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Research paper

Associations between fruit and vegetable intakes and incident depression in middle-aged and older adults from 10 diverse international longitudinal cohorts

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ABSTRACT

Background: Emerging observational evidence supports a role for higher fruit and vegetable intake in protecting against the development of depression. However, there is a scarcity of research in older adults or in low- to middle-income countries (LMICs).
Methods: Participants were 7801 community-based adults (mean age 68.6 ± 8.0 years, 55.8 % female) without depression, from 10 diverse cohorts, including four cohorts from LMICs. Fruit and vegetable intake was self-reported via comprehensive food frequency questionnaire, short food questionnaire or diet history. Depressive symptoms were assessed using validated measures, and depression defined applying validated cut-offs. The associations between baseline fruit and vegetable intakes and incident depression over a follow-up period of three to nine years were examined using Cox regression. Analyses were performed by cohort with results meta-analysed.
Results: There were 1630 cases of incident depression (21 % of participants) over 40,258 person-years of follow-up. Higher intake of fruit was associated with a lower risk of incident depression (HR 0.87, 95%CI [0.77, 0.99], $I^2 = 4$ %). No association was found between vegetable intake and incident depression (HR 0.93, 95%CI [0.84, 1.04], $I^2 = 0$ %).
Limitations: Diverse measures used across the different cohorts and the modest sample size of our study compared with prior studies may have prevented an association being detected for vegetable intake.
Conclusions: Our study supports a role for fruit, but not vegetable intake in protecting against depression. Research investigating different types of fruits and vegetables using standardised measures in larger cohorts of older adults from low- and middle-income countries is warranted.

Abbreviations

COSMIC	Cohort Studies of Memory in an International Consortium
CI	confidence intervals
BMI	body mass index
BPRHS	Boston Puerto Rican Health Study
CVD	cardiovascular disease
EPIDEMCA	Epidemiology of Dementia in Central Africa
EpiFloripa	EpiFloripa Aging Cohort Study
H70-study	Gothenburg H70 Birth cohort studies
HELIAD	Hellenic Longitudinal Investigation of Aging and Diet
HR	Hazard ratio
ISA	Ibadan Study of Aging
LRGS TUA	Long-term Research Grant Scheme -Towards Useful Ageing
MMSE	Mini-Mental State Examination
SLASII	Singapore Longitudinal Aging Study II
MAS	Sydney Memory & Aging Study
PATH	Personality and Total Health Through Life Project 60+ cohort
STROBE	Strengthening the Reporting of Observational Studies in Epidemiology

1. Introduction

Depression is a major public health concern. The global impact of depressive disorders is estimated to be >50 million years lived with disability, making depression the largest contributor to non-fatal burden of disease (World Health Organisation, 2017). More than 80 % of this burden is accounted for by low- and middle-income countries (LMICs) (World Health Organisation, 2017). Estimates of global prevalence of depression in older adults differ widely depending on the population considered and definition of depression used (Beekman et al., 1999). A recently published systematic review and meta-analysis reported an average prevalence of 32 %, with higher prevalence in developing than developed countries (41 % versus 17 %; Zenebe et al., 2021). Compared with depression in younger adults, depression in older adults has a greater impact on physical performance and cognition and is associated with lower quality of life and higher all-cause mortality (Blazer, 2003; Park and Kim, 2018).

A growing body of evidence suggests that dietary behaviours, such as higher fruit and vegetable intake, may be important in reducing the risk of depression (Lassale et al., 2019; Liu et al., 2016; Saghafian et al., 2018). Our earlier systematic review and meta-analysis found four studies examining the associations between fruit and vegetable intake and incident depression in adults aged 45-years and older. The results of these studies were synthesised by meta-analyses, with higher fruit intake associated with a 15 % decreased odds of incident depression and higher vegetable intake associated with a 9 % decrease odds of incident depression (when comparing the highest with the lowest category of consumption) (Matison et al., 2021). However, only a small number of studies have been published, and these were restricted to a limited number of high-income countries (HICs). Evidence of the association between fruit and vegetable intake and depression is lacking in LMICs where dietary patterns (Yusuf et al., 2020) and depression rates (Zenebe et al., 2021) vary from HICs.

The aim of this study was to prospectively examine the associations between baseline fruit and vegetable intake and incidence of depression in adults aged 45-years and older from 10 cohorts across six continents, including participants from four LMICs. We hypothesised that higher baseline intakes of fruit and vegetables would be associated with a lower incidence of depression over the follow-up period.

2. Methods

2.1. Contributing cohorts

Data were collected and harmonised from 10 longitudinal, community-based cohorts. All cohorts were members of the Cohort Studies of Memory in an International Consortium (COSMIC) collaboration (Sachdev et al., 2013). Details of the contributing studies are contained in Table 1. Cohorts were from six different continents (Africa, Asia, Australia, North America, South America and Europe). Cohorts were eligible for inclusion in the current study if they had i) baseline dietary data which could be used to construct servings per day of both fruit and vegetables, ii) baseline depression data and iii) at least one follow-up depression assessment. The number of assessment waves used for each cohort was selected to ensure that the follow-up periods by cohort were comparable. We excluded participants 1) with depression at baseline, 2) no baseline depression data or baseline fruit and vegetable intake data, or 3) no follow-up depression data.

The current study was approved by the University of New South Wales Human Research Ethics Committee (HC 12446, HC 17292 and HC220222) and each individual cohort study was approved by the relevant institutional review board. This study is reported in accord with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines. All participants provided informed consent. All research was conducted in accordance with the guidelines set out in the Declaration of Helsinki.

