

Effects of 100% Orange Juice on Markers of Inflammation and Oxidation in Healthy and At-risk Adult Populations: A Scoping Review, Systematic Review, and Meta-analysis

Cara et al.

Online Supplementary Material

Supplementary Methods¹

To perform meta-analyses, we converted all reported CIs or SEMs to SDs. Rather than reporting net change, all included parallel trials reported only baseline and post-intervention results. Therefore, we calculated within-group change scores by subtracting baseline values from final measures. To estimate intervention effects, we used the difference between within-group change scores as net change. We then imputed missing SDs of net change based on reported baseline and final SDs and a common correlation coefficient of 0.5. Sensitivity analyses using correlation coefficients of 0.2 and 0.8 found no change in overall conclusions for pooled effects.

Similarly, all included crossover trials reported means and SDs or SEMs for each intervention separately rather than reporting net change. To deal with this inappropriate reporting, we approximated paired analyses for these studies by calculating net change means and imputing missing standard deviations of net change. Some crossover trials reported pooled baseline values due to no difference in baseline characteristics between participants assigned to each sequence. We used these pooled results as baseline values for the separate interventions. Next, as outlined in the Cochrane Handbook, we used reported *P* values to determine associated *t*-scores, calculate the standard error and standard deviation of change (1), and estimate correlation coefficients (2). If studies reported upper limits rather than exact *P* values, we adopted the reported upper limits as conservative *P* values for those studies as is recommended (e.g., $P < 0.001$ became $P = 0.001$). No *P* values were reported for OxLDL results, and for IL-6 and MDA, correlation coefficients differed across studies and were at or below |0.5|. Consequently, rather than using change from baseline values, we used post-intervention values to calculate net change means and estimate standard error of net change more precisely, as suggested in the Cochrane Handbook. For these three markers, net change means were calculated as between-group differences for final measurements. Standard errors of net change were calculated from final group SDs and a common correlation coefficient of 0.5. Sensitivity analyses using values of 0.2 and 0.8 produced similar results.

For high-sensitivity C-reactive protein (hs-CRP), correlation coefficients derived from reported *P* values showed some variation but were all > 0.5 , and the average correlation coefficient for the one study reporting *P* values for both baseline and post-intervention between-group differences was 0.78. Here, using change from baseline hs-CRP to calculate means and standard errors of net change was justified, and this was done as described above for parallel trials. A common correlation coefficient of 0.78 was used to impute standard errors of net change, and sensitivity analyses using coefficients of 0.2 and 0.5 resulted in similar findings.

For all markers, data were insufficient to perform pre-specified subgroup meta-analyses by health status of the study population (healthy or at-risk). For one marker, IL-6, data were sufficient to conduct the pre-specified subgroup meta-analysis by orange juice (OJ) preparation type (fresh-squeezed or commercial 100% OJ). In sensitivity meta-analyses, we excluded studies

¹ All citations included in the text, tables, and figures herein are listed under Supplementary References at the end of this document.

rated high risk of bias (ROB), and overall conclusions did not change, or remaining data were insufficient to analyze.

We avoided double counting participants in each meta-analysis. For controlled trials with multiple comparators, we selected interventions most closely matched to the 100% OJ intervention to reduce confounding. For example, if comparators included both water and an isocaloric beverage (e.g., water with glucose), we used only the isocaloric beverage for analysis, as this would control for energy intake. One crossover trial compared two 100% OJ interventions (commercial OJ without pulp and 0.7 g fiber/serving; juice from blended whole orange with 6.3 g fiber/serving) with two fiber-matched comparators (isocaloric sugar-matched control with no fiber; commercial OJ with 5.4 g added fiber/serving) (3). To avoid double counting participants from this study, we included only the non/low-fiber 100% OJ and comparator interventions due to similar fiber content with other meta-analyzed studies. Another crossover trial was conducted once in a polluted area and again in a non-polluted area with no difference in results between environments (4). To avoid double counting these participants, we analyzed only results from the first trial conducted in the polluted area. Each forest plot clearly identifies group comparisons to aid interpretation.

