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Revisión

Ultra-processed food intake and risk of depression: a systematic review

Ingestión de alimentos ultraprocesados y riesgo de depresión: revisión sistemática

Ying-Rui Tian[1,2], Chun-Yan Deng[1], He-Chuan Xie[1], Qian-Jing Long[1], Yuan Yao[1], Yan Deng[1], Hao Zhao[2], Yong Li[2], Hui Liu[2], Lun Xiao[1]

[1]Centers for Disease Control and Prevention. Jiulongpo District, Chongqing. People's Republic of China. [2]Institute of School of Public Health. Lanzhou University. Lanzhou, People's Republic of China

Abstract

Objective: to conduct a systematic review of the observational studies analyzing the association between ultra-processed food (UPF) intake and the risk of depression.

Material and methods: the search adhered to the guidelines of Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA); a search for observational studies published until June 2020 was performed in PubMed, Embase, Cochrane Library, and Web of Science databases, followed by additional manual searches. Eight reviewers, working independently in teams of two, screened studies for eligibility, extracted data, and assessed risk of bias. We resolved disagreements through discussion or, if necessary, through adjudication by a third (LH). And the study assessed cross-sectional studies using the Agency for Healthcare Research and Quality (AHRQ) methodological checklist and cohort and case-control studies using the Newcastle-Ottawa Scale (NOS) for quality. We used a tabular format to summarize the articles.

Results: twenty-eight studies evaluating UPF intake and risk of depression were finally selected, 21 of which had a cross-sectional design, 6 studies had a cohort design, and 1 had a case-control design. Of these, 4 cohort studies and 17 cross-sectional studies found that consumption of UPF were positively associated with depression or depressive symptoms.

Conclusions: our review demonstrated that most studies included in the systematic review showed that UPF consumption is associated with the risk of depression. Future studies should consider the use of validated food intake assessments and standardized depression assessment methods to promote comparability between studies.

Keywords:

Ultra-processed food. Fast food. Depression. Depressive symptoms.

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Correspondence:

Lun Xiao. Centers for Disease Control and Prevention. No. 56 Panglong Road. Jiulongpo District, Chongqing. People's Republic of China
e-mail: 719316527@qq.com

Resumen

Objetivo: realizar una revisión sistemática de los estudios observacionales que analizan la asociación entre la ingesta de alimentos ultraprocesados (UPF) y el riesgo de depresión.

Material y métodos: la búsqueda se adhirió a las directrices Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA); se realizó una búsqueda de estudios observacionales publicados hasta junio de 2020 en las bases de datos PubMed, Embase, Cochrane Library y Web of Science, seguida de búsquedas manuales adicionales. Ocho revisores, que trabajaron de forma independiente en equipos de dos, seleccionaron los estudios para su elegibilidad, extrajeron los datos y evaluaron el riesgo de sesgo. Los desacuerdos se resolvieron a través de la discusión o, si era necesario, a través de la adjudicación de un tercero. Se evaluaron los estudios transversales mediante la lista de comprobación metodológica de la Agency for Healthcare Research and Quality (AHRQ) y los estudios de cohortes y de casos y controles mediante la escala Newcastle-Ottawa (NOS) para la calidad. Se utilizó un formato tabular para resumir los artículos.

Resultados: finalmente se seleccionaron 28 estudios que evaluaban la ingesta de UPF y el riesgo de depresión, 21 de los cuales tenían un diseño transversal, 6 un diseño de cohortes y 1 un diseño de casos y controles. De ellos, 4 estudios de cohortes y 17 estudios transversales encontraron que el consumo de UPF se asociaba positivamente con la depresión o los síntomas depresivos.

Conclusiones: nuestra revisión demostró que la mayoría de los estudios incluidos en la revisión sistemática mostraron que el consumo de UPF está asociado con el riesgo de depresión. Los estudios futuros deberían considerar el uso de evaluaciones validadas del consumo de alimentos y métodos estandarizados de evaluación de la depresión para promover la comparabilidad entre los estudios.

Palabras clave:

Alimentos ultraprocesados. Comida rápida. Depresión. Síntomas depresivos.

INTRODUCTION

Depression refers to a wide range of mental health problems characterized by the absence of positive affect (a loss of interest and enjoyment in ordinary things and experiences), persistent low mood, and a range of associated emotional, cognitive, physical, and behavioral symptoms (1). Affecting more than 264 million people worldwide (2), depression is a leading cause of disease burden and a major contributor to global disability (3). It has been estimated that current treatments reduce only about one-third of the disease burden associated with major depressive disorder (4). However, a recent study has shown that preventative interventions can reduce the incidence of depression by 21 % (5). Therefore, public health interventions to prevent depression are particularly important. In the face of a multitude of preventive measures, we must focus on areas that are malleable or highly influential, while acknowledging the role of other factors, including diet (6). Ultra-processed foods (UPFs) are becoming dominant in the global food system (7), and are generally energy-dense, rich in refined carbohydrates, saturated fats, and salt, and contain low dietary fiber (8). These foods include savory snacks, industrialized candies and desserts, reconstituted meat products, prepared frozen dishes, and soft drinks (9). Therefore, the study of the association between UPF and depression is likely to provide public health strategies for the prevention of depression.

A growing number of studies have demonstrated the potential health hazards of UPF (10), and we suspect that it may contribute to an increase in depression. Several epidemiological studies (11-13) show a positive association between UPF and depression, but some also suggest that consumption of UPF is not linked to a higher prevalence of depression (14,15). In the current study, we systematically reviewed the literature investigating UPF intake and risk of depression in an attempt to synthesize the current state of the literature, to inform further research, and to provide strategies for the prevention of depression.

MATERIALS AND METHODS

STUDY DESIGN

The search used Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, and the review was registered in the International Prospective Register of Systematic Reviews (PROSPERO) database (CRD42020192648) (16). A systematic review of studies published until June 3, 2020, was performed in PubMed, Embase, Cochrane Library, and Web of Science databases with an additional manual search conducted via references of found studies.

INCLUSION/EXCLUSION CRITERIA

Studies were included if they met the following criteria: 1) cohort studies, case-control studies, and cross-sectional studies; 2) the exposure factor was consumption of ultra-processed foods; 3) the outcome factors were depression, depressive symptoms or depressive mood; and 4) the odds ratio (OR), relative risk (RR) or hazard ratio (HR) with 95 % confidence interval (CI) were provided or could be calculated.

Exclusion criteria: 1) Studies of inverse associations (i.e., those that examine the effects of depression, depressive symptoms, or depressed mood on the intake of ultra-processed foods); 2) only the effect of dietary patterns on depression was assessed, and not for a single food group; 3) it did not evaluate the association between UPF and depression risk; and 4) those for which the full text could not be found or that were not published in English.

SEARCH STRATEGY

The search for studies was performed in PubMed, Embase, Cochrane Library, and Web of Science databases up to June 2020;

the search strategy is shown in the supplementary table I. In addition, a manual search for publications was conducted via analyzing the references of the found studies.

Eight reviewers working independently in pairs of two screened all titles and abstracts following training and calibration exercises; a third reviewer adjudicated conflicts. Full texts of these potentially eligible studies were also independently assessed for eligibility by the pair, and any disagreements were resolved through discussion with a third researcher. This procedure is presented in figure 1.

