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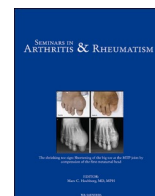
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Does body mass index mediate the relationship between socioeconomic position and incident osteoarthritis?☆

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ABSTRACT

Objectives: To investigate associations of socioeconomic position (SEP) and obesity with incident osteoarthritis (OA), and to examine whether body mass index (BMI) mediates the association between SEP and incident OA.

Methods: Data came from the English Longitudinal Study of Ageing, a population-based cohort study of adults aged ≥ 50 years. The sample population included 9,281 people. Cox regression analyses were performed to investigate the associations between SEP (measured by education, occupation, income, wealth and deprivation) and obesity (BMI ≥ 30 kg/m²) at baseline and self-reported incident OA. The mediating effect of BMI on the relationship between SEP and incident OA were estimated using Structural Equation Models.

Results: After a mean follow-up time of 7.8 years, 2369 participants developed OA. Number of person-years included in the analysis was 65,456. Lower SEP was associated with higher rates of OA (for example, hazard ratio (HR) lowest vs highest education category 1.52 (95% confidence interval (CI) 1.30, 1.79)). Obesity compared with non-obesity was associated with increased rates of incident OA (HR 1.37 (95% CI 1.23, 1.52)). BMI mediated the relationship between a lower SEP and OA ($\beta = 0.005$, $p < 0.001$) and the direct effect was not significant ($\beta = 0.004$, $p = 0.212$).

Conclusions: Strategies to reduce social inequalities and obesity prevalence may help to reduce OA risk.

Introduction

Osteoarthritis (OA) is a common form of arthritis globally and it is a leading cause of years lived with disability [1]. Although both genetic and lifestyle factors play a role in the development of OA [2], obesity is considered as one of the main risk factors for the disease [3]. Underlying mechanisms for the relationship between obesity and the development of OA have been attributed to mechanical stress on load bearing joints

and adipose tissue releasing pro-inflammatory cytokines leading to joint inflammation [4].

Socioeconomic position (SEP) is a multifactorial concept referring to an individual's economic and social position within a society, and can be measured using multiple indicators, including education, occupation, income and deprivation [5]. Whilst all these indicators are interlinked (e.g. education is linked to occupation, which in turn is related to income level [6]), they each have unique properties and are not

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interchangeable [6]. A lower SEP has been associated with increased risk of OA [7–10] in cross-sectional and retrospective studies. However, due to significant limitations of these study designs [11,12], prospective longitudinal studies investigating the temporal association between SEP and incident OA are needed.

SEP is considered a distal factor (indirectly affecting health) and the association between a lower SEP and OA likely occurs via more proximal factors (directly affecting health), such as lifestyle and environmental factors [13]. Identifying mediators through which a lower SEP is associated with incident OA may help to improve targeted prevention strategies. As lower SEP has also been consistently associated with obesity in the general population in high-income countries [14–16], obesity (both total and central [17]) may therefore be a mediator of the relationships between SEP and incident OA. However, this may be different for men and women as previous research suggest that the association between SEP and obesity differs by gender [17].

A recent Mendelian Randomisation study from UK-Biobank reported that body mass index (BMI) mediated the relationship between education and OA (proportion mediated: 23%) [18]. However, UK Biobank is a non-representative sample of the UK population [19], a single indicator as a proxy for SEP (education) was used and the study design was not a prospective longitudinal study. Therefore, the current study aims to 1) assess associations of SEP and obesity (both total and central) with incident OA, 2) whether these associations differ in sub groups (by gender and SEP), and 3) whether BMI mediates any associations observed between SEP and incident OA.

Methods

Participants and study design

Data came from the English Longitudinal Study of ageing (ELSA), a large longitudinal panel study documenting the health, social and economic circumstances of adults aged ≥ 50 years and their partners, living in private households in England [20]. The original sample in 2002 and refreshment samples in 2006, 2008, 2012 and 2014 (to keep the sample representative of the general population) was drawn from the Health Survey of England (HSE). This is a yearly cross-sectional survey aiming to monitor the health of the general population in England, with a multi-stage stratified probability sampling design. The first stage includes a random selection of primary sampling units based on postcodes. In the second stage, a random sample of postal addresses were drawn from the primary sample units. Participants of HSE who were 50 years or older and who agreed to take part in future studies were invited to participate in ELSA.

