

SUPPORTING INFORMATION

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Supplemental Table 1. Literature search strategy

The following databases were searched:

- PubMed
- Scopus
- ISI web of knowledge

PubMed(n=130)

("Vitamin C"[Title/Abstract] OR "ascorbic acid"[MeSH Terms] OR "ascorbate"[Title/Abstract] OR "Dehydroascorbic Acid"[Title/Abstract] OR "ascorbic acid"[Title/Abstract] OR "Antioxidant"(1) OR "multivitamin"(1)) AND ("Blood pressure"[mesh] OR "Blood pressure"[tiab] OR "diastolic pressure"[tiab] OR "systolic pressure"[tiab] OR "pulse pressure"[tiab] OR hypertension[tiab] OR hypertension[mesh] OR "blood pressures"[tiab] OR "arterial pressure"[tiab] OR "Arterial tension"[tiab] OR "arterial tensions"[tiab] OR "systolic blood pressure"[tiab] OR "diastolic blood pressure"[tiab] OR "SBP"[tiab] OR "DBP"[tiab] OR "MAP"[tiab] OR "arterial blood pressure"[tiab] OR "Aortic pressure" [tiab] OR "Aortic pressures"[tiab] OR "Aortic tension"[tiab] OR "Aortic tensions"[tiab] OR "systolic arterial pressure"[tiab] OR "Aortic pressure"[tiab] OR cardiometabolic[tiab] OR cardiovascular [tiab]) AND ("systematic review" [tiab] OR meta-analysis[tiab])

Scopus(n=179)

(TITLE-ABS ("Vitamin C") OR TITLE-ABS ("ascorbic acid") OR TITLE-ABS ("Dehydroascorbic Acid") OR TITLE (Antioxidant) OR TITLE (multivitamin) OR TITLE-ABS- (ascorbate)) AND (TITLE-ABS ("Blood pressure" OR "diastolic pressure" OR "systolic pressure" OR "pulse pressure" OR hypertension OR "blood pressures" OR "arterial pressure" OR "Arterial tension" OR "arterial tensions" OR "systolic blood pressure" OR "diastolic blood pressure" OR "SBP" OR "DBP" OR "MAP" OR "arterial blood pressure" OR "Aortic pressure" OR "Aortic pressures" OR "Aortic tension" OR "Aortic tensions" OR "systolic arterial pressure" OR "Aortic pressure" OR cardiometabolic OR cardiovascular)) AND (TITLE-ABS ("systematic review" OR meta-analysis))

ISI(n=151)

(TI= ("Vitamin C") OR TI= ("ascorbic acid") OR TI= ("Dehydroascorbic acid") OR TI= (ascorbate) OR TI= (Antioxidant) OR TI= (multivitamin) OR AB= ("Vitamin C") OR AB= ("ascorbic acid") OR AB= ("Dehydroascorbic acid") OR AB= (ascorbate)) AND (TI= ("Blood pressure" OR "diastolic pressure" OR "systolic pressure" OR "pulse pressure" OR hypertension OR "blood pressures" OR "arterial pressure" OR "Arterial tension" OR "arterial tensions" OR "systolic blood pressure" OR "diastolic blood pressure" OR "SBP" OR "DBP" OR "MAP" OR "arterial blood pressure" OR "Aortic pressure" OR "Aortic pressures" OR "Aortic tension" OR "Aortic tensions" OR "systolic arterial pressure" OR "Aortic pressure" OR cardiometabolic OR cardiovascular) OR AB= ("Blood pressure" OR "diastolic pressure" OR "systolic pressure" OR "pulse pressure" OR hypertension OR "blood pressures" OR "arterial pressure" OR "Arterial tension" OR "arterial tensions" OR "systolic blood pressure" OR "diastolic blood pressure" OR "SBP" OR "DBP" OR "MAP" OR "arterial blood pressure" OR "Aortic pressure" OR "Aortic pressures" OR "Aortic tension" OR "Aortic tensions" OR "systolic arterial pressure" OR "Aortic pressure" OR cardiometabolic OR cardiovascular)) AND (TI=(systematic review) OR AB=("Systematic review") OR TI=(meta-analysis) OR AB=(meta-analysis))

Cochrane (n=43)