Supplementary Table I

Databases [Platform] *Searches run*		**Results**
PubMed June 3, 2020		4396
Embase 1947 to 2020 June *3* [Ovid]		10869
Cochrane Library June *3* 2020 [Ovid]		1426
Web of science June *3* 2020		1778
	Total	18469
PubMed Jun 3, 2020 Search Strategy:		
#	**Searches**	**Results**
1	"ultra processed "[Title/Abstract] OR "ultraprocessed "[Title/Abstract] OR "ultra-processed "[Title/Abstract]	414
2	"Fast Foods"[MeSH]	2078
3	"ready-to-eat"[Title/Abstract] OR "ready-to-consume"[Title/Abstract] OR "convenience food*"[Title/Abstract] OR "fast-food*"[Title/Abstract] OR "fast food*"[Title/Abstract] OR "fastfood*"[Title/Abstract] OR "junk food*"[Title/Abstract] OR "prepared food*"[Title/Abstract]	7124
4	"Carbonated Beverages"[MeSH]	2905
5	"Carbonated Beverage*"[Title/Abstract] OR "Energy Drink*"[Title/Abstract] OR "soft drink*"[Title/Abstract] OR "soft-drink*"[Title/Abstract] OR "soda"[Title/Abstract]	9464
6	"Sugar-Sweetened Beverages"[MeSH]	104
7	"Sugar-sweetened beverage*"[Title/Abstract] OR "sugar sweetened beverage*"[Title/Abstract] OR "artificially sweetened beverage*"[Title/Abstract] OR "artificially-sweetened beverage*"[Title/Abstract] OR "fruit juice*"[Title/Abstract] OR "juice*"[Title/Abstract]	35613
8	"Candy"[Title/Abstract] OR "sweet"[Title/Abstract] OR "Sweety"[Title/Abstract] OR "sweetie"[Title/Abstract] OR "sweetmeat"[Title/Abstract] OR "Dessert "[Title/Abstract] OR "cake"[Title/Abstract] OR "ice cream"[Title/Abstract] OR "chocolate"[Title/Abstract] OR "snacks"[Title/Abstract] OR "burger"[Title/Abstract] OR "French fries"[Title/Abstract] OR "sausage"[Title/Abstract] OR "banger"[Title/Abstract] OR" wiener"[Title/Abstract] OR "salami" [Title/Abstract] OR "bratwurst"[Title/Abstract] OR "frankfurter" [Title/Abstract] OR "breakfast cereal*"[Title/Abstract]	41799
9	"Feeding Behavior" [MeSH]	168919
10	"dietary pattern*"[Title/Abstract] OR "dietary behavior*"[Title/Abstract] OR "dietary habit*"[Title/Abstract] OR "Feeding Behavior*"[Title/Abstract]	26963
11	OR/1- 10	266843
12	"depressive disorder"[MeSH]	108415
13	"depressive disorder*"[Title/Abstract] OR "Major Depressive Disorder*"[Title/Abstract]	36397
14	"depression"[MeSH]	117732
15	"depression"[Title/Abstract]	335435
16	"adjustment disorders"[MeSH]	4205
17	"Adjustment Disorder*"[Title/Abstract]	1698
18	"mood disorders"[MeSH]	121221
19	"mood disorder*"[Title/Abstract] OR "Affective Disorder*"[Title/Abstract]	33502
20	"bipolar disorder"[MeSH]	40051
21	"Bipolar Disorder*"[Title/Abstract]	28510
22	OR/12-21	454365
23	11 AND 22	4396

(Continues on next page)

Supplementary Table I (Cont.)

Embase Jun 3, 2020 Search Strategy:		
#	**Searches**	**Results**
1	'ultra processed':ab,ti OR 'ultraprocessed':ab,ti OR 'ultra-processed':ab,ti	472
2	'Fast Foods'/exp OR 'ready-to-eat':ab,ti OR 'ready-to-consume':ab,ti OR 'convenience food*':ab,ti OR 'fast-food*':ab,ti OR 'fast food*':ab,ti OR 'fastfood*':ab,ti OR 'junk food*':ab,ti OR 'prepared food*':ab,ti	13437
3	'Carbonated Beverages'/exp OR 'Carbonated Beverages':ab,ti OR 'Energy Drink*':ab,ti OR 'soft drink':ab,ti OR 'soft drinks':ab,ti	8942
4	'Sugar-Sweetened Beverages'/exp OR 'sugar-sweetened beverage*':ab,ti OR 'sugar sweetened beverage*':ab,ti OR 'artificially sweetened beverage*':ab,ti OR 'artificially-sweetened beverage*':ab,ti OR 'fruit juice*':ab,ti OR 'juice*':ab,ti	45425
5	'Candy':ab,ti OR 'sweet':ab,ti OR 'Sweety':ab,ti OR 'sweetie':ab,ti OR 'sweetmeat':ab,ti OR 'Dessert':ab,ti OR 'cake':ab,ti OR 'ice cream':ab,ti OR 'chocolate':ab,ti OR 'snacks':ab,ti OR 'burger':ab,ti OR 'French fries':ab,ti OR 'sausage':ab,ti OR 'banger':ab,ti OR 'wiener':ab,ti OR 'salami':ab,ti OR 'bratwurst':ab,ti OR 'frankfurter':ab,ti OR 'breakfast cereal':ab,ti OR 'Breakfast cereals':ab,ti	54277
6	'Feeding Behavior'/exp OR 'dietary pattern*':ab,ti OR 'dietary behavior*':ab,ti OR 'dietary habit*':ab,ti OR 'Feeding Behavior*':ab,ti	201657
7	OR/1-6	303157
8	'depressive disorder'/exp OR 'depressive disorder*':ab,ti OR 'Major Depressive Disorder*':ab,ti	499118
9	'depression'/exp OR 'depression':ab,ti	698352
10	'adjustment disorder*'/exp OR 'Adjustment Disorder*':ab,ti	5393
11	'mood disorder*'/exp OR 'mood disorder*':ab,ti OR 'Affective Disorder*':ab,ti	75873
12	'bipolar disorder'/exp OR 'Bipolar Disorder*':ab,ti	78442
13	OR/8-12	733423
14	7 AND 13	10869
Cochrane Library Jun 3, 2020 Search Strategy:		
#	**Searches**	**Results**
1	(ultra processed):ti,ab,kw OR (ultraprocessed):ti,ab,kw OR (ultra-processed):ti,ab,kw	52
2	MeSH descriptor: [Fast Foods] explode all trees	98
3	(ready-to-eat):ti,ab,kw OR (ready-to-consume):ti,ab,kw OR (convenience food*):ti,ab,kw OR (fast-food*):ti,ab,kw OR (fast food*):ti,ab,kw OR (fastfood*):ti,ab,kw OR (junk food*):ti,ab,kw OR (prepared food*):ti,ab,kw	3338
4	MeSH descriptor: [Carbonated Beverages] explode all trees	168
5	(Carbonated Beverage*):ti,ab,kw OR (Energy Drink*):ti,ab,kw OR (soft drink*):ti,ab,kw	2108
6	MeSH descriptor: [Sugar-Sweetened Beverages] explode all trees	7
7	(sugar-sweetened beverage*):ti,ab,kw OR (sugar sweetened beverage*):ti,ab,kw OR (artificially sweetened beverage*):ti,ab,kw OR (artificially-sweetened beverage*):ti,ab,kw OR (fruit juice*):ti,ab,kw OR (juice*):ti,ab,kw	4968
8	(Candy):ti,ab,kw OR (sweet):ti,ab,kw OR (Sweety):ti,ab,kw OR (sweetie):ti,ab,kw OR (sweetmeat):ti,ab,kw OR (Dessert):ti,ab,kw OR (cake):ti,ab,kw OR (ice cream):ti,ab,kw OR (chocolate):ti,ab,kw OR (snacks):ti,ab,kw OR (burger):ti,ab,kw OR (French fries):ti,ab,kw OR (sausage):ti,ab,kw OR (banger):ti,ab,kw OR (wiener):ti,ab,kw OR (salami):ti,ab,kw OR (bratwurst):ti,ab,kw OR (frankfurter):ti,ab,kw OR (breakfast cereal):ti,ab,kw OR (Breakfast cereals):ti,ab,kw	4565
9	MeSH descriptor: [Feeding Behavior] explode all trees	8589
10	(Feeding Behavior*):ti,ab,kw OR (dietary pattern*):ti,ab,kw OR (dietary behavior*):ti,ab,kw OR (dietary habit*):ti,ab,kw	14177
11	OR/1-10	30491

