



## Avocado consumption is associated with a reduction in hypertension incidence in Mexican women

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### Abstract

Avocado is a fruit rich in dietary fibre, potassium, Mg, mono and PUFA and bioactive phytochemicals, which are nutritional components that have been associated with cardiovascular health. Yet, despite the boom in avocado consumption, we lack evidence on its association with CVD risk in the general population. To estimate the prospective association between avocado consumption and incident hypertension in Mexican women, we estimated the association in participants from the Mexican Teachers' Cohort who were  $\geq 25$  years, free of hypertension, CVD and cancer at baseline ( $n$  67 383). We assessed baseline avocado consumption with a semi-quantitative FFQ (never to six or more times per week). Incident hypertension cases were identified if participants self-reported a diagnosis and receiving treatment. To assess the relation between categories of avocado consumption (lowest as reference) and incident hypertension, we estimated incidence rate ratios (IRR) and 95 % CI using Poisson regression models and adjusting for confounding. We identified 4002 incident cases of hypertension during a total of 158 706 person-years for a median follow-up of 2.2 years. The incidence rate of hypertension was 25.1 cases per 1000 person-years. Median avocado consumption was 1.0 (interquartile range: 0.23, 1.0) serving per week (half an avocado). After adjustment for confounding, consuming 5 + servings per week of avocado was associated with a 17 % decrease in the rate of hypertension, compared with non- or low consumers (IRR = 0.83; 95 % CI: 0.70, 0.99;  $P_{\text{trend}} = 0.01$ ). Frequent consumption of avocado was associated with a lower incidence of hypertension.

**Key words:** Avocado: Diet: Hypertension: Low- and middle-income countries: Mexican women

Avocado is a widely accepted fruit, and its availability is increasing worldwide<sup>(1)</sup>. This fruit is rich in dietary fibre, potassium, Mg, mono (MUFA) and PUFA and bioactive phytochemicals, which contribute to cardiovascular and metabolic health<sup>(2)</sup>. In the USA alone, demand has tripled over the past two decades<sup>(3)</sup>, and Mexico is the country with the highest avocado consumption (7.2 kg per capita)<sup>(4)</sup> where it has been consumed for centuries<sup>(5)</sup>. Yet, despite the boom in avocado consumption, we lack evidence on its association with CVD risk in the general population<sup>(2,6,7,8)</sup>.

Globally, hypertension is an important modifiable risk factor (its effect can be modified) for CVD and premature death<sup>(9)</sup>. The absolute burden and prevalence of hypertension are increasing worldwide, particularly in low- and middle-income countries<sup>(10)</sup>.

Therefore, effective primary prevention strategies are urgently needed to relieve the growing burden of hypertension. Mexico is the ideal population to evaluate the association between avocado intake and health, as avocado consumption is not a marker of a healthy lifestyle, as opposed to other populations, because avocado it is widely accepted and consumed in our population<sup>(4)</sup>. Furthermore, the distribution of avocado consumption in Mexicans is wide<sup>(4)</sup>.

Among the various preventive strategies to reduce the burden of hypertension, lifestyle modifications, particularly a healthy diet, have gained interest. It is well documented that diet plays an important role in disease and mortality prevention (e.g. CVD, diabetes and cancer)<sup>(11–15)</sup>. Thus, the objective of the present study was to assess the association between avocado

**Abbreviations:** HEI-2015, Healthy Eating Index 2015; IRR, incidence rate ratios; MTC, Mexican Teachers Cohort.

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consumption and hypertension incidence in Mexican women participating in the Mexican Teachers Cohort (MTC).

## Methods

### Study population

In 2006 and 2008, the MTC was established. This study includes 115 312 female teachers from twelve states in Mexico. Details of the cohort's characteristics have been previously reported<sup>(16)</sup>. Briefly, the MTC had two recruiting phases. The first phase began in 2006 with 27 979 teachers from two states: Jalisco and Veracruz. Participants responded to a baseline questionnaire concerning socio-demographic characteristics, reproductive history, lifestyle (e.g. physical activity and tobacco use) and diet, as well as medical conditions. The second phase began in 2008–2010 when we recruited an additional 87 334 teachers from ten other states and were asked to answer the baseline questionnaire as well. Follow-up questionnaires were distributed every 3–4 years to update information on medical conditions and risk factors (e.g. lifestyle factors). In this study, we used the first follow-up cycle in 2011–2013, with an 83% response rate.

