Review began 06/15/2023 Review ended 06/26/2023 Published 06/30/2023 Corrected 02/13/2024

#### © Copyright 2023

Okobi et al. This is an open access article distributed under the terms of the Creative Commons Attribution License CC-BY 4.0., which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

# **Corrected:** Effect of Avocado Consumption on Risk Factors of Cardiovascular Diseases: A Systematic Review and Meta-Analysis

Okelue E. Okobi <sup>1, 2</sup>, Victor A. Odoma <sup>3</sup>, Omolola Okunromade <sup>4</sup>, Olusayo Louise-Oluwasanni <sup>5</sup>, Blessing Itua <sup>6</sup>, Chinonso Ndubuisi <sup>7</sup>, Omosefe E. Ogbeifun <sup>8</sup>, Bright C. Nwatamole <sup>9</sup>, Thomas A. Elimihele <sup>10</sup>, Joy O. Adekunle <sup>11</sup>, Akeem A. Adekunle <sup>12</sup>, Chinedum B. Obi <sup>13</sup>, Endurance O. Evbayekha <sup>14</sup>

1. Family Medicine, Larkin Community Hospital, Miami, USA 2. Family Medicine, Lakeside Medical Center, Belle Glade, USA 3. Cardiology/Oncology, Indiana University (IU) Health Bloomington Hospital, Bloomington, USA 4. Public Health, Jiann-Ping Hsu College of Public Health, Georgia Southern University, Statesboro, USA 5. Genetics, Howard University College of Medicine, Washington, USA 6. Internal Medicine, Annotto Bay Hospital, St. Mary, JAM 7. Family Medicine, Humboldt Park Health, Chicago, USA 8. Public Health, University of West Florida, Florida, USA 9. Cardiology, Calderdale and Huddersfield NHS Foundation Trust, Huddersfield , GBR 10. Clinical Research, Norris Comprehensive Cancer Center, University of Southern California, Los Angeles, USA 11. Internal Medicine, Lagos State Health Service (LHSC), Lagos, NGA 12. Internal Medicine, College of Medicine, University of Lagos, Lagos, NGA 13. Internal Medicine, Imo State University, Owerri, NGA 14. Internal Medicine, St. Luke's Hospital, Chesterfield, USA

Corresponding author: Okelue E. Okobi, drokelue.e.okobi@gmail.com

# This article has been corrected.

Correction date: February 13, 2024. Cite this correction as Okobi O E, Odoma V A, Okunromade O, et al. (February 13, 2024) Correction: Effect of Avocado Consumption on Risk Factors of Cardiovascular Diseases: A Systematic Review and Meta-Analysis. Cureus 16(2): c160. doi:10.7759/cureus.c160.

This article has been corrected to accurately reflect the HDL-C concentrations in Table 3.

Previously the values for the HDL cholesterol (mg/dL) avocado group and HDL cholesterol (mg/dL) control group were incorrectly stated as 146.9  $\pm$  38.6 and 143  $\pm$  38.6, respectively. These values have been corrected to 55  $\pm$  13 for the avocado group (women) and 44  $\pm$  9 for the avocado group (men). Control group (women) is now 56  $\pm$  13 and the control group (men) is 45  $\pm$  10.

The authors and journal regret that these errors were not identified and addressed prior to publication.

## Abstract

High cholesterol levels are a significant risk factor for heart disease, the leading cause of death worldwide. Lowering cholesterol plays a crucial role in maintaining good health. One approach to reducing cholesterol is through dietary modifications, and avocados have been recognized as a potential food choice for this purpose. Avocados are rich in monounsaturated fatty acids (MUFAs), fiber, and plant sterols, which have cholesterol-lowering effects. Incorporating avocados into a low-fat diet can be beneficial. This study design followed the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines and conducted databases in Cochrane, SCOPUS, PubMed, and Web of Science up until May 2023, combining keywords related to avocados and cardiovascular diseases (CVDs). The study focused on randomized clinical trials (RCTs) and excluded observational studies, meta-analyses, surveys, abstracts, and reviews. Seven RCTs were included in the study, all reporting total cholesterol (TC) levels. The findings of the study showed that individuals who followed an avocado diet experienced reduced TC levels compared to those who followed a habitual diet or a low-fat diet. The avocado group exhibited lower TC levels compared to the control group in both the habitual diet and low-fat diet subgroups. When considering high-density lipoprotein (HDL) levels, the control group had higher HDL levels than the avocado group in the habitual diet subgroup, while the avocado group had higher HDL levels than the control group in the low-fat diet subgroup. In both the habitual diet and low-fat diet subgroups, the avocado group had lower levels of low-density lipoprotein (LDL) compared to the control group. The study concluded that incorporating avocados into the diet can be a beneficial dietary strategy for individuals aiming to lower their cholesterol levels and promote heart health. The avocado diet was associated with decreased LDL levels, but it did not significantly impact triglyceride (TG) levels or fasting glucose levels. Systolic blood pressure values showed minimal changes with the avocado diet.

**Categories:** Family/General Practice, Internal Medicine, Cardiology **Keywords:** avocado, cardiovascular disease, avocado diet, risk factors for heart disease, low fat diets, total cholesterol

## Introduction And Background

According to global estimates, poor diet is responsible for 255 million disability-adjusted life years and 11 million deaths [1]. Higher intakes of refined carbohydrates, salt, and saturated fat, as well as lower intakes of fiber-rich foods (vegetables, fruit, and whole grains), are consistently linked to cardiometabolic risk factors [1,2]. High blood cholesterol levels, particularly low-density lipoproteins (LDLs), are usually regarded as a significant risk factor for coronary heart disease (CHD) [3,4]. High levels of high-density lipoprotein (HDL), on the other hand, protect against the development of CHD [5-7]. To reduce blood cholesterol levels, many dietary regimens have been advised [3-5]. These suggestions generally include lowering overall fat and increasing fiber and polyunsaturated fatty acids in the diet. The oxidative alteration of LDL particles is crucial in the pathophysiology of atherosclerosis [8,9]. Oxidized LDL (oxLDL) is taken up by macrophages through the activated scavenger receptor, resulting in significant cholesterol buildup and the production of foam cells. Many longitudinal studies have demonstrated a high plasma oxLDL concentration as an independent risk factor for cardiovascular disease (CVD) [10,11]. Avocados consist of several numbers of phytochemicals and nutrients, and each of them plays a beneficial role in preventing CVD and improving the lipid profile [12]. Avocados contain ~10% monounsaturated fatty acids (MUFAs). According to the American Heart Association guidelines, MUFAs are highly recommended instead of trans fatty acids and saturated fatty acids (SFAs) for the prevention of primary and secondary CVD [13]. When MUFAs replaced carbohydrates in the diet, the HDL cholesterol level showed elevations with decreasing in other lipid markers for CVD [14]. The higher MUFA intake was associated with an overall risk reduction in cardiovascular mortality (12%), all-cause mortality (11%), stroke (17%), and cardiovascular events (9%) than with the lower MUFA intake [15]. Avocados contain magnesium, potassium, and fiber, which are linked to cardiovascular health [12]. Avocado carbohydrates consist of~80% dietary fiber, which is composed of 70% insoluble and 30% soluble fiber [16]. A recent meta-analysis showed that eating more fiber is associated with a decreased risk of CVD [17]. In our study, we aim to compare the efficacy of the avocado-rich diet with that of different avocado-free diets on CVD risk.

