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The potential causal relationship between various lifestyles and depression: a univariable and multivariable Mendelian randomization study

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Background: Previous studies have shown that lifestyle was associated with depression. Thus, the aim of this study was to examine the causality between multiple lifestyles and depression by Mendelian randomization (MR) analysis.

Methods: The single-nucleotide polymorphisms (SNPs) of depression, alcoholic drinks per week, sleeplessness or insomnia, body mass index (BMI), mood swings, weekly usage of mobile phone in the last 3 months, beef intake, cooked vegetable intake, and "smoking status: never" were acquired from the Integrative Epidemiology Unit Open genome-wide association study database. Causal effects of eight exposure factors and depression were investigated using MR-Egger, weighted median, inverse variance weighted (IVW), simple mode, and weighted mode, and results were primarily referred to IVW. Subsequently, univariable MR (UVMR) analysis was performed on eight exposure factors and depression, separately. In addition, sensitivity analysis, including heterogeneity test, horizontal pleiotropy, and leave-one-out (LOO) methods, was conducted to evaluate the stability of MR results. Furthermore, multivariable MR (MVMR) analysis was carried out.

Results: UVMR analysis revealed that all eight exposure factors were causally associated with depression; alcoholic drinks per week, sleeplessness or insomnia, BMI, mood swings, weekly usage of mobile phone in the last 3 months, and cooked vegetable intake were risk factors, and beef intake and "smoking status: never" were protection factors. Heterogeneity tests revealed no heterogeneity for alcoholic drinks per week, sleeplessness or insomnia, mood swings, weekly usage of mobile phone in the last 3 months, and cooked vegetable intake. Meanwhile, there was no horizontal pleiotropy in UVMR, and LOO analysis verified that univariable analysis results were reliable. Moreover, MVMR analysis indicated that mood swings and weekly usage of mobile phone in the last 3 months were risk factors, and beef intake was a protection factor for depression when multiple factors occurred at the same time.

Conclusion: Alcoholic drinks per week, sleeplessness or insomnia, BMI, mood swings, weekly usage of mobile phone in the last 3 months, and cooked vegetable intake were risk factors, and beef intake and "smoking status: never" were protection factors. In addition, mood swings, weekly usage of mobile phone in the last 3 months, and beef intake had a direct effect on depression when multiple factors occurred simultaneously.

KEYWORDS

depression, lifestyle, Mendelian randomization, genome-wide association study, causality

1 Introduction

Depression is a common illness that significantly limits social and psychological functioning and reduces the quality of life (1). More than 300 million people worldwide suffer from depression, making it a significant public health issue that imposes a global burden (2, 3). Depression was ranked as the fourth-leading cause of disease burden in 2000 (4). Mild depression manifests as persistent sadness, loss of interest or pleasure, and feelings of worthlessness. Severe depression, on the other hand, is characterized by recurrent suicidal tendencies (5).

The interplay of genes, biological factors, and the environment leads to the onset of depression (6). Compared to men, women have a higher prevalence of depression (7). Lifestyle is closely related to health; a healthy lifestyle promotes feelings of happiness and reduces feelings of displeasure and misery. Analyses of the correlation between lifestyle and the incidence of depressive symptoms suggest that lifestyle and its various dimensions are related to the onset of depressive symptoms (8). Excessive alcohol consumption increases the risk of depression (9). However, moderate drinking can mitigate or suppress the impact of stress on depression (10). Smoking increases the risk of developing depression (11). Diet and health are closely related, and healthy eating habits can reduce the risk of depression (12). Additionally, there is a close relationship between body mass index (BMI) and depression, with obese individuals being more prone to depression (13). Sleep disturbances are linked to many mental illnesses. Insomnia is a risk factor for depression (14), and sleep interventions can be beneficial in alleviating clinical depressive symptoms (15). Studies have found that frequent mobile phone use is a risk factor for adverse mental health outcomes in young people over a 1-year follow-up (16).

Mendelian randomization (MR) is a method that uses genetic instrumental variables (IVs) to assess the causal direction between exposure and outcome, and it is unaffected by confounding factors and reverse causality (17, 18). In the face of clinical research where randomized controlled trials (RCTs) are challenging to conduct, including but not limited to impractical and unethical RCT studies, MR can strengthen the inference of direct causal relationships between exposure factors and diseases, while avoiding difficult RCT studies (17). Recently, there has been a surge in MR articles related to depression, but most of the content focuses on the application of biomarkers, with few causal studies on various lifestyle factors and depression. In particular, there is a lack of multivariate MR (MVMR) research on the role of various lifestyle factors in depression (19). Therefore, this paper is devoted to study the causal relationships of various lifestyles and depression by means of univariate and multivariate methods. The univariable MR (UVMR) analysis evaluates the influence of a single predictor variable on the outcome (20). MVMR is an extension of UVMR that estimates the direct causal effect of each exposure factor on the outcome, taking into account the pleiotropy among multiple variables (21).

This study, based on single-nucleotide polymorphism (SNP) data of depression and exposure factors (eight lifestyle factors) from public databases, employed both UVMR and MVMR methods to investigate the causal relationship between different lifestyles and depression. Sensitivity analyses were conducted to assess the impact of assumptions on the study findings and to ensure the robustness of the results. From a genetic perspective, this research explored the potential roles of various lifestyles in the progression of depression.

2 Materials and methods

2.1 Source of data

The datasets of depression (finn-b-F5_ DEPRESSIO), alcoholic drinks per week (ieu-b-73), sleeplessness or insomnia (ukb-a-13), BMI (ukb-a-248), mood swings (ebi-a-GCST006944), weekly usage of mobile phone in the last 3 months (ukb-b-17999), beef intake

Abbreviations: MR, Mendelian randomization; BMI, Body mass index; IEU, Integrative epidemiology unit; GWAS, Genome-wide association study; IVW, Inverse variance weighted; UVMR, Univariable Mendelian randomization; LOO, Leave-one-out; MVMR, Multivariable Mendelian randomization; SNPs, Single-nucleotide polymorphisms; IVs, Instrumental variables; OR, Odds ratio; CI, Confidence interval.

