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Association of habitual intake of fruits and vegetables with depressive symptoms: The AusDiab study

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1 **Association of habitual intake of fruits and vegetables with depressive symptoms: the**
2 **AusDiab Study**

3

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38 **Short running head:** Fruit and vegetable intake and depressive symptoms

39

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52 **Ethics statement**

53 The study was approved by The Human Research Ethics Committees of the International
54 Diabetes Institute, and the Alfred Hospital (Melbourne, Australia).

55 **Data Availability**

56 The data that support the findings of this study were available from the Baker Heart and
57 Diabetes Institute, under a license agreement. Data will be available from the Principal
58 Investigator of AusDiab upon reasonable request and approval of the AusDiab Steering
59 Committee.

60 **Authors' contributions**

61 SRB, RA, LCB, JRL and JMH designed the statistical analysis of the study, planned the
62 statistical analysis, interpreted the results and extensively reviewed the manuscript. SRB and
63 NPB analysed the data. RW assisted with the statistical analyses. SRB and RA reviewed the
64 literature and prepared the manuscript. NPB, MS, CPB, CH assisted with the methodology and
65 interpretation of the results. SRB, RA, NPB, MS, CPB, MJS, CH, RW, DJM, JES, RMD, JMH,
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88

89

90 **ABSTRACT**

91 **Purpose:** To investigate the relationship of habitual FV intake, different types of FV and
92 vegetable diversity with depressive symptoms.

93 **Methods:** Australian men and women (n=4,105) aged >25 years from the Australian
94 Diabetes, Obesity and Lifestyle Study were included. Dietary intake was assessed using a
95 Food Frequency Questionnaire at baseline, 5 and 12 years. Depressive symptoms were
96 assessed using the validated 10-item Centre for Epidemiology Studies Short Depression Scale
97 at 12 years. Multiple logistic regression models were used to investigate the association
98 between the exposures of interest and depressive symptoms using odds ratios (OR) and 95%
99 confidence intervals (CI) across quartiles of FV intake and vegetable diversity. Analyses
100 were multivariable adjusted for confounding factors.

101 **Results:** At 12 years, 425 (10.4%) participants had “any depressive symptoms”. Habitual FV
102 intake was inversely associated with depressive symptoms at 12 years. After adjustment,
103 participants in quartile 2 of FV intake (Q2; median 317 g/day) had a 20% lower odds of
104 having any depressive symptoms (OR [95%CI]: 0.80 [0.69, 0.95]) in comparison to those in
105 the lowest quartile of FV intake (Q1; median 223 g/d). Yellow/orange/red and leafy green
106 vegetables were the key vegetable types driving this association. Higher vegetable diversity
107 (4-6 different vegetables per day) was associated with a 24-42% lower odds of having
108 depressive symptoms when compared to <3 different vegetables per day. The associations
109 remained similar after further adjusting for diet quality.

110 **Conclusion:** A FV-rich diet, consisting of a diverse range of vegetables, particularly
111 yellow/orange/red and leafy green vegetables may help to lower depressive symptoms.
112 Promoting such a diet, particularly in men and women with a low FV intake, may have a
113 significant public health impact.

114 **Keywords:** AusDiab, Australian adults, fruits and vegetable intake, vegetable diversity,
115 depressive symptoms.

116 INTRODUCTION

117 Depression, also known as Major Depressive Disorder (MDD) or clinical depression. The
118 two core features of MDD are persistent feeling of sadness and low mood as well loss of
119 interest and pleasure [1]. Depression affects how individuals feel, think and behave and can
120 lead to several emotional and physical problems [1]. Depression affects more than 300
121 million people worldwide [2] and is one of the most common mental disorders in Australia
122 [3,4]. It is the leading contributor to global disability [5] and cause of mental health-related
123 disease burden [6]. Depression is estimated to be responsible for an average of 8.3 deaths by
124 suicide per day among Australian men and women [7], and is also associated with an
125 increased risk of other chronic diseases, particularly impaired cognitive functioning [8] and
126 cardiovascular disease (CVD) [9].

127 Evidence shows that dietary interventions can reduce depressive symptoms [10]. One focus
128 of research has been on the link between habitual intake of fruit and vegetables (FV) and
129 depression. As background, it has been suggested that many vitamins, minerals and
130 phytochemicals found in FV may serve a protective function for aspects of mood with greater
131 consumption of FV being not only associated with lower oxidative stress and inflammation,
132 but also associated with better healthy emotional and cognitive functioning [11]. Evidence
133 suggests a link between FV intake and depression [12-21]. Diets high in fruit (total fruit with
134 and without juice) and vegetables (specifically orange, dark green vegetables and legumes)
135 [22,23,14] have been associated with lower depressive symptomology in different
136 populations. Higher intakes of FV have been associated with fewer symptoms of depression
137 among women in the United Kingdom [12] and for both men and women in Japan [13].
138 Further, the outcomes of Australian longitudinal studies indicate that consuming diets high in
139 FV can improve mood regulation associated with depression [15], and that consuming higher

140 quantities of salad (cucumber, lettuce), fresh vegetables (broccoli, carrots), and fruit (melon,
141 peach, nectarines) was associated with lower depressive symptoms [16].

142 Although these studies have investigated the association of FV intake with depression in
143 specific age populations, the association between long-term habitual FV consumption and
144 depressive symptomology across the adult lifespan remains to be determined. Furthermore,
145 the role of habitual intake of specific FV types as well as the habitual diversity of FV on
146 symptoms of depression requires investigation, which may have significant impact on public
147 health.

