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External reference group – 5 A Day logo

Paper for information: 'Fruit juice and health rapid review – early conclusions'.

Please see attached paper for information. Source of funding added (see tables 1-3).

‘Rapid review on fruit juice and fruit and vegetable consumption- early conclusions’

Background – fruit juice

1. A review of the evidence on fruit juice consumption and cardiovascular disease was requested in order to assess the relationship between fruit juice and health since the 5-a-day message was accepted.

Literature search

2. A literature search was performed in PubMed to identify prospective cohort studies and randomised controlled trials which assessed the relationship between fruit juice intake and cardiovascular disease and markers for disease risk. The risk markers included were blood pressure, total cholesterol, LDL cholesterol, HDL cholesterol, triglycerides and vascular function. No start date was specified for the search, which was conducted up to the middle of November 2014.

3. The search was performed using a set of terms adapted from published systematic reviews to increase the likelihood of capturing the available evidence, but it is important to note that this exercise is not intended to be a systematic review.

Inclusion and exclusion criteria

4. Studies were included if they met the following criteria:

    - prospective cohort studies
    - randomised controlled trials (RCTs)
    - included an appropriate control group
    - published in English
    - conducted in humans
    - participants are healthy or at increased risk of disease
    - investigated fruit juice including tomato juice, as tomatoes are considered as a fruit
    - the endpoint was cardiovascular disease or markers for disease risk such as total cholesterol, LDL, HDL, Triglyceride, blood pressure and vascular function

5. Studies were excluded for the following reasons:

    - ecological, cross-sectional, case control studies, case reports or animal studies

- if trials did not state that participants had been randomly allocated to the intervention group.
- subjects with diabetes mellitus, cardiovascular, lung, liver, kidney or any other chronic disease.
- use of fruit juice powder
- fruit cordial/squash
- vegetable or a combination of fruit and vegetable juice
- the effect of fruit juice alone could not be ascertained, eg RCTs that compared one fruit juice with another, fruit juice fortified with sterols or other components or if the studies included multi-component interventions

Results

Cohort studies

6. In total, two prospective cohort studies and 13 RCTs were identified that met the inclusion criteria. Specific details of these studies can be found in tables 1-2.

7. Both cohort studies were conducted in the US; one reported on fruit juice (Duffey et al., 2010) and the other on tomato juice (Sesso et al., 2003). Duffey et al. (2010) reported on the beverage consumption of 2774 adults and their risk of cardiovascular disease 20 years later. The authors found that increasing fruit juice intake was associated with a significant decrease in the incidence of hypertension. No associations were found for the risk of high triglyceride and LDL concentrations, or low HDL concentrations. Sesso et al. (2003) assessed the diet of 38,445 women who were recruited to a trial involving vitamin E and aspirin supplementation. They found that after a median of 7.2 years of follow up, tomato juice consumption was not associated the incidence of cardiovascular disease. See table 1 for details of these studies.

RCTs

8. Of the 13 RCTs investigating cardiovascular risk, five were conducted in the US, one in Brazil, one in Canada, four in Europe, one in Japan and one in South Korea. The duration of the trials ranged from seven days to 18 months, with only three of the studies being longer than four weeks (see table 2 for details). The fruit juices investigated include orange juice, reduced energy cranberry juice, GoChi^{TM} juice, tomato juice, watermelon juice, pomegranate juice and concord grape juice.

Blood pressure

9. Seven RCTs investigated fruit juice consumption in relation to blood pressure (Amagase and Nance, 2008, Basu et al., 2011, Dohadwala et al., 2010, Lynn et al., 2012, Morand et al., 2011, Park et al., 2004, Ruel et al., 2013). See table 2.

Lynn et al. (2012) found that supplementing participants with 330ml of pomegranate juice for four weeks resulted in significantly lower systolic and diastolic blood pressure compared to the control group. No significant differences in BMI were found between the experimental groups. A cross-over trial found that after four weeks, diastolic blood pressure was significantly lower in overweight men following the consumption of 500ml of orange juice per day compared with the control beverage (Morand et al., 2011). However, no effect on systolic blood pressure was demonstrated in this study. A third trial conducted in mildly hypertensive men found that both diastolic and systolic blood pressure were significantly lower following the consumption of concord grape juice (5.5ml/kg/day) at the end of the intervention compared with baseline (Park et al., 2004). Diastolic blood pressure was also significantly lower compared to baseline after the consumption of the placebo drink, but the reduction was less than the grape juice intervention (-3.2 mm Hg vs. -6.2 mm Hg). Park et al. 2004 did not report between group comparisons so it is not clear whether there was any significant effect of the intervention compared to the control.

