

# **Dimension of pain-related quality of life and self-reported mental health in men and women of the European Prospective Investigation into Cancer–Norfolk cohort: a population-based cross-sectional study**

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## Abstract

Both cognitive and behavioural factors are linked to the experience of pain as well as its interference with quality of life. Psychological distress has been shown to be associated to several emotional and social impairments. Although, the association between pain and mental health has been widely discussed, the understanding of life interference and outcome is not fully understood. This study examined the association of pain dimension and mental health domain in 16,051 participants of the EPIC-Norfolk cohort (mean age =  $58.9 \pm 9.1$  years). Study outcomes were depressive or anxious behaviour and limitations due to emotional problems and impairments in social functioning (mental functional health components of the Short Form-36 (SF-36)). Logistic regression models were constructed controlling for the potentially confounding factors including socio-economic variables (occupational social class, deprivation, marital status, education), lifestyle behaviour (physical activity, smoking, alcohol, dietary) and previous medical history. Strong interference in quality of life due to pain (bottom 20% of pain dimension score of SF-36) was significantly associated with poor MH in men and women (odds ratios (ORs) (95% confidence intervals (CIs)): 1.35 (1.19, 1.54) and 1.39 (1.25, 1.55), respectively;  $p < 0.0001$ ) in fully adjusted models. Moreover, strong interference due to pain was also significantly associated with poor overall MH including emotional and social functioning (ORs (95% CIs): 1.42 (1.25, 1.62) and 1.39 (1.25, 1.55) respectively;  $p < 0.0001$ ) in fully adjusted models; subsidiary analysis using linear regression models demonstrated similar results for these domains. Although a strong association has been shown, further research is needed to provide information on the different site and/or causes of pain which would allow stratification. Moreover, assuming a bi-directional nature of both domains, systematic assessment and management of pain have a lot of potential to improve the MH-related quality of life in the general population and vice versa.

*Keywords:* Pain, mental health, psychosocial functioning, quality of life, SF-36

## Introduction

Both pain and mental health (MH)-related problems are the most common reasons for seeking health care.<sup>1</sup> Individuals reporting ongoing pain report higher levels of psychological distress which ranges from anger,<sup>2</sup> fear or anxiety,<sup>3,4</sup> frustration, low tolerance and self-downing<sup>5</sup> or depression.<sup>6</sup>

Additionally, chronic pain patients show more severe consequences including a higher vulnerability to suicidal ideation or suicide attempts.<sup>7</sup> Cognitive (e.g. expectations) as well as behavioural (e.g. avoidance) factors are closely linked to the subjective experience of pain which possibly prevents therapeutic success.<sup>8</sup> The psychological approach to pain management may have a significant impact on quality-of-life experience and outcome in a long term.<sup>9</sup> The interaction of cognitive factors and environmental influences on human behaviour are often underestimated. Understanding the complexity of pain and its highly personal component is a true challenge especially from a psychological standpoint.

Ample research of the association of pain and MH exists in clinical as well as in general populations. The severe consequences of enduring pain have been extensively documented, for example, in chronic back or neck pain patients,<sup>10</sup> osteoarthritis of hip or knee patients,<sup>11</sup> psychiatric patients with a history of suicidal ideation or attempted suicide<sup>12</sup> or other psychological factors.<sup>13</sup> It has been shown that severity and frequency of pain is linked to a number of objective outcomes including onerous functional or social impairments.<sup>13,14</sup> To date, the subjective interference due to pain, regardless of severity, has been given less attention. The strong relationship between reported functional health and mortality has been previously reported in numerous studies using the Short Form-36 (SF-36), a multipurpose, short-form health survey.<sup>15,16</sup> Although MH-related domains of the SF-36 have been widely discussed, no study to date examined the dimension of pain in relation to depressive and anxious behaviour, social limitations or emotional impairments. Given the linkage of the SF-36 to several objective outcomes, the examination of quality of life due to pain and its association with MH-related problems may give insightful results to the area of functional and psychological health.

In this study, we used data from the European Prospective Investigation into Cancer (EPIC)-Norfolk cohort (a large cohort representative of the general UK population) to address the following

aims: (1) to investigate the association between dimension of pain- related quality of life and self-reported MH; assessed using SF-36 pain and MH domains including depressive and anxious behaviours; (2) to expand previous research by examining further psychosocially relevant outcomes of limitations due to emotional problems, social functioning (SF) and general MH-related quality of life and (3) to provide gender-specific relation- ship between pain dimension and MH; controlling for a variety of potentially confounding factors including personal and lifestyle characteristics and medical history.

## **Methods**

### **Study population**

This study population includes participants of the EPIC-Norfolk cohort who attended the first health-check (1HC; N= 25,633) and completed the anglicised 36-item Short-Form Health Survey (SF-36) 18 months later (n= 19,535). Complete data were available for a total of 16,051 participants (7119 men) as not all participants, who attended the 1HC, completed the survey and vice versa. A detailed study protocol has been described previously.<sup>17</sup> Briefly, the Norfolk cohort of the EPIC includes the city of Norfolk and surrounding small towns and rural areas. Participants were men and women aged between 39 and 78 years (99.6% White British) from general practice age–sex registers (N= 35) at the study baseline during 1993–1997. The cohort characteristics are representative of the UK population apart from the lower prevalence of smokers. Ethical approval was obtained from the Norwich Local Research Ethics Committee and all participants provided written informed consent.