#### Materials and methods

Search Strategy and Information Sources

We conducted our study based on the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) recommendations and guidelines [18]. We developed a search strategy by combining these keywords: ("Avocado" OR "Avocado-rich" or "Avocado-free") AND ("cardiovascular diseases" OR "heart diseases"). Concerning data sources, we utilized Cochrane, SCOPUS, PubMed, and Web of Science databases till May 2023 for articles that matched our inclusion criteria in the search process.

#### **Study selection**

First, we performed both title and abstract screening. After that, we conducted a full-text screening. Finally, we selected eligible articles based on the following criteria:

· Population: The study included individuals who were either at an increased risk of CVD or were healthy.

 $\cdot$  Intervention: The participants were provided with a diet rich in avocados.

· Comparator: The control group consisted of individuals who were given a diet without avocados.

• Outcomes: The outcomes assessed in the study were total cholesterol (TC) levels, triglyceride (TG) levels, LDL cholesterol levels, HDL cholesterol levels, fasting blood glucose (FBG) levels, systolic blood pressure (SBP), and diastolic blood pressure (DBP).

• Study design: We specifically included only randomized clinical trials (RCTs) and excluded observational studies, meta-analyses, surveys, abstracts, and reviews.

For quality assessment regarding the clinical trials, we utilized the Cochrane risk of bias tool, which depends on assessing eight domains in each clinical trial [19]. The tool assesses proper randomization of patients, allocation concealment, and adequate blinding through seven domains. Each domain could be categorized as high, unclear, or low risk of bias.

#### **Data extraction**

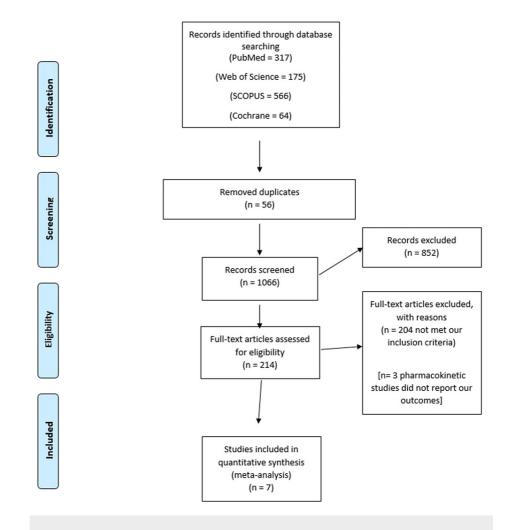
We extracted three types of data from included articles: the first category is the demographic characteristics of the involved individuals, the baseline, and the characteristics of the included trials. The second category was extracting data of the following outcomes for analysis: TC level, TG, LDL, HDL, FBG, SBP, and DBP. The last category was quality assessment data in both trials. The process of data collection was conducted using Microsoft Excel [20].

Data Synthesis and Analysis

We performed the meta-analysis of this study using Review Manager software (The Nordic Cochrane Center, Odense, Denmark) [21]. Our study included continuous outcomes. We analyzed continuous data using mean difference (MD) and 95% confidence interval (CI). The fixed-effects model was used when data were homogeneous, while heterogeneous data were analyzed under a random-effects model. To measure the presence of inconsistency among the studies, in 2 of 11 we used the  $I^2$  value and the *P*-value of the chi-square tests [22]. Values of P < 0.1 or  $I^2 > 50\%$  were significant indicators of the presence of heterogeneity. We tried to solve the inconsistency of heterogeneous outcomes using Cochrane's leave-one-out method [22].

#### Summary of Included Studies

Figure 1 shows the PRISMA flowchart of our literature search process. A total of seven trials [23-29] were included in our meta-analysis. Our meta-analysis included 1,359 patients divided into two groups; the avocado group, which included 683 patients fed an avocado-rich diet, and the control group, which included 676 patients fed an avocado-free diet.



#### FIGURE 1: PRISMA flowchart of selected studies.

PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analysis

The mean age of the avocado group patients was 49.7 years, while the control group was 50.1 years. Tables *1-2* contain baseline characteristics of the included studies related to avocado consumption and its effects.

					Sample si	70	Age (years)		Male (N)		Female (N)		BMI (kg/m2)	
Study ID	Country	Study design	Avocado (g/day)	Control diet	Gample a			5.6,						2)
			(g/uay)		Avocado	Control	Avocado	Control	Avocado	Control	Avocado	Control	Avocado	Control
Pieterse et al. (2005)	South	Randomized clinical trial	200	Energy restricted diet	28	27	40.8 ± 8.9		NR NR		NR	NR	31.9 ± 3.9	
[24]	Africa													
Scott et al. (2017)	United	Randomized controlled trial		One potato or one cup	20	20	63.3 ±	62.5 ±	6	9	14	11	24.1 ±	24.2 ±
[25]	States			of chickpeas			11	9.2					3.1	2.4
Wang et al. (2015) [1]	Australia	Randomized, crossover,	One Hass	AAD-LFD	45		45 ± 13.3		NR		NR		28.2 ± 2.4	
		controlled feeding trial	avocado											
Zhang et al. (2022)	United	Randomized clinical trial	One Hass	Low-fat diet	49	45	40.6 ±	42.7 ±	21	18	28	26	92.2 ±	32.8 ±
[26]	States		avocado				11.8	12.5					14.7	3.88
Colquhoun et al.	Australia	Randomized clinical trial	200-500	Low-fat diet	15	15	49	49	0		15		66.8	
(1992) [27]														
Lichtenstein et al.	United	Randomized, controlled, parallel-	NR	Habitual diet	505	503	50.1 ±	50.4 ±	149	129	356	374	32.9 ±	33.2 ±
(2022) [28]	States	arm, unblinded trial					14.3	13.8					5.3	5.6
Alvizouri-Muñoz et al.	Italy	Randomized clinical trial	NR	Habitual diet	21	21	NR	NR	NR	NR	NR	NR	NR	NR
(1992) [29]														