2.2. Measurements

2.2.1. Fruit and vegetable intake

Fruit and vegetable intake was self-reported at baseline. A variety of dietary assessment methods were used and are detailed in Supplementary Tables S1 for fruit and S2 for vegetables, together with the methods used to harmonise intakes into serves per day. Briefly, four of the studies used comprehensive food frequency questionnaires (FFQs) designed to collect data on all foods consumed, four studies used short questionnaires designed to collect data on specific foods (including fruit and vegetables) and two studies used a diet history to capture all foods eaten. The four comprehensive FFQs collected data on between five and 27 fruit items, and seven to 26 vegetable items. The short questionnaires generally contained one fruit and one vegetable question. Questionnaires were tailored to the population being assessed and included fruit and vegetables commonly consumed by that population. Where fruit juice intake was separately collected it was not included in the total serves of fruit consumed as the percentage fruit juice and whether the juice contained added sugar was not consistently available. For vegetables, potato consumption was generally separately collected, particularly in countries with high potato intake. For the main analysis, potato consumption was not included in total serves of vegetables as the type of potato (e.g. potato mash, potato chips, crisps) were not available. Sensitivity analysis was performed including potatoes within vegetable intake, acknowledging their potential health benefits contingent on method of preparation.

Daily intake data were dichotomised into two categories for both fruit and vegetable intake. Categories were 0–1/serves per day and > 1/serves per day for fruit and 0–1.5/serves per day and > 1.5/serves per day for vegetables. Categories were used consistently across all cohorts. Intakes were analysed as categorical variables to enable comparison with existing studies (a review of the literature found that this was the most commonly used method; Matison et al., 2021) and as four studies used short diet questionnaires, which are more suitable for differentiating between high and low consumers, rather than determining absolute intakes (Perez Rodrigo et al., 2015). The previous studies in this area used either a variety of cut-offs or quintiles. We were unable to use quintiles (or any form of quantile) due to the distribution of intake data. For example, dividing participants into quintiles resulted in participants consuming one fruit serve/day being split into two different quintiles in several of the cohorts. We therefore selected cut-offs using a similar basis as previously used, while maintaining statistical power in each cohort.

2.2.2. Incidence of depression

Depressive symptoms were assessed at baseline and follow-up for all cohorts using validated depression measures. Depression was defined as a depressive symptom score greater than or equal to a cut-off validated for the depression tool used. Details of depression assessment methods and cut-offs to harmonise depression data into depression present/absent are in Supplementary Table S3.

2.2.3. Covariates

All studies collected baseline data on participant age, sex, education (years), marital status, body mass index (BMI), history of cardiovascular

Table 1
Details of contributing studies.

Cohort	Abbreviation	Location	Start date	Number of assessment waves used	Follow-up period (years)	*n*
Boston Puerto Rican Health Study (Tucker, 2005)	BPRHS	Boston, USA	2004	3	6	490
Epidemiology of Dementia in Central Africa (Guerchet et al., 2014)	EPIDEMCA	Republic of Congo	2011	4	3	433
EpiFloripa Aging Cohort Study (Schneider et al., 2017)	EpiFloripa	Florianópolis, Brazil	2009	3	8	790
Gothenburg H70 Birth cohort studies (Wetterberg et al., 2022)	H70-study	Gothenburg, Sweden	2000	3	9	375
Hellenic Longitudinal Investigation of Aging and Diet (Dardiotis et al., 2014)	HELIAD	Larissa and Marousi, Greece	2011	2	3	728
Ibadan Study of Aging (Gureje et al., 2007)	ISA	Nigeria	2003	4	6	933
Long-term Research Grant Scheme - Towards Useful Aging (Shahar et al., 2016)	LRGS TUA	Malaysia	2012	4	5	396
Sydney Memory & Aging Study (Sachdev et al., 2010)	MAS	Sydney, Australia	2005	4	6	778
Personality and Total Health Through Life Project 60+ cohort (Anstey et al., 2012)	PATH	Canberra, Australia	2001	3	8	1469
Singapore Longitudinal Aging Study II (Feng et al., 2013)	SLASII	Singapore	2009	2	4	1409

disease (CVD), presence of hypertension, presence of diabetes and physical activity. Cognition was measured in nine studies, via the Mini-Mental State Examination (MMSE), and used as a continuous variable (Folstein et al., 1975). Energy intake was not included as a covariate as four of the 10 studies did not collect total energy intake data. Harmonisation protocols were established for all covariates to enable comparability across studies. For example, some studies collected education data as continuous number of years, while others collected categorical data (e.g. primary, secondary, tertiary). In cases where categorical data were used, it was converted to the number of years based on the duration required to complete each category of education. For the absence/presence of health conditions, all relevant diagnostic data were utilised. Details of covariate assessment methods, definitions and full details of harmonisation protocols are in Supplementary Tables S4-S10.

2.3. Statistical analysis

Participant characteristics are presented as mean and standard deviation (SD) for continuous data or percentage for categorical data. Continuous data were assessed for normality using skewness and kurtosis statistics, together with visual inspections of histograms.

Missing data were assessed by cohort for all covariates and were generally <1 %. Missing covariate data were imputed by cohort using multiple imputation (20 imputations) with all provided available covariate data as predictors. Data after imputation were checked against original data using summary statistics (mean, minimum, maximum and quartiles for continuous variables and percentage for categorical variables). The mice package version 3.15.0 in R was used to perform the imputation (van Buuren and Groothuis-Oudshoorn, 2011).

Data were analysed for extreme values using box plots and, where necessary, winsorisation was performed to limit the impact of potential outliers. Details of the winsorisation are in Supplementary Table S11.

The associations between baseline fruit and vegetable intakes and incident depression were analysed using Cox proportional hazard regression models, with the lower category of intake used as reference. Hazard ratios (HR) and 95 % confidence intervals (CI) were calculated. Time to event was calculated as the time between baseline and either the first incidence of depression or, for participants without an incidence of depression, the time between baseline and the last completed depression assessment. Proportional hazards assumptions were checked and where non-proportional hazards existed for covariates, time-dependent covariates were used (Zeng et al., 2022). Models were also tested to ensure linearity between the log-hazard and covariates and that there were no outlier observations influencing the models.