### **Study procedure**

Initial instruments used for exposure definition included the Health and Lifestyle Questionnaire (HLQ) with an integrated semi-quantitative Food Frequency Questionnaire (FFQ).<sup>18,19</sup> At the participant's 1HC, anthropometric measurements were taken by a trained research nurse following a standardised protocol. After 18 months, participants received the Health and Life Experiences Questionnaire (HLEQ) including the anglicised version of the SF-36, a widely used and well-validated measurement to assess health- related quality of life.<sup>20,21</sup>

## Measurements

*Anthropometric measures.* At the IHC, a trained research nurse performed several basic measurements according to a standardised protocol.<sup>17</sup> Height was measured using a free-standing stadiometer to the nearest millimetre (without shoes) and weight was recorded to the nearest 0.2 kg (without shoes and in light clothing). Waist and hip circumferences were also recorded to the nearest millimetre.<sup>17</sup> Body mass index (BMI) was calculated using weight in kilogram/height squared in square metres.

*The HLQ.* Personal and demographic information on age, sex, ethnicity, marital status, educational attainment, occupational status and type of occupation(s), smoking status, alcohol consumption, medical history as well as a short section on physical exercise were included in the HLQ. Any dietary data were obtained by integrating the FFQ. Marital status was categorised as being single, married, widowed, separated or divorced. Educational attainment was based on the highest qualification attained at the time of the IHC. This included having a degree (or equivalent), A-levels (or equivalent; UK: Secondary school leaving qualification, students being around 18 years), O-levels (or equivalent; UK: General Certificate of Education (GCE) ordinary level, students being around 16 years) or less than O-levels/no qualification. Occupational social-class categories were classified using the Registrar General's occupation-based classification scheme.<sup>22</sup> Social class I consisted of professionals, class II included all managerial and technical occupations, class III was subdivided into non-manual and manual skilled workers, class IV of partly skilled workers and class V comprised unskilled manual workers. Following the classification scheme, men and women's social class was coded differently. For men, their own occupation was used, and only when participants were unemployed or retired, their partner's social class was used instead. For women, partner's social class was used except when their social class was unclassified or missing. Unemployed men and women without partner were coded as unclassified. To obtain the residential area-based socio-economic measure, the Townsend Deprivation Index was calculated which is based on data from the UK 1991 census.<sup>23</sup> The Townsend Score consists of four indicators, each summarised as a standardised score (z-scores) for the enumeration of district level (about 150 households). Percentage of unemployment in active residents aged over 16 years was used as a measure of lack of material resources and

insecurity, the percentage of private households not owning a car was taken as a proxy indicator of income, and the percentage of households not owner occupied was taken as a proxy indicator of wealth. The percentage of households with more than one person per room was used to determine material living condition. The participant's postcode was assigned to the appropriate deprivation level utilising these data. In general, values  $<0$  were categorised as less deprived and values  $>0$  as highly deprived areas.

Other lifestyle factors relevant for this study were physical activity, smoking status and medical history. Habitual physical activity was assessed asking about physical activity at work and about the amount of time spent (in hours per week) in various activities during winter and summer. Work-related physical activity was divided into four categories: sedentary (spending most of the time sitting), standing (spending most of the time standing or walking without intense physical effort), physical work (involving some physical effort) and heavy manual work (involving very vigorous physical activity). An additional question obtained information about physical activities, such as cycling to work and during leisure time or other physical exercises, such as swimming or jogging, in a typical week during the past 12 months. This was recorded separately for the summer and winter season. Hours per day of recreational activity were computed from the mean of summer and winter hours per week of cycling plus the mean of summer and winter hours per week of other physical activities divided by seven. Finally, individuals were assigned to four categories: inactive, moderately inactive, moderately active and active, which was validated against a heart rate monitor.<sup>24</sup>

Smoking status was categorised based on the question 'Have you ever smoked as much as one cigarette a day for as long as a year?' and was classified as 'never smoked' if answered with 'no'. If answered with 'yes', participants were asked 'Do you smoke cigarettes now?' and were accordingly classified as 'current' or 'former smoker'. Prevalent illnesses were assessed by asking 'Have you ever been told by a doctor that you have, or had, any of the following conditions?' Several common medical conditions were listed including myocardial infarction, stroke, diabetes mellitus, cancer, asthma/chronic obstructive pulmonary disease (COPD) and depression (with required treatment) or any psychiatric illness.

*Dietary assessment methods.* The FFQ listed 130 food items divided into sections according to food type and assessed the average consumption in the last 12 months. Alcohol consumption formed an own subsection and contained additional information about alterations over a lifespan. A specific program, DINER (Data Into Nutrients for Epidemiological Research), was used to transform data for nutritional analyses. Alcohol consumption was transformed in grams/per week and later divided into units/per week with one unit being 8 g of alcohol. For descriptive purpose, data were summarised into three categories (none, <7 units/ per week and  $\geq 7$  units/per week). Similarly, fruit and vegetable consumption was transformed separately into grams, both scores were summarised later and divided into portion/per day with 80 g representing one portion and categorised into three categories (<3, 3–5 and  $\geq 5$  portions/a day).

*Dimension of pain-related quality of life and MH assessment.* Dimension of pain-related quality-of-life and MH domains were assessed using the HLEQ which included the anglicised version of the SF-36. The SF-36 comprised 36 items across eight health dimensions assigned either to a physical component summary (PCS) or mental component summary (MCS) score. Each component referred to a time period over the last 4 weeks. The PCS included information on physical functioning (10 items), role limitations due to physical problems (4 items), bodily pain (2 items) and general health (5 items). The MCS provided information on MH (5 items), role limitations due to emotional problems (3 items), vitality (4 items) and social functioning (2 items). Of interest for this article was the physical dimension of pain in relation to MH, emotional role (ER) and social functioning (SF). For each health dimension, a SF-36 score of 0 represented poor and a score of 100 represented good health.<sup>25</sup> Dimension of pain-related quality of life was measured by asking how much pain participants experienced during the past 4 weeks and how much this interfered with their normal work including both work outside the home and housework.

Psychosocial measures included self-reported psychiatric symptoms following the rules of the Diagnostic and Statistical Manual of Mental Disorders of the American Psychiatric Association in 1994. MH was limited to major depressive disorders and generalised anxiety disorders only. Emotional limitation was measured by asking for any interference in daily activities or work due to

emotional problems. Similarly, social functioning was obtained for any social interference in normal social activities with family, friends, neighbours or groups due to physical or emotional problems.

