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Association of neighbourhood disadvantage and individual socioeconomic position with all-cause mortality: a longitudinal multicohort analysis

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Summary

Background Few studies have examined the interactions between individual socioeconomic position and neighbourhood deprivation and the findings so far are heterogeneous. Using a large sample of diverse cohorts, we investigated the interaction effect of neighbourhood socioeconomic deprivation and individual socioeconomic position, assessed using education, on mortality.

Methods We did a longitudinal multicohort analysis that included six cohort studies participating in the European LIFEPATH consortium: the CoLaus (Lausanne, Switzerland), E3N (France), EPIC-Turin (Turin, Italy), EPIPorto (Porto, Portugal), Melbourne Collaborative Cohort Study (Melbourne, VIC, Australia), and Whitehall II (London, UK) cohorts. All participants with data on mortality, educational attainment, and neighbourhood deprivation were included in the present study. The data sources were the databases of each cohort study. Poisson regression was used to estimate the mortality rates and associations (relative risk, 95% CIs) with neighbourhood deprivation (Q1 being least deprived to Q5 being the most deprived). Baseline educational attainment was used as an indicator of individual socioeconomic position. Estimates were combined using pooled analysis and the relative excess risk due to the interaction was computed to identify additive interactions.

Findings The cohorts comprised a total population of 168 801 individuals. The recruitment dates were 2003–06 for CoLaus, 1989–91 for E3N, 1992–98 for EPIC–Turin, 1999–2003 for EPIPorto, 1990–94 for MCCS, and 1991–94 for Whitehall II. We use baseline data only and mortality data obtained using record linkage. Age-adjusted mortality rates were higher among participants residing in more deprived neighbourhoods than those in the least deprived neighbourhoods (Q1 least deprived neighbourhoods, 369·7 per 100 000 person-years [95% CI 356·4–383·2] *vs* Q5-most deprived neighbourhoods 445·7 per 100 000 person-years [430·2–461·7]), but the magnitude of the association varied according to educational attainment (relative excess risk due to interaction=0·18, 95% CI 0·08–0·28). The relative risk for Q5 versus Q1 was 1·31 (1·23–1·40) among individuals with primary education or less, but less pronounced among those with secondary education (1·12; 1·04–1·21) and tertiary education (1·16; 1·07–1·27). Associations remained after adjustment for individual-level factors, such as smoking, physical activity, and alcohol intake, among others.

Interpretation Our study suggests that the detrimental health effect of living in disadvantaged neighbourhoods is more pronounced among individuals with low education attainment, amplifying social inequalities in health. This finding is relevant to policies aimed at reducing health inequalities, suggesting that these issues should be addressed at both the individual level and the community level.

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Introduction

Socioeconomic status is associated with health and mortality. Yet, an increasing number of studies have shown that residing in deprived neighbourhoods is associated with increased mortality and that this excess risk is still present after accounting for personal socioeconomic factors.[1,2] This association happens because neighbourhood deprivation is a marker for characteristics that can affect health, including the availability of public services and environmental resources, and therefore it can exert an independent effect over an individuals' health.[3,4] Studying the interaction between neighbourhood-level and individual-level socioeconomic deprivation and their effect on health is highly relevant to policies because this knowledge could help to generate targeted and multisectoral actions.

Socioeconomic factors at the individual level and neighbourhood level might act together to influence

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Research in context

Evidence before this study

Low socioeconomic position is a strong predictor of morbidity and premature mortality worldwide. We searched PubMed on Oct 1, 2021, for articles published from 1998 to 2021 with titles or abstracts that included the search terms: "mortality", "death", "survival", "socioeconomic", "poverty", "income", "disadvantage", and "deprivation". The following languages were considered: Portuguese, Spanish, Italian, French, German, and English. Our search yielded more than 15 000 publications. We found evidence of a similar effect of low socioeconomic status on mortality to that of well established risk factors. A growing number of studies (~500 of the >15 000 publications) also showed that the socioeconomic characteristics of the place where individuals live, work, and recreate might affect their health as well. However, the results on whether there is an interaction between neighbourhood socioeconomic deprivation and individual socioeconomic position were conflicting. Although some studies found that individuals of a low socioeconomic position living in disadvantaged neighbourhoods might have a higher mortality risk compared with individuals of a low socioeconomic position living in wealthy neighbourhoods, other studies suggested that individuals of a low socioeconomic position who live in wealthy neighbourhoods have a higher mortality risk than those who live in a disadvantaged neighbourhood. The studies we cite in the present research paper were selected as being representative of high-quality evidence on the topic, and so are not intended to be an exhaustive list of all available research on the subject.

Added value of this study

Part of the conflict in the available evidence might be because of the fact that the interaction effects between neighbourhood deprivation and individual socioeconomic position differ across countries and regions because of the different degrees of socio-spatial segregation (the extent to which similar societal groups are living close to each other) and social integration and interaction, so that previous evidence, based on single settings, does not provide a comprehensive and diverse portrait of these processes. Therefore, it is important to conduct large multi-country prospective studies assembling different countries, regions, and cities.

Our study examines the interaction of individual and neighbourhood socioeconomic factors in six cohorts presenting results from different international settings, comprising more than 3 million person-years and more than 20 000 deaths. Overall, individuals living in more deprived neighbourhoods had a higher mortality, but this association was more pronounced among individuals of a lower socioeconomic position: the age-adjusted mortality rates were the highest among individuals of lower socioeconomic position in the most deprived neighbourhoods and the effect of neighbourhood deprivation was also stronger among individuals of a lower socioeconomic position.

To our knowledge, this is the first study that used multiple cohorts, representing two continents (Europe and Oceania), with different welfare regimens and physical and socioeconomic characteristics, to study the interaction between individual (compositional effect) and neighbourhood (contextual effect) socioeconomic conditions. The examination of this dyad (compositional *vs* contextual) is paramount for the definition of policies aimed at reducing inequalities in health. Additionally, we used robust epidemiological measures of interaction and focused on mortality, a fundamental health endpoint, as opposed to a previous multi-cohort study by Ribeiro and colleagues in 2019 on the topic that only explored risk biomarkers with the potential to increase death risk.

Implications of all the available evidence

We showed that individual and neighbourhood socioeconomic factors might interact to affect mortality. Living in disadvantaged neighbourhoods is more detrimental to individuals with a low income, who are less able to overcome unmet needs, and suggesting that the inadequate public services and environmental resources in these neighbourhoods might amplify their risk of dying, widening socioeconomic inequalities in health. Therefore, policies aiming to narrow health inequalities should simultaneously intervene at an individual and community level.

health in two ways, united in two theories: the deprivation amplification model[5] and the relative standing model.[6] Coming from a low socioeconomic background and residing in deprived neighbourhoods might exert an amplified detrimental influence on health, so that individuals of a low socioeconomic position living in deprived neighbourhoods might have a higher mortality risk compared with individuals of a low socioeconomic position living in less deprived neighbourhoods. This effect might happen because deprived neighbourhoods tend to have fewer community resources (eg, services and jobs) and, simultaneously, individuals of a low socioeconomic position might be more reliant on local resources because they have less ability to purchase goods and services privately.[4] The second model stresses the relative standing of an individual within their neighbourhood—namely, that the discrepancy between individual socioeconomic position and their neighbours' positions might be detrimental to health.