# TABLE 1: Baseline characteristics of the included studies.

AAD-LFD, Average American diet-low-fat diet; NR, not reported

Study ID	Age (years)	Statin use	Socioeconomic status	Control diet
Pieterse et al. (2005) [24]	21 to 57	Six subjects (four in the experimental group and two in the control group) used hypolipidemic agents (statins).	Not reported	Mixed dietary fats such as margarine or oil. (Other specifics of the control diet were not given.)
Scott et al. (2017) [25]	>=50	individuals taking medications interfering with fat absorption (e.g., bile acid sequestrants, ezetimibe) were excluded.	Not reported	One medium potato or one cup of chickpeas a day.
Wang et al (2015) [1]	21-70	All participants were not taking lipid-lowering medications or supplements.	Not reported	The control diet was described as AAD: 34% fat, 51% CHO, and 16% protein.
Zhang et al. (2022) [26]	25-65	Individuals who used medications that would interfere with the study's outcomes, like lipid-lowering medications, were excluded.	Not reported	Participants randomly allocated to the control arm were given control foods in different combinations to match the energy level of one avocado per day as closely as possible. Foods such as mini bagels, pierogis, fruit juice, waffle, instant oatmeal, and others were provided.
Colquhoun et al. (1992) [27]	37 and 58	The study was silent on statins or lipid-lowering agents.	Not reported	High-complex-carbohydrate diet (AHA-III) on blood lipid concentrations. (Specifics of this diet were not reported.)
Lichtenstein et al. (2022) [28]	>25	Statin intake was not reported in the inclusion or exclusion criteria.	Not reported	The control diet was described as a Habitual diet (with no specifics).
Madrigal 2008 [29]	Did not report age range	Was silent on statin.	Not reported	The control diets were labeled as Rich monosaturated, free monosaturated, and Low monosaturated fats (Without specific mention of types of traditional food names). The first and third diets were designed to simulate a usual diet, and volunteers carried on their normal activities during the trial.

## TABLE 2: Age, statin status, and dietary breakdown.

AAD, average American diet; CHO, carbohydrate

Table 3 provides information on various parameters related to the studies that investigated the effects of avocado consumption on cholesterol levels, blood pressure, and glucose levels.

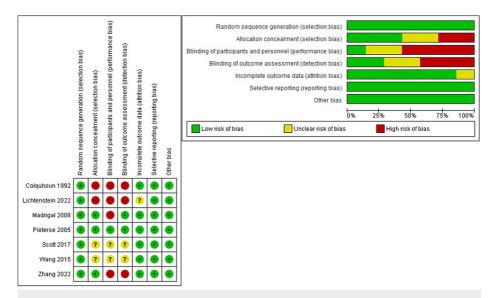
Study ID	Total cholesterol LDL cholesterol (mg/dL) (mg/dL)				HDL cholesterol (mg/dL)	Triglyceri (mg/dL)	de	Systolic b	lood	Diastolic blood pressure		Glucose (mg/dL)			
	Avocado	Control	Avocado	Control	Avocado Control			Avocado Control		Avocado Control		Avocado	Control	Avocado	Control
Pieterse et al. (2005) [24]	5.19 ± 1.17	,	3.45 ± 1.12	2	1.1 ± 0.31	1.73 ± 2.0	3	120 ± 15.6		71 ± 8.2	71 ± 8.2		NR		
Scott et al. (2017) [25]	NR		NR		NR	NR		NR		NR	NR		NR		
Wang et al. (2015) [1]	199.9 ± 32	.4	128.1 ± 26	.1	48.7 ± 12.1			114.0 ± 39	9.6	117.2± 10.4		79.2 ± 7.4		92.2 ± 8.0	
Zhang et al. (2022) [26]	NR		NR		NR			NR		NR		NR		106 ± 9.73	104 ± 11.1
Colquhoun et al. (1992) [27]	NR		NR		NR	NR		NR	NR	NR		NR		NR	
Lichtenstein et al. (2022) [28]	185 ± 40	190 ± 39	110 ± 34	114 ± 34	55 ± 13 WOMEN 44 ± 9 MEN	56 ± 13 WOMEN 10 MEN	45 ±	110 ± 49	107 ± 54	123 ± 16	123 ± 16	77 ± 10	76 ± 11	107 ± 29	107 ± 30
Alvizouri-Muñoz et al. (1992) [29]	212.68 ± 4	2.5	119.9 ± 11	.2	30.9 ± 7.3			336 ± 256		6±256 NR NR		NR	NR	189 ± 70.2	!

# TABLE 3: Table displaying cholesterol levels, blood pressure, and glucose measurements in avocado and control groups from various research papers.

NR, not reported

#### **Results of risk-of-bias assessment**

According to Cochrane's tools, the risk-of-bias evaluation of RCTs indicated an overall low risk of bias. Regarding randomization, all the involved studies were at low risk. Regarding allocation concealment, three studies [23,26,29] were at low risk, and two studies [27,28] were at high risk, but the rest of the studies [24,25] did not report enough data. All the studies were not blinded to the participants and personnel except two studies [24,25] that did not report enough data, and Pieterse et al. [23] were blinded. Three studies [26-28] were not blinded to outcome assessment, two studies [23,29] were blinded, and two studies [24,25] did not report enough data. A summary of the risk of bias in involved trials is demonstrated in Figure 2.



#### FIGURE 2: Risk-of-bias table.

Colquhoun et al. (1992) [27], Lichtenstein et al. (2022) [28], Alvizouri-Muñoz et al. (1992) [29], Pieterse et al. (2005) [24], Scott et al. (2017) [25], Wang et al. (2015) [1], Zhang et al. (2022) [26]

#### **Results**

Analysis of the Outcomes

According to the control group's diet type, we conducted a subgroup analysis and divided the studies into two subgroups: the habitual diet (HD) group and the low-fat (LF) diet group.

