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Adding salt to foods and risk of incident depression and anxiety

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Abstract

Background Diet is a well-known determinant of mental health outcomes. However, epidemiologic evidence on salt consumption with the risk of developing depression and anxiety is still very limited. This study aimed to examine the association between adding salt to foods and incident depression and anxiety longitudinally.

Methods This study used data from 444,787 adults who had never been diagnosed with depression or anxiety at baseline from the UK Biobank, a national community-based cohort from 2006 to 2010. Adding salt to foods was measured using a four-point Likert scale at baseline from a touch-screen questionnaire. The outcomes were incidents of diagnosed depression (F32-F33) and anxiety (F40-F48), defined by the International Statistical Classification of Diseases and Related Health Problems, 10th Revision codes. Cox proportional hazards models were used to investigate the association between the frequency of adding salt to foods and incident depression and anxiety.

Results During a mean follow-up period of 14.5 years, 16,319 incidents of depression and 18,959 incidents of anxiety were documented. A higher frequency of adding salt to foods was associated with elevated risk for depression and anxiety. Compared with the group of never/rarely adding salt to foods, the adjusted HRs of incident depression were 1.07 (95% CI: 1.02–1.12), 1.18 (95% CI: 1.10–1.26), and 1.29 (95% CI: 1.18–1.41) across the groups of sometimes, usually, and always, respectively (P trend < 0.001). Participants who reported always adding salt to foods had a 1.17-fold higher risk for developing anxiety (95% CI: 1.07–1.28) compared with those who never/rarely added salt to foods.

Conclusions A higher frequency of adding salt to foods was independently associated with a higher hazard of depression and anxiety. Interventions such as public awareness campaigns promoting reduced salt consumption may be promising preventative measures to reduce the incidence of depression and anxiety.

Keywords Adding salt to foods, Depression, Anxiety

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Background

Mental disorders are major contributors to the global health-related burden. The Global Burden of Disease Study (GBD) 2021 showed that depressive disorders ranked as the second leading cause of years lived with disability, while anxiety disorders as the sixth [1]. The emergence of the COVID-19 pandemic exacerbated determinants of poor mental health, resulting in a significant increase in the prevalence of both major depressive disorder (27.6%) and anxiety disorders (25.6%) [2]. In 2021, an estimated 332 million (95% UI 298–376) people worldwide were affected by depressive disorders [1]. Given that depressive disorders are rarely detected at their onset and that only a small proportion of individuals receive minimally adequate evidence-based treatment, identifying modifiable factors and developing preventive strategies is crucial [3, 4]. The pressing need for preventative strategies also extends to anxiety disorder, which commonly co-occurs with depressive disorders and exacerbates the disease burden in affected individuals [5, 6].

Diet is a well-known determinant of mental health outcomes. Salt liking, for instance, has been linked to mental disorders. An Australian population survey reported that higher salt liking (pleasantness) was correlated with Depression, Anxiety, and Stress Scale-21 scores indicative of severe depression and anxiety [7]. Similarly, a biomarker study on depression treatment suggested that higher salt liking was associated with longer disease duration in depressive disorders [8]. Furthermore, studies in healthy populations found that individuals with high trait anxiety had higher salt taste thresholds [9, 10]. In addition to self-reported preference for salty foods, salt consumption can be evaluated using the reported frequency of adding salt to food at the table. Adding salt to foods is a common eating behavior shaped by an individual's preference for salt and habitual salt intake over the long term [11, 12]. It accounted for 6–20% of total salt consumption in the Western diet and was less likely to be influenced by day-to-day variations [13, 14]. Therefore, adding salt at the table provides a unique assessment to investigate the association between long-term salt taste preference and depression/anxiety. However, despite mounting evidence pointing toward the potential relationship between salt and mental health, very few studies have examined the association of adding salt to foods with depression and anxiety risk.

In the prospective study, we aimed to evaluate the association between the frequency of adding salts to foods and the risk of developing depression and anxiety and further investigate whether genetic predisposition to depression modifies the association.

Methods

Study population

The UK Biobank is a large population-based prospective cohort including over half a million participants aged 37 to 73 years when recruited from 2006 to 2010. Details of the study design have been described elsewhere [15]. For this study, data from 502,422 participants were available. We excluded 56,620 participants with a baseline diagnosis of depression or anxiety, 1007 participants with incomplete data regarding the frequency of adding salt to foods, and eight participants with missing dates of baseline assessment center attendance. A total of 444,787 participants were included in the final analysis. The flowchart of the study population is presented in Additional file 1: Fig. S1. The UK Biobank was approved by the North West Multi-Centre Research Ethics Committee and all participants provided written informed consent.

