



Fruit and vegetable intake and risk of incident of type 2 diabetes: results from the consortium on health and ageing network of cohorts in Europe and the United States (CHANCES)

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1 Original article

2

3 **Title:** Fruit and vegetable intake and risk of incident of type 2 diabetes: results from the consortium on
4 health and ageing network of cohorts in Europe and the United States (CHANCES)

5

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62 obtained from all participants.

63 **Abstract:**

64 *Background* There is limited information to support definitive recommendations concerning the role
65 of diet in the development of type II Diabetes mellitus (T2DM). The results of the latest meta-
66 analyses suggest that an increased consumption of green leafy vegetables may reduce the incidence
67 of diabetes, with either no association or weak associations demonstrated for total fruit and
68 vegetable intake. Few studies have, however, focused on older subjects.

69 *Methods* The relationship between T2DM and fruit and vegetable intake was investigated using data
70 from the NIH-AARP study and the EPIC elderly study. All participants below the age of 50 and/or with
71 a history of cancer, diabetes or coronary heart disease were excluded from the analysis. Multivariate
72 logistic regression analysis was used to calculate the odds ratio of T2DM comparing the highest with
73 the lowest estimated portions of fruit, vegetable, green leafy vegetables and cabbage intake.

74 *Results* Comparing people with the highest and the lowest estimated portions of fruit, vegetable or
75 green leafy vegetable intake indicated no association with the risk of T2DM. However, although the
76 pooled OR across all studies showed no effect overall, there was significant heterogeneity across
77 cohorts and independent results from the NIH-AARP study showed that fruit and green leafy
78 vegetable intake was associated with a reduced risk of T2DM OR 0.95 (95% CI 0.91,0.99) and OR 0.87
79 (95% CI 0.87,0.90) respectively.

80 *Conclusion* Fruit and vegetable intake was not shown to be related to incident T2DM in older
81 subjects. Summary analysis also found no associations between green leafy vegetable and cabbage
82 intake and the onset of T2DM. Future *dietary pattern* studies may shed light on the origin of the
83 heterogeneity across populations.

84

85 **Introduction**

86 The chronic hyperglycaemia that characterizes Type 2 diabetes mellitus (T2DM) is caused by
87 impaired insulin secretion or action and results from the interaction between a genetic
88 predisposition and environmental risk factors [1]. In 2004, an estimated 3.4 million people died from
89 the consequences of diabetes or pre-diabetes. According to the WHO, this number is rising and will
90 lead to diabetes being the 7th leading cause of death by 2030 [2]. Although the genetic basis of
91 T2DM has yet to be identified, there is strong evidence that modifiable risk factors such as obesity
92 and a sedentary lifestyle are among the non-genetic determinants of the disease [3-6]. However,
93 other than avoidance of obesity, there is limited information for definitive recommendations
94 regarding the role of diet in the development of T2DM [7-9]. The role of fruit and vegetable intake
95 and risk of T2DM is even less recognized, especially with regards to green leafy vegetables, a rich
96 source of polyphenols which are thought to be associated with increased insulin sensitivity [10].

97 The results of a recent meta-analysis suggests that an increased consumption of fruit and
98 green leafy vegetables may be associated with a significantly reduced risk of T2DM, with no
99 association or weak associations demonstrated for total vegetable intake. However, the former
100 observation regarding green leafy vegetables is based on a limited number of studies [11].
101 Conversely, another more up-to-date meta-analysis reported a dose dependent association between
102 fruit and vegetable intakes separately and a reduced risk of T2DM [12]. An earlier a meta-analysis
103 carried out in 2010 [10] included a sub-analysis using studies with information on green leafy
104 vegetable consumption. The summary estimates showed that greater intake of green leafy
105 vegetables was associated with a 14% reduction in risk of T2DM. Similarly a meta-analysis by Cooper
106 et al [13] also included a sub-analysis of green leafy vegetable intake showing an inverse association
107 with T2DM. Neither study, however, was specifically focussed on older subjects. Therefore, the
108 present study was undertaken to examine the association between T2DM and fruit and vegetables
109 intake, including green leafy vegetables.

110 **Methods**

111 **Study population**

112 The aim of the Consortium on Health and Ageing Network of Cohorts in Europe and the United
113 States (CHANCES) was to combine and integrate prospective cohort studies to produce, improve and
114 clarify the evidence on ageing-related health characteristics and risk factors for chronic diseases in
115 the elderly, and their socio-economic implications (www.chancesfp7.eu). Detailed characteristics of
116 the cohorts have previously been described [14]. All variables used in the analyses from different
117 cohorts were harmonised according to pre-agreed CHANCES data harmonisation rules. All of the
118 cohorts obtained ethical approval and written informed consent from all participants.