In the current analysis, we excluded women with prevalent hypertension ( $n$  13 340). We then excluded participants with implausible energy intake ( $500 > \text{kcal} > 3500$  ( $n$  9679))<sup>(17)</sup> or an incomplete semi-quantitative FFQ (responded to  $\leq 50\%$  of items ( $n$  3598) and/or empty staple section ( $n$  4654)). We also excluded women with myocardial infarction, stroke or cancer ( $n$  2036) and pregnant women at baseline ( $n$  1080) because these conditions may result in changes in diet. Participants who did not respond to the follow-up questionnaire were also excluded ( $n$  13 543). The final analytical sample included 67 383 participants.

The present study was developed and performed according to the Declaration of Helsinki guidelines. The Research, Ethics, and Biosecurity Committee at the National Institute of Public Health (INSP, by its Spanish acronym) evaluated and approved the study protocol and informed consent forms. Additionally, we obtained written informed consent from all women.

### Dietary assessment

We collected dietary information with a 140-item semi-quantitative FFQ, previously validated among women in Mexico City<sup>(18)</sup>. Over a 1-year period, they obtained four 4-d 24-h recalls, corresponding to 16 d of diet recall in batches of 4 d to account for all seasons. Pearson correlation coefficients for total energy, carbohydrate, protein and total fat intakes between the FFQ and 24-h dietary recalls were fairly strong, 0.52, 0.57, 0.32 and 0.63, respectively. Participants reported the average frequency of consumption over the previous year of each food item in a commonly used unit or portion size, which we converted to daily intake values. The consumption frequencies ranged from never, once a month or less, two to three times a month, once a week, two to four times a week, five to six times a week, once a day, two to three times a day, four to five times a day and six or more times a day. In the FFQ, we asked participants the frequency of consumption of half an avocado. We defined a serving of

avocado as consumption of half an avocado (defined following the serving size reported by the National Health and Nutrition Examination Survey)<sup>(2)</sup>. Nutrient and energy intake per day was calculated by multiplying the nutrient and energy content of the specified pre-defined portion sizes by the reported daily intake value using the USA Department of Agriculture food-composition database<sup>(19)</sup>, which was complemented with a database used in the National Health and Nutrition Survey (ENSANUT, by its Spanish acronym) in Mexico (personal communication).

### Hypertension assessment

In both the baseline and follow-up questionnaires, we asked participants to report whether a clinician had made a diagnosis of elevated blood pressure in the previous years, if they received treatment and the year of diagnosis. We defined an incident case of hypertension when participants reported having a diagnosis and undergoing treatment. We evaluated the validity of self-reported hypertension diagnosis in a random subsample of 101 participants who reported having elevated blood pressure, using a structured phone interview in which we confirmed the diagnosis, treatment and year of diagnosis. We confirmed the presence of hypertension in 79% of participants who had previously reported having a diagnosis of elevated blood pressure and being under treatment (positive predictive value: 79%; 95% CI 65, 90%) (moderately high)<sup>(20)</sup>.