Exposure assessment

Information on the frequency of adding salt to foods was collected using a touch-screen questionnaire at baseline (2006–2010) [16]. Participants were asked to respond to the question "Do you add salt to your foods? (Do not include salt used in cooking)," and select one answer from four options: (1) never/rarely, (2) sometimes, (3) usually, or (4) always. Those who preferred not to answer were excluded from the final analysis. Additionally, participants were asked, "Have you made any major changes to your diet in the last 5 years?" in the baseline questionnaire. They chose one of the following options: (1) no; (2) yes, because of illness; or (3) yes, because of other reasons.

Outcome identification

Participants diagnosed with depression or anxiety during follow-up were ascertained using the first occurrence of health outcomes in the UK Biobank, which synthesized data from hospital inpatient records, primary care, and death registry data. Incidents of depression and anxiety were defined by International Statistical Classification of Diseases and Related Health Problems, 10th Revision (ICD-10) codes F32-F33 and F40-F48, respectively. Follow-up time was calculated from the date of baseline assessment to diagnosis of depression or anxiety, death, or the censoring date (June 5, 2024), whichever came first.

Statistical analysis

Demographic characteristics were presented as mean with SD for continuous variables and as absolute number (percentage) for categorical variables. The chi-square tests for categorical variables and general linear models for continuous variables were performed to compare

proportions or means of characteristics between participants with different frequencies of adding salt to foods. Cox proportional hazards models were used to evaluate the association between the frequency of adding salt to foods and the risk of developing depression and anxiety. The proportional hazards assumption was tested by the Kaplan–Meier method and Schoenfeld residuals, and no violation was found. Several potential confounders were adjusted in these models, including age (years, continuous), sex (male or female), race (White or non-White), education level (years, continuous), income (< £18,000, £18,000–£30,999, £31,000–£51,999, £52,000–£100,000, > £100,000, or "do not know"), Townsend deprivation index (TDI, continuous), body mass index (BMI, continuous), smoking status (never, past, or current), alcohol consumption (never, past, or current), healthy diet score (0, 1, 2, 3, 4, or 5) [17, 18], physical activity (high, moderate, or low), sleep behaviors (healthy, intermediate, or poor) [19, 20], diabetes (yes or no), hypertension (yes or no), cholesterol (mmol/L, continuous), cardiovascular disease (CVD, yes or no), spot urinary sodium, and depression polygenic risk score (PRS). The definition of healthy diet score was based on the corresponding median consumption (vegetable intake at least 4 tbsp/day, fruit intake at least 3 pieces/day, fish intake at least twice per week, unprocessed red meat intake no more than twice per week, and processed meat intake less than twice per week). Among the covariates, BMI was calculated using weight (kg) measured with a Tanita BC-418 MA body composition analyzer and height (m) measured with a Seca 202 device. Biochemistry markers, including cholesterol levels, were assayed using the AU5800 analytical platform (Beckman Coulter). Sociodemographic factors, dietary intake, and lifestyle factors were self-reported. Baseline health conditions, including diabetes, hypertension, and cardiovascular disease, were identified through hospital inpatient records, primary care data, death registries, and self-reported questionnaires. Detailed assessments for confounders are described in the Additional file 1.

We hypothesized that the association between the frequency of adding salt to foods and incidents of depression or anxiety may be modified by sex (female or male), age (< 60 or ≥ 60 years), TDI (quintiles 1, quintiles 2–4, quintile 5), education level (< 16 years or ≥ 16 years), BMI (18.5–25, 25–30, ≥ 30 kg/m^2), physical activity (high, moderate, or low), 24-h weighted average noise (≤ median or > median), and depression PRS (tertile 1, tertile 2, or tertile 3). Stratified analyses with hazard ratios (HRs) and 95%CIsestimated within the strata were conducted. Multiplicative interaction was assessed by adding interaction terms to the Cox models.

Several sensitivity analyses were performed to verify the robustness of the results. First, to minimize the influence of reverse causation, we excluded depression and anxiety cases that occurred in the first year of follow-up. Second, to control for the impact of diet change on the frequency of adding salt to foods, we excluded participants who had changed their diet in the last 5 years due to illness or other reasons. Third, we performed a sensitivity analysis by further adjusting for total energy intake in participants with available data. Fourth, we excluded individuals with hypertension at baseline. Fifth, we further adjusted the estimated glomerular filtration rate (eGFR). Sixth, we adjusted for education level as a categorical variable (university or nonuniversity) rather than a continuous one. Seventh, we conducted an additional sensitivity analysis, adjusting for further covariates, using "living with a spouse or partner" as an indicator of marital status and "cancer history of father, mother, and siblings" as an indicator of family members' health status. Finally, we conducted another sensitivity analysis by adjusting BMI PRS instead of BMI.

