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REVIEW



Is dairy consumption associated with depressive symptoms or disorders in adults? A systematic review of observational studies

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ABSTRACT

Diet quality is associated with depression risk, however the possible role of dairy products in depression risk is unclear. A number of epidemiological studies have examined associations between dairy consumption and depressive symptoms, but results have been inconsistent. Therefore, this systematic review aimed to examine whether an association exists between dairy consumption and depressive symptoms or disorders in adults. Anxiety symptoms were also explored as a secondary outcome. CINAHL, Cochrane, MEDLINE complete, EMBASE, Scopus and PsycINFO databases were searched from database inception to December 2018. Studies were included if they used a case-control, cross-sectional, or cohort study design, and included community dwelling or institutionalized adults (≥ 18 years). Seven prospective and six cross-sectional studies ($N=58,203$ participants) reported on the association between dairy consumption and depressive symptoms or disorders. Findings were mixed, with one study reporting a positive association; five studies reporting no association; and seven studies reporting mixed associations depending on dairy type, gender or population group. We found conflicting and inconsistent associations in studies that were generally of fair quality. Future longitudinal and intervention studies that employ more rigorous dietary assessment methods are warranted.

KEYWORDS

Diet; depression; dairy; milk; systematic review

Introduction

Depression is a leading contributor to the global burden of disease, affecting approximately 322 million people worldwide (World Health Organisation 2017). The etiology of depression is complex and multifaceted, with inflammation, oxidative stress and the gut-microbiota all proposed to be key mediating pathways (Marx et al. 2017; Berk et al. 2013). Diet has been shown to modulate each of these biological processes and is therefore proposed as an important modifiable factor in the prevention and management of depressive disorders (Marx et al. 2017).

Meta-analyses support that high-quality diets are associated with a reduced risk of depression or depressive symptoms (Sarris et al. 2012; Lassale et al. 2019; Li et al. 2017). Conversely, poor-quality diets such as the Western-style diet, have been associated with an increased risk of depression (Sarris et al. 2012; Lassale et al. 2019; Li et al. 2017). More recently, landmark clinical trials have demonstrated that adherence to a Mediterranean-style diet, as an adjunct to pharmacotherapy, can effectively reduce symptoms of depression (Jacka et al. 2017; Parletta et al. 2017) and a recent meta-analysis has confirmed that dietary change can improve depressive symptoms (Firth et al. 2019). However,

such studies consider a whole-of-diet approach, therefore it is unknown to what extent specific foods within these diets may contribute to the observed findings.

The association between certain food groups and depression risk has been established within the literature. For instance, systematic reviews indicate that fruit and vegetable consumption is protectively associated with depression (Saghafian et al. 2018). Conversely, meat consumption is associated with a moderately higher risk of depression (Zhang et al. 2017). Although a key food group within many traditional diets, no prior reviews have examined the association between dairy consumption and depression.

Dairy products refers to a wide range of milk-based products including milk, yoghurt and cheese (National Health and Medical Research Council 2013). Dairy products are a rich source of protein, micronutrients (e.g. calcium) and bioactive compounds (Muehlhoff, Bennett, and McMahon 2013), however, can vary greatly in their nutritional composition. For instance, processing techniques such as fermentation, pasteurization and filtration can influence overall fatty acid and microbial composition. In theory, these nutritional variations may be protective or deleterious for depression risk. For example, functional microorganisms within fermented dairy products may have a protective benefit by

contributing to the diversity of microorganisms within the gut microbiome (Aslam et al. 2018). Comparatively, increased saturated fatty acid consumption within whole-fat dairy products may promote inflammation (Rocha, Bressan, and Hermsdorff 2017), a central pathway in depression (Berk et al. 2013).

Although current dietary guidelines recommend the inclusion of dairy products within the diet (National Health and Medical Research Council 2013; Public Health England 2016; US Department of Health and Human Services 2015) evidence concerning dairy consumption is inconsistent within the literature. Prior reviews of epidemiological evidence have highlighted contrasting findings for the association between dairy consumption and cardiovascular disease (Qin et al. 2015; Guo et al. 2017), obesity (Louie et al. 2011) and cognitive function (Crichton et al. 2010); conditions of which, share biological similarities with depression.

Similarly, several epidemiological studies indicate that the association between dairy consumption and depression may also be inconsistent. Some studies have shown no association between total dairy consumption and depressive symptoms (Miyake et al. 2016; Tsai, Chang, and Chi 2012), whereas other studies have found significant associations between specific types of dairy products (e.g. yoghurt, milk and cheese) and depressive symptoms (Pasco et al. 2015; Yu et al. 2017; Wolfe et al. 2011). Furthermore, differences have been observed between dairy products that have varied in nutritional composition, such as fat content (Perez-Cornago et al. 2016). Despite heightened public health interest in the putative health effects of dairy fats and fermented foods, evidence concerning their role in depression remains ambiguous. Therefore, the present review aimed to conduct a comprehensive systematic review to summarize available evidence on the association between dairy consumption and depressive symptoms or disorders in adults. As a secondary aim, the association with anxiety symptoms was also explored.

Methods

Protocol and registration

This review was registered with the International Prospective Register of Systematic Reviews (PROSPERO, registration number CRD42018087038) and has been reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Moher et al. 2009).

Eligibility criteria

Studies were included if they used a case-control, cross-sectional, or cohort design; included adults aged 18 years or over; and reported on associations between dairy consumption and depressive symptoms or disorders and/or anxiety symptoms. Studies reporting on depressive symptoms as well as diagnosis of unipolar and postnatal depression were considered. As a small number of studies were expected, studies involving pregnant, lactating and non-pregnant

women – and both community-dwelling and institutionalized participants – were considered for inclusion. For cohort studies, no restrictions were placed on length of follow-up. Studies reporting on dairy products recommended for daily consumption within the Australian dietary guidelines (i.e. milk, yoghurt and cheese) were included (National Health and Medical Research Council 2013). However, dairy products considered as discretionary items (i.e. ice-cream, cream and butter etc.) were outside the scope of this review (National Health and Medical Research Council 2013). Studies were excluded if they grouped dairy products with other foods, to ensure the association observed could be attributable to dairy rather than other food items. Furthermore, studies describing outcomes from intake of beverages where milk was added in negligible amounts (i.e. tea and coffee) were excluded, as were fortified dairy products such as probiotic-fortified milk.