10. The four other RCTs found no significant effect of consuming fruit juice on blood pressure (Amagase and Nance, 2008, Basu et al., 2011, Dohadwala et al., 2010, Ruel et al., 2013).

Blood lipids

11. Eight RCTs explored the effect of fruit juice intake in relation to blood lipid concentrations (Aptekmann and Cesar, 2010, Basu et al., 2011, Collins et al., 2004, Dohadwala et al., 2010, Morand et al., 2011, Mulero et al., 2012, Park et al., 2009, Maruyama et al., 2001). See table 2**.**

12. One RCT conducted in overweight and obese pre-menopausal women instructed participants to engage in aerobic training three times a week; the experimental group consumed 500ml of orange juice each day for 12 weeks whereas the control group received no additional intervention (Aptekmann and Cesar, 2010). At the end of the study period, the group receiving orange juice had significantly lower concentrations of total cholesterol and LDL, but higher concentrations of HDL and improved LDL: HDL ratio compared to baseline values. No significant effect was found for triglyceride concentrations following orange juice consumption. There were no significant effects on any of the blood lipid concentrations in the control group at the end of the intervention. No comparisons between the orange juice and control group were reported. The authors stated that there was no significant difference between body weight, BMI and percentage fat between the intervention and control group; weight loss is also known to lower blood lipids.

13. One RCT in subjects with increased metabolic risk were allocated to either receive 300ml of a citrus-based juice per day or a placebo beverage for six months (Mulero et al., 2012). At the end of the study, concentrations of total cholesterol, LDL and HDL were significantly lower after citrus juice consumption compared to baseline values; no effect was observed for triglyceride levels. No differences were found for any of the blood lipids in the placebo group. No information on background diet, anthropometry or physical activity was provided so it cannot be ascertained if it was the fruit juice intervention that was specifically leading to a reduction in blood lipid concentrations. In addition, no details of the placebo beverage were reported and whether it had the same energy content as the citrus-based drink.

14. Maruyama et al. (2001) recruited 31 female students and allocated them to three groups: 480 g of a control drink, 160g of control drink plus 320g tomato juice or 480g of tomato juice. They were asked to consume the drinks for one menstrual cycle. At the end of the study, the level of free cholesterol in the HDL fraction was significantly higher in the high tomato juice consumers compared to the control group but no other effects were seen amongst the lipid fractions of LDL, HDL and VLDL.

15. The five other RCTs found no significant effect of consuming fruit juice on any of the blood lipid measures (Basu et al., 2011, Collins et al., 2004, Dohadwala et al., 2010, Morand et al., 2011, Park et al., 2009).

Vascular function

16. Five RCTs investigated the effect of fruit juice intake on vascular function using a range of measures (Buscemi et al., 2012, Davidson et al., 2009, Dohadwala et al., 2010, Lynn et al., 2012, Ruel et al., 2013). See table 2.

17. One crossover trial recruited 21 subjects at increased cardiovascular risk who received 500ml of red orange juice per day and 500ml of placebo beverage on separate occasions for a period of 7 days (Buscemi et al., 2012). Twelve healthy, non-obese volunteers were also recruited as controls but did not receive any beverage; therefore, results from these participants have not been captured. Nineteen volunteers completed the study which found that flow mediated dilatation, a measure of arterial function, was significantly higher after consuming orange juice compared to placebo or baseline. Fruit juice intake did not have any significant effect on the markers of vascular function measured in the other four RCTs (Davidson et al., 2009, Dohadwala et al., 2010, Lynn et al., 2012, Ruel et al., 2013).

Discussion

18. One cohort study observed that increasing fruit juice consumption was associated with a lower risk of developing hypertension (Duffey et al., 2010) and three RCTs found that fruit juice (pomegranate, orange juice or concord grape juice) supplementation reduced blood pressure (Lynn et al., 2012, Morand et al., 2011, Park et al., 2004). Two RCTs reported beneficial effects on blood lipids following consumption of orange juice and a citrus based juice containing chokeberry extract (Aptekmann and Cesar, 2010, Mulero et al., 2012) and one RCT found that the intake of orange juice improved vascular function (Buscemi et al., 2012)

19. There are few studies demonstrating that fruit juice reduces the risk of cardiovascular disease. Of the trials that show an effect, all of them involve consuming fruit juice well in excess of the current recommendation of 150ml per day; in addition the trials include a small number of participants and only three studies are longer than four weeks. Therefore it is difficult to apply these findings to the general population. In summary, there is insufficent evidence to show that fruit juice intake reduces cardiovascular disease risk, however, there is no evidence of detrimental effects.