All statistical analyses were conducted using StataMP 17 and R version 4.0.3. All statistical tests were two-sided, and $P < 0.05$ was considered statistically significant. A Bonferroni-corrected 2-sided P value of 0.006 was used as the significance threshold for the eight interaction analyses due to multiple comparisons.

Results

Baseline characteristics of participants according to the frequency of adding salt to foods

Of the participants, 55.7% reported never/rarely adding salt to foods, 28.0% added salt sometimes, 11.6% usually, and 4.7% always (Table 1). Compared with participants with a lower frequency of adding salt to foods, participants with a higher frequency were more likely to be men, non-white, and to have higher TDI and BMI; were less likely to adopt a healthy lifestyle (never smoking, high physical activity, healthy diet); and had a lower prevalence of hypertension but a higher prevalence of CVD.

Association between the frequency of adding salt to foods and depression risk

During a mean follow-up of 14.5 years, 16,319 incident cases of depression were documented. After adjustment for age, sex, race, education, income, TDI, BMI, smoking, alcohol consumption, physical activity, healthy diet score, hypertension, diabetes, cholesterol, CVD, healthy sleep behaviors, spot urinary sodium, and depression PRS, the hazard of depression increased monotonously with increasing frequency of adding salts to foods. The adjusted HRs were 1.00 (reference),

Table 1 Baseline characteristics according to the frequency of adding salt to foods, 2006–2010

Characteristics	Overall (*n* = 444,787)	Never/rarely (*n* = 247,735)	Sometimes (*n* = 124,738)	Usually (*n* = 51,385)	Always (*n* = 20,929)
Age, mean (SD), years	56.6 (8.12)	56.6 (8.10)	56.5 (8.14)	57.1 (8.05)	56.1 (8.30)
Sex					
Male	208,784 (46.9%)	112,108 (45.3%)	59,098 (47.4%)	27,018 (52.6%)	10,560 (50.5%)
Female	236,003 (53.1%)	135,627 (54.7%)	65,640 (52.6%)	24,367 (47.4%)	10,369 (49.5%)
Race					
Whites	418,479 (94.1%)	236,212 (95.3%)	116,170 (93.1%)	47,901 (93.2%)	18,196 (86.9%)
Non-Whites	24,759 (5.6%)	10,664 (4.3%)	8164 (6.5%)	3296 (6.4%)	2635 (12.6%)
Education, mean (SD), years	15.0 (5.06)	15.2 (4.97)	14.8 (5.09)	14.6 (5.14)	13.3 (5.32)
Income, mean (SD)	3.61 (2.54)	3.62 (2.49)	3.61 (2.55)	3.55 (2.55)	3.61 (2.84)
< £18,000	81,249 (18.3%)	42,522 (17.2%)	23,071 (18.5%)	10,222 (19.9%)	5434 (26.0%)
£18,000–£30,999	95,602 (21.5%)	52,924 (21.4%)	26,890 (21.6%)	11,311 (22.0%)	4477 (21.4%)
£31,000–£51,999	99,364 (22.3%)	56,555 (22.8%)	27,884 (22.4%)	11,116 (21.6%)	3809 (18.2%)
£52,000–£100,000	79,305 (17.8%)	46,469 (18.8%)	21,672 (17.4%)	8597 (16.7%)	2567 (12.3%)
> £100,000	21,566 (4.8%)	12,711 (5.1%)	5884 (4.7%)	2380 (4.6%)	591 (2.8%)
Townsend deprivation index, mean (SD)	−1.35 (3.06)	−1.54 (2.96)	−1.26 (3.09)	−1.13 (3.15)	−0.259 (3.49)
BMI (kg/m2), mean (SD)	27.3 (4.71)	27.1 (4.65)	27.6 (4.73)	27.8 (4.72)	28.0 (5.00)
Drinking					
Never	19,548 (4.4%)	10,749 (4.3%)	5110 (4.1%)	2141 (4.2%)	1548 (7.4%)
Past	14,424 (3.2%)	8330 (3.4%)	3560 (2.9%)	1576 (3.1%)	958 (4.6%)
Current	410,330 (92.3%)	228,459 (92.2%)	115,906 (92.9%)	47,593 (92.6%)	18,372 (87.8%)
Smoking					
Never	245,412 (55.2%)	147,782 (59.7%)	65,741 (52.7%)	23,336 (45.4%)	8553 (40.9%)
Past	153,255 (34.5%)	80,346 (32.4%)	45,070 (36.1%)	20,289 (39.5%)	7550 (36.1%)
Current	44,415 (10.0%)	18,772 (7.6%)	13,409 (10.7%)	7540 (14.7%)	4694 (22.4%)
Healthy diet score, mean (SD)	3.06 (1.26)	3.19 (1.24)	2.99 (1.25)	2.79 (1.26)	2.57 (1.27)
IPAQ activity group					
Low	65,972 (14.8%)	35,300 (14.2%)	18,823 (15.1%)	8245 (16.0%)	3604 (17.2%)
Moderate	146,206 (32.9%)	83,394 (33.7%)	40,548 (32.5%)	16,402 (31.9%)	5862 (28.0%)
High	145,721 (32.8%)	82,865 (33.4%)	39,954 (32.0%)	16,421 (32.0%)	6481 (31.0%)
Sleep behaviors					
Healthy	7797 (1.8%)	3690 (1.5%)	2272 (1.8%)	1130 (2.2%)	705 (3.4%)
Intermediate	140,071 (31.5%)	74,350 (30.0%)	39,760 (31.9%)	18,004 (35.0%)	7957 (38.0%)
Poor	217,185 (48.8%)	125,365 (50.6%)	60,241 (48.3%)	23,280 (45.3%)	8299 (39.7%)
Hypertension	243,085 (54.7%)	137,121 (55.3%)	66,908 (53.6%)	27,837 (54.2%)	11,219 (53.6%)
Diabetes	22,982 (5.2%)	12,613 (5.1%)	6553 (5.3%)	2705 (5.3%)	1111 (5.3%)
CVD	30,322 (6.8%)	16,637 (6.7%)	8260 (6.6%)	3680 (7.2%)	1745 (8.3%)
Cholesterol, mean (SD), mmol/L	5.69 (1.10)	5.67 (1.10)	5.71 (1.10)	5.72 (1.11)	5.69 (1.12)