(ukb-b-2862), cooked vegetable intake (ukb-b-8089), and "smoking status: never" (ukb-d-20116_0) were retrieved from the Integrative Epidemiology Unit (IEU) Open Genome-Wide Association Study (GWAS) database (https://gwas.mrcieu.ac.uk/). The finn-b-F5_DEPRESSIO dataset included 16,380,457 SNPs from 215,644 samples. The ieu-b-73 dataset included 11,887,865 SNPs from 335,394 samples. The ukb-a-13 dataset included 10,894,596 SNPs from 336,965 samples. The ukb-a-248 dataset included 10,894,596 SNPs from 336,107 samples. The ebi-a-GCST006944 dataset included 10,894,596 SNPs from 329,428 samples. The ukb-b-17999 dataset included 9,851,867 SNPs from 386,626 samples. The ukb-b-2862 dataset included 9,851,867 SNPs from 461,053 samples. The ukb-b-8089 dataset included 9,851,867 SNPs from 448,651 samples. The ukb-d-20116_0 dataset included 13,586,591 SNPs from 359,706 samples. Details of the above datasets are given in Table 1.

2.2 Pre-processing of data

The adjusted *p*-values of the forward and reverse MR analysis results were calculated by the false discovery rate (FDR) method. The reading and filtering of exposure factors was carried out via the extract_instruments function of the TwoSampleMR package ($p < 5\times10^{-8}$) (22) in forward MR analysis. In the reverse MR analysis, IVs with significant correlation with exposure factors were found through $p < 5\times10^{-6}$. IVs were removed using linkage disequilibrium analysis (LDA) ($r^2 = 0.001$ and kb = 10,000). Three basic premises underlie UVMR studies (1): a robust and significant correlation existed between exposures and IVs (2); IVs were not related to confounding factors; and (3) IVs could only influence outcomes through exposure and not through other channels. Three hypotheses of the MVMR require consideration of all exposures: (1) in the case of other exposures given, SNPs were strongly correlated with the remaining exposures. (2) In conditions that give all exposures, SNPs and outcomes were independent. (3) SNPs were independent of all confounding (23).

2.3 UVMR analysis and sensitivity analysis

Firstly, genetic correlation between exposure factors and outcome was calculated using the ldscr package. Then, five diverse MR methods, MR-Egger (24), weighted median (25), inverse variance weighted (IVW) (26), simple mode, and weighted mode (22, 27), were adopted to explore the causality of eight exposure factors with depression, the most important of which was IVW. In addition, odds ratio (OR) was calculated, and OR > 1 indicated that exposure factor was a risk factor, while OR < 1 revealed that exposure factor was a protection factor. Results were presented using scatter plots, forest plots, and funnel plots. Moreover, sensitivity analysis was conducted to evaluate the reliability of UVMR results. First, heterogeneity test was conducted by Cochran's *Q* test. Namely, there was no heterogeneity when the *p*-value was greater than 0.05 in Cochran's *Q* test. If there was heterogeneity ($p < 0.05$), the IVW test was performed for random effects. Secondly, the horizontal pleiotropy test was performed via TwoSampleMR function mr_pleiotropy_test in *R*, and if $p > 0.05$, it indicated no horizontal pleiotropy, meaning that there were no confounding factors in the study. In addition, horizontal pleiotropy was further validated using MR-Egger analysis (28). Finally, leave-one-out (LOO) analysis was conducted by gradually eliminating each SNP, and if the effect of the remaining SNPs on the outcome variable did not change significantly, this indicates that the results of MR analysis was reliable.

2.4 Multivariable MR analysis

In order to detect causal relations between eight exposure factors and depression at the multivariate level, the TwoSampleMR package was utilized to harmonize effect equivalents and effect sizes followed

TABLE 1 Detailed information about the datasets.

Trait	Year	Population	GWAS ID	Sample size	SNP	Consortium
Depression	2021	European	finn-b-F5_DEPRESSIO	215,644	16,380,457	FinnGen
Alcoholic drinks per week	2019	European	ieu-b-73	335,394	11,887,865	GWAS and Sequencing Consortium of Alcohol and Nicotine use
Sleeplessness/insomnia	2017	European	ukb-a-13	336,965	10,894,596	UK Biobank
Body mass index (BMI)	2017	European	ukb-a-248	336,107	10,894,596	UK Biobank
Mood swings	2017	European	ebi-a-GCST006944	329,428	10,894,596	EBI
Weekly usage of mobile phone in the last 3 months	2018	European	ukb-b-17999	386,626	9,851,867	UK Biobank
Beef intake	2018	European	ukb-b-2862	461,053	9,851,867	UK Biobank
Cooked vegetable intake	2018	European	ukb-b-8089	448,651	9,851,867	UK Biobank
Smoking status: Never	2018	European	ukb-d-20116_0	359,706	13,586,591	UK Biobank

by MVMR analysis. Multiple exposure factor IVs were filtered by the mv_lasso_feature_selection function. Then, ORs were computed as before.

3 Results

3.1 Genetic correlation

The gene correlation between eight exposure factors and outcome was calculated. The results revealed that BMI (r_g = 0.102, p < 0.001), sleeplessness_insomnia (r_g = 0.372, p < 0.001), mood swings (r_g = 0.318, p = 0.002), weekly usage of mobile phone in the last 3 months (r_g = 0.209, p < 0.001), alcoholic drinks per week (r_g = 0.118, p < 0.001), and cooked vegetable intake (r_g = 0.0579, p = 0.049) and depression had positive genetic correlations, while beef intake (r_g = −0.171, p < 0.001) and "smoking status: never" (r_g = −0.324, p< 0.001) showed an inverse genetic association.