Confounders were selected based on their likely relationship with fruit and vegetable intake and depression as identified in the literature. Directed acyclic graphs (DAGs) (Textor et al., 2016) were used to help determine which potential confounders should be adjusted based on the likely direction of their associations with exposure and outcome (Supplementary Fig. S1). The partially adjusted model adjusted for age, sex, education and marital status. To ensure the robustness of the results, the fully adjusted model additionally adjusted for BMI, physical activity, history of CVD, presence of diabetes and presence of hypertension. As MMSE data were only available in nine cohorts, cognition was not included as a covariate in the fully adjusted model. However, in sensitivity analysis MMSE continuous score was added to the fully adjusted model and analysis restricted to the nine cohorts with MMSE data.

Cox proportional hazards regression was performed by cohort and then the results were combined using a random-effects meta-analysis model. Heterogeneity between studies was assessed using I^2. Subgroup analysis was performed by sex (female versus male), age (45–64 years versus 65+ years) and country income level (HICs vs LMICs). The World Bank's classification was used to assign countries to income groups (World Bank Organisation, 2023).

Three sensitivity analyses were performed to assess the robustness of our results. Firstly, potato consumption was included in vegetable intake. Secondly, inverse probability weightings were used in the fully adjusted model to adjust for attrition (e.g. older and less educated participants were upweighted). Weightings were calculated by cohort based on each participant's covariate data. Weightings were performed in the WeightIt package version 0.13.1 in R using the "ps" weighting method (Greifer, 2022). Thirdly, MMSE as a continuous variable was added as a covariate to the fully adjusted model and analysis run based on the nine cohorts where data were available. Post hoc sensitivity analysis was performed to further examine the result from sensitivity analysis three. The one cohort without MMSE data was removed from the main analysis to isolate the impact of removing this cohort, from the impact of including MMSE as a covariate.

3. Results

The total number of individuals across the 10 cohorts was 18,884. Of these, 3686 were excluded for having probable depression at baseline. A further 3706 were excluded due to missing baseline fruit or vegetable intake and 3691 did not have follow-up depression data, resulting in a final sample size of 7801.

Baseline characteristics of participants by category of fruit and vegetable intake are presented in Table 2. The mean baseline age of participants was 68.6 ± 8.0 years and 55.8 % were female. Mean fruit intake was 1.7 ± 1.5 serves/day and mean vegetable intake was 2.0 ± 1.4 serves/day. Details of fruit and vegetable intakes and covariates by cohort are in Supplementary Tables S12 and S13. The breakdown of participants by category of fruit and vegetable intake from each cohort are included in Supplementary Table S14.

A comparison of included participants and participants lost to follow-up revealed significant differences in covariate data (Supplementary Table S15). Participants lost to follow-up were generally older, less educated, less physically active and less physically and cognitively healthy than included participants.

3.1. Fruit and vegetable intake and incidence of depression

There were 1630 incident cases of depression during follow-up (range 3–9 years) over 40,258 person-years, representing 21 % of participants. For fruit, incidence of depression was 26 % in the lower

Table 2
Baseline characteristic of participants by category of fruit and vegetable intake.

	Fruit		Vegetables		
Serves/day category (range)	0–1	> 1	0–1.5	> 1.5	Total
Serves/day mean (SD)	0.6 (0.4)	2.5 (1.4)	0.9 (0.4)	2.8 (1.4)	
n	3270	4531	3171	4630	7801
Age, years (SD)	68.3 (8.0)	68.8 (8.0)	70.8 (8.3)	67.1 (7.4)	68.6 (8.0)
Education, years (SD)	7.4 (5.4)	9.7 (5.6)	7.1 (5.5)	9.9 (5.4)	8.8 (5.6)
BMI, kg/m^2 (SD)	25.5 (5.1)	26.5 (5.2)	25.7 (5.3)	26.4 (5.2)	26.1 (5.2)
MMSE score (SD)	26.7 (3.8)	28.1 (2.5)	26.6 (3.8)	28.0 (2.7)	27.5 (3.2)
Female (%)	53.9 %	57.2 %	53.3 %	57.6 %	55.8 %
Married (%)	61.8 %	65.4 %	56.6 %	68.9 %	63.9 %
CVD history (%)	14.2 %	20.5 %	17.9 %	17.9 %	17.9 %
Hypertension (%)	60.7 %	55.5 %	56.2 %	58.7 %	57.7 %
Diabetes (%)	14.9 %	12.5 %	14.6 %	12.8 %	13.5 %
Low physical activity (%)	28.1 %	23.9 %	26.3 %	25.2 %	25.6 %

SD – standard deviation; BMI – body mass index; CVD – cardiovascular disease, MMSE – Mini-Mental State Examination.

category of intake and 17 % in the higher category. For vegetables, incidence was 30 % in the lower category and 15 % in the higher category. Across all cohorts, in the partially adjusted model, there was a lower risk of incident depression when comparing participants in the higher category of fruit intake with participants in the lower category (HR 0.87, 95%CI [0.77, 0.99]). There was no association between vegetable intake and risk of depression (HR 0.93, 95%CI [0.84, 1.04]). Heterogeneity between studies was low (fruit $I^2 = 5$ %, vegetables $I^2 = 0$ %) (Supplementary Fig. S2). Similar results were found using the fully adjusted model (fruit HR 0.87, 95%CI [0.77, 0.99], $I^2 = 4$ %; vegetables HR 0.93, 95%CI [0.84, 1.04], $I^2 = 0$ %) (Fig. 1).

