BMJ Open

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Journal:	*BMJ Open*
Manuscript ID	bmjopen-2018-027530
Article Type:	Research
Date Submitted by the Author:	29-Oct-2018
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Keywords:	MENTAL HEALTH, PUBLIC HEALTH, Depression & mood disorders < PSYCHIATRY, EPIDEMIOLOGY

The association between area deprivation and major depressive disorder in British men and women: large, population study

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ABSTRACT

OBJECTIVE

Studies have shown area-level deprivation can increase the risk for mental disorders over and above individual-level circumstances, such as education and social class. The objective of this study is to determine whether area deprivation is associated with major depressive disorder (MDD) in British women and men separately while adjusting for individual-level factors.

DESIGN

Large, population study.

SETTING

UK population-based cohort.

PARTICIPANTS

30,445 people from the general population aged 40 years and older and living in England consented to participate at study baseline, and of these, over 21,000 participants completed a structured HLEQ used to capture MDD. Area deprivation was measured in 1991 using Census data, and current MDD was assessed in 1996-2000. 8,239 men and 10,343 women had complete data on all covariates.

PRIMARY OUTCOME MEASURE

MDD identified according to the Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV).

RESULTS

In this study, 3.3% (339/10,343) of women and 2.1% (177/8,239) of men had MDD. Men living in the most deprived areas were 60% more likely to have depression than those living in areas that were not deprived (OR=1.60, 95%CI: 1.09 to 2.35; p=0.018), but this association between deprivation and MDD was not apparent in women (OR=1.25, 95% CI: 0.94 to 1.66; p=0.123).

CONCLUSION

This study shows that the residential environment differentially affects men and women, and this needs to be taken into account by mental health policy-makers. Knowing that men living in deprived conditions are at high risk for having depression helps inform targeted prevention and intervention programs.

Article Summary

Strengths and limitations of this study

- We used a population-based sample of over 20,000 British adults and controlled for important confounders, including social class, medical history, and disability.
- We used a structured questionnaire to determine whether participants met criteria for MDD according to the DSM.
- We used the Townsend index to assess area deprivation. This index is commonly-used by researchers to examine deprivation and is a theoretically sound measure.
- People who took part in EPIC-Norfolk were generally more affluent and healthier than those living in other parts of England. As such, our results may not be generalizable to the most deprived areas.

Introduction

Depression is a common psychiatric disorder affecting approximately 350 million people around the world.[1] According to the Global Burden of Disease Study[2], major depressive disorder (MDD) contributed to 689.9 per 100,000 disability-adjusted life years in men and 1161.2 per 100,000 disability-adjusted life years in women in 2010. Depression can increase the risk for impairment, disability and suicide.[3, 4, 5] It has also been linked to decreased work productivity, poor quality of life, and high health service use.[3, 6, 7]

A number of studies have examined the individual-level risk factors of depression, such as, personal and parental history of psychopathology[8], genetics[9], history of trauma and stressful life events[10, 11], and socioeconomic status.[12] However, the environment or living context can have a profound influence on mental health, over and above individual-level factors.[13, 14, 15] In a systematic review[16] of 14 studies, about half found an association between neighbourhood socioeconomic conditions and depression. Living in an area of low socioeconomic status can expose people to a higher number of stressors, such as, violence, disorder, and noise pollution, and this can have deleterious effects on mental health.[17]

There is a wealth of literature on the effect of the places where people live on mental health. Findings from systematic reviews[18, 19, 20] assessing neighbourhood characteristics and depression show that there is large heterogeneity in findings, because of differences in study populations, the confounders that are adjusted for in analyses, and the measures and definitions used to delineate neighbourhoods.[19] Although there is much evidence on the influence of area-level disadvantage or deprivation on depression, research on this relationship from a gendered perspective is lacking.

In this large, population-based, cohort study, we examine the association between area deprivation and major depressive disorder in men and women separately, while controlling for a range of important confounders, including social class, previous medical conditions, psychiatric co-morbidity, and disability. Area deprivation refers to residential environments or living contexts characterized by factors, such as, high levels of unemployment, non-home

ownership, non-car ownership, and low income.[13] Findings are disaggregated by sex, and this is done for several reasons. Gender frames access to resources derived from the environment.[21, 22] Compared to men, women have been shown to have less access to material and social conditions, and this can influence mental health.

However, there are additional reasons why findings are disaggregated by sex. Women and men tend to react to different kinds of stressors. Recent research has shown that men are more susceptible to work- and finance-related stressors, while women are more affected by deficiencies in their social networks and interpersonal relationships.[23, 24] Hence, living in a deprived area with high levels of unemployment might be particularly detrimental for men's mental health. This was evident when the economy shifted in the UK from a manufacturing- to a service-based one, and many men lost their jobs.[25] Prior to the shift, the local economy had relied on skilled and semi-skilled jobs, typically performed by men. When the economy changed, an increasing number of women entered employment (occupying mainly service industry jobs), and this had implications for traditional sex-defined social roles. Men who experienced reduced economic opportunities may have suffered from loss of role identify and self-esteem, and this had consequences for their physical and mental health.[25] A recent study[23] showed that men's mental health is particularly affected if they fail at key instrumental tasks, such as, work achievements and ability to provide for the family. In contrast, women are more likely to be depressed if they fail to meet their needs for relationship.[23] To this end, it appears that men and women are susceptible to different kinds of stressors.

It remains unclear whether men and women living in deprived areas are differentially susceptible to MDD – the objective of this study will be to assess this. Knowing that one sex is at risk of developing depression when exposed to deprived circumstances helps to tailor interventions and allocate scarce resources according to need.[26] This is particularly important at a time of scarce economic and health-related resources.

Methods

Data were drawn from EPIC-Norfolk, whose design and study methods have been described in detail elsewhere.[27] In brief, a prospective population-based cohort of 30,445 participants ages 40 to 74 years were recruited by post between 1993 and 1997 through general practice age-sex registers in the city of Norwich and the surrounding small towns and rural areas. At baseline (1993-97), participants completed a postal HLQ questionnaire that captured information on sociodemographics, including age, sex, highest educational attainment, marital status, social class, and self-reported physician diagnoses of physical diseases. Using participants' postal codes, a measure of area deprivation was derived based on the 1991 Census. Between 1993 and 2000, participants completed self-reported postal questionnaires provided they: 1) were still alive, 2) did not ask to be removed from the study's mailing list, and 3) had a valid mailing address.

During 1996-2000, 20,919 participants completed a structured, psychosocial Health and Life Experiences (HLEQ) questionnaire. During this time, an assessment of generalized anxiety disorder (GAD) and major depressive disorder (MDD) was made according to the Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV)[28]. Using the HLEQ questionnaire, disability measures based on the SF-36 were also derived.[29]

All participants recruited through general-practice registers and who completed a baseline health questionnaire were eligible to be included in our study; those who completed a psychosocial questionnaire during follow-up were eligible to be included in our analysis.

Dependent variable

The primary outcome in this study was current MDD, which was measured using the HLEQ, a structured self-assessment instrument designed to provide a measure of depression for inclusion in a large-scale epidemiology project.[30, 31] DSM-IV criteria were applied to the psychiatric symptoms to determine whether participants had an episode of MDD that was ongoing at the time of the completion of the HLEQ questionnaire. Participants who reported a psychiatric episode were asked to estimate the onset and offset timings of the episode, and then to report an outline of the history of the problem. Participants were also asked about age at first symptom onset and subsequent episode recurrence.

The dependent variable in this study is current MDD, defined as an episode of MDD reported as ongoing at the time of the completion of the HLEQ.

The following two core criteria of MDD were first evaluated:

1. Have there ever been times in your life when you felt sad or depressed for two weeks or more in a row?
2. Have there ever been times in your life when you lost interest in most things like your work or activities that usually give you pleasure, for two weeks or more in a row?

If participants answered yes to one of these questions, they were then asked to think of the most recent two-week episode during their lives when these feelings of sadness, depression or loss of interest were the worst. They then had to report that these feelings of being sad, depressed, or loss of interest lasted all day or most of the day, and that during these two weeks of their most recent episode, they felt this way every day or almost every day.

In addition, at least five of the following symptoms had to be present: gaining or losing weight, having trouble falling asleep or sleeping too much, feeling tired or low on energy, feeling unable to sit still or feeling slowed down, experiencing guilt or shame, feeling worthless, losing confidence, having trouble concentrating, and thinking a lot about death or suicide. One of these five symptoms had to be one of the two core criteria evaluated at the beginning.

Finally, it was evaluated whether these symptoms interfered with participants' lives and resulted in disability or impairment.

Individual-level measures (potential confounders)

Individual-level measures included age, education, marital status, social class, and prevalent physical disease. The final categorization of the variables took cell size into account and was also done in accordance with previous literature.[31-37] Educational attainment was categorized into high (vocational or formal qualifications at the A- or O-level or degree-level qualifications) vs. low (no formal qualifications). Marital status was categorized into three groups: married, single (or never married), and others (widowed, divorced, separated). Social class was derived using the Computer-Assisted Standard Occupational Coding[38] and categorized as follows: I (professionals), II (managerial and technical occupations), III non-manual and III manual (skilled workers), IV (partly skilled workers), and V (unskilled manual workers). To assign social class to men and women, the male partner's current or past occupation was used. If this information was not available, the female partner's occupation was used. If the social class from either partner was unavailable, then it was coded as missing. The final categorization of social class included manual: skilled manual, partly skilled, and unskilled; and non-manual: professionals, managerial and technical, and skilled non-manual. Individual-level health status was assessed through the construction of a variable capturing major prevalent physical diseases. This was based on HLQ questions asking participants: "Has the doctor ever told you that you have any of the following?", followed by a list of options, such as allergies, asthma, cancer, stroke, heart attack, diabetes, thyroid conditions, etc.

Lifetime history of GAD was also assessed using the self-reported HLEQ questionnaire.[31] Lifetime GAD consisted of having ever had at least one episode that met core criteria stipulated by the DSM-IV. Anxiety was identified if participants reported having uncontrollable, excessive worry for six months or longer on most days than not that resulted in disability or impairment. In addition, at least three of the following symptoms needed to have been present: restlessness, irritability, muscle tension, fatigue, trouble concentrating because of worry, mind going blank, trouble falling asleep, trouble staying asleep, and feeling keyed up or on edge.

To determine disability levels, we used the PCS derived from the HLEQ. The PCS is part of the SF-36, a widely-used, validated self-assessment tool. Higher scores indicate better health.[29] PCS scores were dichotomized above and below the median.

All of these individual-level variables were regarded as potential confounders and selected based on the literature and their association with depression and area-level socioeconomic circumstances.

Area-level measure (exposure variable)

To examine area deprivation, we used one of the most commonly-used measures of area deprivation in the UK: the Townsend Index.[39, 40] This index is a composite measure of four variables obtained from the 1991 Census: 1) percentage of economically active residents over age 16 who are unemployed, 2) percentage of households that do not possess a car, 3) percentage of private households that are not owner occupied, and 4) percentage of private households that are overcrowded (have more than 1 person per room). These variables were obtained at the level of the enumeration district. Each variable was standardized by obtaining Z scores (dividing the mean by the standard deviation across enumeration districts in England). The Z values of the four variables were added together to produce a Townsend index score for each enumeration district. Positive values of the index indicate enumeration districts that are more deprived, while negative values indicate those that are less deprived; 0 represents the national mean. The postal codes of participants were record linked to enumeration districts, and participants were considered to live in deprived areas depending on the Townsend index score assigned to their enumeration district.[39]

The Townsend deprivation index was also disaggregated into its four constituent components to determine whether any one of these is associated with MDD or if it is the effect of the combined components that is important.

Statistical analysis

Characteristics of the participants were compared by GAD status. We used correlated data analysis to assess the association between individual- and area-level risk factors of GAD. A population-average model was constructed, which accounted for the potential correlation introduced by the clustering of individuals within enumeration districts. To estimate the population-average effect of the risk factors of interest on past-year GAD, we used generalized estimating equations. As past-year GAD represents a binary outcome (yes/no) and the intra-cluster correlation is assumed to be equal, GEE with a logit link and an exchangeable correlation structure was used. Adjusted odds ratios (OR) and 95% confidence intervals based on robust standard errors were estimated. Standard multivariate logistic regression was also conducted and compared to the findings based on GEE.

Individual-level measures consisted of demographic and socio-economic status variables, whereas the area-level measure comprised the Townsend index. Townsend index scores were used to create a dichotomous variable, with 0 as the cut-point (representing the national average). Similarly, when the Townsend index was disaggregated into its four consistent components, each variable was dichotomized using 0 (the national average) as the cut-point.

Analyses were conducted separately for men and women. First, unadjusted effect estimates were determined. Next, models were constructed that adjusted for 1) age, educational attainment, marital status, and social class; then for 2) age, educational attainment, marital status, social class, and GAD; and finally for 3) age, educational attainment, marital status, social class, GAD, physical diseases and disability level. Age was first assessed as a categorical variable, and subsequently divided into 10-year bands. Models were constructed for participants with complete measurements on all covariates. It was not possible to group the GAD variable otherwise since it was created and categorized according to the DSM-IV[30, 31], and area deprivation was analysed in accordance with the literature[35, 39].

In a subsequent analysis, a fully-adjusted model was built in which the Townsend index was replaced by its four constituent components to determine whether any one of these four variables is significantly associated with GAD.

Finally, analyses were run with pure MDD as the outcome in which past-year GAD was excluded. All models used two-sided statistical tests and a p-value of <0.05 was considered statistically significant. Analyses were implemented in Statistical Analysis Software (SAS) Version 9.3 (SAS Institute, Cary, NC).

To arrive at the study size, we went through the following steps: of the 30,445 who completed the baseline HLQ, we retained those participants who completed the HLEQ (20,921), and of these, we kept those people with complete data on all covariates (18,584).

Patient involvement

There were no patients involved in the development of the research question and outcome measures, the design of the study, or the recruitment to and conduct of the study.

Results

At baseline, 30,445 participants were recruited from general practices in the city of Norwich and the surrounding towns and rural areas. Of these, 20,919 people completed the HLEQ during the follow-up period. In total, 18,582 out of 20,919 (88.8%) people were available for analysis, because they had complete data on all covariates. The number of missing observations for each covariate were: 9 for education, 47 for marital status, 417 for MDD, 434 for GAD, 458 for social class, 75 for the Townsend index, and 1386 for the SF-36. Participants in this study were followed between 1993 and 2000 for a total of 7 years.

In this sample, there were 8,239 men and 10,343 women over the age of 40 years. Table 1 shows the distribution of individual- and area-level characteristics by current MDD.

Table 1: Distribution of characteristics for women (n=10,343) and men (n=8,239) who completed the HLEQ questionnaire in the EPIC-Norfolk cohort

	Women		Men	
Characteristic	**Number with characteristic**	**Percentage and number with MDD**	**Number with characteristic**	**Percentage and number with MDD**
Individual-level variables				
Socio-demographics				
Age (years)				
<50	1452	5.0 (72)[a]	964	3.4 (33)[a]
50-60	3719	3.9 (145)	2653	3.0 (80)
60-70	3182	2.1 (68)	2744	1.5 (40)
>70	1990	2.7 (54)	1878	1.3 (24)
Education[‡]				
Low	4056	3.5 (141)	2365	2.2 (51)
High	6287	3.2 (198)	5874	2.2 (126)
Marital status				
Single	417	2.4 (10)[a]	303	3.6 (11)[a]
Married	7757	2.7 (207)	7240	1.7 (122)
Other[*]	2169	5.6 (122)	696	6.3 (44)
Social class[¥]				
Manual	3833	3.3 (127)	3288	2.3 (76)
Non-manual	6510	3.3 (212)	4951	2.0 (101)
Health status				
Prevalent physical disease				
Yes[+]	5702	3.8 (214)[b]	3844	2.6 (100)[b]
No	4641	2.7 (125)	4395	1.8 (77)
Disability level				
High[¶]	5299	3.9 (208)[a]	4022	3.0 (119)[a]
Low	5044	2.6 (131)	4217	1.4 (58)
Lifetime GAD				
Yes	448	19.4 (87)[a]	255	22.4 (57)[a]
No	9895	2.6 (252)	7984	1.5 (120)
Area-level variable				
Townsend index				
Deprivation				
Yes (>0)	1646	4.6 (76)[a]	1242	3.6 (45)[a]
No (<=0)	8697	3.0 (263)	6997	1.9 (132)

‡ High education: O-level, A-level, degree; low education: refers to no education

* Other: divorced, separated, widowed

+ Prevalent physical disease: respiratory disease (asthma and bronchitis), allergies (allergies and hay fever), stroke, heart attack, cancer, diabetes, thyroid conditions, arthritis

¥ Manual: skilled manual, semi-skilled, non-skilled; non-manual: professionals, managerial, skilled non-manual

¶ Below the median PCS value of 50.6

[a] $P < 0.001$

[b] $P < 0.05$

The prevalence of (current) MDD was 2.1% (177/8239) for men and 3.3% (339/10343) for women. Women with MDD were younger than 50 years of age, more likely to be single, have prevalent physical disease, high disability, GAD, and live in deprived areas. Among men, similar patterns emerged (table 1).

After performing correlated data analysis, findings showed that the risk of depression in men living in the most deprived areas was 68% higher than in those living in the least deprived areas, even after accounting for age and socio-economic status (OR=1.68, 95% CI: 1.18, 2.40; p=0.004) (table 2).

