

Review

Association between fruit and vegetable consumption and depression symptoms in young people and adults aged 15-45: A systematic review of cohort studies

Putu Novi Arfirsta Dharmayani¹, Melissa Juergens², Margaret Allman Farinelli^{2,3} and Seema Miharshahi^{1,3*}

¹ Department of Health Systems and Populations, Faculty of Medicine, Health and Human Sciences, Macquarie University, NSW 2109, Australia; putu-novi-arfirsta.dharmaya@hdr.mq.edu.au (P.N.A.D)

² Discipline of Nutrition and Dietetics, School of Life and Environmental Sciences, Faculty of Science, University of Sydney, NSW 2006, Australia; mjue0385@uni.sydney.edu.au (M.J); margaret.allman-farinelli@sydney.edu.au (M.A.F)

³ Prevention Research Collaboration, Sydney Medical School & Sydney School of Public Health, University of Sydney, NSW 2006, Australia

* Correspondence: seema.miharshahi@mq.edu.au; Tel.: +61-29850-2468

Abstract: Higher consumption of fruit and vegetables has been associated with a lower risk of various chronic diseases including coronary heart disease, obesity, and certain cancers. Recently, fruit and vegetable intake has also been linked with mental health, including depression. This systematic review aimed to evaluate the association between fruit and vegetable intake and depressive symptoms in young people and adults aged 15-45. The systematic review focused on peer-reviewed cohort studies published from 1 January 2000 to 31 August 2020 using searches of six electronic databases. The exposure was fruit and vegetable consumption analysed both separately and/or together, and the outcome was depression or depressive symptoms. Data from eligible studies were extracted according to predefined criteria and the studies were appraised using the Newcastle-Ottawa Scale (NOS) for Cohort Studies to evaluate for study quality and risk of bias. To evaluate the association between fruit and vegetable consumption and depressive symptoms, a narrative synthesis was conducted. Of 9667 potentially relevant studies that were screened for title and abstracts, 144 full text studies were evaluated, and 12 studies from seven countries were deemed eligible and included in the qualitative synthesis. Using the NOS framework one study was categorised as 'very good' quality, ten studies were 'good' quality, and two studies were 'moderate' quality. With respect to combined fruit and vegetable consumption, two studies demonstrated an inverse association with depression. When the effects of fruit and vegetable on depression were analysed separately, five studies showed significant associations in fruit consumption, and two studies showed significant associations in vegetable consumption. Four studies showed no association between combined fruit and vegetable consumption and depression, one study showed no association between fruit consumption and depression, and two studies showed no association between vegetable consumption and depression. Despite some contradictory results in the studies included in this review, the evidence seems to be building that a possible association exists, and this may have implications for addressing the burden of mental illness in young people and adults aged 15-45 years. Well-designed prospective cohort studies are needed to provide more robust evidence on the diet-depression relationship.

Keywords: fruit, vegetables, depressive symptoms, depression, young people, young adult, nutrition, diet

1. Introduction

Depression is a debilitating, chronic and reoccurring condition that has become a major public health concern worldwide. In 2017 it was estimated that 300 million people, accounting for 4.4% of

the global population, suffered from this disorder [1,2]. The number of incident cases of depression increased by almost 50% between 1990 and 2017 [3]. Major depressive disorder (MDD) is the second leading cause of years lived with disability and a large contributor to the global burden of disease globally[2] making it a substantial economic burden for countries. The peak age of onset of mental disorders, including depression, typically occurs during a period of life transition in early adulthood making it an important time for prevention strategies [4-6]. A recent study showed that depressive disorders are one of the top ten causes of disability-adjusted life-years (DALYs) in aged 10-24 years and 25-49 years globally, ranked fourth and sixth, respectively [7]. Moreover, the percentage change in number of DALYs between 1990-2009 in depressive symptoms has risen dramatically in both age groups, an increase of 20.7% for ages 10-24 years and an increase of 53.2% for ages 25-49 years. These alarming numbers emphasise the importance of preventing the onset on mental disorders as a priority for public health intervention.

The complex nature of the disease makes it difficult to attribute to a particular cause but depression has been linked to numerous biopsychosocial and lifestyle factors [8]. There has been growing interest recently in the plausible role of dietary factors, such as fruit and vegetable intake, as protective factors against depressive symptoms [9-11]. It is widely recognized that sufficient intake of fruit and vegetables is important for improving health status [12-14]. However, the findings from previous studies on the association between the intake of fruit and vegetables and depression in adults have tended to have contradictory conclusions. Some studies showed that higher intake of fruit and vegetables was associated with a lower likelihood of depressive symptoms [9,11], whereas other studies found no significant associations [15,16]. Recent systematic reviews indicated that an increase of fruits and vegetables intake may protect against the risk of depression and depressive symptoms in adults [10,17]. Another systematic review highlighted that emerging adulthood is a risk period for both low diet quality, including inadequate fruit and vegetable intake, and poor mental health [18].

Existing systematic literature reviews examining the diet depression relationship tend to be inclusive of all study designs including those cross-sectional in nature [19-23]. This poses a methodological limitation when inferring causation. Cohort studies have an advantage in that they are prospectively studying the associations between diet and depression, so that there is a clearer sequential relationship seen between exposure and outcome. In this systematic review, we aimed to evaluate the association the between fruit and vegetables intake and depressive symptoms in young people and adults aged 15-45 using longitudinal cohort studies.

2. Materials and Methods

2.1 Study design

The PRISMA framework was used to guide the reporting of methodology and outcomes [24]. The review used a predefined protocol registered with International Prospective Register of Systematic Reviews (PROSPERO) database (ID no: CRD42018091642) and can be accessed at: https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=91642.

2.2 Eligibility criteria

The detailed inclusion and exclusion are shown in Supplementary Table S1. The following criteria was used – (1) studies in healthy individuals aged 15-45 years old; (2) study design was restricted to original cohort studies with a follow up time of a year or longer (3) the exposure was fruit and vegetable intake analysed both separately and/or together; and (4) the outcome of studies was depression or depressive symptoms. Studies were excluded if (1) they had study designs other than a longitudinal cohort (2) they were published prior to 1 January 2000; (3) had a follow up period < 1 year; (4) major dietary patterns were examined without separate analysis of fruit and/ or vegetables; (5) the studies were published in languages other than English; and if the populations included in the studies (6) had pre-existing conditions, including depression; (7) had specific

nutritional needs; and (8) were unique populations which are less likely to be representative of the general population (e.g., monks).

2.3 Search strategy

The systematic review focused on peer-reviewed cohort studies published from 1 January 2000 to 31 August 2020. Prespecified search terms and Medical Subject Headings (MeSH) terms were utilised to identify potentially relevant articles from six databases, namely Medline, EMBASE, PreMedline, and PsycINFO via Ovid, CINAHL via EBSCO, and Scopus. Two reviewers (PNAD & MJ) conducted a comprehensive search using the following keywords: (a) type of food ('fruit' OR 'vegetable' OR 'FV') (b) 'consumption' OR 'intake' (c) mental disorders ('depression' OR 'depressive disorder' OR 'depressive symptoms') (d) population ('young people' OR 'young adults' OR 'adults') (e) study design ('longitudinal stud*' or 'cohort stud*'). Full details of the search strategy can be found in Supplementary Table S2.

2.4 Study selection

All studies identified were imported into EndNote X9 citation management software (Thomson Reuters, Toronto, Canada). At the first stage studies were verified and screened based on title and abstract by two reviewers (PNAD & MJ). At the second stage, all potentially relevant studies were independently screened and scrutinised for eligibility by three reviewers (PNAD, MJ & SM). Any discrepancies in judgement were resolved by discussion between researchers. Reference lists of eligible studies were manually searched to identify any additional studies. The procedure of identification and screening process for selection of cohort studies is presented in Figure 1.