(Continues on next page)

Supplementary Table I (Cont.).

Cochrane Library Jun 3, 2020 Search Strategy:		
#	**Searches**	**Results**
13	(depressive disorder*):ti,ab,kw OR (Major Depressive Disorder*):ti,ab,kw	20467
14	MeSH descriptor: [depression] explode all trees	11836
15	(depression):ti,ab,kw	72816
16	MeSH descriptor: [adjustment disorders] explode all trees	246
17	(adjustment disorder*):ti,ab,kw	2930
18	MeSH descriptor: [mood disorders] explode all trees	12617
19	(mood disorder*):ti,ab,kw OR (Affective Disorder*):ti,ab,kw	12034
20	MeSH descriptor: [bipolar disorder] explode all trees	2638
21	(Bipolar Disorder*):ti,ab,kw	6258
22	OR/12-21	84777
23	11 AND 22	1426
Web of Science Jun 3, 2020 Science Citation Index Expanded (SCI-EXPANDED) – from 1980 to now Social Sciences Citation Index (SSCI) – from 1980 to now Search Strategy:		
#	**Searches**	**Results**
1	TS = ("ultra processed" OR "ultraprocessed" OR "ultra-processed")	519
2	TS = ("ready-to-eat" OR "ready-to-consume" OR "convenience food*" OR "fast-food*" OR "fast food*" OR "fastfood*" OR "junk food*" OR "prepared food*")	10773
3	TS = ("Carbonated Beverage*" OR "Energy Drink*" OR "soft drink*" OR "soft-drink*" OR "soda")	23397
4	TS = ("sugar-sweetened beverage*" OR "sugar sweetened beverage*" OR "artificially sweetened beverage*" OR "artificially-sweetened beverage*" OR "fruit juice*" OR"juice*")	55976
5	TS = ("Candy" OR "sweet" OR "Sweety" OR "sweetie"OR "sweetmeat" OR "Dessert " OR "cake" OR "ice cream"] OR "chocolate" OR "snacks" OR "burger" OR "French fries" OR"sausage"OR "banger" OR"wiener" OR "salami" OR"bratwurst" OR "frankfurter" OR "breakfast cereal*")	114552
6	TS = ("dietary pattern*" OR "dietary behavior*" OR "dietary habit*" OR "Feeding Behavior*")	38372
7	OR/#1-#6	232560
8	TS = ("depressive disorder*" OR "MajorDepressiveDisorder*")	44885
9	TS ="depression"	438927
10	TS ="Adjustment Disorder*"	1546
11	TS = ("mood disorder*" OR "Affective Disorder*")	42795
12	TS ="Bipolar Disorder*"	45764
13	OR/#8-#12	497590
14	#7 AND #13	1778

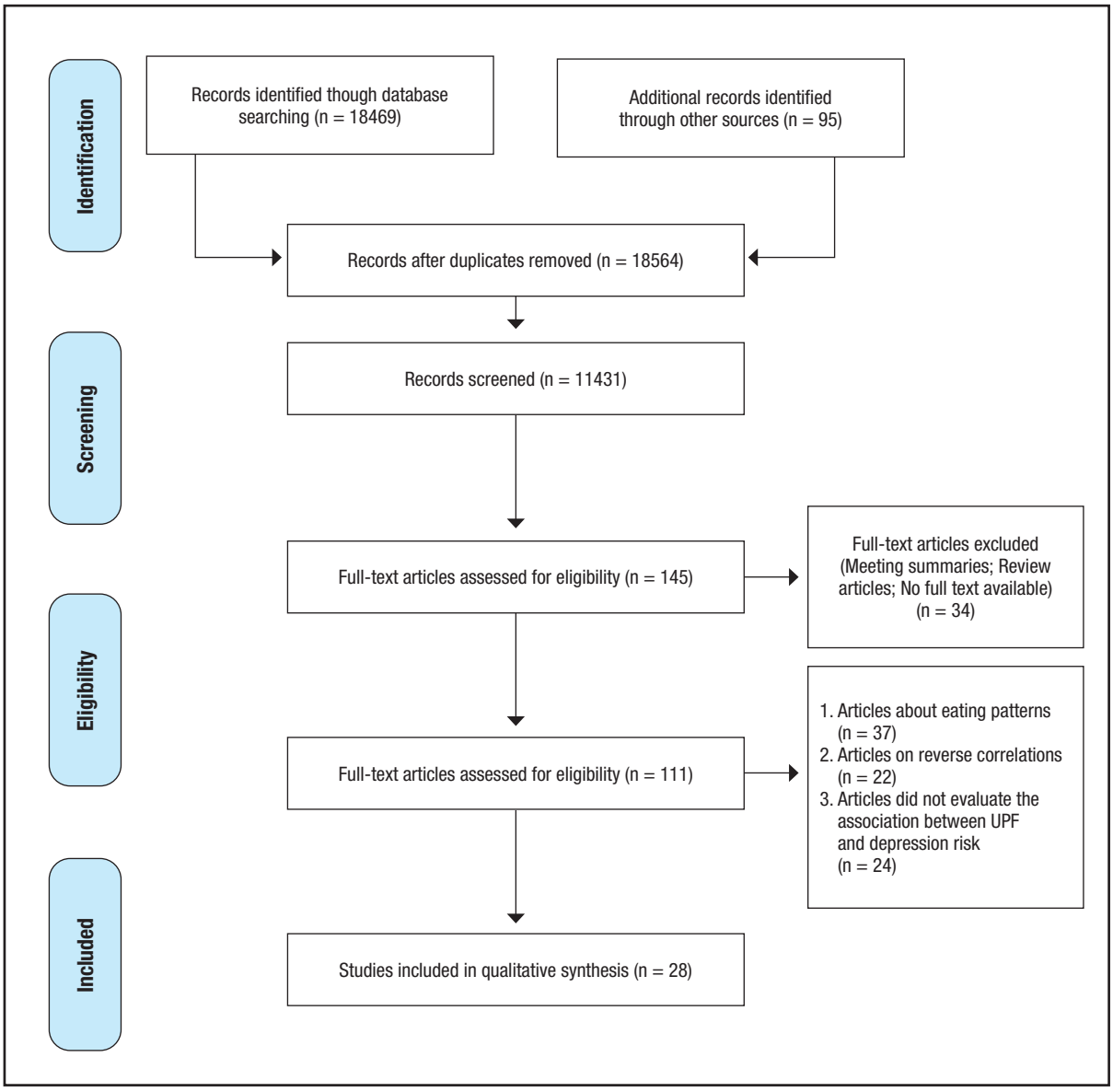

Figure 1.