Investigations exploring the interactions between individual and neighbourhood socioeconomic conditions and their effects on mortality have reached mixed and contradictory findings. In a pioneer study, it was observed that mortality was highest among those who lived in disadvantaged neighbourhoods and were also of a lower socioeconomic position,[7] suggesting that poor neighbourhood environments amplified their risk. Subsequently, other studies have observed such a deprivation amplification pattern.[7–9] Contrastingly, other investigations seem to support the relative standing model, suggesting that individuals of a low socioeconomic position residing in least deprived neighbourhoods are at higher risk of dying than their counterparts who live in more deprived neighbourhoods,[10–13] which implies they do not benefit from the higher quality and availability of resources. Finally, no evidence of an interaction between individual socioeconomic position and neighbourhood deprivation was reported.[14,15] Moreover, the relevance of each model might differ across settings because of the different degrees of socio-spatial segregation and social integration and interaction; so that previous evidence, based on single settings, does not provide a comprehensive and diverse portrait of these processes. Therefore, it is necessary to conduct studies covering different countries, regions, and cities.

Using data from six prospective adult cohorts from Europe and Australia, the objective of this study was to analyse the association between neighbourhood socioeconomic deprivation and all-cause mortality and to investigate the presence of interactions between individual socioeconomic position and neighbourhood deprivation.

Methods

Study design and participants

We did a longitudinal multicohort study that used six adult cohorts participating in the European LIFEPATH consortium, for whom data on individual and neighbourhood deprivation, demographics, and mortality was available for: the CoLaus cohort (Lausanne, Switzerland; N=6733, including both men and women), the E3N cohort (France; N=98 995, including only women), the EPIC-Turin cohort (Turin, Italy; N=8763, including both men and women; data on neighbourhood deprivation was not available for the whole cohort, only for Turin), the EPIPorto cohort (Porto, Portugal; N=2485, including both men and women), the Melbourne Collaborative Cohort Study (MCCS) cohort (Melbourne, VIC, Australia; N=41 514, including both men and women), and Whitehall II (London, UK; N=10 308, including both men and women). Participants from the included cohorts were adults (≥18 years), recruited from the community (except in Whitehall II, where participants were individuals working as civil servants, and in EN3, where participants were individuals working in the education sector) and were followed up regularly from recruitment through telephone questionnaires, in-person evaluations, and record linkage.

Although data availability and being part of the LIFEPATH consortium were factors for the selection of these specific cohorts (for participants to be included in the present investigation, the cohort study had to have information on neighbourhood deprivation, educational attainment, and mortality), it is notable that they represent southern and western Europe, different welfare systems, and various physical and socioeconomic characteristics, and include an Australian cohort, which was crucial to ascertain the generalisability of our findings to other continents.

All cohorts were approved by their respective ethics committees (appendix pp 2–4) and written informed consent was obtained from all participants. This study's protocol was approved by the LIFEPATH Steering Committee. The only deviations from the protocol were the use of Poisson regression instead of survival analysis, and the exclusion of a cohort study because of the absence of data on neighbourhood deprivation. A full description of the study design, ethics, and participants in each cohort is provided in the appendix. We assessed the quality of included studies using the Cochrane Risk of Bias Tool for cohort studies. Three reviewers (AIR, SS, and MK) independently assessed the studies. The quality of the study was considered to be high if all items were assessed favourably (appendix p 6).

See **Online** for appendix

For the **protocol** see https://tinyurl.com/mr4dee2u

This manuscript follows the Strengthening the Reporting of Observational studies in Epidemiology guidelines for cohort studies and the Guidelines for Accurate and Transparent Health Estimates Reporting.

Procedures

Data on educational attainment and covariates at baseline were collected by trained professionals through a questionnaire and physical examination. Data on neighbourhood deprivation were obtained through linkage between the baseline residential location and geographical datasets containing information on neighbourhood deprivation, and mortality data were obtained through record linkage (except for CoLaus, where it was measured through active follow-up).

Educational attainment

Baseline educational attainment was used as an indicator of individual socioeconomic position. Educational attainment was grouped in the following classes: (1) primary and lower secondary school (from 7 to 9 years after preschool with a basic curriculum in languages, mathematics, and other subjects, classified as low educational attainment); (2) upper secondary school (around 4–5 years more than primary and lower secondary, high school diploma level, classified as medium educational attainment); and (3) post-secondary and tertiary education (any degree after high school, such as BSc and MSc, etc, classified as high educational attainment). Low educational attainment corresponds to the International Standard Classification of Education (ISCED) 1–2, medium educational attainment to ISCED 3, and high educational attainment to ISCED 4–8. The harmonisation procedures of the educational data in LIFEPATH are described in the appendix (pp 11–13).

Neighbourhood socioeconomic deprivation
Baseline neighbourhood socioeconomic deprivation was measured using different multivariable indices covering employment, education, wealth, housing conditions, and tenure status (appendix p 8): the Townsend index of deprivation in Whitehall II and CoLaus,[16] the Rey index of deprivation in E3N,[17] the neighbourhood deprivation index in EPIC-Turin,[18] the European Deprivation Index in EPIPorto,[19] and the Socio-Economic Indexes for Areas index of relative socioeconomic disadvantage in MCCS.[20] In CoLaus, the deprivation was assessed for 1000 m² cells of land (calculating the mean of 106 inhabitants per area); in E3N, the deprivation was assessed for communes (the mean of 500 inhabitants per area); in EPIC-Turin, it was assessed for administrative neighbourhoods (the mean of 41 000 inhabitants per area); in EPIPorto, it was assessed for census block groups (the mean of 600 inhabitants per area); in MCCS, it was assessed for postal areas (the mean of 400 inhabitants per area); and in Whitehall II, it was assessed for electoral wards (the mean of 5500 inhabitants per area). Neighbourhood deprivation was categorised according to cohort-specific quintiles of increasing socioeconomic deprivation (Q1 being the least deprived to Q5 being the most deprived).

Mortality follow-up
Each cohort provided participants' vital status, follow-up time, and date of death. In most cohorts, the vital status was assessed through record linkage with administrative data, except in the CoLaus cohort, where it was measured through active follow-up.[21]

Covariates
Estimates were adjusted for the following baseline covariates, harmonised within the LIFEPATH project:[21–23] age, sex, marital status, smoking, alcohol consumption, physical activity, and body-mass index (BMI). Details on the precision of the main exposure variables, outcome, and covariates are provided in the appendix (pp 9–10). Marital status was classified either as married or cohabiting, or living alone. Smoking was categorised into current, former, and never smoker. Alcohol consumption was measured in units per week; participants were categorised as abstainers (0 units per week), moderate (1–21 units per week for men, 1–14 for women), and heavy (>21 units per week for men, >14 for women) drinkers. Physical activity was a dichotomous variable indicating whether the person led an active or sedentary lifestyle. BMI was defined as weight (kg) divided by height (m²).

Statistical analysis
The primary outcome was all-cause mortality and we aimed to study the association of neighbourhood socioeconomic deprivation and educational attainment with all-cause mortality.