### **Statistical Analysis**

Statistical analyses were performed using IBM SPSS Statistics for Windows version 23.0 (Armonk, New York, USA). Of the participants who attended the 1HC and returned the HLEQ in the 18-months follow-up (n = 19,535), complete data for all variables included in this study were available for a total of 16,051 participants (8932 women). Sex-specific analyses were performed to identify gender differences in the relationship of pain dimension and MH as previous research has shown fundamental differences in many biological and psychological factors such as BMI, smoking and alcohol consumption, education, occupation or depression.<sup>26,27</sup> Pain dimension category classification was based on data distribution of the EPIC-Norfolk cohort and was divided into quintiles. An examination of sex-specific cut-off points of this variable showed similar results for both men and women, and thus, for pain dimension categories, same cut-off values were used. Frequency of pain and interference with quality of life increased with each ascending category. Cut-off points were based on SF-36 with 0 indicating frequent pain/high interference and 100 no pain/no interference due to pain. Those were set to 100, 84, 72, 51 and <51.

An analysis of variance (ANOVA) and chi-square test of independence were performed to examine difference in outcome variables of interest (MH, ER, SF, MCS) and socio-economic variables (occupational social class, deprivation, marital status and education), lifestyle behaviour (physical activity, smoking, alcohol and dietary) and medical history across pain dimension quintiles. Unadjusted linear regression models were created to identify the presence or absence of a linear relationship between MH, ER or SF as dependent variables and pain dimension score as the independent variable. For ease of interpreting outcomes, the SF-36 scale for the pain dimension score was reversed so that 0 represented no pain/no reduced quality of life due to pain and 100 represented frequent pain/severely reduced quality of life due to pain for linear models. For descriptive purposes, cut-off points were set up to dichotomise selected outcomes of MH and MCS. These arbitrary cut-off points allow meaningful interpretation of results in terms of population at risk and contextualising



findings for clinicians. Cut-off points for MH and MCS are based on the top and bottom 20th percentile (good MH>92.00, poor MH<64.00, good MCS> 59.35, poor MCS<46.12). Binary logistic regression models were cumulatively adjusted similar to the linear regression models. Pain dimension categories were recoded into a dichotomous variable using Q1-4 as reference category. All analyses were agreed a priori. All p-values reported in this study are for two-sided significance tests and regarded as statistically significant when  $p<0.05$ .

## **Results**

### **Sample characteristics**

Analyses were conducted in 16,051 participants (44.4% male; mean age (standard deviation (SD)) for males and females  $59.7 \pm 9.1$  and  $58.3 \pm 9.1$  years, respectively). Participant characteristics across pain dimension quintiles are shown in Table 1. The majority of participants (62.9%) were categorised into non-manual social classes (which include professional, managerial or technical and non-manual skilled workers). In areas of low deprivation, participant proportions decreased across ascending pain dimension quintiles, whereas in areas of high deprivation, participant proportions increased with ascending quintiles of pain dimension category. The majority of the sample (82.7%) were married. Educational attainment was higher in men with 63.4% attained A-level or degree-level qualifications compared with 49.8% of women. Women were less active than men. Participant proportions in the lowest physical activity level category increased across ascending pain dimension quintiles in both sexes, whereas the opposite association was observed for all other physical activity-level categories. Smoking behaviour was different between sexes with more women (58.5%) than men (34.9%) having never smoked, although the proportion of men and women identified as current smokers was similar (10.3% and 9.9%, respectively).

[Table 1 about here]

Prevalent illness (history of asthma, COPD, cancer, diabetes mellitus, myocardial infarction and/or stroke) was reported in 18.7% of men and 17.9% of women. Self-reported depression (with required treatment) was higher in women (18.0%) than in men (9.3%). Prevalence of other self-

reported psychiatric illness was similar between men and women (2.8% and 3.1%, respectively). Increasing level of self-reported pain was associated with lower level of MH-related quality of life (MH, ER, SF and MCS) in both sexes.

### **Dimension of pain and MH-related status**

Binary logistic regression models reporting on good and poor MH showed reduced odds of having frequent pain and severe interference (Q5) for self-reported quality of life with good MH (adjusted odds ratio (OR) (95% confidence interval (CI) = 0.75 (0.64, 0.88) in men and 0.60 (0.50, 0.72) in women, Model E). Participants with poor MH showed increased odds of having frequent pain and high interference (Q5) for self-reported pain-related quality of life (OR (95% CI) = 1.35 (1.19, 1.54) in men and 1.39 (1.25, 1.55) in women; Model E). Similar associations were found for MCS score (Table 2). Table 3 presents odds ratios for poor MH and MCS for different exposures entered simultaneously into logistic regression models which included highest pain dimension category (low SF-36 pain score/bottom 20% of the sample), manual social class, high deprivation, low educational attainment, low physical activity, smoking, low fruit and vegetable consumption and self-reported illnesses. Frequent pain and showing high interference in quality of life due to pain is most strongly associated with poor MH assessed by MH and MCS of the SF-36. Participants in pain dimension category Q5 (bottom 20%) showed odds ratios of 4.89 (95% CI = 4.00, 5.97) and 4.47 (95% CI = 3.80, 5.25) for poor MH in men and women, respectively, when compared to the other four pain dimension categories. Unadjusted linear regressions models showed a reduction in MH, ER and SF with increasing frequency of pain and interference in quality of life. Scores were adjusted cumulatively and remained relatively stable for each outcome in all models (Models A to E). There was no difference between regression slopes for men and women (Supplementary Table 1).