Search strategy

A systematic search of the literature was conducted using CINAHL, Cochrane, MEDLINE complete, EMBASE, Scopus and PsycINFO databases. Terms were searched from database inception until December 2018. Articles were identified using a combination of free-text terms and controlled vocabulary as follows: (dairy OR milk OR yog*urt OR cheese OR “diet* pattern” OR kefir OR quark OR “food group*”) AND (mood OR anxiety OR depress* OR affective OR mental OR psycholog* OR MDD) NOT “breast milk”. All searches were limited to adults, humans, and studies published in the English language. Reference lists of full-text studies were hand searched to assess eligibility.

Study selection

References were collected and logged in EndNote vX8.0 (Thomson Reuters, New York, U.S.A.). Screening of articles was conducted independently by two reviewers (MH, AR) using the Rayyan web application (Ouzzani et al. 2016). Following de-duplication of search results, relevant articles were screened based on title and abstract. Full-text articles of potentially eligible studies were reviewed, and reasons for exclusion documented. Results were compared, and disagreements resolved by discussion by the two reviewers.

Data extraction

A standardized pre-piloted data extraction form was designed to collate information pertaining to: study design; country and year; population characteristics, including age and gender of participants; total number of participants, including the number of cases of depression; length of follow-up for cohort studies; measurement of depression and dairy intake including assessment methods, unit of measure, and validation methods; and main findings including comparator reference values, description of confounders adjusted for, and information for assessment of risk of bias. Three

reviewers independently performed data extraction (MH, AR, AJM), which were then collated by one reviewer (MH).

Assessment of risk of bias

Three reviewers independently assessed quality of studies (MH, AR, AJM) using the National Institute of Health Quality of Observational Cohort and Cross-Sectional Studies tool (National Institute of Health 2011). This tool comprised 14 items concerning clarity of research question, validity of exposure and outcome assessments, and adequacy of follow-up. The potential responses to questions were as follows: yes, no, cannot determine, not applicable or not reported. To give an overall indication of study quality, studies were categorized as good (score of 10–14), fair (score of 6–9) or poor quality (score of 0–5) based on the number of ‘yes’ responses received. Items were independently rated and then cross-checked, with disagreements between authors resolved through discussion.

Results

Database searches retrieved 3,642 studies, of which 1,334 were duplicates. Following title and abstract screening of 2,308 studies, 32 full-text studies were assessed for inclusion. Thirteen studies met the eligibility criteria and were included in the final review. Figure 1 illustrates the screening process and details reasons for exclusion of full-text papers.

Study characteristics

Seven prospective (Wolfe et al. 2011; Perez-Cornago et al. 2016; Miyake et al. 2016; Miyake et al. 2006; Pasco et al. 2015; Tsai, Chang, and Chi 2012; Almeida et al. 2006) and six cross-sectional (Miyake et al. 2015; Cui et al. 2017; Yu et al. 2017; Stefańska, Wendolowicz, and Cwalina 2014; Meyer et al. 2013; Grossniklaus et al. 2010) studies were included. Studies comprised a total of 58,203 participants, with the characteristics of each study presented in Table 1. Ten studies examined the association using dairy consumption as the exposure. The remaining three studies used depression status as the exposure and examined differences in dairy consumption between depressed and non-depressed participants (Grossniklaus et al. 2010; Stefańska, Wendolowicz, and Cwalina 2014; Meyer et al. 2013). Six studies presented data for more than one type of dairy product (Perez-Cornago et al. 2016; Wolfe et al. 2011; Miyake et al. 2016; Cui et al. 2017; Stefańska, Wendolowicz, and Cwalina 2014; Miyake et al. 2015).

The sample size of studies varied markedly from 87 (Grossniklaus et al. 2010) to 19,596 (Yu et al. 2017) community-dwelling participants. The age of participants spanned from 18 to greater than 85 years. Studies were conducted in both men and women ($n=8$), women ($n=4$) or men only ($n=1$). Studies were geographically dispersed and conducted in Japanese ($n=4$), Australian ($n=3$), American ($n=2$), Spanish ($n=1$), Taiwanese ($n=1$), Chinese ($n=1$) and Polish ($n=1$) populations. Owing to the broad inclusion criteria, three studies examined associations in pregnant

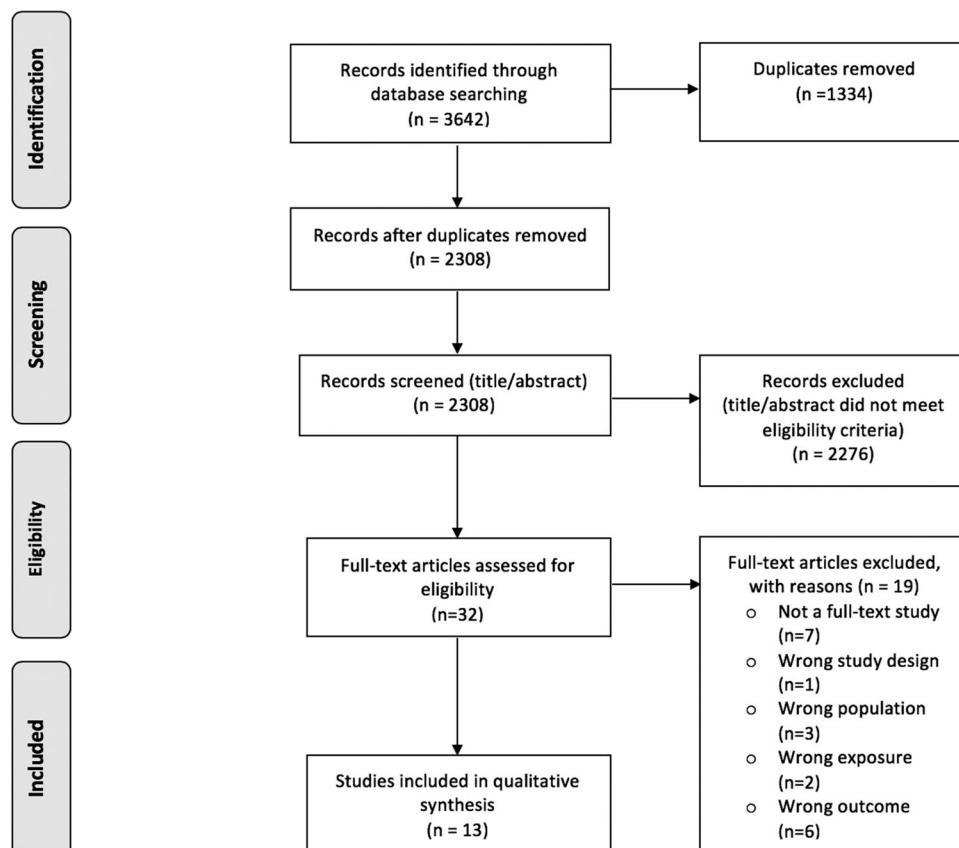


Figure 1. PRISMA flow diagram.

women (Miyake et al. 2006; Miyake et al. 2015; Miyake et al. 2016), and one in pre- and post-menopausal women (Pasco et al. 2015). For prospective studies, the length of follow-up ranged from four (Tsai, Chang, and Chi 2012) to 10.6 years in non-pregnant populations (Wolfe et al. 2011), and two to nine months in pregnant women (Miyake et al. 2006).