119 Participants, aged 50 years and above, were included from the European Prospective Investigation
120 into Cancer and Nutrition elderly study (EPIC Elderly) [15] including Spain, Greece, The Netherlands,
121 and Sweden (EPIC was treated as 4 different cohorts in the analysis); and the National Institutes of
122 Health (NIH)-AARP Diet and Health Study United States [16].

123 **Exclusions**

124 Prior to the analysis, participants at baseline with missing information on chronic diseases
125 (cardiovascular disease, diabetes, and cancer), below 50 years of age, missing or unrealistic
126 information on body mass index (BMI) [if BMI >60 kg/m² or <10 kg/m²] and with extreme energy
127 intake were excluded (applying the cohort specific definitions).

128 **Exposure**

129 Habitual dietary intakes were assessed through compatible methods including food frequency
130 questionnaires (FFQ) and, in some centers within the EPIC elderly study, records of intake over seven
131 or 14 days that had been developed and validated within each center. In addition, a computerized
132 instrument for recall of dietary intake over 24 hours was developed to collect information from a

133 stratified random sample of the aggregate cohort. The aim was to calibrate the measurements
134 across countries [17]. The number of FFQ items differed across cohorts. The number of FFQ items
135 used in EPIC elderly was 200 compared to 124 items used in (NIH)-AARP and were both self-
136 reported. (NIH)-AARP Data were thus harmonized across cohorts regarding definitions of food
137 groups and nutrient units [18]. Fruit and vegetable intakes were calculated in terms of portions per
138 day (1 portion = 80g). Green leafy vegetable and cabbage, which were less frequently consumed,
139 were calculated in portions per week (1 portion = 80g).

140 **Outcome**

141 Information on Incident T2DM was collected through self-administered questionnaires or in
142 interviews. The diagnosis of diabetes after the age of 50 was anticipated to be T2DM, as type 1
143 diabetes usually develops before the age of 40 [19]. All cohorts included in this analysis did not
144 distinguish between type 1 and type 2 diabetes, except for EPIC Elderly Greece.

145 **Covariates**

146 Model A of the analysis was adjusted for age and sex. Model B was adjusted for age, sex, BMI kg/m²;
147 underweight (<18.5), normal (≥18.5–<25), overweight (≥25–<30), moderately obese (≥30–<35) and
148 severely obese (≥35); habitual vigorous physical activity (yes/no) (defined as vigorous exercise at
149 least once per week); energy intake (Kcal); alcohol consumption [Light = men (>0g & <40g daily),
150 women (>0g & <20g daily); moderate = men (≥40g & <60g daily), women (≥20g & <40g daily); and
151 heavy = men (≥60g daily), women (≥40g daily)]; education (primary or less, more than primary,
152 college or university); and smoking (never, former, current) in all cohorts.

153 **Statistical analysis**

154 All analyses were carried out using STATA IC V.11.2 (Stata- Corp, Texas, USA) code available upon
155 request. Multivariate logistic regression analysis was used to calculate the odds ratio (OR) of T2DM
156 and 95 % confidence intervals (CI) comparing the highest with the lowest estimated intakes of fruit,

157 vegetable, green leafy vegetables and cabbage. This type of analysis was used as the majority of the
158 cohorts had no precise date of diagnosis during follow-up; hence cox modelling/time to event was
159 not ideal. This analysis was conducted in two stages: deriving first the study-specific estimates and
160 then a combined overall estimate; thereafter it was also stratified by categories of intake per day
161 and by total intake of each of fruit, vegetable, green leafy vegetable and cabbage. Categories were
162 developed to maintain consistency across cohorts and so that comparisons could be easily made.
163 Categories for fruit and vegetables were <1.5, 1.5-2.4, 2.5-3.9 and ≥ 4 portions per day. For green
164 leafy vegetables and cabbage, the categories were <1.5, 1.5-2.4, 2.5-3.9 and ≥ 4 portions per week.
165 We computed both fixed effects models, and random effects models using the DerSimonian-Laird
166 method [20]. Due to substantial heterogeneity across cohort results as assessed with I^2 - and Q-
167 statistics, random effects estimates are reported as the main results, since random effects models
168 allow for variability of effects across individual studies.

