DOES FRUIT AND VEGETABLE CONSUMPTION IMPACT MENTAL HEALTH? SYSTEMATIC REVIEW AND META-ANALYSES OF PUBLISHED CONTROLLED INTERVENTION STUDIES

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Abbreviations: 95%CI: 95% confidence intervals; BMI: Body Mass Index; C: comparator; DGA: Dietary Guidelines for Americans; F: fruit; FV: fruit and vegetables; HADS: Hospital Anxiety and Depression Scale; ITT: Intention-to-Treat; I: Intervention; NR: not reported; ppts: participants; SMD: standardized mean difference; SF-36: 36-item Short Form Health Survey; V: vegetables



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ABSTRACT

Associations between fruit and vegetable (FV) consumption and mental health are suggested, largely from observational studies. This systematic review aimed to identify and summarize all published controlled intervention studies investigating the effects of FV consumption on mental health in adults. Four academic databases (Medline, PsychInfo, Pubmed, Web of Science) were searched on 16.09.22, over all years, for studies that: used an intervention design; included fruit and/or vegetable consumption; included an appropriate non-FV-consumption control; used a validated measure of mental health; and were conducted in healthy adults or adults with solely a depressive or anxiety-related condition. Study details were tabulated and combined using metaanalyses. Risk of bias was assessed using the domains of the Cochrane Collaboration. Six studies, enrolling 691 healthy adults, and reporting on one or more mental health outcomes were found. Meta-analyses found small and imprecise effects of FV consumption: Psychological Well-being (4 studies, 289 participants) SMD=0.07 (95% confidence intervals (95%CI) -0.17, 0.30), p=0.58, $I^2=0\%$; Depressive Symptomology (3 studies, 271 participants) SMD=-0.15 (95%CI -0.40, 0.10), p=0.23, I²=46%; Anxiety-related Symptomology (4 studies, 298) participants) SMD=-0.15 (95%CI -0.39, 0.08), p=0.20, I^2 =69%. Some benefit for Psychological Well-being was found in change-from-baseline data: SMD=0.28 (95%CI 0.04, 0.52), p=0.02, $I^2=0\%$). Risk of bias was high in many studies. Limitations include the consideration only of published studies, and stem from the studies found. Given the few, limited studies available and the small size of effects, stronger evidence is needed before recommending FV consumption for mental health.

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INTRODUCTION

Fruit and/or vegetable (FV) consumption is robustly associated with reduced risk from a number of global physical health concerns, including cardiovascular disease, type II diabetes, and obesity⁽¹⁻⁴⁾. Recent reviews also suggest some benefits for mental or psychological health⁽⁵⁻¹⁰⁾, and while physical health conditions continue to result in the greatest number of years of life lost globally⁽¹¹⁾, depressive and anxiety disorders contribute increasingly to number of years lived with disability⁽¹¹⁾. Recent estimates suggest increases of 14.3% and 12.8% years lived with disability for depressive and anxiety-related disorders respectively, since 2007, with depressive disorders ranked the third leading cause of years lived with disability in 2017⁽¹¹⁾.

Potential mechanisms for effects of FV consumption on mental health are available. Firstly, some of the biological compounds present in FV are thought to have a direct impact on brain health and function, via roles in neurotransmitter synthesis, activities and reuptake⁽¹²⁻¹⁴⁾. Vitamin C and many of the B vitamins present in FV play a role in the production and activities of serotonin, dopamine, and other monoamine neurotransmitters, known to be important in experiences of mood⁽¹²⁻¹⁴⁾. Secondly, some of the biological compounds in FV which impact physical health may also impact mental health⁽¹²⁻¹⁴⁾. Antioxidants, for example, such as Vitamins E, C, and serum carotenoids, are known to reduce oxidative stress and inflammation; activities associated with reduced depression and increased psychological well-being^(12,14). Other micronutrients, such as phytochemicals, polyphenols and flavanoids, and some minerals, e.g. magnesium, have also been linked to mental state^(13,14). Thirdly, FV consumption may displace the consumption of other foods, resulting in the absence of compounds within the diet, such as saturated fats, that may be deleterious for physical and mental health⁽¹⁴⁻¹⁶⁾. Fourthly, a more psychological route for the impacts of FV consumption on mental health can also be proposed, where FV consumption results in perceptions of self-care, healthiness or expectations of improved mental functioning $^{(14,17,18)}$, which may then improve mental health. Finally, any combination of these suggested mechanisms may apply.

While benefits for mental health have been suggested however, reviews to date, have focused almost solely on observational cross-sectional and prospective studies⁽⁵⁻¹⁰⁾. Using these study designs, direction of effect can only be suggested^(12,19,20), reverse causation remains a concern⁽²¹⁾,

and confounding or secondary variables, such as other dietary, health and lifestyle behaviours and various demographic characteristics, may explain effects^(16,22-26). Reviews of FV consumption using observational studies, thus, may more accurately be described as reviews of the effects of a healthy diet or lifestyle which includes FV, rather than reviews of the effects of FV consumption *per se*. Isolation of the effects of FV consumption is important if FV are to be recommended for benefits for mental health.

This systematic review aimed to identify and summarize all published controlled intervention studies that investigated an effect of FV consumption, as a distinct intervention, on mental health, in adults.

METHODOLOGY

The review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines⁽²⁷⁾, with advice from the Cochrane Collaboration⁽²⁸⁾. A protocol for the work was published following an initial run of all searches on the Open Science Framework (ID: <u>https://osf.io/txcsm/;</u> date of registration: 30.07.22). We adhered to our published protocol in all respects, but extended our search terms from those detailed in the protocol, to also allow the capture of studies measuring 'life satisfaction' and 'quality of life' following recognition that these terms are often used to capture mental health in medical fields. Some additional refinements were also made throughout the review process as detailed below.