Abbreviations: *IPAQ* International Physical Activity Questionnaire, *SD* standard deviation, *CVD* cardiovascular disease

1.07 (95% CI: 1.02–1.12), 1.18 (95% CI: 1.10–1.26), and 1.29 (95% CI: 1.18–1.41) across the groups never/rarely, sometimes, usually, and always, respectively (P trend < 0.001, Table 2).

Association between the frequency of adding salt to foods and anxiety risk

For anxiety, 18,959 incidents were identified during a total of 6,426,051 person-years' follow-up. Participants

Table 2 The association between the frequency of adding salt to foods and hazard of depression and anxiety

	Never/rarely	Sometimes	Usually	Always	*P* value for trend
Depression					
Cases/total	8295/247,735	4667/124,738	2172/51,385	1185/20,929	
Person-years	3,609,878	1,808,201	738,661	295,641	
Unadjusted	1.00 (reference)	1.12 (1.08–1.16)	1.28 (1.22–1.34)	1.74 (1.64–1.85)	< 0.001
Sex and age adjusted	1.00 (reference)	1.13 (1.09–1.17)	1.31 (1.25–1.37)	1.76 (1.66–1.87)	< 0.001
Multivariable adjusted	1.00 (reference)	1.07 (1.02–1.12)	1.17 (1.10–1.25)	1.27 (1.16–1.38)	< 0.001
Further adjusted for depression PRS	1.00 (reference)	1.07 (1.02–1.12)	1.17 (1.10–1.25)	1.28 (1.17–1.40)	< 0.001
Further adjusted for spot urinary sodium	1.00 (reference)	1.07 (1.02–1.12)	1.18 (1.10–1.26)	1.29 (1.18–1.41)	< 0.001
Anxiety					
Cases/total	10,175/247,735	5370/124,738	2219/51,385	1195/20,929	
Person-years	3,591,125	1,801,757	737,896	295,273	
Unadjusted	1.00 (reference)	1.05 (1.02–1.09)	1.06 (1.01–1.11)	1.42 (1.34–1.51)	< 0.001
Sex and age adjusted	1.00 (reference)	1.06 (1.03–1.10)	1.10 (1.05–1.15)	1.46 (1.37–1.55)	< 0.001
Multivariable adjusted	1.00 (reference)	1.02 (0.98–1.07)	1.04 (0.97–1.10)	1.16 (1.07–1.27)	0.003
Further adjusted for depression PRS	1.00 (reference)	1.02 (0.98–1.07)	1.04 (0.98–1.11)	1.17 (1.07–1.28)	0.002
Further adjusted for spot urinary sodium	1.00 (reference)	1.02 (0.98–1.07)	1.04 (0.98–1.11)	1.17 (1.07–1.28)	0.002