169 **Results**

170 The number of diabetes cases at follow up across the cohorts was as follows (data not shown): NIH-
171 AAPP: 22,782; EPIC Elderly All: 1567; EPIC Elderly Spain: 138; EPIC Elderly Greece: 1077; EPIC Elderly
172 Netherlands: 234; and EPIC Elderly Sweden: 118. The characteristics of subjects in each of the
173 cohorts at baseline are presented in Table 1. EPIC Elderly Spain had a higher proportion of
174 individuals in the overweight BMI category, as well as in the moderately obese category. EPIC Elderly
175 Greece, however, had the highest proportion of individuals in the severely obese category. Although
176 the energy intakes (Kcal) were similar across the cohorts, EPIC Elderly Sweden had the lowest
177 intakes. EPIC Elderly Spain had the lowest number of individuals who engaged in vigorous physical
178 activity, while EPIC Elderly Netherlands had the highest proportion of individuals who said they did
179 vigorous activity.

180 The highest proportion of individuals who drank heavily were those of the EPIC Elderly Netherlands
181 cohort. They were also mostly women, with men only making up 5% of the cohort participants. The
182 NIH-AARP study had more highly educated subjects, and the highest number of former smokers.
183 EPIC Elderly Greece had the highest proportion of current smokers.

184 Intakes of fruit and vegetables, which were calculated in portions per day (for fruit and vegetable) or
185 per week (green leafy vegetables and cabbage) are also shown in Table 1. Intakes varied between
186 cohorts especially between subgroups of vegetables. For example, intakes of cabbage were lowest in
187 the EPIC Elderly Sweden and Spain cohorts. EPIC Elderly Greece had the highest intakes across all
188 four categories, across all cohorts, whereas EPIC Elderly Sweden had lowest number of individuals in
189 all four categories.

190 Median intakes and ORs (95% CI) for T2DM are presented in (Table 2) and (Table 3) for categories as
191 well as total intake per day (1 portion = 80g). Compared with the lowest category of intake, the
192 multivariate adjusted OR (Model B) of T2DM across categories of fruit showed a slightly reduced risk
193 of T2DM in the NIH-AARP study; OR: 0.95 (95%CI 0.91-0.99). This, however, was not the case in the

194 EPIC Elderly cohorts where no significant associations were found; for example, EPIC Elderly (all), OR:
195 1.01 (95%CI 0.80-1.28). Figure 1 shows the overall pooled multivariate odds ratio for T2DM
196 comparing the highest with the lowest fruit intakes across the NIH-AARP & EPIC Elderly cohorts. The
197 results show no overall association with the risk of T2DM, OR: 1.00 (95%CI 0.83-1.19). Across
198 categories of vegetable intake, there was no association with risk of T2DM across EPIC Elderly (all
199 and separately) after adjustments were made in Model B. A reduced risk of T2DM, comparing the
200 highest to the lowest category of vegetable intake, was apparent in NIH-AARP, OR: 0.92 (95%CI 0.87-
201 0.97). In the Spanish and Greek EPIC Elderly cohorts there were non-significant increases in risk of
202 T2DM, OR: 1.42 (95%CI 0.78-2.58) and OR: 2.15 (95%CI 0.93-5.03), respectively. Figure 2 shows the
203 pooled analysis for vegetable intake and T2DM risk. The pooled OR in Model B was 1.13 (95%CI 0.77-
204 1.64) indicating no overall association between vegetable intake and incident T2DM.

205 In the NIH-AARP cohort, green leafy vegetable intake was associated with a reduced risk of T2DM
206 which retained its significance in Model B, OR: 0.87 (95%CI 0.84-0.90). However the trends in the
207 EPIC Elderly cohorts were in the opposite direction, with an increase in the odds of developing T2DM
208 in those with the highest intakes of green leafy vegetables; EPIC Elderly All, OR: 1.23(95%CI 1.01-
209 1.50), and EPIC Elderly Greece, OR: 1.52 (1.13-2.04). Nevertheless, the pooled analysis, shown in
210 Figure 3, indicated no overall association between intake of green leafy vegetables and T2DM, OR:
211 1.08 (0.80, 1.46). Finally, when compared to the lowest category of intake, those with highest
212 cabbage intakes had a reduced risk of T2DM across the EPIC Elderly Netherlands cohort after
213 adjustments were made in Model B, OR: 0.61(95%CI 0.35-1.05), though the Confidence Limits could
214 not exclude the null value. In the analysis using the NIH-AARP study, there were also associations
215 found between cabbage intakes and incident T2DM, however these indicated a small increased risk
216 for T2DM , OR: 1.07(0.94-1.21). Thus overall, no association was found between cabbage intake and
217 incident T2DM (Figure 4), OR: 1.03 (95%CI 0.90, 1.18).