### Covariates

We defined covariates by using self-reported information from the baseline (2006–2008) questionnaire. We used internet access at home and the type of insurance women used for serious conditions (public, private or other) as proxies for socio-economic status<sup>(21)</sup>. We defined ethnicity as whether or not women or her parents spoke an indigenous language. We defined menopause using an algorithm that considered post-menopausal status if they had 1) no menstruation over the past 12 months prior or 2) surgical menopause (reported oophorectomy) or were over 51 years old, given that over 90% of women in the cohort have reached menopause at age 51. If they stopped menstruating because of a hysterectomy, chemotherapy or radiation, menopausal status was classified as unknown. We defined family history of hypertension as self-reported hypertension diagnosis in parents, siblings or children. We defined type 2 diabetes as self-reported diagnosis undergoing treatment. We categorised smoking status as current, ever, never or unknown status. We categorised physical activity into tertiles of total metabolic equivalent of task based on self-reported multiple-choice frequencies of different activities per week. The correlation between the MTC questionnaire and the International Physical Activity Questionnaire<sup>(22)</sup> was 0.64 for moderate and vigorous physical activity (Pearson correlation coefficients: 0.64 (95% CI: 0.54, 0.97); intraclass correlation coefficient: 0.77 (95% CI: 0.64, 0.86)) (personal communication). We calculated BMI by dividing self-reported weight in kg by squared height in metres and categorised BMI into normal weight ( $< 25.0 \text{ kg/m}^2$ ), overweight ( $25.0\text{--}30.0 \text{ kg/m}^2$ ), obesity ( $\geq 30.0 \text{ kg/m}^2$ ) and missing. We categorised multivitamin use during the last year as a yes/no question. Finally, we calculated total energy intake and assessed diet quality with the Healthy Eating Index 2015 (HEI-2015). Details on the

development, scoring and components can be accessed in the National Institutes of Health's research resources<sup>(23)</sup>. Briefly, a score for each component of the HEI-2015 is calculated based on the frequency of consumption of the item or items in that component in the FFQ. The HEI-2015 contains thirteen components and sums 100 points (maximum score). Each component is scored on a density basis out of 1000 calories, except fatty acids, which is the ratio of unsaturated to SFA. We took avocado out from the calculation to get a HEI-2015 score without avocado. The validity of the HEI-2015 score has been discussed elsewhere, a study which included Hispanics<sup>(24)</sup>.

### Statistical analyses

We summarised continuous and categorical variables as means  $\pm$  standard deviation (SD) or median and interquartile range and percentages, respectively. We categorised responses to avocado consumption (servings) into never or  $\leq 1$  per month, 2–3 times per month, once a week, 2–4 times per week and 5 or more times per week. We used the lowest (never or  $\leq 1$  per month) category as a reference.

To calculate each participant's person-time, we used the date of response in the baseline questionnaire and either the date of diagnosis of hypertension or the response date from the last follow-up questionnaire. We imputed the date of diagnosis to the midpoint between the date of response to the last questionnaire when they reported being free of hypertension and the date of response to the last follow-up questionnaire where they self-reported a hypertension diagnosis. We estimated age-adjusted and multivariable-adjusted incidence rate ratios (IRR) and 95% CI using Poisson regression models with an offset equal to the natural logarithm of person-time<sup>(25)</sup>. To test for linear trend using the Wald test, we created a continuous variable equal to the value of each category of avocado consumption and the median value for the 5+/day category.

We selected confounders using previous knowledge on biological mechanisms and risk factors for avocado consumption and hypertension<sup>(26)</sup>. In the multivariable models we adjusted first for age (continuous); then for internet access (%), insurance for serious conditions (public, private, other), ethnicity (%), menopausal status (premenopausal, postmenopausal and unknown), family history of hypertension (%), smoking status (current, ever, never, unknown), physical activity (tertiles). We then added BMI status (normal, overweight, obesity, unknown) because we considered BMI a strong confounder of the association since BMI status could influence how much avocado a person consumes and BMI is a risk factor for hypertension. Afterwards, we added multivitamin supplementation (%) to control for a potential threshold effect of micronutrients (e.g. potassium and Mg), total energy intake (continuous) and the HEI-2015 score (continuous). We did not adjust for type 2 diabetes diagnosis in our main model because this disease can be both, a confounder and a mediator in the causal pathway. However, we added this covariate in a separate model. For missing variables on BMI and smoking status, we created a missing indicator category (8.7% and 3.0%, respectively)<sup>(27)</sup>. We also calculated the E-value to estimate the minimum strength of association that an unmeasured confounder would need to have with

both, avocado consumption and hypertension, conditional on the measured covariates, to fully explain away the observed association<sup>(28,29)</sup>.