Total cholesterol: Seven studies [23-29] reported the levels of TC. In the HD subgroup, the avocado group was accompanied by lower levels of TC than the control group (MD = -0.20 [-0.25, -0.14], P = 0.0001). The data were heterogeneous and homogenous after excluding Wang et al. [1] from the leave-one-out method ( $I^2 = 0\%$ , P = 0.48). In the LF diet subgroup, the avocado group was accompanied by lower levels of TC than the control group (MD = -0.18 [-0.24, -0.11], P = 0.0001). The data were heterogeneous and became homogenous after excluding Zhang et al. [26] by the leave-one-out method ( $I^2 = 47\%$ , P = 0.13) (Figure 3).

	Av	ocado		0	Control			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
1.1.1 Habitual Diet									
Lichtenstein 2022	4.66	0.4	505	4.86	0.48	503	30.3%	-0.20 [-0.25, -0.15]	-
Madrigal 2008	4.6	0.99	21	4.6	0.81	21	0.5%	0.00 [-0.55, 0.55]	
Wang 2015 (HD) Subtotal (95% CI)	4.7	0.1	43 526	5.169	0.12	45 524	30.8%	Not estimable -0.20 [-0.25, -0.14]	•
Heterogeneity: Tau <sup>2</sup> =	0.00; C	hi² = 0.	51, df=	= 1 (P =	0.48); l <sup>a</sup>	= 0%			
Test for overall effect									
1.1.2 Low fat diet									
Colquhoun 1992	5.6	0.07	15	5.8	0.08	15	30.9%	-0.20 [-0.25, -0.15]	+
Pieterse 2005		0.39	28	5.26	0.48	27	2.5%	0.07 [-0.16, 0.30]	
Scott 2017	5.4	1.1	20	5.3	1.3	20	0.2%	0.10 [-0.65, 0.85]	
Wang 2015 (LFD)	4.7	0.1	45	4.9	0.13	45	35.6%	-0.20 [-0.25, -0.15]	•
Zhang 2022	4.7	0.12	49	4.6	0.114	45		Not estimable	
Subtotal (95% CI)			108			107	69.2%	-0.18 [-0.24, -0.11]	◆
Heterogeneity: Tau <sup>2</sup> =	0.00; C	hi <sup>2</sup> = 5.	69, df=	= 3 (P =	0.13); P	= 47%			
Test for overall effect	Z= 5.42	? (P < 0	0.00001	)					
Total (95% CI)			634			631	100.0%	-0.19 [-0.23, -0.15]	•
Heterogeneity: Tau <sup>2</sup> =	0.00; C	hi <sup>2</sup> = 6.	22, df=	= 5 (P =	0.29); P	= 20%			-0.5 -0.25 0 0.25 0.5
Test for overall effect	Z=10.1	0 (P <	0.0000	01)					-0.5 -0.25 0 0.25 0.5 Avocado Control
Test for subaroup dif	ferences	: Chi <sup>2</sup>	= 0.20,	df = 1 (f)	P = 0.66	), $ ^2 = 0$	%		Avocado Control

#### FIGURE 3: Analysis of studies that reported total cholesterol.

Colquhoun et al. (1992) [27], Lichtenstein et al. (2022) [28], Alvizouri-Muñoz et al. (1992) [29], Pieterse et al. (2005) [24], Scott et al. (2017) [25], Wang et al. (2015) [1], Zhang et al. (2022) [26]

IV, intravenous; SD, standard deviation; CI, confidence interval

High-density lipoprotein: The levels of HDL were reported by seven studies [23-29]. In the HD subgroup, we found that the control group was associated with higher levels of HDL than the avocado group (MD = -0.04 [-0.06, -0.02], P = 0.0001). The data were heterogeneous and became homogenous after excluding Lichtenstein

et al. [28] by the leave-one-out method ( $I^2 = 0\%$ , P = 1.0). In the LF diet subgroup, the avocado group showed higher levels of HDL than the control group (MD = -0.04 [-0.06, -0.02], P = 0.0001). The data were

heterogeneous and became homogenous after excluding Colquhoun et al. [27] by the leave-one-out method ( $I^2 = 0\%, P = 0.84$ ) (Figure 4).

	Av	ocado	•	0	Control			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
1.2.1 Habitual Diet									
Lichtenstein 2022	0.56	0.16	505	0.55	0.224	503		Not estimable	
Madrigal 2008	0.84	0.16	21	0.88	0.2	21	2.3%	-0.04 [-0.15, 0.07]	
Wang 2015 (HD)	1.21	0.04	43	1.25	0.04	45	97.7%	-0.04 [-0.06, -0.02]	
Subtotal (95% CI)			64			66	100.0%	-0.04 [-0.06, -0.02]	•
Heterogeneity: Tau <sup>2</sup> =	= 0.00; C	hi² = 0	.00, df=	= 1 (P =	1.00); 12	= 0%			
Test for overall effect	Z= 4.74	(P < 0	0.00001	)					
1.2.2 (LFD)									
Colguhoun 1992	1.68	0.03	15	1.49	0.03	15		Not estimable	
Pieterse 2005	1.1	0.16	28	1.1	0.224	27	3.6%	0.00 [-0.10, 0.10]	
Scott 2017	1.5	0.56	20	1.4	0.46	20	0.4%	0.10 [-0.22, 0.42]	
Wang 2015 (LFD)	1.21	0.04	45	1.15	0.38	45	3.1%	0.06 [-0.05, 0.17]	
Zhang 2022	1.25	0.05	49	1.21	0.05	45	93.0%	0.04 [0.02, 0.06]	
Subtotal (95% CI)			142			137	100.0%	0.04 [0.02, 0.06]	•
Heterogeneity: Tau <sup>2</sup> :	= 0.00; C	hi² = 0	.83, df=	= 3 (P =	0.84); l <sup>a</sup>	= 0%			
Test for overall effect	Z = 3.96	6 (P < 0	0.0001)	,					
									-0.2 -0.1 0 0.1 0.2
									-0.2 -0.1 0 0.1 0.2 Control Avocado
Test for subgroup dif	ferences	: Chi <sup>2</sup> :	= 37.04	, df = 1	(P < 0.0	0001),	2 = 97.39	6	Contact Avocado

#### FIGURE 4: Analysis of studies that reported HDL.

Colquhoun et al. (1992) [27], Lichtenstein et al. (2022) [28], Madrigal et al. (2008) [29], Pieterse et al. (2005) [24], Scott et al. (2017) [25], Wang et al. (2015) [1], Zhang et al. (2022) [26]

IV, intravenous; SD, standard deviation; CI, confidence interval; HDL, high-density lipoprotein

Low-density lipoprotein: All the included studies [23-29] reported LDL levels. In both subgroups, HD and LF subgroups, the LDL levels were lower in the avocado group than in the control group (MD = -0.16 [-0.20, -0.12], P = 0.0001) and (MD = -0.13 [-0.25, -0.00], P = 0.04), respectively. In the HD subgroup, the data were heterogeneous and became homogenous after excluding Wang et al. [1] by the leave-one-out method (I2 = 0%, P = 0.77). In the LF subgroup, the data showed heterogeneity ( $I^2 = 95\%$ , P = 0.0001) (Figure 5).