After the approval of the protocol by the LIFEPATH Steering Committee, the individual cohort datasets were stored and harmonised by the Università degli Studi di Torino, the datasets were imported into R software 4.1.0, where data analysis was done by AIR and MS.

To evaluate if the size of the cohorts would be enough to detect significant associations, we used Signorini's formula.[24] Assuming a 5% confidence level and a statistical power of 80%, the minimum sample size for the detection of a relative risk (RR) of 1·1 was 863.

We calculated the absolute frequencies and percentages for categorical variables, and the mean and SD for continuous variables, together with 95% CIs. To assess the differences in covariates according to neighbourhood deprivation, we used measures of effect size: Cohen's ϕ (of a one-way ANOVA test for means) and Cohen's F (of a χ^2 test of association).

Poisson regression models were used to estimate the age-adjusted mortality rates and the associations between neighbourhood deprivation and mortality. For large sample sizes, low incidence, and shorter (≤20 years) follow-up times, Poisson models yield similar results to the Cox's proportional hazard model. The adequacy of Poisson models was formally evaluated using the Brønnesby and Borgan goodness-of-fit statistic.

To account for the time at risk, the logarithm of the person-years was used as offset and, to remove the influence of unequal age distribution, age was added as a continuous variable and centred at the mean of all individuals. Other than age (model 1), the models were adjusted for demographic factors associated with an increased risk of death,[25] more precisely sex and marital status (model 2), and adjusted for the aforementioned factors (smoking, alcohol consumption, physical activity, and BMI; model 3) to test whether these established mortality risk factors explained the differences across deprivation quintiles. The results were presented as age-adjusted mortality rates and RR and corresponding 95% CI, which denote the differences between the least deprived (reference category) and the most deprived neighbourhoods.

Models' goodness of fit was assessed using the likelihood-ratio test. To investigate the presence of interactions between educational attainment and neighbourhood deprivation, we computed the relative excess risk due to the interaction (equation in the appendix p 21), without allowance for multiplicity. The relative excess risk due to the interaction provides a useful metric of departure from the additivity of effects on an RR scale.[26] A value of more than 0 indicates the presence of positive additive interaction and value of exact or less than 0 corresponds to negative additive interaction. Assessment of an interaction on an additive scale is often more meaningful than on a multiplicative scale, because, from a public health perspective, a positive departure from additivity indicates that the number of deaths attributable to two health determinants in combination is larger than

	CoLaus (Lausanne, Switzerland; n=6733)	E3N (France; n=98 995)	EPIC-Turin (Turin, Italy; n=8763)	EPIPorto (Porto, Portugal; n=2485)	MCCS (Melbourne, VIC, Australia; n=41 514)	Whitehall II (London, UK; n=10 308)
Age, years	52·6 (10·7)	49·4 (6·7)	49·8 (7·6)	52·9 (15·5)	55·4 (8·7)	50·3 (6·1)
Missing data for age	1 (<0·1%)	2 (<0·1%)	0	0	0	1493 (14·5%)
Sex						
Male	3189 (47·4%)	0	4884 (55·7%)	946 (38·1%)	17 045 (41·1%)	6057 (68·7%)
Female	3544 (52·6%)	98 995 (100·0%)	3879 (44·3%)	1539 (61·9%)	24 469 (58·9%)	2758 (31·3%)
Missing data for sex	0	0	0	0	0	1493 (14·5%)
Marital status						
Married or cohabiting	3982 (59·2%)	76 959 (81·4%)	6777 (86·1%)	1682 (67·7%)	29 247 (73·7%)	6943 (83·6%)
Living alone	2744 (40·8%)	17 605 (18·6%)	1092 (13·9%)	802 (32·3%)	10 444 (26·3%)	1363 (16·4%)
Missing data for marital status	7 (0·1%)	4431 (4·5%)	894 (10·2%)	1 (<0·1%)	1823 (4·4%)	2002 (19·4%)
Education						
Low	3774 (56·2%)	4909 (5·2%)	5242 (59·9%)	1516 (61·0%)	26 949 (64·9%)	3140 (38·0%)
Medium	888 (13·2%)	55 649 (58·7%)	2298 (26·2%)	320 (12·9%)	4123 (9·9%)	2195 (26·5%)
High	2057 (30·6%)	34 176 (36·1%)	1215 (13·9%)	649 (26·1%)	10 433 (25·1%)	2938 (35·5%)
Missing data for education	14 (0·2%)	4261 (4·3%)	8 (0·1%)	0	9 (<0·1%)	2035 (19·7%)
Neighbourhood deprivation						
Q1, least deprived	1309 (20·2%)	14 043 (20·0%)	2170 (26·0%)	505 (20·3%)	10 836 (26·3%)	1963 (20·0%)
Q2	1287 (19·8%)	14 013 (20·0%)	1891 (22·6%)	492 (19·8%)	7573 (18·4%)	1979 (20·2%)
Q3	1297 (20·0%)	14 077 (20·0%)	1554 (18·6%)	487 (19·6%)	6519 (15·8%)	1936 (19·8%)
Q4	1295 (20·0%)	14 035 (20·0%)	1618 (19·4%)	536 (21·6%)	8721 (21·1%)	1969 (20·1%)
Q5, most deprived	1293 (20·0%)	14 045 (20·0%)	1118 (13·4%)	463 (18·6%)	7613 (18·5%)	1949 (19·9%)
Missing data for deprivation	252 (3·7%)	28 782 (29·1%)	422 (4·8%)	2 (0·1%)	252 (0·6%)	512 (5·0%)
Alcohol intake						
Abstainer	1915 (28·4%)	8977 (12·3%)	750 (8·6%)	829 (34·4%)	13 534 (32·6%)	1625 (19·6%)
Moderate drinker	4276 (63·5)	49 620 (67·9%)	6352 (72·5%)	1095 (45·4%)	22 564 (54·4%)	5399 (65·0%)
Heavy drinker	542 (8·0%)	14 434 (19·8%)	1661 (19·0%)	487 (20·2%)	5377 (13·0%)	1288 (15·5%)
Missing data for alcohol intake	0	25 964 (26·2%)	0	74 (3·0%)	39 (0·1%)	1996 (19·4%)
Smoking						
Never smoker	2732 (40·6%)	53 130 (54·2%)	3757 (42·9%)	1363 (56·3%)	23 819 (57·4%)	3647 (46·7%)
Former smoker	2183 (32·4%)	30 165 (30·8%)	2871 (32·8%)	495 (20·4%)	12 997 (31·3%)	3024 (38·7%)
Current smoker	1812 (26·9%)	14 755 (15·0%)	2135 (24·4%)	564 (23·3%)	4688 (11·3%)	1146 (14·7%)
Missing data for smoking	6 (0·1%)	945 (1·0%)	0	63 (2·5%)	10 (<0·1%)	2491 (24·2%)
Body-mass index						
Underweight	69 (1·3%)	2256 (2·3%)	31 (0·4%)	21 (0·9%)	155 (0·4%)	46 (0·6%)
Healthy	3168 (47·1%)	77 232 (79·9%)	3862 (44·6%)	888 (36·4%)	14 807 (35·7%)	4169 (51·6%)
Overweight	2462 (36·6%)	14 123 (14·6%)	3672 (42·4%)	989 (40·5%)	17 943 (43·3%)	3068 (38·0%)
Obese	1031 (15·3%)	3070 (3·2%)	1102 (12·7%)	541 (22·2%)	8578 (20·7%)	791 (9·8%)
Missing data for body-mass index	3 (<0·1%)	2316 (2·3%)	96 (1·1%)	46 (1·9%)	31 (0·1%)	2234 (21·7%)
Physical activity						
Active lifestyle	4337 (64·8%)	59 540 (77·2%)	6940 (79·2%)	451 (18·6%)	32 282 (77·8%)	6574 (79·0%)
Sedentary lifestyle	2355 (35·2%)	17 626 (22·8%)	1822 (20·8%)	1974 (81·4%)	9223 (22·2%)	1745 (21·0%)
Missing data for physical activity	41 (0·6%)	21 829 (22·1%)	1 (<0·1%)	60 (2·4%)	9 (0·0%)	1989 (19·3%)
Vital status						
Alive	6422 (96·8%)	89 920 (90·8%)	8151 (93·0%)	2072 (83·4%)	32 330 (78·0%)	7666 (87·0%)
Dead	210 (3·2%)	9075 (9·2%)	612 (7·0%)	413 (16·6%)	9122 (22·0%)	1149 (13·0%)
Missing data for vital status	101 (1·5%)	0	0	0	62 (0·0%)	1493 (14·5%)
Time of follow-up, years	6·2 (1·5)	22·9 (3·1)	16·9 (3·0)	16·3 (4·2)	17·5 (3·6)	21·1 (3·4)
Missing data for follow-up	101 (1·5%)	2 (0·0%)	0	37 (1·5%)	0	1502 (14·6%)