[Table 2 about here]

[Table 3 about here]

## Discussion

### Summary of results

This article reports a large-scale, cross-sectional assessment of pain dimension–related quality of life over a period of 4 weeks and its association with MH–related domains in a cohort representative of the general British population. The main findings suggest that after adjusting for multiple potentially confounding factors, there is a strong and significant association between both constructs in men and women. Reporting low quality of life due to pain is independently associated with approximately 4- to 5-fold increased odds of being in poor MH as well as poor mental functional health (MCS) which incorporates ER and SF (see Table 3). These results are extremely relevant if we consider the significant impact of cognitive and behavioural variables on pain experience which has been shown in many previous studies.<sup>4,5,13,28</sup> Although the co-occurrence of depression or anxiety and pain may vary from study to study, both components are accepted and well established as highly influential factors determining the subjective experience of pain and treatment outcome.<sup>6,8,10,29–32</sup>

### Clinical implications

Treatment outcome and efficacy of enduring pain symptoms and its related restrictions in everyday life are closely linked to subjective expectations.<sup>8</sup> This does not only apply to mentally ill individuals but especially to those with depressive thoughts.<sup>28,33</sup> In other words, depressive behaviour might prevent therapeutic success because individuals tend to maintain in a vicious cycle of perpetual treatment failure and continued pain which may result in chronification of disease.<sup>8,28</sup> Research in chronic pain patients suffering from MH issues showed more serious consequences compared to those suffering from pain only. This included more functional impairments and more severe psychological distress.<sup>11,14,34,35</sup> Ratcliffe et al.<sup>7</sup> found a link between several chronic pain conditions and suicidal ideation or suicide attempts and demonstrated that in patients suffering from both conditions, this relationship significantly increased. As our results confirm a strong relationship in a general population, it seems plausible that an early intervention may reduce the risk of chronification and its association with suicidal behaviour.

The study findings also suggest that clinicians should be aware of the full spectrum of MH-related impairments which occur with increased interference in every-day tasks. Therefore, the assessment of mental disorder status in primary and specialised care among patients which report frequent pain and low quality of life due to pain is even more important. Furthermore, it is also important to remember that pain symptoms are even more prevalent in these individuals compared to the general population.<sup>10</sup> The co-occurrence of emotional distress and pain should not be treated as two distinct problems. Rather than focusing on a dualistic view of primary and secondary diagnoses, identifying factors most likely underlying both conditions could provide guidance for intervention and prospective treatment. As further binary logistic regression analyses showed, MH is more strongly related to higher pain dimension categories when compared with other vulnerability variables such as socio-economic factors or lifestyle behaviour. Unexpectedly, men showed higher odds ratios of poor MH when reporting frequent pain and high interference with quality of life due to pain compared to women. This was also the case when including other MH-related scores, such as ER or SF. However, women's MH was more often significantly impaired by other factors such as smoking, which was not the case in men. Research has shown that MH-related disorders, especially depression, are more prevalent in women than in men.<sup>36</sup> However, in this particular study, men seem to be at higher risk to suffer from poor MH when experiencing frequent and interfering pain. This may also contribute to the debate of sex-specific differences in MH-related disorders and may initiate more critical views in the area of gender-specific psychopathology.<sup>26</sup>

### **Strengths, limitations and direction of further research**

It is important to remember that these findings are not necessarily unidirectional and identifying factors for the causality of these associations is not possible using cross-sectional population data. Despite evidence suggests that depressive disorders are accompanied by more vulnerability factors, we do not know whether poor MH is an antecedent or a consequence of pain/ pain dimension or both. Environmental factors such as stress reactions may underlie both pain and MH and therefore increase their co-occurrence.<sup>37</sup> Moreover, information on the different site and/or causes of pain would allow stratification, which would be very informative, but unfortunately this data were not available.

Identifying individuals at risk is probably one of the most challenging research questions in future studies of these conditions. Although, the SF-36 is widely used for medical assessment and research,<sup>38,39</sup> the data of the EPIC- Norfolk cohort were moderately, negatively skewed and showed a categorical rather than a continuous distribution in some of the relevant variables. This might be attributed to the limited number of items tested for each variable. Additionally, the skewed data distribution might also be susceptible to ceiling effects in healthy participants. A noticeable number of healthy individuals reached the SF-36 highest score (100) which made discrimination between subjects more difficult. Using more precise psychiatric measurements to evaluate limitations due to emotional problems or SF would give further insight into their association with dimension of pain. Future studies should bear in mind the complexity of the subjective pain interference with quality of life and its association with MH-related quality of life. Even though correlational studies are an important contribution to understand the association between these two constructs, concrete intervention methods should be tested in order to provide effective guidelines for clinicians. As pain as well as MH conditions are two of the most common reasons to seek health care,<sup>1</sup> effective intervention and prevention of chronification may have a positive impact on excess mortality in chronic pain patients as well as on economical expenses.

## **Conclusion**

Results of this study suggest a strong association between self-reported pain dimension and self-reported mental functional health. Clinicians should be aware of the full spectrum of psychological distress and disorders associated with interference due to pain including any limitations due to emotional problems or SF. Although our findings are not necessarily unidirectional, the strong link supports previous findings in the area of pain research and adds evidence of the association of a general representative population taking into account many potentially confounding factors.<sup>6</sup> Although further research is needed to provide concrete intervention methods for clinicians, these findings provide robust evidence for recommendation of thorough psychological assessment in individuals with pain symptoms. Appropriate pain management is necessary to reduce the burden of poor mental

well-being at a population level. MH assessment should therefore be an integral part of clinical assessment in both primary and secondary care settings.

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#### *Contributorship*

PKM conceived the idea. KTK is one of the PIs of EPIC-Norfolk cohort. RNL was responsible for data management. AW performed literature search, developed analysis plan (supervised by PKM, ADW, and GTJ) and analysed data (supervised by ADW and DV). AW, ADW and PKM drafted the paper. All authors contributed in interpretation of results and in making an important intellectual contribution to the manuscript. PKM is the guarantor.

#### *Declaration of Conflicting Interests*

The Authors declare that there is no conflict of interest.