Study quality

Findings from the assessment of study quality using the Quality of Observational Cohort and Cross-Sectional Studies tool are presented in Appendix 1. Three studies were rated as good (Perez-Cornago et al. 2016; Miyake et al. 2016; Miyake et al. 2006), eight studies as fair (Wolfe et al. 2011; Tsai, Chang, and Chi 2012; Almeida et al. 2006; Pasco et al. 2015; Cui et al. 2017; Yu et al. 2017; Miyake et al. 2015; Grossniklaus et al. 2010), and two studies as poor in quality (Meyer et al. 2013; Stefańska et al. 2015). The majority of studies clearly defined the research question and study population, included greater than 50% of eligible participants and recruited participants from the same or similar population. For prospective studies, all measured dairy consumption prior to the measurement of depressive symptoms. The measurement of depressive symptoms was predominantly self-reported, with the exception of two studies that employed clinician assessments (Pasco et al. 2015; Stefańska, Wendolowicz, and Cwalina 2014). The length of follow-up was deemed sufficient time to allow an association to be seen, with loss to follow-up after baseline 20% or less for most studies. However, no prospective studies measured dairy consumption repeatedly over time. Adjustment for potential confounders varied amongst studies, with four studies (Miyake et al. 2015; Tsai, Chang, and Chi 2012; Pasco et al. 2015; Miyake et al. 2006) failing to or did not report whether they adjusted for energy intake. Furthermore, the measurement of dairy intake varied markedly amongst studies. Consumption data was predominantly derived from self-report measures, such as food frequency questionnaires (Tsai, Chang, and Chi 2012; Perez-Cornago et al. 2016; Miyake et al. 2006; Miyake et al. 2015; Miyake et al. 2016; Wolfe et al. 2011; Cui et al. 2017; Yu et al. 2017) or non-validated self-report questionnaires (Pasco et al. 2015; Stefańska, Wendolowicz, and Cwalina 2014; Almeida et al. 2006). Two studies were the exception and measured intake via 24-hour food recalls (Meyer et al. 2013) and weighed 3-day food records (Grossniklaus et al. 2010). Units of measurement were also inconsistent amongst studies. For example, studies reported dairy consumption as serves per week (Wolfe et al. 2011; Perez-Cornago et al. 2016), times per day or week (Tsai, Chang, and Chi 2012; Cui et al. 2017; Yu et al. 2017; Stefańska, Wendolowicz, and Cwalina 2014), grams or milliliters per day (Pasco et al. 2015; Meyer et al. 2013), mean cups per day (Grossniklaus et al. 2010), or as quartiles of intake (g/day) (Miyake et al. 2016; Miyake et al. 2015). One study also reported consumption as regular or non-regular consumption, although a definition as what constituted as regular was not provided by authors (Almeida

et al. 2006). A further study did not report any data pertaining to dairy consumption (Miyake et al. 2006). Largely, serving sizes were not reported by studies. However, if used, varying definitions of serving sizes were given with arbitrary cutoffs.

Study results

Within study differences were observed between population groups and types of dairy products consumed. This can be expected given changes in metabolism (e.g. during pregnancy) (Lain and Catalano 2017) and the wide nutritional variation between dairy products. Therefore, for the purpose of this review findings have been presented according to population type (e.g. non-pregnant or pregnant) and type of dairy products consumed (e.g. total dairy, milk, yoghurt, and cheese). Of the 13 included studies, two studies reported positive, inverse, and no associations between dairy consumption and self-reported depressive symptoms or medical diagnosis of depression (Perez-Cornago et al. 2016; Wolfe et al. 2011). Additionally, three studies reported both positive and no associations (Pasco et al. 2015; Stefańska, Wendolowicz, and Cwalina 2014; Meyer et al. 2013) and two studies reported both inverse and no associations between dairy consumption and depressive symptoms or risk for de novo major depressive disorder (Cui et al. 2017; Miyake et al. 2015). Furthermore, one study reported a positive association only (Yu et al. 2017) and five studies reported no association between dairy consumption and depressive symptoms (Tsai, Chang, and Chi 2012; Almeida et al. 2006; Miyake et al. 2006; Miyake et al. 2016; Grossniklaus et al. 2010). No studies reported on the association between dairy consumption and anxiety symptoms.

Findings in men and non-pregnant women

Total dairy product consumption. One prospective and one cross-sectional study reported on associations between total dairy consumption and depressive symptoms in adults (Tsai, Chang, and Chi 2012; Cui et al. 2017). One cross-sectional study also reported on total dairy consumption in depressed and non-depressed controls (Meyer et al. 2013). No significant association was found between total dairy consumption (<3 vs ≥ 3 times/week) and depressive symptoms in an elderly Taiwanese cohort (Tsai, Chang, and Chi 2012). However, cross-sectional findings observed that in Japanese adults, more frequent low-fat dairy consumption (≥ 4 times/week) was associated with a lower prevalence of depressive symptoms, compared to less frequent consumption (0 times/week) (Cui et al. 2017). No relationship was observed between whole-fat dairy consumption and depressive symptoms within this population group (Cui et al. 2017). Another cross-sectional study reported that women with depressive symptoms had significantly higher consumption of milk products and dairy dishes, compared to women without depression, although this association was not observed in men (Meyer et al. 2013).

Table 1. Summary of findings from studies reporting on associations between dairy consumption and depressive symptoms/disorders.