Data presented as n (%) or mean (SD).

Table 1: **Sample characteristics of each cohort (N=168 801 in total)**

	Q1 (least deprived)	Q2	Q3	Q4	Q5 (most deprived)	Cohen effect size
Age, years	51·6 (8·1; 51·5–51·7)	51·1 (8·1; 51·0–51·2)	51·2 (8·2; 51·1–51·3)	51·7 (8·4; 51·7–51·8)	51·8 (8·4; 51·7–51·9)	0·02
Sex						
Male	7806 (25·5%; 25·0–26·0%)	6249 (23·1%; 22·6–23·6%)	5627 (22·0%; 21·5–22·5%)	6369 (22·9%; 22·4–23·4%)	5294 (20·3%; 19·8–20·8%)	··
Female	22 798 (74·5%; 74·0–75·0%)	20 766 (76·9%; 76·4–77·4%)	19 982 (78·0%; 77·5–78·5%)	21 485 (77·1%; 76·6–77·6%)	20 790 (79·7%; 79·2–80·2%)	0·04
Marital status						
Married or cohabiting	23 703 (80·2%; 79·7–80·6%)	20 711 (79·7%; 79·2–80·2%)	19 096 (78·0%; 77·5–78·6%)	20 711 (78·2%; 77·7–78·7%)	19 159 (77·1%; 76·6–77·6%)	··
Living alone	5856 (19·8%; 19·4–20·3%)	5270 (20·3%; 19·8–20·8%)	5373 (22·0%; 21·4–22·5%)	5770 (21·8%; 21·3–22·3%)	5690 (22·9%; 22·4–23·4%)	0·03
Education						
Low	7843 (26·1%; 25·6–26·6%)	7693 (29·1%; 28·6–29·7%)	7541 (30·2%; 29·6–30·8%)	9979 (36·7%; 36·2–37·3%)	9462 (37·4%; 36·8–38·0%)	··
Medium	8650 (28·8%; 28·3–29·3%)	9682 (36·7%; 36·1–37·2%)	9744 (39·0%; 38·4–39·6%)	10 427 (38·4%; 37·8–39·0%)	10 736 (42·4%; 41·8–43·0%)	··
High	13 506 (45·0%; 44·5–45·6%)	9029 (34·2%; 33·6–34·8%)	7673 (30·7%; 30·2–31·3%)	6764 (24·9%; 24·4–25·4%)	5126 (20·2%; 19·7–20·7%)	0·13
Alcohol intake						
Abstainer	4982 (16·3%; 15·9–16·7%)	4884 (18·2%; 17·7–18·6%)	4813(18·9%; 18·4–19·3%)	6284 (22·7%; 22·2–23·2%)	6092 (23·5%; 23·0–24·0%)	··
Moderate drinker	20 046 (65·7%; 65·2–66·2%)	17 408 (64·7%; 64·2–65·3%)	16 370 (64·1%; 63·6–64·7%)	17 000 (61·3%; 60·8–61·9%)	15 669 (60·4%; 59·8–61·0%)	··
Heavy drinker	5476 (18·0%; 17·5–18·4%)	4602 (17·1%; 16·7–17·6%)	4336 (17·0%; 16·5–17·5%)	4434 (16·0%; 15·6–16·4%)	4179 (16·1%; 15·7–16·6%)	0·05
Smoking						
Never smoker	16 026 (52·7%; 52·2–53·3%)	14 159 (52·9%; 52·3–53·5%)	13 326 (52·5%; 51·8–53·1%)	14 796 (53·6%; 53·0–54·2%)	14 154 (54·8%; 54·2–55·4%)	··
Former smoker	10 150 (33·4%; 32·9–33·9%)	8785 (32·8%; 32·2–33·4%)	8334 (32·8%; 32·2–33·4%)	8617 (31·2%; 30·7–31·8%)	7757 (30·0%; 29·5–30·6%)	··
Current smoker	4225 (13·9%; 13·5–14·3%)	3840 (14·3%; 13·9–14·8%)	3742 (14·7%; 14·3–15·2%)	4174 (15·1%; 14·7–15·6%)	3918 (15·2%; 14·7–15·6%)	0·02
Body-mass index	24·1 (24·1–24·2)	24·2 (24·2–24·3)	24·3 (24·2–24·3)	24·8 (24·7–24·8)	24·9 (24·9–25·0)	0·04
Physical activity						
Sedentary lifestyle	5838 (21·2%; 78·3–79·3%)	5250 (21·9%; 77·6–78·7%)	5331 (23·6%; 75·8–76·9%)	6098 (24·5%; 74·9–76·0%)	5895 (25·9%; 73·5–74·6%)	··
Active lifestyle	21 730 (78·8%; 20·7–21·7%)	18 775 (78·1%; 21·3–22·4%)	17 235 (76·4%; 23·1–24·2%)	18 743 (75·5%; 24·0–25·1%)	16 914 (74·1%; 25·4–26·5%)	0·04
Vital status						
Dead	3448 (11·3%; 10·9–11·6%)	2941 (10·9%; 10·5–11·3%)	2989 (11·7%; 11·3–12·1%)	3919 (14·1%; 13·7–14·5%)	3754 (14·4%; 14·0–14·8%)	··
Alive	21 127 (88·7%; 88·4–89·1%)	24 045 (89·1%; 88·7–89·5%)	22 589 (88·3%; 87·9–88·7%)	23 906 (85·9%; 85·5–86·3%)	22 287 (85·6%; 85·2–86·0%)	0·04
Length of follow-up, years	19·6 (4·9; 19·6–19·7)	20·0 (5·0; 19·9–20·1)	20·2 (5·0; 20·2–20·3)	20·0 (5·1; 20·0–20·1)	20·1 (5·2; 20·0–20·1)	0·03
Age-adjusted mortality rate per 100 000 person-years	369·7 (356·4–383·2)	368·6 (354·6–383·1)	386·0 (371·3–401·0)	432·0 (417·1–447·2)	445·7 (430·2–461·7)	0·18*

Data presented as n (%; 95% CI) or mean (SD; 95% CI). *Pseudo-R^2.