148 The primary aim of this study was to examine the associations between long-term habitual
149 intake of FV and depressive symptoms among Australian men and women who were part of
150 the Australian Diabetes, Obesity and Lifestyle (AusDiab) Study. Secondary aims were to: (1)
151 examine the association between habitual intake of specific FV types (bananas; apples and
152 pears; oranges and other citrus fruits; cruciferous vegetables; allium vegetables;
153 yellow/orange/red vegetables; leafy green vegetables; and legume vegetables) and depressive
154 symptoms; and (2) examine the association between diversity of vegetable intake and
155 depressive symptoms.

156

157 **METHODS**

158 **Study design**

159 The Australian Diabetes, Obesity and Lifestyle (AusDiab) Study is a large longitudinal
160 population-based study conducted among a diverse group of Australian adults aged 25 years
161 and over, recruited in 1999-2000 and followed up in 2004-05 and 2011-12. A total of 11,247
162 men and women attended a biomedical examination (1999-2000), 6,400 returned for follow-

163 up assessments at 5 years (2004-05), and 4,604 returned at 12 years (2011-12). Methods and
164 response rates have been described previously [24].

165 **Participants**

166 From the 11,247 participants who were initially involved in the AusDiab study, we excluded
167 those who did not complete the CESD-10 questionnaire at 12 years (n=6,768), those who did
168 not complete the Food Frequency Questionnaire (FFQ) at baseline (1999-2000; n=42), and
169 those who did not have at least two repeated measures for FV intake (i.e. those who
170 responded to the FFQ at one time-point only; n=51). We also excluded those with
171 implausible energy intakes (<3300 or >17,500 kJ in men and <2,500 kJ or >14,500 kJ in
172 women; n=89), pregnant women (n=22), and those with missing data for covariates (n=170).
173 After all exclusions (n=7,142), data from 4,105 participants were available for the association
174 between habitual FV intake (main exposure of this study) and depressive symptoms at 12
175 years to be analysed. The consort flow diagram is shown in **Online Resource 1**. A written
176 informed consent was obtained from all participants.

177 **Measures**

178 **Dietary intake**

179 FV intake was assessed using a 74-item FFQ developed by the Cancer Council of Victoria,
180 Australia [25]. Participants self-reported their intake of different food groups including FV
181 over the prior 12 months using 10 possible options ranging from "never" to "3 or more times
182 per day". Nutrient intakes were calculated based on frequency of consumption in the previous
183 12 months and an overall estimate of usual portion size [25]. Energy intake from alcohol was
184 also estimated using the FFQ [25], where frequency of consumption for alcohol ranged from
185 'never' to 'every day'.

186 **Fruit and vegetable exposures**

187 Habitual intake was the average intake of FV, calculated as the sum of FV intake from at
188 least two time-points (baseline, 5 years and 12 years follow-ups), divided by the number of
189 time-points (i.e. baseline + 12-year FV intake)/ 2; or baseline + 5-year + 12-year FV intake)/
190 3).

191 All types of fruits (except for fruit juice, tinned and dried fruits) and vegetables (except
192 potato, roasted and fried, including hot chips) commonly consumed in Australia were
193 assessed in the FFQ. Three types of fruits were included: i) bananas; ii) oranges and other
194 citrus fruits; and iii) apples and pears (pome fruits), as per previous studies [26]. These are
195 the most common fruits consumed in Australia [27]. Vegetable types were determined based
196 on the 2013 Australian Dietary Guidelines [28], and were grouped according to their
197 phytochemical profiles, as previously reported [29]. Briefly, vegetables were combined to
198 form the following subgroups [30,29,31-34]: cruciferous vegetables (cabbage, Brussels
199 sprouts, cauliflower, and broccoli); allium vegetables (onion, leek, and garlic);
200 yellow/orange/red vegetables (tomato, capsicum, carrot, beetroot and pumpkin); leafy green
201 vegetables (lettuce and other salad greens, celery, silver beet, and spinach); and legumes
202 (peas, greens beans, bean sprouts and alfalfa sprouts, baked beans, soy beans, soy bean curd
203 and tofu, and other beans). Habitual intake of the individual FV types was calculated in the
204 same way as the habitual overall FV intake. Vegetable diversity was estimated using the
205 following question from the FFQ: “How many different vegetables do you usually eat in a
206 day?”, with responses ranging from “less than 1” to “6 or more”. The average of at least two
207 time-points (baseline, 5 years and 12 years) were used to calculate the habitual vegetable
208 diversity. An equivalent question to measure fruit diversity was not available from the FFQ.
209 We were, therefore, unable to investigate fruit diversity in our study.

210 **Depressive symptoms outcomes**

211 Depressive symptoms at the 12-year follow-up were assessed using the self-reported 10-item
212 Centre for Epidemiology Studies Short Depression (CESD-10) Scale [35]. The CESD-10 was
213 developed to identify current depressive symptomatology related to major or clinical
214 depression in adults and adolescents, and contains 10 questions about a person's feelings and
215 behaviour over the previous week of completing the questionnaire [35]. Three statements
216 focus on depressed affect (e.g., "I felt depressed"), five question evaluate other symptoms
217 that are part of the diagnostic criteria for depression (e.g., "I could not get going"), or
218 commonly associated with depression (e.g., "I had trouble keeping my mind on what I was
219 doing"), and two items (which are reverse-scored) relate to positive affect (e.g., "I was
220 happy") [36]. The CESD-10 includes questions such as "did you feel depressed", "did you
221 feel afraid", and "were you happy". Respondents rated each symptom of depression as being
222 "rarely or none of the time (less than 1 day)"; "some or a little of the time (1-2 days)";
223 "occasionally or a moderate amount of the time (3-4 days)"; or "most or all of the time (5-7
224 days)" on a four-point Likert scale. Scores on the CESD-10 can range from 0 to 30, with
225 scores ≥ 10 indicating the presence of depressive symptoms [35,37]. In the present study,
226 CESD-10 symptomology was categorised into two groups: no depressive symptoms (score
227 < 10) and any depressive symptoms (score ≥ 10). CESD-10 has been found to be a reliable
228 instrument, presenting high internal consistency (Cronbach's $\alpha=0.86$) and test-retest
229 reliability (ICC=0.85) [38,39]. To test the internal validity of the CESD-10, we categorised
230 question 3 ("do you feel depressed?") into two categories: no (n=3,351) and yes (n=754). We
231 then examined the association between FV intake and this variable. Question 3 ("do you feel
232 depressed?") was the most relevant question to the actual presence of depression.