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**Table 1.** Distribution of characteristics in 16,051 men and women of the EPIC-Norfolk cohort by decreasing quality of life due to pain in increasing quintile categories.

Variable	Total	Pain dimension categories (quintiles) <sup>a</sup>					$\chi^2$ or p-value for trend <sup>b,c</sup>
		Q1	Q2	Q3	Q4	Q5	
<b>Men (n=7119)</b>	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	
By age (years)	59.70 (9.12)	58.80 (9.11)	59.54 (8.85)	59.73 (9.24)	60.04 (9.18)	61.76 (8.92)	<0.0001
By BMI (kg/m <sup>2</sup> )	26.41 (3.20)	26.09 (3.04)	26.20 (3.06)	26.55 (3.08)	26.54 (3.18)	27.28 (3.79)	<0.0001
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	
<i>Socio-economic factors</i>							
Educational attainment							<0.0001
No qualification	1977 (27.8)	593 (26.1)	334 (22.1)	300 (27.4)	436 (31.5)	314 (36.6)	
O-level or equivalent	625 (8.8)	225 (9.9)	138 (9.1)	92 (8.4)	104 (7.5)	66 (7.7)	
A-level or equivalent	3363 (47.2)	1060 (46.7)	729 (48.2)	526 (48.1)	651 (47.1)	397 (46.2)	
Degree or equivalent	1154 (16.2)	392 (17.3)	313 (20.7)	176 (16.1)	191 (13.8)	82 (9.5)	
Marital status							0.67
Single	282 (4.0)	99 (4.4)	67 (4.4)	42 (3.8)	45 (3.3)	29 (3.4)	
Married	6333 (89.0)	2000 (88.1)	1357 (89.6)	983 (89.9)	1232 (89.1)	761 (88.6)	
Widowed	191 (2.7)	65 (2.9)	37 (2.4)	22 (2.0)	40 (2.9)	27 (3.1)	
Separated	59 (0.8)	20 (0.9)	11 (0.7)	8 (0.7)	14 (1.0)	6 (0.7)	
Divorced	254 (3.6)	86 (3.8)	42 (2.8)	39 (3.6)	51 (3.7)	36 (4.2)	
Occupational social class <sup>d</sup>							<0.0001
I	596 (8.4)	212 (9.3)	164 (10.8)	101 (9.2)	86 (6.2)	33 (3.8)	
II	2876 (40.4)	961 (42.3)	664 (43.9)	421 (38.5)	545 (39.4)	285 (33.2)	
III non-manual	928 (13.0)	288 (12.7)	208 (13.7)	139 (12.7)	178 (12.9)	115 (13.4)	
III manual	1653 (23.2)	509 (22.4)	279 (18.4)	273 (25.0)	336 (24.3)	256 (29.8)	
IV	886 (12.4)	249 (11.0)	160 (10.6)	137 (12.5)	204 (14.8)	136 (15.8)	
V	180 (2.5)	51 (2.2)	39 (2.6)	23 (2.1)	33 (2.4)	34 (4.0)	
Townsend category <sup>e</sup>							<0.0001
1 (< -3.81)	1433 (20.1)	464 (20.4)	317 (20.9)	246 (22.5)	262 (19.0)	144 (16.8)	
2 (-3.81 to -2.92)	1588 (22.3)	508 (22.4)	372 (24.6)	241 (22.0)	295 (21.3)	172 (20.0)	
3 (-2.93 to -2.08)	1383 (19.4)	445 (19.6)	288 (19.0)	192 (17.6)	295 (21.3)	163 (19.0)	
4 (-2.09 to -0.61)	1417 (19.9)	475 (20.9)	282 (18.6)	217 (19.8)	266 (19.2)	177 (20.6)	
5 ( $\geq$ -0.62)	1298 (18.2)	378 (16.7)	255 (16.8)	198 (18.1)	264 (19.1)	203 (23.6)	
<i>Lifestyle factors</i>							
Alcohol consumption (units/ week)							<0.0001
None	906 (12.7)	259 (11.4)	179 (11.8)	131 (12.0)	179 (13.0)	158 (18.4)	
Up to <7	5972 (83.9)	1931 (85.1)	1290 (85.2)	922 (84.3)	1156 (83.6)	673 (78.3)	
$\geq$ 7	241 (3.4)	80 (3.5)	45 (3.0)	41 (3.7)	47 (3.4)	28 (3.3)	
Fruit and vegetables (portion/ day)							0.07
<3	844 (11.9)	271 (11.9)	174 (11.5)	117 (10.7)	168 (12.2)	114 (13.3)	
3-5	3381 (47.5)	1059 (46.7)	740 (48.9)	551 (50.4)	613 (44.4)	418 (48.7)	
>5	2894 (40.7)	940 (41.4)	600 (39.6)	426 (38.9)	601 (43.5)	327 (38.1)	
Physical activity category							<0.0001
Inactive	2052 (28.8)	599 (26.4)	399 (26.4)	320 (29.3)	398 (28.8)	336 (39.1)	
Moderately inactive	1788 (25.1)	574 (25.3)	395 (26.1)	287 (26.2)	337 (24.4)	195 (22.7)	
Moderately active	1705 (23.9)	544 (24.0)	390 (25.8)	263 (24.0)	337 (24.4)	171 (19.9)	
Active	1574 (22.1)	553 (24.4)	330 (21.8)	224 (20.5)	310 (22.4)	157 (18.3)	
Smoking status							<0.0001
Current smoker	736 (10.3)	252 (11.1)	126 (8.3)	100 (9.1)	149 (10.8)	109 (12.7)	
Former smoker	3901 (54.8)	1162 (51.2)	823 (54.4)	614 (56.1)	764 (55.3)	538 (62.6)	
Never smoked	2482 (34.9)	856 (37.7)	565 (37.3)	380 (34.7)	469 (33.9)	212 (24.7)	