218 **Discussion**

219 Associations found between intakes of fruits, vegetables, green leafy vegetables and cabbage and
220 incident T2DM varied, as they showed both a reduced risk of T2DM as well as an increased risk
221 across these CHANCES cohorts. Nevertheless, although there was heterogeneity between cohorts,
222 the overall pooled results using multiple cohorts from different countries showed no association
223 with risk of incident T2DM. Being so large, the NIH AARP study has a major impact on our pooled
224 results so in a separate sensitivity analysis we pooled results for all EPIC Elderly cohorts excluding
225 NIH-AARP, which offered the following results per portion: for fruits OR: 1.07 (95%CI 0.77,1.49);
226 vegetables OR 1.49 (95%CI 0.94, 2.36); green leafy vegetables OR: 1.23 (95%CI 0.93, 1.62) and
227 cabbage OR: 0.90 (95%CI 0.66, 1.23), re-affirming the null associations.

228 Similar results have been shown in two meta-analyses [10, 21]. The systematic review by
229 Hamer & Chaida (2007) also included studies measuring antioxidant intake and incidence of T2DM in
230 a separate meta-analysis. The relative risk of T2DM from consuming five or more servings of fruit
231 and vegetables a day was 0.96 (95% CI, 0.79–1.17, $P=0.96$), and 1.01 (0.88–1.15, $P=0.88$) for three or
232 more servings of fruit, and 0.97 (0.86–1.10, $P=0.59$) for three or more servings of vegetables. The
233 authors concluded that the consumption of three or more servings a day of fruit or vegetables is not
234 associated with a reduction in the risk of T2DM. This was similar to the results by Wu et al (2015)
235 which showed that total fruit and vegetable consumption was not significantly associated with risk
236 of T2DM. However, significant heterogeneity was shown for the combined effects of fruit and
237 vegetables intake in the review by Hamer & Chaida (2007) [10, 21]. This was mostly due to the
238 substantially lower risk estimate among women reported by the study by Ford and Mokdad (2001)
239 [22]. Furthermore, showing somewhat different results, a meta-analysis carried out by Carter et al
240 (2010) included six cohort studies, four of which included information on green leafy vegetable
241 consumption. The pooled estimates showed no significant reduced risk from increasing the
242 consumption of vegetables, fruit, or fruit and vegetables combined, results which accord with those
243 in our current study. Nevertheless, the summary estimates from only four studies which assessed

244 green leafy vegetable consumption showed that greater intake of green leafy vegetables was
245 associated with a 14% reduction in risk of T2DM (hazard ratio 0.86, 95% confidence interval 0.77 to
246 0.97). A similar reduced risk for green leafy vegetables was also noted in two recent meta-analysis by
247 Li et al, 2014 [11] and Cooper et al, 2015 [23] . However, most of the studies included in the meta-
248 analysis included females only (4/6) and therefore the results may not be generalizable to a wider
249 population.

250 Several possible mechanisms have been proposed to explain the potential associations between
251 consuming more fruits and vegetables and green leafy vegetables in the diet, and the incidence of
252 T2DM. Fruit and vegetables are rich in fibre, which has been shown to improve insulin sensitivity and
253 insulin secretion [24], though not all studies have found consistent associations with risk of T2DM
254 [25]. On the other hand, many fruits are rich sources of fructose and fructose metabolism may
255 decrease insulin sensitivity and increase risk factors for metabolic syndrome and T2DM [26].

256 Increased intakes of fruit and vegetables have been shown to be inversely associated with obesity
257 [27], which in turn is one of the most established risk factors for T2DM development [28]. The
258 consumption of sugar sweetened fruit juices has also been positively associated with T2DM [29].

259 Green leafy vegetables confer antioxidant properties, which may mitigate T2DM risk through their
260 high concentrations of β carotene, polyphenols and vitamin C [30, 31]. Additionally, green leafy
261 vegetables could reduce the risk of T2DM due to their magnesium content, which has been shown to
262 play a role in glucose control and improving insulin sensitivity [32]. Furthermore they are particularly
263 rich in inorganic nitrate [33] which has been linked to improvement in reaction time in individuals
264 with T2DM [34]. Thus these various putative mechanisms do not point consistently towards a single
265 direction of effect for fruits and vegetable, making the inconsistent findings from observational
266 studies, in which dose and pattern of consumption are recorded with variable precision, hardly
267 surprising. It is also possible that other specific categories of fruit and vegetables are more closely
268 associated with diabetes risk than overall fruit and vegetable intake, however we were not able to
269 assess this in the current analysis. Intakes of fruit and vegetables are highly correlated with other

270 lifestyle and dietary factors, and so it is difficult to isolate the effect of these intakes on T2DM
271 independent of other factors. Consequently, when interpreting such disparate results, attempts
272 must be made to control for some of the important confounders across the cohorts.