233 **Baseline data assessment**

234 Demographic data was collected at baseline (1999-2000) through a household interview and
235 included as covariates in the statistical analyses. Participants provided information on age

236 (based on date of birth), sex (male/female), relationship status (de facto, married, separated,
237 divorced, widowed, never married) education level (never to some high school, completed
238 University or equivalent) and income (based on 6 categories of average weekly income: \$0-
239 199, \$200-399, \$400-599, \$600-799, \$800-1,499, and \$1,500+).

240 Baseline body mass index (BMI) was calculated as weight (kg) divided by height (squared
241 metres). Height was measured to the nearest 0.5 cm without shoes using a stadiometer.

242 Weight was measured without shoes and excess clothing to the nearest 0.1 kg using a
243 mechanical beam balance [40]. Details of anthropometric assessments have been published
244 previously [41,24].

245 Participants self-reported their time spent performing physical activity in the previous week
246 using the Active Australia Survey Questionnaire [42] as described previously [43]. Total
247 physical activity (min per week) was calculated by summing the time spent walking (if
248 continuous for ≥ 10 min) and/or performing moderate-intensity exercise. Time spent
249 performing vigorous-intensity exercise was doubled (i.e. multiplied by two) and then added
250 to the time spent walking and/or performing moderate-intensity exercise to obtain the total
251 minutes of physical activity per week [44]. Physical activity levels were then classified as
252 sedentary (no physical activity), insufficient (below 150 min per week and/or fewer than five
253 sessions per week) and sufficient (above 150 min per week across at least five sessions).

254 Socio-Economic Indexes for Areas (SEIFA) were calculated according to relative socio-
255 economic conditions per geographic area, based on the five-yearly Census [45] from 1999.

256 An interviewer-administered questionnaire [24] was used to assess smoking status.

257 Participants were classified as: current smokers (smoking at least daily); ex-smoker (less than
258 daily for at least the last three months); and never smokers (< 100 cigarettes during life) [46].

259 Self-reported history of CVD (yes/no) and diabetes mellitus (DM) based on plasma glucose

260 levels (known DM, impaired fasting glucose, impaired glucose tolerance, new DM, normal
261 glucose levels) were assessed as previously reported [24].

262 A dietary guideline index [47] reflecting adherence to 5 main food groups based on the
263 Australian Dietary Guidelines [48,28] was calculated and used in our study to help us
264 understand whether a healthy diet could potentially be a confounding factor in our study. The
265 methodology of how this index was calculated has previously been described [47]. Briefly,
266 the dietary guideline index included 15 components representing: 1) dietary variety; 2) fruit;
267 3) vegetables; 4) total cereals; 5) whole-grain cereals; 6) meat and alternatives (i.e. fish,
268 poultry, nuts); 7) lean protein sources; 8) total dairy; 9) reduced/low fat dairy; 10) non-
269 alcoholic beverages; 11) alcoholic beverages; 12) salt intake; 13) saturated fat; 14) added
270 sugars, and; 15) extra foods [47]. A score of 0-10 (from lowest intakes to optimal intake or
271 reaching the recommendations) was given to each component, with a possible total diet score
272 ranging from 0-150 (higher score indicating greater compliance with the dietary guidelines)
273 [47].

274 **Statistical analyses**

275 Analyses were undertaken using IBM SPSS (version 25; IBM, Chicago, IL, USA) [49], and
276 R software (version 3.0.2) [50]. The main exposure of this study was total habitual FV intake
277 (quartiles) and the main outcome was depressive symptoms (CESD-10). Logistic regression
278 models were used to investigate relationships between the exposures of interest (habitual FV
279 intake) and depressive symptoms (no symptoms vs. any symptoms). Odds ratios (ORs) and
280 95% confidence intervals (CIs) were estimated to compare the association between
281 depression and the median of each quartile, with quartile 1 used as a reference value. To
282 assess the linearity of the relationship between habitual FV intake and depressive symptoms,
283 we also modelled the exposures as continuous variables with restricted cubic splines using
284 the 'rms' R package with the rcs() function [51]. The overall effect of the exposure on the

285 outcome for the cubic splines were obtained using Wald's tests. We tested for nonlinearity
286 using a chi-squared test to compare nested models. Odds ratios with 95% CI bands were
287 plotted for each unit increase in the exposure of interest (i.e. FV intake) using the median
288 value in quartile 1 as the reference point. The x-axes of all graphs have been truncated at 3
289 SD above the mean for visual simplicity. Two models of adjustment were used in all
290 analyses: (1) minimally adjusted for age and sex; and (2) multivariable adjusted for age
291 (years), sex (men/women), BMI (kg/m²), energy intake (kcal/day), relationship status (de
292 facto, married, separated, divorced, widowed, never married), physical activity levels
293 (sedentary, insufficient, sufficient), level of education (never to some high school, completed
294 university or equivalent), SEIFA (socio-economic index for areas), smoking status (current
295 smoker, ex-smoker, non-smoker), self-reported history of CVD (yes/no), and diagnosis of
296 diabetes (yes/no). In sensitivity analyses, we further adjusted for income and adherence to the
297 Australian Dietary Guidelines. These analyses were repeated for specific types of FV and
298 habitual vegetable diversity, all entered into models as quartiles. Statistical significance was
299 set at $p \leq 0.05$ (two-tailed) for all tests.