2.5 Data extraction

Data extraction was independently conducted by two reviewers (PNAD & MJ) and then validated by SM using a pre-determined data extraction table. Key study components were extracted including (1) characteristics of participants (age, gender, country of origin), (2) study details (cohort assessed, number of participants, follow up period), (3) outcome and exposure assessment methods (diet and depression), (4) main results (including β coefficients, OR, HR, 95% CI, and P values) and (5) confounding factors (including all models of adjustment).

2.6 Quality Assessment

Two researchers (PNAD & SM) independently appraised the study quality and risk of bias of each eligible studies using the Newcastle-Ottawa Scale (NOS) for Cohort Studies [25]. This framework used following criteria to categorise studies: selection (scale from 0 to 4), comparability (scale from 0 to 2), and outcome (scale from 0 to 3). The overall score of each included study was used to categorise studies as: 'very good' quality (8-9 NOS points), 'good' quality (6-7 NOS points), 'moderate' quality (4-5 NOS points), and 'low' quality (0-3 NOS points) [26]. Differences in scores regarding the quality assessment were resolved by discussion and consensus between the two researchers.

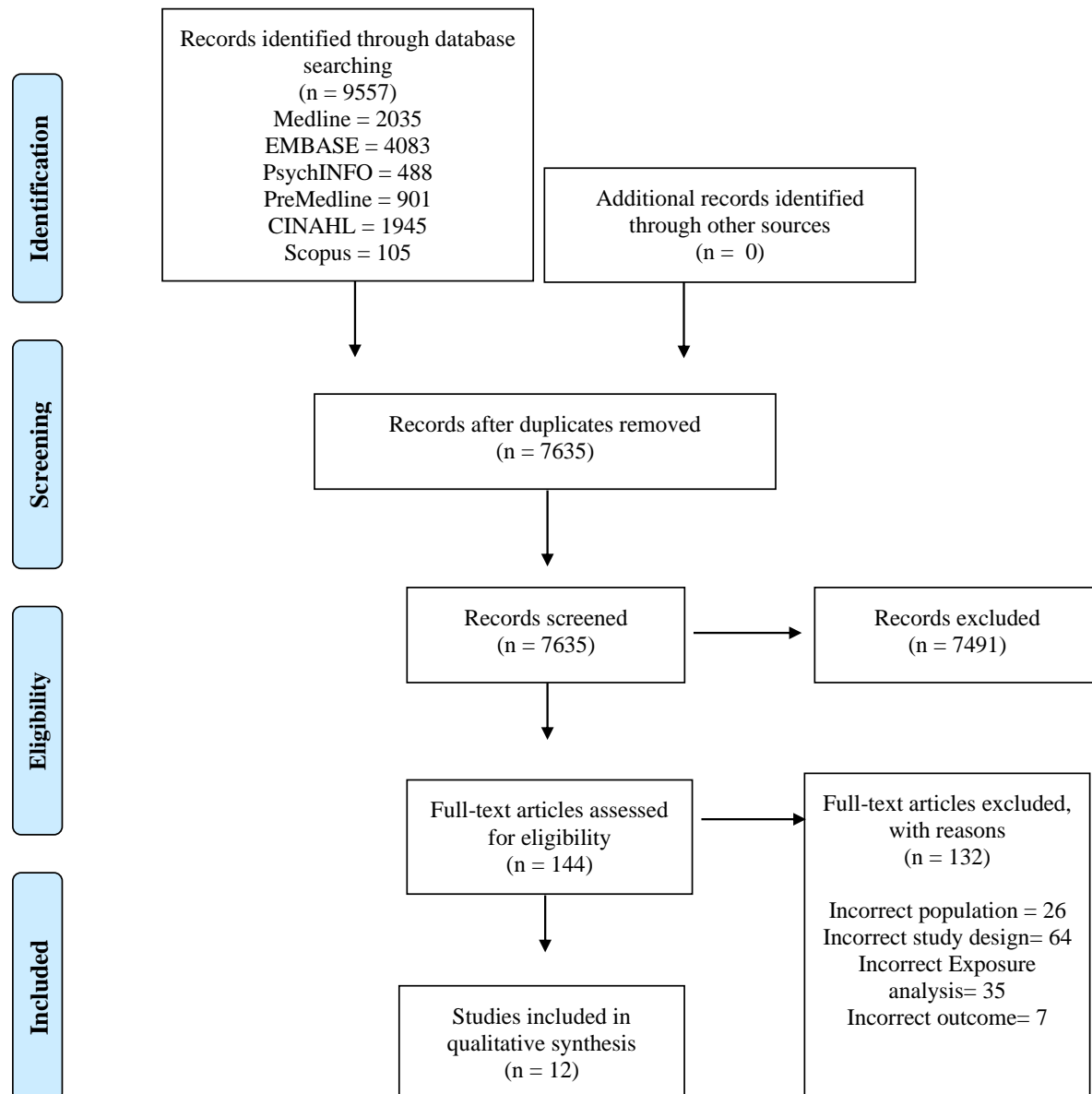


Fig. 1 Flowchart of identification and screening process for selection of cohort studies exploring the association between fruit and vegetable intake and depressive symptoms in young people and adults aged 15-45 years.

3. Results

3.1 Search results

A total of 9557 potentially relevant studies were identified using the search strategy on six electronic databases, (Medline = 2035, EMBASE= 4083, PsychINFO= 488, PreMedline= 901, CINAHL= 1945, Scopus= 105) which was reduced to 7635 after removal of duplicates. After abstract and title screening in the first stage, 7491 studies were excluded leaving 144 full-text articles. Of 144 studies that were screened in full-text publications for eligibility, 12 studies were deemed eligible and included in the qualitative synthesis [27-38]. No additional articles were retrieved from reference list searching. The flowchart in Figure 1 displays the process of selection. Those full-text studies which were deemed ineligible with reasons are reported in Supplementary Table S3.

3.2 Study characteristics

Table 1 shows the study characteristics. Most of the included studies were conducted in European countries; three were based in the UK [29,31,36], one from France [33], one from Spain [38], and one from Sweden [30]. Three studies were conducted in the USA [32,35,37], and the remaining studies were each located in Japan [27] and Australia [28]. The earliest publication date was 2009 and the most recent 2020. Duration of the study follow-up period ranged from 2-14 years with the number of participants varying from 139 to over 45,000. The age ranges at baseline of some of the studies also included participants that were outside the 15-45 years age group, although they were recruited in this age range, as was the nature of the longitudinal cohort. One commentary study [28] was also included as an eligible study because it presented an extra evidence regarding depression and anxiety using the same cohort data from previous study conducted by the same authors [39]. In terms of analysis, one study analysed only vegetable intake [27], and one study exclusively analysed fruit intake [30], while the rest analysed both fruit and vegetable intake [28,29,31-38]. One study consisted of only female participants [35] while the rest comprised of individuals from both genders [27-34,36-38]. For the data extraction, one study [36] reported raw data from only female participants as results in the male participants were not significant. This study also separated analysis into measurements taken at two different time points: 5-years and 10-years.

3.3 Dietary measures

Semi-quantitative food frequency questionnaires were used to assess diet in four studies [27,35,36,38], two studies used country specific food frequency questions, one from the National Cancer Institute [37] and the other from the USA Centres for Disease Control and Prevention [34]. Multiple 24-hour recalls were used in another [33], a 4d diet diary in one study [31], and self-reported questionnaires in four studies [28-30,32]. When looking at the analysis of exposure, three analysed the impact fruits and vegetables had independently on depression [32,36,38], five combined fruits and vegetables in their analysis [28,31,33,34,37], one looked specifically at only flavonoid containing foods which included fruits and vegetables [35], and one study analysed both the impact of fruit and vegetable together and separately [29].