The procedure of identification, screening, eligibility assessment, and inclusion within the conducted systematic review (UPF: ultra-processed foods).

DATA EXTRACTION

Data extraction was conducted independently by two researchers, and disagreements were resolved through discussion with a third researcher.

Data extracted from the studies included the following: author and publication year; country; study design; sample size; age group evaluated; the percentage of females; methods and instruments used to measure the exposure and outcome variables; variables used to control for confounding and in the mediation analysis (when present), and main results.

The quality of the included literature was assessed using the Newcastle-Ottawa Scale (NOS) for cohort and case-control studies (17), and the Agency for Healthcare Research and Quality (AHRQ) methodology checklist for cross-sectional studies (18). The detailed evaluation methods are shown in supplementary table II. The results of case-control studies and cohort studies were interpreted based on the commonly assumed criteria and attributed to the following categories: very high risk of bias (0-3 NOS points), high risk of bias (4-6 NOS points), and low risk of bias (7-9 NOS points) (19). Cross-sectional studies were assessed as follows: low quality = 0-3; moderate quality = 4-7; and high quality = 8-11.

Supplementary Table II

1. NEWCASTLE - OTTAWA QUALITY ASSESSMENT SCALE CASE CONTROL STUDIES									
Note: A study can be awarded a maximum of one star for each numbered item within the Selection and Exposure categories. A maximum of two stars can be given for Comparability.									
	Selection				**Comparability**	**Exposure**			**Total stars**
ID	**1. Is the case definition adequate?**	**2. Representativeness of the cases**	**3. Selection of controls**	**4. Definition of controls**	**1. Comparability of cases and controls on the basis of the design or analysis**	**1. Ascertainment of exposure**	**2. Same method of ascertainment for cases and controls**	**3. Non-response rate**	
5	a) yes with independent validation	a) consecutive or obviously representative series of cases	b) hospital controls	a) no history of disease (endpoint)	c) a and b	b) structured interview where blind to case/ control status	a) yes	a) same rate for both groups	8

2. NEWCASTLE - OTTAWA QUALITY ASSESSMENT SCALE COHORT STUDIES									
Note: A study can be awarded a maximum of one star for each numbered item within the Selection and Outcome categories. A maximum of two stars can be given for Comparability									
	Selection				**Comparability**	**Exposure**			**Total stars**
ID	**1. Representativeness of the exposed cohort**	**2. Selection of the nonexposed cohort**	**3. Ascertainment of exposure**	**4. Demonstration that outcome of interest was not present at start of study**	**1. Comparability of cohorts on the basis of the design or analysis**	**1. Ascertainment of exposure**	**2. Was follow-up long enough for outcomes to occur?**	**3. Adequacy of follow-up of cohorts**	
46	b) somewhat representative of the average _____in the community	a) drawn from the same community as the exposed cohort	a) secure record (e.g. surgical records)	a) yes	c) a and b	b) record linkage	a) yes (select an adequate follow-up period for outcome of interest)	c) follow-up rate < ____% (select an adequate %) and no description of those lost	8
74	b) somewhat representative of the average _____in the community	a) drawn from the same community as the exposed cohort	c) written self report	b) no	c) a and b	a) independent blind assessment	a) yes (select an adequate follow up period for outcome of interest)	d) no statement	6
105	a) truly representative of the average _____(describe) in the community	a) drawn from the same community as the exposed cohort	c) written self report	a) yes	c) a and b	b) record linkage	a) yes (select an adequate follow up period for outcome of interest)	a) complete follow-up - all subjects accounted for	8

(Continues on next page)

Supplementary Table II (Cont.).

2. NEWCASTLE - OTTAWA QUALITY ASSESSMENT SCALE COHORT STUDIES									
Note: A study can be awarded a maximum of one star for each numbered item within the Selection and Outcome categories. A maximum of two stars can be given for Comparability									
	Selection				**Comparability**	**Exposure**			**Total stars**
ID	**1. Representativeness of the exposed cohort**	**2. Selection of the nonexposed cohort**	**3. Ascertainment of exposure**	**4. Demonstration that outcome of interest was not present at start of study**	**1. Comparability of cohorts on the basis of the design or analysis**	**1. Ascertainment of exposure**	**2. Was follow-up long enough for outcomes to occur?**	**3. Adequacy of follow-up of cohorts**	
125	a) truly representative of the average _____(describe) in the community	a) drawn from the same community as the exposed cohort	c) written self report	a) yes	c) a and b	a) independent blind assessment	a) yes (select an adequate follow-up period for outcome of interest)	d) no statement	7
133	a) truly representative of the average _____(describe) in the community	a) drawn from the same community as the exposed cohort	c) written self report	a) yes	c) a and b	a) independent blind assessment	a) yes (select an adequate follow up period for outcome of interest)	a) complete follow-up - all subjects accounted for	8
136	a) truly representative of the average _____(describe) in the community	a) drawn from the same community as the exposed cohort	c) written self report	b) no	c) a and b	c) self report	b) no	c) follow-up rate < ____% (select an adequate %) and no description of those lost	4

3. An 11-item checklist which was recommended by Agency for Healthcare Research and Quality (AHRQ)												
An item would be scored '0' if it was answered 'NO' or 'UNCLEAR'; if it was answered 'YES', then the item scored '1'. Article quality was assessed as follows: low quality = 0–3; moderate quality = 4-7; highquality= 8–11.												
ID	**1. Define the source of information (survey, record review)**	**2. List inclusion and exclusion criteria for exposed and unexposed subjects (cases and controls) or refer to previous publications**	**3. Indicate time period used for identifying patients**	**4. Indicate whether or not subjects were consecutive if not population-based**	**5. Indicate if evaluators of subjective components of study were masked to other aspects of the status of the participants**	**6. Describe any assessments undertaken for quality assurance purposes (e.g., test/retest of primary outcome measurements)**	**7. Explain any patient exclusions from analysis**	**8. Describe how confounding was assessed and/or controlled**	**9. If applicable, explain how missing data were handled in the analysis**	**10. Summarize patient response rates and completeness of data collection**	**11. Clarify what follow-up, if any, was expected and the percentage of patients for which incomplete data or follow-up was obtained**	**Total score**
51	1) yes	2) no	1) yes	1) yes	2) no	2) no	2) no	1) yes	2) no	2) no	2) no	5
52	1) yes	2) no	2) no	1) yes	2) no	1) yes	2) no	1) yes	2) no	2) no	2) no	5

(Continues on next page)

Supplementary Table II (Cont.).