3.2. Subgroup analysis

Subgroup analyses by sex using the fully adjusted model did not detect an association between fruit and vegetable intake and incident depression for either females (fruit: HR 0.88, 95%CI [0.73, 1.06], $I^2 = 9$ %; vegetables: HR 0.88, 95%CI [0.75, 1.02], $I^2 = 0$ %) or males (fruit: HR 0.86, 95%CI [0.71, 1.04], $I^2 = 0$ %; vegetables: HR 1.05, 95%CI [0.84, 1.31], $I^2 = 30$ %) (Supplementary Figs. S3-S4). Subgroup analysis by age only detected a relationship between fruit and incident depression in participants aged 65+ years (fruit: HR 0.85, 95%CI [0.73, 0.99], $I^2 = 7$ %; vegetables: HR 0.96, 95%CI [0.85, 1.09], $I^2 = 0$ %) and not for

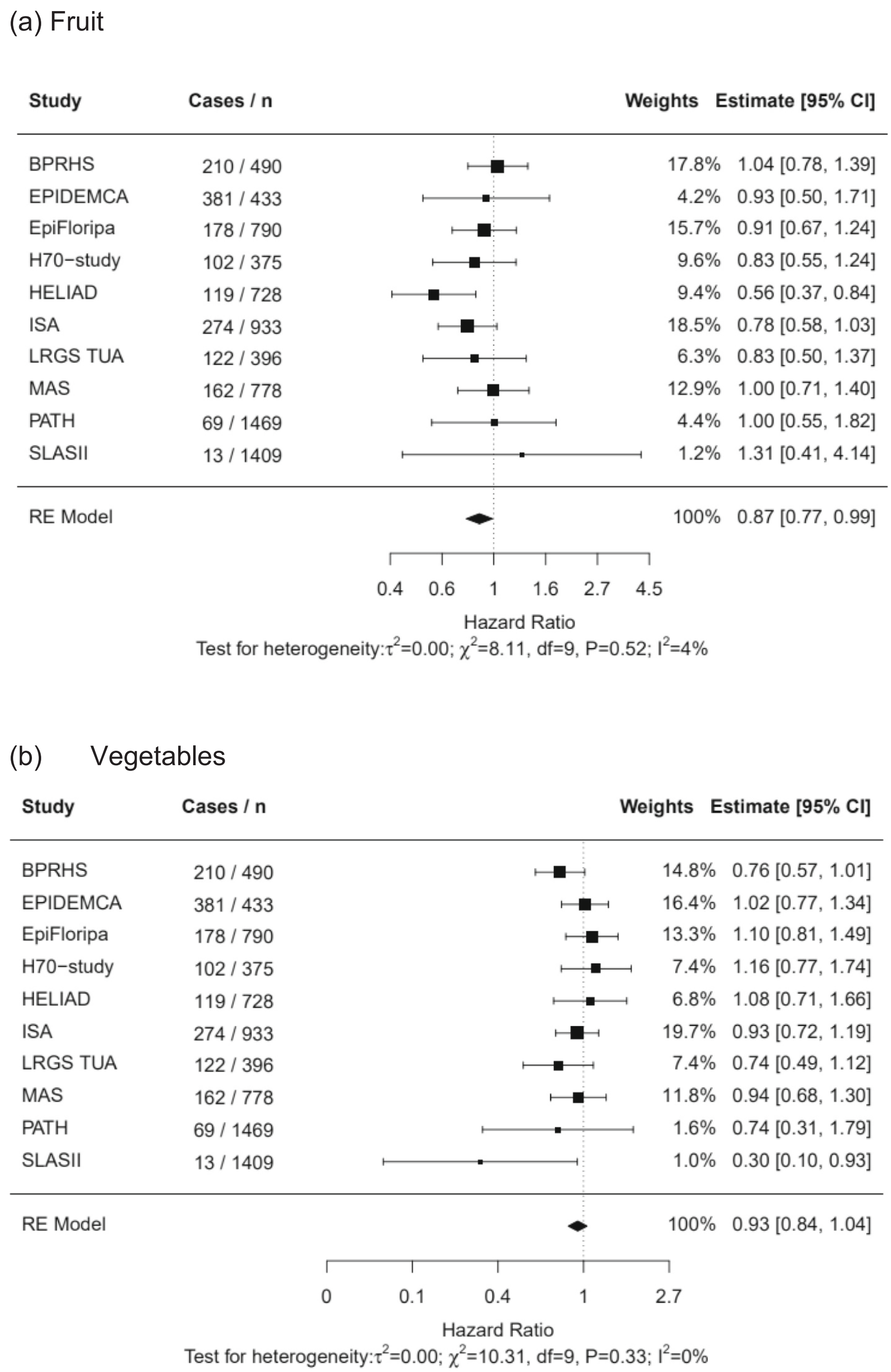

Fig. 1. Fully-adjusted model – Hazard ratio for the association between (a) fruit and (b) vegetable intake and incident depression. Model adjusted for age, sex, education, marital status, body mass index, cardiovascular disease, diabetes, hypertension and physical activity.

those aged 45–64 years (fruit: HR 0.93, 95%CI [0.70, 1.24], $I^2 = 11$ %; vegetables: HR 0.83, 95%CI [0.64, 1.08], $I^2 = 0$ %) (Supplementary Figs. S5-S6). Subgroup analysis by income level of country found no relationship between either fruit or vegetables and incident depression in either HICs or LMICs (fruit: HIC HR 0.88, 95%CI [0.71, 1.10], $I^2 = 36$ %, LMIC HR 0.84, 95%CI [0.70, 1.01], $I^2 = 0$ %; vegetables: HIC HR 0.90, 95%CI [0.74, 1.08], $I^2 = 12$ %, LMIC HR 0.96, 95%CI [0.83, 1.12], $I^2 = 0$ %) (Supplementary Figs. S7-S8).

3.3. Sensitivity analysis

In sensitivity analysis, results were unchanged when potatoes were included in vegetable intake and when inverse probability weighting was used to adjust for attrition. The result for fruit was not significant when the study without MMSE data was removed from the main model, and when MMSE continuous scores were added to this model, there was a marginal effect on the overall fruit result. Results including MMSE as a covariate were unchanged for vegetable intake. Refer to Supplementary Fig. S9 for results including potatoes in vegetable intake, Fig. S10 for results weighted using inverse probability weighting and Figs. S11 and S12 for the model with MMSE scores as an additional covariate.