((("ascorbic acid" OR "Vitamin C" OR "ascorbate" OR "multivitamin" OR "Dehydroascorbic acid" OR "antioxidant"):ti,ab OR [mh "ascorbic acid"] OR [mh antioxidant]) AND ([mh "Blood pressure"] OR [mh hypertension] ("Blood pressure" OR "diastolic pressure" OR "systolic pressure" OR "pulse pressure" OR hypertension OR "blood pressures" OR "arterial pressure" OR "Arterial tension" OR "arterial tensions" OR "systolic blood pressure" OR "diastolic blood pressure" OR "SBP" OR "DBP" OR "MAP" OR "arterial blood pressure" OR "Aortic pressure" OR "Aortic pressures" OR "Aortic tension" OR "Aortic tensions" OR "systolic arterial pressure" OR "Aortic pressure" OR cardiometabolic OR cardiovascular):ti,ab,kw) AND (("systematic review" OR meta-analysis):ti,ab,kw))

Supplemental Table 2. List of excluded studies with reasons

Pregnant women(n=6) (2-7)
Network meta-analysis, umbrella review(n=1) (8)
Not relevant intervention(n=7) (9-15)
Not relevant outcome(n=24) (16-39)
Only systematic review/ review(n=21) (40-60)
Serum vitamin C (n=2) (61, 62)

Supplemental Table 3: Characteristics of the eligible meta-analyses reported investigating the effects of vitamin C supplementation on blood pressure

Outcome	Author; year (Ref)	Num of Primary RCTs extracted from meta study	Num of RCTs excluded from meta study	Reasons for exclusion	Num of non-overlap primary studies from other meta-analyses	Total RCT in main analysis
Systolic blood pressure	Juraschek;2012 (63)	29	20	Short duration(n=4)(64-67) Couldn't extract net effect(n=14)(1, 68-80) Non-English (n=1)(81) No Abstract(n=1)(82)	-	9
	Behers;2023 (83)	5	2	Short duration(n=2)(64, 65)	1	3
	Guan;2020 (84)	8	3	Short duration(n=1)(85) No control(n=2)(86, 87)	1	5
	De Paula;2017 (88)	2	1	Short duration(n=1)(67)	-	1
	Mason;2021 (89)	8	1	Short duration(n=1)(67)	3	7
	Lbban;2023(main) (90)	20	5	Short duration(n=4)(64-67) No Abstract(n=1)(82)	-	15
Diastolic blood pressure	Juraschek;2012 (63)	28	19	Short duration(n=4)(64-67) Couldn't extract net effect(n=13)(1, 69-80) Non-English (n=1)(81) No Abstract(n=1)(82)	-	12
	Behers;2023 (83)	4	2	Short duration(n=2)(64, 65)	1	2
	Guan;2020 (84)	8	3	Short duration(n=1)(85) No control(n=2)(86, 87)	1	5
	De Paula;2017 (88)	2	1	Short duration(n=1)(67)	-	1
	Mason;2021 (89)	8	1	Short duration(n=1)(67)	3	7
	Lbban;2023(main) (90)	20	5	Short duration(n=4)(64-67) No Abstract(n=1)(82)	-	15

Supplemental Table 4. Study quality and risk of bias assessment using ROB 2 tool

Author, Year	Bias arising from random process	Bias due to deviation from intervention	Bias due to missing outcome data	Bias in measurement of the outcome	Bias in selection of reported results	Overall quality
Bhatt, 2012	High	Low	Low	Low	Low	High
Duffy, 2001	Some concerns	Low	Low	Low	Low	Some concerns
El-Aal, 2018	Some concerns	Low	Low	High	Low	High
Fotherby, 2000	Some concerns	Low	Low	Low	Some concerns	Some concerns
Ghosh, 1994	Some concerns	Low	Low	Low	Some concerns	Some concerns
Gokce, 1999	Some concerns	Low	Low	Low	Low	Some concerns
Magen, 2004	Some concerns	Low	Low	Low	Some concerns	Some concerns
Mahajan, 2007	Some concerns	Low	Low	Low	Some concerns	Some concerns
Mason, 2019	Low	Low	Low	Low	Low	Low
Mullan, 2002	Low	Low	Low	Low	Low	Low
Nightingale, 2007	Some concerns	Low	Low	Low	Low	Some concerns
Osilesi, 1991	Some concerns	Some concerns	Low	High	Some concerns	High
Sanguanwong, 2016	Low	Low	Low	Low	Low	Low
Shateri, 2016	Low	High	Low	Low	Low	High
Ward, 2004	Low	Low	Low	Low	Some concerns	Some concerns
Woo, 2020	Some concerns	Low	Low	Low	Low	Some concerns
Yuan, 2017	Some concerns	Some concerns	Low	High	Low	High

Supplemental Table 5. Methodological quality of included meta-analysis using AMSTAR 2.