Background- fruit and vegetables

20. A review of the evidence to determine if there were any grounds for setting specific portion size for children in terms of fruit and vegetable consumption was undertaken.

Literature search

21. A literature search was performed in PubMed to identify studies that assessed the intake of fruit and vegetables during childhood and adolescence and subsequent cardiovascular risk in adulthood.

22. The same cardiovascular search terms were used as for the fruit juice literature search and terms for fruit and vegetables were taken from published reviews.

23. No start date was specified for the search, which was conducted up to the middle of November 2014.

Inclusion and exclusion criteria

24. Studies were included if they met the following criteria:
    - prospective cohort studies
    - randomised controlled trials (unlikely to be identified given the nature of the question)
    - published in English
    - conducted in humans
    - participants are healthy or at increased risk of disease
    - conducted in children and adolescents up to the age of 18 years.

25. Studies were excluded for the following reasons:

    - ecological, cross-sectional, case control studies, case reports or animal studies
    - subjects with cardiovascular, lung, liver, diabetes mellitus, kidney or any other long-term disease
    - studies conducted in adults

Result of search

26. Two prospective cohort studies were identified that met the inclusion criteria (Aatola et al., 2010, Jaaskelainen et al., 2012, Ness et al., 2005). There were no relevant randomised controlled trials found in the search. Specific details of the studies can be found in table 3.

27. Two papers reported on the Cardiovascular Risk in Young Finns study which investigated diet in childhood with cardiometabolic risk in adulthood (Aatola et al., 2010, Jaaskelainen et al., 2012). Jaaskelainen et al. (2012) found that increased vegetable consumption in childhood was associated with a significantly lower risk of high blood pressure and triglyceride concentrations in adulthood. Aatola et al. (2010) reported that higher vegetable consumption in childhood was associated with a significantly lower arterial pulse wave velocity, a measure of vascular function; no significant relationship was found for fruit consumption. Additionally high consumption of fruit and vegetables in both childhood and adulthood was associated with a decreased pulse wave velocity in adulthood.

28. The other study was performed in the UK and recruited families to the Boyd Orr Cohort between1937-39 and followed them until 2000 (Ness et al., 2005). No significant relationship was found between fruit or vegetable consumption in childhood and coronary heart disease mortality in adulthood. However, higher vegetable consumption in childhood was associated with a lower risk of stroke in adulthood, but no association was found for fruit intake.

Discussion

29. Due to the limited nature of the evidence, no firm conclusions can be drawn on whether fruit and vegetable intake in childhood affects cardiovascular risk in adulthood.

Table 1: Fruit juice and cardiovascular disease- prospective cohort studies

Author/ Cohort	Country	No of subjects	Characteristics at baseline	Duration	Fruit juice	Outcome	Contrast	RR (95% CI) P-trend	Adjustments	Funding
Duffey et al. 2010 CARDIA[A]	US	2627	Men and women 18-30yrs	20 years	All fruit juice	High triglycerides[B]	Q4 vs. Q1	0.99 (0.91-1.09) 0.912	Race, sex, exam centre, year 0 age, weight, smoking status, energy from food, total physical activity, energy from low fat milk, whole fat milk and SSBs, and energy from alcohol	Major funding Danone Research Center, National Institute of Health (NIH), Additional funding was received from the NIH, the University of North Carolina– Chapel Hill Center for Environmental Health and Susceptibility, the UNC-CH Clinic Nutrition Research Center, and the Carolina Population Center; and from contracts with the University of Alabama at Birmingham, Coordinating Center; the University of Alabama at

Author/ Cohort	Country	No of subjects	Characteristics at baseline	Duration	Fruit juice	Outcome	Contrast	RR (95% CI) P-trend	Adjustments	Funding
										Birmingham, Field Center; the University of Minnesota, Field Center; Northwestern University, Field Center; and the Kaiser Foundation Research Institute from the National Heart, Lung, and Blood Institute.
		2640				High LDL[C]		0.96 (0.75-1.22) 0.741	Same as above	
		1837				Low HDL[D]		1.00 (0.87-1.16) 0.927	Same as above	
		2639				Hypertension[E]		0.89 (0.82-0.97) 0.007	Same as above	
Sesso et al. 2003 Women's Health Study	US	38,024	Women aged ≥ 45yrs, postmenopausal or not intending to become pregnant	Median 7.2 years	Tomato juice	Cardiovascular disease	Q4 vs. Q1	1.14 (0.83-1.56) 0.24	Age, randomised aspirin, randomised vitamin E, randomised β-carotene, BMI, exercise, smoking, postmenopausal hormone use,	NIH, Roche vitamins Inc

