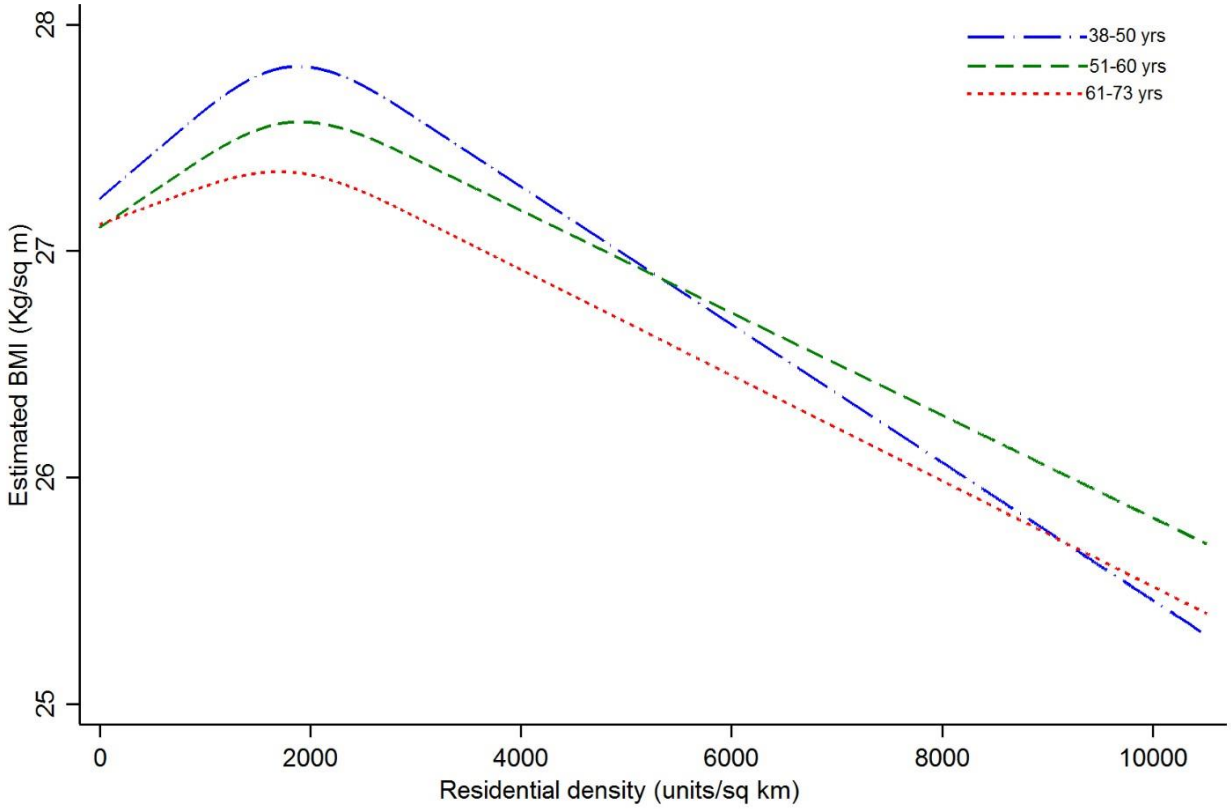
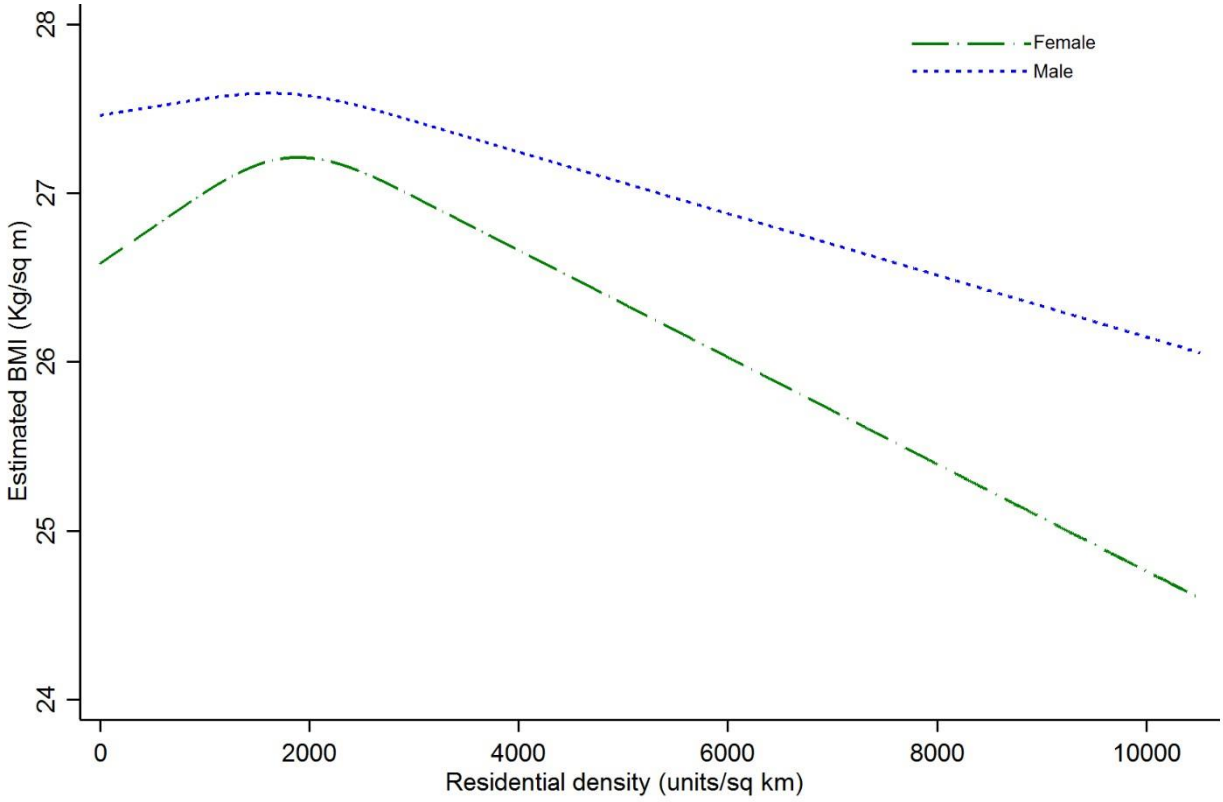