Searches

Electronic databases: Medline, PsychInfo, Pubmed and Web of Science were searched over all years of records. Searches used the search terms (fruit* OR vegetable*) combined with (AND) (anxiety* OR depress* OR "mental health" OR "mental disorders" OR "well being" OR wellbeing OR well-being OR "psychological health" OR "life satisfaction" OR "quality of life"), searched for in 'title' and 'abstract' fields. Phrases were identified as such as necessary in each database. Reference lists of identified papers and review articles were also searched for any papers that may have been missed by our database searches. Our intention was to find as many articles of relevance to our research aim as possible.

Study inclusion

Studies were included in the review if they: were conducted in either healthy adults (aged 18-65 years) or in adults with solely a depressive or anxiety-related condition; included fruit and/or vegetable consumption as an exposure; included a measure of mental health, using a validated measure; used an intervention design with an appropriate non-FV consumption control, and were published in English at the time of our searches.

Only studies in adults (aged 18-65 years) were included; studies in children and adolescents were excluded. Populations were required to be healthy, i.e. were experiencing no major physical or mental health condition, with the exception that studies on individuals with a sole diagnosis of a depressive or anxiety-related condition were considered for inclusion, given the nature of our review. There were no exclusions based on participant gender, age within 18-65 years, or years of condition, if appropriate. Studies were included regardless of the consumption of fruit, vegetables or fruit and vegetables together, to include also the consumption of individual fruits/vegetables and fruit and/or vegetable juices. We did not include studies where the intervention was a fruit/vegetable oil, extract, powder or component, e.g. a vitamin, polyphenol or vegetable protein, or where the intervention was based on a fruit/vegetable with added items. To distinguish between fruit juices, powders and extracts, we included interventions that were commercially available, or that we considered could be made from whole fruit in a home kitchen, e.g., via cooking, while we excluded interventions that were custom-made or required technical processes, such as freeze-drying, or where the process was unclear. We also did not consider studies using herbs, other medicinal plants, or supplements. Studies were excluded if the FV exposure was contaminated by the simultaneous consumption of other foods that may also impact physical and/or mental health, that were not also consumed by the control group; only studies that could ascertain an effect solely due to FV consumption were included. Similarly, we did not include studies using interventions based on dietary patterns high in FV, e.g. the Mediterranean diet, nor did we include studies using interventions where FV consumption was combined with other lifestyle behaviours, such as physical activity. There were no exclusions based on specific FV consumed, type or length of intervention.

We defined mental health as a long-term state of positive well-being or freedom from negative symptomology⁽²⁹⁾. Studies were included in the review if validated measures were used to measure psychological well-being, depressive symptomology, anxiety-related symptomology, mental health, or quality of life, as experiences that last over the long term. We did not consider measures of 'mood' or 'emotion', as these experiences are typically temporary, short-term and transitory in nature, and may be, but are not necessarily, related to longer-term experiences. We also did not consider outcomes that, while psychological in part, may also be physical, such as 'fatigue' or 'vitality', nor did we consider outcomes that are psychological and may be linked to mental health, but are not necessarily markers of good mental health, such as 'self-efficacy' or 'creativity'. 'Life satisfaction' and 'quality of life' were considered as measures that capture mental or psychological health, however, we only included measures of general quality of life, and if possible we used mental health sub-scales; we did not consider studies where quality of life focused on physical symptoms or was measured only in relation to a specific physical condition. We considered only studies that used a controlled intervention design and included a non-FV-consuming control group that allowed assessment of the consumption of FV as a distinct intervention. We did not consider baseline assessments in a pre-post study design to provide sufficient control in this respect. There were no exclusions based on study setting, country or length of follow-up. Only studies that were published and published in English were considered.

Study selection

Searches were conducted by one reviewer (KMA), and search results were then screened independently by two reviewers (KMA, OAA and/or DFS) on title and abstract against our inclusion criteria. All articles of potential relevance were gained in full and screened independently by two reviewers (KMA, LRB, OAA and/or DFS).

Data extraction

Data were extracted and tabulated from all included studies by two independent reviewers (KMA, LRB, OAA and/or DFS), on: number of participants; participant details, including clinical profiles; FV intervention/exposure, including duration; comparator; outcomes assessed; risk of bias and data reported, including authors conclusions. Discordances were resolved by discussion between reviewers.

Risk of Bias

Risk of bias in each study was assessed using the domains and methods suggested by the Cochrane Collaboration⁽²⁸⁾. The domains assessed were: randomization; allocation concealment; blinding of participants and researchers; use of intention-to-treat (ITT) analyses based on number randomized; degree of study non-completion; incomplete outcome reporting and other. Each domain was considered at 'low', 'high' or 'unclear' risk of bias, dependent on the study details as published, either in included papers or from papers detailing the original trial. For the domains randomization, allocation concealment, blinding of participants and researchers and the use of ITT analyses, judgements of low risk were given where details of the methods used and no contra-indications were found, judgements of high risk were given where contra-indications resulting in potential bias were found. For the domain degree of study non-completion, judgements of low risk of bias were given for studies with 20% or lower drop-out and judgements of high risk of bias were given for studies with more than 20% drop-out. For the domain incomplete outcome reporting, judgements of low risk of bias were given where all measures reported in the methods section were reported on in the results section, and judgements of high risk of bias were given where this was not the case. For all domains, an 'unclear' risk of bias judgement was given where information was not reported or unclear. Risk of bias was assessed for each study by two independent reviewers (KMA, LRB, OAA and/or DFS). Discordances were resolved by discussion between reviewers. A-priori, we considered the blinding of participants and researchers and the use of ITT analyses to be the domains most likely to influence our outcomes due to their subjective nature. Studies were included in the review regardless of the risk of bias in each domain.