3. An 11-item checklist which was recommended by Agency for Healthcare Research and Quality (AHRQ)												
An item would be scored '0' if it was answered 'NO' or 'UNCLEAR'; if it was answered 'YES', then the item scored '1'. Article quality was assessed as follows: low quality = 0–3; moderate quality = 4-7; high quality = 8–11.												
ID	**1. Define the source of information (survey, record review)**	**2. List inclusion and exclusion criteria for exposed and unexposed subjects (cases and controls) or refer to previous publications**	**3. Indicate time period used for identifying patients**	**4. Indicate whether or not subjects were consecutive if not population-based**	**5. Indicate if evaluators of subjective components of study were masked to other aspects of the status of the participants**	**6. Describe any assessments undertaken for quality assurance purposes (e.g., test/retest of primary outcome measurements)**	**7. Explain any patient exclusions from analysis**	**8. Describe how confounding was assessed and/or controlled**	**9. If applicable, explain how missing data were handled in the analysis**	**10. Summarize patient response rates and completeness of data collection**	**11. Clarify what follow-up, if any, was expected and the percentage of patients for which incomplete data or follow-up was obtained**	**Total score**
65	1) yes	1) yes	2) no	1) yes	2) no	1) yes	1) yes	1) yes	2) no	2) no	2) no	7
87	1) yes	1) yes	2) no	1) yes	2) no	1) yes	2) no	1) yes	2) no	2) no	2) no	6
89	1) yes	2) no	2) no	1) yes	2) no	1) yes	2) no	1) yes	2) no	1) yes	1) yes	7
99	1) yes	1) yes	2) no	3) unclear	2) no	1) yes	2) no	1) yes	2) no	1) yes	2) no	6
109	1) yes	2) no	2) no	1) yes	2) no	2) no	2) no	1) yes	2) no	1) yes	2) no	4
116	1) yes	1) yes	2) no	1) yes	2) no	1) yes	2) no	1) yes	2) no	1) yes	2) no	7
117	1) yes	2) no	2) no	1) yes	2) no	2) no	2) no	1) yes	2) no	2) no	2) no	5
124	1) yes	1) yes	2) no	1) yes	2) no	1) yes	2) no	1) yes	2) no	1) yes	2) no	6
128	1) yes	1) yes	2) no	1) yes	2) no	1) yes	2) no	1) yes	2) no	2) no	2) no	6
130	1) yes	2) no	2) no	1) yes	2) no	1) yes	2) no	1) yes	2) no	1) yes	2) no	6
132	1) yes	2) no	2) no	1) yes	2) no	2) no	2) no	1) yes	2) no	2) no	2) no	4
159	1) yes	2) no	2) no	1) yes	2) no	2) no	2) no	1) yes	2) no	2) no	2) no	4
160	1) yes	1) yes	2) no	1) yes	2) no	1) yes	2) no	1) yes	2) no	1) yes	2) no	7
167	1) yes	2) no	2) no	1) yes	2) no	1) yes	2) no	1) yes	2) no	2) no	2) no	5
171	1) yes	1) yes	2) no	3) unclear	2) no	1) yes	1) yes	1) yes	2) no	2) no	2) no	6
173	1) yes	2) no	2) no	1) yes	2) no	1) yes	2) no	1) yes	2) no	2) no	2) no	5
179	1) yes	2) no	2) no	1) yes	2) no	1) yes	2) no	2) no	2) no	2) no	2) no	4
181	1) yes	1) yes	2) no	1) yes	2) no	1) yes	1) yes	1) yes	2) no	1) yes	2) no	8
188	1) yes	2) no	2) no	1) yes	2) no	2) no	2) no	2) no	2) no	2) no	2) no	3

Table I. Summary of the selected studies that investigated the association between UPF and depression

Author, year, ref.; country	Study design	Study group age (years), n; female (%)	Exposure	Outcomes	Adjustment variables	Main results	Quality
Xia *et al.* (2017) (30) China	Case-control study	Adults (46.14 ± 12.56) 2,702; 46.33	FFQ: sugared beverages and snacks	SDS: high depressive symptoms	Other food groups intake	Consumption of sugared beverages and snacks ($p = 0.32$) was not associated with a higher prevalence of high depressive symptoms (OR = 1.09; 95 % CI: 0.87-1.35)	8
Kim *et al.* (2020) (33) Korea	Cross-sectional study	Adolescents (12-18) 53,312; 50.58	Specific question: energy drink	Specific question: depressive mood	Age, school grades, economic status, residential status, smoking, drinking, physical activity	The prevalence of students with depressive mood increased as energy drink intake per week increased (boys, 1-2 times/wk: OR = 1.17, 95 % CI: 1.07-1.27; 3 times/wk: OR = 1.40, 95 % CI: 1.25-1.56; girls, 1-2 times/wk: OR = 1.22, 95 % CI: 1.12-1.32; 3 times/wk: OR = 1.61, 95 % CI: 1.44-1.79)	5
Sangsefidi *et al.* (2020) (36) Iran	Cross-sectional study	Adults (20-70) 9,965; 50.3	Questionnaire: sweetened drinks, fast foods, snacks	DASS 21: depression	Age, education level, physical activity, chronic diseases, smoking, and BMI	Consuming sweetened drinks (OR = 0.76; 95 % CI: 0.59-0.96), fast food (OR = 1.61; 95 % CI:1.18-2.18) and snacks (OR = 1.39, 95 % CI: 1.03-1.87) for once or more per week was significantly related to lower odds of depressive features as opposed to its lack of consumption	5
Jackson *et al.* (2019) (26) US	Cross-sectional study	Adults (≥ 20) 13,626; 52.05	24-hr recall: chocolate	PHQ-9: dpressive symptoms	Age, sex, BMI, race, education, annual household income, physical activity, smoking, energy sugar, alcohol and dark chocolate consumption, chronic diseases	A significant association between the highest quartile of total chocolate consumption and clinically relevant depressive symptoms (OR = 0.43, 95 % CI: 0.19-0.96)	7
Pengpid *et al.* (2019) (43); Indonesia, Malaysia *et al.*	Cross-sectional survey	University students (18-30) 3,353; 62.9	Specific question: carbonated soft drinks	CES-D: depression (severe)	Age, country, sex, wealth status, social support, body weight status, and physical activity	Higher frequency of soft drink consumption (two or more times a day) was associated with depression in females (OR = 1.34, 95 % CI: 1.06-1.67)	5
Sousa *et al.* (2019) (38); Brazil	Cross-sectional study	Adults (20-59) 46,785; 52.1	FFQ: sugar sweetened beverages, sweets, snack	PHQ-9: depression	Age, sex, race/color, education, living with a spouse, physical activity, alcohol consumption, and tobacco use	Regular consumption of sweets (OR = 1.53; 95 % CI: 1.33-1.76) and regular replacement of meals for snacks (OR = 1.52; 95 % CI: 1.21-1.90) were positively associated with depression, for regular sugar-sweetened beverages consumption, we found a positive association with depression only in women (OR = 1.27; 95 % CI: 1.10-1.48)	6
Toblin *et al.* (2018) (27); US	Cross-sectional study	Soldiers after deployment (NR) 627; 0	Specific question: energy drink	PHQ-9: depression	Age, rank, education, and deployment history	Soldiers with high frequency of energy drink consumption were more likely to exceed criteria for depression (OR = 2.2; 95 % CI: 0.1-14.6)	7
Wrzosek *et al.* (2018) (20); Europe	Cross-sectional study	Bariatric surgery candidates (43.6 ± 11.5) 361; 73	EDE-Q: snack foods	BDI-II: depressive symptoms	Physical activity, night eating, number of emotions associated with desire to eat	Daily consumption of snack foods ($p < 0.001$) was significantly associated with depression (OR = 2.2; 95 % CI: 0.1-14.6)	6