3.4 Depression measures

Depression assessment methods varied between studies. The most commonly used screening instruments to measure depressive symptomatology were the General Health Questionnaire (GHQ-12) [27,29,30], and the Centre for Epidemiologic Studies Depression Scale, where of two studies used CESD-20 [33,36], and one used both CESD-20 and CESD-10 in different waves of the study [32]. Other instruments included Composite International Diagnostic Interview-Short Form (CIDI-SF) [34], and the Moods and Feelings Questionnaire (MFQ) [31]. One study used a SF-12 Health Survey [37], and was included as it had some measures of depression and mental health. Two studies included questions about diagnosis of depression and/or use of antidepressant medication [28,38] and another used a combination of methods across different assessment time periods [35].

3.5 Quality assessment

The Newcastle-Ottawa Scale for cohort studies was used to assess the study quality. The detailed results of the quality assessment are seen in Supplementary table 5, where the total score for the Newcastle-Ottawa Scale is given. One study was deemed as 'very good' quality,[34] the majority of studies (n= 10) categorised as 'good' quality [27-32,35,36,38], and two studies were categorised as 'moderate' quality [33,37]. Most of the studies failed to meet the requirements on ascertainment of exposure and assessment of outcome because written self-report was used to collect the exposure and outcome information, which was likely to introduce bias. Furthermore, the studies of moderate

quality [33,37] only received one point each for selection and outcome criteria. No studies were excluded on the basis of their quality assessment.

3.6 Outcomes

A pooling of the results was not possible because the differences in the ways that outcomes were reported and thus results were tabulated and described qualitatively. Results are presented in Table 2.

Impact of fruit and vegetable intake on depressive symptoms

Two good quality studies and one moderate quality study explored the impact of fruit and vegetable intake on depressive symptoms [31,33,36]. Two studies used the CES-D instrument [33,36], and one study used the MFQ to assess depressive symptoms [31]. At individual study level, in the 5-year analysis of the Whitehall II cohort [36], a greater consumption of both vegetables and fruit decreased the odds of recurrent depressive symptoms in women while no significant results were seen in men. In the 10-year analysis an improvement or maintenance of vegetable intake was associated with reduced odds of recurrent depressive symptoms in women, while women whose consumption decreased over the same time frame had higher odds of recurrent depressive symptoms. Similarly, an increased fruit intake decreased the odds of depression development in the 10-year analysis, however, no significant association was observed when women maintained or decreased fruit intake. In contrast, Winpenny et al. [31] reported no prospective association between fruit and vegetable intake at age 14 years and depression symptomatology at age 17 years after adjusting for risk factors, such as depressive symptoms at baseline, socio-economic status, physical activity, and total energy intake. Similarly, the finding from the SU.VI.MAX study [33] illustrated that adherence to the French nutrition guidelines resulted in a decrease in depressive symptom development due to an overall healthy diet. This was ascertained by comparing the guidelines score without inclusion of fruit and vegetables and the result was still protective.

Impact of fruit and vegetable intake on depression

One very good quality study and four good quality studies examined the association between fruit and vegetable intake and depression, of which four studies measured the depression doctors diagnosis or medication use [28,34,35,38], and one study used the CES-D instrument [32]. Two good quality studies reported the protective effect of fruit intake against risk of developing depression [35,38]. Moreover, a significant protective effect was observed from greater intakes of legumes and “fruits and nuts” [38]. Citrus fruits and juices were also shown to reduce the odds of depression in women from the Nurses’ Health Study [35]. However, a greater intake of vegetables had no significant effect on the development of depression in individuals in the SUN cohort [38]. One very good quality study showed fruit and vegetable intake not to be associated with depression development or distress after adjusting for the key confounders [34]. Contrastingly, Mujcic and Oswald [28] found an inverse association between fruit and vegetable consumption and the probability of being diagnosed with depression/anxiety within the next 24 months. An interesting finding in the Add Health cohort [32] was that the association between fruit consumption during adolescence and reduced odds of depression in adulthood was not significant after adjustment for adolescent depression. Contrary to that, consuming vegetables once a day was significantly related to reduced odds of adult depression among females after adjustment for adolescent depression, but not at higher intakes (twice or more a day). However, this association was substantially attenuated after further controlling for relevant confounders.

Impact of fruit and vegetable intake on mental health/well-being

Four studies investigated the impact of fruit and/or vegetable intake independently on mental health [27,29,30]. Three good quality studies used the GHQ-12 [27,29,30] and one moderate study

used the SF-12 Health Survey to assess mental health [37]. In the J-MICC study [27], an inverse association between vegetable intake and a GHQ score ≥ 4 was not significant after controlling for confounders. In contrast to that, the study from Sweden highlighted that daily consumption of fruit and berries was a substantial determinant to predict stability in mental health among the 18-29 age group [30]. Similar results were observed in a longitudinal UK study [29] which showed the importance of both frequency and quantity of intake of fruit and vegetables on mental well-being. It was highlighted that daily consumption of fruit and/or vegetable (at least one portion) contributed to maintenance of mental well-being. Moreover, frequent vegetable consumption had a greater effect on mental wellbeing than frequent consumption of fruit. One moderate quality study that assessed emotional and mental health found fruit and vegetable consumption had no significant association with mental health and the results indicated that increased physical activity had a positive association with better mental health, irrespective of fruit and vegetable consumption [37].

Table 1: Characteristics of included studies

Reference/Country/ Year	Participant characteristics (Age range, Mean age at baseline (SD), Gender)	Study characteristics (Number of participants, Follow-up period)	Cohort	Dietary assessment method (Recall period)	Depression assessment method (Analysis assessment)
Choda et al.,[27] Japan, 2020	Age range at baseline: 35-69y Age mean: participants with a GHQ score ≥ 4 is 50.1 (9.1); participants with a GHQ score < 4 is 52.9 (9.5) Gender (female): ~50%	4,701 ~5y (Daiko) ~6y (Shizuoka)	The Japan Multi-Institutional Collaborative Cohort (J-MICC), the Daiko Study and the Shizuoka area	A validated short FFQ (46 food items) (over the past years)	The 12-item General Health Questionnaire (the GHQ-12) (psychological distress and social dysfunction factors)
Mujcic & Oswald,[28] Australia, 2019	Age range: ≥ 15 y Age mean: - Gender (female): -	7,108 2y	The Household, Income, and Labour Dynamics in Australia (HILDA) Survey	<i>Short questions on usual intake and frequency intake: "how many days in a usual week do you eat fruit?" and "how many days in a usual week do you eat vegetables?" "On a day when you eat fruit, how many serves of fruit do you usually eat?" and "On a day when you eat vegetables, how many serves of vegetables do you usually eat?"[39]</i>	"Have you ever been told by a doctor or nurse that you have any of long-term health conditions listed below? Please only include those conditions that have lasted or are likely to last for six months or more: Depression/Anxiety"
Ocean et al.,[29] UK, 2019	Age range at baseline: 15-104y Age mean: 47.1 Gender (female): -	Over 45,000 6y	The UK Household Longitudinal Study (UKHLS)	<i>Short questions on portion intake: "on a day when you eat fruit or vegetables, how many portions of fruit and vegetables in total do you usually eat?"</i>	The 12-item General Health Questionnaire (the GHQ-12) (psychological distress and social dysfunction factors)

Table 1. Cont.