4. Discussion

This study of adults aged 45-years and older from 10 diverse international cohorts revealed a beneficial association between higher fruit intake and lower risk of incident depression over up to nine years, but no association for vegetable intake. Subgroup analysis showed these results to apply only to adults 65+ years. No associations were found with separate analyses for males and females, or for HICs and LMICs.

This study's finding of a protective association between fruit intake and risk of depression is consistent with our published systematic review and meta-analysis of four longitudinal observational studies in middle aged and older adults. Moreover, the effect size and heterogeneity are similar, with the current study reporting a HR of 0.89 and I^2 of 4 % and the meta-analysis showing an OR of 0.85 and I^2 of 0 % (Matison et al., 2021). The low heterogeneity suggests the result is robust across studies. Additionally, a recently published study of adults aged 65+ from the HELIAD cohort (one of the cohorts used in our analysis) found a beneficial relationship between the Mediterranean diet and lower risk of depression (Mamalaki et al., 2023); they also found a beneficial relationship with depression specifically for fruit but not vegetables.

Our finding of no association between vegetable intake and incident depression contrasts with the results of our previous systematic review and meta-analysis (Matison et al., 2021). There was no overlap in the cohorts used, and the sample size of 176,659 was much larger in the previous study. However, only two of the four studies analysed previously reported beneficial associations between higher intakes of vegetables and incident depression, and both studies were of large female-only cohorts (Gangwisch et al., 2015; Shang et al., 2020). Depression rates are generally higher in females (Zenebe et al., 2021), and previous work suggests that a healthy diet may play a more beneficial role in depression in females than in males (Firth et al., 2019). Our subgroup analysis in the current study, however, found no association in either females or males.

It is difficult to draw firm conclusions based on results from our subgroup analysis by age, sex and income level of country as results may be impacted by loss of power. For instance, although no associations were detected in adults 45–64 years, only 35 % of participants were in this age range and five cohorts had no participants younger than 65-years. Similarly, only 33 % of participants were from LMICs potentially contributing to the lack of significance in this subgroup. However, the result for fruit intake in LMICs is suggestive of a beneficial association (HR 0.84, 95%CI [0.70, 1.01]). Consistent with previous estimates (Zenebe et al., 2021), the incidence of depression was notably higher in LMICs than in HICs (37 % and 13 % respectively) and therefore a reduced risk of depression would translate to a greater reduction in cases than in HICs. There may; however, be cost considerations in increasing intakes, as although a diet high in fruits and vegetables appears to be affordable in HICs, this appears not to be the case in many LMICs (Hirvonen et al., 2020). Future research focusing on participants from LMICs is warranted.

Results of sensitivity analysis, which included potatoes in vegetable intake, MMSE scores as a covariate or accounted for attrition, were broadly in line with the main analysis. While the inclusion of MMSE scores as a covariate had little effect on the overall results, the exclusion of the cohort that lacked these data resulted in the fruit association no longer being significant. As the upper end of the confidence interval is close to 1, a small change could lead to the overall result no longer being significant. The observed variability in MMSE scores among cohorts was notably high. This variability could potentially influence the robustness of the reported associations. It is possible that if MMSE data were available for this study the overall result may not be significant, however including MMSE as a covariate had little impact on results across the other cohorts.

It has been suggested that the high levels of antioxidants, dietary fibre and vitamins contained in fruit and vegetables may exert a beneficial influence on depression through numerous mechanisms such as their role in inflammation, oxidative stress and the gut microbiota (Marx et al., 2021). Our results are supported by evidence of an association between higher fruit, but not vegetable intake and greater grey matter volumes in areas of the brain important to depression (Gaudio et al., 2023). The reason we found a beneficial relationship for fruit, but not vegetable intake, may be that vegetables are typically consumed cooked, which may impact their nutrient content, whereas fruit is generally consumed raw (Moore et al., 2016). As fruits and vegetables contain varying nutrients, it also seems likely that different types of fruit and vegetables may have differing impacts on the risk of depression. The evidence for citrus fruits and green leafy vegetables being associated with lower risk of depression is particularly strong (Baharzadeh et al., 2018; Mamplekou et al., 2010). Moreover, the types of fruit and vegetables consumed vary between countries based on local availability, cost and preferences. This has the potential to modify the relationship between intakes and depression in differing countries. Future research should consider the types of fruit and vegetables consumed to better understand the relationships involved and studies should be designed to provide more comparability across cohorts.

Our study has a number of strengths. To our knowledge, it is the first to include middle-aged and older adults from LMICs in a longitudinal analysis of the association between fruit and vegetable intake and depression. Previous studies have focused on HICs, where dietary intakes and rates of depression differ from developing countries. Additionally, by using harmonised data in the current study, we were able to control for the same covariates and standardise the categories of fruit and vegetable intakes across all cohorts, which has been a limitation of previous meta-analyses.