Multivariable model adjusted for age, sex (male or female), ethnicity (White or non-White), education level, income, Townsend deprivation index (TDI), body mass index (BMI), smoking status (never, past, or current), alcohol drinking (never, past, or current), healthy diet score, physical activity (high, moderate, or low), sleep behaviors (healthy, intermediate, poor), diabetes (yes or no), hypertension (yes or no), cholesterol, and cardiovascular disease (CVD, yes or no)

who always added salt to foods were at significantly higher risk for anxiety compared to those who never/rarely added salt (HR 1.17, 95% CI: 1.07–1.28) (Table 2).

Subgroup analysis

No significant multiplicative interaction was observed between self-reported frequency of adding salt to foods and each confounder (e.g., age, sex, BMI, education level, TDI, noise, physical activity, and depression PRS) on developing depression and anxiety, as all *P* values for interaction were greater than the Bonferroni-adjusted threshold of 0.006 (Table 3).

Joint association of the frequency of adding salt to foods and depression prs with risk of depression and anxiety

Participants were classified into joint categories based on the frequency of adding salt to foods and tertiles of depression PRS, with those who never/rarely added salt to foods and were in the lowest depression PRS tertile as the reference (Fig. 1). Participants with the highest frequency of adding salt to foods (always) and the highest depression PRS tertile were at the greatest risk of incident depression (HR 1.78, 95% CI:1.54–2.05) and anxiety (HR 1.30, 95% CI:1.12–1.51). The association between adding salt to foods and the risk of depression appeared to be consistent and significant across all three depression PRS categories.

Sensitivity analysis

The results did not change appreciably after further excluding incidents that occurred during the first year of follow-up, excluding participants with hypertension at baseline, or those who had changed their diet in the last 5 years because of illness or other reasons. The findings remained robust after adjusting for education level as a categorical variable, using BMI PRS instead of BMI, and further adjusting for total energy intake, eGFR, living with a spouse or partner, and family cancer history (Additional file 1: Table S1).

Discussion

In this large prospective study, we observed that a higher frequency of adding salt to foods was associated with an increased risk of incident depression and anxiety, independent of socioeconomic status, lifestyle factors, preexisting diseases, and genetic susceptibility to depression. Furthermore, the association showed a robust dose-dependent increase.

Our findings on the adverse impact of frequently adding salt to foods with depression risk are consistent with previous studies. For instance, data from the National Health and Nutrition Examination Survey (NHANES), including more than 10,000 participants [21], showed that individuals with depression were more likely to add salt to their food. The salt CONNtrol trial demonstrated that salt restriction entailed improvement in depressive symptoms [22].

Several mechanisms could possibly explain the associations between the higher frequency of adding salt to foods and increased risks of depression and anxiety. First, sodium ions play a crucial role in terminating

Table 3 Stratified analyses for the association of self-reported frequency of adding salt to foods and risk of depression and anxiety