*Medical History*

Depression (with treatment)							<0.0001
Yes	661 (9.3)	134 (5.9)	135 (8.9)	96 (8.8)	176 (12.7)	120 (14.0)	
No	6458 (90.7)	2136 (94.1)	1379 (91.1)	998 (91.2)	1206 (87.7)	739 (86.0)	
Psychiatric illness							0.001
Yes	196 (2.8)	47 (2.1)	36 (2.4)	23 (2.1)	55 (4.0)	35 (4.1)	
No	6923 (97.2)	2223 (97.9)	1478 (97.6)	1071 (97.9)	1327 (96.0)	824 (95.9)	
Prevalent illness <sup>f</sup>							<0.0001
Yes	1328 (18.7)	366 (16.1)	231 (15.3)	206 (18.8)	293 (21.1)	232 (27.0)	
No	5791 (81.3)	1904 (83.9)	1283 (84.7)	888 (81.2)	1089 (78.8)	627 (8.8)	
	Mean (SE)	Mean (SE)	Mean (SE)	Mean (SE)	Mean (SE)	Mean (SE)	

*SF-36 Data*

SF-36: Mental health (MH)	79.15 (0.19)	83.56 (0.29)	81.98 (0.35)	78.95 (0.44)	75.03 (0.43)	69.43 (0.64)	<0.0001
SF-36: Emotional role (ER)	85.99 (0.35)	92.63 (0.46)	92.36 (0.55)	86.80 (0.86)	81.26 (0.88)	63.77 (1.46)	<0.0001
SF-36: Social functioning (SF)	87.82 (0.25)	94.34 (0.31)	94.51 (0.34)	89.62 (0.52)	84.18 (0.53)	62.38 (0.96)	<0.0001
SF-36: Mental component score (MCS)	53.02 (0.11)	54.43 (0.16)	54.41 (0.19)	53.12 (0.26)	51.81 (0.26)	48.65 (0.41)	<0.0001

**Women (n=8932)**

	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	
By age (years)	58.33 (9.07)	57.64 (8.92)	57.75 (8.76)	58.19 (9.23)	58.79 (9.11)	59.82 (9.35)	<0.0001
By BMI (kg/m <sup>2</sup> )	26.07 (4.30)	25.42 (3.79)	25.58 (3.94)	26.13 (4.38)	26.49 (4.50)	27.21 (4.93)	<0.0001
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	

*By socio-economic factors*

Educational attainment							<0.0001
No qualification	3353 (37.5)	919 (37.5)	587 (32.3)	468 (35.4)	762 (38.2)	617 (45.7)	
O-level or equivalent	1103 (12.3)	305 (12.5)	231 (12.7)	186 (14.1)	240 (12.0)	141 (10.5)	
A-level or equivalent	3373 (37.8)	932 (38.1)	694 (38.2)	508 (38.4)	764 (38.3)	475 (35.2)	
Degree or equivalent	1103 (12.3)	293 (12.0)	304 (16.7)	160 (12.1)	230 (11.5)	116 (8.6)	
Marital status							<0.0001
Single	364 (4.1)	103 (4.2)	84 (4.6)	58 (4.4)	72 (3.6)	47 (3.5)	
Married	6935 (77.6)	1912 (78.1)	1415 (77.9)	1057 (80.0)	1571 (78.7)	980 (72.6)	
Widowed	913 (10.2)	230 (9.4)	184 (10.1)	119 (9.0)	195 (9.8)	185 (13.7)	
Separated	100 (1.1)	34 (1.4)	18 (1.0)	9 (0.7)	22 (1.1)	17 (1.3)	
Divorced	620 (6.9)	170 (6.9)	115 (6.3)	79 (6.0)	136 (6.8)	120 (8.9)	
Occupational social class <sup>d</sup>							<0.0001
I	620 (6.9)	152 (6.2)	167 (9.2)	80 (6.1)	149 (7.5)	72 (5.3)	
II	3278 (36.7)	915 (37.4)	710 (39.1)	492 (37.2)	726 (36.4)	435 (32.2)	
III non-manual	1801 (20.2)	512 (20.9)	355 (19.5)	259 (19.6)	388 (19.4)	287 (21.3)	
III manual	1808 (20.2)	491 (20.0)	339 (18.7)	289 (21.9)	408 (20.4)	281 (20.8)	
IV	1107 (12.4)	294 (12.0)	191 (10.5)	157 (11.9)	259 (13.0)	206 (15.3)	
V	318 (3.6)	85 (3.5)	54 (3.0)	45 (3.4)	66 (3.3)	68 (5.0)	
Townsend category <sup>e</sup>							0.02
1 (< -3.81)	1777 (19.9)	524 (21.4)	407 (22.4)	257 (19.4)	359 (18.0)	230 (17.0)	
2 (-3.81 to -2.92)	1884 (21.1)	517 (21.1)	386 (21.3)	261 (19.7)	428 (21.4)	292 (21.6)	
3 (-2.93 to -2.08)	1792 (20.1)	482 (19.7)	362 (19.9)	284 (21.5)	396 (19.8)	268 (19.9)	
4 (-2.09 to -0.61)	1782 (20.0)	478 (19.5)	334 (18.4)	277 (21.0)	412 (20.6)	282 (20.9)	
5 (≥ -0.62)	1696 (19.0)	448 (18.3)	327 (18.0)	243 (18.4)	401 (20.1)	277 (20.5)	

*Lifestyle factors*

Alcohol consumption (units/ week)