	A	vocado		C	ontrol			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
1.3.1 (HD)	1. <b>.</b>								
Lichtenstein 2022	2.72	0.31	505	2.88	0.4	503	98.8%	-0.16 [-0.20, -0.12]	
Madrigal 2008	2.5	0.7	21	2.6	0.6	21	1.2%	-0.10 [-0.49, 0.29]	
Nang 2015 (HD)	2.94	0.087	43	3.31	0.1	45		Not estimable	
Subtotal (95% CI)			526			524	100.0%	-0.16 [-0.20, -0.12]	•
Heterogeneity: Tau <sup>2</sup> =	= 0.00; C	hi² = 0.0	9, df =	1 (P = 0)	.77); 1	'= 0%			
Test for overall effect	Z = 7.11	(P < 0.	00001)						
1 2 2 (1 5 0)									
1.3.2 (LFD)									
Colquhoun 1992	3.51	0.05	15	3.76	0.06	15	26.5%	-0.25 [-0.29, -0.21]	-
Pieterse 2005	3.5	0.31	28	3.58	0.4	27	16.5%	-0.08 [-0.27, 0.11]	
Scott 2017	3.38	0.64	20	3.5	1.16	20	3.8%	-0.12 [-0.70, 0.46]	
Wang 2015 (LFD)	2.94	0.087	45	3.1	0.1	45	26.6%	-0.16 [-0.20, -0.12]	+
Zhang 2022	2.8	0.101	49	2.8	0.1	45	26.5%	0.00 [-0.04, 0.04]	+
Subtotal (95% CI)			157			152	100.0%	-0.13 [-0.25, -0.00]	-
Heterogeneity: Tau <sup>2</sup> =	= 0.01; C	hi <sup>2</sup> = 76	.69, df=	= 4 (P <	0.000	01); I <sup>2</sup> =	95%		
Test for overall effect	Z = 2.02	2 (P = 0.	04)						
								•	-0.5 -0.25 0 0.25 0.5
									Avocado Control

Test for subgroup differences: Chi<sup>2</sup> = 0.24, df = 1 (P = 0.63), I<sup>2</sup> = 0%

#### FIGURE 5: Analysis of studies that reported LDL.

Colquhoun et al. (1992) [27], Lichtenstein et al. (2022) [28], Madrigal et al. (2008) [29], Pieterse et al. (2005) [24], Scott et al. (2017) [25], Wang et al. (2015) [1], Zhang et al. (2022) [26]

IV, intravenous; SD, standard deviation; CI, confidence interval; LDL, low-density lipoprotein

Triglyceride: Six studies [23,24,26-29] reported the levels of TG. We found that the TG levels were similar in both groups regarding both subgroups: HD subgroup (MD = 0.00 [-0.08, 0.08], P = 0.98) and LF subgroup (MD = 0.20 [-0.08, 0.47], P = 0.16). The data were homogenous in the HD subgroup ( $I^2$  = 0%, P = 0.7) and heterogeneous in the LF subgroup ( $I^2$  = 95%, P = 0.0001) (Figure 6).

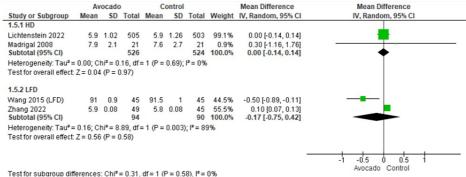
	Av	ocado	•	C	ontrol			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
1.4.1 HD									
Lichtenstein 2022	1.26	0.75	505	1.26	0.5	503	99.4%	0.00 [-0.08, 0.08]	•
Madrigal 2008	2.7	2.1	21	2.5	1.1	21	0.6%	0.20 [-0.81, 1.21]	——————————————————————————————————————
Subtotal (95% CI)			526			524	100.0%	0.00 [-0.08, 0.08]	<b>•</b>
Heterogeneity: Tau <sup>2</sup> :	= 0.00; C	hi <sup>2</sup> = 0.	15, df=	= 1 (P =	0.70);	$ ^{2} = 0\%$			
Test for overall effect	Z = 0.03	8 (P = 0	.98)						
1.4.2 LFD									
Colquhoun 1992	1.41	0.04	15	1.42	0.06	15	30.4%	-0.01 [-0.05, 0.03]	+
Pieterse 2005	1.88	0.7	28	1.28	0.5	27	21.6%	0.60 [0.28, 0.92]	
Scott 2017	0.89	0.64	20	1.05	0.65	20	18.6%	-0.16 [-0.56, 0.24]	
Zhang 2022	3.1	0.28	45	2.76	0.19	45	29.4%	0.34 [0.24, 0.44]	-
Subtotal (95% CI)			108			107	100.0%	0.20 [-0.08, 0.47]	-
Heterogeneity: Tau <sup>2</sup> :	= 0.07; C	hi <sup>2</sup> = 5	5.23, dt	f= 3 (P +	< 0.00	001); I <sup>z</sup>	= 95%		
Test for overall effect	Z = 1.39	9 (P = 0	0.16)						
								0	-1 -0.5 0 0.5 1
									Avocado Control
Test for subgroup dif	ferences	: Chi <sup>2</sup> :	= 1.78,	df = 1 (F	P = 0.1	<ol> <li>I<sup>2</sup> =</li> </ol>	43.8%		

#### FIGURE 6: Analysis of studies that reported TG.

Colquhoun et al. (1992) [27], Lichtenstein et al. (2022) [28], Alvizouri-Muñoz et al. (1992) [29], Pieterse et al. (2005) [24], Scott et al. (2017) [25], Wang et al. (2015) [1], Zhang et al. (2022) [26].

