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Review article

# Diet quality and depression risk: A systematic review and dose-response meta-analysis of prospective studies☆

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ABSTRACT

*Background:* It has been claimed that the quality of a diet is associated with the incidence of depressive disorders. We sought to investigate the evidence for this claim.

*Methods:* Systematic searches were performed up to March 6th, 2017 in order to identify prospective cohort studies that reported on exposure to dietary patterns or food groups and the incidence of depression/depressive symptoms. Data from 24 independent cohorts (totalling 1,959,217 person-years) were pooled in random-effects meta-analyses.

*Results:* Adherence to a high-quality diet, regardless of type (*i.e.,* healthy/prudent or Mediterranean), was associated with a lower risk of depressive symptoms over time (odds ratios ranged 0.64–0.78 in a linear dose-response fashion [$P < 0.01$]). A relatively low dietary inflammatory index was also associated with a somewhat lower incidence of depressive symptom (odds ratio = 0.81), although not in a dose-response fashion. Similar associations were found for the consumption of fish and vegetables (odds ratios 0.86 and 0.82 respectively) but not for other high quality food groups (*e.g.,* fruit). Studies that controlled for depression severity at baseline or that used a formal diagnosis as outcome did not yield statistically significant findings. Adherence to low quality diets and food groups was not associated with higher depression incidence.

*Limitations:* Our ability to detect confounders was only limited.

*Conclusion:* There is evidence that a higher quality of a diet is associated with a lower risk for the onset of depressive symptoms, but not all available results are consistent with the hypothesis that diet influences depression risk. Prospective studies that control for relevant confounders such as obesity incidence and randomized controlled prevention trials are needed to increase the validity of findings in this field.

## 1. Introduction

Adherence to a healthy or high-quality, or healthy, diet has been shown to co-vary with better mental health, with the latter almost always conceptualized as the absence of unipolar depressive symptoms. Conversely, adherence to low-quality diets has been associated with the presence of depressive symptoms (for reviews and meta-analyses see Li et al., 2015, 2017; O'Neil et al., 2014; Quirk et al., 2013).

A difficulty in establishing the diet-depression link however is that not all findings have been consistently replicated (Jacka et al., 2014; Lai et al., 2016). Complicating the issue further is that the larger part of the evidence comes from cross-sectional studies (Khalid et al., 2017; O'Neil et al., 2014). Depression and factors that predispose to its onset (Rucker, 1906; Darmon and Drewnowski, 2015) are associated with altered eating patterns (Stunkard et al., 2003) in many, but not all cases (Jacka et al., 2015). Hence, cross-sectional data cannot differentiate to what extent diet or dietary behaviour is a risk factor, a consequence, or a concomitant phenomenon of depression (Kendler, 2012; Stunkard

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et al., 2003). A final complicating factor is that the mechanistic understanding of the potential association between diet and depression is limited, although hypotheses exist (Jacka, 2017; Sarris et al., 2015b).

In the absence of primary prevention trials on the effects of diet on depression incidence, the best available evidence on this association comes from prospective cohort studies. Here we pool the accumulated prospective evidence on the putative (dose-response) relation between diet quality and the incidence of depression/depressive symptoms and investigate whether the proposed association is influenced by methodological decisions made in individual studies (*e.g.,* statistical control for baseline depressive symptoms).

The experts gathered in the International Society for Nutritional Psychiatry Research [the ISNPR], stated that "diet and nutrition are central determinants of mental health" and that "nutrition is a crucial factor in the high incidence and prevalence of mental disorders" (Sarris et al., 2015a page 271). Hence, we expect consistent associations between dietary exposure and depression incidence.

## 2. Methods

We followed the guidelines stated in the PRISMA statement (Moher et al., 2009). A protocol for this study was drafted and registered at PROSPERO (ID CRD42016041800).

### 2.1. Search strategy

We performed comprehensive literature searches in Embase, PUBMED, and Web of Science to identify relevant articles (up to March 6th, 2017). The set of search terms that was used can be found in the online supplement. Additionally, we checked the references that were made to the two seminal papers on the subject (Hakkarainen et al., 2004; Timonen et al., 2004). Earlier meta-analyses (Lai et al., 2014; Li et al., 2015, 2017; Liu et al., 2016; Psaltopoulou et al., 2013) and reviews (Khalid et al., 2017; O'Neil et al., 2014; Quirk et al., 2013; Rahe et al., 2014; Sanhueza et al., 2013) that partly addressed the topic of the current study also were inspected. Our efforts stand out from earlier meta-analyses in that we pool (dose-response) prospective data only on all age-groups and all dietary patterns and food groups.