Participants of ELSA were surveyed every two years from 2002 to 2019 and, with consent, an additional nurse visit was offered where a series of measurements took place [21]. Waves refer to different cycles of data collection, which includes the follow-up of data collection as well as data collection of newly recruited participants in that particular cycle. Nine waves have been published so far.

Participants were eligible for inclusion in the presented analyses if they had at least one nurse visit with anthropometric measurements. Baseline assessment was defined at the time of first anthropometric measurements. Participants who gave a self-reported diagnosis of OA (i.e. prevalent cases) at baseline assessment were excluded.

Written informed consent was obtained from all participants and ethical approval was acquired from the NHS Research Ethics Committees under the National Research and Ethics Service. The UK Data Service provided anonymized data for this study [22].

Measurements/instruments

Exposure variables: obesity and SEP at baseline (waves 2, 4 or 6)

Height (m), weight (kg) and waist circumference (WC, cm) were measured by nurses following standardised protocols in waves 2, 4 and 6

[21]. The first measurement of total and central obesity for each participant was taken as their baseline measure. Total obesity was defined by baseline BMI ≥ 30 kg/m² and central obesity defined by baseline WC ≥ 102 cm for men or ≥ 88 cm for women.

The following variables were used as indicators of SEP: education (no qualifications, other, National Vocational Qualification (NVQ) 1/Certificate of Secondary Education (CSE) or other grade equivalent, NVQ2/General Certificate of Education (GCE) O level equivalent (qualification normally obtained at age 16 in England), NVQ3/GCE A level equivalent (qualification normally obtained at age 18 in England), higher education/below degree, NVQ4/NVQ5/degree or equivalent), occupation (current or most recent) classified using the UK National Statistics Socioeconomic Classification-5 (NS-SEC5) (semi-routine occupations, lower supervisory and technical occupations, small employers and own account workers, intermediate occupations, managerial and professional occupations), income quintiles, wealth quintiles (includes non-housing and primary housing wealth minus debts) and the Index of Multiple Deprivation (IMD) quintiles (based on area-level instead of personal data) [23]. The IMD is a measure of relative deprivation of small areas in England based on 39 indicators across seven domains of deprivation (income; employment; education, skills and training; health deprivation and disability; crime; barriers to housing and services; and living environment) [23]. IMD 2004, 2007 and 2010 were used for waves 2, 4 and 6, respectively.

Outcome variable: incident OA at follow-up waves (waves 3–9)

The outcome of interest was incident OA. In each wave, participants were asked 'Has a doctor ever told you that you have (or had) any of the following conditions on this card?'. If 'Arthritis' was chosen, they were then asked 'Which type or types of arthritis do you have?', with answer options 'osteoarthritis', 'rheumatoid arthritis' or 'some other kind of arthritis'. Participants who indicated a diagnosis of OA were asked for updates on their condition in subsequent waves, but could not report the same diagnosis again; however, they were able to report diagnoses of other types of arthritis. Participants who did not indicate an arthritis diagnosis in previous waves or newly recruited participants were asked the original question.

Covariates / additional variables

Covariates were identified using directed acyclic graphs. Data on covariates were collected at baseline (waves 2, 4 or 6, depending on when participants entered the study) and were self-reported, including: gender (male, female), age (in years, continuous variable), ethnicity (white, non-white), alcohol consumption (less than monthly, 1x/month–4x/week, (almost) every day), smoking status (never smoked, ex-smoker, current smoker), and physical activity (sedentary, low, moderate, high based on the classification used in the Allied Dunbar Survey of Fitness [24]).

Statistical analysis

Descriptive statistics were used to describe the baseline sample. Cox proportional hazards regression analyses estimated associations between each socioeconomic indicator and incident OA (adjusting for age and gender) as well as for obesity and incident OA (adjusting for age, gender, smoking status, alcohol consumption, physical activity and SEP indicators). Person year follow up was calculated from baseline to either a) date of self-reported OA diagnosis, b) loss to follow-up (including non-response and death), c) end of follow-up (Wave 9). BMI and WC were entered into the models as continuous variables, per 1 kg/m² increment for BMI and 5-cm increment for WC. To investigate whether associations differed by gender (or by SEP for the obesity analyses), interaction terms between obesity/SEP and gender and obesity and SEP were included in the model. The proportional hazard assumption was tested using the Schoenfeld residuals test [25], where a p-value of < 0.05 indicates the proportional hazards assumption holds (Supplementary Table S1).