Reference, year, country	Study design	Population	No. of participants (N depressed)	Length of follow-up	Measurement of depression (assessment method)	Types of dairy (assessment method)	Comparator*	Main findings	Adjustment of confounders	Study quality ¹
Total dairy consumption										
Miyake et al. 2016, Japan	Prospective cohort	Japanese pregnant women. Median age 32yrs (IQR 28-34yrs)	1,319 (108)	5 th -39 th week of pregnancy to 3-4 months postpartum	Self-reported post-partum depressive symptoms (EPDS-10)	Total dairy products (Diet History Questionnaire)	18.5 median g/d (Q1) vs 258.6 median g/d (Q4)	No association with risk of post-partum depressive symptoms (Adjusted OR 0.75, 95% CI 0.41-1.37, p for trend 0.34)	Age, gestation, region of residence, number of children, family structure, history of depression, family history of depression, job type, education, body mass index, having smoked during pregnancy, cesarean delivery, baby's sex, baby's birth weight, and total energy intake	Good
Tsai, Chang, and Chi 2012, Taiwan	Prospective cohort	Taiwanese elderly men and women. Aged ≥ 65 yrs	1,609 (N.R.)	4.0yrs	Self-reported depressive symptoms (CESD-10)	Total dairy products (Food frequency questionnaire)	<3 times/wk vs ≥ 3 times/wk	No association with risk of elevated depressive symptoms (Adjusted OR 0.87, 95% CI 0.61-1.24, p = 0.426)	Baseline age, gender, education, satisfaction with economic status, living setting, smoking status, alcohol drinking, betel-nut chewing, functional status, physical activity, cognitive status, and the presence of major chronic co-morbidities	Fair
Miyake et al., 2006, Japan	Prospective cohort	Japanese pregnant women. Age categories (mean, SD): <29 yrs (324, 37.5), 29-31yrs (253, 29.3), 32yrs+ (288, 33.3)	865 (121)	During pregnancy (gestation week N.R.) to 2-9 months postpartum	Self-reported post-partum depressive symptoms (EPDS-10)	Total dairy products (Diet history questionnaire)	N.R.	No association with risk of post-partum depressive symptoms (Adjusted OR N.R, p value N.R)	Age, gestation, parity, cigarette smoking, family structure, family income, education, changes in diet in the previous month, season when data at baseline were collected, body mass index, time of delivery before the second survey, medical problems in pregnancy, baby's sex and baby's birthweight	Good
Cui et al. 2017, Japan	Cross-sectional	Japanese men and women. Age range 19-83 yrs	1,159 (363)	-	Self-reported depressive symptoms	Total whole-fat and low-fat dairy products (Brief	0 times/wk (T1) vs ≥ 4 times/wk (T3)	Whole-fat dairy No association with prevalence of self-reported depressive	Age, sex, intake of total energy, protein, folate, BMI, drinking and smoking habits,	Fair

(continued)

(continued)

Table 1. Continued.

Reference, year, country	Study design	Population	No. of participants (N depressed)	Length of follow-up	Measurement of depression (assessment method)	Types of dairy (assessment method)	Comparator*	Main findings	Adjustment of confounders	Study quality ¹
Miyake et al. 2015, Japan	Cross-sectional	Japanese pregnant women. Mean age (SD) 31.2yrs (4.3 yrs)	1,745 (337)	–	Self-reported depressive symptoms (Japanese CESD-20)	diet history questionnaire	29.1 median g/d (Q1) vs 257.1 median g/d (Q4)	No association with prevalence of self-reported depressive symptoms (Adjusted OR 0.93, 95% CI 0.66–1.32, p for trend 0.47)	Age, gestation, region of residence, number of children, family structure, history of depression, family history of depression, smoking, second hand smoke exposure at home and at work; job type, household income, education, body mass index, and intake of saturated fatty acids, eicosapentaenoic acid plus docosahexaenoic acid and vitamin D	Fair
Meyer et al. 2013, Australia	Cross-sectional	Australian men and women. Age range 18–79 yrs	10,986 (224)	–	Self-reported depression (ICD diagnosis of depression)	Milk products and dishes (24-hr diet recall)	Intake between depressed v non-depressed (mean \pm SD g/d)	Men No association between intake in men with and without depression (With depression mean 318 \pm 260g/d, without depression mean 327g/d \pm 336g/d, $p \geq 0.05$) Women Women with depression had significantly increased intakes of milk products and dishes (mean 331 \pm 295g/d compared to women without depression (mean 259 \pm 248 g/d, $p < 0.05$)	No adjustments made (univariate model)	Poor
Milk consumption Miyake et al. 2016, Japan	Prospective cohort	Japanese pregnant women. Median age	1,319 (108)	5 th –39 th week of pregnancy to 3–4 months postpartum	Self-reported post-partum depressive	Milk (Diet History Questionnaire)	0 median g/d (Q1) vs 187.5 median g/d (Q4)	No association with risk of post-partum depressive symptoms (Adjusted OR	Age, gestation, region of residence, number of children, family structure, history of	Good

32yrs (IQR 28–34yrs)	symptoms (EPDS-10)								0.51, 95% CI 0.28–0.93, p for trend 0.12)	depression, family history of depression, job type, education, body mass index, having smoked during pregnancy, cesarean delivery, baby's sex, baby's birth weight, and total energy intake	Fair
Pasco et al. 2015, Australia	Prospective cohort	Pre- and post- menopausal Australian women. Age range 29.8–70.3yrs	691 (N.R)	Median 9.3yrs (IQR 9.2–10.0yrs)	Clinician diagnosed depression (SCID)	Milk (Self- administreated questionnaire -not validated)	<250ml vs ≥250mL per day	Higher consumption associated with an increased risk of de novo depression in post- menopausal women (Adjusted HR 3.71, 95% CI 1.04 – 13.27, p value N.R.), but not in pre- menopausal women (N.S findings reported, data N.R.)		Smoking only, however, with further adjustments for dietary calcium intake, BMI, alcohol, physical activity and SES the results remained significant	Fair
Wolfe et al. 2011, USA	Prospective cohort	American men and women. Age range 25–74yrs	4,856 (753)	Mean 10.6yrs (range 8.0–12.5yrs)	Self-reported depressive symptoms (CESD-20)	Milk (Food frequency questionnaire)	≥1 serves/d vs ≤1 serve/wk	Men Lower consumption associated with an increased risk of depressive symptoms (Adjusted RR 1.93, 95% CI 1.11–3.37, p for trend 0.0254) Women No association with risk of depressive symptoms (Adjusted OR 1.31, 95% CI 0.95, 1.81, p for trend 0.0813)		Total energy intake, age, ethnicity, family income level, education, marital status, type of residence area, smoking, alcohol drinking, body mass index (baseline), self- evaluated health status (follow-up) and history of major physical diseases (follow-up)	Fair
Almeida et al. 2006, Australia	Prospective cohort	Australian older men. Aged ≥80yrs	601 (53)	Mean 4.8yrs (range 3.3–6.8yrs)	Self-reported depressive symptoms (GDS-15)	Full-cream milk (Self- report questionnaire – not validated)	Irregular vs regular consumption of full-cream milk (not defined)	No association with risk of elevated depressive symptoms (HR 0.80, 95% CI 0.46–1.39, p value N.R)	No adjustments made (univariate models)		Fair
Miyake et al. 2015, Japan	Cross-sectional	Japanese pregnant women. Mean age (SD) 31.2yrs (4.3yrs)	1,745 (337)	–	Self-reported depressive symptoms (Japanese CESD-20)	Milk (Diet history questionnaire)	8.9 median g/d (Q1) vs 194.7 median g/d (Q4)	No association with prevalence of self- reported depressive symptoms (Adjusted OR 0.89, 95% CI 0.63–1.25, p for trend 0.39)		Age, gestation, region of residence, number of children, family structure, history of depression, family history of depression, smoking, second hand smoke exposure at home and at work; job type, household income, education, body mass index, and intake of saturated fatty acids, eicosapentaenoic acid	Fair