Reference/Country/ Year	Participant characteristics (Age range, Mean age at baseline (SD), Gender)	Study characteristics (Number of participants, Follow-up period)	Cohort	Dietary assessment method (Recall period)	Depression assessment method (Analysis assessment)
Winzer et al.,[30] Sweden, 2018	Age range: 18-29y Age mean: - Gender (female): 61.8%	1,704 ~12y	The Stockholm Public health Cohort (SPHC)	Short questions on frequency intake: How often do you eat Fruit and berries (an apple, an orange, a banana, a glass of juice, grapes, strawberries)?	The 12-item General Health Questionnaire (the GHQ-12) (psychological distress and social dysfunction factors)
Winpenney et al.,[31] UK, 2018	Age range at baseline: 14y Age mean: 14.5 (0.3) Gender (female): 60%	603 3y	The ROOTS study	A 4d diet diary (two weekdays and two weekend days)	The Moods and Feelings Questionnaire (MFQ) (depressive symptoms)
Hoare et al.,[32] USA, 2018	Age range at baseline: 12-18 years Age mean at baseline: 15.9 (1.7) Age mean at follow up: 28.9 (1.7) Gender (female): -	3,696 ~14y	Add Health	Short questions on frequency intake: “How often did you eat fruit or drink fruit juice yesterday?” The same item with response options was asked for vegetable consumption (previous day)	The Center for Epidemiologic Studies Depression Scale CES-D 20 (Wave 1) CES-D 10 (Wave 4) (depressive symptoms)
Kingsbury et al.,[34] Canada, 2016	Age range: 18-104 y Age mean: 44.16 (18.41) Gender (female): 52.8%	8353 Continuous every 2y (1994/1995- 2010-2011)	Canadian Longitudinal Survey	Food frequency questions: from the fruit and vegetable module in the behavioural risk factor surveillance system of the USA Centres for Disease Control and prevention (Usual intake)	CIDI-SF (Major depression) K6 (Distress)
Collin et al.,[33] France, 2016	Age range: 35-60y Age mean: 49.5 (6.2) Gender (female): 56.2%	3328 11y*	Supplementation en Vitamines et Mineraux Antioxydants (SU.VI.MAX)	Multiple (3-6) 24-hour recalls (Usual intake)	CES-D 20 (Chronic or recurrent depressive symptoms)

Table 1. Cont.

Reference/Country/ Year	Participant characteristics (Age range, Mean age at baseline (SD), Gender)	Study characteristics (Number of participants, Follow-up period)	Cohort	Dietary assessment method (Recall period)	Depression assessment method (Analysis assessment)
Chang et al.,[35] USA, 2016	Age*** range: 36-55 y Age mean: ~46.3 (4.6) Gender (female): 100%	36,658 10y	Nurses' Health Study II** (NHSII)	Semi-quantitative FFQ (130 food items) (Previous years usual intake)	MHI-5 (1993, 1997) Antidepressant use (1997) Doctor diagnosis (2001) (Depression)
Akbaraly et al.,[36] UK, 2013	Age range at baseline: 35-55 y Age at initial measurement for this analysis: 39-64y Gender (female): 25.1%	4215 (5y) 4053 (10y)	Whitehall II study, UK civil servants	Semi-quantitative FFQ (127 food items) (Previous years usual intake)	CES-D 20 or/and use of antidepressant medication (Depressive symptoms)
Chai et al.,[37] USA, 2010	Age: 18 years + Age mean: 55.3 (15.5) Gender (female): 74.1%	139 2y	Multiethnic sample of adults living in Hawaii	Food Frequency questions: National Cancer Institute fruit and vegetable questionnaire. (Previous months intake)	SF-12 Health Survey (SF-12)
Sanchez-Villegas et al.,[38] Spain, 2009	Age range at baseline: 18-104y Age mean male: 42.7 (13.3)[40] Age mean female: 35.1 (10.7)[40] Gender (female): ~58.4%	10,094 4.4y	The Seguimiento Universidad de Navarra' Study cohort, alumni of the University in Spain (SUN cohort)	Semi-quantitative FFQ (136 food items) (Usual intake)	Positive response to "Have you ever been diagnosed as having depression by a medical doctor" or/and who reported the habitual use of antidepressant drugs. (Clinical depression)

4 **Abbreviations:** SD; standard deviation, y; years, UK: United Kingdom, FFQ: Food frequency questionnaire, CES-D: Center for epidemiologic studies depression scale, SU.VI.MAX:
5 Supplementation en Vitamines et Mineraux Antioxydants, USA; United States of America, CIDI-SF: Composite International Diagnostic interview- Short form, K6; Kessler
6 psychological Distress Scale, SUN: Seguimiento Universidad de Navarra/University, NHS; Nurses' Health Study, 4d; 4day, MHI-5; 5-item Mental health index, QOL: quality of life.

7 *Follow up 1996-1997 to 2007-2009

8 **Study included data from NHS as well however characteristics were described independently and thus those from the NHSII are only presented in this table

Table 2: Results table

Reference/ Country/Year	Results			Confounders	Quality
	Exposure	Outcome	Key results		
Choda et al.,[27] Japan, 2020	Vegetable intake (frequency)	Mental Health (GHQ-12)	Model 2 <i>P</i> -trend = 0.291 Ref: lowest quartile of exposure (Q1) OR: Q2 = 1.20 (0.95-1.50) OR: Q3 = 0.98 (0.77-1.25) OR: Q4 = 1.21 (0.95-1.55)	Main findings: Vegetable consumption was not associated with GHQ score before or after adjustment of confounders using prospective logistic regression Adequate consumption of certain nutrients and foods may lead to better mental health in Japanese adults Associations between fruit and mental health were not reported in this study.	Model 2: Adjusted for sex, age, area, employment, smoking, drinking, sleeping time, leisure time exercise, eating breakfast, and total energy.
Mujcic & Oswald,[28] Australia, 2019	Fruit and vegetable (portions/day)	Depression/ Anxiety (Doctor diagnosis)	β = -0.0041 (-0.008, -0.001) <i>p</i> = 0.017**	Main findings: Individuals who increased fruit and vegetable intake from 0 to 8 portions/day were on average 3.2% points less likely to experience depression or anxiety within the next 24 months. Fruit and vegetable consumption may help to protect against future risk of clinical depression and anxiety	Adjusted for household income, age, gender, education, occupation, marital status, long-term health condition, having children, alcohol, smoking, never eat red meat, never eat fish, eat breakfast regularly, drink low fat of skim milk, avoid fatty foods, BMI, exercise
	<u>Reverse causality</u> Diagnosed with depression/ Anxiety	Fruit and vegetable	β = -0.0718 (-0.174, 0.031) <i>p</i> = 0.170	There is no decisive evidence whether fruit and vegetable consumption in the future can be predicted from the rate of depression or anxiety in the current period.	

Table 2. Cont.

Reference/ Country/Year	Results				Confounders	Quality
	Exposure	Outcome	Key results	Summary		
Ocean et al.,[29] UK, 2019	Fruit and vegetable (portions/day)	Well-being (GHQ-12)	Specification (2) = 0.118*** (0.0220) Specification (3) = 0.133*** (0.0245)	Main findings: Mental well-being responds in a dose-response fashion to increases in both the quantity and the frequency of fruits and vegetables consumed.	Specification (2): controlling for standard socio-demographic variables	Good
	Days each week eat fruit (frequency)		Specification (4) Ref: never 1-3 days = 0.259*** (0.0896) 4-6 days = 0.423*** (0.0989) Every day = 0.613*** (0.0982)	Increasing one's consumption of fruit and vegetables by one portion (on a day where at least one portion is consumed) leads to a 0.133-unit increase in mental well-being ($p < 0.01$).	Specification (3): controlling for standard socio-demographic variables, lifestyle/health behaviours, consumption of bread/dairy, smoking status, walking frequency, presence of a long standing-health condition	
	Days each week eat vegetables (frequency)		Specification (4) Ref: never 1-3 days = 0.518*** (0.171) 4-6 days = 0.803*** (0.175) Every day = 0.925*** (0.177)	The more often fruit and vegetables are consumed in a week, the more likely individuals have a higher mental well-being.	Specification (4): same as specification 2	
Winzer et al.,[30] Sweden, 2018	Consumption of fruit and berries (frequency)	Mental Health (GHQ-12)	P-trend = 0.071 Ref: rare consumption of fruit and berries OR: Daily consumption = 1.39 (1.05-1.84)** OR: Weekly consumption = 1.25 (0.94-1.67)	Main findings: Consuming fruit and berries in daily basis were considered as a determinant for stable mental health. Having healthy food intake, demonstrated by consuming fruit and berries, was one of six determinants to predict stability in mental health.	Gender, country of birth, occupational status, financial strain, housing, emotional support, instrumental support, interpersonal trust, community trust, societal participation, voting, nutrition – consumption of breakfast, physical activity, tobacco smoking, victim of threat and violence	Good

Table 2. Cont.