Table 2: **Participants' characteristics according to neighbourhood socioeconomic deprivation (N=168 801)**

the sum of the deaths that would be caused by each determinant separately. To generate the 95% CI of the relative excess risk due to the interaction, we used the R package boot version 1.3-28, using 199 samples and a normal distribution. The stability of the bootstrapping was ascertained through the inspection of the histograms, which were revealed to be unimodal, symmetrical, and normally distributed. The results were also presented separately for each education level because of the presence of a significant interaction.

Analyses were initially done separately for each study. The results were subsequently combined using a pooled analysis by including the cohort as a fixed effect in the Poisson models and in the relative excess risk because of the interaction equation. To reduce biases caused by missing data and attrition, we produced a multiple imputation model using chained equations implemented in the R package mice version 3.14.0. Imputed variables and the numbers of missing data are depicted in table 1.

Sensitivity analysis

To guarantee that the results were not driven by imputation, we fitted the models using the original non-imputed dataset. The results were mostly similar (appendix p 22). For the cohorts with the geocode of the neighbourhood of residence, a random effect at neighbourhood-level was added to the models. Previous analyses were reproduced and the results were mostly similar (appendix p 24).

To account for the shorter period of follow-up of the CoLaus cohort, we obtained pooled estimates without this cohort, which yielded similar results (appendix p 23). Finally, to ascertain the effect of data quality and the modifiable areal unit problem, sensitivity analyses were conducted, revealing that the results were robust to those issues (appendix p 27).

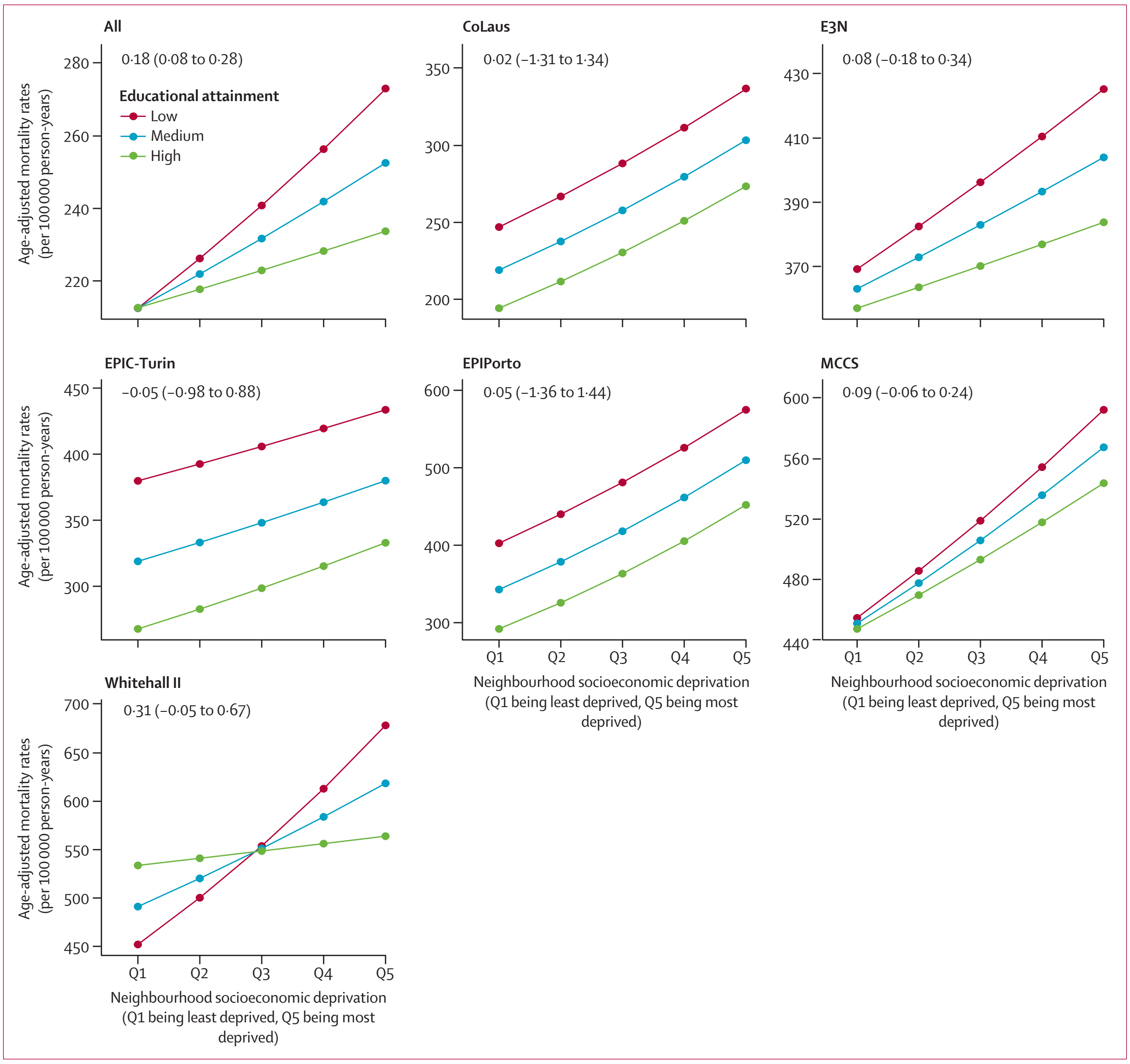

Figure: **Age-adjusted mortality rates (per 100 000 person-years) and relative excess risk due to the interaction between neighbourhood deprivation and educational attainment, by cohort**

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The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

Table 1 shows the characteristics of each individual cohort, comprising a total population of 168 801 individuals. The mean age at baseline was 51·1 (SD 8·0), ranging from 49·4 (6·7) in the E3N cohort to 55·4 (8·7) in the MCCS cohort. The mean time follow-up was 20·3 (5·1) years, ranging from 6·2 (1·5) in the CoLaus cohort to 22·9 (3·1) in the E3N cohort. At the end of the last available follow-up, 20 581 (12·3%) participants died, with this proportion ranging from 210 (3·2%) of 6734 in the CoLaus cohort to 9122 (22·0%) of 41 514 in the MCCS cohort. Overall, 45 530 (28·0%) of the 162 474 participants that we had information on their education status had a low education level, but this varied substantially between cohorts (from 26 949 [64·9%] of 41 505 in the MCCS cohort to 4909 [5·2%] of 94734 in the E3N cohort).