Analysis

Data were combined both narratively and statistically. Statistical combination was undertaken to provide estimations of effect sizes, although caution should be exercised, considering the low number of studies. Meta-analyses were conducted for three outcomes of mental health identified during the review process: psychological well-being, depressive symptomology, and anxiety-related symptomology, with each outcome analysed separately. Each outcome was also analysed twice, once using data recorded at the end of the intervention (end-of-intervention data) and once using data on change from baseline to the end of the intervention (change-from-baseline data).

Mean and standard deviation data for each intervention and comparator group, corrected to ensure comparable direction, were analysed as standardized mean difference (SMD) (Cohen's d) with 95% confidence intervals (95%CI), using unadjusted ITT data (based on number of participants randomized), where possible^(30,31). Estimates were made using fixed effect models primarily, due to low heterogeneity between studies. Random effects models were also applied as sensitivity analyses^(30,31). Effect size estimates were subsequently converted into meaningful units for each outcome, using the most commonly used measure for the outcome in the contributing studies and the standard deviations reported^(28, section 15.5). Where studies included multiple treatment or comparator groups, each treatment or comparator group was treated as an independent comparison, and participant numbers in single comparison groups were divided.

Authors were contacted by email for original data where these were missing from publications. Complete unadjusted data on baseline, end-of-intervention and change-from-baseline were obtained for the study by Smith & Rogers⁽³²⁾. Where change-from-baseline data could not be obtained⁽³³⁾, these data were calculated based on reported means, and estimated from mean standard deviations. No other study used the same measures, so alternative estimates for standard deviations were not possible⁽³⁴⁾.

Heterogeneity between studies was investigated using Higgins' I^2 statistic^(35,36). The I^2 statistic can be interpreted such that 0% to 40% heterogeneity might not be important, 30% to 60% heterogeneity may represent moderate heterogeneity, 50% to 90% heterogeneity may represent substantial heterogeneity and 75% to 100% heterogeneity may represent considerable heterogeneity⁽²⁸⁾, but caution is again urged given the low number of studies included in all analyses. Possible sources of heterogeneity were identified a-priori to include publication bias and risk of bias, but insufficient studies were available to allow the systematic consideration of these sources of bias in our analyses.

Analyses were undertaken in RevMan (www.cochrane.org) (version 5.4.1) and Stata, Stata Corp Inc. (version 17).

RESULTS

Searches were conducted on the 16th Sept., 2022, to result in the identification of 5136 articles of potential relevance. Title and abstract screening resulted in the retention of 68 of these articles. All full texts were obtained and screened to result in the final inclusion of six articles in the review^(15,17,32,33,37,38). These articles detailed six studies, one of which included two relevant intervention groups⁽¹⁷⁾, and one included two relevant control groups⁽³⁷⁾. Together, these studies enrolled a total of 691 individuals. The PRISMA flow diagram is given in Figure 1.

Characteristics of Included Studies

Methodological details of all studies are provided in Table 1. Three studies were designed to investigate mental health^(32,33,37), the reports by De Leon et al.⁽¹⁵⁾ and Conner et al.⁽¹⁷⁾ were secondary reports of trials by Casperson et al.⁽³⁹⁾ and Brookie et al.⁽⁴⁰⁾, respectively, and the study by Plaisted et al.⁽³⁸⁾ is described as a sub-study of a larger trial by Appel et al.⁽⁴¹⁾. A correction to the trial by Conner et al.⁽³⁷⁾ detailing concerns with randomization, has also been published⁽⁴²⁾, but these concerns do not render this trial ineligible for our review.

Studies included between 35 and 174 participants at trial conception, but only 27 to 171 participants provided data for the outcomes in this review. In all studies, the majority of participants was female with the exception of one study where the sample consisted of 36% females⁽³⁸⁾. In three studies, participants were young adults^(17,32,37), and in three studies, participants were low consumers of FV or not reaching current recommendations^(15,17,37). None of the studies were undertaken specifically among depressive or anxiety-related clinical populations, or reported inclusion of individuals with depressive or anxiety-related conditions.

Studies tested an intervention which provided fruit^(32,37), vegetables⁽¹⁵⁾, fruit and vegetables^(17,38), a fruit and vegetable juice⁽³³⁾ or provided participants with a voucher for a greengrocers and used text-messaging and behavioural change techniques to encourage them to increase their FV intake⁽¹⁷⁾. Comparators were the provision of alternative foods (chocolate and crisps)⁽³²⁾, sugar-free chewing gum⁽¹⁷⁾, an artificial coloured beverage⁽³³⁾, Vitamin C or placebo tablets⁽³⁷⁾, nothing⁽³⁸⁾ or an attention control⁽¹⁵⁾. Participants were randomized to result in intervention and control groups that were roughly equal in size, and compliance with the intervention or

comparator was assessed and reported as good in four studies^(15,17,37,38). Interventions and comparisons lasted for 10 days⁽³²⁾, 14 days⁽¹⁷⁾, 4 weeks⁽³⁷⁾, 45 days over 9 weeks⁽³³⁾ and 8 weeks^(15,38).

Studies measured psychological well-being^(15,37,38), depressive symptomology^(17,32) and anxietyrelated symptomology^(17,32,33), plus several additional mood, physical or mental attributes not considered suitable for inclusion in our review. Psychological well-being was assessed using the Subjective Happiness Scale⁽⁴³⁾, the Warwick–Edinburgh Mental Well-being Scale⁽⁴⁴⁾ and the 36item short form Health Survey (SF-36)⁽⁴⁵⁾. Depressive symptomology was assessed using the Hospital Anxiety and Depression scale⁽⁴⁶⁾ and the Center for Epidemiological Studies Depression Scale⁽⁴⁷⁾. Anxiety-related symptomology was assessed using the Hospital Anxiety and Depression scale⁽⁴⁶⁾ and the Beck Anxiety Inventory⁽⁴⁸⁾.