Reference/ Country/Year	Results			Confounders	Quality
	Exposure	Outcome	Key results		
Winpenny et al.,[31] UK, 2018	Fruit and vegetables (servings/day)	Depressive symptoms (MFQ)	Model 1: $\beta = 0.17$ (-0.10, 0.45) Model 2: $\beta = 0.16$ (-0.21, 0.43) Model 3: $\beta = 0.14$ (-0.15, 0.43) Model 3 (male): $\beta = 0.06$ (-0.32, 0.44) Model 3 (female): $\beta = 0.21$ (-0.22, 0.64)	Main findings: Fruit and vegetable consumption at age 14 years were not significantly associated with depressive symptoms at age 17 years based on based on prospective logistic regression. Diet quality was not significantly associated with depressive symptoms.	Model 1: Adjusted for sex and socio-economic status Model 2: Adjusted for sex, socio-economic status, smoking level, alcohol consumption, physical activity, and sleep Model 3: Adjusted for model 2 + friendship quality, self-esteem, family functioning, medication use, percentage body fat and total energy intake
Hoare et al.,[32] USA, 2018	Fruit consumption (quantity/day)	Depression (CES-D 10 & CES-D 20)	Model 1 (pro) In males results Ref: no fruit consumption OR: Once = 0.62 (0.41, 0.94)** OR: Twice + = 0.64 (0.44, 0.94)** Model 3 (pro) In males results Ref: no fruit consumption OR: Once = 0.72 (0.46, 1.11) OR: Twice + = 0.71 (0.47, 1.07) In females results Ref: no fruit consumption OR: Once = 0.92 (0.63, 1.33) OR: Twice + = 0.73 (0.62, 1.26)	Main findings: Fruit and vegetable consumption could be a protective factor against adult depression. Fruit consumption among males and vegetable consumption among females were prospectively associated with a reduced risk of adult depression in unadjusted models (Model 1).	Model 2 (pro): Adjusted for adolescent depression Model 3 (pro): Adjusted for adolescent depression, age, household income, ethnicity, physical activity, and body mass index

Table 2. Cont.

Reference/ Country/Year	Results				Confounders	Quality
	Exposure	Outcome	Key results	Summary		
Hoare et al.,[32] USA, 2018	Vegetable consumption (quantity/day)	Depression (CES-D 10 & CES-D 20)	Model 1 (pro) In females results Ref: no vegetable consumption OR: Once = 0.66 (0.48, 0.89)*** OR: Twice + = 0.68 (0.49, 0.94)**	Then, vegetable consumption among female remained significant after adjusting for adolescent depression (Model 2).	Model 2 (pro): Adjusted for adolescent depression	Good
			Model 2 (pro) In females results Ref: no vegetable consumption OR: Once = 0.79 (0.53, 1.00)** OR: Twice + = 0.79 (0.57, 1.10)	However, the association diminished after further adjusting age, household income, ethnicity, physical activity, and overweight/obesity (Model 3) on both groups.	Model 3 (pro): Adjusted for adolescent depression, age, household income, ethnicity, physical activity, and body mass index	
			Model 3 (pro) In males results Ref: no vegetable consumption OR: Once = 1.07 (0.72, 1.57) OR: Twice + = 1.02 (0.66, 1.56)			
			In females results Ref: no vegetable consumption OR: Once = 0.74 (0.54, 1.02) OR: Twice + = 0.80 (0.57, 1.12)			
Collin et al.,[33] France, 2016	mPNNS-GS ^a	Depressive symptoms (CES-D 20)	P trend= <0.001(Model 4b) Ref: Lowest quartile of exposure (Q1) OR: Q2= 0.76 (0.55, 1.05) OR: Q3= 0.72 (0.51, 0.99) OR: Q4= 0.51 (0.35, 0.73)	Main findings: There was a 49% reduced odds of developing chronic or recurrent depressive symptoms with better adherence to diet-related recommendations of the French nutrition guidelines.	Model 4b: Adjusted for age, energy intake, education level, marital status, tobacco, supplementation group, number of 24-hour dietary records, BMI and physical activity	Moderate

Table 2. Cont.

Reference/ Country/Year	Results			Confounders	Quality
	Exposure	Outcome	Key results		
Collin et al.,[33] France, 2016	PNNS-GS without Fruits and vegetables	Depressive symptoms (CES-D 20)	OR: 0.84 (0.77, 0.91) P=<0.0001 When adjusted for fruit and vegetable intake the PNNS-GS score remained statistically significant	Higher adherence to the French nutritional guideline assessed by PNNS-GS was associated with a lower likelihood of chronic or recurrent depressive symptoms. This association was not driven by any specific component of the PNNS-GS (including Fruit and vegetables) but was a result of an overall healthy diet.	PNNS-GS adjustments: Adjusted for gender, age, energy intake, educational level, tobacco, supplementation group, number of 24-hour dietary records and removed component
Kingsbury et al.,[34] Canada, 2016	<u>Direct association</u>			Main finding: A greater fruit and vegetable consumption at the initial measurement was associated with a lower risk of depression at the next. This association was evident in Model 2 adjustments however disappeared once obesity was included in the adjustment (Model 3).	Model 2 (dep): Adjusted for age, sex, history of depression, Socioeconomic status, education, chronic disease and binge drinking
	Fruit and vegetable intake (daily frequency)	Depression (CIDI-SF)	Model 2 (dep): β = -0.03 (-0.05 to -0.01) Model 3 (dep): β = 0.001 (-0.03 to 0.04)		Model 3 (dep): Adjusted for Model 2+ obesity, social support, smoking, energy expenditure
	Fruit and vegetable intake (daily frequency)	Distress (K6)	Model 2 (dis): β = -0.03 (-0.05 to -0.01) Model 3 (dis): β = 0.02 (-0.01 to 0.04)	A greater fruit and vegetable consumption at the initial measurement was associated with lower distress scores at the next. This association was evident in Model 2 adjustments however disappeared once social support smoking and physical activity were added to the model (Model 3).	Model 2 (dis): Adjusted for age, sex, history of depression, SES, education, chronic disease, binge drinking and obesity Model 3 (dis): Adjusted for Model 2 + Social support, smoking and energy expenditure

Table 2. Cont.