Table 2: Odds ratios for MDD according to individual- and area-level characteristics for men (n=8,239) who completed the HLEQ questionnaire in the EPIC-Norfolk cohort

	Odds ratios and 95% CI				
Characteristic*	**Unadjusted**	**Model A[1]**	**Model B[2]**	**Model C[3]**	**P-value for Model C**
Individual-level variables					
Socio-demographics					
Age					
(per 10 years)	0.65 (0.55, 0.77)	0.63 (0.53, 0.74)	0.69 (0.58, 0.82)	0.61 (0.51, 0.73)	<0.0001
Education‡					
Low	1.01 (0.72, 1.40)	1.11 (0.76, 1.60)	1.07 (0.73, 1.55)	1.00 (0.69, 1.46)	0.996
High	1.00	1.00	1.00	1.00	
Marital status					
Single	2.20 (1.17, 4.12)	1.87 (0.99, 3.55)	1.64 (0.86, 3.12)	1.62 (0.84, 3.14)	<0.0001
Married	1.00	1.00	1.00	1.00	
Other*	3.94 (2.76, 5.61)	3.97 (2.77, 5.71)	3.69 (2.47, 5.51)	3.82 (2.58, 5.66)	
Social class¥					
Manual	1.14 (0.84, 1.54)	0.99 (0.71, 1.36)	1.12 (0.80, 1.56)	1.04 (0.75, 1.45)	0.799
Non-manual	1.00	1.00	1.00	1.00	
Health status					
Lifetime GAD					
Yes	18.87 (13.36, 26.65)		16.80 (11.64, 24.25)	14.08 (9.72, 20.39)	<0.0001
No	1.00		1.00	1.00	
Prevalent physical disease					
Yes+	1.50 (1.11, 2.02)			1.30 (0.94, 1.81)	0.117
No	1.00			1.00	
Disability level					
High¶	2.19 (1.59, 3.00)			2.20 (1.55, 3.12)	<0.0001
Low	1.00			1.00	
Area-level variable					
Townsend index					
Deprivation					
Yes (>0)	1.96 (1.39, 2.76)	1.68 (1.18, 2.40)	1.66 (1.13, 2.44)	1.60 (1.09, 2.35)	0.018
No (<=0)	1.00	1.00	1.00	1.00	

1. Adjusted for age, SES (education, marital status, social class)

2. Adjusted for age, SES, lifetime MDD
3. Adjusted for age, SES, lifetime MDD, physical diseases and disability
[+] Prevalent physical disease: respiratory disease (asthma, bronchitis), allergies (allergies, hay fever), stroke, heart attack, cancer, diabetes, thyroid conditions, arthritis
[¥] Manual: skilled manual, semi-skilled, non-skilled; non-manual: professionals, managerial, skilled non-manual
[‡] High education: O-level, A-level, degree; low education: refers to no education
[*] Other: divorced, separated, widowed
[¶] Above the median PCS value of 50.6

*The brackets show the reference categories that were used for each categorical variable when it was entered in the models - deprivation: no [ref] vs. yes; GAD: no [ref] vs. yes; education: high [ref] vs. low; marital status: married [ref], single, others; social class: non-manual [ref] vs. manual; lifetime MDD: no [ref] vs. yes; prevalent physical disease: no [ref] vs. yes; disability level: low [ref] vs. high. These reference categories were based on the literature. Choosing other groupings for the potential confounders would not have changed the results.

The OR reduced slightly after controlling for lifetime GAD (OR=1.66, 95% CI: 1.13, 2.44; p=0.009), but remained highly significant. After additionally adjusting for prevalent physical diseases and disability, the effect estimate became somewhat attenuated (OR=1.60, 95% CI: 1.09, 2.35; p=0.018), however, a strong association between area derivation and depression remained. (table 2) To determine the aspect of deprivation that is specifically associated with depression, the Townsend index was disaggregated into its four constituent components. Results showed that the OR was highest for unemployment (OR=1.82, 95% CI: 1.19, 2.77; p=0.005), followed by non-car ownership (OR=1.23, 95% CI: 0.72, 2.09; p=0.450), and lowest for overcrowding (OR=0.94, 95% CI: 0.62, 1.44; p=0.777) and non-home ownership (OR=0.82, 95% CI: 0.50, 1.35; p=0.439). Of these, only the effect estimate for unemployment was statistically significant. Men living in area characterized by high levels of unemployment were over 80% more likely to have depression than those living in areas with low levels of unemployment. Next, we wanted to determine whether deprivation is associated with pure MDD, and thus excluded past-year GAD; the association with depression remained statistically significant (OR=1.69, 95% CI: 1.10, 2.58; p=0.016).

In women, while there was a statistically significant association in the model adjusting for age, education, marital status, and social class (OR=1.41, 95% CI: 1.08, 1.84; p=0.012), the association lost its significance in the fully-adjusted model (OR=1.25, 95%CI: 0.94, 1.66; p=0.123) (table 3).

I had similar findings when the models were run with logistic regression instead of generalised estimating equations. This suggests that the intra-class correlation is negligible (findings not shown).

Table 3: Odds ratios for MDD according to individual- and area-level characteristics for women (n=10,343) who completed the HLEQ questionnaire in the EPIC-Norfolk cohort

	Odds ratios and 95% CI				
Characteristic*	**Unadjusted**	**Model A[1]**	**Model B[2]**	**Model C[3]**	**P-value for Model C**
Individual-level variables					
Socio-demographics					
Age					
(per 10 years)	0.75 (0.66,0.85)	0.66 (0.58, 0.76)	0.72 (0.63, 0.83)	0.68 (0.58, 0.78)	<0.0001
Education‡					
Low	1.11 (0.89, 1.38)	1.26 (0.99, 1.60)	1.32 (1.03, 1.69)	1.33 (1.04, 1.70)	0.023
High	1.00	1.00	1.00	1.00	
Marital status					
Single	0.90 (0.47, 1.70)	0.96 (0.50, 1.83)	0.92 (0.48, 1.78)	0.92 (0.48, 1.77)	<0.0001
Married	1.00	1.00	1.00	1.00	
Other*	2.17 (1.73, 2.73)	2.51 (1.96, 3.21)	2.38 (1.85, 3.07)	2.34 (1.82, 3.01)	
Social class¥					
Manual	1.02 (0.81, 1.27)	0.96 (0.75, 1.21)	0.99 (0.77, 1.27)	0.97 (0.76, 1.24)	0.805
Non-manual	1.00	1.00	1.00	1.00	
Health status					
Lifetime GAD					
Yes	9.22 (7.07, 12.03)		8.37 (6.31, 11.09)	7.67 (5.76, 10.20)	<0.0001
No	1.00		1.00	1.00	
Prevalent physical disease+					
Yes	1.41 (1.13, 1.76)			1.27 (1.00, 1.61)	0.051
No	1.00			1.00	
Disability level					
High¶	1.53 (1.23, 1.91)			1.45 (1.14, 1.84)	0.003
Low	1.00			1.00	
Area-level variable					
Townsend index					
Deprivation					
Yes (>0)	1.55 (1.20, 2.02)	1.41 (1.08, 1.84)	1.28 (0.96, 1.69)	1.25 (0.94, 1.66)	0.123
No (<=0)	1.00	1.00	1.00	1.00	

1. Adjusted for age, socioeconomic status (education, marital status, social class)

2. Adjusted for age, socioeconomic status, lifetime GAD

3. Adjusted for age, socioeconomic status, lifetime GAD, physical diseases and disability

‡ High education: O-level, A-level, degree; low education: refers to no education

* Other: divorced, separated, widowed

¥ Manual: skilled manual, semi-skilled, non-skilled; non-manual: professionals, managerial, skilled non-manual

+ Prevalent physical disease: respiratory disease (asthma, bronchitis), allergies (allergies, hay fever), stroke, heart attack, cancer, diabetes, thyroid conditions, arthritis

¶ Below the median PCS value of 50.6

*The brackets show the reference categories that were used for each categorical variable when it was entered in the models - deprivation: no [ref] vs. yes; GAD: no [ref] vs. yes; education: high [ref] vs. low; marital status: married [ref], single, others; social class: non-manual [ref] vs. manual; lifetime MDD: no [ref] vs. yes; prevalent physical disease: no [ref] vs. yes; disability level: low [ref] vs. high. These reference categories were based on the literature. Choosing other groupings for the potential confounders would not have changed the results.

Discussion

In this analysis of data from a population-based, cohort study we show, for the first time that area deprivation is significantly associated with increased risk for major depressive disorder (MDD) in men, but not in women. The association in men persisted after accounting for characteristics measured at the level of the individual, including sociodemographics and major medical conditions. When we assessed the specific aspects of deprivation associated with depression in men, we found that living in areas characterized by a high level of unemployment contributed to a high risk of depression.

Potential mechanisms

The living context, as measured by a Census deprivation index, appears to have a different relationship with the mental health of men and women after adjusting for a number of potential confounders. Several reasons can account for this. First, men appear to be more sensitive to stressful events occurring in their environment compared to women, especially if the stress is relating to financial and work-related problems.[23] The reason for this is that occupational and financial success is particularly important for men's mental health. Second, when living in disadvantaged regions, the possibility of hearing about job loss from others increases and this can promote anticipatory stress in those who are still working, which can increase their risk of depression.[41] This is particularly problematic for men who are perceived by their families as the main provider and head of household. In contrast, women's risk of depression seems to be influenced more by the social networks they are embedded in, the quality and continuity of relationships, the social support derived from neighbours and communities, and marital satisfaction.[23, 24] Women are more likely to experience depression as a result of unmet needs in relationships. Deficiencies in interpersonal relationships in women can lead to a perception that the self is unable to meet needs for self-worth and achievements, and this can increase their risk of poor mental health.[23] Men, on the other hand, have been shown to be more prone to depression as a result of failure in key instrumental tasks, including achievements at work and inability to provide for the family.[23, 42]

Unemployment, often accompanied by low social ranking, can lead to loss of self-esteem and role identity in men. This was seen in the United Kingdom after the 1970's, when the economy shifted from a manufacturing to a service-based one.[25] The shift was accompanied by a loss of skilled and semi-skilled jobs among men, while women had to enter the workforce and partake in jobs that were primarily service-based. The loss of employment opportunities among men might have contributed to a loss of role identity and self-esteem in this group.[25] However, even more than a decade later after this shift in economy, men who lost their employment and were in low social class groups showed poorer self-rated health compared to women.[43] This is also mirrored by recent research.[23] This again supports the notion that men are affected by failure at key instrumental tasks.[23] The same phenomenon occurred in rural areas of Midwestern United States after the farm crisis and related events occurred in the 1980s.[44] Rural areas held agrarian values, characterized by male provider norms and 'rugged independence'.[44] After the farm crisis hit, men were no longer able to fulfil their economic provider role, and both sexes had to take on multiple jobs to make ends meet. This shook the traditional system, and created stress and contributed to high rates of depression in men. During this time, men also showed susceptibility to a wider range of stressors compared to women.[44]

Men and women also tend to experience and manifest the effect of stress in different ways. Women living in deprived areas have been shown to be more prone to anxiety[26], while men living in disadvantage are more likely to have depression. This could be a result of evolutionary, survival functions. Women have traditionally had the responsibility of childcare and ensuring the successful survival of future generations.[45] Therefore, living in deprived circumstances can trigger the fight or flight reaction, which can increase stress in findings ways to make ends meet so that they can raise their children. In this context, anxiety might be seen as protective, ensuring the survival of future generations. This is why women also tend to be more concerned about community features that can disrupt their caregiving role and negatively impact their family, such as, lack of safe play areas for children.[45, 46] Men have traditionally had the responsibility of being the provider, and if they are not able to fulfil this role, they are more likely to become depressed and potentially commit suicide.[23, 25] This is a problem in India, where suicide rates are high among male farmers whose crops have failed.[47, 48] In the UK, men with depression are also more likely than women to commit

suicide. Taken together, these findings suggest that women may actually be more resilient than men when encountering adversity. However, very little research has examined this, and previous studies in the mental health literature have typically described women as vulnerable. Further research on health from a gendered perspective is needed.[26]

When exposed to the stresses and strains of deprivation, men are also more likely to develop substance abuse and this, in turn, can increase the risk for depression. The National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) study[49] showed that total number of stressors experienced in life had a significantly stronger association with heavy drinking in men than in women. Finally, when men experience mental health issues, they are less likely to seek help than women [44].

Strengths and weaknesses and future research

This study reveals that depression in men is strongly linked with area disadvantage. It has several strengths. We had a large, population-based sample of middle- and older-aged adults and adequately adjusted for a range of possible confounders. We used a structured, self-reported questionnaire to assess presence of past-year GAD, and participants were followed for a long period of time. We overcome methodological limitations of previous studies by employing a commonly-used, theoretically-sound measure of area deprivation capturing important features of the environment, such as, unemployment and non-home ownership. We also had a large list of self-reported physician diagnoses of chronic physical diseases that we used to establish medical histories. Despite this, the residual effect of diseases not captured by our study, but that are associated with GAD may be present. Past illness may have been underreported, which may have introduced measurement error and attenuated effect estimates towards the null. Participants were required to complete detailed dietary and lifestyle questionnaires and undergo periodic health assessments. Because those who participated in EPIC-Norfolk were somewhat less deprived and healthier than individuals living in other parts of England[27], our results may not generalize to people living in extremely deprived circumstances.

Future research should assess the risk of depression not only in countries, such as, the US or UK where there is higher gender equality, but also in parts of the world where social roles and

gendered norms for men and women have shown much less change over time. Countries with higher gender equality also show some of the highest rates of depression and other mental disorders in the world.[50] In Europe, the discrepancy in depression rates between men and women in highly-developed countries is greater than in less-developed countries where there is also greater gender inequality.[51] In Eastern European countries, levels of depression are similar between men and women[51], while in Western Europe, women are twice as affected as men.[52] More studies are needed to explore the influence of area deprivation on the mental health of men and women separately, and to do this in different contexts (ex. rural, urban) and countries around the world. Further, the reasons behind gender differences need to be better elucidated.

Placing our research in context

Although other studies have shown that the places where people live have a substantial impact on health[14, 15], studies on the links between area deprivation and mental disorders from a gendered perspective are limited. A recent study[53] of over 1000 African American and non-Hispanic white adults living in the US showed that men who had experienced stressful life events in 1983-1986 were more likely to have depression in 2011, while this was not observed in women. This study, however, has limited generalizability, because it excluded other ethnicities. Also, the reliability and validity of the measure of stressful life events was not reported – the measure was based on a checklist of 'major negative events' that had occurred in the previous 3 years. Finally, exposure to stressful life events at the individual-level were investigated, rather than the effect of the place people live in.

A number of studies have assessed individual-level risk factors of depression, but substantially fewer have examined the influence of the environment on mental health. Nonetheless, studies of individual-level risk factors provide an important starting point in understanding relationships. Another prospective UK study of over 500 people[25] showed that the socioeconomic status of men at midlife was associated with depression at midlife, while this was not observed in women. For women, their socioeconomic status at birth influenced their levels of depression at midlife. Also, men who had experienced downward social mobility or a reduction in their socioeconomic status from adulthood to midlife were at high risk of having poor mental health at midlife, but this was not found in women.[25] These results suggest that women are more sensitive to the social class group they are in very early in life, while for men, social mobility over the life course, as well as the socioeconomic status group they are in during later life are more important for their mental health. This study, however, was limited, because it was based on a small sample size, assessed only individual-level measures rather than area-level level effects, and failed to adjust for a number of important confounders, such as, demographic factors. Failure to properly adjust for potential confounders can lead to overestimation of the effect estimate. Finally, this study examined general mental health, rather than individual psychiatric disorders.

A recent US study showed that the types of stressors that influence men's risk of depression are those related to work, finances, and legal matters.[23] In this study, stressors were not

linked to depression risk in women. Again, this research only assessed individual-level data. Our study shows, for the first time that living in a deprived area increases the risk of depression in men, while less so in women. Area deprivation was measured in our study at midlife and beyond, the time period which seems to have the greatest influence on men's mental health.[23]

Interpretation

The absolute number of people living in deprived areas across the globe is large. When this is considered along with the growing mental health burden worldwide, our findings are highly relevant. There is a need to reduce social and health inequalities, and we provide a strong evidence base in support of this. When developing mental health policy, the places where people live need to be taken into account and greater investments in relation to employment opportunities in deprived communities need to be made. We show that gender is an important factor when it comes to assessing the impact of the environment, and promoting good mental health. Our findings also suggest that financial investments made to local areas will not benefit everyone equally, and this is particularly important at a time of scarce economic- and health-related resources. Regarding clinical implications, health professionals should consider assessing depression in men living in deprived areas.

Acknowledgements: OR received PhD funding from the National Institute for Health Research.

Competing interest: All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: no support from any organisation for the submitted work; no financial relationships with any organizations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

Funding: This work was supported by the Medical Research Council UK (grant number SP2024-0201 and SP2024-0204) and Cancer Research UK (grant number G9502233).

Author contributions: OR (corresponding author) had the idea for and conducted the analysis, and wrote the article, along with CB, KK, LL, PS, and NW. All authors provided feedback into the analysis and critically reviewed drafts of the manuscript. All authors have seen and approved the final version. The authors had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. OR acts as guarantor of the study.

Transparency declaration: OR affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

Role of study sponsors and statement of independence: The funding sources had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; and preparation, review, or approval of the manuscript.

Ethical approval: The study has ethics committee approval from Norfolk Ethics Committee (Rec Ref: 98CN01) and all participants gave informed consent.

Data sharing: No additional data available.

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Please see the article line numbers (column on the right) and the explanations provided.