Results from all studies are given in Table 2. Scores at baseline in all studies suggested good psychological well-being and low depressive and anxiety-related symptomology at study start. Studies reported small statistically-significant increases in psychological well-being following FV consumption, and some reductions in depressive and anxiety-related symptomology, although effects were small, and did not reach statistical significance in all studies. No improvements in these outcomes were reported in comparator groups, and in the study by Smith & Rogers⁽³²⁾, marked increases in depressive symptomology scores were found in the comparator group following the consumption of alternate unhealthy foods. Authors of all studies concluded possible benefits for mental health from the consumption of FV. There are also suggestions that providing participants with FV may have a greater impact than simply asking them to consume more $FV^{(17)}$, that effects may be greater in participants who have lower circulating levels of some of the biological compounds in $FV^{(37)}$, and that effects may occur quickly, then reduce over time⁽³⁷⁾.

Risk of Bias

When assessing risk of bias, we considered three studies to have used randomization methods, that were low in risk of bias^(15,17,32), and that resulting intervention and comparator groups were comparable in nature in three studies^(17,32,33). Some concerns were noted for the study by Conner

et al.⁽³⁷⁾, where randomization was not implemented as intended⁽⁴¹⁾ and level of education differed between randomization groups; a variable known to be associated with healthy eating and mental health^(25,26). Groups in the study by Plaisted et al.⁽³⁸⁾ also differed in gender, another variable known to be associated with healthy eating and mental health^(25,26). Allocation concealment was rarely reported. In all studies, blinding of participants was not possible, with the exception of the study by Chiochetta et al.⁽³³⁾, where participants were blinded to juice received (FV vs non-FV). In one study⁽³⁸⁾, researchers were blinded, in three studies, the researchers undertaking the outcome assessments were not blinded^(15,33,37), while in the other two studies, blinding of researchers (or not) was not reported^(17,32). Data were analysed on an ITT basis in only one study⁽³²⁾. Number of participants with incomplete data was low in three studies^(17,32,37). All pre-specified outcomes were reported in all studies. One additional source of possible bias was also found, where in one study⁽¹⁵⁾ assessments of psychological well-being were not implemented until part way through running the trial. Risk of bias for all studies is given in Table 3.

Statistical Combination

Psychological well-being: Three studies^{15,37,38} (one with two control groups)⁽³⁷⁾ contributed data for these analyses. Analyses of end-of-intervention data using fixed effect models (4 studies, 289 participants) revealed a SMD of 0.07 (95% CI -0.17, 0.30), p=0.58, I²=0%. Analyses using random effects models found the same effects. Analyses of change-from-baseline data using fixed effect and random effects models (4 studies, 289 participants) revealed a SMD of 0.28 (95% CI 0.05, 0.52), p=0.02, I²=0%. Forest plots for analyses on end-of-intervention and change-from-baseline data are provided in Figure 2. One study used a control group who consumed Vitamin C capsules to assess the possibility that the Vitamin C in fruit was the mechanism by which FV impact mental health⁽³⁷⁾. Analyses without this study on end-of-intervention data using fixed effect and random effects models (3 studies, 237 participants) revealed a SMD of 0.12 (95% CI -0.14, 0.37), p=0.37, I²=0%. Analyses without this study on change-from-baseline data using fixed effect and random effects models (3 studies, 237 participants) revealed a SMD of 0.35 (95% CI 0.09, 0.61), p=0.01, I²=0%. Effects favour FV, but effect sizes are small, and when converted into units on the SF-36 are equivalent to an

improvement in psychological well-being from 0.8 (-1.9 - 3.4) units to 3.8 (-1.0 - 6.6) units on a 100-point scale.

Depressive Symptomology: Two studies^(17,32), one with two intervention groups⁽¹⁷⁾, contributed data. Analyses of end-of-intervention data using fixed effect models (3 studies, 271 participants) revealed a SMD of -0.15 (95% CI -0.40, 0.10), p=0.23, I²=47%. Analyses using random effects models revealed a SMD of -0.14 (95% CI -0.48, 0.20), p=0.43, I²=47%. The Forest plot for the analysis on end-of-intervention data is provided in Figure 3, panel a. Analyses of change-from-baseline data using fixed effect and random effects models (3 studies, 271 participants) revealed a SMD of -0.21 (95% CI -0.45, 0.04), p=0.10, I²=0%. Effects favour FV, but effect sizes are small, and when converted into units on the HADS are equivalent to an improvement in depressive symptomology of 0.4 (-0.1 to 0.9) units on a 21-point scale.

Anxiety-related Symptomology: Three studies^(17,32,33), one with two intervention groups⁽¹⁷⁾, contributed data. Analyses of end-of-intervention data using fixed effect models (4 studies, 298 participants) revealed a SMD of -0.15 (95% CI -0.39, 0.08), p=0.20, I²=71%. Analyses using random effects models revealed a SMD of -0.06 (95% CI -0.51, 0.38), p=0.78, I²=71%. The Forest plot for the analysis on end-of-intervention data is provided in Figure 3, panel b. Analyses of change-from-baseline data using fixed effects models revealed a SMD of -0.10 (95% CI -0.34, 0.13), p=0.40, I²=39%. Analyses using random effects models (4 studies, 298 participants) revealed a SMD of -0.08 (95% CI -0.39, 0.23), p=0.61, I²=39%. Effects favour FV, but effect sizes are small, and when converted into units on the HADS are equivalent to an improvement in anxiety-related symptomology of 0.2 (-1.1 to 1.7) units on a 21-point scale.