Author, Year	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Q13	Q14	Q15	Q16
Behers, 2023	Y	PY	Y	Y	Y	Y	Y	PY	Y	N	Y	N	Y	Y	Y	Y
de Paula, 2017	Y	PY	Y	PY	Y	Y	N	Y	Y	N	Y	N	N	N	N	Y
Guan, 2020	Y	PY	Y	N	N	N	N	N	Y	N	Y	N	N	Y	Y	N
Juraschek, 2012	Y	PY	Y	PY	N	N	Y	Y	Y	N	Y	N	N	Y	Y	N
Lbban, 2023	Y	Y	Y	PY	Y	N	N	Y	N	N	Y	N	Y	N	Y	N
Mason, 2021	Y	Y	Y	Y	Y	Y	Y	PY	Y	N	Y	Y	Y	Y	Y	Y

Supplemental Table 6: GRADE assessment of vitamin c supplementation on blood pressure

Certainty assessment							№ of patients		Effect	Certainty without imprecision
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	(91)	[comparison]	Mean difference (95%CI)	
Systolic blood pressure										
17	randomised trials	Serious ¹	not serious ²	not serious	Serious ³	none	611	511	MD 3.75 mmHg lower (5.67 Lower to 1.84 lower)	⊕⊕○○ Low
Diastolic blood pressure										
17	randomised trials	Serious ¹	Serious ⁴	not serious	not serious ⁵	none	611	511	MD 1.43 mmHg lower (2.96 Lower to 0.10 higher)	⊕⊕○○ Low

¹ Most studies were at risk of bias due to issues arising from the randomization process, selection of reported results, and measurement of outcomes. Although studies with a low risk of bias showed results similar to the main analysis, their number was small. Therefore, we conservatively chose to downgrade the certainty of the evidence

² There was evidence of substantial heterogeneity in the data ($I^2 = 61.8\%$, $P_{het} < 0.001$); however, out of 17 trials included in the analysis, 16 trials reported consistent decreasing effects. Indeed, there was high consistency in terms of the direction of the effects and, thus, the large heterogeneity in the data is due to difference in the magnitude of the effects. Not downgraded.

³ The point estimate exceeded the MID (2 mmHg) for systolic blood pressure reduction; however, the upper bound of the confidence interval crossed the threshold (-2 mmHg), indicating that the true effect might be smaller than the MID, leading to downgrading.

⁴ There was evidence of substantial heterogeneity in the data ($I^2 = 72.88\%$, $P_{het} < 0.001$); however, this heterogeneity was accounted for by a priori subgroup analysis based on study quality, and therefore, the certainty of evidence was not downgraded.

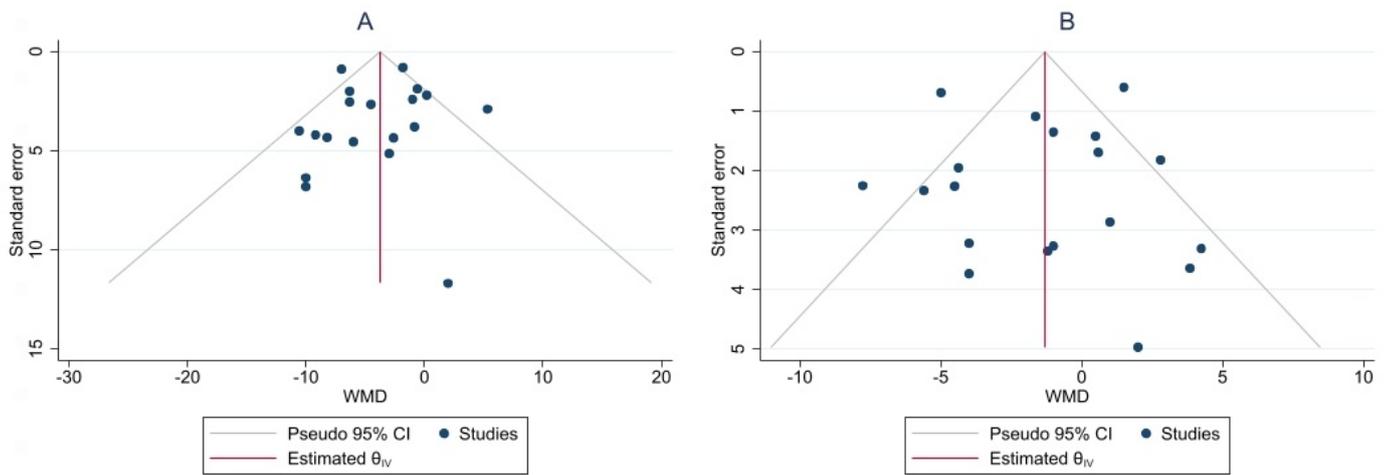
⁵ The point estimate and its confidence interval surpassed the threshold set as the MID for diastolic blood pressure (2 mmHg) and were not downgraded.