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Table I (Cont.). Summary of the selected studies that investigated the association between UPF and depression

Author, year, ref.; country	Study design	Study group age (years), n; female (%)	Exposure	Outcomes	Adjustment variables	Main results	Quality
Lazarevich *et al.* (2018) (41); Mexico	Cross-sectional study	Freshman students (19.6 ± 2.4) 1,104; 59.7	FFQ: fast food, sweetened drinks	CES-D: depressive symptoms	Age and BMI	In women, the frequent consumption of fast food (OR = 2.07, 95 % CI: 1.13-3.78; $p = 0.018$) was associated with a higher depression score. No association was observed between depression score and food variables in men.	4
Hong *et al.* (2017) (34); Korea	Cross-sectional study	Adolescents (12-18) 65,528; 47.8	Questionnaire: soft drinks, sweetened drinks, fast foods	Questionnaire: depression symptoms	Age, sex, socioeconomic status, school level, school types, BMI, physical activity, and substance use	Consuming soft drinks (OR = 2.07, 95 % CI: 1.75-2.44), sweetened drinks (OR = 1.97, 95 % CI: 1.67-2.32), fast foods (OR = 3.57, 95 % CI: 2.62-4.87) for 3+ times/day was significantly related to higher odds of depression as opposed to its lack of consumption	4
Ruiz-Cabello *et al.* (2017) (21); Spain	Cross-sectional study	Women (52.2 ± 8.0) 486; 100	FFQ: sweets, sweetened beverages	BDI-II: depressive symptoms	Age and percent body fat	Cereals ($p = 0.215$, OR = 0.632, 95 % CI: 0.307, 1.304), sweets ($p = 0.215$, OR = 0.632, 95 % CI: 0.307, 1.304) and sweetened beverages ($p = 0.524$, OR = 1.257, 95 % CI: 0.622, 2.540) were not associated with depression	6
Pabayo *et al.* (2016) (28); USA	Cross-sectional study	High-school students (13-19) 1,611; 54.3	Questionnaire: soda, fruit drink, sweetened beverage	MDS: depressive symptoms	NR	Consuming soda 2-6 times/week ($\beta = 0.18$; 95 % CI: 0.04-0.32) and ≥ 1 times/d ($\beta = 0.29$; 95 % CI: 0.13-0.45) had significantly greater depressive scores. Consuming drank fruit drinks 2-6 times/week ($\beta = 0.14$; 95 % CI: 0.00-0.28) and ≥ 1 times/d ($\beta = 0.22$; 95 % CI: 0.04-0.40) had significantly greater depressive scores	7
Takahashi *et al.* (2016) (42); Japan	Cross-sectional study	Pregnant women (31.0 ± 5.0) 9,030; 100	FFQ: lactic acid beverage	K6: depressed feeling	Only crude analysis	No associations between psychological distress and the intake of lactic acid beverages (OR = 1.334, 95 % CI: 0.961-1.744)	8
Richards *et al.* (2016) (22); England	Cross-sectional study	Students (11-17) 3323; 51.5	DABS: energy drink	WPQ: depression	NR	No associations between depression and energy drinks (OR = 1.334, 95 % CI: 0.961-1.744)	3
Park *et al.* (2016) (35); Korea	Cross-sectional study	Adolescents (12-18) 68,043; 47.87	Questionnaire: energy drink	Questionnaire: depressed feeling	Age, gender, school type, area of residence, residential type, academic achievement, junk food and alcohol consumption, and physical activity	Participants who used energy drinks highly frequently (OR = 2.59, 95 % CI: 2.54-2.65) and moderately frequently (OR = 1.51, 95 % CI: 1.49-1.52) were more likely to experience depressive mood, compared to participants who used energy drinks infrequently or did not use energy drinks	5

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Table I (Cont.). Summary of the selected studies that investigated the association between UPF and depression

Author, year, ref.; country	Study design	Study group age (years), n; female (%)	Exposure	Outcomes	Adjustment variables	Main results	Quality
Yu *et al.* (2015) (31); China	Cross-sectional study	Adults (42.5 ± 12.1) 3,667; 39.82	FFQ: soft drink	SDS: depression symptoms	Age, sex, body mass index, smoking status, drinking status, physical activity, marital status, total energy intake, household incomes, employment status, educational levels, visiting friends, green tea,black tea, coffee, and juices	The ORs for depressive symptoms (SDS ≥ 50) for each level of soft drink consumption were < 1 cup/week (OR = 1.00); 1-3 cups/week (OR = 1.43, 95 % CI: 1.01-2.01); and ≥ 4 cups/week (OR = 2.00, 95 % CI: 1 .15-3.37); $p < 0.01$. Compared to participants who consumed < 1 cup/week, consumption of ≥ 4 cups/week of soft drinks doubled the prevalence of depressive symptoms	6
Azagba *et al.* (2014) (39); Canada	cross-sectional study	High school students (15.2 ± 0.06) 8,210; 51.8	Questionnaire: energy drink	CES-D: depressive symptoms	Unequal probabilities of selection	There was a clear dose-response pattern for the association between depressive symptoms and energy drink. An OR of 1.40 for consuming energy drinks one or two times per year; an OR of 1.14 for consuming energy drinks three to eight times per year; an OR of 2.08 for consuming energy drinks once per month; and an OR of 2.73 when consuming energy drinks more than once per month	6
Ansari *et al.* (2014) (23); The United Kingdom	cross-sectional survey	University students (24.9 ± 8.6) 3,706; 72.83	FFQ: sweets/ cookies/ snacks/ fast food, lemonade/soft drinks	MBDI: depressive symptoms	University and for all other variables	As for sweets/cookies/snacks/fast food (Female: $p = 0.001$, estimate = 0.072; male: $p < 0.001$, estimate = 0.158) more frequent consumption of these foods was significantly associated with higher depressive symptoms for both males and females. But consuming lemonade/soft drinks (female: $p = 0.128$, estimate = 0.032; male: $p = 0.270$, estimate = -0.047) was not associated with depressive symptoms	6
Zahedi et al. (2014) (37); Iran	Cross-sectional survey	Students (6-18); 13,486 49.24	Questionnaire: sweets, sweetened beverages, fast foods, salty snacks	Questionnaire: depression	Age, sex, family history of chronic diseases, mother's education, screen time, physical activity, socioeconomic status, and BMI	The students with daily consumption of sweetened beverages (OR = 1.41, 95 % CI: 1.23-1.61), fast foods (OR = 1.50, 95 % CI: 1.16-1.94), and salty snacks (OR = 1.24, 95 % CI: 1.07-1.43) (compared with seldom eaters) had a significantly higher risk of self-reported psychiatric distress	4

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Table I (Cont.). Summary of the selected studies that investigated the association between UPF and depression