We also conducted several sensitivity analyses. First, we used a broader definition of the outcome, where we defined an incident hypertension case as having responded to any one of the three questions on high blood pressure described previously. This analysis was carried out considering that some participants could have been diagnosed but are either not treated<sup>(30)</sup>, not aware of taking medication or omitted certain questions on the questionnaire. Second, we ran two different analyses as another way to assess confounding (unmeasured and residual). (1) We ran the analysis among women without type 2 diabetes, since it may be a confounder in the association between avocado consumption and incident hypertension<sup>(31)</sup>. (2) We explored whether the association between avocado consumption and incident hypertension was due to avocado being a marker of a healthy diet and/or a healthy lifestyle. Thus, we ran the analysis excluding participants with the highest tertile of a 'healthy lifestyle score', composed of four proxies for a healthy lifestyle. The components were physical activity, diet quality, weight and smoking status. For each component, participants would score a point if they were normal weight ( $< 25 \text{ kg/m}^2$ ), never smokers, in the highest tertile of physical activity and/or in the highest tertile of the HEI-2015 score. The total 'healthy lifestyle score' ranged from 0 to 4. We assumed that participants had a 'true' healthy lifestyle if they scored in the highest tertile of this score. However, since type 2 diabetes, BMI and a healthy diet and/or lifestyle could be mediators in the causal pathway between avocado consumption and hypertension, stratifying analyses by these variables could have induced selection bias. We also stratified for a 'healthy diet', defined as those who scored in the highest tertile of the HEI-2015 score. Finally, we ran another analysis using a food substitution model ( $\log(b(t; x)) = \log(b_0(t)) + \delta_1 \text{food}_{1(\text{avocado})} + \delta_2 \text{food}_{2(\text{added fats})} + \delta_3 \text{food}_{3(\text{other foods})} + \delta_4 \text{total energy intake} + \alpha_3 \text{covariates}$ ) instead of a non-specified food substitution model ( $\log(b(t; x)) = \log(b_0(t)) + \alpha_1 \text{food}_{1(\text{avocado})} + \alpha_2 \text{total energy intake} + \alpha_3 \text{covariates}$ )<sup>(32)</sup>. We modelled the substitution of 161 kcal of added fats (cream, margarine or butter) for the same amount of avocado (161 kcal =  $\frac{1}{2}$  avocado), adjusting only for those foods which could be confounders of the substitution of avocado and added fats (red meat, processed meats, fast foods and fruits and vegetables). This model was adjusted for age, internet access, insurance for serious conditions, ethnicity, menopausal status, family history of hypertension, smoking status, physical activity (tertiles), BMI, energy intake and multivitamin intake.

We used the Statistical Analysis System statistical software package version 9.4 (SAS Institute Inc.) to perform all analyses.

### Results

We followed a total of 67 383 teachers for a median 2.2 years (interquartile range: 1.8, 2.3) and a total of 158 706 person-years. We identified 4002 incident cases of hypertension with an incidence rate of 25.2 cases per 1000 person-years.



Participants had a mean age of  $41.9 \pm 7.1$  years and a mean BMI of  $26.9 \pm 4.4$  kg/m<sup>2</sup>. The median avocado consumption was one (interquartile range: 0.23, 1.0) serving per week or half an avocado per week. Women with a higher consumption of avocado were less likely to be obese and current smokers and more likely to have internet access at home, consume multivitamins, be physically active and have a higher diet quality as per the HEI (Table 1). The mean age and energy-adjusted contribution of MUFA and fibre were higher in those who consumed more avocado compared with those who consumed less avocado. Potassium and Mg intake were higher in those with the highest intake of avocado. (online Supplementary Table 1).

Crude incidence rates for extreme categories of avocado consumption were 26.7 (never or 1 month) and 24.3 (5 + servings per week) cases of hypertension per 1000 person-years. When comparing age-adjusted extreme categories of avocado consumption, a higher avocado consumption was associated with a 14% lower rate of hypertension (IRR = 0.86; 95% CI: 0.79, 0.94; *P*-trend = 0.003). After adjusting for covariates, consuming 5 + servings per week of avocado was associated with a 17% decrease in the rate of hypertension compared with non- or low-consumers (IRR = 0.83; 95% CI: 0.70, 0.99; *P*-trend = 0.01) (Table 2).