300

301 **RESULTS**

302 *Baseline characteristics*

303 Participants' flow chart is shown in **Online Resource 1**. Baseline characteristics of the 4,105
304 participants overall, and stratified by quartiles of habitual FV intake, are presented in **Table**
305 **1**. Briefly, 55.7% (n=2,285) were women and the mean (\pm SD) age of participants was 49 ± 11
306 years. The majority (53.9%) were considered sufficiently active, 10.7% were current
307 smokers, 4.1% reported a history of CVD, and more than 80% presented with normal glucose
308 levels.

309 At baseline, average energy intake was $2,022 \pm 666$ kcal/day (mean \pm SD), and total FV
310 intake was 380 ± 148 g/day. At 12 years, average CESD-10 score for depression was $4.0 \pm$
311 4.4 : 10.4% (n=425) had “any depressive symptoms (CESD-10 score ≥ 10)” and 89.6%
312 (n=3,680) had “no depressive symptoms (CESD-10 < 10)”. Of those participants with a
313 CESD-10 score ≥ 10 , 272 (6.6% of the overall sample) reported mild symptoms of depression
314 (CESD-10 score 10-14)” and 153 of the participants (3.7% of the total sample) reported
315 severe depressive symptoms (CESD-10 score > 14).

316 *Associations of habitual dietary intake of FV and types of fruit and vegetable intake with*
317 *depressive symptoms at 12 years*

318 The association between FV intake and depressive symptoms at 12 years was nonlinear (**Fig.**
319 **1**): the inverse association appeared to plateau at FV intakes of approximately 300 g/day (i.e.
320 the relationship was somewhat “L-shaped”). Similar-shaped associations were seen for
321 intakes of fruit and vegetables, discretely (Fig. 1).

322 Odds ratios for any depressive symptoms (CESD-10 score ≥ 10), by quartiles of FV intake,
323 are shown in **Table 2**. For FV, participants in Q2 (median habitual intake of 317 g/day) had a
324 20% lower odds of depressive symptoms (OR [95% CI]: 0.80 [0.69, 0.95]), compared to
325 participants in Q1 (median intake 223 g/day; Model 2; **Table 2**); ORs were not lower for
326 higher intake categories, which is also reflected by the splines. For vegetable intake, those in
327 Q2 (median intake 148 g/day) had 18% lower odds of depressive symptoms in comparison to
328 those in Q1 (median intake 105 g/day) (**Table 2**). For question 3 of the CESD-10 (“do you
329 feel depressed?”; no [n=3,351] and yes [n=754]), those in Q2 (median 317 g/day), Q3
330 (median intake 410 g/day) and Q4 (median intake 550 g/day) of FV intake had a 26% (OR
331 [95% CI] 0.74 [0.65, 0.84]), 27% (0.73 [0.61, 0.87]) and 24% (0.76 [0.10, 0.95]) lower odds
332 for depression, respectively, in comparison to those in Q1 (median intake 223 g/day).

333 The multivariable-adjusted cubic splines for associations between types of fruit and
334 depression are shown in **Online Resource 2**. There was no evidence of an association
335 between individual fruits (bananas, oranges and other citrus; or apples and pears) and
336 depressive symptoms (**Table 3**).

337 Intakes of yellow/orange/red vegetables in Q3 (median intake 51 g/day) and Q4 (median
338 intake 71 g/day) were associated with a 24% (0.76 [0.61, 0.95]) and 31% (0.69 [0.52, 0.92])
339 lower odds of depressive symptoms, respectively, in comparison to Q1 (median intake 25
340 g/day) (**Table 3**). A lower odds of depressive symptoms (38%) was also identified among
341 those with a higher intake of leafy green vegetables (Q4; median intake 26 g/day: 0.62 [0.47,
342 0.82] vs. Q1; median intake 7 g/day). In addition, **Online Resource 3** shows the cubic spline-
343 based association between the habitual intake of types of vegetables examined in the present
344 study and symptoms of depression.

345 An average vegetable diversity of 4, 5 and 6 or more different types of vegetables per day
346 was associated with a 24% (Q2: 0.76 [0.63, 0.92]), 42% and (Q3: 0.58 [0.43, 0.77]) 41% (Q4:
347 0.59 [0.43, 0.82]) lower odds of depressive symptoms, respectively, compared to 3 or less
348 (**Table 4**). In addition to the above findings, **Fig. 2** shows the cubic spline-based association
349 between average vegetable diversity and depressive symptoms. We have also further adjusted
350 the aforementioned analysis for vegetable intake and the associations remained significant,
351 suggesting that the results are robust and independent of total vegetable intake (Q2: 0.74
352 [0.60, 0.92], Q3: 0.55 [0.39, 0.77], Q4: 0.54 [0.35, 0.84] vs. Q1).

353 **Sensitivity analyses**

354 We added income to the multivariable-adjusted model, as a further adjustment for socio-
355 economic status. The association between consumption of FV and depressive symptoms (Q2:
356 0.81 [0.69, 0.95] vs. Q1) remained similar. To further explore whether an optimal healthy diet

357 could be a confounding factor in our study, we added the dietary guideline index in the
358 multivariable-adjusted model 2 (except for energy intake, which is accounted for in the
359 dietary guideline index). Similar relationships were observed for FV intake and depressive
360 symptoms, with those in Q2 (317 g/day) of FV intake having a 17% (0.83 [0.71, 0.98]) lower
361 odds of presenting depressive symptoms compared to Q1 (223 g/day).