Author, year, ref.; country	Study design	Study group age (years), n; female (%)	Exposure	Outcomes	Adjustment variables	Main results	Quality
Shi *et al.* (2010) (40); Australia	Cross-sectional survey	Adults (≥ 16) 4,741; 51.3	Questionnaire: soft drink	Self report: depression	Age, gender, education, income, area of residence, smoking, drinking, physical activity, overweight, diabetes, asthma, CVD, arthritis, osteoporosis, chronic obstructive pulmonary disease, intake of fruit and vegetables	The intake of soft drinks was significantly associated with depression (OR = 1.63, 95 % CI: 1.03, 2.58)	4
Mikolajczyk *et al.* (2009) (24); Germany, Poland, Bulgaria	cross-sectional survey	Students (20.6 ± 2.3) 1,839; 65.3	FFQ: sweets/ cookies/ snacks/fast food, soft drinks, cereal products	M-BDI: depressive symptoms	Country and for all other variables in the table, separate models for males and females and for both mental health indicators	Higher consumption of carbohydrate-dense foods such as sweets, cookies, snacks, and fast food was not associated with depressive symptoms scores (For male: $p = 0.30$, estimate = -0.89; for female: $p = 0.15$, estimate = 0.96). Soft drinks and cereal products also were not associated with depressive symptoms score.	7
Liu *et al.* (2007) (32); China	cross-sectional survey	College students (about 20.4) 2.541; 42.1	Questionnaire: ready-to-eat food, snack food, fast food	CES-D: depression	Gender, grade, city, perceived weight, smoking, and alcohol use	Depression increased with the frequency of ready-to-eat food (OR = 0.70, 95 % CI: 0.57-0.86) and fast food (OR = 0.40, 95 % CI: 0.12-1.37) consumption	5
Gómez -Donoso *et al.* (2020) (11); Spain	cohort study	University graduates (36.7 ± 11.7) 14, 907; 58.85	FFQ: UPF	Diagnosis: incident depression	Sex, BMI, total energy intake, physical activity, smoking, marital status, living alone, employment status, working hours per week, health-related career, education, adherence to Trichopoulou's MeDiet Score, self-perception of competitiveness, anxiety, and dependence levels	Higher consumption of UPF was directly associated with the risk of developing depression during the follow-up (HR = 1.33, 95 % CI: 1.07-1.64; $p = 0.004$)	8
Adjibade *et al.* (2019) (12); France	cohort study	Adults (≥ 18) 26,730; 76.24	24-hr recall: UPF	CES-D: depressive symptoms	Age, sex, and MBI, marital status, educational level, occupational categories, household income, residential area, 24-h dietary records, inclusion month, energy intake, alcohol intake, smoking, and physical activity	Consumption of UPF was significantly associated with depressive symptoms (HR for a 10% increase in UPF in the diet = 1.14, 95 % CI: 1.09-1.20)	7

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Table I (Cont.). Summary of the selected studies that investigated the association between UPF and depression

Author, year, ref.; country	Study design	Study group age (years), n; female (%)	Exposure	Outcomes	Adjustment variables	Main results	Quality
Elstgeest *et al.* (2019) (14); Italy	cohort study	Older adults (65.8 ± 15.2) 1,058; 55	FFQ: savory snacks, sugar sweetened beverages + fruit juices	CES-D: depressive symptoms	Age, sex, baseline CES-D score, marital status, education level, physical activity, smoking, instrumental activities of daily living disabilities, alcohol intake, and energy intake	Consumption of savoury snacks (B = -0.01, 95 % CI: 0.55-0.54; p = 0.984) and sugar-sweetened beverages + fruit juices (B = -0.23, 95 % CI = 0.78-0.32; p = 0.420) were both not associated with a higher prevalence of depressive symptoms	6
Sanchez -Villegas *et al.* (2018) (15); Spain	cohort study	University graduates (33.4 ± 10.3-40.0 ± 12.7) 15,546; NR	FFQ: energy-adjusted sweetened drink	Diagnosis: depression	Sex, smoking, BMI, physical activity, energy intake, Mediterranean diet, the prevalence of CVD, hypertension, or dyslipidemia and recruitment period	Participants in the upper quartiles of energy-adjusted sweetened drinks consumption(p = 0.090) did not show a significant increment in the risk of depression (HR for the third quartile in the multivariable-adjusted model = 1.04, 95 % CI: 0,83-1.32; HR for the highest quartile = 1.12, 95 % CI: 0.9-1.41)	8
Guo *et al.* (2014) (29); US	cohort study	Older adults (50-71) 263,923; 39.34	FFQ: soft drinks, fruit drinks	Self report: depression	Age, sex, race, education, marital status, smoking, alcoholic beverage intake, physical activity, BMI, and energy intake	Overall, higher consumption of soft drinks or fruit drinks at baseline was monotonically associated with a higher risk of depression. Between the extreme drinking categories (≧ 4 cans/day versus none), the multivariate OR for soft drinks = 1.30, 95 % CI: 1.17-1.44; and OR for fruit drinks = 1.38, 95 % CI: 1.15-1.65; (both p < 0.001). Similar results were found in both genders, except for fruit drinks, where the association was restricted to men	4
Villegas *et al.* (2012) (13); Spain	cohort study	University graduates (NR) 8,964; 58.7	FFQ: fast-food, commercial baked goods	SCID-I: depression	Sex, smoking, physical activity, total energy intake, BMI, and healthy food items consumption	Consumption of fast food in the highest category was associated with a 40 % higher risk of depression (HR = 1.40; 95 % CI: 1.05, 1.86). Moreover, a significant dose-response relationship was found (p = 0.001). And a direct association was also found between commercial baked goods consumption and depression	8

NR: not reported; DABS: Diet and Behaviour Scale; EDE-Q: Eating Disorders Examination-Questionnaire; SDS: Chinese version of Zung Self-Rating Depression Scale; DASS 21: Iranian validated version of depression, anxiety, and stress scale questionnaire 21; PHQ-9: Patient Health Questionnaire-9; CES-D: Center for Epidemiologic Studies Depression Scale; BDI-II: Beck Depression Inventory-II; MDS: Modified Depression Scale; K6: Kessler 6-item psychological distress scale; WPQ: Wellbeing Process Questionnaire; M-BDI: modification of the Beck Depression Inventory; SCID-I: Structured Clinical Interview for DSM-IV; BMI: body mass index.