273 Our study has specific strengths and limitations. The main strength was the ability to compare
274 cohorts from different countries which have harmonised the vast majority of variables using
275 individual participant data. However, high levels of heterogeneity were found for the leafy green
276 vegetable analysis ($I^2=79.3\%$, $p=0.002$) and differences in the classification of leafy green vegetables
277 may exist between cohorts. Although all data were harmonised based on agreed rules
278 (www.chancesfp7.eu; [16]), the data from the different cohorts are not perfectly comparable, due to
279 differences in study design and data collection procedures, with the potential for residual
280 inconsistencies in variable definitions. Although we made strenuous effort at harmonisation, the
281 dietary assessment methods used in these studies differed with, for example, the total number of
282 FFQ items differing across the cohorts and with EPIC elderly using more than one method (FFQ/24
283 hour diet recall). This may be a possible explanation for differences found across the cohorts.

284 Similarly, the strengths of the meta-analysis may also be weaknesses where the possibility of the
285 exposure is still heterogeneous for the same reason mentioned above. Individual study odds ratios
286 are presented in Figures 1-4 and show the effects that each study has on the pooled effect estimate.

287 Additionally, under-reporting and selective recall (of healthier foods) can be a problem with
288 unpredictable consequences since dietary constituents are not consumed in isolation. Although we
289 adjusted for several pertinent confounders, residual confounding from unmeasured risk factors
290 cannot be ruled out. We were unable, for example, to analyse dietary *patterns* and had this been
291 possible it may have shed additional light on the heterogeneity across cohorts, as in some countries
292 the consumption of vegetables by older people correlates highly with intakes of red meat [35] and
293 intakes of meat may be associated with diabetes risk [36]. A further consideration, which was not
294 possible to explore in this study, is the impact of different cooking methods and of the ways fruits

295 and vegetables are incorporated into meals, and the impact of both on overall micronutrient content
296 [37].

297 Imprecision arising from a single measurement of diet at baseline may also have introduced
298 some bias into this study, though classically this is often assumed to be towards the null [38]. In
299 addition to this, lack of corroboration that the outcome used in this analysis is T2DM, which was an
300 assumption made based on self-reported age of diagnosis, is a limitation of the study, though we do
301 not believe that the precision of outcome verification should be differentially associated with the
302 accuracy of any particular nutrient intake. Furthermore, the risk of under-ascertainment of diabetes
303 might be greater in people who don't visit their doctor very often and these are likely to be the
304 people on healthier diets. This would however not be an explanation of our lack of finding an inverse
305 association. Finally, although having a precise date of diagnosis for the cases ascertained in these
306 CHANCES cohorts would have been preferable, the essentially null findings suggest that a time-to-
307 event analysis may not have been particularly illuminating.

308 In summary, while there was some notable heterogeneity across cohorts, this study suggests
309 that in older subjects there was no overall association between fruit, vegetable, green leafy
310 vegetable, or cabbage and incident T2DM. Further studies are needed to assess these effects on
311 T2DM risk in older people.