The minimum strength of the association that an unmeasured confounder would need to have with both the exposure and the outcome (E-value) to explain away the observed association was 1.70, and the lower limit for the CI was 1.11. We considered type 2 diabetes as a mediator in the association between avocado consumption and the incidence of hypertension. However, running the models with type 2 diabetes diagnosis as a covariate did not change the main result (IRR = 0.83; 95% CI: 0.70, 0.99; *P*-trend: 0.01) (data not shown).

As a sensitivity analysis, we ran the analysis on a different definition for hypertension. When comparing age-adjusted extreme categories of avocado consumption, results were slightly strengthened (IRR = 0.81; 95% CI: 0.71, 0.92; *P*-trend < 0.0001) (online Supplementary Table 2). We also explored two different ways to adjust for potential unmeasured or residual confounding. First, we ran the analysis among women without type 2 diabetes, and results remained similar to the main analysis (IRR = 0.83; 95% CI: 0.69, 0.99; *P*-trend 0.01). Second, we assessed whether the association between avocado consumption and incident hypertension was due to avocado being a marker of a healthy lifestyle. Thus, we ran the analysis in participants with a low healthy lifestyle score (excluding the highest tertile of the healthy lifestyle score), which did not change the main results; we also stratified by a 'healthy diet' (T1 & 2 *v.* T3 of HEI-2015) and results were consistent with the main analysis (online Supplementary Table 3).

Finally, we ran a food substitution model in which 161 kcal of added fats such as cream, margarine or butter substituted avocado. We found that none of these substitutions were associated with incidence of hypertension: IRR Cream = 1.03 (95% CI 0.95, 1.12), IRR Margarine = 0.97 (95% CI 0.88, 1.06) and IRR = butter 0.97 (95% CI 0.89, 1.05) (Fig. 1). We believe the protective effect of avocado on hypertension is given by the other substitutions not specified when adjusting for energy, shown on Table 2.

## Discussion

In the present prospective cohort study of Mexican women, we found that a higher avocado consumption was associated with a lower rate of hypertension.

Several animal and small clinical trials have shown the health benefits of avocado consumption<sup>(6,7,33,34)</sup>. In a previous study in hypertensive rats, avocado oil decreased diastolic and systolic blood pressure by 21.2% and 15.5%, respectively<sup>(33)</sup>. A randomised clinical trial compared three diets on lipid risk factors in overweight and obese individuals: (a) low fat, (b) moderate fat and (c) moderate fat with one avocado per day. The avocado per day diet compared with low fat and moderate fat diets reduced LDL-cholesterol, non-high-density lipoprotein cholesterol (non-HDL-cholesterol), LDL-cholesterol particle number, small dense LDL-cholesterol and the ratio of LDL-cholesterol/HDL-cholesterol<sup>(6)</sup>. Another randomised clinical trial on overweight and obese participants which assessed the effects of replacing carbohydrate energy with avocado on postprandial indices of metabolic and vascular health also found improvement in endothelial function and lipid profile<sup>(7)</sup>, which could be related to better cardiovascular health. More recently, another randomised clinical trial showed the effect of consuming one avocado per day *v.* an isoenergetic diet on reduced abdominal fat<sup>(34)</sup>. Observational studies have also shown avocado's health benefits. Avocado consumption has been associated with a diet with a healthier nutrient profile in National Health and Nutrition Examination Survey<sup>(2)</sup>. A recent observational study also found an association between avocado consumption and CVD: two or more servings/week were associated with 16% lower risk of CVD<sup>(8)</sup>. This study also found that substituting 40 g of several foods with 40 g of avocado was associated with 16–22% lower risk of CVD. Contrary to this study, we did not find an association between substituting 161 kcal of cream, butter or margarine with the equivalent amount of avocado and hypertension. We carefully selected the foods which would be natural substitutes of avocado in this population and carefully chose to model kcal instead of grams/servings so as to not have confusion due to residual energy<sup>(32)</sup>.