3.2 Eight exposure factors were significantly causally associated with depression

Following screening, 34 IVs for alcoholic drinks per week, 28 IVs for sleeplessness or insomnia, 297 IVs for BMI, 40 IVs for mood swings, 10 IVs for weekly usage of mobile phone in the last 3 months, 14 IVs for beef intake, 11 IVs for cooked vegetable intake, and 76 IVs for "smoking status: never" were obtained (Supplementary Tables 1–8). The IVW method revealed a causal relationship between alcoholic drinks per week (adj.p = 0.015, OR = 1.484), sleeplessness or insomnia (adj.p = 0.009, OR = 1.873), BMI (adj.p = 0.031, OR = 1.104), mood swings (adj.p < 0.001, OR = 2.099), weekly usage of mobile phone in the last 3 months (adj.p = 0.021, OR = 1.799), cooked vegetable intake (adj.p = 0.021, OR = 2.508), beef intake (adj.p < 0.001, OR = 0.224), and "smoking status: never" (adj.p < 0.001, OR = 0.515) and depression (Figure 1). Scatter plots for alcoholic drinks per week, sleeplessness or insomnia, BMI, mood swings, weekly usage of mobile phone in the last 3 months, and cooked vegetable intake had positive slopes, suggesting that they were risk factors, while beef intake and "smoking status: never" had negative slopes, indicating that they were protection factors for depression (Figures 2A–H). The symmetrical distribution of the samples along both sides of the IVW line in the funnel plot revealed that UVMR analysis results conforms to the second law of MR grouping (Figures 3A–H). The results of forest plots were consistent with the previous results (Figures 4A–H).

3.3 Sensitivity analysis of eight exposure factors revealed UVMR analysis results were reliable

In this study, there was no heterogeneity for alcoholic drinks per week (p = 0.070), sleeplessness or insomnia (p = 0.106), mood swings (p = 0.129), weekly usage of mobile phone in the last 3 months (p = 0.267), and cooked vegetable intake (p = 0.902) as exposure factors, respectively (Table 2). The heterogeneity test results for BMI (p = 0.006), beef intake (p = 0.022), and "smoking status: never" (p = 0.002) showed that p was less than 0.05 in Cochran's Q test, but p < 0.05 in IVW and so it did not affect the results (Table 1) and all p-values in MR-Egger analysis were greater than 0.05 (Figure 1). Horizontal pleiotropy showed that there was no horizontal pleiotropy between eight exposure factors and depression (p > 0.05, Table 3). Furthermore, there were no points of serious bias in the results of LOO analysis, indicating that the results were reliable (Figures 5A–H). Thus, eight exposure factors, alcoholic drinks per week, sleeplessness or insomnia, BMI, mood swings, weekly usage of mobile phone in the last 3 months, beef intake, cooked vegetable intake, and "smoking status: never", were causally associated with the occurrence of depression.

3.4 No causal relationship between depression and eight exposure factors based on reverse MR analysis

Since the relationship between exposure factors and outcome was not one-way and may be two-way, reverse MR analysis was performed to further confirm the causal relationship between depression and eight lifestyle types. The results revealed that there was no significant causal relationship between the eight outcomes and exposure factor (depression), which further confirmed the relationship between the eight lifestyles and the risk of depression (Supplementary Figure 1).

3.5 Mood swings, weekly usage of mobile phone in the last 3 months, and beef intake had a direct effect on depression when multiple factors occurred simultaneously

Following screening, 141 SNPs from six exposure factors, alcoholic drinks per week, sleeplessness or insomnia, mood swings, weekly usage of mobile phone in the last 3 months, beef intake, and "smoking status: never", were utilized as IVs for the MVMR analysis. MVMR analysis suggested that mood swings (p = 0.001, OR = 1.737) and weekly usage of mobile phone in the last 3 months (p = 0.013, OR = 1.619) were risk factors and beef intake (p = 0.015, OR = 0.490) was a protection factor. Moreover, mood swings, weekly usage of mobile phone in the last 3 months and beef intake had a direct effect on depression when multiple factors occurred simultaneously (Figure 6).

4 Discussion

Depression is a global disease, greatly exacerbating socio-economic burdens (1, 2, 29). Healthy lifestyle habits help reduce the risk of depression. MR treats genetic variations as natural

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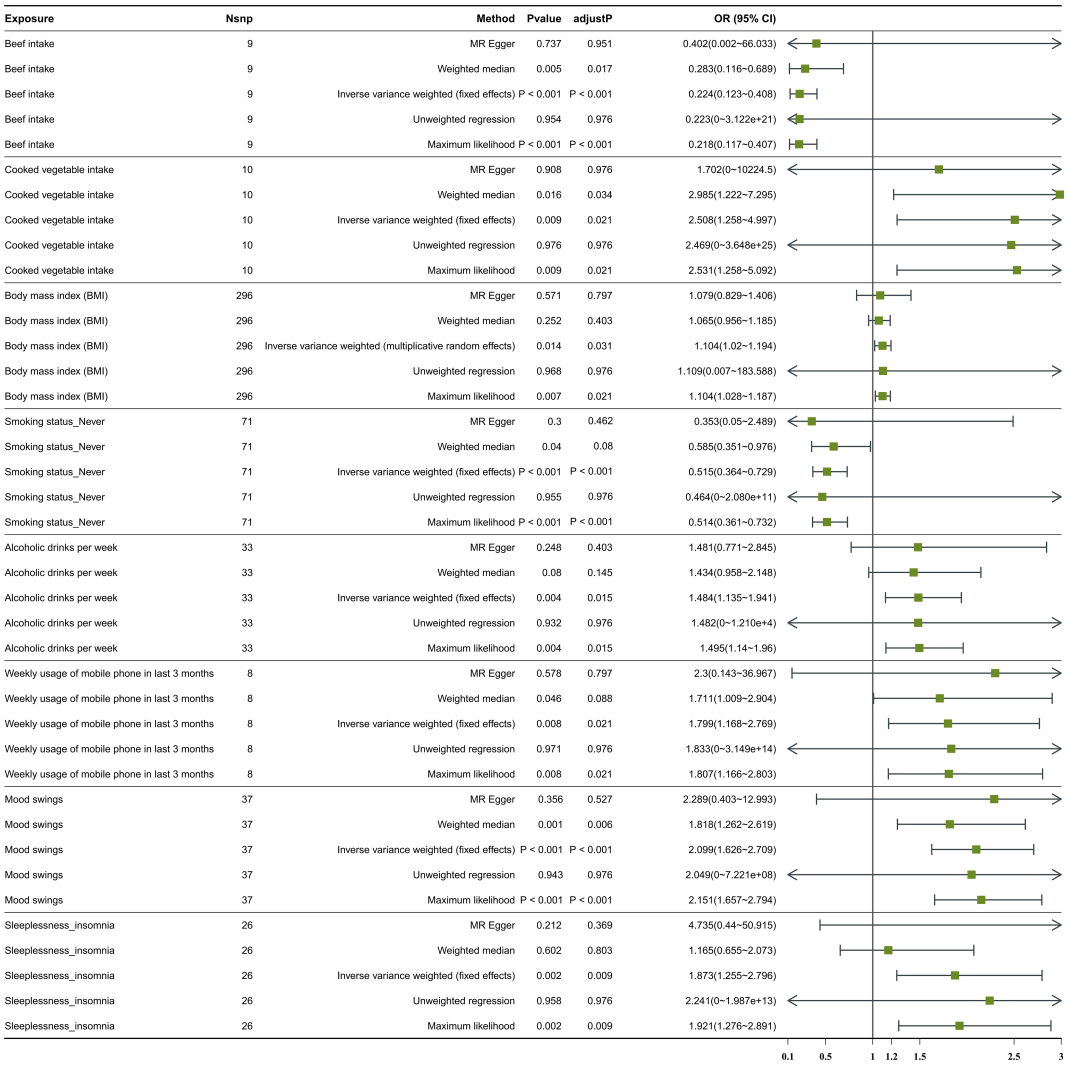