Exposure variables and covariates had missing data (all <5%, except for alcohol which had 11%). To account for missing data, multiple imputation using chained equations was performed with 10 cycles [26]. Moreover, longitudinal survey weights were used to correct for historical non-response, improving the representativeness of the sample [27]. These analyses were performed in Stata v14.

To estimate the mediating effect of BMI on the relationship between SEP and incident OA, mediation analyses were performed. A mediator (i.e. BMI) is an intermediate variable between an exposure (i.e. SEP) and an outcome (i.e. incident OA) [28]. The total effect of SEP on incident OA can be divided into the indirect effect (i.e. effect mediated by BMI) and direct effect (i.e. effect not explained by BMI). Different statistical methods of analysing mediating effects exist, including structural equation modelling (SEM) and causal mediation analysis. SEM includes path analysis with latent variables [29], where direct and indirect effects are measured simultaneously. The advantage of using SEM is that 'latent variables' can be constructed and these allow multiple observed indicators to be captured within one unobserved construct. This is specifically useful for the operationalisation of SEP, since no single observed variable can capture SEP in its totality. However, using mediation analyses in a SEM approach has been criticised as associations between variables represent descriptive rather than causal relationships [30]. Causal mediation analysis, using counterfactuals, is an alternative approach. The outcome is modelled assigning all participants as first exposed and then unexposed, and the causal/total effect is defined as the difference between those two predicted outcomes [31,32]. Here, we estimated the mediating effect of BMI on the relationship between SEP and incident OA using SEM as the main analysis and causal mediation analysis as a sensitivity analysis.

SEM was performed using the lavaan package [33] in R v4.1.1 [34]. Using confirmatory factor analysis, SEP was defined as a latent variable with education, occupation, wealth and income as indicators. Initially, IMD was also added as an observed indicator for SEP; however, as the factor loading was non-significant ($p < 0.05$), it was therefore not included in the final model. The following fit indices assessed model fit: comparative fit index (CFI) (≥ 0.95 indicates good fit), root mean square error of approximation (RMSEA) (≤ 0.08 indicates good fit) and standardised root mean square residual (SRMSR) (≤ 0.08 indicates good fit) [35]. As the indicators for SEP were non-normally distributed ordinal variables, the diagonally weighted least squares estimator was used (WLSMV in Lavaan) [36]. Bootstrapping was used to calculate confidence intervals around the indirect effects, as recommended by Pesigan et al. [37]. As previous research indicated that the association between SEP and obesity differs by gender [17], stratified analyses were performed. Causal mediation analysis was performed using the R package for Causal Mediation Analysis [38] for each SEP indicator individually.

Results

Description of the cohort

Of the people who had at least one nurse visit at waves 2, 4 or 6 ($n = 11,848$), 2567 people were excluded due to having prevalent OA at baseline, resulting in a final sample of 9281 participants. Number of person-years included in the analysis was 65,456. After a mean follow-up of 7.8 years, 2369 participants (25.5% of the sample) developed OA. Table 1 presents the characteristics at baseline for those who developed OA and those who did not. Those who developed OA were more often women, older, had a lower education and higher total and central obesity rates at baseline compared with those who did not develop OA.

Associations between socioeconomic position and incident osteoarthritis

Participants with lower SEP were more likely to develop OA than those with higher SEP (Table 2). For example, the HR of the lowest vs highest education category was 1.52 (95% CI 1.30, 1.79). Formal tests

Table 1

Baseline characteristics of the sample, stratified by those who developed OA and those who did not.