Author/ Cohort	Country	No of subjects	Characteristics at baseline	Duration	Fruit juice	Outcome	Contrast	RR (95% CI) P-trend	Adjustments	Funding
									parental history of MI <60yrs, diabetes, hypertension, high cholesterol, and intake of fruit and vegetables, alcohol, fibre, folate, non-supplemental vitamin E and saturated fat	

[A] CARDIA, Coronary Artery Risk Development in Young Adults cohort
[B] High triglycerides ≥ 150 mg/dL (≥ 1.7 mmol/L) or use of cholesterol-lowering medication.
[C] High LDL ≥ 130 mg/dL or use of cholesterol-lowering medication.
[D] High HDL< 40 mg/dL [<1.04 mmol/L (men)], < 50 mg/dL [<1.3 mmol/L (women)], or use of cholesterol-lowering medication.
[E] High blood pressure ≥ 130 mm Hg/ ≥ 85 mm Hg or use of antihypertensive medication.

Table 2: Fruit juice and cardiovascular disease- randomised controlled trials

Author/design	Country	No of subjects	Characteristics	Duration	Fruit juice	Control	Background diet	Results	Funding
Aptekmann and Cesar 2010 Parallel Blinding not stated	Brazil	30 (26 finished study)	Premenopausal overweight/ obese women 30-48yrs	12 weeks	Orange juice 500ml/day aerobic training 3x week (frozen and reconstitute)	Aerobic training 3x week	Not specified	Orange juice group baseline vs. end of study: total cholesterol, LDL-C, and LDL:HDL ratio significantly ↑ ($p<0.05$), HDL significantly ↓ ($p<0.05$) Triglycerides not reported as significant (p-values not given) Control baseline vs. end of trial: no significant effect on total cholesterol, LDL-C, LDL:HDL ratio, HDL and triglycerides	Fischer Group/ Asscociacao Laranja Brasil (PhD)
Amagase and Nance 2008 Parallel Double blind	US	35 (34 completed)	Healthy men and women Mean age 32.2 (juice), 30.5 (placebo)	14 days	GoChi™ (*L. barbarum*) 120ml/day	Placebo	Usual diet but asked to discontinue use of any foods with *L. barbarum, dietary supplements, energy drinks or green tea*	GoChi™ vs. placebo: no significant effect SBP ($p= 0.0528$) and DBP ($p= 0.3326$)	FreeLife International
Basu et al. 2011 Parallel Double blind	US	36 (31 completed)	Metabolic syndrome, women, mean age 52yrs	8 weeks	Reduced energy cranberry juice 480ml/day – contained sucralose and acesulfame K	Placebo juice made to emulate cranberry taste 480ml/day	Usual diet but asked to avoid berries, green tea, cocoa and soy products	Reduced energy cranberry juice vs. placebo no significant effect reported: SBP, DBP, total cholesterol, LDL-C, HDL-C, VLDL-c and triglycerides.	Cranberry Institute and Wisconsin Cranberry Board Inc. NIH and two grants from