Supplementary Tables

Supplemental Table 1. Eligibility criteria for inclusion of studies in this review of the effect of 100% orange juice on markers of inflammation or oxidative stress

Category	Inclusion criteria	Exclusion criteria
Study design	Any intervention study: <ul style="list-style-type: none"> • Randomized controlled trials including those with crossover designs • Non-randomized controlled trials including quasi-experimental, crossover, and controlled before-after studies • Uncontrolled trials (e.g., single arm studies) Prospective cohort studies Nested case-control studies Case-cohort studies	Mendelian randomization studies Retrospective cohort studies Cross-sectional studies Narrative reviews Systematic reviews Meta-analyses Letters to the editor Case studies or case series Conference proceedings Abstracts
Study duration	No restriction	None
Sample size	No restriction	None
Intervention/exposure	100% orange juice (other terms could be “fresh,” “pure,” “whole,” “natural,” or “not from concentrate”) Juice made from whole oranges where variety is specified (e.g., mandarin, bergamot, satsuma, etc.)	Interventions other than 100% orange juice (e.g., juice from concentrate, juice with additives or where something has been removed, studies where only “orange juice” is specified)
Comparator	Comparisons across different 100% orange juice amounts. Comparisons of 100% orange juice to other foods/beverages (including comparison to usual diet in the case of single-arm studies). Comparison(s) to a placebo.	None
Outcomes	Oxidative stress and inflammatory markers such as (but not limited to): <ul style="list-style-type: none"> • Cytokines such as TNFα, IL-1, IL-6, and C-reactive protein • Toll-like receptors and transcription nuclear factors such as NFκB, 	Other outcomes

Category	Inclusion criteria	Exclusion criteria
	cyclooxygenase-2, and lipopolysaccharides	
Date of publication	No restriction	None
Publication status	Articles published in peer-reviewed journals	Articles not published in peer-reviewed journals, including unpublished data, manuscript reports, abstracts, pre-prints, and conference proceedings
Language of publication	English	Languages other than English
Country	No restriction	None
Study participants	Human subjects	Non-human subjects Pregnant and lactating women
Age of study participants	Adults, 18-years or older (based on mean/median if available or mid-point of reported age range)	None
Health status of participants	<p>Healthy populations</p> <ul style="list-style-type: none"> • Includes observational studies with <20% disease at baseline • Includes studies with overweight populations that are otherwise healthy <p>At-risk populations such as those with the following:</p> <ul style="list-style-type: none"> • Metabolic syndrome • Obesity • Mild hypercholesterolemia • Prediabetes • Hypertension 	Other diseased populations

Supplemental Table 2. Publications excluded from the review with reasons for exclusion

First author	Year	Title	Reason for excluding
None listed (5)	2009	Sugar-sweetened drinks and fructose linked to gout	Wrong publication type
Alvarez-Parrilla (6)	2010	Daily consumption of apple, pear and orange juice differently affects plasma lipids and antioxidant capacity of smoking and non-smoking adults	Wrong intervention
Aptekmann (7)	2010	Orange juice improved lipid profile and blood lactate of overweight middle-aged women subjected to aerobic training	Wrong intervention
Baird (8)	1979	The effects of ascorbic acid and flavonoids on the occurrence of symptoms normally associated with the common cold	Wrong outcome
Bond (9)	2014	Cardiorespiratory function associated with dietary nitrate supplementation	Wrong intervention
Brain (10)	2019	The effect of a pilot dietary intervention on pain outcomes in patients attending a tertiary pain service	Wrong intervention
Bub (11)	2003	Fruit juice consumption modulates antioxidative status, immune status and DNA damage	Wrong intervention
Büsing (12)	2017	Impact of regular orange juice or cola consumption on uric acid levels in healthy adults	Wrong publication type
Cerletti (13)	2012	Blood cell response to a fatty meal in healthy subjects at different degree of cardiovascular risk: Effect of orange juice (OJ) intake	Wrong publication type
Cerletti (14)	2013	Blood cell response to a fatty meal in healthy subjects at different degree of cardiovascular risk: Effect of orange juice intake	Wrong publication type
Choi (15)	2010	Fructose-rich beverages and risk of gout in women	Wrong intervention
Chrysohoou (16)	2011	Cardiovascular disease-related lifestyle factors and longevity	Wrong publication type
Cilla (17)	2009	Impact of fruit beverage consumption on the antioxidant status in healthy women	Wrong intervention
Constans (18)	2015	Marked antioxidant effect of orange juice intake and its phytonutrients in a preliminary randomized cross-over trial on mild hypercholesterolemic men	Wrong intervention
Coppola (19)	2004	Impairment of coronary circulation by acute hyperhomocysteinaemia and reversal by antioxidant vitamins	Wrong intervention
Crutchley (20)	2013	Effect of sugar-sweetened soft drinks on serum uric acid and associated metabolic risk factors	Wrong intervention
Devaraj (21)	2011	Effect of orange juice and beverage with phytosterols on cytokines and PAI-1 activity	Wrong intervention