Reference/ Country/Year	Exposure	Outcome	Results Key results	Summary	Confounders	Quality
Kingsbury et al.,[34] Canada, 2016	<u>Inverse association</u> Depression	Fruit and vegetable intake	Model 2: $\beta = -0.27$ (-0.42 to -0.11) Model 3: $\beta = -0.10$ (-0.22 to 0.02)	Inverse association showed that depression and distress at initial measurements predicted lower consumption of fruits and vegetables at the next measurement.	Model 2: Adjusted for Age, sex, history of depression, SES, education, chronic disease, binge drinking and obesity	Very Good
	Distress	Fruit and vegetable intake	Model 2: $\beta = -0.02$ (-0.03 to -0.01) Model 3: $\beta = 0.01$ (-0.01 to 0.02)	These associations were no longer evident once social support, smoking and physical activity were added to the model.	Model 3: Adjusted for Model 2 + Social support, smoking and energy expenditure	
Chang et al.,[35] USA, 2016	Citrus fruit and Juice combined (servings/day)	Depression (MHI-5, antidepressant use, doctor diagnosis)	P= <0.0001*** Ref: Lowest quintile of exposure (Q1) HR: Q2= 0.94 (0.85, 1.05) HR: Q3= 0.89 (0.78, 1.02) HR: Q4= 0.85 (0.75, 0.97) HR: Q5= 0.82 (0.74, 0.91)	Main findings: Citrus intake (fruit and juice) ≥ 2 servings/d was associated with an 18% reduction in depression risk ^b .	Adjusted for: Age, questionnaire cycle, total energy intake, social network (quintiles), alternate Mediterranean score, census-tract family income, alcohol intake, subjective self-rate societal position, cigarette smoking, physical activity (METs), BMI, actual sleep hours, frequency of difficulty falling or staying asleep, bodily pain, current multivitamin use, coffee consumption, menopausal status and postmenopausal hormone use, history of hypertension, history of CVD, history of diabetes, history of hypercholesterolemia.	Good
	Citrus fruit (servings/day)		P= 0.001*** Ref: Lowest quintile of exposure (Q1) HR: Q2= 0.93 (0.88, 0.99) HR: Q3= 0.91 (0.86, 0.96) HR: Q4= 0.97 (0.83, 1.13) HR: Q5= 0.87 (0.75, 1.01)	Independently both citrus fruit and juice showed significant associations to a reduction in depression. This was true for moderate to high intakes of citrus fruit but only high intakes of juice		

Table 2. Cont.

Reference/ Country/Year	Results			Confounders	Quality
	Exposure	Outcome	Key results		
Chang et al.,[35] USA, 2016	Onions (servings/day)	Depression (MHI-5, antidepressant use, doctor diagnosis)	P= 0.25 Ref: Lowest quintile of exposure (Q1) HR: Q2= 1.00 (0.94, 1.06) HR: Q3= 0.98 (0.92, 1.05) HR: Q4= 0.96 (0.89, 1.02) HR: Q5= 0.99 (0.89, 1.09)	Main findings: Onion intake was not associated with depression risk Diet higher in flavonoids results in a moderate reduction in risk of depression- especially in older women	Adjusted for: Age, questionnaire cycle, total energy intake, social network (quintiles), alternate Mediterranean score, census-tract family income, alcohol intake, subjective self-rate societal position, cigarette smoking, physical activity (METs), BMI, actual sleep hours, frequency of difficulty falling or staying asleep, bodily pain, current multivitamin use, coffee consumption, menopausal status and postmenopausal hormone use, history of hypertension, history of CVD, history of diabetes, history of hypercholesterolemia.
Akbaraly et al.,[36] UK, 2013	5-year analysis (Phase 7) AHEI ^a score	Depressive symptoms (CES-D 20 or/and use of antidepressant medication)	In women only a 1SD increase in AHEI score resulted in a 41% decreased odds of recurrent depression. OR: 0.59 (0.47, 0.75)*** (Model 2) When AHEI was computed without each AHEI component, the modified AHEI-recurrent-DepS association remained significant. (Model 3)	Main findings: Large differences observed between men and women with regard to association between diet and depression. In women a higher adherence to the AHEI was related to lower risk of DepS assessed over 5 years. In women as AHEI score increased odds of recurrent depression decreased. No such association was observed in men.	Model 2: Adjusted for model 1 (age, ethnicity and total EI) +SES, retirement status, marital status, smoking, physical activity, CAD, T2D, hypertension, HDL cholesterol, use of lipid-lowering drugs, central obesity and cognitive impairment. Model 3: Adjusted for model 2 + 8 other AHEI- component scores.

Table 2. Cont.

Reference/ Country/Year	Results			Confounders	Quality
	Exposure	Outcome	Key results		
Akbaraly et al.,[36] UK, 2013	<u>5-year analysis</u> (Phase 7)	Depressive symptoms (CES-D 20 or/and use of antidepressant medication)	OR: ~0.65 ^c (0.51, 0.88) (Model 3) OR: ~ 0.68 ^c (0.58, 0.97) (Model 3)	High consumption of fruits and vegetables was associated with lower odds of recurrent depression	Model 3: Adjusted for model 2 + 8 other AHEI- component scores.
	<u>10-year analysis</u> (Phase 9)	AHEI score	In women results (Model 2) Ref: Those who maintained low OR: Maintained high= 0.35 (0.19, 0.64)*** OR: Improved = 0.32 (0.13, 0.18)** Ref: Those who maintained high OR: Decreased = 2.15 (1.09, 4.22)**	Main findings: Women who increased or maintained a high AHEI score over the 10y period resulted in 68% and 65% lower odds of subsequent depression, respectively, compared to women who maintained a low AHEI score. Women who decreased AHEI score over the 10y had a 2 fold increased odds of developing subsequent depression than those who maintained a high AHEI score. No association was observed in men	Model 2: Adjusted for model 1 (age, ethnicity and total EI) +SES, retirement status, marital status, smoking, physical activity, CAD, hypertension, HDL cholesterol and central obesity at phase 3.
	Vegetable intake (servings/day)		Ref: Those who maintained low OR: Maintaining= ~0.50 ^c (0.30, 0.90) OR: Improving2 = ~0.45 ^c (0.27, 0.91) Ref: Those who maintained high OR: Decreasing = ~2.6 ^c (1.35, 5.35)		

Table 2. Cont.

Reference/ Country/Year	Exposure	Outcome	Results		Confounders	Quality
Akbaraly et al.,[36] UK, 2013	10-year analysis (Phase 9) Fruit intake (servings/day)	Depressive symptoms (CES-D 20 or/and use of antidepressant medication)	Ref: Those who maintained low OR: Maintaining= ~0.60 ^c (0.40, 1.01) OR: improving= ~0.30 ^c (0.25, 0.60) Ref: Those who maintained high OR: Decreasing= ~1.55 ^c (0.90, 3.01) (NS)	Improvement in fruit and vegetable score led to lower odds of subsequent depressive symptoms compared to those who maintained low scores. Decrease in AHEI score led to higher odds of depression in vegetables but not fruit.	Model 2: Adjusted for model 1 (age, ethnicity and total EI) +SES, retirement status, marital status, smoking, physical activity, CAD, hypertension, HDL cholesterol and central obesity at phase 3.	Good
Chai et al.,[37] USA, 2010	Fruit and vegetable intake (servings/day)	Quality of Life (SF-12)	MCS scores P>0.05 at all-time points (T1-T7) Correlation co-efficient ranged from: -0.06 to 0.13	Main findings: There was no significant association between MCS score and daily fruit and vegetable consumption. Increasing weekly physical activity levels was significantly associated with increasing MCS at all time points. Physical activity predictive of positive mental health irrespective of other behaviours such as fruit and vegetable intake and TV/video watching	Adjusted for: ethnicity, gender, age, BMI, and education	Moderate

Table 2. Cont.