	Frequency of adding salt to foods					
	Never/rarely	**Sometimes**	**Usually**	**Always**	***P* value for trend**	***P* for interaction**
Depression						
Sex						0.1892
Male	1.00 (reference)	1.01 (0.94–1.10)	1.13 (1.02–1.24)	1.17 (1.02–1.34)	0.004	
Female	1.00 (reference)	1.11 (1.04–1.18)	1.21 (1.11–1.32)	1.37 (1.22–1.54)	< 0.001	
Age						0.6223
< 60	1.00 (reference)	1.05 (0.99–1.12)	1.14 (1.05–1.24)	1.31 (1.17–1.46)	< 0.001	
≥ 60	1.00 (reference)	1.09 (1.01–1.18)	1.22 (1.10–1.35)	1.25 (1.07–1.46)	< 0.001	
TDI						0.4838
Quintile 1	1.00 (reference)	1.02 (0.90–1.15)	1.27 (1.08–1.49)	1.38 (1.08–1.77)	0.001	
Quintiles 2–4	1.00 (reference)	1.09 (1.02–1.16)	1.15 (1.05–1.25)	1.35 (1.19–1.52)	< 0.001	
Quintile 5	1.00 (reference)	1.06 (0.96–1.17)	1.18 (1.04–1.34)	1.17 (1.00–1.38)	0.005	
Education level						0.1179
< 16 years	1.00 (reference)	1.12 (1.05–1.20)	1.15 (1.05–1.26)	1.33 (1.19–1.49)	< 0.001	
≥ 16 years	1.00 (reference)	1.01 (0.94–1.09)	1.21 (1.10–1.33)	1.23 (1.06–1.42)	< 0.001	
BMI						0.5084
18.5–25 kg/m^2	1.00 (reference)	1.08 (0.98–1.19)	1.16 (1.02–1.32)	1.16 (0.96–1.40)	0.009	
25–30 kg/m^2	1.00 (reference)	1.05 (0.97–1.14)	1.20 (1.08–1.33)	1.42 (1.24–1.62)	< 0.001	
≥ 30 kg/m^2	1.00 (reference)	1.07 (0.98–1.17)	1.17 (1.04–1.31)	1.21 (1.04–1.42)	0.001	
IPAQ activity group						0.2569
Low	1.00 (reference)	1.12 (1.01–1.24)	1.14 (1.00–1.30)	1.12 (0.94–1.35)	0.025	
Moderate	1.00 (reference)	1.08 (1.00–1.17)	1.19 (1.07–1.33)	1.29 (1.11–1.51)	< 0.001	
High	1.00 (reference)	1.02 (0.94–1.11)	1.18 (1.07–1.32)	1.39 (1.21–1.60)	< 0.001	
24-h weighted average noise						0.6815
≤ median	1.00 (reference)	1.04 (0.97–1.12)	1.16 (1.06–1.28)	1.26 (1.10–1.44)	< 0.001	
> median	1.00 (reference)	1.10 (1.03–1.18)	1.22 (1.12–1.34)	1.34 (1.18–1.52)	< 0.001	
Depression PRS						0.0195
Tertile 1	1.00 (reference)	1.10 (1.00–1.21)	1.21 (1.08–1.37)	1.27 (1.07–1.50)	< 0.001	
Tertile 2	1.00 (reference)	1.02 (0.94–1.12)	1.31 (1.18–1.46)	1.23 (1.05–1.44)	< 0.001	
Tertile 3	1.00 (reference)	1.09 (1.00–1.18)	1.03 (0.92–1.15)	1.36 (1.18–1.56)	0.001	
Anxiety						
Sex						0.2447
Male	1.00 (reference)	0.97 (0.90–1.05)	1.07 (0.97–1.18)	1.15 (1.00–1.32)	0.055	
Female	1.00 (reference)	1.05 (0.99–1.11)	1.01 (0.93–1.10)	1.18 (1.05–1.32)	0.019	
Age						0.5202
< 60	1.00 (reference)	1.02 (0.96–1.08)	1.01 (0.93–1.10)	1.21 (1.09–1.35)	0.013	
≥ 60	1.00 (reference)	1.02 (0.95–1.10)	1.07 (0.97–1.18)	1.11 (0.96–1.29)	0.079	
TDI						0.0301
Quintile 1	1.00 (reference)	1.11 (1.00–1.23)	1.01 (0.86–1.17)	0.96 (0.74–1.24)	0.608	
Quintiles 2–4	1.00 (reference)	1.01 (0.95–1.07)	1.03 (0.95–1.12)	1.30 (1.16–1.46)	0.001	
Quintile 5	1.00 (reference)	0.98 (0.89–1.08)	1.07 (0.94–1.21)	1.03 (0.87–1.22)	0.474	
Education level						0.6640
< 16 years	1.00 (reference)	1.01 (0.95–1.08)	1.04 (0.96–1.13)	1.15 (1.02–1.29)	0.036	
≥ 16 years	1.00 (reference)	1.04 (0.97–1.11)	1.04 (0.95–1.14)	1.22 (1.06–1.41)	0.016	
BMI						0.5611
18.5–25 kg/m^2	1.00 (reference)	1.03 (0.95–1.11)	0.98 (0.87–1.11)	1.05 (0.88–1.24)	0.720	
25–30 kg/m^2	1.00 (reference)	0.99 (0.93–1.07)	1.02 (0.92–1.12)	1.21 (1.06–1.39)	0.060	
≥ 30 kg/m^2	1.00 (reference)	1.06 (0.97–1.16)	1.14 (1.02–1.29)	1.24 (1.06–1.46)	0.001	
IPAQ activity group						0.1005

Table 3 (continued)