DISCUSSION

This review aimed to identify and summarize all published controlled intervention studies that have investigated an effect of FV consumption as a distinct intervention on mental health in adults. Only six studies were found, involving a total of 691 individuals. Studies used a range of FV interventions. Three studies reported on psychological well-being, two reported on depressive symptomology and three studies reported on anxiety-related symptomology. All studies were relevant to our research question, but mental health was a secondary outcome in

some studies and risk of bias in the included studies was high. In only one study was it possible to blind participants⁽³³⁾, in only one study were researchers reported to be blinded⁽³⁸⁾, and in only one study were data analysed on an ITT basis based on number randomized⁽³²⁾. The evidence available to draw conclusions on the impacts of FV consumption on mental health is thus, extremely limited.

Considering all eligible studies, our analyses revealed limited effects of FV consumption on three outcomes related to mental health. Psychological well-being, depressive symptomology and anxiety-related symptomology were all improved by FV consumption, but these effects are not statistically significant and effect sizes are small. Effects are equivalent to a 1- to 4-point improvement on a 100-point scale of psychological well-being, and less than a single point improvement on a 21-point scale of depressive or anxiety-related symptomology. Confidence intervals are also wide, thus the effect estimates are imprecise, ranging from very small negative or null effects to small positive effects. Heterogeneity between studies was low in analyses on psychological well-being, suggesting these effects are consistent across the studies included, but heterogeneity was moderate to substantial in analyses on depressive and anxiety-related symptomology suggesting inconsistency. Measures of heterogeneity can be difficult to interpret where few studies are included in analyses. The low number of studies available also precluded any assessment of possible sources of heterogeneity.

We find some suggestion that effects in psychological well-being and depressive symptomology may be stronger if baseline scores are considered, i.e. in change-from-baseline data. Effect sizes remain small, but may be important at the upper end of our confidence intervals. Importantly, however, no studies were found that were specifically conducted in individuals with poor mental health, high depressive or anxiety-related symptomology, or a depressive or anxiety-related clinical condition. Further investigation in these populations may be of value.

Effects size estimates in psychological well-being were also found to increase if a study with a control group who consumed Vitamin C capsules was removed from the analyses. These findings suggest that the Vitamin C in FV may contribute to the effects of FV consumption on psychological well-being. A similar conclusion is offered by the authors of the primary study⁽³⁷⁾,

with the addition that Vitamin C from whole FV may have a greater impact than that that may be gained from supplements, due to the provision of other biological compounds, such as fibre, folate or potassium, which may also impact psychological well-being⁽³⁷⁾. We were unable to investigate these mechanisms in our analyses due to the few studies available, but studies based on likely mechanisms could be important.

Taken together, our findings suggest small and imprecise effects of FV consumption on all three aspects of mental health, although very few, limited studies and few participants contribute to our review. Our conclusions are comparable with those of other reviews with regard to the limited number of intervention studies currently available, but our conclusions differ from the majority of these reviews⁽⁵⁻¹⁰⁾, from the studies included^(15,17,32,37,38), and from the majority of studies published in this area^(e.g.12,16,18,19,23,49-51), as we find very little evidence to suggest a beneficial effect. Some independent studies also report no association between FV consumption and mental health. For example, Kingsbury et al.⁽²⁴⁾ and Pengpid & Peltzer⁽⁵²⁾ report no associations in longitudinal analyses of cohort studies using multiple measures once confounding factors are controlled, although Pengpid & Peltzer⁽⁵²⁾ do report associations between vegetable consumption and one outcome measure. We were unable to investigate differing effects as a result of fruit versus vegetable consumption^(10,18,52), due to the limited number of studies available.

We were also unable to investigate differing effects as a result of the consumption of specific fruits, vegetables or FV forms^(5,7,17,53,54), the differing outcomes assessed^(17,51,52), or the differing assessment time-frames^(16,17,19,37).

Further study may be desirable to provide more conclusive evidence. This evidence will only be gained from adequately-powered randomized trials using appropriate control conditions and study procedures. Importantly, control conditions must allow the independent and isolated investigation of FV consumption, to consider not only aspects of diet and lifestyle, but also comparable treatment of study participants by study researchers, e.g. through researcher blinding and the use of comparable gift-giving, and the potential deleterious effects of the consumption of other (less healthy) foods^(32,55). Blinding of those making the outcome assessments is also important for subjective outcomes, and while it may not be possible to blind participants to an

increased consumption of FV, it will be possible to blind participants to other study conditions and to study aims. Consideration of study non-completion will also be important where participants may fail to complete studies following both positive and negative experiences⁽⁵⁶⁾. Studies based on potential mechanisms will be of particular value, as will studies involving realistic and sustainable interventions that can be transferred to the public health setting, where outcomes are also assessed over sufficient time frames for meaningful interpretation. Considering our effects in change-from-baseline data, advantages may be gained from the study specifically of those with low mood at baseline or those presenting with clinical conditions. Some advantage may also be gained from a focus on those who are low consumers of $FV^{(15,17,37)}$. Comparison with other dietary components, dietary interventions and other lifestyle interventions may also be of value. Recent meta-analyses of meta-analyses investigating the effects of physical activity on mental health, for example, report convincing beneficial effect size estimates of SMD=-0.50 (95% CI -0.93 to -0.06), I^2 =0%, 92 studies, 4310 participants) for depressive symptomology, and SMD=-0.38 (95% CI -0.66 to -0.11) I^2 =4%, 306 studies, 10,755 participants) for anxiety-related symptomology, in non-clinical populations⁽⁵⁷⁾.

Limitations

Our review is limited by the very small number of studies available, the limited number of participants and the high risk of bias in most domains in many studies. Our searches were confined to articles published in English in full papers, and while we sought to include as many studies as possible, we only included studies that used a distinct FV consumption intervention; we did not look at multi-component interventions that were only effective for changing FV consumption, nor did we look at alternate interventions that may be expected to increase FV consumption, such as vegetable gardening⁽⁵⁸⁾. Consideration of these studies may enhance the evidence base, but confounding must remain a consideration. Our conclusions are limited by the very small number of studies available and the specific nature of these studies. Notably, the studies included in our review were conducted in predominantly female samples, of young age, and from Western populations, thus generalizability to other population groups may be limited. Due to the very small number of studies available in our analyses, we were also unable to investigate possible sources of heterogeneity or confounding.