First author	Year	Title	Reason for excluding
Devaraj (22)	2006	Reduced-calorie orange juice beverage with plant sterols lowers C-reactive protein concentrations and improves the lipid profile in human volunteers	Wrong intervention
Di Folco (23)	2018	Effects of a nutraceutical multicomponent including bergamot (<i>Citrus Bergamia</i> Risso) juice on metabolic syndrome: A pilot study	Wrong intervention
do Rosario (24)	2021	Food anthocyanins decrease concentrations of TNF-alpha in older adults with mild cognitive impairment: A randomized, controlled, double blind clinical trial	Wrong intervention
Ekhlesi (25)	2015	Effects of pomegranate and orange juice on antioxidant status in non-alcoholic fatty liver disease patients: a randomized clinical trial	Wrong population
Ghanim (26)	2007	Orange juice or fructose intake does not induce oxidative and inflammatory response	Wrong intervention
Giordano (27)	2012	Four-week ingestion of blood orange juice results in measurable anthocyanin urinary levels but does not affect cellular markers related to cardiovascular risk: a randomized cross-over study in healthy volunteers	Wrong outcome
Goncalves (28)	2017	Orange juice as dietary source of antioxidants for patients with hepatitis C under antiviral therapy	Wrong population
Goszcz (29)	2019	Consumption of antioxidant-rich drinks does not protect against endothelial dysfunction associated with a high-calorie meal challenge	Wrong intervention
Goszcz (30)	2019	Co-ingestion of antioxidant drinks with an unhealthy challenge meal fails to prevent post-prandial endothelial dysfunction: an open-label, crossover study in healthy older adults	Wrong intervention
Harima-Mizusawa (31)	2016	Citrus juice fermented with <i>Lactobacillus plantarum</i> YIT 0132 alleviates symptoms of perennial allergic rhinitis in a double-blind, placebo-controlled trial	Wrong population
Hofmann (32)	2006	Intervention with polyphenol-rich fruit juices results in an elevation of glutathione S-transferase P1 (hGSTP1) protein expression in human leucocytes of healthy volunteers	Wrong intervention
Johnston (33)	2003	Orange Juice Ingestion and Supplemental Vitamin C Are Equally Effective at Reducing Plasma Lipid Peroxidation in Healthy Adult Women	Wrong intervention
Joosten (34)	2014	Effect of moderate alcohol consumption on fetuin-A levels in men and women: Post-hoc analyses of three open-label randomized crossover trials	Wrong intervention
Joosten (35)	2012	Moderate alcohol consumption alters both leucocyte gene expression profiles and circulating proteins related to immune response and lipid metabolism in men	Wrong intervention
Kirkhus (36)	2012	Effects of similar intakes of marine n-3 fatty acids from enriched food products and fish oil on cardiovascular risk markers in healthy human subjects	Wrong intervention

First author	Year	Title	Reason for excluding
Ko (37)	2005	Comparison of the antioxidant activities of nine different fruits in human plasma	Wrong outcome
Kurowska (38)	2000	HDL-cholesterol-raising effect of orange juice in subjects with hypercholesterolemia	Wrong outcome
Li (39)	2018	Effects of blood orange juice consumption on vascular function in healthy overweight subjects of European origin	Wrong intervention
Li (40)	2020	Blood Orange Juice Consumption Increases Flow-Mediated Dilation in Adults with Overweight and Obesity: a Randomized Controlled Trial	Wrong intervention
Liu (41)	2017	Association Between Inflammatory Diet Pattern and Risk of Colorectal Carcinoma Subtypes Classified by Immune Responses to Tumor	Wrong intervention
Milenkovic (42)	2011	Hesperidin displays relevant role in the nutrigenomic effect of orange juice on blood leukocytes in human volunteers: a randomized controlled cross-over study	Wrong intervention
Milenkovic (43)	2009	Identification of molecular targets of hesperidin, the major flavonoid of orange juice, in relation to its beneficial vascular action in healthy men	Wrong intervention
Milenkovic (44)	2013	The role of hesperidin in the nutrigenomic effect of orange juice on blood leukocytes in human volunteers	Wrong intervention
Morand (45)	2011	Hesperidin contributes to the vascular protective effects of orange juice: a randomized crossover study in healthy volunteers	Wrong intervention
Mullan (46)	2016	Effects of a beverage rich in (poly)phenols on established and novel risk markers for vascular disease in medically uncomplicated overweight or obese subjects: A four week randomized placebo-controlled trial	Wrong intervention
Murphy (47)	2013	The effect of post-match alcohol ingestion on recovery from competitive rugby league matches	Wrong intervention
Nakamura (48)	2017	Effect of β -cryptoxanthin-rich Satsuma mandarin juice supplementation on pulse wave velocity: A randomized controlled trial	Wrong intervention
Napoleone (49)	2012	Orange juice intake decreases the procoagulant activity of whole blood: A randomized crossover study in healthy volunteers	Wrong intervention
Napoleone (50)	2013	Both red and blond orange juice intake decreases the procoagulant activity of whole blood in healthy volunteers	Wrong outcome
Nasser (51)	2011	Evaluation of serum oxidative stress in regular consumers of orange juice	Wrong intervention
Nishino (52)	2009	Cancer prevention by carotenoids	Wrong intervention
Numminen (53)	2000	The effect of acute ingestion of a large dose of alcohol on the hemostatic system and its circadian variation	Wrong intervention