362

363 **DISCUSSION**

364 In this population-based cohort of Australian men and women, we found an association
365 between higher habitual intake of FV and lower depressive symptoms. This relationship was
366 non-linear, with the largest dietary benefit seen from increasing individuals' consumption
367 beyond 250 g/day – the upper range of the lowest quartile. Our results showed that
368 consuming sufficient amounts of vegetables is associated with lower depressive symptoms.
369 When examining the associations of habitual intake of specific types of vegetables, a higher
370 consumption of total vegetables, and in particular yellow/orange/red vegetables and leafy
371 green vegetables, was associated with a lower odds of depressive symptoms at 12 years.
372 Potential benefits of habitual intake of vegetables were observed for median intakes of ~148
373 g/day (~2 servings of vegetables per day).

374 Our findings support previous studies that reported associations between FV intake and
375 depression [12-21]. A meta-analysis [52] reported that a higher intake of vegetables was
376 associated with a 14% lower risk of depression in 9 prospective cohort studies, and 25%
377 lower risk of depression in 16 cross-sectional studies. The same meta-analysis reported that
378 for each 100 g/day higher in vegetable intake there was an associated 3% lower risk of
379 depression in prospective cohort studies (RR=0.97; 95% CI 0.95, 0.98), and a 5% lower risk
380 of depression in cross-sectional studies (RR=0.95; 95% CI 0.91, 0.98) [52].

381 Individuals with depression also have lower levels of certain nutrients found in FV, such as
382 beta carotene, vitamin C, fiber, and folate [53-55], as well as higher oxidative stress and
383 lower antioxidant capacity [56,57] than those without depression. In addition, the association
384 between intakes of FV and depressive symptoms might be partly mediated by minerals and
385 amino acids found in FV, which are precursors of particular neurotransmitters [58] (e.g.
386 Gamma aminobutyric acid (GAMA), serotonin, norepinephrine and dopamine) that regulate
387 mood [59]. The association may also be attributed to higher levels of 8-hydroxy-
388 deoxyguanosine, a marker of oxidative damage to DNA, that has been found to be associated
389 with depression [60]. Particular nutrients and phytochemicals found in FV, such as vitamin E,
390 vitamin C, carotenoids, and nitrate, can reduce oxidative stress [61] and mitigate
391 inflammation [62,63], both which are associated with depression [64], thereby potentially
392 reducing the risk of depression [65,66] or reducing depressive symptoms [18].

393 The association between FV intake and depressive symptoms was also observed for specific
394 types of vegetables; a higher habitual intake of yellow/orange/red vegetables and leafy green
395 vegetable were each associated with lower odds of having depressive symptoms. The
396 potential health benefits of vegetable compounds, such as lycopene present in red vegetables
397 (i.e. tomatoes), could be attributable to their antioxidant activities that decreases oxidative
398 stress and free radical cell damage [67], with potential benefits on depressive disorders [68].
399 Carotenoids, phytochemicals also present in yellow/orange/red and dark green leafy
400 vegetables [69,30], reduce oxidative stress and inflammation, potentially through the
401 activation of transcription factors, such as nuclear factor κ B (NF κ B) or nuclear factor
402 erythroid 2-related factor 2 (Nrf2). Carotenoids may also influence transcription factors'
403 targets (i.e. interleukin 8 [IL-8], prostaglandin E2 [PGE2], heme oxygenase [Hmox-1] and
404 superoxide dismutase [SOD]) [70], which leads to a decrease in oxidative stress and
405 inflammation. Leafy green vegetables are the richest source of dietary nitrate, which has been

406 shown to reduce inflammation [63]. Dietary nitrate present in leafy green vegetables could,
407 therefore, play a role in alleviating depressive symptoms. The reported consumption of green
408 leafy vegetables and lower odds of experiencing depressive symptoms is in line with previous
409 studies [14]. A cross-sectional study including 422 participants aged 18 to 25 years conducted
410 in New Zealand and the United States, also reported an association between consuming
411 vegetables, such as dark green leafy vegetables, and better mental health outcomes [22].
412 Similarly, a study including adolescents who participated in the Western Australian
413 Pregnancy Cohort (Raine) Study reported a correlation between higher intakes of leafy green
414 vegetables and more favourable mental health outcomes [23].

415 To the best of our knowledge this is the first observational study to investigate vegetable
416 diversity and depressive symptoms in a large number of adults across the lifespan. In the
417 current study, we found that consumption of a greater diversity of vegetables (≥ 4 types/day)
418 was associated with a 24-42% lower odds of having depressive symptoms (CESD-10 score
419 ≥ 10). Similarly, a randomised controlled trial that included Australian adults between the
420 ages of 18–65 years reported that consumption of a diversity of vegetables and
421 Mediterranean-style diet plus fish oil supplementation improved mental health ($r=-0.303$,
422 $p=0.01$) [71]. Taken together, these results suggest that consuming ≥ 4 types/day of vegetables
423 may contribute to lowering depressive symptoms.

424 Collectively, the findings from the present study support an association between FV intake
425 and depressive symptoms, strengthening the findings from previous studies [72]. Currently,
426 approximately 350 million people are affected by depression [73] and depression is predicted
427 to outpace CVD as the number one cause of disease burden worldwide by 2030 [73].
428 Although diets rich in vegetables have been linked with more favourable mental health
429 outcomes, only one in 13 Australians (7.5%) meet the recommended intake of ≥ 5 serves of
430 vegetables per day in 2017-18 [74]. This highlights the importance of our results and the need

431 to improve public health messages around increasing FV intake, in particular the
432 consumption of specific types of vegetables and diversity of vegetables. These may be simple
433 protective measures to prevent the onset of depression and/or improve mental health, and
434 therefore of crucial importance given the increasing rate of depression worldwide. Given the
435 global burden of depression [3] and its impact on quality of life [13], modifiable lifestyle
436 factors, such as recommendations to increase FV intake, should be considered to help
437 improve mental health [14].