Many FFQ used in prospective cohort studies based in the USA do not contain avocados as an item. This is one of the reasons why there have been so few epidemiologic studies on avocados and chronic disease risk. Also, randomised clinical trials are done in a carefully selected population, which is why future studies need to address this. Nutritional epidemiologists have long tried to find the best way to study how diet affects health in order to advise the public which foods to prefer or avoid, sometimes without success. Our findings suggest that consuming 2.5+ (whole) avocados per week reduces hypertension by 17% compared with non- or low consumers. Similar to the National Health and Nutrition Examination Survey study<sup>(2)</sup>, MTC participants who consumed more avocado, compared with non- or low-consumers, also had a higher fibre and fat intake (%kcal/d). Total fat intake was driven by MUFA consumption.

Multiple mechanisms have described the possible protective effect of avocado against hypertension, including its antioxidant capacity<sup>(1)</sup> and its improvement of the lipid profile<sup>(1)</sup>. Also, avocados are rich in dietary fibre (4.6 g/half an avocado)<sup>(35)</sup>, potassium,



**Table 1.** Age-Standardised characteristics of 67 383 mexican women from the Mexican teachers' cohort at baseline by categories of avocado consumption frequency\*,‡

	Avocado consumption, frequency of consumption of half an avocado														
	Never or ≤ 1/month (n 16 992)			2–3 month (n 16 294)			1 week (n 17 275)			2–4 week (n 12 700)			5+ week (n 4122)		
	%	Mean	SD	%	Mean	SD	%	Mean	SD	%	Mean	SD	%	Mean	SD
Added fats intake, servings		1.9	2.5		2.1	2.6		2.4	2.7		2.7	3.1		2.8	3.6
Age, years†		41.5	7.1		41.4	7.1		42.1	7.1		42.7	7.0		43.1	7.3
BMI, kg/m <sup>2</sup>		27.3	4.6		27.0	4.5		26.9	4.3		26.6	4.3		26.5	4.3
BMI, categories															
Normal weight, %	30.8			33.3			34.2			36.7			38.1		
Overweight, %	38.0			38.4			38.7			37.6			36.5		
Obese, %	21.8			19.8			18.7			17.1			16.8		
Unknown, %	9.4			8.5			8.4			8.6			8.6		
Insurance – serious condition															
Social Security, %	69.9			70.6			71.1			69.6			69.3		
Private, %	18.8			17.9			17.5			18.1			18.1		
Other, %	11.3			11.5			11.4			12.3			12.7		
Internet use, %	44.7			47.9			50			53.8			56.6		
Family history of hypertension, %	53.9			53.6			54			54.6			53.4		
Type 2 Diabetes, %	3.1			2.8			2.9			2.5			2.8		
Hypercholesterolemia, %	9.8			9.3			9.4			9.7			9.4		
Menopausal status															
Premenopausal, %	77.0			78			78.5			78.2			77.9		
Postmenopausal, %	13.4			13.5			13.2			13.3			13.1		
Unknown, %	9.6			8.6			8.3			8.5			9.1		
Multivitamin intake, %	29.2			29.9			31.4			33.5			34.2		
Smoking, categories															
Current smoker, %	9.5			9.6			9.1			8.7			9.4		
Past smoker, %	11.6			11.3			11.3			11.3			12.6		
Never smoker, %	75.2			76.4			76.6			77.1			75.5		
Unknown, %	3.6			2.7			3			2.9			2.5		
Physical Activity, MET/week															
Low activity, %	36.7			33.1			30.8			27.4			27.5		
Medium activity, %	33.5			34.8			34.5			34.1			33		
High activity, %	29.8			32.2			34.7			38.5			39.5		
Total energy, kcal/d		1593	603		1680	581		1870	580		2056	588		2324	609
Healthy eating index score		66.7	9.9		68.3	9.2		69.4	8.8		71.0	8.6		72.5	9.1

\* Values are mean ± SD for continuous variables and percent for categorical variables. Values are age standardised to the age distribution of the study population. Values of categorical variables may not add up to 100 % due to rounding. We assessed avocado and added fats consumption as servings per week. We defined one serving as ½ an avocado and one serving of added fats (cream, margarine and butter) as 15 g.