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Line numbers within the article
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	6, 43
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	35-41
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	87-114
Objectives	3	State specific objectives, including any prespecified hypotheses	140-144
Methods			
Study design	4	Present key elements of study design early in the paper	148-149
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	148-151, 154-161
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	165-167, 148-151, 156-158 The manuscript also mentions that the EPIC-Norfolk cohort was record linked to hospitalization databases (follow-up).
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	171-205, 206-236, 243-256
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is	There were two variables of interest in this study: area deprivation and major depressive disorder (243-256,

		more than one group	171-203. The others are potential confounders – in the methods I list them all, indicate how they were assessed, and mention that they were collected through the baseline, self-reported postal HLQ questionnaire.
Bias	9	Describe any efforts to address potential sources of bias	282-284
Study size	10	Explain how the study size was arrived at	299-302
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	How variables were handled in analyses: 206-236 Which grouping were chosen and why: I describe the reference categories of the variables in the footnotes under tables 2 and 3. I mention that the categorization of the variables was done in accordance with the literature and provide the relevant citations in the methods section (line 207-208). How the dependent variable was created: 171-203 How area-level measure was created: 243-256 Individual-level measures: 206-236
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	263-299
		(*b*) Describe any methods used to examine subgroups and interactions	Similar to other studies, I conducted analyses separately for men and women. I did not do this because of p-value considerations (statistical significance), but rather, because I felt it was important to do. In the introduction, I provide the rationale for conducting sex-specific analyses. Knowing which gender group is more affected can help with the tailoring of targeted interventions.
		(*c*) Explain how missing data were addressed	We indicated that this was a complete-case analysis.
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed	Loss to follow-up was not a problem in this study. We were able to track down all participants using various means, unless they expressed that they wished

Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy	to be removed from the mailing list. We elaborate on this in the manuscript.
(*e*) Describe any sensitivity analyses	This paper conducted two sensitivity analyses: in one analysis, the relationship between area deprivation and pure MDD (in which past-year GAD was excluded) was assessed. In another analysis, logistic regression was conducted in place of correlated data analysis. The methods and results sections elaborate on these.

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	310-311
		(b) Give reasons for non-participation at each stage	We do not have the reasons for non-participation, because these data were not collected when the study was initiated in 1993.
		(c) Consider use of a flow diagram	We reference a paper which describes the EPIC-Norfolk study further. This paper contains a flow diagram. Also, our previously-published BMJ Open paper upon which this one was based contains a flow diagram also – we reference this paper.
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	We included characteristics for those with vs. without MDD, because we felt it was important to show the characteristics of those exposed vs. non-exposed (see also Table 1)
		(b) Indicate number of participants with missing data for each variable of interest	314-316
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	316
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	331
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Tables 2 and 3 contain unadjusted and progressively adjusted estimates. We also discussed the findings within the text, and provide odds ratios and 95% confidence intervals (336-339, 360-383). We included the confounders based on the literature – we mention this in the paper and cite relevant literature. As per strobe, we included this information

			in the methods section; and we omitted repeating this in the results section to reduce redundancy. However, if the editor would like us to repeat this information in the results, we are happy to do so.
		(*b*) Report category boundaries when continuous variables were categorized	This age cut-offs are provided. In regards to the Tosi-Laird index, the methods section states that those below and above the cut-point of zero were compared.
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Sensitivity analyses: 1) relationship between area deprivation and pure MDD (past-year GAD excluded) – findings remained the same; 2) correlated data analysis replaced with logistic regression – findings remained the same. This is reported in the paper.
Discussion			
Key results	18	Summarise key results with reference to study objectives	404-410
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	486-499
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	541-552 (We also have a section comparing our study results to those of others: 509-544, as well as a section on potential mechanisms explaining our findings: 413-472)
Generalisability	21	Discuss the generalisability (external validity) of the study results	489-492
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	567-569

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

The association between area deprivation and major depressive disorder in British men and women: large, cohort study

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2018-027530.R1
Article Type:	Research
Date Submitted by the Author:	22-Mar-2019
Complete List of Authors:	Remes, Olivia; University of Cambridge, Public Health and Primary Care LaFortune, Louise; University of Cambridge, Institute of Public Health Wainwright, Nick; University of Cambridge, Public Health and Primary Care (retired) Surtees, Paul; University of Cambridge, Department of Public Health and Primary Care Khaw, Kay-Tee; University of Cambridge, Department of Public Health and Primary Care Brayne, Carol; University of Cambridge, Institute of Public Health
Primary Subject Heading:	Epidemiology
Secondary Subject Heading:	Mental health, Public health
Keywords:	MENTAL HEALTH, PUBLIC HEALTH, Depression & mood disorders < PSYCHIATRY, EPIDEMIOLOGY

The association between area deprivation and major depressive disorder in British men and women: large cohort study

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Tables: 3

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ABSTRACT

OBJECTIVE

Studies have shown area-level deprivation can increase the risk for mental disorders over and above individual-level circumstances, such as education and social class. The objective of this study is to determine whether area deprivation is associated with major depressive disorder (MDD) in British women and men separately while adjusting for individual-level factors.

DESIGN

Large, population study.

SETTING

UK population-based cohort.

PARTICIPANTS

30,445 people from the general population aged 40 years and older and living in England consented to participate at study baseline, and of these, over 20,000 participants completed a structured Health and Life Experiences Questionnaire (HLEQ) used to capture MDD. Area deprivation was measured in 1991 using Census data, and current MDD was assessed in 1996-2000. 8,236 men and 10,335 women had complete data on all covariates.

PRIMARY OUTCOME MEASURE

MDD identified according to the Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV).

RESULTS

In this study, 3.3% (339/10,335) of women and 2.1% (177/8,236) of men had MDD. Men living in the most deprived areas were 51% more likely to have depression than those living in areas that were not deprived (OR=1.51, 95% CI: 1.01 to 2.24; p=0.043), but the association between deprivation and MDD was not statistically significant in women (OR=1.24, 95%CI: 0.93 to 1.65; p=0.143).

CONCLUSION

This study shows that the residential environment differentially affects men and women, and this needs to be taken into account by mental health policy-makers. Knowing that men living in deprived conditions are at high risk for having depression helps inform targeted prevention and intervention programs.

Article Summary

Strengths and limitations of this study

- We used a population-based sample of over 20,000 British adults and controlled for important confounders, including social class, medical history, and disability.
- We used a structured questionnaire (the Health and Life Experiences Questionnaire of the EPIC-Norfolk study) to determine whether participants met criteria for MDD according to the DSM.
- We used the Townsend index to assess area deprivation. This index is commonly-used by researchers to examine deprivation and is a theoretically sound measure.
- People who took part in EPIC-Norfolk were generally more affluent and healthier than those living in other parts of England. As such, our results may not be generalizable to the most deprived areas.

Introduction

Depression is a common psychiatric disorder affecting approximately 350 million people around the world.[1] According to the Global Burden of Disease Study[2], major depressive disorder (MDD) contributed to 689.9 per 100,000 disability-adjusted life years in men and 1161.2 per 100,000 disability-adjusted life years in women in 2010. Depression can increase the risk for impairment, disability and suicide.[3, 4, 5] It has also been linked to decreased work productivity, poor quality of life, and high health service use.[3, 6, 7]

A number of studies have examined the individual-level risk factors of depression, such as, personal and parental history of psychopathology[8], genetics[9], history of trauma and stressful life events[10, 11], and socioeconomic status.[12] However, the environment or living context can have a profound influence on mental health, over and above individual-level factors.[13, 14, 15] In a systematic review[16] of 14 studies, about half found an association between neighbourhood socioeconomic conditions and depression. Living in an area of low socioeconomic status can expose people to a higher number of stressors, such as, violence, disorder, and noise pollution, and this can have deleterious effects on mental health.[17]

There is a wealth of literature on the effect of the places where people live on mental health. Findings from systematic reviews[18, 19, 20] assessing neighbourhood characteristics and depression show that there is large heterogeneity in findings, because of differences in study populations, the confounders that are adjusted for in analyses, and the measures and definitions used to delineate neighbourhoods.[19] Although there is much evidence on the influence of area-level disadvantage or deprivation on depression, research on this relationship from a gendered perspective is lacking.

In this large, population-based, cohort study, we examine the association between area deprivation and major depressive disorder in men and women separately, while controlling for a range of important confounders, including social class, previous medical conditions, psychiatric co-morbidity, and disability. Area deprivation refers to residential environments or living contexts characterized by factors, such as, high levels of unemployment, non-home

ownership, non-car ownership, and low income.[13] Findings are disaggregated by gender, and this is done for several reasons. Gender frames access to resources derived from the environment.[21, 22] Compared to men, women have been shown to have less access to material and social conditions, such as income, power, and social status, and this can influence mental health. Women have historically been the victims of discrimination, and because of this have had limited opportunities for education, and well-remunerated and respected forms of employment.[23] Women have taken on different job roles and tasks than men, which has exposed them to different hazards and contaminants affecting their health. Women have traditionally been seen as 'care-takers' in society and involved in domestic work, which might have led to an interruption in their education or career paths. As such, they have derived fewer resources with which they could maintain or improve their health.[23, 24]

However, there are additional reasons why findings are disaggregated by gender. Women and men tend to react to different kinds of stressors. Recent research has shown that men are more susceptible to work- and finance-related stressors, while women are more affected by deficiencies in their social networks and interpersonal relationships.[25, 26] This research is based on a study conducted in the US and other parts of the world. Hence, living in a deprived area with high levels of unemployment might be particularly detrimental for men's mental health. This was evident when the economy shifted in the UK from a manufacturing- to a service-based one, and many men lost their jobs.[27] Prior to the shift, the local economy had relied on skilled and semi-skilled jobs, typically performed by men. When the economy changed, an increasing number of women entered employment (occupying mainly service industry jobs), and this had implications for traditional gender-defined social roles. Men who experienced reduced economic opportunities may have suffered from loss of role identify and self-esteem, and this had consequences for their physical and mental health.[27] A recent study[25] showed that men's mental health is particularly affected if they fail at key instrumental tasks, such as, work achievements and ability to provide for the family. In contrast, women are more likely to be depressed if they fail to meet their needs for relationship.[25] To this end, it appears that men and women are susceptible to different kinds of stressors.

It remains unclear whether men and women living in areas of above average deprivation are differentially susceptible to MDD – the objective of this study will be to assess this. Knowing that one gender is at risk of developing depression when exposed to deprived circumstances helps to tailor interventions and allocate scarce resources according to need.[28] This is particularly important at a time of scarce economic and health-related resources.

Methods

Data were drawn from EPIC-Norfolk, whose design and study methods have been described in detail elsewhere.[29] In brief, a prospective population-based cohort of 30,445 participants ages 40 to 74 years were recruited by post between 1993 and 1997 through general practice age-sex registers in the city of Norwich and the surrounding small towns and rural areas. At baseline (1993-97), participants completed a postal Health and Life Experiences (HLQ) questionnaire that captured information on sociodemographics, including age, gender, highest educational attainment, marital status, social class, employment status, ethnicity and self-reported physician diagnoses of physical diseases. Using participants' postal codes, a measure of area deprivation was derived based on the 1991 Census. Between 1993 and 2000, participants completed self-reported postal questionnaires provided they: 1) were still alive, 2) did not ask to be removed from the study's mailing list, and 3) had a valid mailing address.

During 1996-2000, 20,919 participants completed a structured, psychosocial Health and Life Experiences (HLEQ) questionnaire. During this time, an assessment of generalized anxiety disorder (GAD) and major depressive disorder (MDD) was made according to the Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV)[30]. Using the HLEQ questionnaire, disability measures based on the SF-36 were also derived.[31]

All participants recruited through general-practice registers and who completed a baseline health questionnaire were eligible to be included in our study; those who completed a psychosocial questionnaire during follow-up were eligible to be included in our analysis.

In regards to the study size, an initial sample of 30,445 participants completed the baseline HLQ and of these, 20,921 filled out the psychosocial HLEQ. After retaining the people with complete measures on all covariates, the final sample size was 18,571.

Although EPIC-Norfolk is a prospective study and area derivation was measured in 1991 and anxiety in 1996-2000, this analysis should be considered cross-sectional.

Dependent variable

The primary outcome in this study was current MDD, which was measured using the HLEQ, a structured self-assessment instrument designed to provide a measure of depression for inclusion in a large-scale epidemiology project.[32, 33] DSM-IV criteria were applied to the psychiatric symptoms to determine whether participants had an episode of MDD that was ongoing at the time of the completion of the HLEQ questionnaire. Participants who reported a psychiatric episode were asked to estimate the onset and offset timings of the episode, and then to report an outline of the history of the problem. Participants were also asked about age at first symptom onset and subsequent episode recurrence.

The dependent variable in this study is current MDD, defined as an episode of MDD reported as ongoing at the time of the completion of the HLEQ.

The following two core criteria of MDD were first evaluated:

1. Have there ever been times in your life when you felt sad or depressed for two weeks or more in a row?
2. Have there ever been times in your life when you lost interest in most things like your work or activities that usually give you pleasure, for two weeks or more in a row?

If participants answered yes to one of these questions, they were then asked to think of the most recent two-week episode during their lives when these feelings of sadness, depression or loss of interest were the worst. They then had to report that these feelings of being sad, depressed, or loss of interest lasted all day or most of the day, and that during these two weeks of their most recent episode, they felt this way every day or almost every day.

In addition, at least five of the following symptoms had to be present: gaining or losing weight, having trouble falling asleep or sleeping too much, feeling tired or low on energy, feeling unable to sit still or feeling slowed down, experiencing guilt or shame, feeling worthless, losing confidence, having trouble concentrating, and thinking a lot about death or suicide. One of these five symptoms had to be one of the two core criteria evaluated at the beginning.

Finally, it was evaluated whether these symptoms interfered with participants' lives and resulted in disability or impairment.

Individual-level measures (potential confounders)

Individual-level measures included age, education, employment status, marital status, social class, prevalent physical disease, and ethnicity. The final categorization of the variables took cell size into account and was also done in accordance with previous literature.[33-39] Age was divided into 10-year bands. Educational attainment was categorized into high (vocational or formal qualifications at the A- or O-level or degree-level qualifications) vs. low (no formal qualifications). Further details on the meaning of A- and O-level can be found elsewhere[40, 41]; the appendix also contains definitions of these (appendix 1). Employment was divided into yes vs. no. Marital status was categorized into three groups: married, single (or never married), and others (widowed, divorced, separated). Social class was derived using the Computer-Assisted Standard Occupational Coding[42] and categorized as follows: I (professionals), II (managerial and technical occupations), III non-manual and III manual (skilled workers), IV (partly skilled workers), and V (unskilled manual workers). To assign social class to men and women, the male partner's current or past occupation was used. If this information was not available, the female partner's occupation was used. If the social class from either partner was unavailable, then it was coded as missing. The final categorization of social class included manual: skilled manual, partly skilled, and unskilled; and non-manual: professionals, managerial and technical, and skilled non-manual. Individual-level health status was assessed through the construction of a variable capturing major prevalent physical diseases. This was based on HLQ questions asking participants: "Has the doctor ever told you that you have any of the following?", followed by a list of options, such as allergies, asthma, cancer, stroke, heart attack, diabetes, thyroid conditions, etc. Ethnicity was based on a self-reported question asking participants to tick the relevant box: 'white', 'black Caribbean', 'black other', 'Indian', 'Pakistani', 'Bangladeshi', 'Chinese', 'other'.

Lifetime history of GAD was also assessed using the self-reported HLEQ questionnaire.[33] Lifetime GAD consisted of having ever had at least one episode that met core criteria stipulated by the DSM-IV. Anxiety was identified if participants reported having uncontrollable, excessive worry for six months or longer on most days than not that resulted

in disability or impairment. In addition, at least three of the following symptoms needed to have been present: restlessness, irritability, muscle tension, fatigue, trouble concentrating because of worry, mind going blank, trouble falling asleep, trouble staying asleep, and feeling keyed up or on edge.

To determine disability levels, we used the physical component summary (PCS) derived from the HLEQ. The PCS is part of the SF-36, a widely-used, validated self-assessment tool. The SF-36 is a 36-item measure capturing 8 health dimensions: physical functioning, social functioning, role limitations due to physical problems, role limitations due to emotional problems, mental health, energy/vitality, bodily pain, and general health perception. The eight dimensions of the SF-36 were used to create two higher order scores, one of which was the PCS. Higher scores indicate better health.[31] PCS scores were dichotomized above and below the median.

All of these individual-level variables were regarded as potential confounders and selected based on the literature and their association with depression and area-level socioeconomic circumstances.

Area-level measure (exposure variable)

To examine area deprivation, we used the Townsend Index.[43, 44] This is one of the most commonly-used measures of area deprivation in the UK and particularly appropriate for the time of the original EPIC-Norfolk study. This index is a composite measure of four variables obtained from the 1991 Census: 1) percentage of economically active residents over age 16 who are unemployed, 2) percentage of households that do not possess a car, 3) percentage of private households that are not owner occupied, and 4) percentage of private households that are overcrowded (have more than 1 person per room). These variables were obtained at the level of the enumeration district, which is a geographic area used for census purposes in Britain. Each variable was standardized by obtaining Z scores (dividing the mean by the standard deviation across enumeration districts in England). The Z values of the four variables were added together to produce a Townsend index score for each enumeration district. A score of 0 represents the national mean, while positive values of the index indicate enumeration districts that are above average deprivation, while negative values indicate

those that are below average deprivation. The postal codes of participants were record linked to enumeration districts, and participants were considered to live in areas of above average deprivation depending on the Townsend index score assigned to their enumeration district.[43]

The Townsend deprivation index was also disaggregated into its four constituent components to determine whether any one of these is associated with MDD or if it is the effect of the combined components that is important.