FIGURE 1
The forest plot of studies that evaluated the causal effect between exposures and depression using values obtained by the IVW MR method. Nsnp stands for the number of SNPs. An OR value greater than 1 indicates a risk factor, whereas a value less than 1 suggests a protective factor. This is in reference to a binary variable. IVW, inverse variance weighted; MR, Mendelian randomization; SNPs, single-nucleotide polymorphisms; OR, odds ratio; CI, confidence interval.

experiments to evaluate the causal relationship between two variables (30). We assessed the causal relationship between eight different lifestyles and depression through UVMR and MVMR.

In this study, we observed a causal relationship between multiple lifestyle-related exposure factors and depression. The UVMR analysis showed that alcoholic drinks per week, sleeplessness or insomnia, BMI, mood swings, weekly usage of mobile phones in the last 3 months, and cooked vegetable intake were risk factors, while beef intake and never smoking were protective factors.

Prospective studies have shown deep connections between alcohol consumption and smoking with depression (31, 32). One study showed that alcohol consumption and headache were negatively correlated and that the comorbidity of headache with depression was common (33). A study of 6,646 ordinary people over 3 and 6 years found that reducing smoking and alcohol consumption were associated with improvements in depressive symptoms through multiple cross-sectional analyses (34). Risky drinking and alcohol abuse may increase the risk of depression (9). However, surveys indicate that moderate alcohol intake (5–15 g/day) can reduce the risk of developing depression (35, 36). Some drugs that treat depression can also treat alcohol dependence (37). SEMA3A may be a common genetic risk gene for alcohol dependence and depression (38). There is a potential bidirectional relationship between smoking and depression: smokers may have