438 **Limitations of the study**

439 A limitation of the study is observational nature which does not allow evidence for causality.
440 Another limitation is that depressive symptoms were measured only once in 2011-2012
441 which means we cannot rule out the possibility for reverse causality (low intake of FV could
442 be a consequence of depression) [72], although higher intakes of FV have previously been
443 found to lower the risk of onset of depression [75]. In addition, there may be a possibility of
444 selection bias given only 37% of the baseline participants remained after excluding those lost
445 to follow up, or with missing data. Our results may not therefore be generalisable to all
446 Australian adults. Residual confounding also remains a possibility, given the self-reported
447 nature of data on FV consumption. A further limitation is that depression-related hormones,
448 such as dopamine and cortisol, were not available in this study.

449 **Strengths of the study**

450 A major strength of the study is its large sample size, being one of the largest observational
451 studies to analyse the association between types of FV intake and depressive symptoms in
452 adults across a wide age range. This is the first observational study to report that a diverse
453 range of vegetables are associated with a lower odds of depressive symptoms, which has
454 significant implications for public health messaging. A further strength is the use of the same

455 validated FFQ to assess dietary intake across all three time-points over a 12-year period
456 which allowed us to generate a reliable measure for habitual FV intake. Depressive symptoms
457 were measured using a well-established and validated questionnaire (CESD-10) and the
458 detailed survey allowed us to account for a large number of important lifestyle confounders.

459 **Conclusion**

460 A habitual FV intake above that of the lowest quartile was associated with approximately
461 20% lower odds of having any depressive symptoms. Yellow/orange/red and leafy green
462 vegetables, in particular, as well as consuming a variety of vegetables (4 or more types of
463 vegetables per day) were associated with lower depressive symptoms. These associations
464 were independent of factors known to be associated with a healthier lifestyle, such as being
465 more physically active and not smoking. These results suggest that healthy diet rich in FV,
466 with an emphasis on yellow/orange/red and leafy green vegetables, may benefit mental
467 health. These benefits are likely to have more impact in those consuming low intakes of FVs.

468

469 **Conflict of Interest Statement**

470 DJM and JES report grants from Abbott Australasia Pty Ltd, Alphapharm Pty Ltd,
471 AstraZeneca, Bristol-Myers Squibb, Eli Lilly Australia, GlaxoSmithKline, Janssen-Cilag,
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478

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TABLES

Table 1. Baseline characteristics by quartiles of habitual fruit and vegetable intake among Australian men and women

Baseline characteristics	Quartiles of habitual/average FV intake				
	All participants n=4,105	Q1 (0-273) g/day n=1,027	Q2 (274-361) g/day n=1,026	Q3 (362-464) g/day n=1,027	Q4 (≥465) g/day n=1,025
Age (years)	49 ± 11	46 ± 11	49 ± 11	49 ± 11	51 ± 11
Sex, n (%) - female	2,285 (55.7)	561 (54.6)	600 (58.5)	599 (58.3)	525 (51.2)
BMI (kg/m ²), mean ± SD	27 ± 5	26 ± 5	26 ± 5	27 ± 5	27 ± 5
Energy intake (kcal/day)	2,022 ± 666	1,883 ± 654	1,946 ± 623	2,007 ± 637	2,253 ± 690
Physical activity, n (%)					
<i>Sedentary</i>	630 (15.3)	209 (20.4)	151 (14.7)	158 (15.4)	112 (10.9)
<i>Insufficient (<150min/w)</i>	1,263 (30.8)	344 (33.5)	335 (32.7)	321 (31.3)	263 (25.7)
<i>Sufficient (>150min/w)</i>	2,212 (53.9)	474 (46.2)	540 (52.6)	548 (53.4)	650 (63.4)
Smoking status, n (%)					
<i>Current</i>	438 (10.7)	183 (17.8)	119 (11.6)	81 (7.9)	55 (5.4)
<i>Ex-smoker</i>	1,180 (28.7)	268 (26.1)	299 (29.1)	310 (30.2)	303 (29.6)
<i>Non-smoker</i>	2,487 (60.6)	576 (56.1)	608 (59.3)	636 (61.9)	667 (65.1)
SEIFA, mean ± SD	1,029 ± 80	1,029 ± 82	1,028 ± 80	1,031 ± 75	1,029 ± 84
Relationship status, n (%)					
<i>Married</i>	3,180 (77.5)	760 (74.9)	812 (79.1)	794 (77.3)	805 (78.5)
<i>De facto</i>	183 (4.5)	48 (4.7)	52 (5.1)	42 (4.1)	41 (4.0)
<i>Separated</i>	80 (1.9)	22 (2.1)	18 (1.8)	19 (1.9)	21 (2.0)
<i>Divorced</i>	233 (5.7)	60 (5.8)	49 (4.8)	67 (6.5)	57 (5.6)
<i>Widowed</i>	103 (2.5)	18 (1.8)	25 (2.4)	31 (3.0)	30 (2.9)
<i>Single</i>	325 (7.9)	110 (10.7)	70 (6.8)	74 (7.2)	71 (6.9)
Level of education, n (%)					
<i>Never to some high school</i>	1,355 (33.0)	353 (34.4)	355 (34.6)	328 (31.9)	319 (31.1)
<i>Completed university or equivalent</i>	2,750 (67.0)	674 (65.6)	671 (65.4)	699 (68.1)	706 (68.9)
Prevalent CVD, n (%)	168 (4.1)	39 (3.8)	37 (3.6)	47 (4.6)	45 (4.4)
Diabetes, n (%)					