Missing data

The number of missing observations for each covariate were: 9 for education, 47 for marital status, 417 for MDD, 434 for GAD, 458 for social class, 75 for the Townsend index, and 1386 for the SF-36, 52 for employment status.

Statistical analysis

First, we compared participants on sociodemographic, and medical and psychiatric history characteristics, and the prevalence of MDD was computed for sub-groups. Next, we undertook correlated data analysis based on generalized estimating equations (GEE)[45, 46] to determine the population-average effect of living in an area of above average deprivation on risk of having depression while controlling for confounders. MDD is a dichotomous outcome and the intra-cluster correlation was assumed to be equal. As such, we used GEE with a logit link and an exchangeable correlation structure.

First, we ran unadjusted analyses between deprivation and MDD. To determine the influence of potential confounders on risk of having depression, we progressively adjusted the models and accounted for 1) age, educational attainment, marital status, and social class; then for 2) age, educational attainment, marital status, social class, and GAD; and finally for 3) age, educational attainment, marital status, social class, GAD, physical diseases and disability level. We conducted separate analyses for men and women. The individual-level covariates were sociodemographics, and medical and psychiatric history, while the area-level covariate was the Townsend index score. The progressively adjusted models allowed us to estimate adjusted odds ratios (OR) and 95% confidence intervals based on robust standard errors.

A dichotomous variable was created using the Townsend index scores, and 0 was used as the cut-point (considered to be the national average). The variable was dichotomized, because we wanted to compare participants' scores to the national average[47] - scores above the cut-point of 0 were considered above average deprivation. A binary variable was also used in accordance with previous research[47] and because of cell size considerations – we wanted to ensure that there were sufficient people with MDD in each category of the deprivation variable.

Models were constructed for participants with complete measurements on all covariates. It was not possible to group the MDD variable otherwise since it was created and categorized according to the DSM-IV[32, 33], and area deprivation was analysed in accordance with the literature[37, 43].

Several sensitivity analyses were undertaken. We ran fully-adjusted models using pure MDD as the outcome, in which those with past-year GAD were excluded. It should be mentioned that although GAD and MDD have been regarded as closely correlated by many researchers, they are independent disorders. The high GAD-MDD comorbidity found in older literature was due to the use of clinical populations with multiple co-occurring conditions.

Next, we disaggregated the index used to measure disadvantage. If a significant relationship was found between area deprivation and depression for one of the genders in a fully-adjusted model, we investigated further. We disaggregated the Townsend index into its 4 constituent components (unemployment, non-home ownership, non-car ownership, and overcrowding) to determine whether any aspect of deprivation is associated with increased risk of having depression in that gender group. Each component was dichotomized using a cut-point of 0, because it represents the national average.

Then we determined whether relationships held after dividing the Townsend index into quintiles and adjusting for sociodemographic and health status variables. Further, we examined whether the inclusion of additional covariates or recategorization of variables made any difference to the effect estimates. We included ethnicity as a potential confounder

in a fully-adjusted model, and assessed whether the division of the education variable into four categories influenced the associations.

Finally, we conducted logistic regression, which does not take the intra-cluster correlation into account, and compared the findings to those from GEE. Similar results between the models suggests that the intraclass correlation is negligible.

All models used two-sided statistical tests, and a p-value of <0.05 was considered statistically significant. Statistical Analysis Software (SAS) Version 9.3 (SAS Institute, Cary, NC) was used in these analyses.

Patient and Public Involvement:

There were no patients or public involved in the development of the research question, outcome measures, design of the study, or recruitment to and conduct of the study.

Results

At baseline, 30,445 participants were recruited from general practices in the city of Norwich and the surrounding towns and rural areas. Of these, 20,919 people completed the HLEQ during the follow-up period. In total, 18,571 out of 20,919 (89%) people were available for analysis, because they had complete data on all covariates.

In this sample, there were 8,236 men and 10,335 women over the age of 40 years. Table 1 shows the distribution of individual- and area-level characteristics by current MDD.

Table 1: Distribution of characteristics for women and men who completed the HLEQ questionnaire in the EPIC-Norfolk cohort

	Women (n=10,335)		Men (n=8,236)	
Characteristic	**Number with characteristic**	**Percentage and number with MDD**	**Number with characteristic**	**Percentage and number with MDD**
Individual-level variables				
Socio-demographics				
Age (years)				
<50	1450	5.0 (72)[a]	964	3.4 (33)[a]
50-60	3716	3.9 (145)	2651	3.0 (80)
60-70	3180	2.1 (68)	2743	1.5 (40)
>70	1989	2.7 (54)	1878	1.3 (24)
Education[‡]				
Low	4050	3.5 (141)	2365	2.2 (51)
High	6285	3.2 (198)	5871	2.1 (126)
Marital status				
Single	417	2.4 (10)[a]	303	3.6 (11)[a]
Married	7750	2.7 (207)	7237	1.7 (122)
Other[*]	2168	5.6 (122)	696	6.3 (44)
Social class[¥]				
Manual	3829	3.3 (127)	3286	2.3 (76)
Non-manual	6506	3.3 (212)	4950	2.0 (101)
Employment				
Yes	4075	128 (3.1)	3821	68 (1.8)[b]
No	6260	(3.4) 211	4415	109 (2.5)
Health status				
Prevalent physical disease				
Yes[+]	5698	3.8 (214)[b]	3843	2.6 (100)[b]
No	4637	2.7 (125)	4393	1.8 (77)
Disability level				
High[¶]	5296	3.9 (208)[a]	4021	3.0 (119)[a]
Low	5039	2.6 (131)	4215	1.4 (58)
Lifetime GAD				
Yes	448	19.4 (87)[a]	255	22.4 (57)[a]
No	9887	2.5 (252)	7981	1.5 (120)
Area-level variable				
Townsend index				
Deprivation				

Above average deprivation (>0)	1646	4.6 (76)[a]	1242	3.6 (45)[a]
Below average deprivation (<=0)	8689	3.0 (263)	6994	1.9 (132)

** Please see appendix 2 for the distribution of the Townsend index scores in men and women.

‡ High education: O-level, A-level, degree; low education: refers to no education

* Other: divorced, separated, widowed

+ Prevalent physical disease: respiratory disease (asthma and bronchitis), allergies (allergies and hay fever), stroke, heart attack, cancer, diabetes, thyroid conditions, arthritis

¥ Manual: skilled manual, semi-skilled, non-skilled; non-manual: professionals, managerial, skilled non-manual

¶ Below the median PCS value of 50.6

[a] $P < 0.001$

[b] $P < 0.05$

The prevalence of (current) MDD was 2.1% (177/8236) for men and 3.3% (339/10335) for women. Women with MDD were younger than 50 years of age, more likely to be divorced/separated/widowed, have prevalent physical disease, high disability, GAD, and live in areas of above average deprivation. Among men, similar patterns emerged (table 1). Men with MDD were also more likely to be unemployed.

After performing correlated data analysis based on GEE, findings showed that the risk of depression in men living in areas of above average deprivation was 95% higher in an unadjusted analysis (OR=1.95, 95% CI: 1.39, 2.76; p=0.0001). After accounting for sociodemoraphics, the odds ratio attenuated slightly to 1.57 (OR=1.57, 95% CI: 1.09, 2.26; p=0.0152) (table 2).

Table 2: Odds ratios for MDD according to individual- and area-level characteristics for men (n=8,236) who completed the HLEQ questionnaire in the EPIC-Norfolk cohort

	Odds ratios and 95% CI					
Characteristic*	**Model A[1]**	**P-value for model A**	**Model B[2]**	**P-value for model B**	**Model C[3]**	**P-value for Model C**
Individual-level variables						
Socio-demographics						
Age						
(per 10 years)	0.40 (0.32, 0.50)	<0.0001	0.50 (0.40, 0.63)	<0.0001	0.47 (0.38, 0.60)	<0.0001
Education‡						
Low	1.10 (0.76, 1.61)	0.6081	1.06 (0.72, 1.54)	0.7813	1.00 (0.68, 1.46)	0.9978
High	1.00		1.00		1.00	
Marital status						
Single	1.46 (0.76, 2.83)	<0.0001	1.39 (0.71, 2.68)	<0.0001	1.41 (0.72, 2.76)	<0.0001
Married	1.00		1.00		1.00	
Other*	3.66 (2.53, 5.28)		3.48 (2.31, 5.22)		3.58 (2.39, 5.35)	
Social class¥						
Manual	1.02 (0.73, 1.41)	0.9161	1.14 (0.81, 1.59)	0.4612	1.06 (0.76, 1.48)	0.7298
Non-manual	1.00		1.00		1.00	
Employment¥						
No	3.69 (2.48, 5.50)	<0.0001	2.64 (1.74, 4.03)	<0.0001	2.24 (1.46, 3.45)	0.0002
Yes			1.00		1.00	
Health status						
Lifetime GAD						
Yes			14.33 (9.84, 20.87)	<0.0001	12.65 (8.68, 18.44)	<0.0001
No			1.00		1.00	
Prevalent physical disease						
Yes+					1.25 (0.89, 1.75)	0.1977

No					1.00	
Disability level						
High¶					1.98 (1.39, 2.82)	0.0002
Low					1.00	
Area-level variable						
Townsend index						
Deprivation						
Above average deprivation (>0)	1.57 (1.09, 2.26)	0.0152	1.56 (1.05, 2.31)	0.0287	1.51 (1.01, 2.24)	0.0434
Below average deprivation (<=0)	1.00		1.00		1.00	

1. Adjusted for age, SES (education, marital status, social class, employment status)
2. Adjusted for age, SES, lifetime GAD
3. Adjusted for age, SES, lifetime GAD, physical diseases and disability

⁺ Prevalent physical disease: respiratory disease (asthma, bronchitis), allergies (allergies, hay fever), stroke, heart attack, cancer, diabetes, thyroid conditions, arthritis

¥ Manual: skilled manual, semi-skilled, non-skilled; non-manual: professionals, managerial, skilled non-manual

‡ High education: O-level, A-level, degree; low education: refers to no education

* Other: divorced, separated, widowed

¶ Above the median PCS value of 50.6

*The brackets show the reference categories that were used for each categorical variable when it was entered in the models - deprivation: below average deprivation [ref] vs. above average deprivation; education: high [ref] vs. low; marital status: married [ref], single, others; social class: non-manual [ref] vs. manual; employment: yes [ref] vs. no; lifetime GAD: no [ref] vs. yes; prevalent physical disease: no [ref] vs. yes; disability level: low [ref] vs. high. These reference categories were based on the literature. Choosing other groupings for the potential confounders would not have changed the results.

The OR reduced slightly after controlling for lifetime GAD (OR=1.56, 95% CI: 1.05, 2.31; p=0.029), but remained highly significant. After additionally adjusting for prevalent physical diseases and disability, the effect estimate became somewhat attenuated (OR=1.51, 95% CI: 1.01, 2.24; p=0.043), however, a statistically significant association between area derivation and depression remained (table 2). To determine the aspect of deprivation that is specifically linked to depression, the Townsend index was disaggregated into its four constituent components. Results showed that the OR was highest for unemployment (OR=1.77, 95% CI: 1.16, 2.71; p=0.008), followed by non-car ownership (OR=1.20, 95% CI: 0.70, 2.04; p=0.507), and lowest for overcrowding (OR=0.93, 95% CI: 0.60, 1.42; p=0.727) and non-home ownership (OR=0.81, 95% CI: 0.49, 1.34; p=0.422). Of these, only the effect estimate for unemployment was statistically significant. Men living in area characterized by high levels of unemployment were almost 80% more likely to have depression than those living in areas with low levels of unemployment. Next, we wanted to determine whether deprivation is associated with pure MDD, and thus excluded past-year GAD; the association with depression remained statistically significant (OR=1.64, 95% CI: 1.06, 2.52; p=0.025).

In women, while there was a statistically significant association in the unadjusted analysis (OR=1.55, 95% 1.19, 2.01; p=0.0010) as well as in the model adjusting for sociodemographics (OR=1.40, 95% CI: 1.07, 1.84; p=0.013), the association lost its significance in the fully-adjusted model (OR=1.24, 95%CI: 0.93, 1.65; p=0.143) (table 3).

We also conducted some sensitivity analyses. First, we divided the Townsend index into quintiles. Results showed that men living in the most deprived quintile had a statistically significantly increased risk for depression (OR=1.68, 95% CI: 1.01, 2.79; 0.0472), while none of the quintiles for women showed statistically significant findings. Second, we wanted to determine whether there was any change in findings after incorporating ethnicity in the original fully-adjusted models. The associations remained the same (men: OR=1.53, 95% CI: 1.03, 2.27 and women: OR=1.25, 95% CI: 0.94, 1.66). Second, we undertook analyses in which the education variable was left in its original form (divided into 4 categories: no education, O-level, A-level, degree and beyond) in fully-adjusted models, and similar findings were again obtained (men: OR=1.51, 95% CI: 1.02, 2.24) and women: OR= OR=1.23, 95% CI: 0.92, 1.63). Third, we re-ran the fully-adjusted models using logistic regression rather than correlated

data analysis based on GEE (Appendix 3), and results remained essentially unchanged (men: OR=1.51, 95% CI: 1.03, 2.21 and women: OR=1.24, 95% CI: 0.94, 1.64). This shows that there indeed is a robust association between area deprivation and depression in men, while there is no statistically significant effect in women.

Table 3: Odds ratios for MDD according to individual- and area-level characteristics for women (n=10,335) who completed the HLEQ questionnaire in the EPIC-Norfolk cohort

	Odds ratios and 95% CI					
Characteristic*	**Model A[1]**	**P-value for model A**	**Model B[2]**	**P-value for model B**	**Model C[3]**	**P-value for Model C**
Individual-level variables						
Socio-demographics						
Age						
(per 10 years)	0.54 (0.46, 0.64)	<0.0001	0.62 (0.52, 0.74)	<0.0001	0.59 (0.50, 0.71)	<0.0001
Education‡						
Low	1.23 (0.97, 1.56)	0.0890	1.29 (1.01, 1.65)	0.0412	1.30 (1.02, 1.66)	0.0356
High	1.00		1.00		1.00	
Marital status						
Single	0.93 (0.48, 1.78)	<0.0001	0.91 (0.48, 1.75)	<0.0001	0.91 (0.47, 1.75)	<0.0001
Married	1.00		1.00		1.00	
Other*	2.56 (2.00, 3.27)		2.41 (1.87, 3.10)		2.36 (1.83, 3.04)	
Social class¥						
Manual	0.95 (0.75, 1.21)	0.6964	0.99 (0.77, 1.27)	0.9530	0.97 (0.76, 1.25)	0.8225
Non-manual	1.00		1.00		1.00	
Employment¥						
No	1.87 (1.42, 2.48)	<0.0001	1.62 (1.21, 2.15)	0.0010	1.55 (1.17, 2.06)	0.0026
Yes			1.00		1.00	
Health status						
Lifetime GAD						
Yes			7.97 (5.99, 10.60)	<0.0001	7.37 (5.52, 9.83)	<0.0001
No			1.00		1.00	
Prevalent physical disease						
Yes+					1.25 (0.98, 1.59)	0.0682
No					1.00	

Disability level						
High¶					1.41 (1.11, 1.79)	0.0045
Low					1.00	
Area-level variable						
Townsend index						
Deprivation						
Above average deprivation (>0)	1.40 (1.07, 1.84)	0.0132	1.26 (0.95, 1.67)	0.1081	1.24 (0.93, 1.65)	0.1425
Below average deprivation (<=0)	1.00		1.00		1.00	

1. Adjusted for age, socioeconomic status (education, marital status, social class, employment status)
2. Adjusted for age, socioeconomic status, lifetime GAD
3. Adjusted for age, socioeconomic status, lifetime GAD, physical diseases and disability

‡ High education: O-level, A-level, degree; low education: refers to no education

* Other: divorced, separated, widowed

¥ Manual: skilled manual, semi-skilled, non-skilled; non-manual: professionals, managerial, skilled non-manual

+ Prevalent physical disease: respiratory disease (asthma, bronchitis), allergies (allergies, hay fever), stroke, heart attack, cancer, diabetes, thyroid conditions, arthritis

¶ Below the median PCS value of 50.6

*The brackets show the reference categories that were used for each categorical variable when it was entered in the models - below average deprivation [ref] vs. above average deprivation; education: high [ref] vs. low; marital status: married [ref], single, others; social class: non-manual [ref] vs. manual; employment: yes [ref] vs. no; lifetime GAD: no [ref] vs. yes; prevalent physical disease: no [ref] vs. yes; disability level: low [ref] vs. high. These reference categories were based on the literature. Choosing other groupings for the potential confounders would not have changed the results.

Discussion

This research is an analysis based on EPIC-Norfolk data, and findings showed that living in an area of above average deprivation was associated with a significantly increased the risk of depression in men; the relationship with depression was not statistically significant in women. The association in men endured after adjusting for important individual-level confounders, such as serious physical health conditions, disability, and history of generalized anxiety disorder (GAD). When we looked closer to determine the specific component of area deprivation that has the greatest influence on men's mental health, unemployment emerged as an important factor. Men living in areas characterized by high unemployment had a 77% greater chance of having depression than those living in areas with low levels of unemployment.