First author	Year	Title	Reason for excluding
O'Neil (54)	2012	100% orange juice consumption is associated with better diet quality, improved nutrient adequacy, decreased risk for obesity, and improved biomarkers of health in adults: National Health and Nutrition Examination Survey, 2003-2006	Wrong study design
Perche (55)	2014	Orange juice and its major polyphenol hesperidin consumption do not induce immunomodulation in healthy well-nourished humans	Wrong intervention
Pereira-Caro (56)	2015	Chronic administration of a microencapsulated probiotic enhances the bioavailability of orange juice flavanones in humans	Wrong intervention
Rangel (57)	2012	Evolution of plasma inflammatory biomarkers after the intake of an orange-based beverage enriched with polyphenols in overweight adults (BIONAOS Study)	Wrong intervention
Rangel (58)	2013	Consumption of a polyphenol-rich orange juice improves endothelial biomarkers in overweight and obese adults(bionaos study)	Wrong outcome
Rendeiro (59)	2016	Flavanone-rich citrus beverages counteract the transient decline in postprandial endothelial function in humans: a randomised, controlled, double-masked, cross-over intervention study	Wrong outcome
Rocha (60)	2017	Orange juice modulates proinflammatory cytokines after high-fat saturated meal consumption	Wrong intervention
Rouyer (61)	2019	Effects of a high fat meal associated with water, juice, or champagne consumption on endothelial function and markers of oxidative stress and inflammation in young, healthy subjects	Wrong intervention
Smith (62)	1997	Caffeine and the common cold	Wrong intervention
Szeto (63)	2013	A study of DNA protective effect of orange juice supplementation	Wrong intervention
Teng (64)	2013	Consumption of green tea and alcohol, and serum urate levels: The singapore chinese health study	Wrong intervention
Valls (65)	2020	Effects of hesperidin in orange juice on blood and pulse pressures in mildly hypertensive individuals: a randomized controlled trial (Citrus study)	Wrong outcome
Venneria (66)	2013	Potential beneficial effects of anthocyanins on nutritional status of obese human subjects	Wrong intervention
Volman (67)	2010	Effects of α -glucans from <i>Agaricus bisporus</i> on ex vivo cytokine production by LPS and PHA-stimulated PBMCs; A placebo-controlled study in slightly hypercholesterolemic subjects	Wrong intervention

Supplemental Table 3. GRADE evidence profiles for commonly reported markers assessed by included studies¹

Outcome	Quality assessment							Summary of findings	Strength of evidence ²
	Total studies	n studies by design	Limitations	Imprecision	Inconsistency	Indirectness	Publication bias		
C-reactive protein (CRP) measured in plasma or serum	2	1 Crossover RCT (3) 1 Before-after (68)	Very serious limitations: Information is from studies at moderate and high ROB. The crossover RCT was rated <i>some concern</i> for overall ROB and bias due to period and carryover effects and selection of reported results. The before-after study had <i>high</i> overall ROB due to study design.	Very serious imprecision: Both the crossover RCT (n=36) and the before-after study (n=20) had small sample sizes. Both studies reported no effect of 100% OJ, and CIs were not sufficiently narrow for either study.	No serious inconsistency: Both studies showed no effects with 100% OJ.	No serious indirectness: Clinical outcome.	Unlikely: Both studies showed no effect. One study was industry funded.	100% OJ interventions may have no effects on CRP levels.	⊕○○○ VERY LOW
High-sensitivity C-reactive protein (hs-CRP) measured in serum	7	3 Crossover RCTs (69-71) 1 Parallel RCT (72) 1 Non-randomized parallel controlled intervention (73) 2 Before-after (74, 75)	Very Serious limitations: Most of the information is from studies at high ROB. Two crossover and one parallel RCT were rated <i>some concern</i> for overall ROB due to either randomization and/or reporting. Two trials were rated <i>high</i> overall ROB including one crossover RCT for period and carryover effects and one parallel trial with ROB due to randomization and adherence to assigned intervention. The two before-after studies have	Very serious imprecision: A forest plot of two crossover RCTs and two parallel controlled trials had a small total sample size (n=139). Two of these studies found no effect for 100% OJ, and the CIs for three of these studies were not sufficiently narrow. One other crossover RCT (n=45) had no non-100% OJ comparator and reported no effect with either 100% OJ intervention. The two before-after studies had small sample	Serious inconsistency: A random effects meta-analysis of the four controlled trials with non-100% OJ comparators showed no effect of 100% OJ, widely overlapping CIs, and high significant heterogeneity ($I^2=78.8%$, $P=0.003$). Separate random effects meta-analyses by study design showed two crossover RCTs had high significant heterogeneity ($I^2=86.5%$, $P=0.007$) that may be explained by differing study characteristics (health status and/or juice preparation). Results for	No serious indirectness: Clinical outcome.	Unlikely: Three studies showed no effect. Two studies were industry funded.	100% OJ interventions may have beneficial effects on hs-CRP levels.	⊕○○○ VERY LOW