(continued)

(continued)

Table 1. Continued.

Reference, year, country	Study design	Population	No. of participants (N depressed)	Length of follow-up	Measurement of depression (assessment method)	Types of dairy (assessment method)	Comparator*	Main findings	Adjustment of confounders	Study quality ¹
Stefańska, Wendolowicz, and Cwalina 2014, Poland	Cross-sectional	Polish men and women. Age range 18–75yrs	150 (75)	–	Clinician diagnosed depression (According to ICD-10 criteria)	Milk (Questionnaire – not validated)	Intake between depressed vs healthy controls (median times/wk)	Men No difference in milk intake between depressed and healthy controls ($p = 0.29$) Women No difference in milk intake between depressed and healthy controls ($p = 0.81$)	plus docosahexaenoic acid, and vitamin D. No adjustments made (univariate model)	Poor
Grossniklaus et al., 2010	Cross-sectional	Overweight American men and women. Mean age (SD) 41.3yrs (10.2yrs)	87 (19)	–	Self-reported depressive symptoms (BDI-II)	Milk (Weighed 3-d food record)	Intake between those with vs without depressive symptoms (mean \pm SD cups/d)	No difference in milk intake in those with (0.9 ± 0.7 cups/d) and without (1.2 ± 1.0 cups/d) self-reported depressive symptoms ($p = 0.23$)	No adjustments made (univariate model)	Fair
Yoghurt consumption Perez-Cornago et al. 2016, Spain	Prospective cohort	Spanish university graduate and women. Mean age 37yrs (SD N.R.)	14,539 (727)	Median 9.3yrs (IQR N.R.)	Self-reported medical diagnosis of depression	Total, whole- and low-fat yoghurt (Food frequency questionnaire)	<0.5 serves/wk (<63 g/wk) vs ≥ 7 serves/wk (≥ 875 g/wk)	Total yoghurt No significant association with risk of self-reported depression (Adjusted HR 1.00, 95% CI 0.81–1.25, p for trend 0.83) Whole-fat yoghurt Higher consumption associated with a decreased risk of self-reported depression (HR 0.78, 95% CI 0.63–0.98, p for trend 0.02). In stratified analyses this association was shown only in women (HR 0.66, 95% CI 0.50–0.87, p for trend 0.004), not men (p for trend 0.86) Low-fat yoghurt Higher consumption associated with an increased risk of self-reported depression (HR 1.32, 95% CI 1.06–1.65, p for trend 0.001). In stratified analyses this association was shown only in women (HR 1.37, 95% CI 1.07–1.76, p for trend <0.001), not men (p for trend 0.53)	Age, sex, smoking, physical activity, total energy intake, baseline BMI, living alone, unemployment, marital status, and personality traits.	Good
Miyake et al. 2016, Japan	Prospective cohort	Japanese pregnant women.	1,319 (108)	5 th –39 th week of pregnancy to 3–4	Self-reported post-partum depressive	Yoghurt (Diet History Questionnaire)	0 median g/d (Q1) vs 75 median g/d (Q4)	No association with risk of post-partum depressive symptoms (Adjusted OR	Age, gestation, region of residence, number of children, family	Good

Table 1. Continued.

Reference, year, country	Study design	Population	No. of participants (N depressed)	Length of follow-up	Measurement of depression (assessment method)	Types of dairy (assessment method)	Comparator*	Main findings	Adjustment of confounders	Study quality ¹
Wolfe et al. 2011, USA	Prospective cohort	American men and women. Age range 25–74yrs	4,856 (753)	Mean 10.6yrs (range 8.0–12.5yrs)	Self-reported depressive symptoms (CESD-20)	Cheese/buttermilk (Food frequency questionnaire)	≥3 serves/wk vs <1 serve/wk	Men Lower consumption associated with a decreased risk of depressive symptoms (Adjusted RR 0.56, 95% CI 0.32–0.98, p for trend 0.0076) Women No association with risk of depressive symptoms (Adjusted RR 0.99, 95% CI 0.69–1.43, p for trend 0.8591)	Total energy intake, age, ethnicity, family income level, education, marital status, type of residence area, smoking, alcohol drinking, body mass index (baseline), self-evaluated health status (follow-up) and history of major physical diseases (follow-up)	Fair
Miyake et al. 2015, Japan	Cross-sectional	Japanese pregnant women. Mean age (SD) 31.2yrs (4.3yrs)	1,745 (337)	–	Self-reported depressive symptoms (Japanese CESD-20)	Cheese (Diet history questionnaire)	0.1 median g/d (Q1) vs 11.4 median g/d (Q4)	No association with prevalence of self-reported depressive symptoms (Adjusted OR 0.86, 95% CI 0.59–1.24, p for trend 0.58)	Age, gestation, region of residence, number of children, family structure, history of depression, family history of depression, smoking, second hand smoke exposure at home and at work; job type, household income, education, body mass index, and intake of saturated fatty acids, eicosapentaenoic acid plus docosahexaenoic acid, and vitamin D.	Fair
Stefańska, Wendolowicz, and Cwalina 2014, Poland	Cross-sectional	Polish men and women. Age range 18–75yrs	150 (75)	–	Clinician diagnosed depression (According to ICD-10 criteria)	Cheese (Questionnaire – not validated)	Intake between depressed vs healthy controls (median times/wk)	Men No difference in cheese intake between depressed and healthy controls (p = 0.45) Women Women with depression consumed cheese more often (2–3 times/wk) compared to women without depression (once/wk) (p = 0.02).	No adjustments made (univariate model)	Poor

*Reference in bold.