Potential mechanisms

An environment in which deprivation is above average according to the Townsend index appears to differentially affect men and women's mental health after accounting for a number of potential confounders. A number of reasons can explain this. First, men appear to be more sensitive to stressful events occurring in their environment compared to women, especially if the stress is relating to financial and work-related problems.[25] The reason for this is that occupational and financial success is particularly important for men's mental health. Second, when living in disadvantaged regions, the possibility of hearing about job loss from others increases and this can promote anticipatory stress in those who are still working, which can increase their risk of depression.[48] This is particularly problematic for men who are perceived by their families as the main provider and head of household. In contrast, women's risk of depression seems to be influenced more by the social networks they are embedded in, the quality and continuity of relationships, the social support derived from neighbours and communities, and marital satisfaction.[25, 26] Women are more likely to experience depression as a result of unmet needs in relationships. Deficiencies in interpersonal relationships in women can lead to a perception that the self is unable to meet needs for self-worth and achievements, and this can increase their risk of poor mental health.[25] Men, on the other hand, have been shown to be more prone to depression as a

result of failure at key instrumental tasks, including achievements at work and inability to provide for the family.[25, 49]

Unemployment, often accompanied by low social ranking, can lead to loss of self-esteem and role identity in men. This was seen in the United Kingdom after the 1970's, when the economy shifted from a manufacturing to a service-based one.[27] The shift was accompanied by a loss of skilled and semi-skilled jobs among men, while women had to enter the workforce and partake in jobs that were primarily service-based. The loss of employment opportunities among men might have contributed to a loss of role identity and self-esteem in this group.[27] However, even more than a decade later after this shift in economy, men who lost their employment and were in low social class groups showed poorer self-rated health compared to women.[50] This is also mirrored by recent research.[25] This again supports the notion that men are affected by failure at key instrumental tasks.[25] The same phenomenon occurred in rural areas of Midwestern United States after the farm crisis and related events occurred in the 1980s.[51] Rural areas held agrarian values, characterized by male provider norms and 'rugged independence'.[51] After the farm crisis hit, men were no longer able to fulfil their economic provider role, and both genders had to take on multiple jobs to make ends meet. This shook the traditional system, and created stress and contributed to high rates of depression in men. During this time, men also showed susceptibility to a wider range of stressors compared to women.[51]

Men and women also tend to experience and manifest the effect of stress in different ways. Women living in deprived areas have been shown to be more prone to anxiety[28], while men living in disadvantage are more likely to have depression. This could be a result of evolutionary, survival functions. Women have traditionally had the responsibility of childcare and ensuring the successful survival of future generations.[52] Therefore, living in circumstances of (above average) deprivation can trigger the fight or flight reaction, which can increase stress in finding ways to make ends meet so that they can raise their children. In this context, anxiety might be seen as protective, ensuring the survival of future generations. This is why women also tend to be more concerned about community features that can disrupt their caregiving role and negatively impact their family, such as, lack of safe play areas for children.[52, 53] Men have traditionally had the responsibility of being the

provider, and if they are not able to fulfil this role, they are more likely to become depressed and potentially commit suicide.[25, 27] This is a problem in India, where suicide rates are high among male farmers whose crops have failed.[54, 55] In the UK, men with depression are also more likely than women to commit suicide. Taken together, these findings suggest that women may actually be more resilient than men when encountering adversity. However, very little research has examined this, and previous studies in the mental health literature have typically described women as vulnerable. Further research on health from a gendered perspective is needed.[28]

When exposed to the stresses and strains of deprivation, men are also more likely to develop substance abuse and this, in turn, can increase the risk for depression. The National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) study[56] showed that total number of stressors experienced in life had a significantly stronger association with heavy drinking in men than in women. Experiencing stressors can also lead to unhealthy means of coping with the hardships, such as smoking and physical inactivity, and this can lead to sequelae.[24, 57] Finally, when men experience mental health issues, they are less likely to seek help than women [51].

Strengths and weaknesses and future research

This study shows that there is a statistically significant association between area deprivation and depression in men, while this relationship is not apparent in women. There are a number of strengths associated with our research. Our study used a structured questionnaire, the HLEQ, to assess mental health, and a measure of MDD was created using valid and reliable criteria stipulated by the DSM. Also, we were able to adjust for a number of important confounders, such as medical and psychiatric history, and sociodemographic factors, including unemployment measured at the level of the individual. Nonetheless, residual confounding may be present in our research if certain covariates were not adequately adjusted for. With respect to the medical history covariate, it is possible that some participants may have omitted disclosing or had difficulty recalling medical diagnoses and this might have introduced measurement error. Our measure of area deprivation also may not capture features of the environment that may affect mental health; however, all indexes designed to measure environmental effects suffer from this limitation. The Townsend index

is theoretically sound and commonly used in research assessing these types of relationships. One of the limitations of this variable is that it is somewhat biased towards urban populations, particularly as it is capturing aspects that are more reflective of urban settings (ex. car ownership). Given that it may not be capturing rural deprivation as well as it should, measurement error may be an issue. This is an area of further research.

Because of healthy volunteer bias, it is possible that some of the sickest, most deprived people who would have been eligible to take part in EPIC-Norfolk, did not participate. This means that our results may not generalize to those individuals.

Also, we did not have information on length of living in the area for participants, however, migration in EPIC-Norfolk is minimal and unlikely to have biased the findings. People who took part in this study tended to reside in the same areas their whole lives. This is why Norfolk and the surrounding towns and rural areas were selected for participant recruitment.[58]

Another issue is the fact that EPIC-Norfolk only included people over the age of 40. As critical time periods for the development of depression include young adulthood[59], it would be useful if future research examined these relationships with deprivation using a younger sample. Nonetheless, depression can still develop at midlife and beyond, and many times, this is triggered by stressful life events, such as adverse social conditions.

Subjective deprivation as a study limitation

A mechanism linking socioeconomic circumstances with depression in general involves subjective relative deprivation. Living in a deprived area can trigger comparison of the self to others, and this can in turn, lead to stress and poor mental health. A number of people living in deprived areas may experience negative emotions because they lack the necessary means to survive or are unable to achieve desired outcomes compared to those who are more affluent. Perceptions of lack can thus lead to poor health outcomes. Relative deprivation is composed of "affective and cognitive (i.e., appraisal) responses to perceived unfair outcomes."[60] Thus, social comparisons and stress arising from deprivation can contribute to increased risk of depression. A recent study has indeed shown that subjective relative deprivation is linked to depressive symptoms.[60] Living in a deprived area can give rise to subjective feelings of deprivation, which can subsequently lead to poor mental health. Although we did not have information on subjective feelings of deprivation, future studies should assess this.

Future research

Future research should assess the risk of depression not only in countries, such as, the US or UK where there is higher gender equality, but also in parts of the world where social roles and gendered norms for men and women have shown much less change over time. Countries with higher gender equality also show some of the highest rates of depression and other mental disorders in the world.[61] In Europe, the discrepancy in depression rates between men and women in highly-developed countries is greater than in less-developed countries where there is also greater gender inequality.[62] In Eastern European countries, levels of depression are similar between men and women[62], while in Western Europe, women are twice as affected as men.[63] More studies are needed to explore the influence of area deprivation on the mental health of men and women separately, and to do this in different contexts (ex. rural, urban) and countries around the world. Further, the reasons behind gender differences need to be better elucidated.

Finally, future studies should assess area deprivation and mental health at multiple points in time using a repeated measures analysis, because both may change over the follow-up period.

Placing our research in context

Although other studies have shown that the places in which people live have a substantial impact on health[14, 15], studies on the links between area deprivation and mental disorders from a gendered perspective are limited. A recent study[64] of over 1000 African American and non-Hispanic white adults living in the US showed that men who had experienced stressful life events in 1983-1986 were more likely to have depression in 2011, while this was not observed in women. This study, however, has limited generalizability, because it excluded other ethnicities. Also, the reliability and validity of the measure of stressful life events was not reported – the measure was based on a checklist of 'major negative events' that had occurred in the previous 3 years. Finally, exposure to stressful life events at the individual-level were investigated, rather than the effect of the place people live in.

A number of studies have assessed individual-level risk factors of depression, but substantially fewer have examined the influence of the environment on mental health. Nonetheless, studies of individual-level risk factors provide an important starting point in understanding relationships. Another prospective UK study of over 500 people[27] showed that the socioeconomic status of men at midlife was associated with depression at midlife, while this was not observed in women. For women, their socioeconomic status at birth influenced their levels of depression at midlife. Also, men who had experienced downward social mobility or a reduction in their socioeconomic status from adulthood to midlife were at high risk of having poor mental health at midlife, but this was not found in women.[27] These results suggest that women are more sensitive to the social class group they are in very early in life, while for men, social mobility over the life course, as well as the socioeconomic status group they are in during later life are more important for their mental health. This study, however, was limited, because it was based on a small sample size, assessed only individual-level measures rather than area-level level effects, and failed to adjust for a number of important confounders, such as, demographic factors. Failure to properly adjust for potential confounders can lead to overestimation of the effect estimate. Finally, this study examined general mental health, rather than individual psychiatric disorders.

A recent US study showed that the types of stressors that influence men's risk of depression are those related to work, finances, and legal matters.[25] In this study, stressors were not

linked to depression risk in women. Again, this research only assessed individual-level data. Our study shows, for the first time that living in an area of above average deprivation increases the risk of depression in men, while less so in women. Area deprivation was measured in our study at midlife and beyond, the time period which seems to have the greatest influence on men's mental health.[25]

Interpretation

The genders seem to be differentially affected by the environment, and we believe it is important to highlight this for policy-makers, clinicians, and public health authorities. Knowing that men living in areas of above average deprivation are more susceptible to depression can be used to tailor treatment and prevention efforts – and knowing how to best tailor treatment efforts and targeted interventions is important at a time when there are scarce health resources, such as now.

Acknowledgements: OR received PhD funding from the National Institute for Health Research.

Competing interest: All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: no support from any organisation for the submitted work; no financial relationships with any organizations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

Funding: This work was supported by the Medical Research Council UK (grant number SP2024-0201 and SP2024-0204) and Cancer Research UK (grant number G9502233).

Author contributions: OR (corresponding author) had the idea for and conducted the analysis, and wrote the article, along with CB, KK, LL, PS, and NW. All authors provided feedback into the analysis and critically reviewed drafts of the manuscript. All authors have seen and approved the final version. The authors had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. OR acts as guarantor of the study.

Transparency declaration: OR affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

Role of study sponsors and statement of independence: The funding sources had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; and preparation, review, or approval of the manuscript.

Ethical approval: The study has ethics committee approval from Norfolk Ethics Committee (Rec Ref: 98CN01) and all participants gave informed consent.

Data sharing: No additional data available.

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Appendix 1

Further information on A- and O-levels:

A-levels are advanced level qualifications, which "are subject-based qualifications that can lead to university, further study, training, or work." (UCAS)

According to IGCSE Centre, "O-Level is the abbreviation of Ordinary Level. It is one of the two-part GCE (General Certificate of Education). The other part of GCE is Advanced Level (A-Level), which students enter after completing O-Level. O-Level is the final certification for secondary school, to be taken at fifth form or year 11 at approximately age 17 (or age group 14-16). Students that have completed O-Level are considered to have complemented formal education." (IGCSE Centre)

Appendix 2

Distribution of Townsend index scores

1. Above average deprivation

Men

Mean: 1.96

Standard deviation: 1.49

Range: 0.01 to 6.09

Women

Mean: 1.93

Standard deviation: 1.47

Range: 0.01 to 6.98

2. Below average deprivation

Men

Mean: -2.85

Standard deviation: 1.21

Range: -6.73 to -0.02

Women

Mean: -2.83

Standard deviation: 1.21

Range: -6.10 to -0.02

Appendix 3

Odds ratios for MDD according to individual- and area-level characteristics for men and women who completed the HLEQ questionnaire in the EPIC-Norfolk cohort

	Men (n=8,236)		Women (n=10,335)	
	Odds ratios and 95% CI[1]		Odds ratios and 95% CI[1]	
Characteristic*				
Individual-level variables				
Socio-demographics				
Age				
(per 10 years)	0.47 (0.38, 0.59)	<0.0001	0.59 (0.51, 0.69)	<0.0001
Education‡				
Low	1.00 (0.69, 1.45)	0.9977	1.30 (1.01, 1.67)	0.0384
High	1.00		1.00	
Marital status				
Single	1.41 (0.72, 2.79)	0.3181	0.91 (0.47, 1.75)	0.7737
Married	1.00		1.00	
Other*	3.58 (2.42, 5.28)	<0.0001	2.36 (1.85, 3.02)	<0.0001
Social class¥				
Manual	1.06 (0.76, 1.49)	0.7340	0.97 (0.76, 1.24)	0.8204
Non-manual	1.00		1.00	
Employment¥				
No	2.24 (1.49, 3.37)	0.0001	1.55 (1.18, 2.04)	0.0019
Yes	1.00		1.00	
Health status				
Lifetime GAD				
Yes	12.65 (8.71, 18.37)	<0.0001	7.37 (5.57, 9.75)	<0.0001
No	1.00		1.00	
Prevalent physical disease				
Yes+	1.25 (0.90, 1.73)	0.1842	1.25 (0.99, 1.59)	0.0658
No	1.00		1.00	
Disability level				
High¶	1.98 (1.38, 2.83)	0.0002	1.41 (1.11, 1.80)	0.0048
Low	1.00		1.00	
Area-level variable				
Townsend index				
Deprivation				
Above average	1.51 (1.03, 2.21)	0.0358	1.24 (0.94, 1.64)	0.1325

deprivation (>0)		
Below average deprivation (<=0)	1.00	1.00

1. Adjusted for age, socioeconomic status, lifetime GAD, physical diseases and disability

‡ High education: O-level, A-level, degree; low education: refers to no education

* Other: divorced, separated, widowed

¥ Manual: skilled manual, semi-skilled, non-skilled; non-manual: professionals, managerial, skilled non-manual

+ Prevalent physical disease: respiratory disease (asthma, bronchitis), allergies (allergies, hay fever), stroke, heart attack, cancer, diabetes, thyroid conditions, arthritis

¶ Below the median PCS value of 50.6

*The brackets show the reference categories that were used for each categorical variable when it was entered in the models - below average deprivation [ref] vs. above average deprivation; education: high [ref] vs. low; marital status: married [ref], single, others; social class: non-manual [ref] vs. manual; employment: yes [ref] vs. no; lifetime GAD: no [ref] vs. yes; prevalent physical disease: no [ref] vs. yes; disability level: low [ref] vs. high. These reference categories were based on the literature. Choosing other groupings for the potential confounders would not have changed the results.

Please see the article line numbers (column on the right) and the explanations provided.

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Line numbers within the article
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	6, 4
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	34-4
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	89-1
Objectives	3	State specific objectives, including any prespecified hypotheses	156-
Methods			
Study design	4	Present key elements of study design early in the paper	113-
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	158-17 273
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	159-17 We specify in the paper that the Townsend index was is record linked to the cohort.
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	187-29
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is	There were two variables of interest in this study: area deprivation and major depressive disorder. The others

		more than one group	are potential confounders – in the methods I list them all, indicate how they were assessed and mention that they were collected through the baseline, self-reported postal LLQ questionnaire.
Bias	9	Describe any efforts to address potential sources of bias	324
Study size	10	Explain how the study size was arrived at	180
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	How variables were handled in analyses: 306-313 (the methods section describes how the variables were categorized/which categories were used) Which grouping were chosen and why: I describe the reference categories of the variables in the footnotes under Tables 2 and 3. I mention that the categorization of variables was done in accordance with the literature and provide the relevant citations in the method section. How the dependent variable was created: 187-220 How area-level measure was created: 269-286 Individual-level measures: 222-267
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	297-356
		(*b*) Describe any methods used to examine subgroups and interactions	Similar to other studies, I conducted analyses separately for men and women. I did not do this because of p-value considerations (statistical significance), but rather, because I felt it was important to do. In the introduction, I provide the rationale for conducting sex-specific analyses. Knowing which gender group is more affected can help with the tailoring of targeted interventions.
		(*c*) Explain how missing data were addressed	We indicated that this was a complete-case analysis.
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed	Loss to follow-up was not a problem in this study.

Case-control study—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	We were able to track down all participants using various means, unless they expressed that they wished to be removed from the mailing list. We elaborate on this in the manuscript.
(*e*) Describe any sensitivity analyses	329-335

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	180-184
		(b) Give reasons for non-participation at each stage	We do not have the reasons for non-participation, because these data were not collected when the study was initiated in 1993.
		(c) Consider use of a flow diagram	We reference a paper which describes the EPIC-Norfolk study further. This paper contains a flow diagram. Also, our previously-published BMJ Open paper upon which this one was based contains a flow diagram also – we reference this paper.
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	We added characteristics for those with vs. without MDD, because we felt it was important to show the characteristics of those exposed vs. non-exposed (see also Table 1)
		(b) Indicate number of participants with missing data for each variable of interest	292-295 – we had to move this section to the Methods because one of the reviewers had asked us to do so.
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	Initially we mentioned that participants were followed for 7 years, however, we had to delete this phrase because one of the reviewers had asked us to do so. The Townsend index was record linked to the cohort.
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	380-383
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Tables 2 and 3 contain unadjusted and progressively adjusted estimates. We also discussed the findings within the text, and provide odds ratios and 95%

			confidence intervals. We included the confounders based on the literature – we mention on this in the paper and cite relevant literature. As per strobe, we included this information in the methods section; and we omitted repeating this in the results section to reduce redundancy. However, if the editor would like us to repeat this information in the results, we are happy to do so.
		(*b*) Report category boundaries when continuous variables were categorized	The cut-offs are provided. In regards to the Townsend index, the methods section states that those below and above the cut-point of zero were compared.
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Sensitivity analyses: 1) relationship between area deprivation and pure MDD (past-year GAD excluded); 2) correlated data analysis replaced with logistic regression ; 3) analyses run with education re-categorized and ethnicity included ; 4) Townsend index divided into quintiles. In all these instances, the associations remained the same. This is reported in the paper.
Discussion			
Key results	18	Summarise key results with reference to study objectives	470-474
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	556-596
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	655-668 (We also have a section comparing our study results to those of others: 616-652, as well as a section on potential mechanisms explaining our findings: 481-

			547)
Generalisability	21	Discuss the generalisability (external validity) of the study results	566-57
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	676-67

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

The association between area deprivation and major depressive disorder in British men and women: a cohort study

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2018-027530.R2
Article Type:	Research
Date Submitted by the Author:	23-May-2019
Complete List of Authors:	Remes, Olivia; University of Cambridge, Public Health and Primary Care LaFortune, Louise; University of Cambridge, Institute of Public Health Wainwright, Nick; University of Cambridge, Public Health and Primary Care (retired) Surtees, Paul; University of Cambridge, Department of Public Health and Primary Care Khaw, Kay-Tee; University of Cambridge, Department of Public Health and Primary Care Brayne, Carol; University of Cambridge, Institute of Public Health
Primary Subject Heading:	Epidemiology
Secondary Subject Heading:	Mental health, Public health
Keywords:	MENTAL HEALTH, PUBLIC HEALTH, Depression & mood disorders < PSYCHIATRY, EPIDEMIOLOGY

The association between area deprivation and major depressive disorder in British men and women: a cohort study

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Tables: 3

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ABSTRACT

OBJECTIVE

Studies have shown area-level deprivation can increase the risk for mental disorders over and above individual-level circumstances, such as education and social class. The objective of this study is to determine whether area deprivation is associated with major depressive disorder (MDD) in British women and men separately while adjusting for individual-level factors.