Table 2 shows the distribution of the variables examined according to neighbourhood deprivation for the six cohorts altogether. Health-related variables, such as current smoking and a higher BMI, were generally more prevalent among participants residing in the more deprived neighbourhoods, although the effect sizes were rather small. The proportion of less-educated individuals increased with neighbourhood deprivation. Similarly, the proportion of deaths and age-standardised mortality rates increased with increasing deprivation, being approximately 21% higher among those residing in the

	RR (model 1)*	RR (model 2)†	RR (model 3)‡
Pooled estimate			
Low education	1·31 (1·23–1·40)	1·31 (1·23–1·39)	1·20 (1·13–1·28)
Medium education	1·12 (1·04–1·21)	1·11 (1·03–1·20)	1·09 (1·01–1·18)
High education	1·16 (1·07–1·27)	1·14 (1·04–1·25)	1·12 (1·03–1·22)
CoLaus			
Low education	1·33 (0·82–2·15)	1·24 (0·76–2·01)	1·19 (0·73–1·93)
Medium education	1·69 (0·54–5·24)	1·59 (0·51–5·00)	1·40 (0·43–4·56)
High education	1·32 (0·56–3·11)	1·23 (0·52–2·90)	1·20 (0·50–2·86)
E3N			
Low education	1·14 (0·86–1·50)	1·14 (0·87–1·51)	1·12 (0·85–1·47)
Medium education	1·10 (1·01–1·21)	1·10 (1·01–1·21)	1·11 (1·01–1·21)
High education	1·14 (1·01–1·28)	1·13 (1·00–1·28)	1·15 (1·02–1·29)
EPIC-Turin			
Low education	1·16 (0·88–1·54)	1·14 (0·86–1·50)	1·08 (0·82–1·43)
Medium education	1·03 (0·61–1·74)	1·02 (0·60–1·73)	0·97 (0·57–1·65)
High education	1·47 (0·65–3·31)	1·34 (0·58–3·09)	1·32 (0·57–3·05)
EPIPorto			
Low education	1·45 (1·03–2·05)	1·47 (1·04–2·08)	1·44 (1·02–2·04)
Medium education	1·73 (0·61–4·87)	1·48 (0·56–3·93)	1·69 (0·59–4·84)
High education	1·27 (0·45–3·54)	1·49 (0·51–4·34)	1·62 (0·53–4·92)
MCCS			
Low education	1·32 (1·23–1·41)	1·30 (1·21–1·39)	1·20 (1·12–1·28)
Medium education	1·13 (0·95–1·34)	1·05 (0·88–1·26)	0·99 (0·83–1·18)
High education	1·24 (1·07–1·43)	1·17 (1·01–1·36)	1·09 (0·93–1·27)
Whitehall II			
Low education	1·50 (1·15–1·96)	1·64 (1·24–2·18)	1·39 (1·04–1·86)
Medium education	1·35 (0·95–1·94)	1·26 (0·87–1·83)	1·10 (0·75–1·61)
High education	1·02 (0·74–1·41)	0·98 (0·70–1·37)	0·87 (0·62–1·22)

N=168 801. Data presented as RR (95% CI). RR=relative risk. *Adjusted for age and years of follow-up. †Adjusted for age, years of follow-up, marital status, and sex. ‡Adjusted for age, years of follow-up, marital status, sex, and risk factors (smoking, alcohol intake, physical activity, and body-mass index).

Table 3: **Associations between neighbourhood socioeconomic deprivation and mortality according to educational attainment**

most deprived neighbourhoods (Q1, least deprived neighbourhoods, 369·7 per 100 000 person-years [95% CI 356·4–383·2] *vs* Q5, most deprived neighbourhoods 445·7 per 100 000 person-years [430·2–461·7]). As shown in the appendix (pp 14–19), a pattern of increasing mortality with greater deprivation was observed in all cohorts, although in the CoLaus and EPIC-Turin cohorts it was not statistically significant.

The figure shows the age-adjusted mortality rates for the six cohorts according to neighbourhood socioeconomic deprivation and educational attainment. Overall, among individuals with the lowest educational attainment, the age-adjusted mortality rate was 273·0 per 100 000 person-years (95% CI 237·1–314·2) in those residing in the most deprived neighbourhoods; among individuals attaining medium level education, it was 252·57 per 100 000 person-years (219·67–290·39); and among individuals attaining higher education the rate was 233·7 per 100 000 person-years (201·8–270·7). A statistically significant, positive additive interaction between education and neighbourhood socioeconomic deprivation was observed (pooled relative excess risk due to the interaction=0·18; 95% CI 0·08–0·28), indicating that the effect of neighbourhood deprivation was stronger among less-educated individuals. The relative excess risk due to the interaction was positive in all cohorts, although the cohort-specific results were not statistically significant. As depicted in table 3, the RR was 1·31 (1·23–1·40) in model 1 among individuals with a low education; that is, mortality was 31% higher among those residing in the most deprived neighbourhoods compared with those in the least deprived neighbourhoods. The RR was 1·12 (1·04–1·21) among individuals with a medium level of education and 1·16 (1·07–1·27) among individuals with a high level of education. The stronger effect of neighbourhood deprivation among less-educated individuals was observed in the EPIPorto, MCCS, and Whitehall II cohorts. However, in the E3N cohort, neighbourhood deprivation was associated with a higher risk of death among individuals with a medium and high education.

In general, the strength of the association between neighbourhood deprivation and mortality did not change after adjustment for additional demographic factors (RR 1·31 [1·23–1·39] among individuals with the lowest educational attainment; table 3), but effect estimates were slightly attenuated after accounting for well established risk factors (1·20 [1·13–1·28] among individuals with the lowest educational attainment; table 3).

Discussion

Using data from six well established adult cohorts, comprising more than 3 million person-years and more than 20 000 deaths, we assessed the association between neighbourhood deprivation and all-cause mortality, exploring interactions between individual and neighbourhood socioeconomic conditions. Age-adjusted mortality rates increased with neighbourhood deprivation, with individuals residing in the most deprived neighbourhoods being associated with a 21% higher risk of dying. Yet, the influence of neighbourhood deprivation was different according to individual socioeconomic position, being more pronounced among those with a low level of education.

One systematic review and meta-analysis of 18 studies presented an overall RR of 1·07 for all-cause mortality among inhabitants living in areas of low socioeconomic status,[1] but it is important to stress that there was a large heterogeneity between studies, with study-specific death risk estimates ranging from 1·35 to 0·99. However, the interaction between individual and neighbourhood socioeconomic position was not tested. In our study, we found that the influence of neighbourhood deprivation was more pronounced among those with a lower education. The age-adjusted mortality rates were highest among individuals with a low education residing in the most deprived neighbourhoods, and the effect of neighbourhood deprivation was also stronger among these individuals, whose RR was 1·31 versus 1·06 in individuals with medium levels of education and 1·13 in highly educated individuals. Similarly, in the USA, participants with a low income living in the most disadvantaged neighbourhoods had the highest risk of death (2·87 in White individuals and 2·61 in African American individuals).[7] In Canada, a survival gap of 10% between disadvantaged individuals residing in the least and the most deprived neighbourhoods was observed, but no differences existed among wealthier individuals.[9] This association of deprivation with mortality was particularly noticeable in the EPIPorto, MCCS, and Whitehall II cohorts. A possible explanation is that two of these cohorts—namely, EPIPorto and MCCS—have the highest values of socio-spatial segregation, as measured by the Massey and Denton's[27] formula (appendix p 28), potentially accentuating socio-spatial injustices in the distribution of community resources.