	Total cohort (N = 9281)	
	Non-OA cases (N = 6912)N (%)	OA cases* (N = 2369) N (%)
Gender (female,%)	3295 (47.7%)	1468 (62.0%)
Age (mean (SD))	63.4 (9.8)	64.0 (9.3)
Ethnic group		
- White	6692 (96.9%)	2308 (97.5%)
- Non-white	218 (3.2%)	59 (2.5%)
- Missing	2 (0.0%)	0 (0.0%)
Education		
- Degree/NVQ4/5	1146 (16.6%)	320 (13.5%)
- Higher education/below degree	914 (13.2%)	296 (12.5%)
- A level/NVQ3	566 (8.2%)	154 (6.5%)
- O level/NVQ2/GCE	1284 (18.6%)	454 (19.2%)
- CSE/NVQ1	323 (4.7%)	88 (3.7%)
- Other	531 (7.7%)	222 (9.4%)
- No qualification	2139 (31.0%)	832 (35.1%)
- Missing	9 (0.0%)	3 (0.1%)
Occupation (NS-SEC5) (current or most recent occupation if retired)		
- Managerial/professional	2376 (35.3%)	735 (31.0%)
- Intermediate	869 (12.9%)	338 (14.3%)
- Small employers	794 (11.8%)	246 (10.4%)
- Lower supervisory/technical	677 (10.1%)	236 (10.0%)
- Semi-routine	2020 (30.0%)	756 (31.9%)
- Missing	176 (2.5%)	58 (2.4%)
Smoking status		
- Never smoked	2695 (39.1%)	913 (38.5%)
- Ex-smoker	3087 (44.8%)	1093 (46.1%)
- Current smoker	1116 (16.2%)	357 (15.1%)
- Missing	14 (2.0%)	6 (0.3%)
Alcohol consumption		
- Less than monthly	1457 (24.0%)	566 (23.9%)
- 1x/month-4x/week	3172 (52.2%)	1118 (47.2%)
- (Almost) every day	1452 (23.9%)	455 (19.2%)
- Missing	831 (12.0%)	230 (9.7%)
BMI (mean (SD)) [kg/m ²]	27.5 (4.7)	28.7 (5.2)
- Missing	270 (3.9%)	111 (4.7%)
WHO BMI categories†		
- Underweight	78 (1.1%)	15 (0.6%)
- Normal weight	2003 (29.0%)	496 (20.9%)
- Overweight	2869 (41.5%)	959 (40.5%)
- Obesity	1692 (25.5%)	788 (33.3%)
WC (mean (SD)) [cm]	95.17 (13.3)	96.6 (13.4)
- Missing	160 (2.3%)	55 (2.3%)
Central obesity‡	3117 (46.2%)	1333 (56.3%)

BMI, body mass index; cm, centimetres; NS-SEC, National Statistics Socio-economic classification; NVQ, National Vocational Qualification; OA, osteoarthritis; SD, standard deviation; WC, waist circumference. *Characteristics defined at baseline, when participants are recruited (not at OA onset) †WHO categories defined as: underweight (BMI <18.5 kg/m²), normal weight (BMI 18.5–24.9 kg/m²), overweight (BMI 25.0–29.9 kg/m²), obese (BMI >30.0 kg/m²). ‡Central obesity defined as: WC ≥ 102 cm for men or ≥ 88 cm for women.

of interaction between SEP indicators and gender/obesity were not statistically significant ($0.08 \leq p \leq 0.89$) except for between gender and deprivation ($p = 0.014$). Stratified analyses (Supplementary Table S2) showed that the relationship between higher deprivation and incident OA was stronger for men (most vs least deprived HR 1.89 (95% CI 1.46, 2.46)) than women (HR 1.33 (95% CI 1.07, 1.64)).

Associations between obesity and incident osteoarthritis

Total and central obesity were both associated with incident OA and these associations were maintained after adjustment for covariates, including SEP indicators (Table 3). Risk of OA incidence increased by 1% for each 1 kg/m² increase in BMI and increased by 3% for each 5 cm increase in WC. There was no evidence of gender or SEP differences in

Table 2
Weighted* Cox proportional hazards regression for the associations between different SEP indicators and RA/OA incidence.