DESIGN

Large, population study.

SETTING

UK population-based cohort.

PARTICIPANTS

30,445 people from the general population aged 40 years and older and living in England consented to participate at study baseline, and of these, over 20,000 participants completed a structured Health and Life Experiences Questionnaire (HLEQ) used to capture MDD. Area deprivation was measured in 1991 using Census data, and current MDD was assessed in 1996-2000. 8,236 men and 10,335 women had complete data on all covariates.

PRIMARY OUTCOME MEASURE

MDD identified according to the Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV).

RESULTS

In this study, 3.3% (339/10,335) of women and 2.1% (177/8,236) of men had MDD. Men living in the most deprived areas were 51% more likely to have depression than those living in areas that were not deprived (OR=1.51, 95% CI: 1.01 to 2.24; p=0.043), but the association between deprivation and MDD was not statistically significant in women (OR=1.24, 95%CI: 0.93 to 1.65; p=0.143).

CONCLUSION

This study shows that the residential environment differentially affects men and women, and this needs to be taken into account by mental health policy-makers. Knowing that men living in deprived conditions are at high risk for having depression helps inform targeted prevention and intervention programs.

Article Summary

Strengths and limitations of this study

- We used a population-based sample of over 20,000 British adults and controlled for important confounders, including social class, medical history, and disability.
- We used a structured questionnaire (the Health and Life Experiences Questionnaire of the EPIC-Norfolk study) to determine whether participants met criteria for MDD according to the DSM.
- We used the Townsend index to assess area deprivation. This index is commonly-used by researchers to examine deprivation and is a theoretically sound measure.
- People who took part in EPIC-Norfolk were generally more affluent and healthier than those living in other parts of England. As such, our results may not be generalizable to the most deprived areas.

Introduction

Depression is a common psychiatric disorder affecting approximately 350 million people around the world.[1] According to the Global Burden of Disease Study[2], major depressive disorder (MDD) contributed to 689.9 per 100,000 disability-adjusted life years in men and 1161.2 per 100,000 disability-adjusted life years in women in 2010. Depression can increase the risk for impairment, disability and suicide.[3, 4, 5] It has also been linked to decreased work productivity, poor quality of life, and high health service use.[3, 6, 7]

A number of studies have examined the individual-level risk factors of depression, such as, personal and parental history of psychopathology[8], genetics[9], history of trauma and stressful life events[10, 11], and socioeconomic status.[12] However, the environment or living context can have a profound influence on mental health, over and above individual-level factors.[13, 14, 15] In a systematic review[16] of 14 studies, about half found an association between neighbourhood socioeconomic conditions and depression. Living in an area of low socioeconomic status can expose people to a higher number of stressors, such as, violence, disorder, and noise pollution, and this can have deleterious effects on mental health.[17]

There is a wealth of literature on the effect of the places where people live on mental health. Findings from systematic reviews[18, 19, 20] assessing neighbourhood characteristics and depression show that there is large heterogeneity in findings, because of differences in study populations, the confounders that are adjusted for in analyses, and the measures and definitions used to delineate neighbourhoods.[19] Although there is much evidence on the influence of area-level disadvantage or deprivation on depression, research on this relationship from a gendered perspective is lacking.

In this large, population-based, cohort study, we examine the association between area deprivation and major depressive disorder in men and women separately, while controlling for a range of important confounders, including social class, previous medical conditions, psychiatric co-morbidity, and disability. Area deprivation refers to residential environments or living contexts characterized by factors, such as, high levels of unemployment, non-home

ownership, non-car ownership, and low income.[13] Findings are disaggregated by gender, and this is done for several reasons. Gender frames access to resources derived from the environment.[21, 22] Compared to men, women have been shown to have less access to material and social conditions, such as income, power, and social status, and this can influence mental health. Women have historically been the victims of discrimination, and because of this have had limited opportunities for education, and well-remunerated and respected forms of employment.[23] Women have taken on different job roles and tasks than men, which has exposed them to different hazards and contaminants affecting their health. Women have traditionally been seen as 'care-takers' in society and involved in domestic work, which might have led to an interruption in their education or career paths. As such, they have derived fewer resources with which they could maintain or improve their health.[23, 24]

However, there are additional reasons why findings are disaggregated by gender. Women and men tend to react to different kinds of stressors. Recent research has shown that men are more susceptible to work- and finance-related stressors, while women are more affected by deficiencies in their social networks and interpersonal relationships.[25, 26] This research is based on a study conducted in the US and other parts of the world. Hence, living in a deprived area with high levels of unemployment might be particularly detrimental for men's mental health. This was evident when the economy shifted in the UK from a manufacturing- to a service-based one, and many men lost their jobs.[27] Prior to the shift, the local economy had relied on skilled and semi-skilled jobs, typically performed by men. When the economy changed, an increasing number of women entered employment (occupying mainly service industry jobs), and this had implications for traditional gender-defined social roles. Men who experienced reduced economic opportunities may have suffered from loss of role identify and self-esteem, and this had consequences for their physical and mental health.[27] A recent study[25] showed that men's mental health is particularly affected if they fail at key instrumental tasks, such as, work achievements and ability to provide for the family. In contrast, women are more likely to be depressed if they fail to meet their needs for relationship.[25] To this end, it appears that men and women are susceptible to different kinds of stressors.

It remains unclear whether men and women living in areas of above average deprivation are differentially susceptible to MDD – the objective of this study will be to assess this. Knowing that one gender is at risk of developing depression when exposed to deprived circumstances helps to tailor interventions and allocate scarce resources according to need.[28] This is particularly important at a time of scarce economic and health-related resources.

Methods

Data were drawn from EPIC-Norfolk, whose design and study methods have been described in detail elsewhere.[29] In brief, a prospective population-based cohort of 30,445 participants ages 40 to 74 years were recruited by post between 1993 and 1997 through general practice age-sex registers in the city of Norwich and the surrounding small towns and rural areas. At baseline (1993-97), participants completed a postal Health and Life Experiences (HLQ) questionnaire that captured information on sociodemographics, including age, gender, highest educational attainment, marital status, social class, employment status, ethnicity and self-reported physician diagnoses of physical diseases. Using participants' postal codes, a measure of area deprivation was derived based on the 1991 Census. Between 1993 and 2000, participants completed self-reported postal questionnaires provided they: 1) were still alive, 2) did not ask to be removed from the study's mailing list, and 3) had a valid mailing address.

During 1996-2000, 20,919 participants completed a structured, psychosocial Health and Life Experiences (HLEQ) questionnaire. During this time, an assessment of generalized anxiety disorder (GAD) and major depressive disorder (MDD) was made according to the Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV)[30]. Using the HLEQ questionnaire, disability measures based on the SF-36 were also derived.[31]

All participants recruited through general-practice registers and who completed a baseline health questionnaire were eligible to be included in our study; those who completed a psychosocial questionnaire during follow-up were eligible to be included in our analysis.

In regards to the study size, an initial sample of 30,445 participants completed the baseline HLQ and of these, 20,921 filled out the psychosocial HLEQ. After retaining the people with complete measures on all covariates, the final sample size was 18,571.

Although EPIC-Norfolk is a prospective study and area derivation was measured in 1991 and anxiety in 1996-2000, this analysis should be considered cross-sectional.

Dependent variable

The primary outcome in this study was current MDD, which was measured using the HLEQ, a structured self-assessment instrument designed to provide a measure of depression for inclusion in a large-scale epidemiology project.[32, 33] DSM-IV criteria were applied to the psychiatric symptoms to determine whether participants had an episode of MDD that was ongoing at the time of the completion of the HLEQ questionnaire. Participants who reported a psychiatric episode were asked to estimate the onset and offset timings of the episode, and then to report an outline of the history of the problem. Participants were also asked about age at first symptom onset and subsequent episode recurrence.

The dependent variable in this study is current MDD, defined as an episode of MDD reported as ongoing at the time of the completion of the HLEQ.

The following two core criteria of MDD were first evaluated:

1. Have there ever been times in your life when you felt sad or depressed for two weeks or more in a row?
2. Have there ever been times in your life when you lost interest in most things like your work or activities that usually give you pleasure, for two weeks or more in a row?

If participants answered yes to one of these questions, they were then asked to think of the most recent two-week episode during their lives when these feelings of sadness, depression or loss of interest were the worst. They then had to report that these feelings of being sad, depressed, or loss of interest lasted all day or most of the day, and that during these two weeks of their most recent episode, they felt this way every day or almost every day.

In addition, at least five of the following symptoms had to be present: gaining or losing weight, having trouble falling asleep or sleeping too much, feeling tired or low on energy, feeling unable to sit still or feeling slowed down, experiencing guilt or shame, feeling worthless, losing confidence, having trouble concentrating, and thinking a lot about death or suicide. One of these five symptoms had to be one of the two core criteria evaluated at the beginning.

Finally, it was evaluated whether these symptoms interfered with participants' lives and resulted in disability or impairment.

Individual-level measures (potential confounders)

Individual-level measures included age, education, employment status, marital status, social class, health status, ethnicity, history of anxiety, and prevalent physical disease. The final categorization of the variables took cell size into account and was also done in accordance with previous literature.[33-39] Age was divided into 10-year bands. Educational attainment was categorized into high (vocational or formal qualifications at the A- or O-level or degree-level qualifications) vs. low (no formal qualifications). Further details on the meaning of A- and O-level can be found elsewhere[40, 41]; the appendix also contains definitions of these (appendix 1). Employment was divided into yes vs. no. Marital status was categorized into three groups: married, single (or never married), and others (widowed, divorced, separated). Social class was derived using the Computer-Assisted Standard Occupational Coding[42] and categorized as follows: I (professionals), II (managerial and technical occupations), III non-manual and III manual (skilled workers), IV (partly skilled workers), and V (unskilled manual workers). To assign social class to men and women, the male partner's current or past occupation was used. If this information was not available, the female partner's occupation was used. If the social class from either partner was unavailable, then it was coded as missing. The final categorization of social class included manual: skilled manual, partly skilled, and unskilled; and non-manual: professionals, managerial and technical, and skilled non-manual. Individual-level health status was assessed through the construction of a variable capturing major prevalent physical diseases. This was based on HLQ questions asking participants: "Has the doctor ever told you that you have any of the following?", followed by a list of options, such as allergies, asthma, cancer, stroke, heart attack, diabetes, thyroid conditions, etc. Ethnicity was based on a self-reported question asking participants to tick the relevant box: 'white', 'black Caribbean', 'black other', 'Indian', 'Pakistani', 'Bangladeshi', 'Chinese', 'other'.

Lifetime history of GAD was also assessed using the self-reported HLEQ questionnaire.[33] Lifetime GAD consisted of having ever had at least one episode that met core criteria stipulated by the DSM-IV. Anxiety was identified if participants reported having uncontrollable, excessive worry for six months or longer on most days than not that resulted

in disability or impairment. In addition, at least three of the following symptoms needed to have been present: restlessness, irritability, muscle tension, fatigue, trouble concentrating because of worry, mind going blank, trouble falling asleep, trouble staying asleep, and feeling keyed up or on edge.

To determine disability levels, we used the physical component summary (PCS) derived from the HLEQ. The PCS is part of the SF-36, a widely-used, validated self-assessment tool. The SF-36 is a 36-item measure capturing 8 health dimensions: physical functioning, social functioning, role limitations due to physical problems, role limitations due to emotional problems, mental health, energy/vitality, bodily pain, and general health perception. The eight dimensions of the SF-36 were used to create two higher order scores, one of which was the PCS. Higher scores indicate better health.[31] PCS scores were dichotomized above and below the median.

All of these individual-level variables were regarded as potential confounders and selected based on the literature and their association with depression and area-level socioeconomic circumstances.

Area-level measure (exposure variable)

To examine area deprivation, we used the Townsend Index.[43, 44] This is one of the most commonly-used measures of area deprivation in the UK and particularly appropriate for the time of the original EPIC-Norfolk study. This index is a composite measure of four variables obtained from the 1991 Census: 1) percentage of economically active residents over age 16 who are unemployed, 2) percentage of households that do not possess a car, 3) percentage of private households that are not owner occupied, and 4) percentage of private households that are overcrowded (have more than 1 person per room). These variables were obtained at the level of the enumeration district, which is a geographic area used for census purposes in Britain. Each variable was standardized by obtaining Z scores (dividing the mean by the standard deviation across enumeration districts in England). The Z values of the four variables were added together to produce a Townsend index score for each enumeration district. A score of 0 represents the national mean, while positive values of the index indicate enumeration districts that are above average deprivation, while negative values indicate

those that are below average deprivation. The postal codes of participants were record linked to enumeration districts, and participants were considered to live in areas of above average deprivation depending on the Townsend index score assigned to their enumeration district.[43]

Depending on the results from the main analysis (association between overall area deprivation and depression), the Townsend deprivation index was disaggregated into its four constituent components to determine whether any one of these is associated with MDD.

Missing data

The number of missing observations for each covariate were: 9 for education, 47 for marital status, 417 for MDD, 434 for GAD, 458 for social class, 75 for the Townsend index, and 1386 for the SF-36, 52 for employment status.

Statistical analysis

First, we compared participants on sociodemographic, and medical and psychiatric history characteristics, and the prevalence of MDD was computed for sub-groups. Next, we undertook correlated data analysis based on generalized estimating equations (GEE)[45, 46] to determine the population-average effect of living in an area of above average deprivation on risk of having depression while controlling for confounders. MDD is a dichotomous outcome and the intra-cluster correlation was assumed to be equal. As such, we used GEE with a logit link and an exchangeable correlation structure.

First, we ran unadjusted analyses between deprivation and MDD. To determine the influence of potential confounders on risk of having depression, we progressively adjusted the models and accounted for 1) age, educational attainment, marital status, and social class; then for 2) age, educational attainment, marital status, social class, and GAD; and finally for 3) age, educational attainment, marital status, social class, GAD, physical diseases and disability level. We conducted separate analyses for men and women. The individual-level covariates were sociodemographics, and medical and psychiatric history, while the area-level covariate was the Townsend index score. The progressively adjusted models allowed us to estimate adjusted odds ratios (OR) and 95% confidence intervals based on robust standard errors.

A dichotomous variable was created using the Townsend index scores, and 0 was used as the cut-point (considered to be the national average). The variable was dichotomized, because we wanted to compare participants' scores to the national average[47] - scores above the cut-point of 0 were considered above average deprivation. A binary variable was also used in accordance with previous research[47] and because of cell size considerations – we wanted to ensure that there were sufficient people with MDD in each category of the deprivation variable.

Models were constructed for participants with complete measurements on all covariates. It was not possible to group the MDD variable otherwise since it was created and categorized according to the DSM-IV[32, 33], and area deprivation was analysed in accordance with the literature[37, 43].

Several sensitivity analyses were undertaken. We ran fully-adjusted models using pure MDD as the outcome, in which those with past-year GAD were excluded. It should be mentioned that although GAD and MDD have been regarded as closely correlated by many researchers, they are independent disorders. The high GAD-MDD comorbidity found in older literature was due to the use of clinical populations with multiple co-occurring conditions.

Next, we disaggregated the index used to measure disadvantage. If a significant relationship was found between area deprivation and depression for one of the genders in a fully-adjusted model, we investigated further. We disaggregated the Townsend index into its 4 constituent components (unemployment, non-home ownership, non-car ownership, and overcrowding) to determine whether any aspect of deprivation is associated with increased risk of having depression in that gender group. Each component was dichotomized using a cut-point of 0, because it represents the national average.

Then we determined whether relationships held after dividing the Townsend index into quintiles and adjusting for sociodemographic and health status variables. Further, we examined whether the inclusion of additional covariates or recategorization of variables made any difference to the effect estimates. We included ethnicity as a potential confounder

in a fully-adjusted model, and assessed whether the division of the education variable into four categories influenced the associations.

Finally, we conducted logistic regression, which does not take the intra-cluster correlation into account, and compared the findings to those from GEE. Similar results between the models suggests that the intraclass correlation is negligible.