Additional information on neighbourhood structure could be helpful to better understand if individuals of a lower socioeconomic position are particularly susceptible to the poorer environment of disadvantaged neighbourhoods as advocated by the deprivation amplification model, which proposes that neighbourhoods composed of residents of a low socioeconomic position suffer from an underinvestment in public services and resources, increased exposure to contaminants, and detrimental environment, which ultimately can affect health and chances of survival.[5,27] Additionally, because of reduced personal resources, individuals of low socioeconomic status are particularly susceptible to those detrimental environments.

Although we could not assess the mediation effect of the neighbourhood attributes on mortality, other studies suggest that the most deprived neighbourhoods have the worst physical environments: in Porto, Portugal, access to green space was lower in the most deprived neighbourhoods than in the least deprived neighbourhoods[28] and, in France[29] and London, UK, deprived neighbourhoods were the most exposed to pollutants and noise.[30] Nevertheless, we were able to measure the effect of demographic variables and health-related behaviours on the model estimates, which were slightly attenuated after accounting for those factors. So, although we could not directly infer from our study, it is possible that both behaviours and environmental factors contribute to the observed associations.

The present study has some limitations. Different indexes of neighbourhood deprivation were used, hampering between-cohort comparisons. However, it has been shown that different deprivation indices—namely the European Deprivation Index and Townsend—perform similarly.[31] Because there was no data on neighbourhood characteristics, we could not explore the mechanisms that drove the observed associations. The areal units differed substantially between the cohorts, which might generate inconsistencies, a feature known as the Modifiable Areal Unit Problem.[32] Although most cohorts used small areas allowing the capture of local variation, in EPIC-Turin and Whitehall II, the use of larger geographies could potentially smooth socio-spatial differences. In fact, in the EPIC-Turin cohort, associations with neighbourhood deprivation were lower than all other cohorts except COLAUS, although we were still able to identify important neighbourhood effects in the Whitehall II cohort. Because of insufficient longitudinal data about the residential histories of individuals, we could not assess the health effects of the cumulative lifelong exposure to deprivation nor of early-life exposures and exposure trajectories, which could provide important information on the temporality and mechanisms (eg, residualisation and segregation) behind the observed associations. Additionally, because of data unavailability, we could not fit multilevel models, making our study more prone to type 1 errors. However, for the three cohorts with information on the unit of aggregation, a sensitivity analysis was done and results did not seem to be much affected by clustering effects. Although all-cause mortality is commonly used as a general marker of health, is free of diagnostic errors, and is associated with the most important causes of mortality,[15] analysis by cause of death could provide clues about the possible pathways (behavioural and psychosocial) by which neighbourhood deprivation affects health.

We used a single marker of individual socioeconomic position, educational attainment, although we acknowledge that socioeconomic position is a multidimensional construct. Data on occupational status were available too, missing data were greater for this variable than for education. Moreover, occupational status was not available for all cohorts, whereas educational attainment, through its stability throughout life, consistent associations with health-related behaviours, and easy harmonisation between countries, offers notable advantages as an indicator of socioeconomic position. We conducted a sensitivity analysis based on the cohorts with data on occupation and results, and despite not being statistically significant, it also revealed mostly positive interactions and stronger effects among those in manual occupations (appendix p 25).

Although we used multivariable adjustment strategies, observational studies are limited in their capacity to account for individual-level variables related to place of residence, which might also be related to mortality. Residual confounding is particularly important when measuring the effects of socioeconomically patterned exposures, such as place of residence and the corresponding level of deprivation. Moreover, housing prices dictate people's place of residence, so that disadvantaged individuals are less able to afford to live in wealthy neighbourhoods. That fact diminishes the power to find statistically significant interactions, because of the low number of disadvantaged individuals in wealthy neighbourhoods and vice versa. This might constitute a source of selection bias. Finally, there are potential limitations related with the composition of the cohort studies. Whitehall II only includes individuals who were originally civil servants and therefore is not representative of the general population. MCCS purposely includes a large share of the immigrant population of Melbourne (ie, predominantly southern European individuals). Although this inclusion that widens the behavioural and socioeconomic features of the cohort,[33] results from the MCCS cohort might not fully compare with those obtained from the other cohorts, composed essentially of non-migrants. Additionally, E3N (in addition to being formed of women only) includes a high proportion of teachers and school staff and, therefore, few people with low education, reducing the opportunity to detect interactions and potentially explaining the somewhat unexpected results obtained in this cohort. However, the representativeness of the cohort itself does not in principle influence associations that you find between a variable and an outcome in the cohort. Representativeness would be a larger issue if we were assessing prevalence.

Our study has notable strengths. We used prospective and harmonised data from six well established cohorts covering six countries and resulting in a large sample size, which allowed us to generate solid and comparable estimates about the association between neighbourhood deprivation and mortality. Also, most of these cohorts had an extended follow-up of approximately 20 years, whereas most previous studies dealt with shorter follow-up periods. Strict and validated geocoding methods were used in these cohorts, leading to high geocoding rates and good accuracy, and theoretical and methodologically sound multivariate indexes of deprivation were applied to characterise neighbourhood socioeconomic structure.

Our findings show that neighbourhood deprivation is associated with socioeconomic inequalities in mortality. Neighbourhood deprivation seems to exert a stronger influence among the most disadvantaged individuals, contributing to amplify their already higher mortality risk. These conclusions suggest that neighbourhood-based interventions to improve neighbourhood structures might contribute to reduce mortality rates across all populations, but particularly among individuals of a low socioeconomic position. Because we observed between-cohort differences in the magnitude of the association between mortality and neighbourhood deprivation, our investigation also suggests that the national policies and context—namely, the various degrees of residential segregation and social integration and the different welfare regimes—could modify the associations between socioeconomic position, neighbourhood deprivation, and mortality. Our results support the idea that the characteristics of places where people live (contextual effects) influence health by interacting with an individuals' personal characteristics (compositional effects). Such knowledge is crucial for decision makers to decide if they should guide policies towards individuals or neighbourhoods. In light of our findings, a three-level approach should be implemented. Place-based and individual-based solutions cannot be excluded as part of planning strategies to reduce inequalities but should be coupled with equalitarian country-level policies towards socio-spatial cohesion and social welfare.

LIFEPATH Consortium

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Contributors

AIR conceptualised the study, conducted the analysis, and wrote the initial draft of the manuscript. MS conducted the statistical analysis together with AIR. SF, MS, MK-I, CD, SS, MK, SJ, IG, GS, GG, CS, and PV reviewed and edited the final version of the manuscript. HB supervised the study and reviewed and edited the final version of the manuscript. AIR and MS accessed and verified the data used in the study. All authors revised the manuscript critically for important intellectual content. All authors approved the final version of the manuscript.

Declaration of interests

We declare no competing interests.