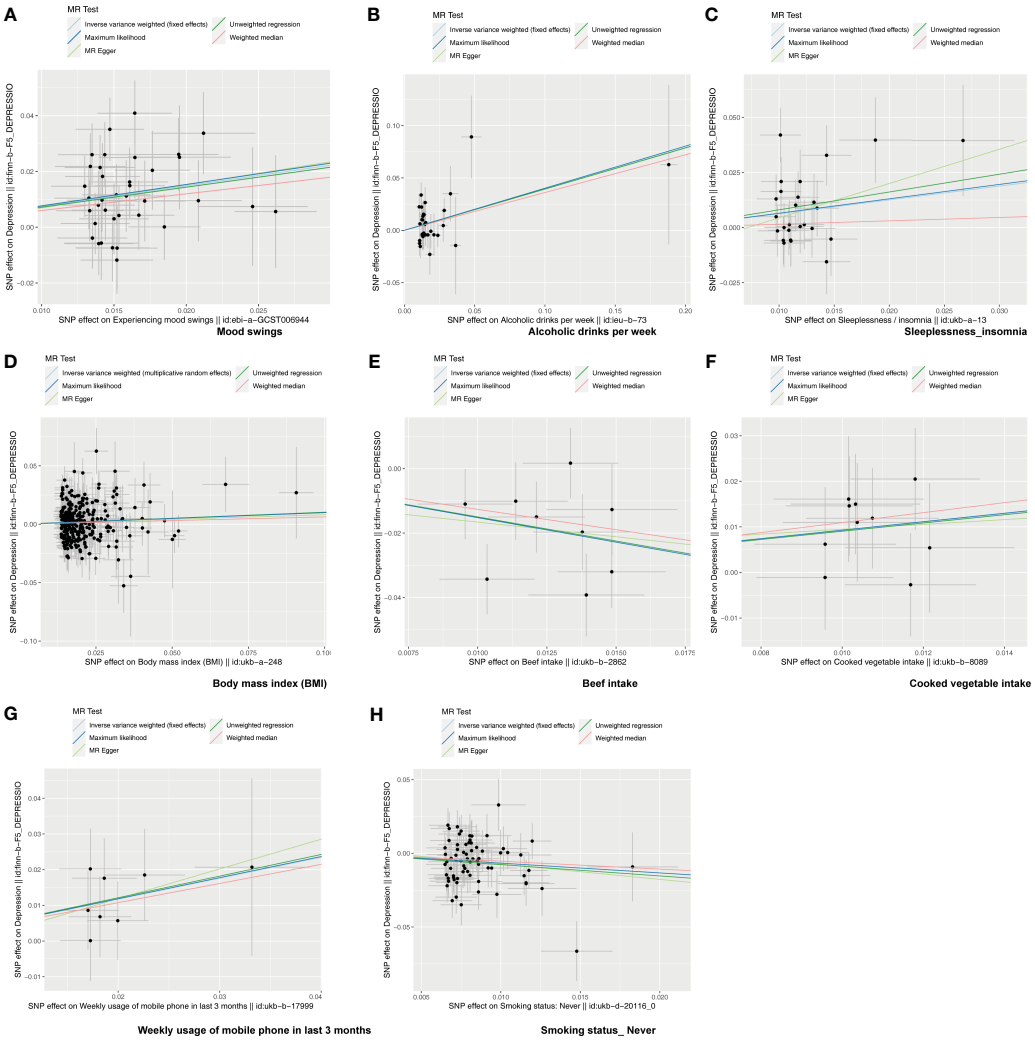

FIGURE 2
The scatter plot of MR analysis. **(A–H)** Scatter plots for the causal association between depression and mood swings **(A)**, alcoholic drinks per week **(B)**, sleeplessness/insomnia **(C)**, body mass index **(D)**, beef intake **(E)**, cooked vegetable intake **(F)**, weekly usage of mobile phone in the last 3 months **(G)**, and "smoking status: never" **(H)**. Each point on the graph represents an SNP locus. The *x*-axis represents the effect of the SNP on the exposure, while the *y*-axis represents the effect of the SNP on the outcome. The colored lines represent the fit results of different MR algorithms. A positive slope of the line indicates a risk factor, while a negative slope indicates a protective factor.

an increased risk of developing depression, and among those with depression, the smoking rate is higher than among non-smokers. Cross-sectional studies show that smokers are more likely to develop depression, and a higher proportion of people with depression smoke (31). Longitudinal studies suggest that smoking is a potential factor for developing depression (39). Recent MR studies indicate that smoking is a causal risk factor for diagnosed depression (40), and inflammation is likely involved in at least part of the connection between smoking and depression (41). Our UVMR showed a causal relationship between weekly alcohol consumption and never smoking with depression. Combined with MVMR, weekly drinking is a risk factor, while never smoking is a protective factor.

The relationship between diet and depression is profound. Healthy dietary habits and avoiding pro-inflammatory foods can prevent depression to a certain extent (12). Multiple studies suggest that the Mediterranean diet can reduce the risk of depression (12, 42, 43). The Mediterranean diet emphasizes the consumption of plant-based foods rich in fruits, vegetables, whole grains, nuts, seeds, and legumes (44). Interestingly, the intake of raw vegetables seems to have a more significant effect on mental health than cooked vegetables (45). Through a UVMR analysis, we found a direct causal relationship between cooked vegetables and depression. Intriguingly, cooked vegetables act as a risk factor for depression. This might be because cooking can destroy some beneficial components in vegetables, such as

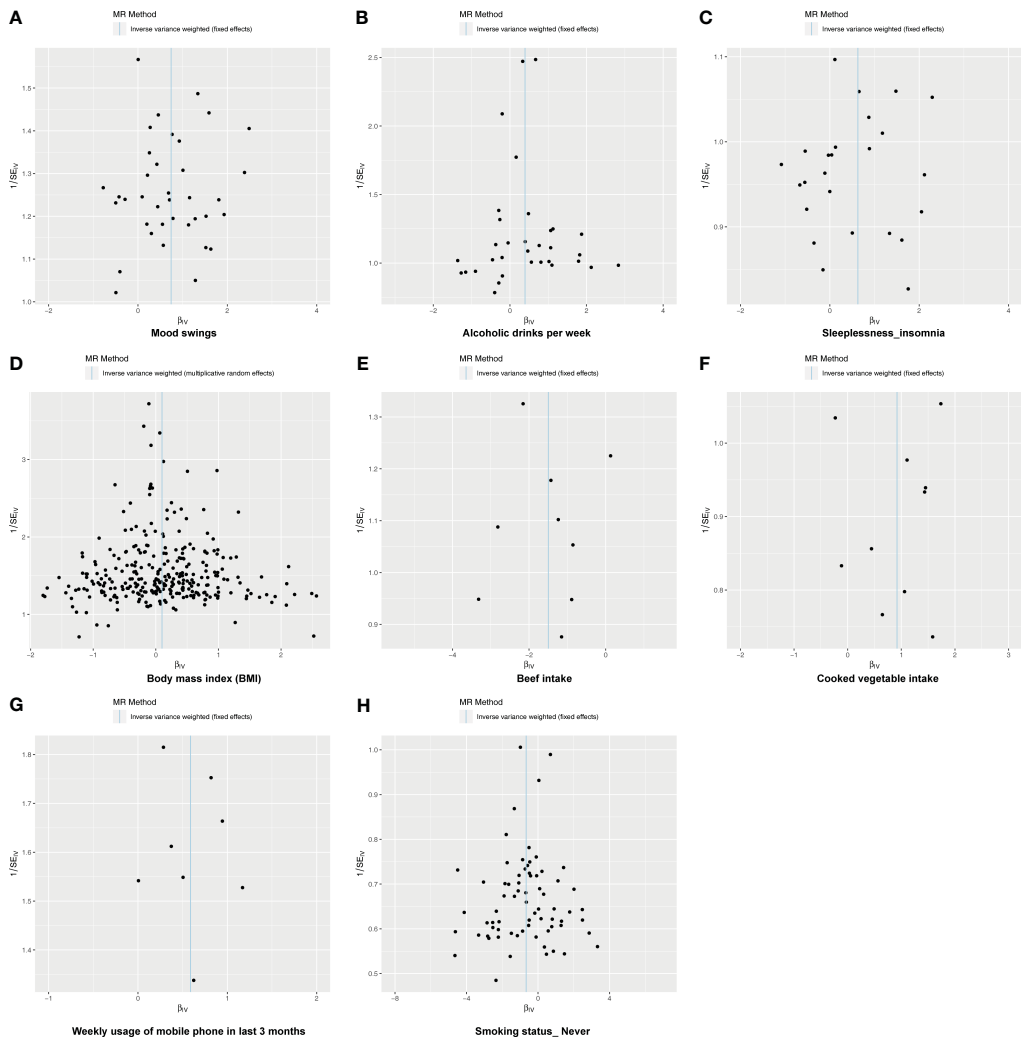

FIGURE 3
The funnel plot of MR analysis. **(A–H)** Funnel plots to show the overall heterogeneity of MR analysis for the effect of mood swings **(A)**, alcoholic drinks per week **(B)**, sleeplessness/insomnia **(C)**, body mass index **(D)**, beef intake **(E)**, cooked vegetable intake **(F)**, weekly usage of mobile phone in the last 3 months **(G)**, and "smoking status: never" **(H)** on depression. If samples are symmetrically distributed on both sides of the IVW line, then the MR conforms to Mendel's second law of random assortment.