All models used two-sided statistical tests, and a p-value of <0.05 was considered statistically significant. Statistical Analysis Software (SAS) Version 9.3 (SAS Institute, Cary, NC) was used in these analyses.

Patient and Public Involvement:

There were no patients or public involved in the development of the research question, outcome measures, design of the study, or recruitment to and conduct of the study.

Results

At baseline, 30,445 participants were recruited from general practices in the city of Norwich and the surrounding towns and rural areas. Of these, 20,919 people completed the HLEQ during the follow-up period. In total, 18,571 out of 20,919 (89%) people were available for analysis, because they had complete data on all covariates.

In this sample, there were 8,236 men and 10,335 women over the age of 40 years. Table 1 shows the distribution of individual- and area-level characteristics by current MDD.

Table 1: Distribution of characteristics for women and men who completed the HLEQ questionnaire in the EPIC-Norfolk cohort

	Women (n=10,335)		Men (n=8,236)	
Characteristic	**Number with characteristic**	**Percentage and number with MDD**	**Number with characteristic**	**Percentage and number with MDD**
Individual-level variables				
Socio-demographics				
Age (years)				
<50	1450	5.0 (72)[a]	964	3.4 (33)[a]
50-60	3716	3.9 (145)	2651	3.0 (80)
60-70	3180	2.1 (68)	2743	1.5 (40)
>70	1989	2.7 (54)	1878	1.3 (24)
Education[‡]				
Low	4050	3.5 (141)	2365	2.2 (51)
High	6285	3.2 (198)	5871	2.1 (126)
Marital status				
Single	417	2.4 (10)[a]	303	3.6 (11)[a]
Married	7750	2.7 (207)	7237	1.7 (122)
Other[*]	2168	5.6 (122)	696	6.3 (44)
Social class[¥]				
Manual	3829	3.3 (127)	3286	2.3 (76)
Non-manual	6506	3.3 (212)	4950	2.0 (101)
Employment				
Yes	4075	128 (3.1)	3821	68 (1.8)[b]
No	6260	(3.4) 211	4415	109 (2.5)
Health status				
Prevalent physical disease				
Yes[+]	5698	3.8 (214)[b]	3843	2.6 (100)[b]
No	4637	2.7 (125)	4393	1.8 (77)
Disability level				
High[¶]	5296	3.9 (208)[a]	4021	3.0 (119)[a]
Low	5039	2.6 (131)	4215	1.4 (58)
Lifetime GAD				
Yes	448	19.4 (87)[a]	255	22.4 (57)[a]
No	9887	2.5 (252)	7981	1.5 (120)
Area-level variable				
Townsend index				
Deprivation				

Above average deprivation (>0)	1646	4.6 (76)[a]	1242	3.6 (45)[a]
Below average deprivation (<=0)	8689	3.0 (263)	6994	1.9 (132)

** Please see appendix 2 for the distribution of the Townsend index scores in men and women.

‡ High education: O-level, A-level, degree; low education: refers to no education

* Other: divorced, separated, widowed

+ Prevalent physical disease: respiratory disease (asthma and bronchitis), allergies (allergies and hay fever), stroke, heart attack, cancer, diabetes, thyroid conditions, arthritis

¥ Manual: skilled manual, semi-skilled, non-skilled; non-manual: professionals, managerial, skilled non-manual

¶ Below the median PCS value of 50.6

[a] $P < 0.001$

[b] $P < 0.05$

The prevalence of (current) MDD was 2.1% (177/8236) for men and 3.3% (339/10335) for women. Women with MDD were younger than 50 years of age, more likely to be divorced/separated/widowed, have prevalent physical disease, high disability, GAD, and live in areas of above average deprivation. Among men, similar patterns emerged (table 1). Men with MDD were also more likely to be unemployed.

After performing correlated data analysis based on GEE, findings showed that the risk of depression in men living in areas of above average deprivation was 95% higher in an unadjusted analysis (OR=1.95, 95% CI: 1.39, 2.76; p=0.0001) (results not shown). After accounting for sociodemoraphics, the odds ratio attenuated slightly to 1.57 (OR=1.57, 95% CI: 1.09, 2.26; p=0.0152) (table 2).

Table 2: Odds ratios for MDD according to individual- and area-level characteristics for men (n=8,236) who completed the HLEQ questionnaire in the EPIC-Norfolk cohort

	Odds ratios and 95% CI					
Characteristic*	**Model A[1]**	**P-value for model A**	**Model B[2]**	**P-value for model B**	**Model C[3]**	**P-value for Model C**
Individual-level variables						
Socio-demographics						
Age						
(per 10 years)	0.40 (0.32, 0.50)	<0.0001	0.50 (0.40, 0.63)	<0.0001	0.47 (0.38, 0.60)	<0.0001
Education‡						
Low	1.10 (0.76, 1.61)	0.6081	1.06 (0.72, 1.54)	0.7813	1.00 (0.68, 1.46)	0.9978
High	1.00		1.00		1.00	
Marital status						
Single	1.46 (0.76, 2.83)	<0.0001	1.39 (0.71, 2.68)	<0.0001	1.41 (0.72, 2.76)	<0.0001
Married	1.00		1.00		1.00	
Other*	3.66 (2.53, 5.28)		3.48 (2.31, 5.22)		3.58 (2.39, 5.35)	
Social class¥						
Manual	1.02 (0.73, 1.41)	0.9161	1.14 (0.81, 1.59)	0.4612	1.06 (0.76, 1.48)	0.7298
Non-manual	1.00		1.00		1.00	
Employment¥						
No	3.69 (2.48, 5.50)	<0.0001	2.64 (1.74, 4.03)	<0.0001	2.24 (1.46, 3.45)	0.0002
Yes			1.00		1.00	
Health status						
Lifetime GAD						
Yes			14.33 (9.84, 20.87)	<0.0001	12.65 (8.68, 18.44)	<0.0001
No			1.00		1.00	
Prevalent physical disease						
Yes+					1.25 (0.89, 1.75)	0.1977

No					1.00	
Disability level						
High¶					1.98 (1.39, 2.82)	0.0002
Low					1.00	
Area-level variable						
Townsend index						
Deprivation						
Above average deprivation (>0)	1.57 (1.09, 2.26)	0.0152	1.56 (1.05, 2.31)	0.0287	1.51 (1.01, 2.24)	0.0434
Below average deprivation (<=0)	1.00		1.00		1.00	

1. Adjusted for age, sociodemographics (education, marital status, social class, employment status)
2. Adjusted for age, sociodemographics, lifetime GAD
3. Adjusted for age, sociodemographics, lifetime GAD, physical diseases and disability

⁺ Prevalent physical disease: respiratory disease (asthma, bronchitis), allergies (allergies, hay fever), stroke, heart attack, cancer, diabetes, thyroid conditions, arthritis

¥ Manual: skilled manual, semi-skilled, non-skilled; non-manual: professionals, managerial, skilled non-manual

‡ High education: O-level, A-level, degree; low education: refers to no education

* Other: divorced, separated, widowed

¶ Above the median PCS value of 50.6

*The brackets show the reference categories that were used for each categorical variable when it was entered in the models - deprivation: below average deprivation [ref] vs. above average deprivation; education: high [ref] vs. low; marital status: married [ref], single, others; social class: non-manual [ref] vs. manual; employment: yes [ref] vs. no; lifetime GAD: no [ref] vs. yes; prevalent physical disease: no [ref] vs. yes; disability level: low [ref] vs. high. These reference categories were based on the literature.

The OR reduced slightly after controlling for lifetime GAD (OR=1.56, 95% CI: 1.05, 2.31; p=0.029), but remained highly significant. After additionally adjusting for prevalent physical diseases and disability, the effect estimate became somewhat attenuated (OR=1.51, 95% CI: 1.01, 2.24; p=0.043), however, a statistically significant association between area derivation and depression remained (table 2). As the association with area deprivation emerged to be statistically significant for men (table 2), we took this finding further and wanted to determine the specific component of deprivation that was related to men's risk of having poor mental health (by disaggregating the Townsend index into its constituent components). Results showed that the OR was highest for unemployment (OR=1.77, 95% CI: 1.16, 2.71; p=0.008), followed by non-car ownership (OR=1.20, 95% CI: 0.70, 2.04; p=0.507), and lowest for overcrowding (OR=0.93, 95% CI: 0.60, 1.42; p=0.727) and non-home ownership (OR=0.81, 95% CI: 0.49, 1.34; p=0.422). Of these, only the effect estimate for unemployment was statistically significant (Appendix 3). Men living in areas characterized by high levels of unemployment were almost 80% more likely to have depression than those living in areas with low levels of unemployment. Next, we wanted to determine whether deprivation is associated with pure MDD, and thus excluded past-year GAD; the association with depression remained statistically significant (OR=1.64, 95% CI: 1.06, 2.52; p=0.025).

In women, while there was a statistically significant association in the unadjusted analysis (OR=1.55, 95% 1.19, 2.01; p=0.0010) as well as in the model adjusting for sociodemographics (OR=1.40, 95% CI: 1.07, 1.84; p=0.013), the association lost its significance in the fully-adjusted model (OR=1.24, 95%CI: 0.93, 1.65; p=0.143) (table 3). Thus, we did not carry out further analyses using the Townsend index.

We also conducted some sensitivity analyses. First, we divided the Townsend index into quintiles. Results showed that men living in the most deprived quintile had a statistically significantly increased risk for depression (OR=1.68, 95% CI: 1.01, 2.79; 0.0472), while none of the quintiles for women showed statistically significant findings. Second, we wanted to determine whether there was any change in findings after incorporating ethnicity in the original fully-adjusted models. The associations remained the same (men: OR=1.53, 95% CI: 1.03, 2.27 and women: OR=1.25, 95% CI: 0.94, 1.66). Second, we undertook analyses in which the education variable was left in its original form (divided into 4 categories: no education, O-

level, A-level, degree and beyond) in fully-adjusted models, and similar findings were again obtained (men: OR=1.51, 95% CI: 1.02, 2.24) and women: OR= OR=1.23, 95% CI: 0.92, 1.63). Third, we re-ran the fully-adjusted models using logistic regression rather than correlated data analysis based on GEE (Appendix 4), and results remained essentially unchanged (men: OR=1.51, 95% CI: 1.03, 2.21 and women: OR=1.24, 95% CI: 0.94, 1.64). This shows that there indeed is a robust association between overall area deprivation and depression in men, while there is no statistically significant effect in women.

Table 3: Odds ratios for MDD according to individual- and area-level characteristics for women (n=10,335) who completed the HLEQ questionnaire in the EPIC-Norfolk cohort

	Odds ratios and 95% CI					
Characteristic*	**Model A[1]**	**P-value for model A**	**Model B[2]**	**P-value for model B**	**Model C[3]**	**P-value for Model C**
Individual-level variables						
Socio-demographics						
Age						
(per 10 years)	0.54 (0.46, 0.64)	<0.0001	0.62 (0.52, 0.74)	<0.0001	0.59 (0.50, 0.71)	<0.0001
Education‡						
Low	1.23 (0.97, 1.56)	0.0890	1.29 (1.01, 1.65)	0.0412	1.30 (1.02, 1.66)	0.0356
High	1.00		1.00		1.00	
Marital status						
Single	0.93 (0.48, 1.78)	<0.0001	0.91 (0.48, 1.75)	<0.0001	0.91 (0.47, 1.75)	<0.0001
Married	1.00		1.00		1.00	
Other*	2.56 (2.00, 3.27)		2.41 (1.87, 3.10)		2.36 (1.83, 3.04)	
Social class¥						
Manual	0.95 (0.75, 1.21)	0.6964	0.99 (0.77, 1.27)	0.9530	0.97 (0.76, 1.25)	0.8225
Non-manual	1.00		1.00		1.00	
Employment¥						
No	1.87 (1.42, 2.48)	<0.0001	1.62 (1.21, 2.15)	0.0010	1.55 (1.17, 2.06)	0.0026
Yes			1.00		1.00	
Health status						
Lifetime GAD						
Yes			7.97 (5.99, 10.60)	<0.0001	7.37 (5.52, 9.83)	<0.0001
No			1.00		1.00	
Prevalent physical disease						
Yes+					1.25 (0.98, 1.59)	0.0682
No					1.00	

Disability level						
High¶					1.41 (1.11, 1.79)	0.0045
Low					1.00	
Area-level variable						
Townsend index						
Deprivation						
Above average deprivation (>0)	1.40 (1.07, 1.84)	0.0132	1.26 (0.95, 1.67)	0.1081	1.24 (0.93, 1.65)	0.1425
Below average deprivation (<=0)	1.00		1.00		1.00	

1. Adjusted for age, sociodemographics (education, marital status, social class, employment status)
2. Adjusted for age, sociodemographics, lifetime GAD
3. Adjusted for age, sociodemographics, lifetime GAD, physical diseases and disability

‡ High education: O-level, A-level, degree; low education: refers to no education

* Other: divorced, separated, widowed

¥ Manual: skilled manual, semi-skilled, non-skilled; non-manual: professionals, managerial, skilled non-manual

+ Prevalent physical disease: respiratory disease (asthma, bronchitis), allergies (allergies, hay fever), stroke, heart attack, cancer, diabetes, thyroid conditions, arthritis

¶ Below the median PCS value of 50.6

*The brackets show the reference categories that were used for each categorical variable when it was entered in the models - below average deprivation [ref] vs. above average deprivation; education: high [ref] vs. low; marital status: married [ref], single, others; social class: non-manual [ref] vs. manual; employment: yes [ref] vs. no; lifetime GAD: no [ref] vs. yes; prevalent physical disease: no [ref] vs. yes; disability level: low [ref] vs. high. These reference categories were based on the literature.

Discussion

This research is an analysis based on EPIC-Norfolk data, and findings showed that living in an area of above average deprivation was associated with a significantly increased the risk of depression in men; the relationship with depression was not statistically significant in women. The association in men endured after adjusting for important individual-level confounders, such as serious physical health conditions, disability, and history of generalized anxiety disorder (GAD). When we looked closer to determine the specific component of area deprivation that has the greatest influence on men's mental health, unemployment emerged as an important factor. Men living in areas characterized by high unemployment had a 77% greater chance of having depression than those living in areas with low levels of unemployment.

Potential mechanisms

An environment in which deprivation is above average according to the Townsend index appears to differentially affect men and women's mental health after accounting for a number of potential confounders. A number of reasons can explain this. First, men appear to be more sensitive to stressful events occurring in their environment compared to women, especially if the stress is relating to financial and work-related problems.[25] The reason for this is that occupational and financial success is particularly important for men's mental health. Second, when living in disadvantaged regions, the possibility of hearing about job loss from others increases and this can promote anticipatory stress in those who are still working, which can increase their risk of depression.[48] This is particularly problematic for men who are perceived by their families as the main provider and head of household. In contrast, women's risk of depression seems to be influenced more by the social networks they are embedded in, the quality and continuity of relationships, the social support derived from neighbours and communities, and marital satisfaction.[25, 26] Women are more likely to experience depression as a result of unmet needs in relationships. Deficiencies in interpersonal relationships in women can lead to a perception that the self is unable to meet needs for self-worth and achievements, and this can increase their risk of poor mental health.[25] Men, on the other hand, have been shown to be more prone to depression as a

result of failure at key instrumental tasks, including achievements at work and inability to provide for the family.[25, 49]

Unemployment, often accompanied by low social ranking, can lead to loss of self-esteem and role identity in men. This was seen in the United Kingdom after the 1970's, when the economy shifted from a manufacturing to a service-based one.[27] The shift was accompanied by a loss of skilled and semi-skilled jobs among men, while women had to enter the workforce and partake in jobs that were primarily service-based. The loss of employment opportunities among men might have contributed to a loss of role identity and self-esteem in this group.[27] However, even more than a decade later after this shift in economy, men who lost their employment and were in low social class groups showed poorer self-rated health compared to women.[50] This is also mirrored by recent research.[25] This again supports the notion that men are affected by failure at key instrumental tasks.[25] The same phenomenon occurred in rural areas of Midwestern United States after the farm crisis and related events occurred in the 1980s.[51] Rural areas held agrarian values, characterized by male provider norms and 'rugged independence'.[51] After the farm crisis hit, men were no longer able to fulfil their economic provider role, and both genders had to take on multiple jobs to make ends meet. This shook the traditional system, and created stress and contributed to high rates of depression in men. During this time, men also showed susceptibility to a wider range of stressors compared to women.[51]

Men and women also tend to experience and manifest the effect of stress in different ways. Women living in deprived areas have been shown to be more prone to anxiety[28], while men living in disadvantage are more likely to have depression. This could be a result of evolutionary, survival functions. Women have traditionally had the responsibility of childcare and ensuring the successful survival of future generations.[52] Therefore, living in circumstances of (above average) deprivation can trigger the fight or flight reaction, which can increase stress in finding ways to make ends meet so that they can raise their children. In this context, anxiety might be seen as protective, ensuring the survival of future generations. This is why women also tend to be more concerned about community features that can disrupt their caregiving role and negatively impact their family, such as, lack of safe play areas for children.[52, 53] Men have traditionally had the responsibility of being the

provider, and if they are not able to fulfil this role, they are more likely to become depressed and potentially commit suicide.[25, 27] This is a problem in India, where suicide rates are high among male farmers whose crops have failed.[54, 55] In the UK, men with depression are also more likely than women to commit suicide. Taken together, these findings suggest that women may actually be more resilient than men when encountering adversity. However, very little research has examined this, and previous studies in the mental health literature have typically described women as vulnerable. Further research on health from a gendered perspective is needed.[28]

When exposed to the stresses and strains of deprivation, men are also more likely to develop substance abuse and this, in turn, can increase the risk for depression. The National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) study[56] showed that the total number of stressors experienced in life had a significantly stronger association with heavy drinking in men than in women. Experiencing stressors can also lead to unhealthy means of coping with the hardships, such as smoking and physical inactivity, and this can lead to sequelae.[24, 57] Finally, when men experience mental health issues, they are less likely to seek help than women [51].