† Variable is not age adjusted.

‡ MET, Metabolic equivalents.

**Table 2.** Multivariable adjusted incidence rate ratios (95 % confidence interval) of incident hypertension by avocado consumption frequency in 67 383 women from the Mexican teachers' cohort study\*

Model	Never or ≤ 1/ month (n 16 992)	2–3 month (n 16 294)		1 week (n 17 275)		2–4 week (n 12 700)		5+ week (n 4122)		P-Trend
		Incidence Rate Ratio	95 % CI	Incidence Rate Ratio	95 % CI	Incidence Rate Ratio	95 % CI	Incidence Rate Ratio	95 % CI	
Cases	1067	953		1008		735		239		
Person-years	40 010	38 244		40 556		30 069		9827		
Age adjusted†	Reference	0.94	0.83, 1.07	0.91	0.80, 1.04	0.87	0.77, 1.00	0.85	0.72, 1.01	0.01
Multivariable‡	Reference	0.94	0.83, 1.07	0.91	0.80, 1.04	0.88	0.77, 1.01	0.87	0.74, 1.03	0.03
+ BMI status§	Reference	0.96	0.84, 1.09	0.93	0.82, 1.06	0.92	0.81, 1.05	0.92	0.78, 1.09	0.19
+ Diet	Reference	0.95	0.84, 1.08	0.91	0.80, 1.03	0.87	0.76, 0.99	0.83	0.70, 0.99	0.01

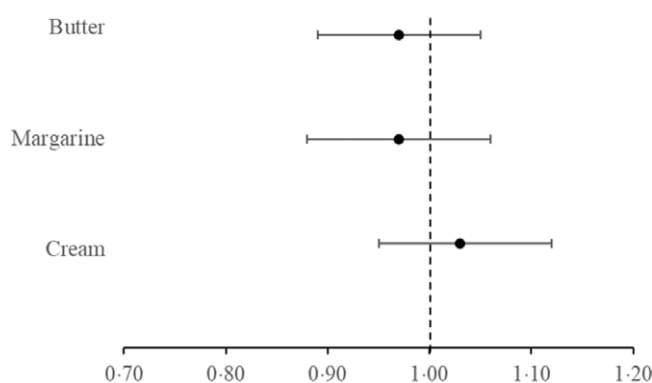
\* We assessed avocado consumption as servings per week and defined one serving as ½ an avocado.

† Age-adjusted model: age adjusted (continuous).

‡ Multivariable: previous plus smoking (never, ever, current, missing), indigenous (yes/no), internet at home (yes/no), insurance (private, public, other), family history of hypertension (yes/no), menopause (pre, post, unknown) and physical activity (continuous).

§ Multivariable: previous plus BMI status (normal weight, overweight and obese, missing).

|| Multivariable: previous plus total energy intake (continuous) + Healthy Eating Index score (continuous) and multivitamin intake (yes/no).



**Fig. 1.** Multivariable adjusted incidence rate ratios (95 % CI) of incident hypertension in 67 383 women from the Mexican Teachers' Cohort study: substitution analyses of added fats: cream, margarine and butter for avocado.