polyphenols, which are known to alleviate depression (46, 47). Meat intake is an integral part of the Mediterranean diet (44). Our UVMR and MVMR analyses indicate a direct causal relationship between beef intake and depression, with beef acting as a protective factor. Other MR studies support this viewpoint (48). Interestingly, several studies suggest that excessive beef consumption is linked to an increased risk of depression (49). It is undeniable that beef contains vitamins and minerals that have a positive effect on mood. Thus, moderate beef intake might have beneficial effects on reducing the risk of depression. The Mediterranean diet helps maintain a healthy weight range. An abnormal BMI is closely linked to depression. Individuals with metabolic health issues have a higher risk of depression than those without such issues (50, 51). A joint survey questionnaire of 18,025 participants showed that the prevalence of depression was highest among those with unhealthy metabolic obesity, accompanied by an abnormal elevation of C-reactive protein. This seems to indicate that inflammation caused by metabolic anomalies might increase the risk of depression (52). A longitudinal study also linked the inflammatory consequences of obesity to depression (53). However, through our MR analysis, there is a direct causal relationship between BMI and depression. An MR study showed that being overweight does not increase the risk of depression due to inflammation marked by an abnormal C-reactive protein caused by metabolic abnormalities. Instead, being overweight directly increases the risk of depression, fully supporting our analysis (54).

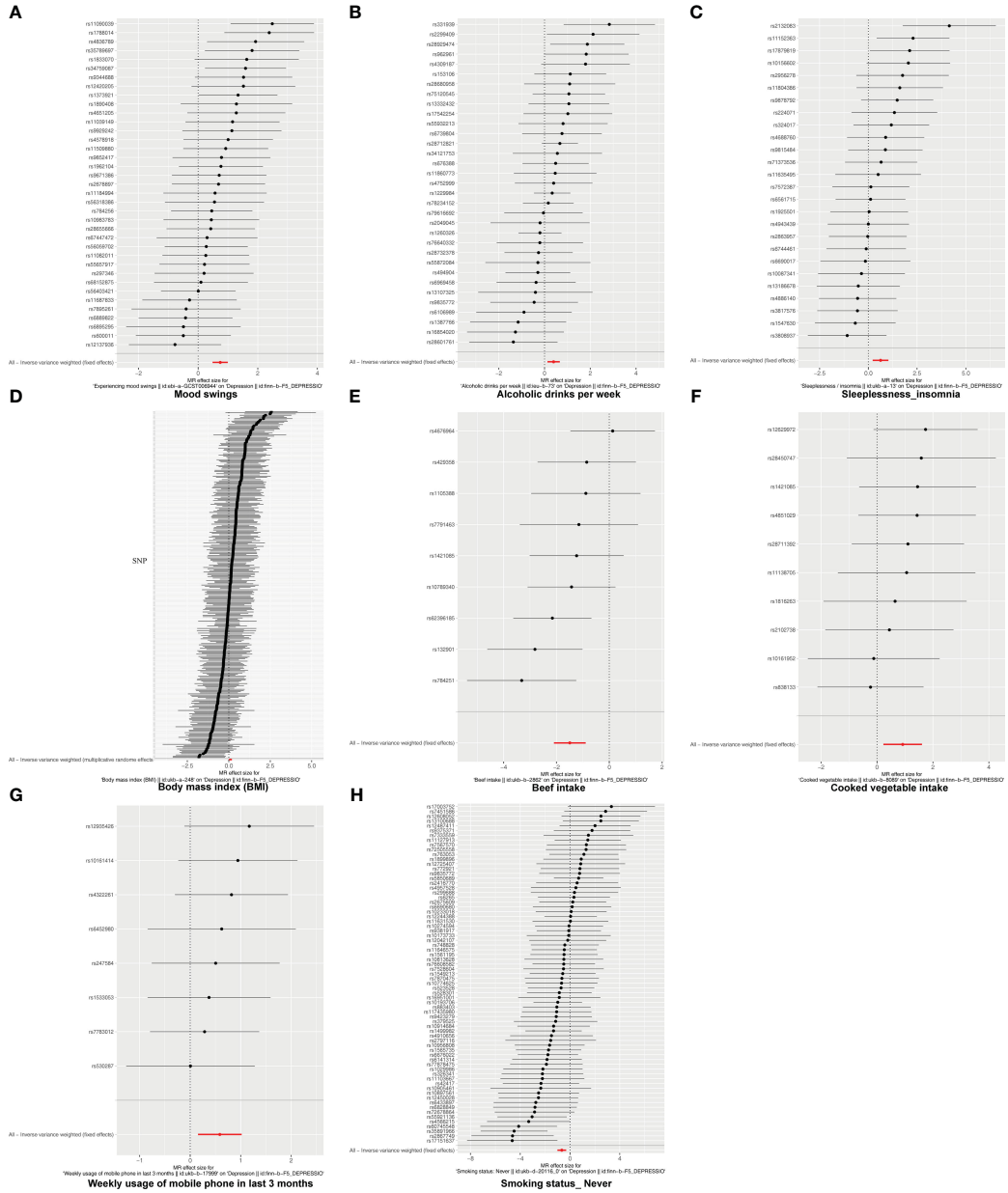

FIGURE 4
The forest plot of studies that determined the diagnostic efficacy between exposures and depression using values obtained by the IVW MR method. **(A)** Mood swings; **(B)** alcoholic drinks per week; **(C)** sleeplessness/insomnia; **(D)** body mass index; **(E)** beef intake; **(F)** cooked vegetable intake; **(G)** weekly usage of mobile phone in the last 3 months; **(H)** "smoking status: never". Solid points on the left indicate a reduction, while those on the right indicate an increase.