BDI-II, Beck Depression Inventory Second Edition; CESD, Center for Epidemiological Studies Depression Scale; CI, confidence interval; EPDS, Edinburgh Postnatal Depression Scale; hsCRP, high sensitivity C-reactive protein; ICD, International Classification of Diseases; N.A., not applicable; OR, odds ratio; Q, quartile; SD, standard deviation; SDS, self-rating depression scale; times/wk, times per week; twice/d, twice per day; T, tertile; wks, weeks

Milk consumption. Three prospective studies examined associations between milk consumption and depressive symptoms or risk for de novo major depressive disorder in adults (Almeida et al. 2006; Pasco et al. 2015; Wolfe et al. 2011). Further, two cross-sectional studies examined differences between milk consumption in those with and without depression or depressive symptoms (Stefańska, Wendolowicz, and Cwalina 2014; Grossniklaus et al. 2010). Studies reported conflicting findings with positive associations (Pasco et al. 2015; Wolfe et al. 2011), no associations (Pasco et al. 2015; Wolfe et al. 2011; Almeida et al. 2006; Grossniklaus et al. 2010; Stefańska, Wendolowicz, and Cwalina 2014), and inverse associations observed (Wolfe et al. 2011). Specifically, compared to high milk consumption (≥ 1 serves/day), drinking milk once or less per week was associated with an almost doubled risk for depressive symptoms in men (Wolfe et al. 2011). However, no association was observed in women (Wolfe et al. 2011). Further, the definition of what constituted a serve of milk was not reported by the authors. Conversely, compared to low milk intake (< 250 mL/day), post-menopausal women with high milk intake (≥ 250 mL/day) were found to be at an increased risk for de novo major depressive disorder. Findings were not consistent for pre-menopausal women, with no association found between milk consumption and major depressive disorder in this population group (Pasco et al. 2015). Similarly, compared to non-regular consumption, the regular consumption of full-cream milk was not associated with risk of elevated depressive symptoms in older Australian men (Almeida et al. 2006). Although, the definition of regular and non-regular consumption was not defined by authors, limiting the interpretability of these findings. Furthermore, no significant difference was observed in milk consumption between depressed and healthy Polish adults (Stefańska, Wendolowicz, and Cwalina 2014), and American overweight adults with and without depressive symptoms (Grossniklaus et al. 2010).

Yoghurt consumption. One prospective (Perez-Cornago et al. 2016) and one cross-sectional study (Yu et al. 2017) examined associations between yoghurt consumption and self-reported diagnosis of depression or depressive symptoms in adults. A further cross-sectional study also examined associations between yoghurt consumption in depressed and healthy controls (Stefańska, Wendolowicz, and Cwalina 2014). No association was found between total yoghurt consumption and risk of self-reported depression in a Spanish cohort (Perez-Cornago et al. 2016). However, differences were observed between whole- and low-fat yoghurt. For instance, compared to less frequent consumption (< 0.5 serves/week), more frequent consumption of whole-fat yoghurt (≥ 7 serves/week) was associated with a decreased risk of self-reported depression (Perez-Cornago et al. 2016). However, in stratified analyses, this association was shown only in women (Perez-Cornago et al. 2016). Conversely, compared to less frequent consumption (< 0.5 serves/week), increased low-fat yoghurt consumption (≥ 7 serves/week) was associated with an increased risk of self-reported depression (Perez-Cornago et al. 2016). However, findings were no longer statistically significant after removing cases

of self-reported depression that occurred within the initial two years of follow-up, and in stratified analyses, this association was shown only in women (Perez-Cornago et al. 2016). In a large study involving Chinese men and women, more frequent yoghurt consumption (\geq twice/day) was associated with a significantly greater odds of both moderately severe and severe depressive symptoms, compared to less frequent consumption ($<$ once/week) (Yu et al. 2017). However, no significant differences were observed in yoghurt consumption between depressed and healthy Polish adults (Stefańska, Wendolowicz, and Cwalina 2014).

Cheese consumption. Two studies reported on the association between cheese consumption and depression (Wolfe et al. 2011; Stefańska, Wendolowicz, and Cwalina 2014). One prospective study grouped cheese and buttermilk intake together and reported on combined intake and depressive symptoms (Wolfe et al. 2011). A further cross-sectional study reported on the association between cheese consumption only, in depressed and healthy adults (Stefańska, Wendolowicz, and Cwalina 2014). Compared to high cheese and buttermilk consumption (≥ 3 serves/week), low consumption (< 1 serve/week) was associated with a decreased risk of depressive symptoms in American men, but not in women (Wolfe et al. 2011). Gender specific associations were also reported by one cross-sectional study (Stefańska, Wendolowicz, and Cwalina 2014). Polish women with depression significantly more often consumed cheese (median intake 2–3 times/week) compared to women without depression (median intake once/week) (Stefańska, Wendolowicz, and Cwalina 2014). However, no association was found between cheese intake in depressed and non-depressed Polish men (Stefańska, Wendolowicz, and Cwalina 2014).

Findings in pregnant women

Associations between dairy consumption and risk of postpartum depressive symptoms were examined by two prospective studies (Miyake et al. 2006; Miyake et al. 2016). One cross-sectional study also examined the association between dairy consumption and prevalence of depressive symptoms during pregnancy (Miyake et al. 2015). No significant associations were found between total dairy, milk or cheese intake, and the risk of postpartum depression or depressive symptoms during pregnancy (Miyake et al. 2006; Miyake et al. 2015; Miyake et al. 2016). However, cross-sectional analyses revealed that higher intake levels of yoghurt were independently associated with a lower prevalence of depressive symptoms during pregnancy (Miyake et al. 2015).