Outcome	Quality assessment							Summary of findings	Strength of evidence ²
	Total studies	n studies by design	Limitations	Imprecision	Inconsistency	Indirectness	Publication bias		
			<i>high</i> overall ROB due to study design.	sizes (n=50 and 35). Both reported significant effects with 100% OJ where one study had sufficiently narrow CIs, but participants served as their own controls.	the two parallel controlled trials showed no heterogeneity ($I^2=0.0\%$, $P=0.945$) and a beneficial effect with 100% OJ. A crossover RCT with two 100% OJ interventions found no effect with 100% OJ, but the two before-after studies reported significant benefits with 100% OJ.				
Interleukin 6 (IL-6) measured in serum	4	Crossover RCTs (3, 69, 70, 76)	Serious limitations: Most of the information is from studies at moderate ROB. Of the 4 crossover RCTs, 3 were rated <i>some concern</i> for overall ROB due to randomization, period and carryover effects, or selection of reported results. The other RCT was rated <i>high</i> overall ROB due to period and carryover effects.	Very serious imprecision: A random effects meta-analysis on the 4 trials had a small total sample size (n=88). The significant pooled net difference CI was not sufficiently narrow (-2.3, -0.70).	No serious inconsistency: A random effects meta-analysis on the four crossover RCTs showed widely overlapping CIs, low non-significant heterogeneity ($I^2=23.0\%$, $p=0.27$), and significantly beneficial effects with 100% OJ.	No serious indirectness: Clinical outcome.	Unlikely: One trial showed no effects. One study was industry funded.	100% OJ interventions may have beneficial effects on IL-6 levels.	⊕○○○ VERY LOW
Tumor necrosis factor alpha (TNF- α) measured in plasma or serum	4	2 Crossover RCTs (3, 70) 2 Before-after (68, 74)	Very serious limitations: Most of the information is from studies at high ROB. Of crossover RCTs, one was rated <i>some concern</i> and one was rated <i>high</i> for overall ROB due to period and carryover effects.	Very serious imprecision: The crossover RCTs had small sample sizes (n=21 and 39). One crossover RCT found significant effects with 100% OJ, but the CIs were not sufficiently narrow. The	Serious inconsistency: One crossover RCT showed significantly beneficial effects with 100% OJ. One crossover RCT and two before-after studies	No serious indirectness: Clinical outcome.	Unlikely: Three studies showed no effect. Two studies were industry funded.	100% OJ interventions may have no effect on TNF- α levels.	⊕○○○ VERY LOW