Reference/ Country/Year	Exposure	Outcome	Results Key results	Summary	Confounders	Quality
Sanchez-Villegas et al.,[38] Spain, 2009	Mediterranean diet pattern ^a	Depression (doctor diagnosis or antidepressant use)	P trend =0.007*** Ref: Lowest quintile of exposure (Q1) HR: Q2= 0.79 (0.57-1.09) HR: Q3= 0.67 (0.48-0.93) HR: Q4= 0.56 (0.39-0.80) HR: Q5= 0.69 (0.50-0.96)	Main findings: Greater adherence to the Mediterranean dietary pattern resulted in more than a 30% reduction in depression development.	Mediterranean diet adjusted for: Sex, age, smoking status, BMI, physical activity during leisure time, energy intake, employment status and excludes participants who reported the use of antidepressant medication during follow up by not a physician-made diagnosis of depression.	Good
	Fruits and nuts (grams/day)		P trend=0.007*** Ref: Lowest quintile of exposure (Q1) HR: Q2= 0.69 (0.53-0.91) HR: Q3= 0.67 (0.51-0.88) HR: Q4.= 0.69 (0.52-0.91) HR: Q5= 0.61 (0.45-0.82) Merged Q3-Q5: 0.67 (0.54-0.84)	Compared to participants with the lowest consumption fruit and nut those with the highest intake had a 39% decreased risk of developing depression.	Fruits and nuts, vegetables, and legumes adjusted for: Sex, age, smoking status, BMI, physical activity during leisure time, energy intake, employment status.	
	Vegetables (grams/day)		P trend=0.81 Ref: Lowest quintile of exposure (Q1) HR: Q2= 0.88 (0.67-1.17) HR: Q3= 0.87 (0.66-1.16) HR: Q4= 0.94 (0.71-1.25) HR: Q5= 0.93 (0.69-1.24)	There was no significant association between vegetable intake and depression.		
	Legumes (grams/day)		P trend=0.03** Ref: Lowest quintile of exposure (Q1) HR: Q2=0.76 (0.58-1.00) HR: Q3=0.73 (0.55-0.96) HR: Q4= 0.65 (0.49-0.86) HR: Q5= 0.76 (0.57-1.00) Merged Q3-Q5: 0.71 (0.57-0.88)	Compared to participants with lowest consumption of legumes those with highest intake had a 27% decreased risk of developing depression.		

Abbreviations: UK; United Kingdom, AHEI; Alternate healthy eating index, SD; standard deviation, OR; odds ratio, DepS; depression symptoms, total EI; total energy intake, SES; socioeconomic status, CAD; coronary artery disease, T2D; type 2 diabetes, HDL; high density lipoproteins, Ref; reference, NS; not significant, mPNNS-GS; only the dietary components of the PNNS-GS, PNNS-GS; French Programme National Nutrition Sante'- Guidelines Score, Q; quartile/quintile, BMI; body mass index, Dep; depression, Dis; distress, HR; hazard ratio, MDP; Mediterranean dietary pattern, USA; United States of America, METs: metabolic equivalents, CVD; cardiovascular disease, MCS; Mental component summary score, CES-D: Center for epidemiologic studies depression scale, USA; United States of America, GHQ; General Health Questionnaire, CIDI-SF; Composite International Diagnostic interview- Short form, K6; Kessler psychological Distress Scale, MHI-5; 5-item Mental health index, SF-12; The 12-item Short Form Survey, MFQ; Mood and Feelings Questionnaire.

****** $p < 0.05$

******* $p < 0.01$

^aRefer to Appendix A

^bThis trend was consistent for both NHS and NHSII cohort

^cRaw data not reported- only graphically represented estimate provided

4. Discussion

This systematic review aimed to evaluate the association between fruit and vegetable intake and depressive symptoms in young people and adults aged 15-45 years. We identified 12 cohort studies from seven countries. Among six cohort studies which analysed the impact of combined fruit and vegetable consumption [28,29,31,33,34,37], only two studies demonstrated an inverse association with depressive symptoms [28,29]. Varying results were observed when the effects of fruit and vegetables were analysed separately. Among the five studies which showed an inverse association between fruit consumption and depression after adjusting for key confounders [29,30,35,36,38], two studies showed that the association was observed in women [35,36]. Two studies showed an inverse association between vegetable consumption and depressive symptoms [29,36]. Two studies, although initially showing a significant association in unadjusted models, showed no association between fruit and vegetable intake and depression after adjustment for confounders, such as obesity, physical activity, and BMI [32,34]. Four studies showed no association between fruit and vegetable consumption and depression [31,33,34,37], one study showed no association between fruit consumption and depression [32], and two studies showed no association between vegetable consumption and depression [27]. Two studies reported possible gender effects, because there were different impacts of fruit and vegetable consumption on depression between women and men [32,36]. Although we are unable to make definite assertions, the evidence seems to be building that a possible association exists, and this may have implications for addressing the burden of mental illness in young people and adults aged 15-45 years.

Existing literature reviews conducted on the diet-depression relationship have shown varying results. While some have illustrated positive effects around healthy dietary patterns and decreased risk of depression [10,23,41], others have detected no association [21]. Furthermore, in line with the results obtained from this review, most existing work recommended the need for additional research in this area [20,22,42]. This study looks solely at the impact of fruits and vegetables because few systematic reviews [4,10,19] examined its impact on depression and most of them examined the impact of dietary patterns on depression. We chose this option because findings will be able to be translated more readily into recommendations for whole foods. In addition, this review exclusively examined the association in young people and adults aged 15-45 years which is the age transition where most mental health issues arise.

A common finding across the 12 studies was the low intake of fruit and vegetables generally, and the failure to meet recommended guidelines. According to the Understanding Society study [29], 87% of 15-29 year-olds and 80% of 30-41 year-olds consumed fewer than five portions a day in the UK. Despite the low rate of adherence to guidelines, the study found that even small increases in the consumption patterns of individuals may translate into substantive positive effects for the well-being [29]. Also, the more often fruits and vegetables are eaten in a week, the better mental well-being is likely to be. The study by Winzer et al. [30] for example concluded that consuming fruit and berries on daily basis is a determinant of stability in mental health in the 18-29 age group. Another study also illustrated that vegetable consumption once a day among women was prospectively associated with a reduced risk of adult depression although the association diminished after further adjustment for key confounders [32]. These findings indicate that even one portion of fruit and vegetable daily is likely to reduce the risk of depression in adults.

There were large variations in the methods used to assess intake of fruits and vegetables. For example, four studies used serving size [31,35-37], while three studies used frequency of consumption [29,30,34], and another used meeting the national guidelines [27]. This may have contributed to the variations in results seen. When analysed separately, the independent effects of fruits and vegetables on depression and depressive symptoms differed. The inverse relationship was more likely to be observed between fruit intake and depressive symptoms than vegetable intake. Such disparities were also seen in a study conducted in Australian middle-aged women [43]. A higher intake of fruits was seen to be protective of depressive symptoms in both cross sectional and longitudinal analyses whereas vegetables were only protective using cross sectional analyses. Authors from this study suggested that the discrepancy between the two food groups could be a

93 result of differing chemical composition, whereby fruits tended to contain higher levels of
94 antioxidants and anti-inflammatory components such as carotenoids, flavonoids, and resveratrol.
95 While this is a possibility, it may also be hypothesised that in these studies the vegetable intake is not
96 consumed in quantities high enough to see protective effects, or that the types of vegetables
97 consumed in larger amounts do not contain the corresponding nutrients suggested to be protective.

98 Interestingly, of the two good quality studies, there was evidence of differences in the
99 association according to gender [32,36]. The results demonstrated that vegetable consumption
100 among females is inversely associated with future depressive symptoms. The association was
101 attenuated in a US study by further adjustment for potential confounders [32], while the other
102 remained significant [36]. In terms of fruit consumption, no significant association was observed in
103 both genders in the US study [32], whereas an inverse association was significantly observed in
104 women only in the Whitehall II study from the UK [36]. A plausible explanation for the gender
105 differences, may be explained by psychosocial factors. According to Emanuel et al., [44] a gender
106 difference in fruit and vegetable intake may be attributable to attitudes and perceived behavioural
107 control. Furthermore, women reported more favourable attitudes and perceived behavioural control
108 towards fruit and vegetable intake than men.