None	2143 (24.0)	570 (23.3)	390 (21.5)	274 (20.7)	461 (23.1)	448 (33.2)	<0.0001
Up to <7	6767 (75.8)	1869 (76.3)	1421 (78.2)	1046 (79.1)	1532 (76.8)	899 (66.6)	
≥7	22 (0.2)	10 (0.4)	5 (0.3)	2 (0.2)	3 (0.2)	2 (0.1)	
Fruit and vegetables (portion/ day)							0.001
<3	518 (5.8)	154 (6.3)	86 (4.7)	58 (4.4)	110 (5.5)	110 (8.2)	
3-5	3303 (37.0)	878 (35.9)	692 (38.1)	493 (37.3)	750 (37.6)	490 (36.3)	
>5	5111 (57.2)	1417 (57.9)	1038 (57.2)	771 (58.3)	1136 (56.9)	749 (55.5)	
Physical activity category							<0.0001
Inactive	2371 (26.5)	609 (24.9)	404 (22.2)	342 (25.9)	524 (26.3)	492 (36.5)	
Moderately inactive	2949 (33.0)	763 (31.2)	642 (35.4)	437 (33.1)	706 (35.4)	401 (29.7)	
Moderately active	2124 (23.8)	607 (24.8)	481 (26.5)	312 (23.6)	458 (22.9)	266 (19.7)	
Active	1488 (16.7)	470 (19.2)	289 (15.9)	231 (17.5)	308 (15.4)	190 (14.1)	
Smoking status							<0.0001
Current smoker	888 (9.9)	236 (9.6)	148 (8.1)	133 (10.1)	196 (9.8)	175 (13.0)	
Former smoker	2822 (31.6)	678 (27.7)	560 (30.8)	417 (31.5)	668 (33.5)	499 (37.0)	
Never smoked	5222 (58.5)	1535 (62.7)	1108 (61.0)	772 (58.4)	1132 (56.7)	675 (50.0)	
<i>Medical History</i>							
Depression (with treatment)							<0.0001
Yes	1609 (18.0)	319 (13.0)	277 (15.3)	223 (16.9)	437 (21.9)	353 (26.2)	
No	7323 (82.0)	2130 (87.0)	1539 (84.7)	1099 (83.1)	1559 (78.1)	996 (73.8)	
Psychiatric illness							0.06
Yes	280 (3.1)	68 (2.8)	49 (2.7)	40 (3.0)	64 (3.2)	59 (4.4)	
No	8652 (96.9)	2381 (97.2)	1767 (97.3)	1282 (97.0)	1932 (96.8)	1290 (95.6)	
Prevalent illness <sup>f</sup>							<0.0001
Yes	1603 (17.9)	371 (15.1)	260 (14.3)	230 (17.4)	402 (20.1)	340 (25.2)	
No	7329 (82.1)	2078 (84.9)	1556 (85.7)	1092 (82.6)	1594 (79.9)	1009 (74.8)	
	Mean (SE)	Mean (SE)	Mean (SE)	Mean (SE)	Mean (SE)	Mean (SE)	
<i>SF-36 Data</i>							
SF-36: Mental health (MH)	76.13 (0.17)	81.35 (0.29)	79.37 (0.33)	75.79 (0.41)	73.26 (0.37)	66.87 (0.49)	<0.0001
SF-36: Emotional role (ER)	82.70 (0.34)	90.61 (0.50)	89.18 (0.60)	84.33 (0.83)	79.63 (0.76)	62.58 (1.17)	<0.0001
SF-36: Social functioning (SF)	86.45 (0.22)	93.41 (0.31)	93.62 (0.33)	89.50 (0.45)	84.92 (0.43)	63.42 (0.72)	<0.0001
SF-36: Mental component score (MCS)	51.76 (0.10)	53.31 (0.17)	53.12 (0.19)	51.77 (0.25)	51.24 (0.23)	47.85 (0.32)	<0.0001

Note. SF-36 data was recorded 18 months after the first health check (1HC).

<sup>a</sup> Quality of life in relation to pain decreases with each ascending category; Q1 presenting no interference and Q5 severe interference with quality of life. Quintile cut-off points are based on the SF-36 scale with 0 indicating severe and 100 no interference due to pain, they are the same for men and women. Pain dimension cut-offs are Q1=100, Q2= 84, Q3=72, Q4= 51, Q5<51. In general, SF-36 scores of 0 represents poor and 100 represents good health.

<sup>b</sup> Based on ANOVA (1) with age/ BMI as dependent or (2) SF-36 data as dependent variable and pain quintile categories as fixed factor.

<sup>c</sup> Based on Chi-Square ( $\chi^2$ ) Test of Independence for all categorical variables.

<sup>d</sup> Occupational social class: I= professional, II= managerial and technical, III= non-manual skilled, III manual skilled, IV partly skilled manual, V= unskilled manual.

<sup>e</sup> Townsend categories are presented as 1= least deprived to 5= highly deprived.

<sup>f</sup> Prevalent illnesses: Asthma/ COPD, cancer, diabetes mellitus, myocardial infarct and/ or stroke.

**Table 2.** Binary logistic regression models presenting odds ratio and corresponding 95% confidence intervals reporting good and poor mental health defined by using SF-36 mental health (MH) and the mental component summary (MCS) top and bottom 20<sup>th</sup> percentile scores, respectively, in 7119 men and 8932 women of the EPIC-Norfolk cohort.