### 2.2. Inclusion and exclusion criteria

We retained studies that reported on the association between dietary patterns or the consumption of food groups and the incidence of depression (DSM-IV APA, 2000; DSM-5 APA 2013; ICD 10 WHO, 2016) *and/or* changes in depressive symptoms. We considered a dietary pattern or food group to be of high-quality when the *a priori* definition or the factor loadings derived through factor- or principal component analysis aligned with the food groups mentioned by the experts (Sarris et al., 2015a, 2015b) as being healthy or when they were defined as such by the authors of the paper. In a similar manner, we defined unhealthy dietary patterns and food groups. Tables S1 and S2 in the online supplement specify the categorization and operationalization of the exposure- and outcome variables. We also defined a neutral exposure category; food groups on which no predictions have been made with regard to depression risk (*e.g.,* eggs). Jacka et al. (2015) only reported results that were in line with the study hypothesis, which was evident in 1 of 3 age cohorts. For analyses, we estimated the OR for the entire sample (*i.e.,* we bootstrapped between OR's = 0.85 and 1.14 for high- and low-quality diets respectively [the observed effects in 1 cohort] and OR = 1 (the estimated effects in the other two age cohorts)).

Papers that reported on the association between the dietary inflammatory index and incidence of depression or depressive symptoms were also subjected to a meta-analysis. This analysis was not *a priori* registered but performed at request of one of the reviewers, recognizing that inflammatory processes may play a part in the pathophysiology of depressive disorder (*e.g.,* Miller and Raison, 2016).

Studies had to be written in English, Dutch, French, German, or Spanish in order to be retained. In case multiple articles reported on data that were derived from the same cohort, using the same exposure variable, we excluded the article with the shortest follow-up. This occurred in one instance in which Sánchez-Villegas et al. (2015a), (2015b) was chosen over Sánchez-Villegas et al. (2009).

### 2.3. Data extraction and quality assessment

We extracted data on demographic, clinical, and methodological characteristics and effect-sizes and corresponding 95% Confidence Intervals (CI) on the association of interest. We extracted effect-size estimates from the model with the largest degree of statistical control for potential confounders (see Table S3). The methodological quality of the retained articles was assessed using the method proposed by Lievense et al. (2002) and is presented in Tables S4 and S5.

### 2.4. Statistical analysis

Statistical analyses were performed in STATA (StataCorp, 2013) with statistical significance set at $P < 0.05$. As effect-size measure we used the odds ratio (OR).

We pooled the data on depression/depressive symptom incidence as a function of highest compared to lowest category of adherence to (a) high-quality dietary patterns and food groups and (b) low-quality dietary patterns and food groups. In case a study provided input on > 1 exposure variable for one of the meta-analyses (*e.g.,* on the association between vegetable- and fruit intake and depression risk) and hence could be included twice in the healthy food group analysis, we averaged the effect-sizes over exposure variables and initially ran meta-analysis using this within-study pooled effect size (see the online supplement). Next, we stratified effect-size estimates by the components that made up the primary exposure variables (*e.g.,* a meta-analysis on the effect of fruit rather than pooling effect-size estimates over types of healthy food groups). We presented results from random-effects models (Borenstein et al., 2009). Outcomes were weighted using inverse variance methods.

After evaluating the pooled effects of highest compared to lowest exposure (*e.g.,* fifth *versus* first quintile), we calculated the risk of depression in the intermediate exposure categories compared to the lowest category (*e.g.,* fifth *versus* second quintile). Dose-response associations were estimated by pooling the reported *P*-values for trends over exposure categories using Edgington's additive method (Edgington, 1972). To illustrate the clinical relevance of our findings we calculated the number of persons (and 95% CI) that would need to change their diets in order to prevent one case of depression (Number Needed to Benefit; NNB).

To assess potential sources of heterogeneity, we ran meta-analyses as a function of method of exposure assessment (*i.e.,* FFQ *vs* other), outcome assessment (*i.e.,* diagnosis *vs* self-report), whether the study controlled for depressive symptoms at baseline (yes *vs* no), geographic region where the study was performed (in line with Li et al., 2017 defined as: European an American *vs* Asian and others and additionally as Mediterranean *vs* non-Mediterranean) and whether analyses were controlled for time-varying covariates (*e.g.,* diabetes onset; yes *vs* no). Additionally, we related mean age and sex distribution of the sample, depression incidence, months of follow-up, and the methodological quality of a study to individual study outcome. Analyses on geographic region were requested by a reviewer and were not *a priori* registered.

Publication bias was assessed by means of visual inspection of funnel plots and Egger's tests (Egger et al., 1997).

## 3. Results

### 3.1. Study selection

Our initial search yielded 39,153 records (*k*). Of these, 32,433 were