Conclusions

In conclusion, we found very few controlled intervention studies that investigated the effects of FV consumption on psychological well-being, depressive symptomology and anxiety-related symptomology, and the majority of these studies were considered at high risk of bias on many important criteria. Thus, the evidence available to draw conclusions on the impacts of FV consumption on mental health is extremely limited. Meta-analyses suggest some benefits of FV consumption, but effects sizes are small and imprecise. Given the limited evidence available and the small size of effects, stronger evidence is needed before recommending FV consumption for mental health. Further research to provide more definitive conclusions would be of value.

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Table 1: Methodological details for all included studies

Referenc	N in study	Population – gender,	Intervention	Comparator	Trial	Outcomes
e	(Interventi	age, BMI, clinical			duratio	measured
	on/	status			n	
	Control)					
De Leon	110	73% female; age: 43	Vegetable Intervention – ppts	Attention Control – ppts	8 weeks	Psychological
et al.	(55 / 55)	(15) years; BMI: 35	provided with a variety of	not provided V,	(plus 8	well-being
2022 ^{(15)a}		(7) kg/m ² ; clinical	pre-packaged, minimally	consumed usual diet,	weeks	
		status: NR; low V	prepared fresh or frozen V in	completed the same test	follow-	
		consumers.	Dietary Guidelines for	schedule with the same	up)	
			Americans (DGA)	interaction with research		
			recommended types and	staff as the V group. No		
			amounts. Greater V intake at	change in V intake at		
			end vs baseline, based on	end vs baseline, based on		
			weekly logs and skin	weekly logs and skin		
			carotenoid levels.	carotenoid levels.		
Conner	167	61% female; age:	Ppts supplemented with either	1) Ppts supplemented	4 weeks	Psychological
et al.	(57 /	21.7 (3.5) years;	two Sun Gold kiwifruit per	with chewable vitamin C	(plus 2	well-being,
2020 ^{(37)b}	56/54)	BMI: 23.8 (4.4)	day (~150g containing	tablets (250mg). Good	weeks	Other mood
		kg/m ² ; clinical	~250mg vitamin C). Greater	tablet intake – greater	lead-in	and fatigue /
		status: "not	F intake at end vs baseline,	plasma Vitamin C levels	and 2	vigour

		distressed" based on	based on plasma Vitamin C	at end vs baseline;	weeks	measures
		outcome scores at	levels.	2) Ppts supplemented	follow-	
		baseline/lead-in;		with chewable placebo	up)	
		consuming less than		tablets (no active vitamin		
		5 FV/day; low		C ingredients). No		
		plasma Vitamin C		change in plasma		
		levels.		Vitamin C levels at end		
				vs baseline.		
Chiochet	35	81% female; age: I:	Ppts received a FV juice,	Ppts received an	45 days	Anxiety-
ta et al.	(18 / 17)	31.1 (11.1), C: 30.2	composed of apple, orange,	artificial green beverage	-	related
2018 ⁽³³⁾		(8.5) years; BMI: I:	and green vegetables such as	of powdered gelatin and	weekda	symptomolog
		25.4 (4.1), C: 23.5	lettuce, green cabbage, head	powdered drink mixes,	ys for 9	у,
		(2.9) kg/m ² ; clinical	cabbage, and cucumber,	300ml/day.	weeks	Other
		status: no diseased	300ml/day.	Compliance: NR, but		psychological
		pathology	Compliance: NR, but doses	doses given under		measures
			given under supervision	supervision		
Conner	174 (57/57	67% female; age:	1) Ecological momentary	Control intervention -	14 days	Depressive
et al.	/ 60)	19.4 (1.5) years,	intervention (EMI) - ppts sent	ppts given a 14-piece		symptomolog
2017 ^{(17)c}		BMI: 24.1 (3.9);	twice daily text-messages	packet of sugar-free		y, Anxiety-
		kg/m ² , clinical	using behavioural change	chewing gum, and asked		related
		status: not taking	techniques to increase FV	to consume one piece a		symptomolog
		anti-depressant	consumption, and given \$10	day, and provided with a		y, Other

		medication; low FV	voucher for a local	\$10 voucher for a local		mood and
		consumers	greengrocer to purchase FV;	greengrocer. No change		vitality
			2) FV intervention (FVI) –	in FV intake vs baseline		measures
			ppts given two weeks' worth	based on self-report,		
			of FV, and asked to consume	plasma Vitamin C and		
			at least 1 F and 1 V daily on	carotenoid levels.		
			top of their regular FV			
			consumption. Greater FV			
			intake vs baseline for both			
			interventions based on self-			
			report, and plasma Vitamin C			
			and carotenoid levels.			
Smith &	100	73% female, age: 19	Fruit condition - ppts given	Chocolate/crisps	10 days	Depressive
Rogers,	(50 / 50)	(0.79) years; BMI:	10 pieces of F and told to	condition – ppts given		symptomolog
2014 ⁽³²⁾		NR; clinical status:	consume 1 piece each	10 snacks (crisps and		y, Anxiety-
		NR	afternoon for 10 days.	chocolate wafers), and		related
			Compliance – NR	told to consume 1 each		symptomolog
				afternoon for 10 days.		y, Fatigue-
				Compliance – NR		related
						symptoms
Plaisted	105 (NR /	36% female; age: I:	FV Diet – ppts provided	Control Diet - reflected	8 weeks	Quality of
et al.	NR (NR))	47.8 (10.9), C: 44.7	additional servings of FV but	typical American dietary	(after a	life, including