	Frequency of adding salt to foods					
	Never/rarely	Sometimes	Usually	Always	*P* value for trend	*P* for interaction
Low	1.00 (reference)	1.05 (0.95–1.16)	1.10 (0.96–1.26)	0.99 (0.81–1.20)	0.373	
Moderate	1.00 (reference)	1.06 (0.98–1.13)	1.01 (0.91–1.12)	1.17 (1.01–1.36)	0.075	
High	1.00 (reference)	0.97 (0.90–1.05)	1.04 (0.94–1.15)	1.28 (1.12–1.47)	0.013	
24-h weighted average noise						0.9328
≤ median	1.00 (reference)	1.02 (0.95–1.08)	1.04 (0.95–1.14)	1.18 (1.04–1.34)	0.026	
> median	1.00 (reference)	1.04 (0.97–1.10)	1.05 (0.96–1.15)	1.16 (1.02–1.31)	0.021	
Depression PRS						0.3283
Tertile 1	1.00 (reference)	0.97 (0.90–1.06)	0.94 (0.83–1.06)	1.23 (1.06–1.44)	0.376	
Tertile 2	1.00 (reference)	1.03 (0.95–1.11)	1.07 (0.96–1.19)	1.15 (0.98–1.34)	0.053	
Tertile 3	1.00 (reference)	1.06 (0.98–1.14)	1.10 (0.99–1.22)	1.14 (0.98–1.32)	0.016	

Abbreviations: *TDI* Townsend deprivation index, *IPAQ* International Physical Activity Questionnaire, *PRS* polygenic risk score, *BMI* body mass index

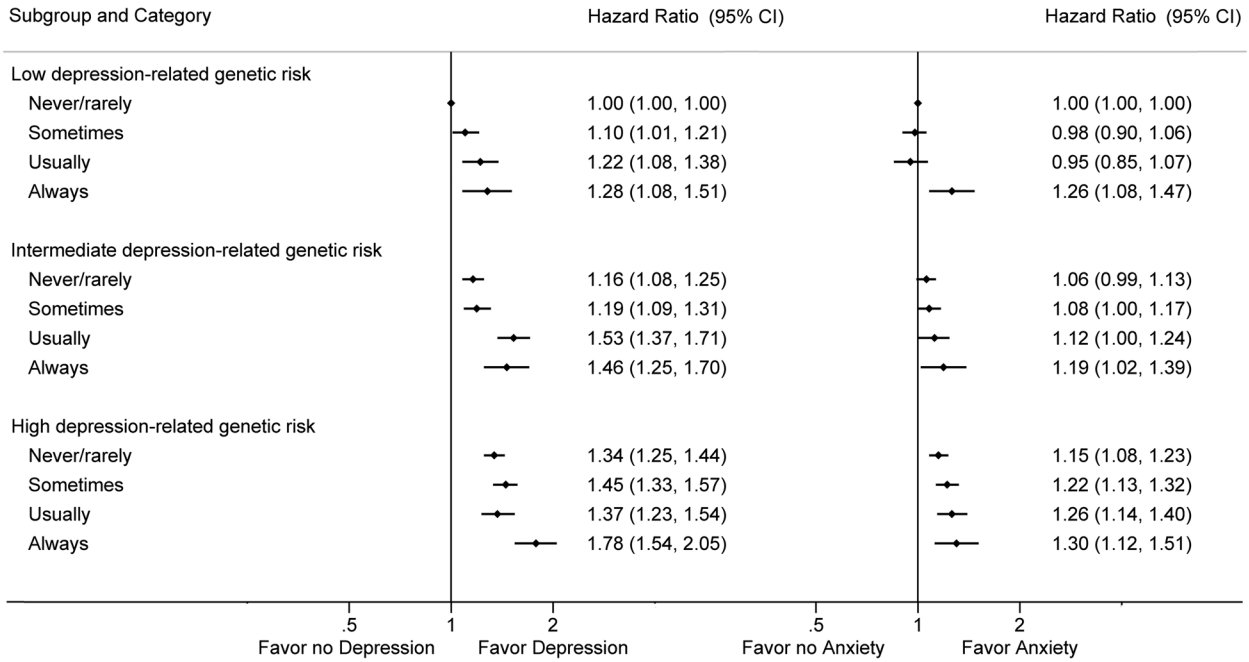

Fig. 1 The joint association of adding salt and depression PRS with incident depression and anxiety