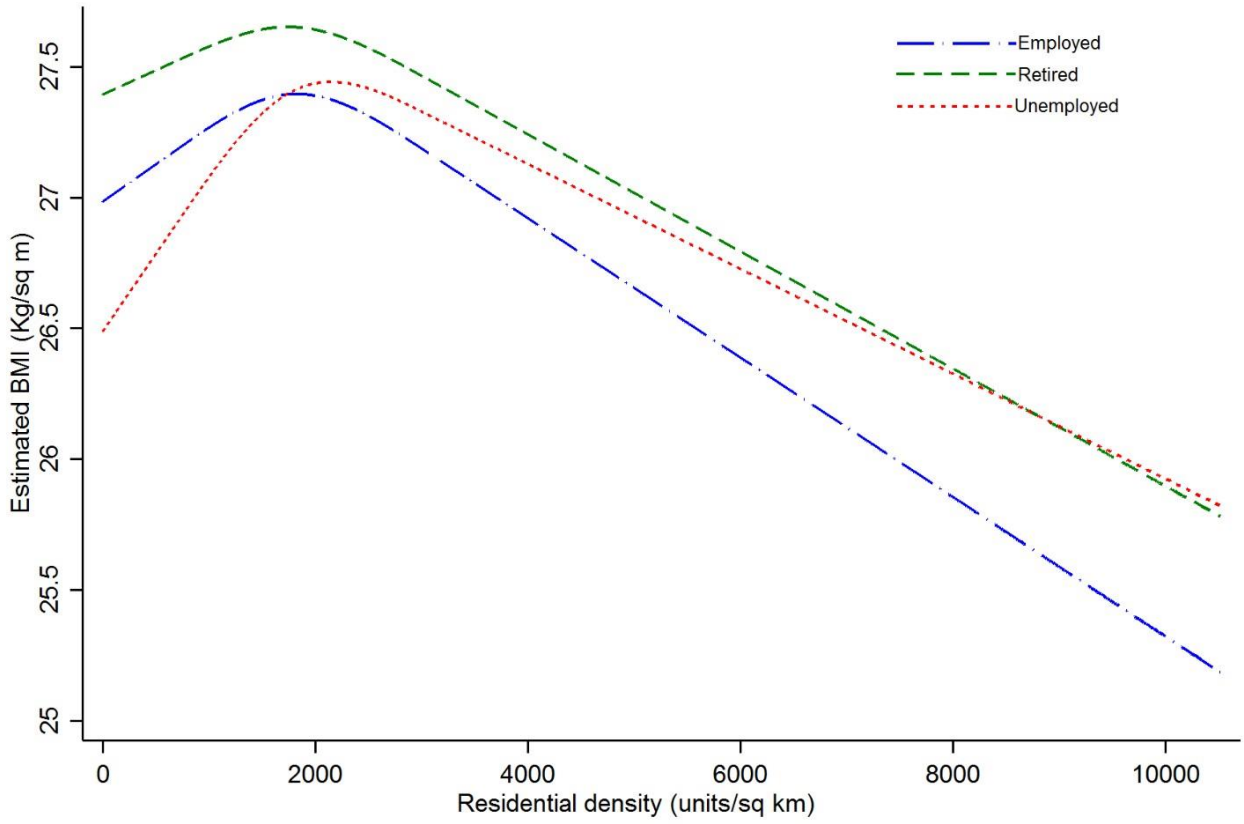
Figure 2. Association between physical activity (log transformed MET-h/week) and residential density, allowing for non-linear effects, with 95% CIs.