1999 ^{(38)d}	(11.2); BMI: 29%	otherwise was similar to the	intake. Compliance –	3 week	mental health
	obese; clinical	control diet. Compliance –	reported as excellent,	lead-in)	subscale
	status: NR.	reported as excellent, based	based on self-report and		
		on self-report and urinary	urinary markers. The		
		markers.	study also included a		
			Combination Diet group		
			(not considered further		
			here)		

Data provided as means (and standard deviations). BMI: Body Mass Index; C: comparator; F: fruit; FV: fruit and vegetables; I:

intervention; NR: not reported; Ppts: participants; V: vegetable

^aAdditional detail gained from Casperson et al. 2021⁽³⁹⁾

^bAdditional detail gained from Conner et al. 2022⁽⁴²⁾

^cAdditional detail gained from Brookie et al. 2017⁽⁴⁰⁾

^dAdditional detail gained from Appel et al. 1997⁽⁴¹⁾

Table 2: Findings for all included studies

Referenc e	Outcome	Measure	N in analyse s (Inter- vention / Control)	I – base- line	I – end ^a	I – chang e	C – base -line	C – end ^a	C – chang e	Authors Conclusions
De Leon et al. 2022 ^{(15)b}	Psycho- logical well- being	Subjective Happiness Scale ⁽⁴³⁾ , scored 1- 7.	75 of 110 (37 / 38)	5.1 (1.1)	5.4 (1.0)	0.23 (0.67) c	5.3 (1.4)	5.1 (1.3)	-0.15 (0.67) c	Greater mean subjective happiness scores were observed after increasing V consumption to meet DGA recommendations in low V consumers with overweight or obesity. Adhering to DGA V guidance may help promote psychological well-being.
Conner et al. 2020 ^{(37)d}	Psycho- logical well- being	Warwick– Edinburgh Mental Well- being Scale ⁽⁴⁴⁾ , scored 14- 70.	159 of 167 (55 / 52/52)	48.04 (9.31)	50.55 (8.88)	2.4 (7.0) ^e	1: 48.5 6 (9.6 4) 2: 49.0 (7.9 0)	1: 51.06 (10.73) 2: 49.17 (7.50)	1: 1.8 (7.8) ^e 2: 0.2 (6.6) ^e	Improvements in mood and well-being in the group consuming F, whereas improvements in fatigue and well-being were found in the group consuming vitamin C, but only if they had low baseline levels of vitamin C. No changes in any outcomes in the placebo group.
Chiochet ta et al. 2018 ⁽³³⁾	Anxiety- related symptom ology	Beck Anxiety Inventory ⁽ ⁴⁸⁾ ,	27 of 35 (14 / 13)	7.86 (4.22)	9.07 (6.33)	NR 1.21 (5.28) ^f	4.64 (2.7 3)	5.27 (4.29)	NR 0.63 (3.51) ^f	We suggest that green juice did not cause an improvement in metabolic function or quality of life, and there is a need for

		Scoring NR; standard scoring 0- 63.								further research on this issue.
Conner et al. 2017 ^{(17)g}	Depressi ve symptom ology	Centre for Epidemiol ogical Studies Depressio n Scale ⁽⁴⁷⁾ , scored 0- 60	171 of 174 (55/57 / 59)	1: 13.73 (9.01) ; 2: 14.70 (7.06)	1: 13.07 (8.37) ; 2: 13.25 (7.65)	1: 0.66 (8.38) ^h ; 2. 1.46 (5.36) ^h ;	14.4 4 (9.8 2)	12.78 (10.07)	1.66 (6.14)	Providing young adults with high-quality FV (FVI), rather than reminding them to eat more FV with a voucher to purchase FV (EMI), resulted in significant short-term improvements to their psychological well-being.
	Anxiety- related symptom ology	Hospital Anxiety and Depressio n Scale ⁽⁴⁶⁾ , scored 0- 21	171 of 174 (55/57 / 59)	1: 5.40 (3.17) 2: 6.25 (3.5)	1: 4.80 (3.02) 2: 5.84 (3.29)	1: 0.60 (3.26) h 2. 0.40 (3.17) h	5.68 (3.6 6)	5.44 (3.54)	0.24 (2.30) h	
Smith & Rogers, 2014 ⁽³²⁾ⁱ	Depressi ve symptom ology	Hospital Anxiety and Depressio n Scale ⁽⁴⁶⁾ , scored 0- 21	100 (50 / 50)	NR (NR)	2.40 (1.77)	-0.5% (NR)	NR (NR)	3.32 (1.77)	46.6% (NR)	The consumption of fruit was associated with lower anxiety, depression and emotional distress than consumption of crisps/chocolate.
	Anxiety- related symptom	Hospital Anxiety and	100 (50 / 50)	NR (NR)	5.46 (2.33)	- 31.8% (NR)	NR (NR)	6.77 (2.33)	- 18.5% (NR)	

	ology	Depressio n Scale ⁽⁴⁶⁾ , scored 0- 21								
Plaisted et al. 1999 ^{(38)j}	Quality of Life	SF-36 ⁽⁴⁵⁾ - whole scale, scored 0- 100	83 of 105 (26 / 29 / (28))	NR (NR)	NR (NR)	5% (10%)	NR (NR)	NR (NR)	4% (23%)	These data suggest that the FV diet can not only lower blood pressure, but may also improve the perception of health-related quality of life.
	Mental well- being	SF-36 ⁽⁴⁵⁾ - mental health subscale, scored 0- 100	83 of 105 (26 / 29 / (28))	78.7 (15.0)	82.7 (10.8)	3.9 (10.2)	82.2 (15. 0)	84.7 (11.9)	2.5 (11.5)	

Data provided as means (and standard deviations). C: comparator; DGA: Dietary Guidelines for Americans; F: fruit; FV: fruit and vegetables; I: intervention; NR: not reported; V: vegetables

^aAll end assessments made at end of intervention.