IV, intravenous; SD, standard deviation; CI, confidence interval; TG, triglyceride

Fasting blood glucose: The outcome was reported by four studies [25,26,28,29]. We found that the FBG levels were similar in both groups regarding both subgroups: HD subgroup (MD = 0.00 [-0.14, 0.14], P = 0.97) and LF subgroup (MD = -0.17 [-0.75, 0.42], P = 0.58). The data were homogenous in the HD subgroup ( $I^2 = 0\%$ , P = 0.17) 0.69) and heterogeneous in the LF subgroup ( $I^2 = 89\%$ , P = 0.003) (Figure 7).



#### FIGURE 7: Analysis of studies that reported FBG.

Colquhoun et al. (1992) [27], Lichtenstein et al. (2022) [28], Alvizouri-Muñoz et al. (1992) [29], Pieterse et al. (2005) [24], Scott et al. (2017) [25], Wang et al. (2015) [1], Zhang et al. (2022) [26].

IV, intravenous; SD, standard deviation; CI, confidence interval, FBG, fasting blood glucose

Systolic blood pressure: SBP was reported by four studies [23,25,26,28]. Regarding the HD subgroup, the SBP was the same in both the avocado and the control group (MD = -1.21 [-3.10, 0.68], P = 0.21). The data showed heterogeneity ( $I^2 = 97\%$ , P = 0.0001). Regarding the LF subgroup, the SBP decreased with the avocado group than the control group (MD = -1.71 [-2.21, -1.21], P = 0.001). The data were heterogeneous and became homogeneous after excluding Zhang et al. [26] by the leave-one-out method ( $I^2 = 0\%$ , P = 0.48) (Figure 8).

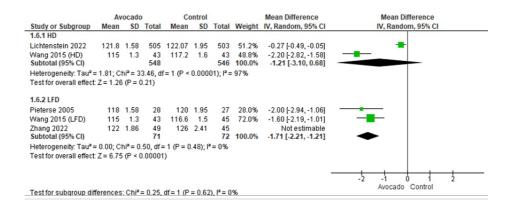
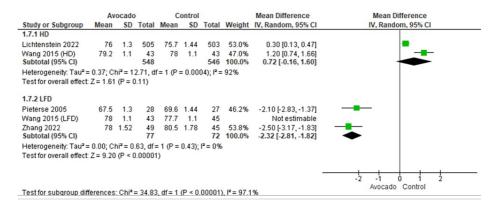


FIGURE 8: Analysis of studies that reported systolic blood pressure.

Colquhoun et al. (1992) [27], Lichtenstein et al. (2022) [28], Alvizouri-Muñoz et al. (1992) [29], Pieterse et al. (2005) [24], Scott et al. (2017) [25], Wang et al. (2015) [1], Zhang et al. (2022) [26].

IV, intravenous; SD, standard deviation; CI, confidence interval

Diastolic blood pressure: DBP was reported by four studies [23,25,26,28]. Regarding the HD subgroup, the DBP was the same in both the avocado and the control group (MD = 0.72 [-0.16, 1.60], P = 0.11). The data showed heterogeneity ( $I^2 = 92\%$ , P = 0.0004). Regarding the LF subgroup, the DBP decreased with the avocado group than the control group (MD = -2.32 [-2.81, -1.82], P = 0.0001). The data were heterogeneous and became homogeneous after excluding Wang et al. [1] by the leave-one-out method ( $I^2 = 0\%$ , P = 0.43) (Figure 9).



#### FIGURE 9: Analysis of studies that reported diastolic blood pressure.

Colquhoun et al. (1992) [27], Lichtenstein et al. (2022) [28], Alvizouri-Muñoz et al. (1992) [29], Pieterse et al. (2005) [24], Scott et al. (2017) [25], Wang et al. (2015) [1], Zhang et al. (2022) [26].

IV, intravenous; SD, standard deviation; CI, confidence interval

#### **Review**

In this meta-analysis, we investigated the efficacy of the avocado-rich diet in reducing the risk of CVDs compared with HD and LF diets. Our analysis showed that the avocado group was accompanied by lower levels of TC than the HD and LF diets. Concerning HDL, we found that HD was associated with higher levels of HDL compared with the avocado diet. On the other hand, populations in the LF diet group had higher levels of HDL compared with the group following the avocado-rich diet. Regarding the LDL levels, the avocado diet was associated with lower levels of LDL. We also found that TG levels were similar in different diet groups.

A randomized trial by Wang et al. [1] found that consuming one avocado per day for six weeks resulted in lower levels of circulating oxLDL and increased plasma lutein concentrations. This effect was observed compared to a typical Western diet, a moderate-fat diet with matched macronutrients and fatty acids, and a high-carbohydrate, low-fat diet. The benefits were attributed to the bioactive compounds present in avocados, which go beyond their fatty acids. The reduction in small LDL particles may have contributed to lowering oxLDL on the avocado diet. Furthermore, increasing the intake of fruits, vegetables, and whole grains may protect against the oxidation of atherogenic lipoproteins even on a high-carbohydrate, low-fat diet that increases small, dense LDL (sdLDL) particles [30].

Pacheco et al. [31] conducted a comprehensive study on American men and women, revealing that consuming avocados regularly can significantly reduce the risk of developing CVDs and coronary heart diseases. However, no significant association was found between avocado intake and total or ischemic stroke. The study also suggested replacing unhealthy food items such as margarine, butter, processed meats, cheese, and eggs with avocados can lower the incidence of CVD. This study provides further evidence that incorporating plant-based unsaturated fats in our diet can improve its quality and play a crucial role in preventing CVD in the general population.

Wang et al. [1] found that consuming one Hass avocado per day can have positive effects on reducing LDL and other emerging risk factors for CVD beyond just its fatty acid content. This study also shows that a moderate-fat diet low in saturated fat and high in monounsaturated fat from avocados can lead to greater reductions in various cholesterol markers compared to a high-monounsaturated fat diet with similar macronutrient and fatty acid profiles. Therefore, incorporating a food source rich in monounsaturated fats and bioactive compounds can provide additional cardiovascular benefits compared to a low-saturated-fat diet with matched levels of monounsaturated fats. They also discovered that individuals who followed a high-fat diet had higher HDL levels than those who followed an avocado diet. Conversely, those in the lowfat diet group had higher HDL levels than the avocado diet group, which is similar to our results.