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431

Table 1. Baseline characteristics of CHANCES participants

Baseline variables	CHANCES cohort					
	NIH-AARP	EPIC Elderly All	EPIC Elderly Spain	EPIC Elderly Greece	EPIC Elderly The Netherlands	EPIC Elderly Sweden
Total N	401909	20629	4309	7567	5786	2967
Mean follow up time of study (years)	10.6	11.8	13.1	10.0	12.6	13.3
Age at baseline ¹	62 ± 5	64 ± 4	63 ± 2	67 ± 5	64 ± 3	60 ± 1
BMI (Kg/m ²) ²						
Underweight	4,343 (1)	134 (0.65)	4 (0.09)	29 90.380	69 (1)	32 (1)
Normal	145,197 (37)	5,650 (27)	496(12)	1,292 (170)	2,518 (44)	1,344 (45)
Overweight	166,893 (43)	,850 (43)	2,041 (47)	3,184 (42)	2,412 (42)	1,213 (41)
Modestly obese	56,134 (14)	4,531 (22)	1,367 (32)	2,257 (30)	639 (11)	268 (9)
Severely obese	20,096 (5)	1,464 (7)	401 (9)	805 (11)	148 (3)	110 (4)
Vigorous Physical activity ²	186,334 (46)	5,080 (29)	222 (5)	1,603 (22)	3,255 (58)	na
Energy intake in Kcal ¹	1,822 ± 651	1,835 ± 583	2,036 ± 674	1,842 ± 586	1,772 ± 429	1,647 ± 600
Alcohol consumption/day ²						
0	88,022 (22)	5,771 (28)	1,722 (40)	2,479 (33)	1,197 (21)	373 (13)
1	274,779 (68)	13,031 (63)	1,987 (46)	4,690 (62)	3,701 (65)	2,593 (87)
2	19,638 (5)	1,257 (6)	344 (8)	243 (3)	669 (12)	1 (0.03)
3	19,470 (5)	570 (3)	256 (6)	155 (2)	159 (30)	-
Sex ²						
Male	231,259 (58)	6,394 (31)	1,858 (43)	2,873 (38)	263 (5)	1,400 (47)
Education ²						
Primary or less	2,592 (0.6)	14,071 (68)	3,674 (85)	6,883 (91)	1,896 (33)	1,618 (55)
More than primary	95,522 (24)	4,927 (24)	308 (7)	417 (6)	3,228 (56)	974 (33)
College or University	293,119 (73)	1,523 (7)	277 (6)	238 (3)	655 (11)	353 (12)
Smoking status ²						
Never	147,429 (37)	12,745 (62)	2,896 (67)	5,269 (70)	2,778 (48)	1,802 (61)
Former	190,969 (48)	4,475 (22)	676 (16)	1,230 (16)	1,960 (34)	609 (21)
Current	48,597 (12)	3,126 (15)	734 (17)	857 (11)	1,047 (18)	488 (16)
Fruits and Vegetables ³						
Fruits p/day	3.7 (2.1-5.9)	3.2 (1.9-4.7)	3.6 (2.3-5.7)	4.0 (2.9-5.3)	2.9 (1.6-3.9)	1.7 (0.9-2.9)
Vegetables p/day	3.2 (2.1-4.6)	2.4 (1.4-4.5)	2.5 (1.6-3.8)	4.8 (3.7-6.2)	1.6 (1.2-2.0)	0.7 (0.4-1.4)
Green leafy vegetables p/w	2.3 (0.9-4.8)	2.7 (1.2-5.0)	3.9 (1.7-7.7)	4.1 (2.5-6.2)	2.4 (1.4-3.5)	0.03 (0.01-0.3)
Cabbage p/w	0.3 (0.08-0.6)	1.2 (0.3-2.4)	0.1 (0.0-0.8)	1.9 (0.9-2.8)	1.7 (1.0-2.7)	0.2 (0.02-0.37)

Abbreviations: N: number, BMI: body mass index, kcal: kilocalorie, na: not available, p: portion, w: week. Exclusions: Age<50, History of Coronary Heart Disease, Cancer and Diabetes. Alcohol consumption/day= 0:non-drinker, 1: Light = men (>0g & <40g daily), women (>0g & <20g daily); 2: Moderate = men (≥40g & <60g daily), women (≥20g & <40g daily); 3: Heavy = men (≥60g daily), women (≥40g daily).

¹Mean and standard deviation

²Number and percentage

³Median and Interquartile range

Table 2. Association between Diabetes, fruits and vegetables in CHANCES participants