Restricted cubic splines with Harrell's knots adjusting for age, sex, education, employment, car ownership, housing tenureship, smoking, processed meat intake, mother's illness and medication use, physical activity, retail, public transport, street-level movement density and neighbourhood deprivation was fitted. Point 'a' indicates the detected turning point of the adiposity – residential density curve (Figure 1), observed at a density of 1,800 units/Km^2. The odds ratios for doing low physical activity (<7.5 MET-h/week) are reported on either side of point 'a'.

*Statistically significant effect estimates.


38-50 yrs
51-60 yrs
61-73 yrs
Estimated BMI (Kg/sq m)
25
26
27
28
0
2000
4000
6000
8000
10000
Residential density (units/sq km)


Female
Male
Estimated BMI (Kg/sq m)
24
25
26
27
28
0
2000
4000
6000
8000
10000
Residential density (units/sq km)


Employed
Retired
Unemployed
Estimated BMI (Kg/sq m)
25
25.5
26
26.5
27
27.5
0
2000
4000
6000
8000
10000
Residential density (units/sq km)

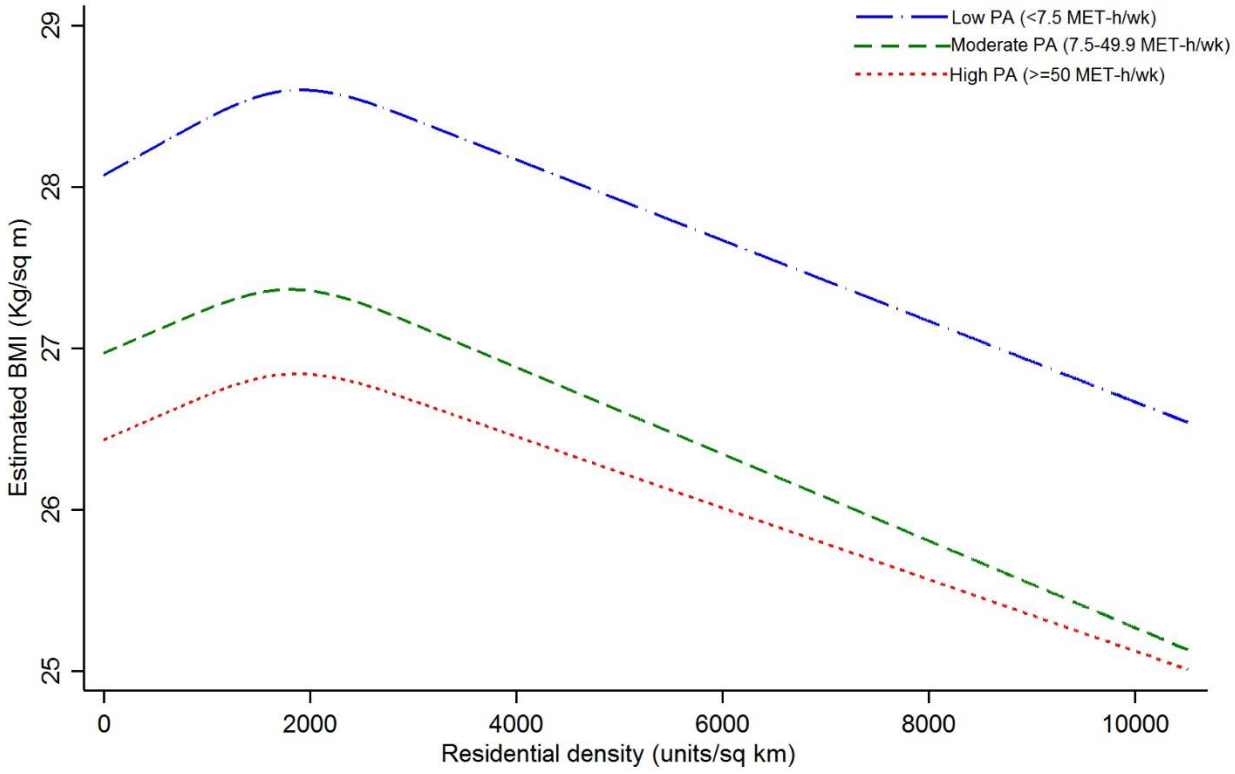

Low PA (<7.5 MET-h/wk)
Moderate PA (7.5-49.9 MET-h/wk)
High PA (>=50 MET-h/wk)
Estimated BMI (Kg/sq m)
25
26
27
28
29
0
2000
4000
6000
8000
10000
Residential density (units/sq km)

Figure 3. Association between body mass index and housing density with effects modification by age, gender, employment status and physical activity (MET-h/wk).