<i>Known Diabetes Mellitus</i>	97 (2.4)	21 (2.0)	22 (2.1)	35 (3.4)	19 (1.9)
<i>Impaired fasting glucose</i>	233 (5.7)	55 (5.4)	71 (6.9)	47 (4.6)	60 (5.9)
<i>Impaired glucose tolerance</i>	391 (9.5)	100 (9.7)	100 (9.7)	93 (9.1)	98 (9.6)
<i>New Diabetes Mellitus</i>	110 (2.7)	22 (2.1)	27 (2.6)	28 (2.7)	33 (3.2)
<i>Normal glucose levels</i>	3,274 (78.8)	829 (80.7)	806 (78.6)	824 (80.2)	815 (79.5)
CESD-10 score, mean \pm SD	4.0 \pm 4.4	4.7 \pm 4.8	4.0 \pm 4.3	3.9 \pm 4.2	3.7 \pm 4.2
Any depressive symptoms (CESD-10 \geq 10), n (%)	425 (10.4%)	133 (13.0)	105 (10.2)	102 (9.9)	85 (8.3)

Data is shown as mean \pm SD (standard deviation), or number (%).

BMI, Body Mass Index; SEIFA, Socio-Economic Index For Areas; CVD, Cardiovascular Disease; CESD-10, Centre for Epidemiology Studies Short Depression Scale – 10 item version; FV, Fruit and Vegetable.

Table 2. Odds ratio for depressive symptoms at 12 years by quartiles of the habitual FV intake in men and women

Depressive symptoms (CESD-10 ≥ 10 ; n=425)	Quartiles of the habitual intake of FV intake (n=4,105)			
	Q1 n=1,027	Q2 n=1,026	Q3 n=1,027	Q4 n=1,025
	Fruit and vegetables (g/day)			
Median (IQR)	223 (187 – 249)	317 (295 – 339)	409 (383 – 433)	547 (502 – 629)
<i>Model 1</i> ^a	Reference	0.76 (0.65, 0.89)	0.77 (0.62, 0.96)	0.72 (0.55, 0.95)
<i>Model 2</i> ^b	Reference	0.80 (0.69, 0.95)	0.83 (0.66, 1.03)	0.79 (0.59, 1.05)
	Fruit (g/day)			
Median (IQR)	80 (63 – 98)	149 (132 – 168)	227 (206 – 249)	349 (306 – 406)
<i>Model 1</i> ^a	Reference	0.73 (0.59, 0.90)	0.72 (0.58, 0.91)	0.72 (0.55, 0.94)
<i>Model 2</i> ^b	Reference	0.81 (0.65, 1.00)	0.83 (0.65, 1.05)	0.84 (0.63, 1.11)
	Vegetables (g/day)			
Median (IQR)	105 (84 – 118)	148 (138 – 157)	188 (177 – 199)	249 (228 – 280)
<i>Model 1</i> ^a	Reference	0.80 (0.71, 0.91)	0.82 (0.67, 1.02)	0.78 (0.60, 1.03)
<i>Model 2</i> ^b	Reference	0.82 (0.72, 0.94)	0.82 (0.66, 1.03)	0.77 (0.58, 1.02)

Odds ratios (OR) and 95% CI (95% Confidence Intervals) for depressive symptoms at 12 years, obtained from restricted cubic splines based on logistic regression models.

^aModel 1: minimally adjusted for age and sex

^bModel 2: multivariable adjusted for age, sex, BMI (body mass index), energy intake, relationship status, physical activity, level of education, SEIFA (Socio-economic index for areas), smoking status, diabetes and self-reported history of cardiovascular disease

Total n=4,105 (No depressive symptoms: 3,680)

CESD-10, Centre for Epidemiology Studies Short Depression Scale; FV, Fruit and Vegetables.

Table 3. Odds ratio for depressive symptoms at 12 years by quartiles of the habitual intake of types of fruit and vegetables in men and women