Supplemental Table 7: Sensitivity analysis of the effect of vitamin C supplementation on systolic blood pressure

Omitted study	WMD (95% CI)	p value
Woo, 2021	-3.785 (-5.755, -1.814)	0.000
Woo, 2021	-3.684 (-5.656, -1.713)	0.000
Yuan, 2019	-4.039 (-6.050, -2.027)	0.000
Mason, 2019	-3.303 (-5.232, -1.375)	0.001
El-Aal, 2018	-3.894 (-5.884, -1.905)	0.000
El-Aal, 2018	-4.216 (-5.958, -2.475)	0.000
Sanguanwong, 2016	-3.724 (-5.765, -1.682)	0.000
Shateri, 2016	-3.591 (-5.541, -1.640)	0.000
Bhatt, 2012	-3.465 (-5.365, -1.565)	0.000
Mahajan, 2007	-3.584 (-5.593, -1.576)	0.000
Nightingale, 2007	-3.794 (-5.719, -1.869)	0.000
Ward, 2005	-4.005 (-6.095, -1.915)	0.000
Magen, 2004	-4.066 (-6.039, -2.093)	0.000
Mullan, 2002	-3.542 (-5.476, -1.608)	0.000
Duffy, 2001	-3.629 (-5.560, -1.698)	0.000
Fotherby, 2000	-3.969 (-5.991, -1.947)	0.000
Gokce, 1999	-3.643 (-5.574, -1.713)	0.000
Ghosh, 1994	-3.808 (-5.795, -1.822)	0.000
Osilesi, 1991	-3.544 (-5.562, -1.526)	0.001
θ (Pooled Estimate)	-3.754 (-5.665, -1.842)	0.000

Supplemental Table 8: Sensitivity analysis of the effect of vitamin C supplementation on dystopic blood pressure

Omitted Study (Author, Year)	WMD (95% CI)	p-value
Woo, 2021	-1.447 (-3.036 to 0.142)	0.074
Woo, 2021	-1.335 (-2.914 to 0.244)	0.098
Yuan, 2019	-1.411 (-3.069 to 0.247)	0.095
Mason, 2019	-1.077 (-2.586 to 0.432)	0.162
El-Aal, 2018	-1.600 (-3.144 to -0.055)	0.042
El-Aal, 2018	-1.636 (-3.170 to -0.101)	0.037
Sanguanwong, 2016	-1.262 (-2.844 to 0.319)	0.118
Shateri, 2016	-1.212 (-2.764 to 0.340)	0.126
Bhatt, 2012	-1.096 (-2.561 to 0.370)	0.143
Mahajan, 2007	-1.578 (-3.196 to 0.041)	0.056
Nightingale, 2007	-1.501 (-3.057 to 0.055)	0.059
Ward, 2005	-1.726 (-3.291 to -0.162)	0.031
Magen, 2004	-1.715 (-3.244 to -0.185)	0.028
Mullan, 2002	-1.248 (-2.834 to 0.337)	0.123
Duffy, 2001	-1.352 (-2.924 to 0.220)	0.092
Fotherby, 2000	-1.462 (-3.110 to 0.186)	0.082
Gokce, 1999	-1.537 (-3.121 to 0.047)	0.057
Ghosh, 1994	-1.439 (-3.026 to 0.148)	0.076
Osilesi, 1991	-1.571 (-3.181 to 0.040)	0.056
θ (Pooled Estimate)	-1.433 (-2.964 to 0.098)	0.067



Supplemental Figure 1: Funnel plots with pseudo 95% CI limits for (A) SBP and (B) DBP. No significant publication bias (Egger's $p = 0.42$ and 0.72 ; Begg's $p = 0.62$ and 0.83 , respectively). DBP: diastolic blood pressure, SBP: systolic blood pressure

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