In terms of FBG levels, our analysis showed that different diet groups were not associated with significant changes in glucose levels. Lichtenstein et al. [28] reported no notable variations in the FBG between the HD and avocado diet after six months of providing one avocado daily. In addition, Wang et al. [1] showed that fasting blood sugar did not differ between HD, LF diet, avocado diet, and moderate-fat diet.

Normal ranges of high blood pressure have evolved over the years and diet composition may play an important role [32-33]. We studied the effect of an avocado-rich diet on blood pressure and found that the SBP was the same in both the avocado and HD groups. However, the SBP decreased with the avocado group than with the LF diet group. We noticed similar results concerning the DBP. The DBP remained consistent between the avocado and HD groups, but the avocado group showed a more significant decrease in DBP than the LF diet group.

Cheng et al. [32] suggested that consuming tomato products and taking lycopene supplements can benefit cardiovascular risk factors such as blood pressure, blood lipids, and endothelial function. This supports the idea of developing personalized nutritional plans that incorporate tomatoes to combat CVD. Lichtenstein et al. [28] Reported that SBP and DBP did not differ significantly between diet groups.

Pieterse et al. [24] showed that neither avocado (MUFA) nor weight loss had any impact on serum lipid levels, plasma fibrinogen, arterial compliance, SBP, or DBP. However, the limited sample size may have obscured any potential effects on these variables. A prior meta-analysis conducted by Mahmassani et al. examined the impact of avocado consumption on CVDs. The findings indicated that incorporating avocados into one's diet may enhance HDL cholesterol levels. Nonetheless, avocado intake did not significantly influence serum TC, LDL cholesterol, or TG values [34].

#### **Study limitations**

One of the main limitations of our meta-analysis is the number of studies and the significant heterogeneity in some outcomes. However, we managed to solve the heterogeneity through the leave-one-out method. The analysis showed significant differences among studies due to variations in factors such as the types of participants, their dietary habits, the control groups used, and the length of the intervention. We performed a subgroup analysis according to the control group, which provided more homogenous results.

Another limitation is that the studies included in the analysis had small sample sizes and significant variations in the results. Therefore, this finding should be interpreted with caution, and further long-term trials are needed to fully understand the impact of avocado consumption on blood lipid levels and other risk factors for CVD.

### Conclusions

After analyzing the data, we discovered that individuals in the avocado group had lower levels of TC than those in the HD and low-fat diet groups. The HD group had higher levels of HDL than the avocado group, while the low-fat diet group had higher levels of HDL than the avocado group. The avocado diet was associated with lower LDL levels. The avocado diet did not affect the TG and fasting glucose levels with minimal effect on SBP values. While our analysis revealed significant differences in cholesterol levels among individuals in the avocado, HD, and low-fat diet groups, further research is needed to explore several aspects. First, future studies should investigate the long-term effects of the avocado diet on cholesterol levels to determine if the observed differences persist over time. Additionally, it would be valuable to examine the potential mechanisms by which avocados may impact cholesterol metabolism, shedding light on the underlying biological processes involved. Furthermore, considering the differing effects on HDL levels between the avocado group and the HD and low-fat diet groups, future research could focus on identifying the specific dietary components responsible for these variations. Moreover, it would be beneficial to investigate the impact of the avocado diet on other cardiovascular risks factors, such as stroke, myocardial infarction, and other vasculo-cardiac comorbid outcomes of cardiovascular disease to gain a more comprehensive understanding of its overall effects on cardiometabolic health.

# **Additional Information**

#### Disclosures

**Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

#### Acknowledgements

The authors of this manuscript, Victor A. Odoma, Okelue E. Okobi, Olusayo Louise-Oluwasanmi, Omolola Okunromade, Blessing Itua, Chinonso Ndubuisi, Bright C. Nwatamole, Omosefe E. Ogbeifun, Thomas A. Elimihele, Joy Adekunle, Akeem A. Adekunle, Chinedum B. Obi, and Endurance O. Evbayekha, made significant contributions to the writing of the manuscript according to the guidelines set forth by the International Committee of Medical Journal Editors. These authors were involved in various aspects of the research process, including conceptualization, design, data acquisition, formal analysis, and interpretation of data, as well as writing the original draft, reviewing it for intellectual content, and finalizing the manuscript. They have also provided their final approval for the publication of the manuscript.