		Odds Ratio (95% confidence intervals)			
		Men	Women	Men	Women
		Good MH		Good MCS	
Model <sup>a-e</sup>	A	0.77 (0.66, 0.90)**	0.60 (0.50, 0.72)***	1.02 (0.91, 1.15)	0.94 (0.84, 1.05)
	B	0.73 (0.62, 0.86)***	0.59 (0.49, 0.70)***	0.97 (0.86, 1.09)	0.90 (0.80, 1.01)
	C	0.74 (0.63, 0.86)***	0.59 (0.49, 0.70)***	0.97 (0.86, 1.09)	0.90 (0.80, 1.01)
	D	0.74 (0.63, 0.87)***	0.59 (0.50, 0.71)***	0.97 (0.86, 1.10)	0.91 (0.81, 1.02)
	E	0.75 (0.64, 0.88)***	0.60 (0.50, 0.72)***	0.99 (0.87, 1.12)	0.92 (0.82, 1.03)
		Poor MH		Poor MCS	
Model <sup>a-e</sup>	A	1.37 (1.22, 1.56)***	1.43 (1.30, 1.58)***	1.45 (1.28, 1.65)***	1.43 (1.30, 1.59)***
	B	1.41 (1.25, 1.60)***	1.44 (1.30, 1.60)***	1.48 (1.31, 1.68)***	1.45 (1.31, 1.60)***
	C	1.41 (1.24, 1.59)***	1.44 (1.31, 1.60)***	1.48 (1.30, 1.68)***	1.44 (1.30, 1.60)***
	D	1.40 (1.23, 1.58)***	1.43 (1.29, 1.58)***	1.46 (1.29, 1.66)***	1.43 (1.29, 1.58)***
	E	1.35 (1.19, 1.54)***	1.39 (1.25, 1.55)***	1.42 (1.25, 1.62)***	1.39 (1.25, 1.55)***

*Note.* Cut-off points for the dependent variables (MH, MCS) are based on the SF-36 scale with 0 indicating poor and 100 good health, they are the same for men and women with MH SF-36 scores of <64.00 (bottom 20<sup>th</sup> percentile) and >92.00 (top 20<sup>th</sup> percentile) and MCS SF-36 scores of <46.12 (bottom 20<sup>th</sup> percentile) and >59.35 (top 20<sup>th</sup> percentile). The cut-off point for the predictor variable (pain dimension score) is the bottom 20<sup>th</sup> percentile with a score of <51 (Q5=severe interference in quality of life due to pain). Any significant p-values are marked with \*\* p=0.001 and \*\*\* p<0.0001. SF-36 data (pain, MH, ER, SF) was measured at the 18-months follow-up.

<sup>a</sup> Model A is unadjusted with MH or MCS as dependent variables and pain categories as independent variable.

<sup>b</sup> Model B is adjusted for age and BMI measured at the first health check.

<sup>c</sup> Model C is adjusted for age, BMI and socio-economic factors (occupational social class, townsend category, marital status, educational attainment).

<sup>d</sup> Model D is adjusted for age, BMI, socio-economic factors and lifestyle (physical activity, smoking status, alcohol, fruit and vegetable consumption).

<sup>e</sup> Model E is adjusted for age, BMI, socio-economic factors, lifestyle and medical history (self-reported depression with required treatment, self-reported psychiatric illness, prevalent illness (Asthma/ COPD, cancer, diabetes mellitus, myocardial infarct and/ or stroke).

**Table 3.** Binary logistic regression models presenting odds ratio and corresponding 95% confidence intervals reporting poor mental health defined by using SF-36 mental health (MH) and the mental component summary (MCS) bottom 20<sup>th</sup> percentile scores in 7119 men and 8932 women of the EPIC-Norfolk cohort.

	Odds ratio (95% confidence interval)			
	Men	Women	Men	Women
	Poor MH		Poor MCS	
Severe interference in quality of life due to pain <sup>a</sup>	4.89 (4.00, 5.97)***	4.47 (3.80, 5.25)***	4.64 (3.80, 5.66)***	3.74 (3.18, 4.39)***
Being in manual social class categories <sup>b</sup>	1.12 (0.98, 1.29)	1.15 (1.03, 1.28)*	1.13 (0.99, 1.30)*	1.01 (0.90, 1.13)
Living in highly deprived areas <sup>c</sup>	1.27 (1.07, 1.51)*	1.15 (1.00, 1.33)*	1.35 (1.13, 1.60)**	1.28 (1.11, 1.47)**
Low educational attainment <sup>d</sup>	0.95 (0.83, 1.09)	1.16 (1.04, 1.29)*	0.96 (0.83, 1.10)	0.97 (0.87, 1.08)
Being physical inactive	1.02 (0.89, 1.16)	1.07 (0.96, 1.19)	1.06 (0.93, 1.21)	1.09 (0.98, 1.22)
Being a current smoker	1.05 (0.86, 1.29)	1.47 (1.25, 1.73)***	1.11 (0.91, 1.37)	1.52 (1.30, 1.79)***
Low fruit and vegetable consumption <sup>e</sup>	1.31 (1.09, 1.58)*	1.51 (1.23, 1.85)***	1.17 (0.96, 1.42)	1.30 (1.05, 1.60)*
Self-reported prevalent illness <sup>f</sup>	1.19 (1.02, 1.39)*	1.04 (0.91, 1.19)	1.24 (1.05, 1.45)*	1.09 (0.95, 1.24)

*Note.* Cut-off points for the dependent variables are based on the SF-36 scale with 0 indicating poor and 100 good health, they are the same for men and women. Cut-off for poor MH is a SF-36 score of <64.00 and for poor MCS a SF-36 score of <46.12. Both represent the bottom 20<sup>th</sup> percentile of the population, the 80<sup>th</sup> percentile is used as reference category. Any significant p-values are marked with \* p<0.05, \*\* p=0.001 and \*\*\* p<0.0001. All independent variables are adjusted by any relevant co-variables occurring in this table, plus additionally, for self-reported depression (with required treatment) and psychiatric illness at the baseline. SF-36 data (pain dimension score, MH, MCS) was measured at the 18-months follow-up.

<sup>a</sup> Presented by the bottom 20% of the sample; Q5 cut-off point is a SF-36 score of <51.

<sup>b</sup> Manual occupational social classes include manual skilled, partly skilled and unskilled manual workers.

<sup>c</sup> Any values <0 are classified as less deprived, any values ≥0 are classified as highly deprived.

<sup>d</sup> Low educational attainment includes no qualification or equivalent and O-Levels or equivalent.

<sup>e</sup> Eating less than 3 portions/ day.

<sup>f</sup> Prevalent illnesses: Asthma/ COPD, cancer, diabetes mellitus, myocardial infarct and/ or stroke.