Author/design	Country	No of subjects	Characteristics	Duration	Fruit juice	Control	Background diet	Results	Funding
					as sweeteners. Contained sugars from fruit			(p-values not given)	Oklahoma State University
Buscemi et al. 2012 Cross over Single blind	Italy	31 (all completed)	19 Increased cardiovascular risk (CVR) and 12 healthy non-obese controls Mean age CVR 35yrs, control 48yrs	7d	Red orange juice 500ml/d	Placebo drink 500ml/d (water, orange aroma, and colorants)	Usual diet	Red orange juice vs. placebo significantly improved (increased) flow mediated dilatation (p<0.005)	No funding received
Collins et al. 2004 Cross over	US	10 (all completed)	Men and women mean age 49 and 51yrs	3 weeks	Watermelon juice 3x 260g Tomato juice 3x 122g	Details of control not given	Not specified but all meals were prepared at research facility	Watermelon/ tomato juice vs. control period: no significant effect on total cholesterol, triglyceride and HDL-c (p-values not given)	Supported in part by National Watermelon Promotion Board [other source/s of funding was not stated]
Davidson et al. 2009 Parallel Double blind	US	383 (289 completed)	Men and women increased CVD risk 45-74yrs	18 months	Pomegranate juice 240ml/day	Control beverage similar colour and energy content	Subjects instructed that study drink should replace a food or beverage of a similar energy content	Pomegranate juice vs. control: no significant effect on carotid intima-media thickness progression (p= 0.654)	Roll International Corporation
Dohadwala et al. 2010 Cross over Double blind	US	83 (64 completed)	Men and women with stage 1 hypertension and upper end of pre-hypertension Mean age grape	4 weeks	Concord grape juice 7ml/kg/d	Concord grape flavoured placebo beverage matched flavour,	Maintain diet that met recommendations for sodium intake and to consume study beverages in place of other juice	Concord grape juice vs. placebo: no significant effect on SBP (p=0.67), DBP (p=0.90), total cholesterol (p=0.41), LDL (p=0.27), HDL (p=0.68), triglyceride	Welch Foods, NIH and Boston Medical Center General Clinical

Author/design	Country	No of subjects	Characteristics	Duration	Fruit juice	Control	Background diet	Results	Funding
			fruit 41yrs, placebo 44yrs			colour, calorie and sugar profile	or other sugar sweetened drinks.	(p=0.54), pulse wave velocity carotid-femoral (p=0.92), pulse wave velocity carotid-radial (p=0.82)	research Center
Lynn et al. 2012 Parallel Open label	UK	51	Healthy non-smoking men and women mean age pomegranate juice 39yrs, control 36.1yrs	4 weeks	Pomegranate juice 330ml/day	Lemonade 330ml/day	Usual diet	Pomegranate juice vs. placebo: significantly ↓SBP and DBP (p<0.001 for both), no significant effect on pulse wave velocity	Funding not stated
Maruyama et al. 2001[A] Parallel Blinding not stated	Japan	31	Female students mean age 21.3yrs	One menstrual cycle	Tomato juice 480g	Control drink 480g	Not stated	Tomato juice vs. control: free cholesterol fraction in HDL particle is significantly increased. No other significant effects in any of the other lipid fractions in LDL and HDL particles	Funding not stated
Morand et al. 2011 Cross over Open for fruit juice but double blind for control and placebo drink[B]	France	24	Healthy overweight men Mean age 56yrs	4 weeks	Orange juice 500ml	Placebo drink 500ml (starch capsule)	Usual diet but to refrain from citrus containing foods and limit flavonoid rich beverages	Orange juice vs. placebo: significantly ↓ DBP (p= **<**0.05). No significant effect on SBP, DBP, total cholesterol, LDL-c, HDL-C, triglycerides (p values for this comparison not provided)	Florida Dept of Citrus
Mulero et al. 2012[C] Parallel	Spain	53	Men and women who are healthy or have metabolic	6 months	Citrus based juice (mixture of juice plus *5% Aronia*	Placebo beverage 300ml	Not stated	Citrus juice baseline vs. end of trial: significant ↓LDL-c and HDL-C, no significant effect on	Comisión Interministerial de Ciencia y Tecnología

Author/design	Country	No of subjects	Characteristics	Duration	Fruit juice	Control	Background diet	Results	Funding
Blinding not stated			syndrome Age range 50-65yrs		*melanocarpa extract-Chokeberry*) 300ml			triglycerides. (p-value not given)	(CICYT)
Park et al 2004, Park et al. 2009 Parallel Double blind	Korea	40	Men with mild hypertension (>130/90mm/Hg) Mean age grape juice 43yrs and placebo 46yrs	8 weeks	Concord grape juice 5.5ml/kg body weight	Placebo-calorie matched control drink which looked and smelt like juice drink	Maintain usual energy intake	Concord grape juice baseline vs. end of trial: significant ↓SBP (p=0.005), DBP (p=0.001). Placebo drink baseline vs. end of trial: significant ↓DBP but no effect on SBP. No significant effect on total cholesterol, LDL-C, HDL-C, triglyceride (p-value not given)	Michigan Department of Agriculture, Welch Foods Inc and Korea Research Foundation Grant
Ruel et al. 2013 Cross over Double blind	Canada	35	Healthy overweight men mean age 45yrs	4 weeks	Low calorie cranberry juice 500ml	Placebo juice 500ml	Usual diet but to limit consumption of alcohol to maximum of 1 drink per day and restrain from consuming vitamin, antioxidant or mineral supplement	Pomegranate juice vs. control: no significant effect on SBP, DBP or augmentation index.	Canadian Institute of Health Research, Guillame Ruel supported by Fonds de la Recherche

SBP, systolic blood pressure; DBP, diastolic blood pressure; LDL-c, low density lipoprotein cholesterol, HDL-c, high density lipoprotein cholesterol
Flow mediated dilatation, carotid intima thickness, augmentation Index and pulse wave velocity are all measures of vascular function.