Lifestyle habits are closely linked to depression. With the increasing prevalence and frequency of smartphone use, the relationship between smartphones and depression has attracted widespread attention and research. Overuse of phones might elevate the risk of developing depression (55). Excessive smartphone use can increase transient negative emotions in users, and repeated or persistent negative emotions can heighten the risk of depression. Reducing smartphone usage might have long-term positive effects (56). Another piece of evidence suggests that frequent phone use can decrease physical activity in users, thereby raising the risk of depression (57, 58). Prolific smartphone use can also deteriorate sleep quality, indirectly increasing the risk of depression (59). A study indicates that over-reliance on smartphones might be a strategy driven by an escapist motive linked to depression (60). However, most studies focus primarily on adolescent populations, and many of the findings are

TABLE 2 Heterogeneity test between eight exposure factors and depression.

Outcome	Exposure	Q	Q_df	Q_pval
Depression	Beef intake	25.2289	13.0000	0.0215
Depression	Cooked vegetable intake	4.8372	10.0000	0.9018
Depression	Body mass index (BMI)	360.9072	296.0000	0.0058
Depression	Smoking status: Never	115.5257	75.0000	0.0018
Depression	Alcoholic drinks per week	45.7001	33.0000	0.0697
Depression	Weekly usage of mobile phone in the last 3 months	11.1234	9.0000	0.2673
Depression	Mood swings	49.0984	39.0000	0.1289
Depression	Sleeplessness_insomnia	36.4613	27.0000	0.1056

indirect, which imposes certain limitations on the research methods. Our UVMR analysis indicates a direct causal relationship between excessive smartphone use and depression. Sleep-related characteristics are connected to depression. There might be a unidirectional relationship between sleep disturbances and depression, meaning that insomnia might precede depression (61). A meta-analysis suggests that sleep disturbances could be a harbinger of depression and may serve as one of its risk factors (62). The process through which insomnia affects depression might begin with alterations in the arousal system, affecting biological substrates related to emotional processing, eventually influencing cognitive systems and leading to depression (63, 64). Another piece of evidence posits that treating insomnia symptoms in depression patients can alleviate their depressive symptoms (65). A separate MR study reveals that insomnia might have a causal relationship with coronary artery disease, depressive symptoms, and subjective wellbeing (66). Diurnal mood variations, characterized by worse moods upon waking and improved moods in the evening, are a core feature of depression (67, 68). Neuroendocrine measurements have shown that depressed patients exhibit significantly elevated levels of cortisol and adrenocorticotropic hormone in the morning (69), potentially linked to the diurnal mood fluctuations seen in depression. Another finding attributes these mood fluctuations in depression to diurnal metabolic activities in areas like the ventrolateral–prefrontal, parietal, temporal, and frontal regions, as well as the cerebellum (70). Our results obtained from the UVMR analysis have further confirmed that mood swings are a significant risk factor for depression. This discovery enhances our understanding of the relationship between mood swings and depression, providing a valuable scientific basis for more in-depth research into this complex relationship.

Further MVMR analysis indicates that after considering behaviors such as alcoholic drinks per week, sleeplessness or insomnia, mood swings, weekly usage of mobile phone in the last 3 months, beef intake, and never smoking status, mood swings, weekly usage of mobile phone in the last 3 months, and beef intake have a strong causal relationship with depression. Our research findings are consistent with previous studies, which showcased the relationship between mood swings, weekly mobile phone usage in the last 3 months, and beef intake with depression (48, 55, 71). Healthy lifestyle habits can help reduce the risk of depression. Increased phone usage can lead to reduced sleep duration; hence, limiting phone usage among adolescents can help reduce insomnia, subsequently lowering the risk of depression (72). Mood swings are related to sleep duration (67), with the correlation of IL6 being significantly associated with emotional ratings (73). For those with depression, sleep deprivation is more likely to intensify diurnal mood fluctuations

TABLE 3 Horizontal pleiotropy test between eight exposure factors and depression.

Outcome	Exposure	Egger_intercept	SE	Q_pval
Depression	Beef intake	0.0137	0.0293	0.6499
Depression	Cooked vegetable intake	−0.0140	0.0432	0.7537
Depression	Body mass index (BMI)	−0.0003	0.0024	0.8885
Depression	Smoking status: Never	0.0073	0.0076	0.3370
Depression	Alcoholic drinks per week	−0.0009	0.0063	0.8854
Depression	Weekly usage of mobile phone in the last 3 months	−0.0007	0.0280	0.9802
Depression	Mood swings	−0.0103	0.0144	0.4755
Depression	Sleeplessness_insomnia	0.0017	0.0078	0.8335