Depressive symptoms (CESD-10 ≥ 10 ; n=425)	Quartiles of the habitual intake of types of fruit and vegetables (n=4,105)			
	Q1 n=1,027	Q2 n=1,026	Q3 n=1,027	Q4 n=1,025
	Bananas (g/day)			
Median (IQR)	8 (4 – 11)	22 (18 – 26)	39 (34 – 44)	68 (58 – 83)
<i>Model 1^a</i>	Reference	0.92 (0.74, 1.13)	0.77 (0.61, 0.97)	0.65 (0.49, 0.85)
<i>Model 2^b</i>	Reference	0.96 (0.77, 1.13)	0.87 (0.68, 1.10)	0.75 (0.56, 1.00)
	Oranges and other citrus (g/day)			
Median (IQR)	5 (3 – 8)	17 (13 – 21)	36 (31 – 43)	80 (63 – 108)
<i>Model 1^a</i>	Reference	0.95 (0.77, 1.18)	0.84 (0.66, 1.06)	0.76 (0.58, 1.01)
<i>Model 2^b</i>	Reference	1.04 (0.84, 1.30)	0.96 (0.75, 1.23)	0.89 (0.67, 1.19)
	Apples and pears (g/day)			
Median (IQR)	15 (8 – 20)	38 (32 – 45)	71 (62 – 82)	130 (110 – 168)
<i>Model 1^a</i>	Reference	0.86 (0.70, 1.06)	0.81 (0.65, 1.01)	0.75 (0.58, 0.99)
<i>Model 2^b</i>	Reference	0.93 (0.75, 1.11)	0.90 (0.72, 1.14)	0.86 (0.65, 1.14)
	Cruciferous vegetables (g/day)			
Median (IQR)	9 (6 – 12)	18 (16 – 20)	26 (24 – 29)	41 (36 – 51)
<i>Model 1^a</i>	Reference	0.92 (0.77, 1.10)	0.87 (0.71, 1.07)	0.87 (0.66, 1.14)
<i>Model 2^b</i>	Reference	0.95 (0.79, 1.13)	0.88 (0.71, 1.09)	0.85 (0.64, 1.12)
	Allium vegetables (g/day)			
Median (IQR)	2 (1 – 3)	5 (4 – 5)	8 (7 – 8)	12 (11 – 15)
<i>Model 1^a</i>	Reference	0.88 (0.72, 1.07)	0.87 (0.70, 1.08)	0.85 (0.65, 1.12)
<i>Model 2^b</i>	Reference	0.93 (0.76, 1.14)	0.94 (0.75, 1.17)	0.91 (0.69, 1.20)
	Yellow/orange/red vegetables (g/day)			
Median (IQR)	25 (19 – 29)	39 (36 – 42)	51 (48 – 55)	71 (64 – 83)
<i>Model 1^a</i>	Reference	0.85 (0.73, 0.99)	0.74 (0.60, 0.91)	0.67 (0.51, 0.88)
<i>Model 2^b</i>	Reference	0.89 (0.76, 1.05)	0.76 (0.61, 0.95)	0.69 (0.52, 0.92)
	Leafy green vegetables (g/day)			
Median (IQR)	7 (5 – 8)	12 (11 – 13)	17 (16 – 19)	26 (23 – 30)
<i>Model 1^a</i>	Reference	0.83 (0.71, 0.97)	0.68 (0.55, 0.85)	0.56 (0.42, 0.73)
<i>Model 2^b</i>	Reference	0.89 (0.76, 1.05)	0.75 (0.60, 0.93)	0.62 (0.47, 0.82)

	Legumes (g/day)			
Median (IQR)	13 (10 – 16)	23 (21 – 25)	32 (30 – 35)	47 (42 – 56)
<i>Model 1</i> ^a	Reference	0.84 (0.71, 0.99)	0.92 (0.75, 1.14)	0.97 (0.74, 1.26)
<i>Model 2</i> ^b	Reference	0.84 (0.71, 1.00)	0.91 (0.73, 1.12)	0.92 (0.70, 1.21)

Odds ratios (OR) and 95% CI (95% Confidence Intervals) for depressive symptoms at 12 years, obtained from restricted cubic splines based on logistic regression models.

^aModel 1: minimally adjusted for age and sex

^bModel 2: multivariable adjusted for age, sex, BMI (body mass index), energy intake, relationship status, physical activity, level of education, SEIFA (Socio-economic index for areas), smoking status, diabetes and self-reported history of cardiovascular disease

Total n=4,105 (No depressive symptoms: 3,680)

CESD-10, Centre for Epidemiology Studies Short Depression Scale; FV, Fruit and Vegetables.

Table 4. Odds ratio for depressive symptoms at 12 years by habitual vegetable diversity in men and women

Depressive symptoms (CESD-10 ≥ 10 ; n=425)	Habitual vegetable diversity (number of types of vegetables consumed per day) ^c			
	≤ 3	4	5	≥ 6
<i>Model 1</i> ^a	Reference	0.71 (0.59, 0.85)	0.54 (0.40, 0.71)	0.51 (0.38, 0.70)
<i>Model 2</i> ^b	Reference	0.76 (0.63, 0.92)	0.58 (0.43, 0.77)	0.59 (0.43, 0.82)

Odds ratios (OR) and 95% CI (95% Confidence Intervals) for depressive symptoms at 12 years, obtained from restricted cubic splines based on logistic regression models.

^aModel 1: minimally adjusted for age and sex

^bModel 2: multivariable adjusted for age, sex, BMI (body mass index), energy intake, relationship status, physical activity, level of education, SEIFA (Socio-economic index for areas), smoking status, diabetes and self-reported history of cardiovascular disease

Total n=4,105 (No depressive symptoms: n=3,680)

^cValues represent a range of number of different vegetables consumed in a day, based on the average of at least 2 measures (≤ 3 , 4, 5, ≥ 6)

CESD-10, Centre for Epidemiology Studies Short Depression Scale.

694 **LEGENDS FOR FIGURES**695 **Fig. 1 Association between habitual FV intake and depressive symptoms at 12 years.**

696 Odds ratios from logistic regression models with restricted cubic spline curves describing the
697 association between the habitual intake of: a) Fruit and vegetable (g/day); b) Fruit (g/ day)
698 and; c) Vegetable (g/ day) intake over 12 years, and depressive symptoms at 12 years
699 (vertical axis). Odds ratios are based on models adjusting for age, sex, BMI, energy intake,
700 relationship status, physical activity, level of education, SEIFA (Socio-economic index for
701 areas), smoking status, diabetes status, and self-reported history of cardiovascular disease,
702 and are comparing the specific level of intake (horizontal axis) to the median (IQR) intake for
703 participants in the lowest intake quartile (fruit and vegetable: 223 [187 – 249] g/day; fruit: 80
704 [63 – 98] g/day; vegetable: 105 [84 – 118] g/day)

705 **Fig. 2 Association between habitual vegetable diversity and depressive symptoms at 12**

706 **years.** Odds ratios from logistic regression models with restricted cubic spline curves
707 describing the association between habitual vegetables diversity (horizontal axis), and
708 depressive symptoms at 12 years (vertical axis) ($p < 0.05$). Odds ratios are based on models
709 adjusting for age, sex, BMI, energy intake, relationship status, physical activity, level of
710 education, SEIFA (Socio-economic index for areas), smoking status, diabetes status, and self-
711 reported history of cardiovascular disease

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