Outcome	Quality assessment							Summary of findings	Strength of evidence ²
	Total studies	n studies by design	Limitations	Imprecision	Inconsistency	Indirectness	Publication bias		
			Both trials showed <i>some concern</i> for bias due to reporting of results. The two before-after studies have <i>high</i> overall ROB due to study design.	other crossover RCT reported no effect, and CI could not be determined. The before-after studies had small sample sizes (n=20 and 50) with no effect from 100% OJ when participants served as their own controls. CIs were not sufficiently narrow.	showed no effects with 100% OJ.				
Malondialdehyde (MDA) measured in plasma or serum	6	3 Crossover RCTs (4, 77, 78) 1 Parallel RCT (72) 1 Non-randomized parallel controlled intervention (79) 1 Before-after (74)	Very serious limitations: Most of the information is from studies at high ROB. One crossover and one parallel RCT were rated <i>some concern</i> for overall ROB due to randomization and reporting of results. Three trials rated <i>high</i> overall ROB included one crossover RCT and one parallel trial with ROB due to adherence to the assigned intervention and one crossover RCT with period and carryover effects. The before-after study had <i>high</i> overall ROB due to study design.	Very serious imprecision: A random effects meta-analysis on 3 crossover RCTs had a small total sample size (n=127) and non-significant pooled effects for 100% OJ with a sufficiently narrow CI (-0.19, 0.08). A forest plot of the two parallel trials with a small total sample size (n=100) showed the CIs for individual studies were not sufficiently narrow, and one study reported significant effects with 100% OJ. The before-after study had a small sample size (n=50) and reported a significant effect with 100% when participants	Serious inconsistency: A random effects meta-analysis on the five controlled trials showed no effects for 100% OJ, widely overlapping CIs among four studies, and high significant heterogeneity ($I^2=78.3%$, $p=0.001$). Separate random effects meta-analyses by study design showed moderate non-significant heterogeneity in three crossover RCTs ($I^2=45.3%$, $p=0.16$), and high significant heterogeneity in two parallel trials ($I^2=86.2%$, $p=0.007$). Heterogeneity may be explained by health status differences (healthy vs. at-risk).	No serious indirectness: Clinical outcome.	Unlikely: Four studies showed no effect. Three studies were industry funded.	100% OJ interventions may have no effect on MDA levels.	⊕○○○ VERY LOW

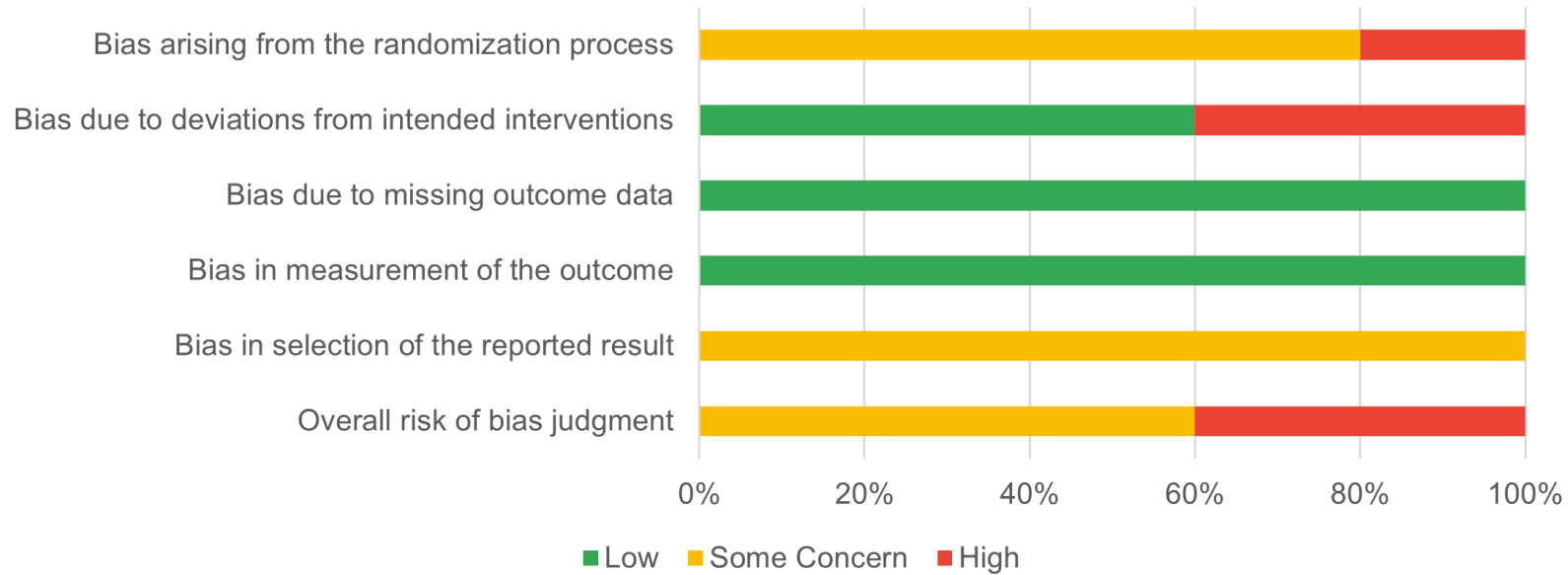
Outcome	Quality assessment							Summary of findings	Strength of evidence ²
	Total studies	n studies by design	Limitations	Imprecision	Inconsistency	Indirectness	Publication bias		
				served as their own controls, but CIs were not sufficiently narrow.	The before-after study and one of the parallel trials found significant benefits with 100% OJ.				
Oxidized LDL (oxLDL) measured in plasma	3	2 Crossover RCTs (3, 77) 1 Non-randomized parallel controlled intervention (73)	Serious limitations: Most of the information is from studies at moderate ROB. Two crossover RCTs had <i>some concern</i> for overall ROB due to randomization, period and carryover effects, and/or reported results. The parallel trial was rated <i>high</i> overall ROB due to randomization and adherence issues.	Very serious imprecision: A forest plot with 2 crossover RCTs and one non-randomized parallel controlled intervention showed a small total sample size (n=156), and no individual study reported significant effects for 100% OJ. The CIs for individual studies were not sufficiently narrow.	No serious inconsistency: A random effects meta-analysis for all three studies showed no effects with 100% OJ, widely overlapping CIs, and no heterogeneity ($I^2=0.0%$, $p=0.846$)	No serious indirectness: Clinical outcome.	Unlikely: All three studies showed no effect. Two studies were industry funded.	100% OJ interventions may have no effect on oxLDL levels.	⊕○○○ VERY LOW