Predictors	UnadjustedHR (95% CI)	Age and gender adjustedHR (95% CI)
<i>Education</i>		
No qualification	1.86 (1.59, 2.16)	1.52 (1.30, 1.79)
Other	1.63 (1.33, 2.00)	1.35 (1.10, 1.66)
NVQ1/CSE	1.28 (0.97, 1.68)	1.23 (0.93, 1.61)
O level/NVQ2/GCE	1.44 (1.22, 1.70)	1.30 (1.10, 1.54)
A level/NVQ3	1.08 (0.87, 1.36)	1.05 (0.84, 1.31)
Higher education/below degree	1.26 (1.05, 1.52)	1.20 (1.00, 1.45)
Degree/NVQ4/5	ref	ref
<i>Occupation (NS-SEC5)</i>		
Semi-routine	1.47 (1.30, 1.66)	1.28 (1.13, 1.45)
Lower supervisory/technical	1.28 (1.07, 1.53)	1.28 (1.07, 1.53)
Small employers	1.08 (0.91, 1.29)	1.07 (0.90, 1.28)
Intermediate	1.34 (1.15, 1.55)	1.09 (0.93, 1.27)
Managerial/professional	ref	ref
<i>Wealth (1=lowest wealth, 5=highest wealth)</i>		
Quintile 1	1.81 (1.54, 2.11)	1.65 (1.41, 1.94)
Quintile 2	1.50 (1.29, 1.74)	1.44 (1.24, 1.68)
Quintile 3	1.37 (1.19, 1.59)	1.31 (1.13, 1.52)
Quintile 4	1.20 (1.04, 1.38)	1.17 (1.01, 1.35)
Quintile 5	ref	ref
<i>Income (1=lowest income, 5=highest income)</i>		
Quintile 1	1.47 (1.26, 1.71)	1.26 (1.07, 1.47)
Quintile 2	1.56 (1.35, 1.82)	1.36 (1.16, 1.59)
Quintile 3	1.42 (1.22, 1.64)	1.29 (1.11, 1.50)
Quintile 4	1.15 (1.00, 1.33)	1.11 (0.96, 1.28)
Quintile 5	ref	ref
<i>Index of Multiple Deprivation (1= most deprived, 5= least deprived)</i>		
Quintile 1	1.56 (1.33, 1.84)	1.53 (1.30, 1.80)
Quintile 2	1.18 (1.01, 1.38)	1.14 (0.98, 1.33)
Quintile 3	1.16 (1.01, 1.34)	1.13 (0.98, 1.30)
Quintile 4	1.03 (0.90, 1.18)	0.99 (0.87, 1.14)
Quintile 5	ref	ref

CI, confidence interval; HR, hazard ratio; NS-SEC, national statistic socioeconomic classification; NVQ, National Vocational Qualification; OA, osteoarthritis; ref, reference category. *Longitudinal survey weights were used to correct for historical non-response. Formal tests of interaction between SEP and gender/obesity were run but in all cases $0.08 < p < 0.89$ except for gender*IMD ($p = 0.014$). Stratified analyses for this can be found in Supplementary Table S2.

Table 3
Weighted* Cox proportional hazards regression for the associations between different definitions of obesity and OA.

Predictors	UnadjustedHR (95% CI)	Fully adjustedHR (95% CI)
<i>Total obesity (BMI ≥ 30 kg/m²)</i>		
Obesity	1.54 (1.39, 1.71)	1.37 (1.23, 1.52)
No obesity	ref	ref
<i>Central obesity (WC ≥ 102 cm for men and ≥ 88 cm for women)</i>		
Central obesity	1.46 (1.33, 1.62)	1.29 (1.17, 1.43)
No central obesity	ref	ref
<i>Continuous</i>		
BMI per 1 kg/m ² increment	1.01 (1.00, 1.02)	1.01 (1.00, 1.02)
WC per 5 cm increment	1.01 (1.00, 1.03)	1.03 (1.01, 1.05)

CI, confidence interval; HR, hazard ratio; NS-SEC, national statistic socioeconomic classification; ref, reference category; WC, waist circumference. Fully adjusted model for obesity/central obesity: adjusted for gender, age, alcohol, smoking, physical activity, education, occupation, wealth, income and IMD. *Longitudinal survey weights were used to correct for historical non-response. Formal tests of interaction between obesity and gender/SEP were run but in all cases $0.08 < p < 0.97$.

the associations between total obesity and OA (p -values from tests of interaction $0.25 < p < 0.93$).

The mediating effect of body mass index on the relationship between socioeconomic position and incident osteoarthritis

The confirmatory factor analysis indicated a good fit for the definition of the latent variable SEP, using four indicators: education, NS-SEC5, wealth quintiles and income quintiles (CFI 0.998, RMSEA 0.038, SRMR 0.007). The fit indices of the different SEMs are shown in Supplementary Table S3.

The total, direct and indirect effects via BMI of a lower SEP on OA incidence in the total population and stratified for women and men are shown in Table 4 and Fig. 1 (results for WC are shown in Supplementary Table S4). The indirect pathway (i.e. SEP->BMI->OA) was statistically significant (0.005 (95% CI 0.004, 0.006), but not the direct effect (0.004 (95% CI -0.002, 0.011)). This indicates that BMI mediates the relationship between a lower SEP and incident OA. Causal mediation analyses showed similar results for the separate indicators for SEP (Supplementary Table S5).