There are limitations to our study. The modest sample size, compared with prior studies in the literature, may have prevented the detection of an association between vegetable intake and incident depression, as has been reported in previous studies. Previous studies have used up to five categories (Gangwisch et al., 2015) and compared intakes in the highest versus lowest of the five categories. In harmonising cohorts with a wide variation of intakes, we chose to use only two categories of intake to increase the number of participants per category. These categories may not have been optimal for detecting associations in the individual cohorts. Another limitation of the current study is the low overall fruit and vegetable intake. Global dietary recommendations generally suggest a combined intake of fruit and vegetables of at least 5 serves/day (Herforth et al., 2019). Total mean fruit and vegetable intake of participants in our highest categories of intake was 5.3 ± 2.8 serves, suggesting many in our higher category had intakes below the level at which we would expect to see a benefit. Additionally, fruit and vegetable intakes were collected using a variety of different self-report measurement tools. Three of these tools were unvalidated short questionnaires. All self-report dietary collection methods are subject to inaccuracies. Reporting of fruit and vegetable intake is known to be subject to over-reporting across a wide variety of ethnic groups (Martínez-Arroyo et al., 2022; Mendez et al., 2004; Ovaskainen et al., 2008). Errors in reporting of intake may have reduced the potential of detecting relationships between intakes and depression. Nevertheless, even brief self-report dietary questionnaires are useful in categorising dietary intakes of individuals (Perez Rodrigo et al., 2015), which is central to our study. It is also possible that other foods which correlate with fruit and vegetable intakes are responsible for the association detected. However, previous meta-analyses have not detected a relationship between either a "healthy" or a Mediterranean diet and incident depression in adults 45+ years (Matison et al., 2021). Cases of depression were identified based on validated cut-off scores for measures of depressive symptoms in our study. However, clinical diagnosis is the gold standard, and we may have misclassified the depression status of participants. We also may have missed any cases of incident depression that occurred and were resolved between assessment waves. Although our study is longitudinal and we have identified new cases of depression over a three-to-nine-year period, we cannot rule out the possibility of reverse causation and that the association detected was due to participants with subclinical depressive symptoms at baseline who had altered their intakes because of subclinical depressive symptoms. Finally, although we adjusted for a range of confounders based on a review of relevant literature, using DAGs to determine which potential confounders should be adjusted, the possibility of residual confounding remains due to unknown or unmeasured confounders (Mendez et al., 2004).

5. Conclusion

A beneficial association between higher fruit, but not vegetable, intake and incident depression was found in our analysis of adults 45+ years from 10 diverse international cohorts. Future research considering the consumption of different types of fruit and vegetables using standardised measures and focusing on larger cohorts of older adults from LMICs is warranted.

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CRediT authorship contribution statement

Annabel P. Matison: Writing – review & editing, Writing – original draft, Methodology, Formal analysis, Conceptualization. **Victoria M. Flood:** Writing – review & editing, Supervision, Methodology, Conceptualization. **Ben C.P. Lam:** Writing – review & editing, Methodology, Conceptualization. **Darren M. Lipnicki:** Writing – review & editing, Methodology, Data curation, Conceptualization. **Katherine L. Tucker:** Data curation. **Pierre-Marie Preux:** Data curation. **Maëlenn Guerchet:** Data curation. **Eleonora d'Orsi:** Data curation. **Anna Quialheiro:** Data curation. **Cassiano R. Rech:** Data curation. **Ingmar Skoog:** Data curation. **Jenna Najar:** Data curation. **Therese Rydberg Sterner:** Data curation. **Nikolaos Scarmeas:** Data curation. **Mary H. Kosmidis:** Data curation. **Mary Yannakoulia:** Data curation. **Oye Gureje:** Data curation. **Akin Ojagbemi:** Data curation. **Toyin Bello:** Data curation. **Suzana Shahar:** Data curation. **Nik N.I.N.M. Fakhruddin:** Data curation. **Nurul F.M. Rivan:** Data curation. **Kaarin J. Anstey:** Data curation. **Nicolas Cherbuin:** Data curation. **Moyra E. Mortby:** Data curation. **Roger Ho:** Data curation. **Henry Brodaty:** Data curation. **Perminder S. Sachdev:** Data curation. **Simone Reppermund:** Writing – review & editing, Supervision, Methodology, Conceptualization. **Karen A. Mather:** Writing – review & editing, Supervision, Methodology, Conceptualization.

Declaration of competing interest

Henry Brodaty is or has been an advisory board member or consultant to Biogen, Eisai, Eli Lilly, Roche and Skin2Neuron. He is a Medical/Clinical Advisory Board member for Montefiore Homes and Cranbrook Care.

Data availability

Data were provided by the contributing studies to COSMIC on the understanding and proviso that the relevant study leaders be contacted for further use of their data and additional formal data sharing agreements be made. Researchers can apply to use COSMIC data by completing a COSMIC Research Proposal Form available from https://cheba.unsw.edu.au/consortia/cosmic/research-proposals.

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Appendix A. Supplementary data

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References

Anstey, K.J., Christensen, H., Butterworth, P., Easteal, S., Mackinnon, A., Jacomb, T., Maxwell, K., Rodgers, B., Windsor, T., Cherbuin, N., Jorm, A.F., 2012. Cohort profile: the PATH through life project. Int. J. Epidemiol. 41, 951–960.

Baharzadeh, E., Siassi, F., Qorbani, M., Koohdani, F., Pak, N., Sotoudeh, G., 2018. Fruits and vegetables intake and its subgroups are related to depression: a cross-sectional study from a developing country. Ann. General Psychiatry 17, 46.

Beekman, A.T., Copeland, J.R., Prince, M.J., 1999. Review of community prevalence of depression in later life. Br. J. Psychiatry 174, 307–311.

Blazer, D.G., 2003. Depression in late life: review and commentary. J. Gerontol. A Biol. Sci. Med. Sci. 58, 249–265.

van Buuren, S., Groothuis-Oudshoorn, K., 2011. Mice: multivariate imputation by chained equations in R. J. Stat. Softw. 45, 1–67.

Dardiotis, E., Kosmidis, M.H., Yannakoulia, M., Hadjigeorgiou, G.M., Scarmeas, N., 2014. The Hellenic longitudinal investigation of aging and diet (HELIAD): rationale, study design, and cohort description. Neuroepidemiology 43, 9–14.

Feng, L., Chong, M.S., Lim, W.S., Lee, T.S., Collinson, S.L., Yap, P., Ng, T.P., 2013. Metabolic syndrome and amnestic mild cognitive impairment: Singapore longitudinal ageing Study-2 findings. J. Alzheimers Dis. 34, 649–657.