## References

- Wang L, Bordi PL, Fleming JA, Hill AM, Kris-Etherton PM: Effect of a moderate fat diet with and without avocados on lipoprotein particle number, size and subclasses in overweight and obese adults: a randomized, controlled trial. J Am Heart Assoc. 2015, 4:e001355. 10.1161/JAHA.114.001355
- Health effects of dietary risks in 195 countries, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet. 2019, 393:1958-72. 10.1016/S0140-6736(19)30041-8
- Drake I, Sonestedt E, Ericson U, Wallström P, Orho-Melander M: A Western dietary pattern is prospectively associated with cardio-metabolic traits and incidence of the metabolic syndrome. Br J Nutr. 2018, 119:1168-76. 10.1017/S000711451800079X
- Islam MM, Hlushchenko I, Pfisterer SG: Low-density lipoprotein internalization, degradation and receptor recycling along membrane contact sites. Front Cell Dev Biol. 2022, 10:826379. 10.3389/fcell.2022.826379
- Willeit P, Yeang C, Moriarty PM, Tschiderer L, Varvel SA, McConnell JP, Tsimikas S: Low-density lipoprotein cholesterol corrected for lipoprotein(A) cholesterol, risk thresholds, and cardiovascular events. J Am Heart Assoc. 2020, 9:e016318. 10.1161/JAHA.119.016318
- Jomard A, Osto E: High density lipoproteins: metabolism, function, and therapeutic potential . Front Cardiovasc Med. 2020, 7:39. 10.3389/fcvm.2020.00039
- Huang S, Zhou C, Yuan Z, Xiao H, Wu X: The clinical value of high-density lipoprotein in the evaluation of new coronavirus pneumonia. Adv Clin Exp Med. 2021, 30:153-6. 10.17219/acem/130606
- Grao-Cruces E, Varela LM, Martin ME, Bermudez B, Montserrat-de la Paz S: High-density lipoproteins and Mediterranean diet: a systematic review. Nutrients. 2021, 13:10.3390/nu13030955
- Tsimikas S: Oxidized low-density lipoprotein biomarkers in atherosclerosis. Curr Atheroscler Rep. 2006, 8:55-61. 10.1007/s11883-006-0065-1
- Itabe H: Oxidized low-density lipoprotein as a biomarker of in vivo oxidative stress: from atherosclerosis to periodontitis. J Clin Biochem Nutr. 2012, 51:1-8. 10.3164/jcbn.11-00020R1
- 11. Strobel NA, Fassett RG, Marsh SA, Coombes JS: Oxidative stress biomarkers as predictors of cardiovascular disease. Int J Cardiol. 2011, 147:191-201. 10.1016/j.ijcard.2010.08.008
- 12. Tsimikas S, Mallat Z, Talmud PJ, et al.: Oxidation-specific biomarkers, lipoprotein(a), and risk of fatal and nonfatal coronary events. J Am Coll Cardiol. 2010, 56:946-55. 10.1016/j.jacc.2010.04.048
- Dreher ML, Davenport AJ: Hass avocado composition and potential health effects. Crit Rev Food Sci Nutr. 2013, 53:738-50. 10.1080/10408398.2011.556759
- Lichtenstein AH, Appel LJ, Brands M, et al.: Diet and lifestyle recommendations revision 2006: a scientific statement from the American Heart Association Nutrition Committee. Circulation. 2006, 114:82-96. 10.1161/CIRCULATIONAHA.106.176158
- Mensink RP, Zock PL, Kester AD, Katan MB: Effects of dietary fatty acids and carbohydrates on the ratio of serum total to HDL cholesterol and on serum lipids and apolipoproteins: a meta-analysis of 60 controlled trials. Am J Clin Nutr. 2003, 77:1146-55. 10.1093/ajcn/77.5.1146
- 16. Schwingshackl L, Hoffmann G: Monounsaturated fatty acids, olive oil and health status: a systematic review and meta-analysis of cohort studies. Lipids Health Dis. 2014, 13:154. 10.1186/1476-511X-13-154
- Ayogu R, Edeh R, Madukwe E, Ene-Obong H: Commonly consumed foods: nutritional quality and contributions to recommended nutrient intakes of school children in rural Southeastern Nigeria. Food Nutr Bull. 2017, 38:65-77. 10.1177/0379572116689627
- Threapleton DE, Greenwood DC, Evans CE, et al.: Dietary fibre intake and risk of cardiovascular disease: systematic review and meta-analysis. BMJ. 2013, 347:f6879. 10.1136/bmj.f6879

- Moher D, Liberati A, Tetzlaff J, Altman DG: Preferred reporting items for systematic reviews and metaanalyses: the PRISMA statement. PLoS Med. 2009, 6:e1000097. 10.1371/journal.pmed.1000097
- Higgins JP, Altman DG, Gøtzsche PC, et al.: The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ. 2011, 343:d5928. 10.1136/bmj.d5928
- 21. Katz A: Excel 2010 Made Simple. DeKalb IL (ed): Apress Berkeley, USA; 2010.
- 22. Lebowitz F: Endnote. Aperture. 2021. 10.4324/9781315251714-10
- Julian PT, Higgins J, Thomas J, et al.: Cochrane Handbook for Systematic Reviews of Interventions . Julian PT, Higgins J, Thomas J, et al. (ed): 2019. 10.1002/9781119536604
- Pieterse Z, Jerling JC, Oosthuizen W, Kruger HS, Hanekom SM, Smuts CM, Schutte AE: Substitution of high monounsaturated fatty acid avocado for mixed dietary fats during an energy-restricted diet: effects on weight loss, serum lipids, fibrinogen, and vascular function. Nutrition. 2005, 21:67-75. 10.1016/j.nut.2004.09.010
- 25. Scott TM, Rasmussen HM, Chen O, Johnson EJ: Avocado consumption increases macular pigment density in older adults: a randomized, controlled trial. Nutrients. 2017, 9:10.3390/nu9090919
- Zhang X, Xiao D, Guzman G, Edirisinghe I, Burton-Freeman B: Avocado consumption for 12 weeks and cardiometabolic risk factors: a randomized controlled trial in adults with overweight or obesity and insulin resistance. J Nutr. 2022, 152:1851-61. 10.1093/jn/nxac126
- Colquhoun DM, Moores D, Somerset SM, Humphries JA: Comparison of the effects on lipoproteins and apolipoproteins of a diet high in monounsaturated fatty acids, enriched with avocado, and a highcarbohydrate diet. Am J Clin Nutr. 1992, 56:671-7. 10.1093/ajcn/56.4.671
- Lichtenstein AH, Kris-Etherton PM, Petersen KS, et al.: Effect of incorporating 1 avocado per day versus habitual diet on visceral adiposity: a randomized trial. J Am Heart Assoc. 2022, 11:e025657. 10.1161/JAHA.122.025657
- Alvizouri-Muñoz M, Carranza-Madrigal J, Herrera-Abarca JE, Chávez-Carbajal F, Amezcua-Gastelum JL: Effects of avocado as a source of monounsaturated fatty acids on plasma lipid levels . Arch Med Res. 1992, 23:163-7.
- 30. Wang L, Tao L, Hao L, Stanley TH, Huang KH, Lambert JD, Kris-Etherton PM: A moderate-fat diet with one avocado per day increases plasma antioxidants and decreases the oxidation of small, dense LDL in adults with overweight and obesity: a randomized controlled trial. J Nutr. 2020, 150:276-84. 10.1093/jn/nxz231
- Pacheco LS, Li Y, Rimm EB, et al.: Avocado consumption and risk of cardiovascular disease in US adults . J Am Heart Assoc. 2022, 11:e024014. 10.1161/JAHA.121.024014
- Cheng HM, Koutsidis G, Lodge JK, Ashor A, Siervo M, Lara J: Tomato and lycopene supplementation and cardiovascular risk factors: a systematic review and meta-analysis. Atherosclerosis. 2017, 257:100-8. 10.1016/j.atherosclerosis.2017.01.009
- Evbayekha EO, Okobi OE, Okobi T, et al.: The evolution of hypertension guidelines over the last 20+ years: a comprehensive review. Cureus. 2022, 14:e31437. 10.7759/cureus.31437
- Mahmassani HA, Avendano EE, Raman G, Johnson EJ: Avocado consumption and risk factors for heart disease: a systematic review and meta-analysis. Am J Clin Nutr. 2018, 107:523-36. 10.1093/ajcn/nqx078