Discussion

To our knowledge, this is the first systematic review to examine whether an association exists between dairy consumption and depressive and anxiety symptoms or disorders in adults. Overall, the findings from 13 prospective and cross-sectional studies were conflicting and inconsistent. Two studies reported positive, inverse and no associations between dairy consumption and self-report depression or

depressive symptoms (Perez-Cornago et al. 2016; Wolfe et al. 2011). Additionally, three studies reported both positive and no associations (Pasco et al. 2015; Stefańska, Wendolowicz, and Cwalina 2014; Meyer et al. 2013), two studies reported both inverse and no associations (Cui et al. 2017; Miyake et al. 2015) and one study reported a positive association only (Yu et al. 2017). Of the 13 studies, five reported no association between dairy consumption and depressive or post-partum depressive symptoms (Tsai, Chang, and Chi 2012; Almeida et al. 2006; Miyake et al. 2006; Miyake et al. 2016; Grossniklaus et al. 2010). Associations were found between depressive symptoms/risk and consumption of total dairy (Meyer et al. 2013), low-fat dairy (Cui et al. 2017), milk (Pasco et al. 2015; Wolfe et al. 2011), cheese (Stefańska, Wendolowicz, and Cwalina 2014; Wolfe et al. 2011) and total (Yu et al. 2017; Miyake et al. 2015), whole- and low-fat yoghurt (Perez-Cornago et al. 2016). However, the directions of these associations were not consistent across studies and differences were observed between sexes and population groups. Studies pertaining to dairy consumption and anxiety symptoms were not identified, representing a gap in the literature.

Methodological appraisal highlighted that studies included within this review were generally of fair quality. No obvious differences were observed in quality scores between studies that reported no association, or studies that found an inverse or positive association. However, significant heterogeneity existed between study designs, which may account for the conflicting findings that were observed. In particular, there were widespread variations in definitions and categorization of dairy products. For example, one study defined total dairy intake as the sum of milk and yoghurt intake (Cui et al. 2017), whereas another included milk, yoghurt, cheese and cottage cheese within this definition (Miyake et al. 2016). Most studies presented dairy consumption as a range where multiple categories of level of consumption were assessed. However, measurement units largely varied with one study reporting yoghurt consumption as serves per week (Perez-Cornago et al. 2016) and another as times per week (Yu et al. 2017). As most studies did not report serving sizes, we could not convert the reported serves into a consistent measurement across studies (e.g. grams per day). Therefore, precise comparisons of dairy consumption between studies could not be made. This lack of detailed reporting with regard to dairy intake has been identified as a major limitation of similar reviews examining dairy consumption and health outcomes (Crichton et al. 2010). Similarly, the categorization of dairy intake, as high versus low, also varied across studies. In many instances, intake categorized as high (e.g. 250 ml of milk per day) (Pasco et al. 2015) was still well below dietary guidelines for the recommended serves of dairy (National Health and Medical Research Council 2013); thus, caution should be exercised when extrapolating findings to a population health setting.

Whilst the majority of studies controlled for age and gender, few controlled for energy intake and/or diet quality. Individuals who consume more energy also consume on average more total nutrients, which may lead to the

confounding of results (Arija et al. 2015; Willett, Howe, and Kush 1997). Further, the consumption of specific dairy products, such as yoghurt, may be proxies for other healthful dietary choices which are protective against depression. For instance, yoghurt consumption has been associated with better diet quality in adults (Wang et al. 2013), which is a known protective factor for depression (Lassale et al. 2019). Therefore, diet quality may represent a confounder in the relationship between dairy consumption and depressive symptoms. Furthermore, there was a lack of reporting of sample size justifications, which was consistent amongst all studies. Thus, it is unknown whether studies were powered to detect an association if one truly existed. Studies with large sample sizes (Yu et al. 2017; Meyer et al. 2013; Perez-Cornago et al. 2016) all found evidence of an association, although the direction of association differed between the studies. Three studies with the smallest sample sizes (Almeida et al. 2006; Grossniklaus et al. 2010; Stefańska, Wendolowicz, and Cwalina 2014) mostly found no evidence of an association, although Stefańska et al. reported a positive association with cheese consumption. Whilst it is possible that these smaller studies were not adequately powered to detect an association, it cannot be ruled out that a single dietary factor, particularly consumed in small quantities, may not be strongly associated with depressive symptoms.

The conflicting findings we observed are concordant with the wider literature in health. A systematic review reported that dairy consumption may have a protective effect on overall risk for overweight and obesity, however the results were not consistent (Louie et al. 2011). Further, a meta-analysis with 934,663 participants reported inverse associations between dairy consumption and overall risk of cardiovascular disease (Qin et al. 2015). Conversely, a second meta-analysis involving 938,465 participants demonstrated neutral associations between dairy products and cardiovascular disease (Guo et al. 2017). The association between dairy consumption and metabolic syndrome and cognitive function is also inconsistent, which is proposed to be due to methodological differences between study designs (Crichton et al. 2011; Crichton et al. 2010).

As not all dairy products are nutritionally equal, it can be expected that the association varies depending on dairy type. For instance, fermented dairy products such as yoghurt may have positive effects on the intestinal microbiota (Lordan et al. 2018; Aslam et al. 2018), which is proposed to be a key mediating pathway in depression (Dash et al. 2015). On the other hand, cheese is often higher in sodium and saturated fat, which may unfavorably effect cardiovascular function (Lordan et al. 2018), and in turn, depressive symptoms. It is postulated that inconsistent findings within the same dairy category may be explained by a lack of distinction between low- and whole-fat dairy products or between fermented and non-fermented dairy products. In particular, of the 13 studies only two performed separate analyses for low- and whole-fat dairy products (Perez-Cornago et al. 2016; Cui et al. 2017), with one additional study reporting results for whole-fat milk only (Almeida et al. 2006). Contrary to previous assumptions, low-fat yoghurt was associated with

an increased risk for depressive symptoms whereas whole-fat yoghurt was inversely associated (Perez-Cornago et al. 2016). While this may be a chance finding, another plausible explanation may relate to differences in the fatty acid composition of these two products. Compared to low-fat varieties, whole-fat dairy products contain increased amounts of beneficial fatty acids (e.g. conjugated linoleic acid) and phospholipids which are proposed to have numerous health benefits (Lordan et al. 2018). It may be possible that these beneficial fatty acids negate the deleterious effects of saturated fat, in addition to contributing to satiety and increased fat-soluble vitamin intake within the diet (Lordan et al. 2018). Conversely, low-fat yoghurt may be associated with an increased risk for symptoms due to increased sugar intake, as total sugar content has been found to be significantly higher in low-fat foods, compared to whole-fat foods (Nguyen, Lin, and Heidenreich 2016). Given that high consumption of added sugars has been associated with an increased risk of depression (Gangwisch et al. 2015), and population dietary guidelines advise the consumption of low-fat dairy (National Health and Medical Research Council 2013) further investigation into these differences are warranted.