Firth, J., Marx, W., Dash, S., Carney, R., Teasdale, S.B., Solmi, M., Stubbs, B., Schuch, F. B., Carvalho, A.F., Jacka, F., Sarris, J., 2019. The effects of dietary improvement on symptoms of depression and anxiety: a Meta-analysis of randomized controlled trials. Psychosom. Med. 81, 265–280.

Folstein, M.F., Folstein, S.E., McHugh, P.R., 1975. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. J. Psychiatr. Res. 12, 189–198.

Gangwisch, J.E., Hale, L., Garcia, L., Malaspina, D., Opler, M.G., Payne, M.E., Rossom, R. C., Lane, D., 2015. High glycemic index diet as a risk factor for depression: analyses from the Women's Health Initiative. Am. J. Clin. Nutr. 102, 454–463.

Gaudio, S., Rukh, G., Di Ciommo, V., Berkins, S., Wiemerslage, L., Schioth, H.B., 2023. Higher fresh fruit intake relates to larger grey matter volumes in areas involved in dementia and depression: a UK biobank study. Neuroimage 283, 120438.

Greifer, N., 2022. WeightIt: Weighting for Covariate Balance in Observational Studies.

Guerchet, M., Mbelesso, P., Ndamba-Bandzouzi, B., Pilleron, S., Desormais, I., Lacroix, P., Aboyans, V., Jesus, P., Desport, J.C., Tchalla, A.E., Marin, B., Lambert, J. C., Clement, J.P., Dartigues, J.F., Preux, P.M., Group, E., 2014. Epidemiology of dementia in Central Africa (EPIDEMCA): protocol for a multicentre population-based study in rural and urban areas of the Central African Republic and the republic of Congo. Springerplus 3, 338.

Gureje, O., Kola, L., Afolabi, E., 2007. Epidemiology of major depressive disorder in elderly Nigerians in the Ibadan study of ageing: a community-based survey. Lancet 370, 957–964.

Herforth, A., Arimond, M., Alvarez-Sanchez, C., Coates, J., Christianson, K., Muehlhoff, E., 2019. A global review of food-based dietary guidelines. Adv. Nutr. 10, 590–605.

Hirvonen, K., Bai, Y., Headey, D., Masters, W.A., 2020. Affordability of the EAT-lancet reference diet: a global analysis. Lancet Glob. Health 8, e59–e66.

Lassale, C., Batty, G.D., Baghdadli, A., Jacka, F., Sanchez-Villegas, A., Kivimaki, M., Akbaraly, T., 2019. Healthy dietary indices and risk of depressive outcomes: a systematic review and meta-analysis of observational studies. Mol. Psychiatry 24, 965–986.

Liu, X., Yan, Y., Li, F., Zhang, D., 2016. Fruit and vegetable consumption and the risk of depression: a meta-analysis. Nutrition 32, 296–302.

Mamalaki, E., Ntanasi, E., Hatzimanolis, A., Basta, M., Kosmidis, M.H., Dardiotis, E., Hadjigeorgiou, G.M., Sakka, P., Scarmeas, N., Yannakoulia, M., 2023. The Association of adherence to the Mediterranean diet with depression in older adults Longitudinally taking into account cognitive status: results from the HELIAD study. Nutrients 15.

Mamplekou, E., Bountziouka, V., Psaltopoulou, T., Zeimbekis, A., Tsakoundakis, N., Papaerakleous, N., Gotsis, E., Metallinos, G., Pounis, G., Polychronopoulos, E., Lionis, C., Panagiotakos, D., 2010. Urban environment, physical inactivity and unhealthy dietary habits correlate to depression among elderly living in eastern Mediterranean islands: the MEDIS (MEDiterranean ISlands elderly) study. J. Nutr. Health Aging 14, 449–455.

Martínez-Arroyo, A., Duarte Batista, L., Corvalán Aguilar, C., Fisberg, R.M., 2022. Misreporting of energy intake is related to specific food items in low-middle income Chilean adolescents. Children 9.

Marx, W., Lane, M., Hockey, M., Aslam, H., Berk, M., Walder, K., Borsini, A., Firth, J., Pariante, C.M., Berding, K., Cryan, J.F., Clarke, G., Craig, J.M., Su, K.P., Mischoulon, D., Gomez-Pinilla, F., Foster, J.A., Cani, P.D., Thuret, S., Staudacher, H. M., Sanchez-Villegas, A., Arshad, H., Akbaraly, T., O'Neil, A., Segasby, T., Jacka, F. N., 2021. Diet and depression: exploring the biological mechanisms of action. Mol. Psychiatry 26, 134–150.

Matison, A.P., Mather, K.A., Flood, V.M., Reppermund, S., 2021. Associations between nutrition and the incidence of depression in middle-aged and older adults: a systematic review and meta-analysis of prospective observational population-based studies. Ageing Res. Rev. 70, 101403.

Mendez, M.A., Wynter, S., Wilks, R., Forrester, T., 2004. Under- and overreporting of energy is related to obesity, lifestyle factors and food group intakes in Jamaican adults. Public Health Nutr. 7, 9–19.

Moore, L.V., Hamner, H.C., Kim, S.A., Dalenius, K., 2016. Common ways Americans are incorporating fruits and vegetables into their diet: intake patterns by meal, source and form, National Health and nutrition examination survey 2007-2010. Public Health Nutr. 19, 2535–2539.

Ovaskainen, M.L., Paturi, M., Reinivuo, H., Hannila, M.L., Sinkko, H., Lehtisalo, J., Pynnönen-Polari, O., Männistö, S., 2008. Accuracy in the estimation of food servings against the portions in food photographs. Eur. J. Clin. Nutr. 62, 674–681.

Park, H., Kim, K., 2018. Depression and its association with health-related quality of life in postmenopausal women in Korea. Int. J. Environ. Res. Public Health 15.

Perez Rodrigo, C., Moran Fagundez, L.J., Riobo Servan, P., Aranceta Bartrina, J., 2015. Screeners and brief assessment methods. Nutr. Hosp. 31 (Suppl. 3), 91–98.