Mg, phytosterols and MUFA (~10%), such as oleic fatty acids, which have been associated with a healthy blood lipid profile and cardiovascular health<sup>(1)</sup>. In this study, the contribution of avocado to these nutrients was 35.4% (first contributor) campesterol, 30% (1st contributor) stigmaterol, 6.0% (second contributor) to total MUFA, 2.9% (8th contributor) of total dietary fibre, 2% (14th contributor) potassium and 1.0% (33rd contributor) to Mg. Studies have shown that dietary fibre (Dietary Reference Intake for adult women: 25 g/d)<sup>(36)</sup> is associated with lower cardiovascular risk factors, including lower blood pressure or hypertension risk<sup>(37,38)</sup>. Avocado's high potassium and Mg content may also contribute to lowering blood pressure<sup>(39–41)</sup>. Additionally, phytosterols may promote cardiovascular health in moderate doses by eating a healthy diet through altering the cholesterol metabolism<sup>(42)</sup>. Finally, a recent meta-analysis showed that supplementation with phytosterol supplementation, via different spreads and drinks, decreased both systolic blood pressure and decreased diastolic in patients with hypercholesterolaemia (≥ 2000 mg for systolic blood pressure and < 2000 mg for decreased diastolic)<sup>(43)</sup>. While the phytosterol content of avocados is higher than in other fruits and vegetables (57 v. 3 mg/d)<sup>(1)</sup>, it is lower than most supplementation doses used in these trials (100–4000 mg/d)<sup>(43)</sup>.

This study has several strengths. It is a population-based cohort, with a prospective design and a large sample size, there are available data on known risk factors for hypertension. Nevertheless, our study also has some limitations: hypertension cases were self-reported; however, other cohort studies have used a self-reported diagnosis of hypertension, and it has been found to be valid in Hispanics<sup>(44,45)</sup>. In our study, while we had a moderately high positive-predictive value of the self-report, measurement error could still be possible. Nonetheless, this error is likely to be non-differential since the exposure was assessed before the outcome; and when running the analysis on a broader definition of hypertension, results were consistent. The exposure (avocado consumption) was assessed through a validated FFQ. However, the validation was done at the nutrient level and not for single food items. In other FFQ used in different Latin America, fruits and vegetables have shown to have a high percentage of exact agreement in quantile categorisation in comparison to multiple 24 h dietary recalls<sup>(46,47)</sup>. Yet, non-differential misclassification of the exposure cannot be ruled out. Our median follow-up was 2.2 years, which limits our conclusions for long-term effects of avocado consumption on hypertension incidence. We also had ~17% loss to follow-up, which

may have introduced selection bias. Thus, we compared the baseline characteristics of women that were part of our study population and those lost to follow-up and found that the two groups were slightly different; participants with a follow-up questionnaire had higher internet use, multivitamin use and family history of hypertension (online Supplementary Table 4). Despite these differences, we do not believe any bias has been introduced because the distribution of major confounders was similar between groups. Around 17% of participants were excluded due to an invalid FFQ so we compared the baseline characteristics of those who were not excluded and those who were. We found that the two groups were different only in that excluded participants were more likely to have lower physical activity, less family history of hypertension and less likely to take multivitamins (online Supplementary Table 5). We also do not believe these slight differences could have introduced bias as the distribution of major confounders was similar between groups. The observational nature of our study means we cannot rule out residual confounding nor unmeasured confounding. However, the E-value (IRR: 1.70) showed that the unmeasured confounder would have to have a high point estimate to fully explain away the association. It is unlikely that we did not adjust for main confounders of the association between avocado consumption and hypertension. Avocado consumption might be a marker of a healthy lifestyle, which is why we conducted a sensitivity analysis to assess whether avocado still had an effect in participants with an unhealthy lifestyle or an unhealthy diet. Results are consistent with our hypothesis that the effect of avocado consumption on hypertension is not due to it being a marker of a healthy lifestyle nor a healthy diet. Lastly, we conducted this study exclusively in female teachers, which increases the internal validity of our findings but can decrease the generalisability of our results. However, we do not believe that teachers differ biologically to women with other occupations or age distribution.

In conclusion, frequent consumption of avocado (2.5+ whole avocados per week) was associated with a lower incidence of hypertension in a cohort of Mexican women. Our study suggests that health professionals could recommend consumption of avocados as part of a healthy diet, and it suggests evidence for policy makers to promote access and affordability of this fruit. However, further research is needed to confirm this finding.

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### Supplementary material

For supplementary material/s referred to in this article, please visit <https://doi.org/10.1017/S0007114522002690>

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