Strengths and weaknesses and future research

This study shows that there is a statistically significant association between overall area deprivation and depression in men, while this relationship is not apparent in women. There are a number of strengths associated with our research. Our study used a structured questionnaire, the HLEQ, to assess mental health, and a measure of MDD was created using valid and reliable criteria stipulated by the DSM. Also, we were able to adjust for a number of important confounders, such as medical and psychiatric history, and sociodemographic factors, including unemployment measured at the level of the individual. Nonetheless, residual confounding may be present in our research if certain covariates were not adequately adjusted for. With respect to the medical history covariate, it is possible that some participants may have omitted disclosing or had difficulty recalling medical diagnoses and this might have introduced measurement error. Our measure of area deprivation also may not capture features of the environment that may affect mental health; however, all indexes designed to measure environmental effects suffer from this limitation. The Townsend index

is theoretically sound and commonly used in research assessing these types of relationships. One of the limitations of this variable is that it is somewhat biased towards urban populations, particularly as it is capturing aspects that are more reflective of urban settings (ex. car ownership). Given that it may not be capturing rural deprivation as well as it should, measurement error may be an issue. This is an area of further research.

Because of healthy volunteer bias, it is possible that some of the sickest, most deprived people who would have been eligible to take part in EPIC-Norfolk, did not participate. This means that our results may not generalize to those individuals.

Also, we did not have information on length of living in the area for participants, however, migration in EPIC-Norfolk is minimal and unlikely to have biased the findings. People who took part in this study tended to reside in the same areas their whole lives. This is why Norfolk and the surrounding towns and rural areas were selected for participant recruitment.[58]

Another issue is the fact that EPIC-Norfolk only included people over the age of 40. As critical time periods for the development of depression include young adulthood[59], it would be useful if future research examined these relationships with deprivation using a younger sample. Nonetheless, depression can still develop at midlife and beyond, and many times, this is triggered by stressful life events, such as adverse social conditions.

Subjective deprivation as a study limitation

A mechanism linking socioeconomic circumstances with depression in general involves subjective relative deprivation. Living in a deprived area can trigger comparison of the self to others, and this can in turn, lead to stress and poor mental health. A number of people living in deprived areas may experience negative emotions because they lack the necessary means to survive or are unable to achieve desired outcomes compared to those who are more affluent. Perceptions of lack can thus lead to poor health outcomes. Relative deprivation is composed of "affective and cognitive (i.e., appraisal) responses to perceived unfair outcomes."[60] Thus, social comparisons and stress arising from deprivation can contribute to increased risk of depression. A recent study has indeed shown that subjective relative deprivation is linked to depressive symptoms.[60] Living in a deprived area can give rise to subjective feelings of deprivation, which can subsequently lead to poor mental health. Although we did not have information on subjective feelings of deprivation, future studies should assess this.

Future research

Future research should assess the risk of depression not only in countries, such as, the US or UK where there is higher gender equality, but also in parts of the world where social roles and gendered norms for men and women have shown much less change over time. Countries with higher gender equality also show some of the highest rates of depression and other mental disorders in the world.[61] In Europe, the discrepancy in depression rates between men and women in highly-developed countries is greater than in less-developed countries where there is also greater gender inequality.[62] In Eastern European countries, levels of depression are similar between men and women[62], while in Western Europe, women are twice as affected as men.[63] More studies are needed to explore the influence of area deprivation on the mental health of men and women separately, and to do this in different contexts (ex. rural, urban) and countries around the world. Further, the reasons behind gender differences need to be better elucidated.

Finally, future studies should assess area deprivation and mental health at multiple points in time using a repeated measures analysis, because both may change over the follow-up period.

Placing our research in context

Although other studies have shown that the places in which people live have a substantial impact on health[14, 15], studies on the links between area deprivation and mental disorders from a gendered perspective are limited. A recent study[64] of over 1000 African American and non-Hispanic white adults living in the US showed that men who had experienced stressful life events in 1983-1986 were more likely to have depression in 2011, while this was not observed in women. This study, however, has limited generalizability, because it excluded other ethnicities. Also, the reliability and validity of the measure of stressful life events was not reported – the measure was based on a checklist of 'major negative events' that had occurred in the previous 3 years. Finally, exposure to stressful life events at the individual-level were investigated, rather than the effect of the place people live in.

A number of studies have assessed individual-level risk factors of depression, but substantially fewer have examined the influence of the environment on mental health. Nonetheless, studies of individual-level risk factors provide an important starting point in understanding relationships. Another prospective UK study of over 500 people[27] showed that the socioeconomic status of men at midlife was associated with depression at midlife, while this was not observed in women. For women, their socioeconomic status at birth influenced their levels of depression at midlife. Also, men who had experienced downward social mobility or a reduction in their socioeconomic status from adulthood to midlife were at high risk of having poor mental health at midlife, but this was not found in women.[27] These results suggest that women are more sensitive to the social class group they are in very early in life, while for men, social mobility over the life course, as well as the socioeconomic status group they are in during later life are more important for their mental health. This study, however, was limited, because it was based on a small sample size, assessed only individual-level measures rather than area-level level effects, and failed to adjust for a number of important confounders, such as, demographic factors. Failure to properly adjust for potential confounders can lead to overestimation of the effect estimate. Finally, this study examined general mental health, rather than individual psychiatric disorders.

A recent US study showed that the types of stressors that influence men's risk of depression are those related to work, finances, and legal matters.[25] In this study, stressors were not

linked to depression risk in women. Again, this research only assessed individual-level data. Our study shows, for the first time that living in an area of above average deprivation increases the risk of depression in men, while less so in women. Area deprivation was measured in our study at midlife and beyond, the time period which seems to have the greatest influence on men's mental health.[25]

Interpretation

The genders seem to be differentially affected by the environment, and we believe it is important to highlight this for policy-makers, clinicians, and public health authorities. Knowing that men living in areas of above average deprivation are more susceptible to depression can be used to tailor treatment and prevention efforts – and knowing how to best tailor treatment efforts and targeted interventions is important at a time when there are scarce health resources, such as now.

Acknowledgements: OR received PhD funding from the National Institute for Health Research.

Competing interest: All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: no support from any organisation for the submitted work; no financial relationships with any organizations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

Funding: This work was supported by the Medical Research Council UK (grant number SP2024-0201 and SP2024-0204) and Cancer Research UK (grant number G9502233).

Author contributions: OR (corresponding author) had the idea for and conducted the analysis, and wrote the article, along with CB, KK, LL, PS, and NW. All authors provided feedback into the analysis and critically reviewed drafts of the manuscript. All authors have seen and approved the final version.

Role of study sponsors and statement of independence: The funding sources had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; and preparation, review, or approval of the manuscript.

Ethical approval: The study has ethics committee approval from Norfolk Ethics Committee (Rec Ref: 98CN01) and all participants gave informed consent.

Data sharing: The data for this study are available in the supplementary materials. Further questions could be sent to OR (or260@medschl.cam.ac.uk).

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Appendix 1

Further information on A- and O-levels:

A-levels are advanced level qualifications, which "are subject-based qualifications that can lead to university, further study, training, or work." (UCAS)

According to IGCSE Centre, "O-Level is the abbreviation of Ordinary Level. It is one of the two-part GCE (General Certificate of Education). The other part of GCE is Advanced Level (A-Level), which students enter after completing O-Level. O-Level is the final certification for secondary school, to be taken at fifth form or year 11 at approximately age 17 (or age group 14-16). Students that have completed O-Level are considered to have completed formal education." (IGCSE Centre)

Appendix 2

Distribution of Townsend index scores

1. Above average deprivation

Men

Mean: 1.96

Standard deviation: 1.49

Range: 0.01 to 6.09

Women

Mean: 1.93

Standard deviation: 1.47

Range: 0.01 to 6.98

2. Below average deprivation

Men

Mean: -2.85

Standard deviation: 1.21

Range: -6.73 to -0.02

Women

Mean: -2.83

Standard deviation: 1.21

Range: -6.10 to -0.02

Appendix 3

Odds ratios for MDD according to individual- and area-level characteristics for men who completed the HLEQ questionnaire in the EPIC-Norfolk cohort

	Odds ratios and 95% CI	
Characteristic*	**Model C[1]**	**P-value for Model C**
Individual-level variables		
Socio-demographics		
Age		
(per 10 years)	0.47 (0.38, 0.59)	<0.0001
Education[‡]		
Low	1.01 (0.69, 1.48)	0.9420
High	1.00	
Marital status		
Single	1.39 (0.71, 2.69)	<0.0001
Married	1.00	
Other[*]	3.51 (2.32, 5.29)	
Social class[¥]		
Manual	1.05 (0.75, 1.47)	0.7747
Non-manual	1.00	
Employment[¥]		
No	2.23 (1.45, 3.42)	0.0002
Yes	1.00	
Health status		
Lifetime GAD		
Yes	12.65 (8.68, 18.43)	<0.0001
No	1.00	
Prevalent physical disease		
Yes[+]	1.24 (0.88, 1.74)	0.2176
No	1.00	
Disability level		
High[¶]	2.01 (1.41, 2.86)	0.0001
Low	1.00	
Area-level variable		
Townsend index		
Deprivation		
Unemployment		
Yes (>0)	1.77 (1.16, 2.71)	0.0084
No (<=0)	1.00	
Non-car ownership		
Yes (>0)	1.20 (0.70, 2.04)	0.5067
No (<=0)	1.00	
Non-home ownership		
Yes (>0)	0.81 (0.49, 1.34)	0.4220
No (<=0)	1.00	

Overcrowding		
Yes (>0)	0.93 (0.60, 1.42)	0.7272
No (<=0)	1.00	

1. Adjusted for age, sociodemographics, lifetime GAD, physical diseases and disability

‡ High education: O-level, A-level, degree; low education: refers to no education

* Other: divorced, separated, widowed

¥ Manual: skilled manual, semi-skilled, non-skilled; non-manual: professionals, managerial, skilled non-manual

+ Prevalent physical disease: respiratory disease (asthma, bronchitis), allergies (allergies, hay fever), stroke, heart attack, cancer, diabetes, thyroid conditions, arthritis

¶ Below the median PCS value of 50.6

*The brackets show the reference categories that were used for each categorical variable when it was entered in the models - below average deprivation [ref] vs. above average deprivation; education: high [ref] vs. low; marital status: married [ref], single, others; social class: non-manual [ref] vs. manual; employment: yes [ref] vs. no; lifetime GAD: no [ref] vs. yes; prevalent physical disease: no [ref] vs. yes; disability level: low [ref] vs. high. These reference categories were based on the literature.

Appendix 4

Odds ratios for MDD according to individual- and area-level characteristics for men and women who completed the HLEQ questionnaire in the EPIC-Norfolk cohort

	Men (n=8,236)		Women (n=10,335)	
	Odds ratios and 95% CI[1]		Odds ratios and 95% CI[1]	
Characteristic*				
Individual-level variables				
Socio-demographics				
Age				
(per 10 years)	0.47 (0.38, 0.59)	<0.0001	0.59 (0.51, 0.69)	<0.0001
Education‡				
Low	1.00 (0.69, 1.45)	0.9977	1.30 (1.01, 1.67)	0.0384
High	1.00		1.00	
Marital status				
Single	1.41 (0.72, 2.79)	0.3181	0.91 (0.47, 1.75)	0.7737
Married	1.00		1.00	
Other*	3.58 (2.42, 5.28)	<0.0001	2.36 (1.85, 3.02)	<0.0001
Social class¥				
Manual	1.06 (0.76, 1.49)	0.7340	0.97 (0.76, 1.24)	0.8204
Non-manual	1.00		1.00	
Employment¥				
No	2.24 (1.49, 3.37)	0.0001	1.55 (1.18, 2.04)	0.0019
Yes	1.00		1.00	
Health status				
Lifetime GAD				
Yes	12.65 (8.71, 18.37)	<0.0001	7.37 (5.57, 9.75)	<0.0001
No	1.00		1.00	
Prevalent physical disease				
Yes+	1.25 (0.90, 1.73)	0.1842	1.25 (0.99, 1.59)	0.0658
No	1.00		1.00	
Disability level				
High¶	1.98 (1.38, 2.83)	0.0002	1.41 (1.11, 1.80)	0.0048
Low	1.00		1.00	
Area-level variable				
Townsend index				
Deprivation				
Above average	1.51 (1.03, 2.21)	0.0358	1.24 (0.94, 1.64)	0.1325

deprivation (>0)		
Below average deprivation (<=0)	1.00	1.00

1. Adjusted for age, sociodemographics, lifetime GAD, physical diseases and disability
‡ High education: O-level, A-level, degree; low education: refers to no education
* Other: divorced, separated, widowed
¥ Manual: skilled manual, semi-skilled, non-skilled; non-manual: professionals, managerial, skilled non-manual
+ Prevalent physical disease: respiratory disease (asthma, bronchitis), allergies (allergies, hay fever), stroke, heart attack, cancer, diabetes, thyroid conditions, arthritis
¶ Below the median PCS value of 50.6
*The brackets show the reference categories that were used for each categorical variable when it was entered in the models - below average deprivation [ref] vs. above average deprivation; education: high [ref] vs. low; marital status: married [ref], single, others; social class: non-manual [ref] vs. manual; employment: yes [ref] vs. no; lifetime GAD: no [ref] vs. yes; prevalent physical disease: no [ref] vs. yes; disability level: low [ref] vs. high. These reference categories were based on the literature.

Please see the article line numbers (column on the right) and the explanations provided.

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Line numbers within the article
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	6, 4
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	34-4
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	89-1
Objectives	3	State specific objectives, including any prespecified hypotheses	156-
Methods			
Study design	4	Present key elements of study design early in the paper	113-
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	158-17 273
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	159-17 We specify in the paper that the Townsend index was record linked to the cohort.
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	187-29
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is	There were two variables of interest in this study: area deprivation and major depressive disorder. The others

		more than one group	are potential confounders – in the methods I list them all, indicate how they were assessed and mention that they were collected through the baseline, self-reported postal LLQ questionnaire.
Bias	9	Describe any efforts to address potential sources of bias	323
Study size	10	Explain how the study size was arrived at	180
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	How variables were handled in analyses: 306-313 (the methods section describes how the variables were categorized/which categories were used) Which grouping were chosen and why: I describe the reference categories of the variables in the footnotes under tables 2 and 3. I mention that the categorization of the variables was done in accordance with the literature and provide the relevant citations in the method section. How the dependent variable was created: 187-220 How area-level measure was created: 269-286 Individual-level measures: 222-267
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	297-356
		(*b*) Describe any methods used to examine subgroups and interactions	Similar to other studies, I conducted analyses separately for men and women. I did not do this because of p-value considerations (statistical significance), but rather, because I felt it was important to do. In the introduction, I provide the rationale for conducting sex-specific analyses. Knowing which gender group is more affected can help with the tailoring of targeted interventions.
		(*c*) Explain how missing data were addressed	We indicated that this was a complete-case analysis.
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed	Loss to follow-up was not a problem in this study.

Case-control study—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	We were able to track down all participants using various means, unless they expressed that they wished to be removed from the mailing list. We elaborate on this in the manuscript.
(e) Describe any sensitivity analyses	328-335

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	180-184
		(b) Give reasons for non-participation at each stage	We do not have the reasons for non-participation, because these data were not collected when the study was initiated in 1993.
		(c) Consider use of a flow diagram	We reference a paper which describes the EPIC-Norfolk study further. This paper contains a flow diagram. Also, our previously-published BMJ Open paper upon which this one was based contains a flow diagram also – we reference this paper.
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	We included characteristics for those with vs. without MDD, because we felt it was important to show the characteristics of those exposed vs. non-exposed (see also Table 1)
		(b) Indicate number of participants with missing data for each variable of interest	292-295 – we had to move this section to the Methods because one of the reviewers had asked us to do so.
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	Initially we mentioned that participants were followed for 7 years, however, we had to delete this phrase because one of the reviewers had asked us to do so. The Townsend index was record linked to the cohort.
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	385.
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Tables 2 and 3 contain unadjusted and progressively adjusted estimates. We also discussed the findings within the text, and provide odds ratios and 95%

			confidence intervals.
			We included the confounders based on the literature – we mention on this in the paper and cite relevant literature. As per strobe, we included this information in the methods section; and we omitted repeating this in the results section to reduce redundancy. However, if the editor would like us to repeat this information in the results, we are happy to do so.
		(*b*) Report category boundaries when continuous variables were categorized	The cut-offs are provided. In regards to the Townsend index, the methods section states that those below and above the cut-point of zero were compared.
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Sensitivity analyses: 1) relationship between area deprivation and pure MDD (past-year GAD excluded); 2) correlated data analysis replaced with logistic regression ; 3) analyses run with education re-categorized and ethnicity included ; 4) Townsend index divided into quintiles. In all these instances, the associations remained the same. This is reported in the paper.
Discussion			
Key results	18	Summarise key results with reference to study objectives	474-484
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	560-606
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	658-664 (We also have a section comparing our study results to those of others: 620-656, as well as a section on potential mechanisms explaining our findings: 485-

			551
Generalisability	21	Discuss the generalisability (external validity) of the study results	571-577
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	674-677

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.