Discussion

In this English study including adults aged >50 years, both total and central obesity, as well as a lower SEP at baseline were associated with increased rates of OA over an average follow-up of 7.8 years. BMI/WC mediated the relationship between a lower SEP and incident OA. There were no notable differences between measurements of obesity, i.e. BMI or WC.

The relationships of both total and central obesity with OA have been demonstrated previously [3]; however, for central obesity, most studies to date were cross-sectional in design and did not adjust for SEP [39,40]. This study indicates that there is a longitudinal association for both types of obesity independent from SEP, strengthening the view that in addition to mechanical stress on joints, inflammation induced by central adiposity may also be an important factor in the disease process of developing OA [4].

Moreover, cross-sectional and retrospective studies have linked a lower SEP with OA [7–10]; however, prospective cohort studies were lacking. A recent study, only using education as SEP indicator, also found a mediating effect of BMI for the association between lower education and OA incidence [18]. To our knowledge, ours is the first study investigating the mediating effect of BMI on the causal pathway between multiple indicators of SEP and the development of OA. We did not find gender differences in the associations of individual SEP indicators included in the SEM (education/occupation/wealth/income) and obesity with incident OA; however, stratified analysis in the SEM indicated that the mediated effect (i.e. the indirect effect) was higher in women than men. This might be driven by the relationships between SEP and obesity, as previous research suggest that the SEP-obesity relationship is stronger among women compared with men [17].

Notably, we found that the relationship between higher area-level deprivation and incident OA was stronger for men than women. This may be due to higher rates of manual occupations among men living in deprived areas, which is associated with the development of OA in part through increased loading on joints and increased risk for joint trauma [41]. However, we did not see gender differences for the relationship between individual SEP indicators, including occupation, and incident OA in our study. This discrepancy may be explained by the fact that the IMD is an area-level variable and does not fully capture an individual's experience of deprivation [42]. Further research should investigate what specific neighbourhood factors are important for the development of OA.

Our study has limitations. Firstly, the OA diagnosis was self-reported, which may lead to recall bias or misclassification. A previous systematic review and meta-analysis by Peeters et al. (2015) studied the sensitivity

Table 4
The total, direct and indirect effect via BMI of SEP on incident OA adjusted for age and gender.

	Total		Direct		Indirect	
	Regression estimate (95% CI)	p-value	Regression estimate (95% CI)	p-value	Regression estimate (95% CI)	p-value
Combined	0.009 (0.002, 0.016)	$p = 0.009$	0.004 (-0.002, 0.011)	$p = 0.212$	0.005 (0.004, 0.006)	$p < 0.001$
Women	0.012 (0.002, 0.023)	$p = 0.021$	0.004 (-0.007, 0.015)	$p = 0.463$	0.008 (0.006, 0.011)	$p < 0.001$
Men	0.006 (-0.004, 0.015)	$p = 0.162$	0.005 (-0.005, 0.013)	$p = 0.310$	0.002 (0.001, 0.003)	$p = 0.002$

CI, confidence interval; OA, osteoarthritis. Proportion mediated (indirect effect/total effect*100%) not calculated as complete mediation was observed (only the indirect effect of BMI was statistically significant).