Sachdev, P.S., Brodaty, H., Reppermund, S., Kochan, N.A., Trollor, J.N., Draper, B., Slavin, M.J., Crawford, J., Kang, K., Broe, G.A., Mather, K.A., Lux, O., Memory, Ageing Study, T, 2010. The Sydney memory and ageing study (MAS): methodology and baseline medical and neuropsychiatric characteristics of an elderly epidemiological non-demented cohort of Australians aged 70-90 years. Int. Psychogeriatr. 22, 1248–1264.

Sachdev, P.S., Lipnicki, D.M., Kochan, N.A., Crawford, J.D., Rockwood, K., Xiao, S., Li, J., Li, X., Brayne, C., Matthews, F.E., Stephan, B.C., Lipton, R.B., Katz, M.J., Ritchie, K., Carriere, I., Ancelin, M.L., Seshadri, S., Au, R., Beiser, A.S., Lam, L.C., Wong, C.H., Fung, A.W., Kim, K.W., Han, J.W., Kim, T.H., Petersen, R.C., Roberts, R.O., Mielke, M.M., Ganguli, M., Dodge, H.H., Hughes, T., Anstey, K.J., Cherbuin, N., Butterworth, P., Ng, T.P., Gao, Q., Reppermund, S., Brodaty, H., Meguro, K., Schupf, N., Manly, J., Stern, Y., Lobo, A., Lopez-Anton, R., Santabarbara, J., Cosmic, 2013. COSMIC (cohort studies of memory in an international consortium): an international consortium to identify risk and protective factors and biomarkers of cognitive ageing and dementia in diverse ethnic and sociocultural groups. BMC Neurol. 13, 165.

Saghafian, F., Malmir, H., Saneei, P., Milajerdi, A., Larijani, B., Esmaillzadeh, A., 2018. Fruit and vegetable consumption and risk of depression: accumulative evidence from an updated systematic review and meta-analysis of epidemiological studies. Br. J. Nutr. 119, 1087–1101.

Schneider, I.J.C., Confortin, S.C., Bernardo, C.O., Bolsoni, C.C., Antes, D.L., Pereira, K.G., Ono, L.M., Marques, L.P., Borges, L.J., Giehl, M.W.C., Krug, R.R., Goes, V.F., Boing, A.C., Boing, A.F., d'Orsi, E., 2017. EpiFloripa aging cohort study: methods, operational aspects, and follow-up strategies. Rev. Saude Publica 51, 104.

Shahar, S., Omar, A., Vanoh, D., Hamid, T.A., Mukari, S.Z.M.-S., Din, N.C., Rajab, N.F., Mohammed, Z., Ibrahim, R., Loo, W.H., Meramat, A., Kamaruddin, M.Z.A., Bagat, M. F., Razali, R., 2016. Approaches in methodology for population-based longitudinal study on neuroprotective model for healthy longevity (TUA) among Malaysian older adults. Aging Clin. Exp. Res. 28, 1089–1104.

Shang, X., Hodge, A.M., Peng, W., He, M., Zhang, L., 2020. Are leading risk factors for cancer and mental disorders multimorbidity shared by these two individual conditions in community-dwelling middle-aged adults? Cancers 12, 1–15.

Textor, J., van der Zander, B., Gilthorpe, M.S., Liskiewicz, M., Ellison, G.T., 2016. Robust causal inference using directed acyclic graphs: the R package 'dagitty'. Int. J. Epidemiol. 45, 1887–1894.

Tucker, K.L., 2005. Stress and nutrition in relation to excess development of chronic disease in Puerto Rican adults living in the northeastern USA. J. Med. Investig. 52 (Suppl), 252–258.

Wetterberg, H., Ryden, L., Ahlner, F., Falk Erhag, H., Gudmundsson, P., Guo, X., Joas, E., Johansson, L., Kern, S., Mellqvist Fassberg, M., Najar, J., Ribbe, M., Sterner, T.R., Samuelsson, J., Sacuiu, S., Sigstrom, R., Skoog, J., Waern, M., Zettergren, A., Skoog, I., 2022. Representativeness in population-based studies of older adults: five waves of cross-sectional examinations in the Gothenburg H70 birth cohort study. BMJ Open 12, e068165.

World Bank Organisation, 2023. World Bank Group Country Classifications by Income Level for FY24 (July 1, 2023- June 30, 2024). World Bank Blogs.

World Health Organisation, 2017. Depression and Other Common Mental Disorders: Global Health Estimates. WHO.

Yusuf, S., Joseph, P., Rangarajan, S., Islam, S., Mente, A., Hystad, P., Brauer, M., Kutty, V. R., Gupta, R., Wielgosz, A., AlHabib, K.F., Dans, A., Lopez-Jaramillo, P., Avezum, A., Lanas, F., Oguz, A., Kruger, I.M., Diaz, R., Yusoff, K., Mony, P., Chifamba, J., Yeates, K., Kelishadi, R., Yusufali, A., Khatib, R., Rahman, O., Zatonska, K., Iqbal, R., Wei, L., Bo, H., Rosengren, A., Kaur, M., Mohan, V., Lear, S.A., Teo, K.K., Leong, D., O'Donnell, M., McKee, M., Dagenais, G., 2020. Modifiable risk factors, cardiovascular disease, and mortality in 155 722 individuals from 21 high-income, middle-income, and low-income countries (PURE): a prospective cohort study. Lancet 395, 795–808.

Zenebe, Y., Akele, B., M, W.S., Necho, M., 2021. Prevalence and determinants of depression among old age: a systematic review and meta-analysis. Ann. General Psychiatry 20, 55.

Zeng, Z., Gao, Y., Li, J., Zhang, G., Sun, S., Wu, Q., Gong, Y., Xie, C., 2022. Violations of proportional hazard assumption in cox regression model of transcriptomic data in TCGA pan-cancer cohorts. Comput. Struct. Biotechnol. J. 20, 496–507.