^bAdditional detail gained from Casperson et al. 2021⁽³⁹⁾

^cDe Leon et al. 2022⁽¹⁵⁾: Standard deviations for change were calculated from published standard errors.

^dAdditional detail gained from Conner et al. 2022⁽⁴²⁾

^eConner et al. 2020⁽³⁷⁾: Means and standard deviations for change were gained from Conner et al. 2022⁽⁴¹⁾.

^fChiochetta et al. 2018⁽³³⁾: Means and standard deviations for change were calculated based on reported means, and estimated from mean standard deviations.

^gAdditional detail gained from Brookie et al. 2017⁽⁴⁰⁾

^hConner et al. 2017⁽¹⁷⁾: Standard deviations for change were calculated from published confidence intervals.

ⁱSmith & Rogers, 2014⁽³²⁾: Published data are adjusted means and standard errors for baseline and end, and percentage change from baseline. Unadjusted means and standard deviations for analyses were gained from authors.

^jAdditional detail gained from Appel et al. 1997⁽⁴¹⁾

Table 3: Risk of bias in all included studies

Reference Authors, date	Randomizati on and are groups well matched	Allocatio n conceale d	Blinding – participant s	Blinding – researcher s	ITT based on random	% sample with incomplet e data	Outcomes reported – all mental health, all	Other
De Leon et al. $2022^{(15)a}$	Low and Unclear	Unclear	Not possible	Researche rs - High Analysts – Low	-ization High	32% - High	others Low, Low	Psychological well- being measure not implemented until after the trial start
Conner et al. $2020^{(37)b}$	High and High	Unclear	Not possible	High	High	5% - Low	Low, Low	
Chiochetta et al. 2018 ⁽³³⁾	Unclear and Low	Unclear	Low	High	High	23% - High	Low, Low	
Conner et al. $2017^{(17)c}$	Low and Low	Unclear	Not possible	Unclear	High	2% - Low	Low, Low	
Smith & Rogers, 2014 ⁽³²⁾	Low and Low	Unclear	Not possible	Unclear	Low	0% - Low	Low, Low	
Plaisted et al. 1999 ^{(38)d}	Unclear and High	Unclear	Not possible	Low	High	21% - High	Low, Low	

ITT: Intention-to-Treat

^aAdditional detail gained from Casperson et al. 2021⁽³⁹⁾

^bAdditional detail gained from Conner et al. 2022⁽⁴²⁾

^cAdditional detail gained from Brookie et al. 2017⁽⁴⁰⁾

^dAdditional detail gained from Appel et al. 1997⁽⁴¹⁾

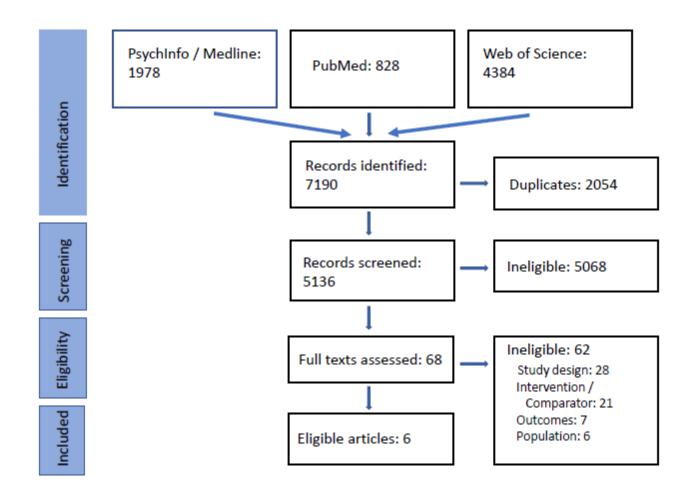


Figure 1: PRISMA Flow Diagram

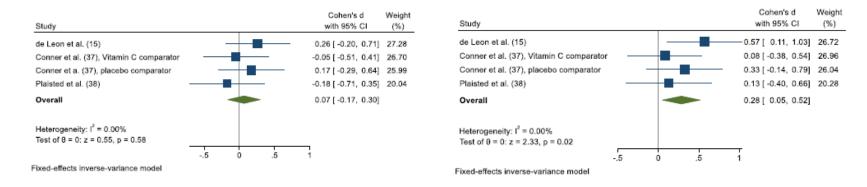


Figure 2: Forest plots for meta-analyses on Psychological Well-being, fixed effect models; panel a: end-of-intervention data, panel b: change-from baseline data. Each Forest plot demonstrates effects in individual studies (effect size, 95% confidence intervals, and % contribution of the study to the overall result), while the standardized mean difference (SMD) and 95% CI for all studies combined is represented by the diamond at the base. Effects to the right of the null line represent better psychological health.

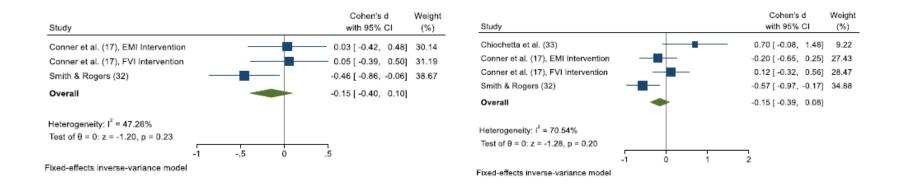


Figure 3: Forest plots for meta-analyses, fixed effect models on end-of-intervention data; panel a: Depressive Symptomology, panel b: Anxiety-related Symptomology. Plots demonstrate effects in individual studies (effect size, 95% confidence intervals, and % contribution of the study to the overall result), while the standardized mean difference (SMD) and 95% CI for all studies combined is represented by the diamond at the base. Effects to the right of the null line represent greater symptomology, so poorer mental health.