A surprising finding was that a small subset of Chinese participants who consumed yoghurt greater than twice per day were at increased of depressive symptoms (Yu et al. 2017). Per capita dairy consumption is low in China relative to Western countries such as the United States and United Kingdom (Muehlhoff, Bennett, and McMahon 2013; Government of Canada 2015). Among consumers, high income earners and urban residents are the highest consumers of dairy in China (Muehlhoff, Bennett, and McMahon 2013). Therefore, it may be likely that high dairy consumption is a proxy for a Western style diet, which has been consistently associated with increased depression risk (Li et al. 2017). Furthermore, reverse causality cannot be excluded due to the cross-sectional nature of this study (Cainzos-Achirica et al. 2018). Individuals with depression may select more 'healthful foods', such as yoghurt, in an attempt to improve their residual symptoms. This behavior has been confirmed in a prior study, where it was postulated that previously depressed individuals sought to improve depressive symptoms through dietary modification (Jacka et al. 2015).

Subgroup inspection of findings also revealed gender differences in the association between dairy consumption and depression. For example, milk intake was associated with less depressive symptoms in men (Wolfe et al. 2011), but associated with increased symptoms in post-menopausal women (Pasco et al. 2015). This may be due to gender-specific differences in metabolism which are driven by sex hormones (Leblanc et al. 2014; Mauvais-Jarvis 2015). However, findings may also be attributable to underlying differences in food choices between men and women, with Australian statistics indicating that men, on average, are greater consumers of dairy compared to women (Australian Bureau of Statistics 2016).

Strengths and limitations

The present review has several strengths. To the best of our knowledge, this is the first systematic review to examine the

association between dairy consumption and depressive and anxiety symptoms. The review had no date restrictions and included a thorough assessment of study quality. It is recognized that inclusion of intervention studies would add to the strength of evidence, however, preliminary literature searches failed to identify intervention studies that matched the research question. Although 13 studies were included within the review, only a small number of studies reported on each of the dairy sub-types (e.g. milk, yoghurt and cheese). Further, many studies did not adjust for energy intake and diet quality, which may confound the association between dairy consumption and depressive symptoms. Heterogeneity amongst studies, including inconsistent measures of dairy intake, limited the ability to perform a meta-analysis. In particular, serves of dairy could not be quantified due to the lack of reporting of serving sizes by studies. Furthermore, given the projected small number of studies, our inclusion criteria set no limitations on the study sample size, length of the follow-up and participant characteristics. Consequently, our search retrieved studies with large variations in samples. Thus, caution should be exercised in comparing findings between studies. Lastly, a reductionist approach that only focuses on a single food fails to consider the synergistic and antagonistic interactions with other foods in the diet and may result in misleading conclusions (Tapsell et al. 2016). Thus, it is recommended that this research should be interpreted in the context of the broader diet.

Future recommendations

Future research would benefit from adequately powered longitudinal and intervention studies that examine the effects of long-term dairy consumption on both depressive and anxiety symptoms. Within these studies, consideration should be given to potential confounders, including energy intake and diet quality. Future research should also consider the use of more rigorous dietary assessment methods, to capture data on nutritional variations between dairy product's including fat, sugar and probiotic content. For instance, as research develops and more reliable markers are identified, biomarkers of intake such as fatty acid biomarkers may be useful to estimate short-term and average intake of dairy products (Munger et al. 2018). Given gender differences have been noted within the literature, future studies should also perform subgroup analyses of associations in both men and women.

Conclusion

Our findings indicate that the association between dairy consumption and depressive symptoms is conflicting and inconsistent. There is some evidence to suggest that dairy consumption is associated with depressive symptoms, however methodological differences and a small number of studies reporting on sub-types of dairy limits our ability to make conclusions. Furthermore, this review identified a need for studies that examine whether an association exists between dairy consumption and anxiety symptoms. Future longitudinal and intervention studies, of more rigorous design, are required

prior to drawing firm conclusions on the association between dairy consumption and depressive and anxiety symptoms.

Author contribution statement

MH developed the protocol, conducted the literature search, screened articles, extracted data, assessed study quality and drafted the manuscript. AR screened articles, extracted data, assessed study quality, contributed to the manuscript and revised for intellectual content. AJM extracted data, assessed study quality and revised the manuscript for intellectual content. WM, TR, FNJ revised the manuscript for intellectual content. All authors read and approved the final draft for submission.

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Appendix 1

Assessment of risk of bias

Reference	1	2	3	4	5	6	7	8	9	10	11	12	13	14*
Prospective studies														
Perez-Cornago et al. 2016	Y	Y	Y	Y	N	Y	Y	Y	Y	N	Y	NA	Y	Y
Wolfe et al. 2011	N	Y	Y	Y	N	Y	Y	Y	N	N	Y	NA	Y	Y
Tsai, Chang, and Chi 2012	Y	Y	Y	N	N	Y	Y	Y	Y	N	Y	NA	Y	N
Pasco et al. 2015	Y	Y	Y	Y	N	Y	Y	Y	N	N	Y	Y	N	N
Almeida et al. 2006	Y	Y	Y	Y	N	Y	Y	N	N	N	N	NA	N	N
Miyake et al. 2006	Y	Y	N	Y	N	Y	Y	Y	Y	N	Y	NA	Y	Y
Miyake et al. 2016	Y	Y	N	Y	N	Y	Y	Y	Y	N	Y	NA	Y	Y
Cross-sectional studies														
Dairy consumption as exposure variable														
Cui et al. 2017	Y	Y	Y	Y	N	N	N	Y	Y	NA	Y	NA	NA	Y
Yu et al. 2017	Y	Y	Y	Y	N	N	N	Y	Y	NA	Y	NA	NA	Y
Miyake et al. 2015	Y	Y	Y	Y	N	N	N	Y	Y	NA	Y	NA	NA	Y
Depression as exposure variable														
Meyer et al. 2013	Y	Y	Y	Y	N	N	N	N	Y	NA	N	NA	NA	N
Grossniklaus et al. 2010	Y	Y	Y	Y	Y	N	N	NA	Y	NA	Y	N.R.	NA	NR
Stefańska, Wendolowicz, and Cwalina 2014	Y	Y	N.R.	N.R.	N	N	N	NA	Y	NA	N	N.R.	NA	NR

*Energy intake identified as key potential confounding variable