109 While all studies adjusted for most key potential confounders, it is difficult to say with certainty
110 that all confounding factors were accounted for, due to the complex nature of both depression and
111 diet. For instance, the studies that showed protective effects against depression did not adjust for
112 BMI in their analysis [29,30,36]. BMI has been shown to have a non-linear association with
113 depression, whereby those who are underweight or obese tend to have higher odds of depression
114 compared to individuals that are normal weight or overweight [45,46]. Thus failure to adjust for
115 BMI, despite adjustment for central obesity, may have obscured the effects observed in the Canadian
116 longitudinal study [34]. Additionally, none of the included studies adjusted for fish intake in their
117 analysis. Greater intakes of fish and omega-3 fatty acids have been associated with lower odds of
118 depression development and thus could be an important confounding factor [47-49]. Not adjusting
119 for all confounders may mean that the associations observed are a result of an unmeasured variable
120 and thus not a true reflection of the association between exposure and outcome. This influence was
121 evident in two included studies [32,34] where consuming vegetable once a day were shown to be
122 protective against depression development in women until adjustments of age, household income,
123 ethnicity, physical activity, and body mass index were made [32], and fruits and vegetables were
124 shown to be protective against depression development until additional adjustments of social
125 support, obesity, and smoking were made in Canadian longitudinal study [34].

126 Different measurement tools in exposure and outcome may also contribute to the current
127 conflicting results. In terms of dietary assessment, fruit and vegetable consumption was reported
128 based on frequency, portions, servings, or quantity per day. A study by Offringa et al., [50]
129 illustrated that the total fiber content of vegetables consumed by 100-kcal portions was significantly
130 higher compared to the total fiber content of vegetables consumed per serving. Therefore, this
131 difference may interfere with the impact of vegetable consumption on predictive depressive
132 symptoms. The dynamic and varying nature of diet means that there may be unavoidable errors in
133 dietary measurements. Therefore, it is important to determine the strengths and weaknesses of the
134 assessment methods used within each study. Reporting bias may be present in all studies as food
135 intake relies on the participants' recall ability and assumption that reported intake close to the true
136 intake. Participants may be inclined to over emphasize their usual intake towards including
137 healthier food choices as this appears more socially desirable [51]. Often, the use of a sensitivity
138 analysis would tend to negate the effects of misreporting, however, none were conducted in any of
139 the included studies. Validation of the dietary assessment method is therefore necessary to ensure
140 the results are accurate. Despite the individual dietary assessment methods having their own
141 limitations, most of the included studies used validated tools. Similarly, different instruments across
142 the studies were used for defining depression, which not limited to clinical diagnosis or
143 antidepressant use. Despite the use of validated instruments, such as CES-D, GHQ-12, to define
144 depression, using different ways of scoring and cut-off points might affect the results [4].

4.1 *Strengths and limitations*

The exclusive use of cohort studies poses both a limitation and strength to this review. The inclusion of only a single study design is a form of selection bias. However, by reviewing only cohort studies, the direction of causation is easier to infer as there is more likely to be a temporal association between exposure and outcome, provided subjects with the outcome at baseline are excluded from the analysis. Additional strengths of this review include the comprehensive nature of the search strategy, thorough quality analysis and the large sample sizes seen in 10 of the 12 studies may have led to a higher statistical power to ascertain an effect. To our knowledge, this is the first systematic review of cohort studies to evaluate the association between fruit and vegetable intake and depressive symptoms in young people and adults aged 15-45.

The strict inclusion criteria for our systematic review resulted in only 12 studies eligible for review and between studies, there were also considerable methodological differences which made direct comparisons challenging. Most of included studies used dietary recall to assess fruit and vegetable consumption. This methodology might be liable to recall bias although it has higher precision in assessing dietary intakes. In terms of exposure assessment, measurement of fruit and/or vegetable consumption varies from grams/day, to portions, serving sizes, quantity, and frequency. Different instruments were used across studies to assess depressive symptomatology, which not limited to clinical diagnosis or antidepressant use. Inconsistency in the outcome measures resulted in different definitions of depression or depressive symptomatology, which also might affect the results. Further, the validity of results may be limited because the age range in majority of studies were slightly extended outside of young people and adults aged 15-45 years. Other limitations include language bias, as studies published in languages other than English were excluded and publication bias may be present.

5. **Conclusions**

Despite a paucity of cohort studies, this study complements existing work evaluating the evidence on the impact of fruit and vegetable consumption on depression. Unique aspects of this systematic review include the exclusive use of cohort studies, specifically in young people and adults aged 15-45, an age group where the prevalence of depression is seen to dramatically increase [52,53]. Overall, there is inconclusive evidence on the effect fruits and vegetables have on reducing the odds of developing depression and depressive symptoms. However, two good quality studies have shown protective effects and reduced odds of depression with frequent intakes of fruit and vegetables. Additionally, four good quality studies indicated a strong inverse association between fruit consumption and development of depressive symptoms. Drawing on this evidence, our findings highlight the potential importance of the association between fruit and vegetable consumption and depressive symptoms in young people and adults aged 15-45 years. More robust evidence is needed to address the specific aspects of diet that could prevent the development of depression. Thus, we recommend the diet-depression relationship be examined in well-designed prospective cohort studies. With the evidence building there is potential to inform public policy and add positive mental health outcomes to an already extensive list of reasons as to why people should prioritise a healthy diet.

Supplementary Materials: The following are available online at www.mdpi.com/xxx/s1, Table S1: Inclusion and exclusion criteria for study designs; Table S2: Full electronic search strategy applied for Medline, Embase, and PsycInfo; Table S3: Justification of exclusion at full text screening; Table S4: The Newcastle-Ottawa Scale results

Author Contributions: S.M. (Seema Mahrshahi) and M.A-F. (Margaret Allman-Farinelli) conceptualised the study including the scope and preliminary search terms. P.N.A.D. (Putu Novi Arfirsta Dharmayani) and M.J. (Melissa Juergens) identified and screened potentially relevant studies. P.N.A.D. (Putu Novi Arfirsta Dharmayani), M.J. (Melissa Juergens), and S.M. (Seema Mahrshahi) screened and scrutinised full-text studies for eligibility. P.N.A.D. (Putu Novi Arfirsta Dharmayani) and M.J. (Melissa Juergens) undertook data extraction which was validated by S.M. (Seema Mahrshahi). P.N.A.D. (Putu Novi Arfirsta Dharmayani) and

S.M. (Seema Mahrshahi) appraised the study quality and risk of bias. P.N.A.D. (Putu Novi Arfirsta Dharmayani) and M.J. (Melissa Juergens) wrote the paper, then S.M (Seema Mahrshahi) and M.A-F. (Margaret Allman-Farinelli) reviewed and edited the paper. All authors read and approved the final manuscript.

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Appendix A

Diet types explained

Alternate healthy eating index (AHEI): Alternate healthy eating index comprises of summing 9 component scores (Fruit, vegetable, ratio of white meat (seafood and poultry) and red meat, trans fat, ratio of PUFA to SFA, total fibre, nuts and soy, alcohol consumption and long-term multivitamin use) where by a higher score corresponds to a healthier diet.[36]

mPNNS-GS: Based on the Program National Nutrition Sante’ the mPNNS-GS contains 12 dietary components. 8 of the components referred to meeting the food serving recommendations, while four of the components are markers of limited consumption for recommendations without providing quantified frequency.[54]

Mediterranean diet pattern (MDP): consists of 9 components: high ration of MUFA to SFA, moderate alcohol intake, high intake of legumes, high intake of cereal, high intake of fruit and nuts, high intake of vegetables, low intake of meat and meat products, moderate intake of milk and dairy products and high intake of fish. The score was positive for intake above the median for 6 components (MUFA/SFA ratio, legumes, cereal, fruit and nuts, vegetables or fish), and intake below the median for 2 components (meat and dairy). For alcohol, points were given if intake was within a sex specific range. [38]

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