RESULTS

STUDY CHARACTERISTICS

The list of studies included and details on the studies are presented in table I. All studies in the table are listed according to study design and year of publication. Among the 28 included studies, the majority were conducted in European countries (10 studies) (11-14,20-25), with additional studies from United States (4 studies) (26-29), China (3 studies) (30-32), Korea (3 studies) (33-35), Iran (2 studies) (36,37), Brazil (1 study) (38), Canada (1 study) (39), Australia (1 study) (40), Mexico (1 study) (41), Japan (1 study) (42), or a combination of countries (1 study) (43). The studied population primarily comprised adults (12 studies) (11-13,21,25-27,30,31,36,38,40), while two focused on the elderly (2 studies) (14,29). Additional studies also examined adolescents (7 studies) (22,28,33-35) and university students (5 studies) (23,24,32,41,43). Two other studies were conducted in special populations, and the inclusion criteria for the subjects were pregnant women and bariatric surgery candidates (20,42). Of the 28 studies, there were cross-sectional studies (21 studies) (20-24,26-28,31-43), cohort studies (6 studies) (11,12,14,15,25,29), and a case-control study (1 study) (30). In 28 studies, the exposure factors were a combination of fast food and soft drinks (10 studies) (14,21,23,24,30,34,36-38,41), soft drinks (7 studies) (25,28,31,40,42,43), energy drinks (5 studies) (22,27,33,35,39), fast food and snacks (3 studies) (13,20,32), ultra-processed foods (2 studies) (11,12), and chocolate (1 study) (26). With regard to sex, the majority of studies were on male and female subjects (24 studies), females only (2 studies) (21,42), and males only (1 study) (27). No gender-related information was reported for 1 additional study (15). The instruments used to measure food consumption included the Food Consumption Frequency Questionnaire (13 studies) (11,13-15,21,23,24,29-31,38,41,42), a questionnaire (8 studies) (28,32,34-37,39,40), specific questions (3 studies) (27,33,43), 24-hour dietary recall (2 studies) (12,26), the Eating Disorders Examination-Questionnaire (1 study) (20), and the Diet and Behaviour Scale (1 study) (22). The Agency for Healthcare Research and Qualification (AHRQ) has recommended quality assessment criteria for observational studies, including the NOS scale for cohort and case-control studies, and 11 items for cross-sectional studies. Of all studies included in the systematic evaluation, 1 case-control study showed low risk of bias (30), 2 of 6 cohort studies were medium risk of bias (14,29) and the remaining 4 showed low risk of bias (11-13,15); and 1 of 21 cross-sectional studies indicated high quality (42), 1 indicated low quality (22), and the rest were ranked as having medium quality (20,21,23,24,26-28,31-41,43). The full details of this evaluation are shown in supplementary table II.

GROUPS OF ULTRA-PROCESSED FOODS CONSUMPTION AND DEPRESSION

Four cohort studies included in the systematic review concerned groups of UPF consumption and depression. Three of these showed that UPF consumption was associated with depression risk (11-13). However, one study (14) found that consumption of savory snacks was not associated with a higher prevalence of depressive symptoms. Seven cross-sectional studies showed that the UPF consumption was significantly associated with depression, while a different study (41) indicated the association was only true in women. It therefore may be that eating behaviors are more typical in women, while men may have other ways to manage their negative emotions and stressful situations. It should be noted that a different study (24) also observed that higher consumption of carbohydrate-dense foods such as sweets, cookies, snacks, and fast food was not associated with depressive symptoms scores.

SOFT DRINKS/SWEETENED BEVERAGES/ ENERGY DRINKS CONSUMPTION AND DEPRESSION

Several studies explored the relationship between soft drinks and depression, including seven cross-sectional studies (23,24,31,34,40,43) and one cohort study (29). Four studies (29,31,34,40) showed a positive association between soft drink intake and depressive symptoms, but others (23,24,43) showed no such association. For sweetened beverages, one study (30) found no relationship between consumption of sugared beverages and snacks and a prevalence of high depressive symptoms in a case-control study. In the cohort studies (14,15), Elstgeest *et al*. found a positive association only among women, while Sanchez-Villegas *et al*. explained sugar-sweetened beverage intake was not associated with a higher prevalence of depressive symptoms. Several cross-sectional studies further observed no association between sugary drink consumption and depression (21,28,41), but Sangsefidi *et al*. found an inverse association between sweetened drink consumption and depressive features (34,36,37). Regarding the relationship between energy drinks intake and depression, four studies (27,33,35,39) observed that participants who regularly used energy drinks were more likely to be depressed; however, Richards *et al*. observed no such association (22).

OTHER ULTRA-PROCESSED FOODS CONSUMPTION AND DEPRESSION

In studies assessing the risk of depression with other UPFs (desserts, chocolate, processed cereals), three (26,37,38) found a positive association between regular consumption of sweets and chocolate and depression. However, one study by Mikolajczyk *et al*. (21,24) controlled for the consumption of cereal products, and no longer found an association between sweet consumption and depressive symptoms.

DISCUSSION

In summary, the majority of studies included in this systematic review showed that UPF consumption is associated with the risk of depression. A lack of correlations in some studies may be due to methodological issues. First, the majority of the study population was generally well represented across the lifespan, but unbalanced samples tended to find no association. For example, people aged ≥ 90 years were oversampled in Elstgeest's study. Intake of UPFs is inherently low in these populations, and other factors such as sleep, socioeconomic status, and other illnesses, may be more important risk factors for depression in older populations (44,45). Furthermore, studies with no or incomplete data on depressive symptoms at baseline or on any follow-up measure were excluded for analysis. This selection bias may also underreport the relationship between them. Meanwhile, Takahashi *et al*. obtained negative results in pregnant women. Such a finding may be due to the fact that pregnant women's diets change considerably after pregnancy, making it difficult to detect a potential relationship between dietary and the risk of depression (46).

Second, different instruments for depression and food consumption evaluation may also partially explain the differences among studies (47). For example, the included studies utilized more than 10 depression assessment instruments, potentially undermining comparability between studies. In addition, Asian researchers tend to use "Western" measures and criteria when conducting research on mental disorders, and cultural differences may lead to the neglect of symptoms specific to Asian populations (48), leading to an underestimation of any potential associations.

Moreover, adjusting for different confounds when constructing regression models can also lead to differences between findings. In the study of Xia *et al*., UPF intake was not associated with high depressive symptoms after adjusting for other dietary pattern factor scores. This may be due to the concomitant consumption of large amounts of fruit, offsetting the impact of intake of UPFs. Moreover, among those that did not find any association, most did not adjust for physical activity, educational attainment, income level, or marital status (21-24,30,39,42), because these are important factors in the incidence of depression (49,50). Thus, it is possible that the relationship between food groups and risk of depression may be difficult to detect without consideration of these other factors. Furthermore, these differences may also be related to a number of characteristics, such as the characteristics of subjects, environment, policies, region, or country and its political and health positions.

It is important to note that when analyzing the relationship between UPFs and the risk of depression, we must focus on those cohort studies with a low risk of bias (11-13,15). In these studies, we observed that consumption of UPFs was associated with an increased risk of depression, especially among participants with low physical activity. This suggests that inadequate micronutrient intake may play an important role in the relationship between UPF consumption and depression. In addition, there was compelling evidence that nutrients in processed foods are not accurately delivered to the brain, but that affect physiology in unexpected ways, such as via promoting metabolic dysfunction in instigating depression (11,51). Furthermore, the pro-inflammatory trans-fatty acids rich in UPFs may increase the risk of depression (11,25), and the association between UPF consumption and depression has been observed to be partly due to some of the non-nutritional components used or produced during processing (13). In fact, UPF often contains product additives such as emulsifiers or molecules produced by high-temperature heating that may lead to alterations in the gut microbiota, which are thought to be important in the onset of depression (52). While these aspects were briefly described in some of the included studies, most focused more heavily on the association between UPF and the risk of depression.

There are a few limitations in this systematic review, such as the heterogeneity of UPF consumption and depression assessments, which prevented us from conducting meta-analysis. In addition, most of the included studies were cross-sectional, and it was therefore not possible to determine a causal relationship between UPF and depression.

However, this is the first systematic review to our knowledge that explores UPF consumption and the risk of depression. We showed that majority of studies on the topic of UPF consumption and risk of depression shows a positive association. Future studies should consider the use of validated food intake assessments and standardized depression assessment methods to promote comparability between studies.

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