¹GRADE, Grades of Recommendation, Assessment, Development, and Evaluation; OJ, orange juice; RCT, randomized controlled trial; ROB, risk of bias.

²Symbols indicate the following strength of evidence: ⊕⊕⊕⊕, High (We are very confident that the true effect lies close to that of the estimate of the effect.); ⊕⊕⊕○, Moderate (We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.); ⊕⊕○○, Low (Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.); and ⊕○○○, Very low (We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect.).

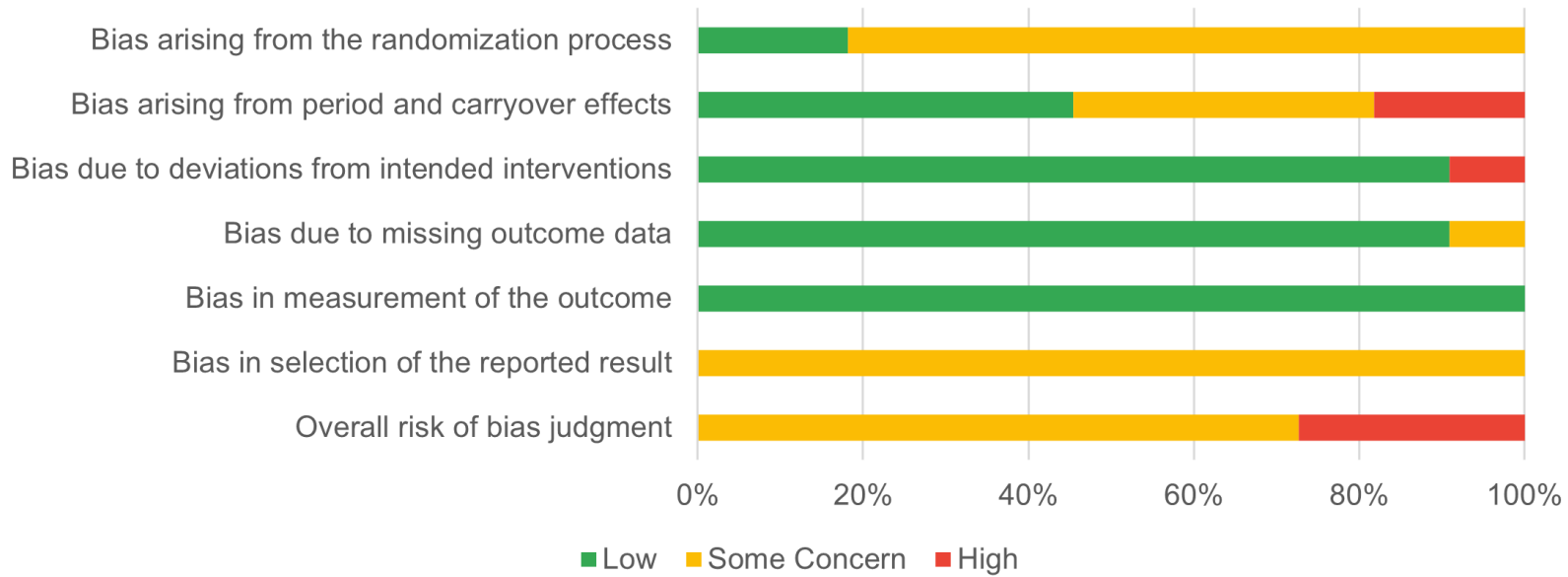
Supplementary Figures

Parallel Trials (n=5 studies)