	Portions/day of fruit intake				P	Total intake 1 portion/day	Portions/day of vegetable intake				P	Total intake
	<1.5	1.5-2.4	2.5-3.9	≥4			<1.5	1.5-2.4	2.5-3.9	≥4		
NIH-AARP												
Median	0.82	1.99	3.24	7.73			1.04	2.02	3.20	6.41		
Model A ^a : OR (95% CI)	1.00 (Ref)	0.93(0.88-0.97)	0.86(0.82-0.89)	0.86(0.83-0.89)	<0.0	1.00(1.00-1.00)	1.00 (Ref)	0.91(0.87-0.95)	0.89(0.85-0.93)	0.98(0.93-1.02)	0.03	1.02(1.01-1.02)
Model B ^b : OR (95% CI)	1.00 (Ref)	0.96(0.91-1.02)	0.95(0.91-0.99)	0.95(0.91-0.99)	0.04	1.00(0.99-1.01)	1.00 (Ref)	0.92(0.87-0.97)	0.88(0.84-0.94)	0.92(0.87-0.97)	0.14	1.00(0.99-1.01)
EPIC Elderly (All)												
Median	0.87	1.89	3.18	5.3			0.97	1.9	3.18	5.5		
Model A ^a : OR (95% CI)	1.00 (Ref)	0.86(0.69-1.07)	0.96(0.79-1.16)	1.01(0.83-1.22)	0.24	1.01(0.98-1.04)	1.00 (Ref)	0.98(0.79-1.21)	1.19(0.95-1.51)	1.23(0.97-1.56)	0.05	1.03(0.99-1.06)
Model B ^b : OR (95% CI)	1.00 (Ref)	0.95(0.73-1.23)	1.01(0.80-1.28)	1.01(0.80-1.28)	0.88	1.00(0.97-1.03)	1.00 (Ref)	0.99(0.79-1.26)	1.11(0.86-1.45)	1.05(0.79-1.37)	0.72	0.99(0.96-1.03)
EPIC Elderly Spain												
Median	0.57	1.94	3.21	5.98			1.05	1.98	3.11	5.03		
Model A ^a : OR (95% CI)	1.00 (Ref)	1.59(0.82-3.13)	1.15(0.61-2.18)	1.47(0.82-2.63)	0.36	1.02(0.96-1.08)	1.00 (Ref)	1.76(1.04-2.96)	1.52(0.90-2.56)	1.35(0.76-2.37)	0.76	0.99(0.91-1.99)
Model B ^b : OR (95% CI)	1.00 (Ref)	1.83(0.91-3.67)	1.28(0.66-2.54)	1.75(0.94-3.26)	0.17	1.04(0.98-1.0)	1.00 (Ref)	1.89(1.10-3.26)	1.66(0.96-2.87)	1.42(0.78-2.58)	0.72	0.99(0.90-1.00)
EPIC Elderly Greece												
Median	1.06	2.08	3.28	5.29			1.15	2.12	3.39	5.61		
Model A ^a : OR (95% CI)	1.00 (Ref)	1.04(0.72-1.49)	1.08(0.78-1.49)	1.13(0.83-1.56)	0.24	1.01(0.98-1.04)	1.00 (Ref)	2.14(0.88-5.16)	2.62(1.14-6.07)	2.73(1.19-6.27)	0.05	1.03(0.99-1.07)
Model B ^b : OR (95% CI)	1.00 (Ref)	1.12(0.77-1.64)	1.09(0.77-1.54)	1.09(0.77-1.55)	0.88	1.00(0.96-1.04)	1.00 (Ref)	1.96(0.81-4.77)	2.29(0.99-5.36)	2.15(0.93-5.03)	0.72	0.99(0.95-1.04)
EPIC Elderly Netherlands												
Median	0.96	1.73	3.14	4.80			1.17	1.86	2.81	4.33		
Model A ^a : OR (95% CI)	1.00 (Ref)	0.59(0.39-0.88)	0.84(0.58-1.21)	0.73(0.49-1.09)	0.63	0.96(0.89-1.04)	1.00 (Ref)	0.80(0.6-1.06)	0.87(0.56-1.37)	0.71(0.09-5.33)	0.29	0.97(0.79-1.19)
Model B ^b : OR (95% CI)	1.00 (Ref)	0.57(0.37-0.88)	0.89(0.61-1.32)	0.73(0.48-1.12)	0.74	0.96(0.88-1.04)	1.00 (Ref)	0.72(0.54-0.98)	0.73(0.46-1.17)	0.92(0.12-7.12)	0.09	0.90(0.73-1.12)
EPIC Elderly Sweden												
Median	0.81	1.89	3.08	4.50			0.58	1.89	2.96	4.67		
Model A ^a : OR (95% CI)	1.00 (Ref)	0.78(0.49-1.27)	0.88(0.52-1.49)	1.21(0.68-2.16)	0.59	1.07(0.96-1.19)	1.00 (Ref)	0.75(0.41-1.39)	2.17(1.17-4.00)	0.53(0.07-3.92)	0.42	1.11(0.93-1.32)
Model B ^b : OR (95% CI)	1.00 (Ref)	0.72(0.43-1.19)	0.87(0.50-1.52)	1.16(0.62-2.15)	0.67	1.07(0.95-1.20)	1.00 (Ref)	0.68(0.35-1.29)	2.17(1.14-4.13)	0.46(0.06-3.46)	0.59	1.09(0.91-1.31)

Abbreviations: g: grams; OR: odds ratio; CI: confidence Intervals. ^aModel A: adjusted for sex and age. ^bModel B: adjusted for age, sex, BMI, physical activity, energy intake, alcohol consumption, education and smoking. P is for trend across categories.

Table 3. Association between Diabetes, green leafy vegetables and cabbage in CHANCES participants