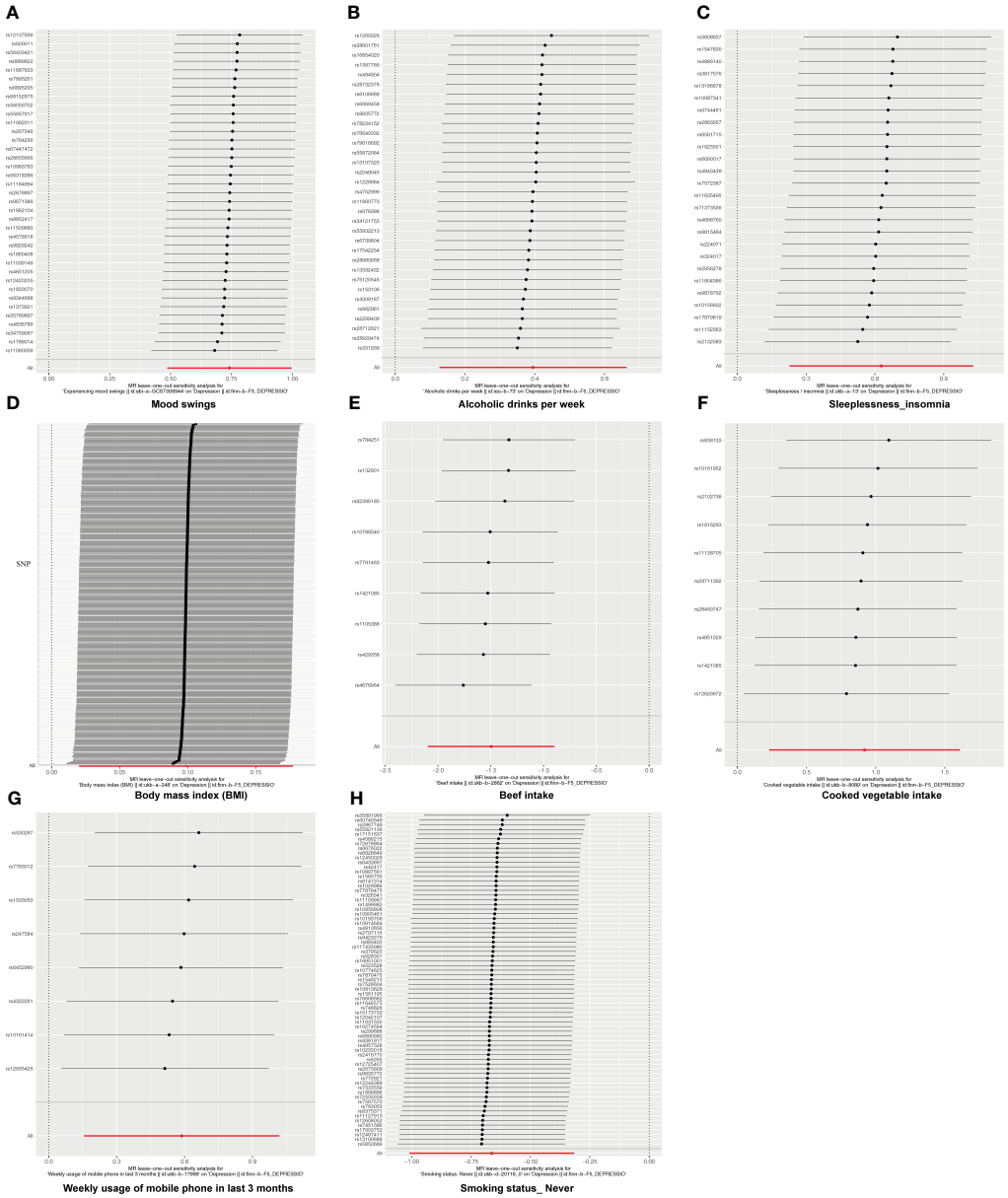

FIGURE 5
The leave-one-out analysis of MR analysis. **(A)** Mood swings; **(B)** alcoholic drinks per week; **(C)** sleeplessness/insomnia; **(D)** body mass index; **(E)** beef intake; **(F)** cooked vegetable intake; **(G)** weekly usage of mobile phone in the last 3 months; **(H)** "smoking status: never".

(74), which could further elevate the risk of depression. Healthy dietary habits help in reducing the risk of depression. While beef intake is essential for those with depression, it is crucial to maintain it within a certain limit. Overconsumption of beef might actually exacerbate the risk of depression (49).

5 Conclusion

Our study indicates that various lifestyle factors have both univariable and multivariable causal relationships with depression, and we have drawn corresponding conclusions. Our analysis focusing on dietary habits primarily targets the European population, and comparatively, there is a lack of analysis concerning the dietary habits of the Asian population. Furthermore, in exploring the causal relationship between cooked vegetable intake and beef intake with depression, we cannot completely rule out the influence of cultural differences on the results. In future studies, we will consider more deeply the impact of cultural factors on depression. The sample population for mobile phone usage frequency is mostly adolescent depression patients, and there is a relative scarcity of

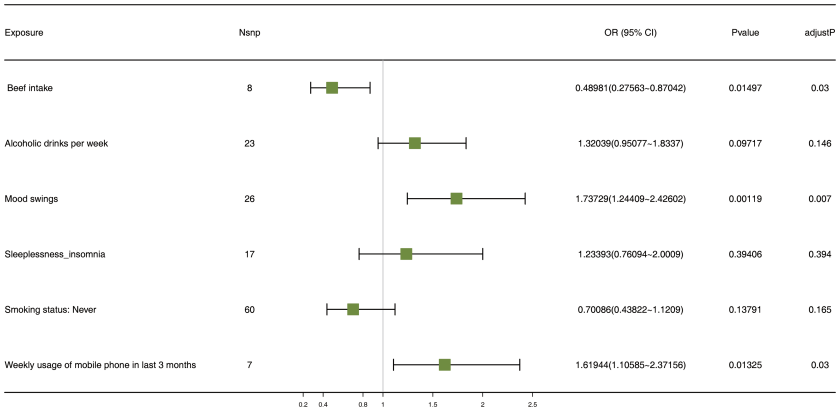

FIGURE 6
The forest plot of MVMR analysis. Nsnp stands for the number of SNPs. An OR value greater than 1 indicates a risk factor, whereas a value less than 1 suggests a protective factor. This is in reference to a binary variable. MVMR: multivariate Mendelian randomization; SNPs: single-nucleotide polymorphisms; OR, odds ratio; CI: confidence interval.

data from other age groups. We need to further investigate the accuracy and consistency of our results, but we will continue to monitor research related to different lifestyles and depression.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary Material. Further inquiries can be directed to the corresponding author.

Ethics statement

Ethical approval was not required for the study involving humans in accordance with the local legislation and institutional requirements. Written informed consent to participate in this study was not required from the participants or the participants' legal guardians/next of kin in accordance with the national legislation and the institutional requirements.

Author contributions

SG: Data curation, Formal analysis, Visualization, Writing – original draft. WZ: Writing – review & editing. LY: Writing – original draft. LJ: Visualization, Writing – original draft. DT: Investigation, Writing – review & editing. TZ: Writing – review & editing. BQZ: Writing – review & editing. BZ: Methodology, Project administration, Supervision, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpsyt.2024.1343132/full#supplementary-material

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