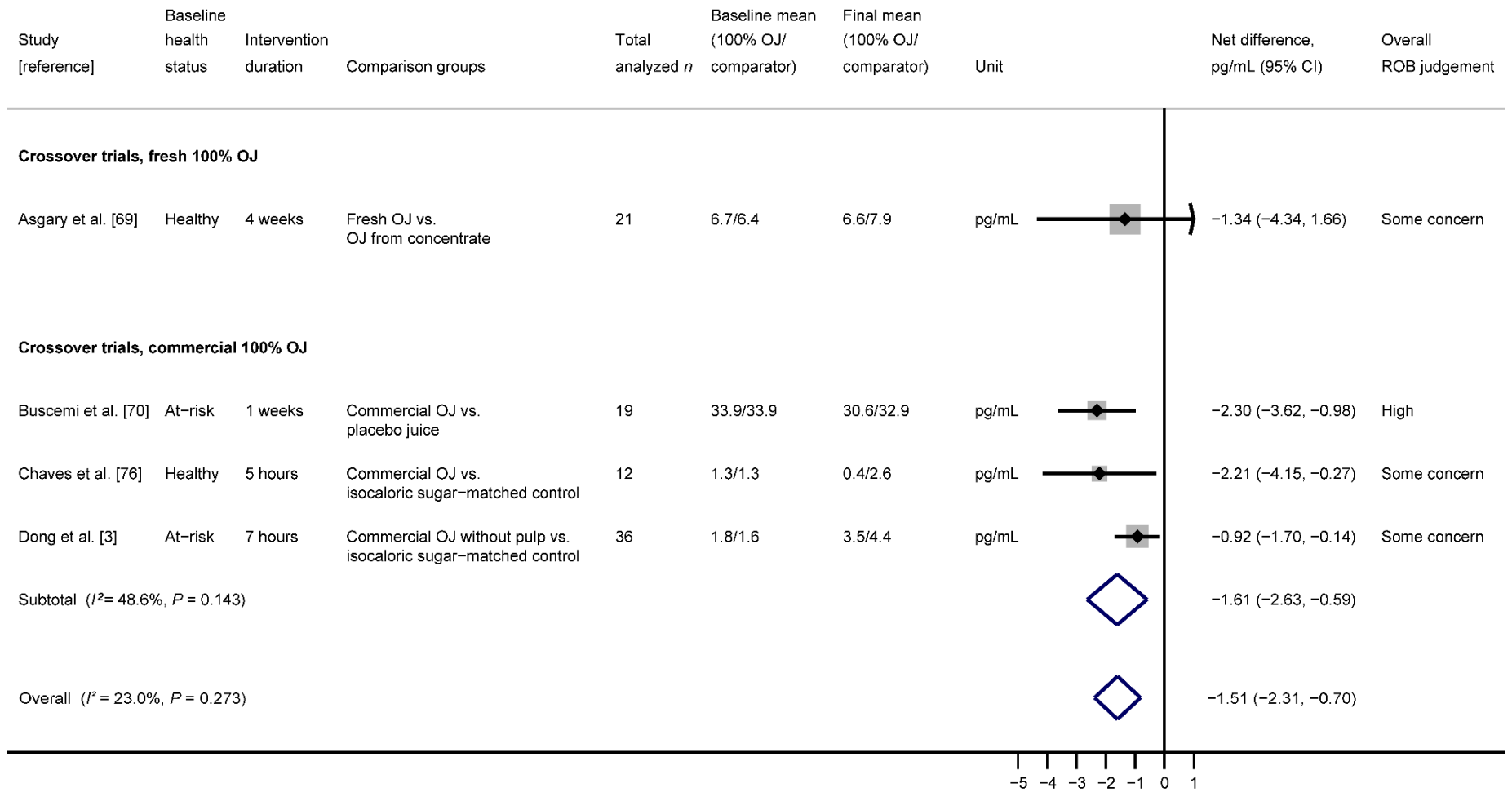


Supplemental Figure 1. Domain-specific and overall risk of bias judgment results for five included parallel trials

Crossover Trials (n=11 studies)



Supplemental Figure 2. Domain-specific and overall risk of bias judgment results for 11 included crossover trials



Supplemental Figure 3. Random-effects model meta-analysis of crossover trials measuring IL-6 in participants given 100% OJ and non-100% OJ interventions with subgroup analysis by juice preparation type (fresh or commercial). Box sizes represent study weight; OJ, orange juice; ROB, risk of bias.

Supplementary References

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