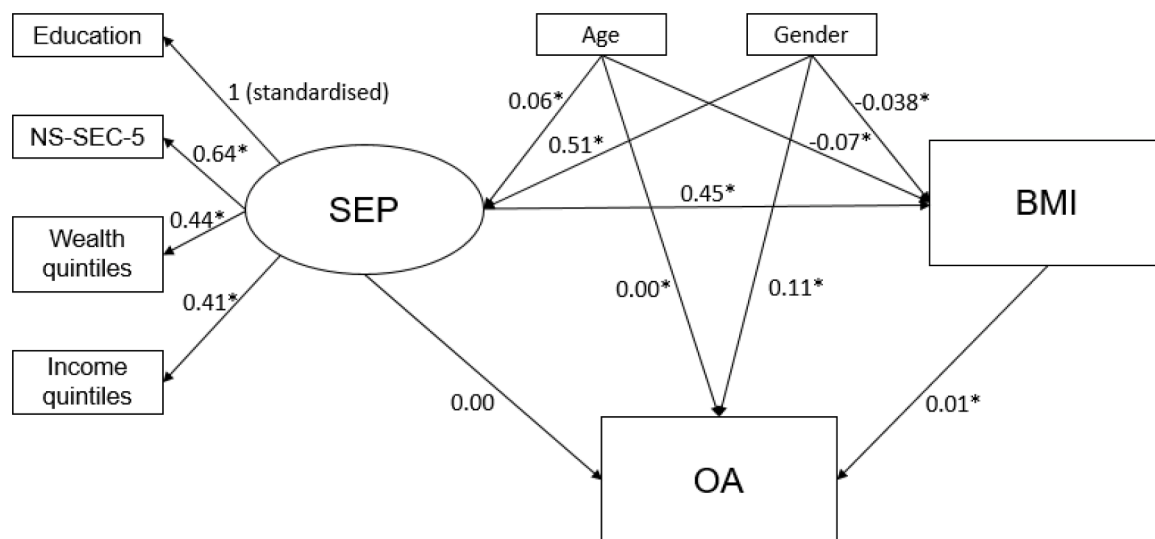


Fig. 1. The structural equation model for the relationships between SEP, BMI and incident OA adjusted for age and gender
*statistically significant ($p < 0.05$). BMI, body mass index; NS-SEC, national statistics socioeconomic classification; OA, osteoarthritis; SEP, socioeconomic position.

and specificity of self-reported OA in population-based studies compared to medical records or American College of Rheumatology (ACR) criteria. This study showed a high sensitivity and specificity for self-reported OA (0.75 and 0.89, respectively) [43]. We expect the remaining misclassification to be non-differential (i.e. it is equally distributed among obese vs non-obese; high vs low SEP); in this case, the true effect will be underestimated. Secondly, we only included BMI and WC at baseline (i.e. the first point of measurement at either wave 2, 4 or 6) and we did not take into account change of BMI/WC over time or life course effects of high BMI/WC as no early life data on BMI/WC were available in this study. However, additional analysis suggested that BMI/WC in this study population remained constant over different waves (Supplementary Table S6) and adjusting for BMI/WC changes over different waves suggested little change to the estimates for the relationships of obesity with incident OA (Supplementary Table S7). Lastly, this study is only generalizable to the older population (aged ≥ 50 years) of England; the associations between SEP, obesity and incident OA may be different for a younger population. Risk factors may differ between early and later onset OA, for example, the main risk factor for early OA is joint injuries [44] whereas for later onset OA this is obesity [3]. In addition, recent improvements of educational and occupational opportunities, especially for women, may not reflect the social environment of the ELSA population.

A strength of this study is that we were able to use nurse-measured heights, weights and waist circumferences, reducing social desirability bias [45]. Moreover, using a latent variable for SEP in the SEMs, we were able to capture SEP indicators reflecting early life (i.e. education), later life (i.e. occupation and income) and current life (i.e. accumulated wealth) in one measure. However, we cannot be certain that our latent

variable represents SEP in its entirety and we may have missed other important factors not captured in ELSA. For instance, when we included IMD, the confirmatory factor analysis for the latent variable ‘SEP’ indicated poor fit, indicating that our latent variable is a better measure for individual rather than neighbourhood SEP. Including a sensitivity analysis using a causal mediation analysis approach increased the robustness of our findings. Lastly, the longitudinal data and large sample size allowed the study of incidence and more precise estimates.

OA is not only a debilitating disease for the individual [1], but also comes at substantial societal cost, both in terms of loss of productivity and healthcare costs [46]. Our research shows that preventing obesity may contribute to reducing incident OA and the aforementioned individual and societal impacts of OA. Further research should focus on effective treatment and prevention interventions with the aim to reduce obesity. However, social inequalities in health will not be solved by focussing on intermediate factors, such as obesity, alone. Public health approaches should also focus on improving upstream structural factors (e.g. education, occupation, income), which will increase the opportunities and reduce the barriers for people to lead healthy lives [47].

In conclusion, our results indicate that both SEP and obesity are associated with the development of OA in both men and women. BMI mediated the relationship between a lower SEP and incident OA. Efforts to reduce obesity, specifically in low SEP groups, may help to decrease the risk for OA.

Data access statement

The anonymised data used in this study is available via the UK Data Service (22).

Declaration of Competing Interest

The authors declare no conflicts of interest.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at [doi:10.1016/j.semarthrit.2022.152063](https://doi.org/10.1016/j.semarthrit.2022.152063).

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