	Portions/week of leafy green vegetables intake				P	Total intake 1 portion/day	Portions/week of cabbage intake				P	Total intake
	<1.5	1.5-2.4	2.5-3.9	≥4			<1.5	1.5-2.4	2.5-3.9	≥4		
NIH-AARP												
Median	0.65	1.98	3.10	8.06			0.32	1.63	3.90	9.79		
Model A ^a : OR (95% CI)	1.00 (Ref)	0.86(0.83-0.89)	0.81(0.77-0.85)	0.82(0.79-0.85)	<0.01	0.98(0.98-0.98)	1.00 (Ref)	1.09(1.05-1.15)	1.24(1.16-1.33)	1.19(1.06-1.33)	<0.01	1.04(1.03-1.05)
Model B ^b : OR (95% CI)	1.00 (Ref)	0.90(0.86-0.94)	0.89(0.85-0.94)	0.87(0.84-0.90)	<0.01	0.98(0.98-0.99)	1.00 (Ref)	1.06(1.01-1.12)	1.09(1.00-1.18)	1.07(0.94-1.21)	<0.01	1.02(1.01-1.03)
EPIC Elderly (All)												
Median	0.32	2.04	3.14	6.18			0.37	1.99	3.07	4.96		
Model A ^a : OR (95% CI)	1.00 (Ref)	1.11(0.89-1.38)	1.28(1.05-1.57)	1.30(1.09-1.59)	<0.01	1.02(0.99-1.03)	1.00 (Ref)	0.94(0.82-1.09)	1.16(1.00-1.34)	0.98(0.80-1.19)	0.02	1.00(0.97-1.04)
Model B ^b : OR (95% CI)	1.00 (Ref)	1.09(0.87-1.37)	1.25(1.01-1.53)	1.23(1.01-1.50)	0.02	1.00(0.99-1.02)	1.00 (Ref)	0.89(0.76-1.04)	1.09(0.94-1.27)	0.96(0.77-1.19)	0.15	0.99(0.94-1.03)
EPIC Elderly Spain												
Median	0.55	1.93	3.14	7.66			0	2.11	2.93	4.95		
Model A ^a : OR (95% CI)	1.00 (Ref)	1.77(1.01-3.14)	1.28(0.73-2.24)	1.02(0.64-1.62)	0.44	0.98(0.95-1.02)	1.00 (Ref)	0.79(0.38-1.63)	0.96(0.38-2.39)	0.79(0.37-1.73)	0.49	0.94(0.83-1.06)
Model B ^b : OR (95% CI)	1.00 (Ref)	1.74(0.97-3.11)	1.39(0.79-2.47)	1.04(0.64-1.68)	0.52	0.98(0.95-1.01)	1.00 (Ref)	0.86(0.41-1.78)	0.96(0.38-2.40)	0.80(0.37-1.75)	0.54	0.95(0.84-1.07)
EPIC Elderly Greece												
Median	0.87	2.13	3.13	6.18			0.84	2.06	3.06	4.88		
Model A ^a : OR (95% CI)	1.00 (Ref)	1.26(0.92-1.72)	1.57(1.18-2.11)	1.61(1.22-2.12)	<0.01	1.03(1.01-1.05)	1.00 (Ref)	0.99(0.83-1.18)	1.28(1.09-1.51)	1.14(0.90-1.43)	0.02	1.03(0.99-1.07)
Model B ^b : OR (95% CI)	1.00 (Ref)	1.23(0.89-1.71)	1.55(1.14-2.11)	1.52(1.13-2.04)	0.02	1.02(0.99-1.04)	1.00 (Ref)	0.93(0.77-1.11)	1.21(1.07-1.44)	1.09(0.85-1.41)	0.15	1.02(0.98-1.07)
EPIC Elderly Netherlands												
Median	0.97	1.99	3.14	4.95			0.92	1.92	3.08	4.97		
Model A ^a : OR (95% CI)	1.00 (Ref)	0.88(0.61-1.29)	0.99(0.65-1.33)	1.13(0.77-1.68)	0.49	1.05(0.97-1.14)	1.00 (Ref)	0.82(0.59-1.12)	0.74(0.51-1.08)	0.57(0.33-0.97)	0.01	0.86(0.79-0.96)
Model B ^b : OR (95% CI)	1.00 (Ref)	0.89(0.61-1.31)	0.87(0.60-1.26)	1.03(0.69-1.54)	0.86	1.02(0.94-1.10)	1.00 (Ref)	0.81(0.58-1.11)	0.79(0.54-1.16)	0.61(0.35-1.05)	0.04	0.87(0.78-0.97)
EPIC Elderly Sweden												
Median	0.03	1.77	3.52	7.04			0.17	1.88	3.75	5.25		
Model A ^a : OR (95% CI)	1.00 (Ref)	0.88(0.12-6.56)	2.86(0.52-9.60)	-	0.60	1.12(0.89-1.42)	1.00 (Ref)	0.85(0.27-2.75)	1.50(0.68-3.31)	0.67(0.09-4.90)	0.73	1.07(0.92-1.23)
Model B ^b : OR (95% CI)	1.00 (Ref)	0.76(0.09-5.86)	2.98(0.85-10.4)	-	0.67	1.12(0.87-1.43)	1.00 (Ref)	0.77(0.23-2.59)	1.53(0.68-3.48)	0.76(0.10-5.71)	0.69	1.04(0.90-1.21)

Abbreviations: g: grams; OR: odds ratio; CI: confidence Intervals. ^aModel A: adjusted for sex and age. ^bModel B: adjusted for age, sex, BMI, physical activity, energy intake, alcohol consumption, education and smoking. P is for trend across categories.