synaptic transmission and recycling neurotransmitters for reuse [23–25]. Disruptions of sodium ion balance can affect the functioning of neurotransmitters (e.g., dopamine, noradrenaline, and 5-hydroxytryptamine) vital for locomotion, autonomic function, hormone secretion, and complex behaviors, which are all associated with emotions, and the development of mood disorders [26–30]. Second, high salt consumption hyperactivates the hypothalamic–pituitary–adrenal (HPA) axis and amplifies stress response [31, 32]. Stress-induced hyperactivity of the HPA axis leads to excessive glucocorticoid release, which continuously and intensely stimulates the glucocorticoid receptors of neurons in the hippocampus and other brain regions, causing symptoms such as neuronal atrophy, loss of dendritic spines, neurogenesis damage, and reduced synthesis of brain-derived neurotrophic factor (BDNF) [33–38]. These neurobiological processes are commonly observed among patients with depression and anxiety [39–41]. Third, high salt intake is associated with disturbance in the gut microbiota, which could induce the production of inflammatory cytokines and cause glial cell changes by passing through the blood–brain barrier, potentially contributing to depression and anxiety [42–48].

To our knowledge, this is the first large-scale prospective cohort study with the longest follow-up duration that highlights the relationship between the frequency of adding salt to foods and incident depression and anxiety. Moreover, the incident of depression and anxiety was recorded using linkage data from hospital inpatient records, primary care records, and death registries. This method avoids information bias and increases the accuracy and reliability of the records.

Limitations

Several limitations should be acknowledged. First, the self-reported nature of adding salt frequency, sociodemographic factors, and lifestyle factors could be subject to recall bias and misclassification. Second, despite our attempt to exclude individuals who had changed their diet in the past 5 years due to illnesses or other reasons, other lifestyle changes were likely to occur during the long follow-up period. Although the sensitivity analysis indicated the robustness of the principal findings, future studies may consider examining the modifying effect of other lifestyle changes on this relationship. Third, while we adjusted for a wide range of potential confounders, residual confounding cannot be entirely ruled out. Fourth, volunteer selection bias may exist in our study because the response rate at baseline in the UK Biobank was only 5.5% [49]. However, many associations observed in other studies could be replicated in the UK Biobank, suggesting that selection bias, if existent in this study, is not greater than that in others [50]. Fifth, another potential limitation of this study is the possibility of response style bias, which occurs when participants tend to respond to questionnaire items in a systematic manner that may not accurately reflect their true behaviors or experiences [51]. Finally, the possibility of reverse causality cannot be eliminated. While evidence from animal models provided the physiologic underpinning of reverse causality, its assessment in humans remains challenging [52–54]. Future large-scale clinical trials on salt reduction, assessing changes in depressive and anxiety symptoms, are needed to obtain higher-level evidence to support the findings of this study.

Conclusions

In conclusion, this study revealed a significant association between a higher frequency of adding salt to foods and increased risks of incident depression and anxiety. These findings suggest that adding salt to foods could be a potential target for intervention strategies aimed at reducing incidence of these mental disorders. Further multiple population-representative research would be warranted to demonstrate generalizability.

Abbreviations

GBD	Global Burden of Disease
ICD-10	International Statistical Classification of Diseases and Related Health Problems, 10th Revision
TDI	Townsend deprivation index
BMI	Body mass index
CVD	Cardiovascular disease
PRS	Polygenic risk score
eGFR	Estimated glomerular filtration rate
NHANES	National Health and Nutrition Examination Survey
HPA	Hypothalamic-pituitary-adrenal
BDNF	Brain-derived neurotrophic factor

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12916-025-03865-x.

Additional file 1: S1. Supplementary Methods. Fig. S1. Provides the participant flow chart. Table S1. Results of sensitivity analyses.

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Authors' contributions

TW, MW, JH, and WW conceptualized the study. WW and MW analyzed the data. WW drafted the manuscript. MW, WW, FL, LF, and TW contributed to discussion. TW, MW, XC, FL, and JH reviewed and edited the manuscript. WW, TW, MW, XC, FL, LF, and JH are the guarantors of this work and, as such, 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. All authors read and approved the final manuscript.

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Data availability

The data that support the findings of this study are available from the UK Biobank. Access to the UK Biobank resource is available via an approved application (http://www.ukbiobank.ac.uk). Analytic codes are available upon reasonable request.

Declarations

Ethics approval and consent to participate

This study was conducted according to the Declaration of Helsinki. The generic ethical approval was obtained by UK Biobank from the NHS National Research Ethics Service (approval letter dated June 17th 2011, Ref 11/NW/0382). All participants provided written informed consent to participate in the UK Biobank.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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