Data sharing

Data cannot be made freely available because of restrictions imposed by the Project Steering Board of the LIFEPATH project. However, the aggregated data are available for other researchers, on request. Requests should be sent to the Principal Investigator of the LIFEPATH Project, Paolo Vineis (p.vineis@imperial.ac.uk). The statistical analyses' code can be obtained upon request to Milton Severo (milton@ispup.up.pt).

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References

1 Meijer M, Röhl J, Bloomfield K, Grittner U. Do neighborhoods affect individual mortality? A systematic review and meta-analysis of multilevel studies. *Soc Sci Med* 2012; **74:** 1204–12.
2 Riva M, Gauvin L, Barnett TA. Toward the next generation of research into small area effects on health: a synthesis of multilevel investigations published since July 1998. *J Epidemiol Community Health* 2007; **61:** 853–61.
3 Ribeiro AI. Public health: why study neighborhoods? *Porto Biomed J* 2018; **3:** e16.
4 Stafford M, Marmot M. Neighbourhood deprivation and health: does it affect us all equally? *Int J Epidemiol* 2003; **32:** 357–66.
5 Macintyre S, Maciver S, Sooman A. Area, class and health: should we be focusing on places or people? *J Soc Policy* 1993; **22:** 213–34.
6 Åberg Yngwe M, Fritzell J, Lundberg O, Diderichsen F, Burström B. Exploring relative deprivation: is social comparison a mechanism in the relation between income and health? *Soc Sci Med* 2003; **57:** 1463–73.
7 Borrell LN, Diez Roux AV, Rose K, Catellier D, Clark BL. Neighbourhood characteristics and mortality in the Atherosclerosis Risk in Communities Study. *Int J Epidemiol* 2004; **33:** 398–407.
8 Hagedoorn P, Vandenheede H, Vanthomme K, Willaert D, Gadeyne S. A cohort study into head and neck cancer mortality in Belgium (2001-11): are individual socioeconomic differences conditional on area deprivation? *Oral Oncol* 2016; **61:** 76–82.
9 Ross NA, Oliver LN, Villeneuve PJ. The contribution of neighbourhood material and social deprivation to survival: a 22-year follow-up of more than 500,000 Canadians. *Int J Environ Res Public Health* 2013; **10:** 1378–91.
10 Winkleby M, Cubbin C, Ahn D. Effect of cross-level interaction between individual and neighborhood socioeconomic status on adult mortality rates. *Am J Public Health* 2006; **96:** 2145–53.
11 Yen IH, Kaplan GA. Neighborhood social environment and risk of death: multilevel evidence from the Alameda County Study. *Am J Epidemiol* 1999; **149:** 898–907.
12 Chen C-H, Huang K-Y, Wang J-Y, Huang H-B, Chou P, Lee C-C. Combined effect of individual and neighbourhood socioeconomic status on mortality of rheumatoid arthritis patients under universal health care coverage system. *Fam Pract* 2015; **32:** 41–48.
13 Jaffe DH, Eisenbach Z, Neumark YD, Manor O. Individual, household and neighborhood socioeconomic status and mortality: a study of absolute and relative deprivation. *Soc Sci Med* 2005; **60:** 989–97.
14 Bosma H, van de Mheen HD, Borsboom GJJM, Mackenbach JP. Neighborhood socioeconomic status and all-cause mortality. *Am J Epidemiol* 2001; **153:** 363–71.
15 Major JM, Doubeni CA, Freedman ND, et al. Neighborhood socioeconomic deprivation and mortality: NIH-AARP diet and health study. *PLoS One* 2010; **5:** e15538.
16 Townsend P, Phillimore P, Beattie A. Health and deprivation: inequality and the north. London: Croom Helm, 1988.
17 Rey G, Jougla E, Fouillet A, Hémon D. Ecological association between a deprivation index and mortality in France over the period 1997 – 2001: variations with spatial scale, degree of urbanicity, age, gender and cause of death. *BMC Public Health* 2009; **9:** 33.
18 Marinacci C, Spadea T, Biggeri A, Demaria M, Caiazzo A, Costa G. The role of individual and contextual socioeconomic circumstances on mortality: analysis of time variations in a city of north west Italy. *J Epidemiol Community Health* 2004; **58:** 199–207.
19 Ribeiro AI, Mayer A, Miranda A, Pina MF. The Portuguese version of the European deprivation index: an instrument to study health inequalities. *Acta Med Port* 2017; **30:** 17–25.
20 Australian Bureau of Statistics. Socio-Economic Indexes for Areas (SEIFA). March 27, 2018. https://www.intelia.com.au/wp-content/uploads/2020/09/SEIFA-2016-Technical-Paper.pdf (accessed May 1, 2021).
21 Stringhini S, Carmeli C, Jokela M, et al. Socioeconomic status and the 25×25 risk factors as determinants of premature mortality: a multicohort study and meta-analysis of 1·7 million men and women. *Lancet* 2017; **389:** 1229–37.
22 d'Errico A, Ricceri F, Stringhini S, et al. Socioeconomic indicators in epidemiologic research: a practical example from the LIFEPATH study. *PLoS One* 2017; **12:** e0178071.
23 Ribeiro AI, Fraga S, Kelly-Irving M, et al. Neighbourhood socioeconomic deprivation and allostatic load: a multi-cohort study. *Nature* 2019; **9:** 8790.
24 Signorini DF. Sample size for Poisson regression. *Biometrika* 1991; **78:** 446–50.
25 Zueras P, Rutigliano R, Trias-Llimós S. Marital status, living arrangements, and mortality in middle and older age in Europe. *Int J Public Health* 2020; **65:** 627–36.
26 Richardson DB, Kaufman JS. Estimation of the relative excess risk due to interaction and associated confidence bounds. *Am J Epidemiol* 2009; **169:** 756–60.
27 Macintyre S. Deprivation amplification revisited; or, is it always true that poorer places have poorer access to resources for healthy diets and physical activity? *Int J Behav Nutr Phys Act* 2007; **4:** 32.
28 Hoffimann E, Barros H, Ribeiro AI. Socioeconomic inequalities in green space quality and accessibility-evidence from a southern European city. *Int J Environ Res Public Health* 2017; **14:** 916.
29 Padilla CM, Kihal-Talantikite W, Vieira VM, et al. Air quality and social deprivation in four French metropolitan areas – a localized spatiotemporal environmental inequality analysis. *Environ Res* 2014; **134:** 315–24.
30 Tonne C, Milà C, Fecht D, et al. Socioeconomic and ethnic inequalities in exposure to air and noise pollution in London. *Environ Int* 2018; **115:** 170–79.
31 Bryere J, Pornet C, Copin N, et al. Assessment of the ecological bias of seven aggregate social deprivation indices. *BMC Public Health* 2017; **17:** 86.
32 Wong DWS. The Modifiable Areal Unit Problem (MAUP). In: Janelle DG, Warf B, Hansen K (eds) WorldMinds: geographical perspectives on 100 problems. Dordrecht; Springer, 2004.
33 Milne RL, Fletcher AS, MacInnis RJ, et al. Cohort profile: the Melbourne Collaborative Cohort Study (Health 2020). *Int J Epidemiol* 2017; **46:** 1757–57i.