[A] Maruyama et al. 2001 also had low lycopene intervention which included 160g tomato juice plus 320g control drink unclear as to whether this was diluted so only the tomato juice results have been extracted.

[B] Morand et al. 2011 A control drink containing the flavonoid hesperidin(also present in orange juice) was also provided but results from this intervention period were not captured.

[C] Mulero et al. 2012-data only extracted for subjects with metabolic syndrome as the healthy control group only consumed citrus juice and not the placebo drink.

Table 3: Fruit and vegetable intake in childhood and cardiovascular disease risk in adulthood- prospective cohort studies

Author/ Cohort	Country	No of subjects	Characteristics at baseline	Duration	Fruit/ Vegetables	Outcome	Contrast	Result	Adjustments	Funding
Aatola et al., 2010 Cardiovascular Risk in Young Finns study	Finland	1622	Male and female 3-18yrs	27yrs	Fruit	Pulse wave velocity	Continuous	β coefficient (SE) -0.02 (0.03) p-value 0.44	Sex, age, vegetable consumption, alcohol consumption, smoking, physical activity index	Academy of Finland, Social Insurance Institu-tion of Finland, Kuopio, Tampere, and Turku University Hospital Medical Funds Juho Vainio Foundation, Paavo Nurmi Foundation, Finnish Foundation of Cardiovascular Research, Finnish Cultural Foundation, Orion-Farmos Research Founda-tion, Sigrid Juselius Foundation, Tampere Tuberculosis Foundation,

Author/ Cohort	Country	No of subjects	Characteristics at baseline	Duration	Fruit/ Vegetables	Outcome	Contrast	Result	Adjustments	Funding
										and Emil Aaltonen Foundation
Aatola et al., 2010 Cardiovascular Risk in Young Finns study					Vegetables		Continuous	β coefficient (SE) -0.07(0.03) p-value 0.0007	Sex, age, smoking, HDL-c, LDL-c cholesterol, triglycerides, BMI, SBP	Same as above
Jaaskelainen et al., 2012 Cardiovascular Risk in Young Finns study	Finland	2128	Male and female 3-18yrs	27yrs	Vegetables	High blood pressure	Continuous	OR 0.88 95%CI 0.80-0.98 p-value 0.01	Sex, age, HDL-c, LDL-c, triglycerides, SBP, CRP, insulin, physical activity index, fruit, fish & meat consumption, butter use on bread, family history of hypertension and diabetes, parents education, high plasma glucose, large waist circumference, low HDL cholesterol, high triglycerides	Same as above
Jaaskelainen et al., 2012 Cardiovascular Risk in Young Finns study					Vegetables	High triglyceride concentrations	Continuous	OR 0.88 95%CI 0.79-0.99 p-value 0.03	Same as above except for high triglycerides	Same as above

Author/ Cohort	Country	No of subjects	Characteristics at baseline	Duration	Fruit/ Vegetables	Outcome	Contrast	Result	Adjustments	Funding
Ness et al. 2005 Boyd Orr Cohort	UK	4028	Male and female mean age 7.5 years	Max 63yrs	Fruit	Coronary heart disease mortality	Q4 vs. Q1	RR 1.19 95%CI 0.76-1.87 Ptrend 0.7	Within family clustering of the diet, childhood family food expenditure, father's social class, district of residence as a child, period of birth, season when studied as a child, and Townsend score for current address or place of death	World Cancer Research Fund, Medical Research Council and British Heart Foundation.
Ness et al. 2005 Boyd Orr Cohort					Vegetables	Coronary heart disease mortality	Q4 vs. Q1	RR 1.01 95%CI 0.70-1.63 Ptrend 0.07	Same as above	Same as above
Ness et al. 2005 Boyd Orr Cohort					Fruit	Stroke mortality	Q4 vs. Q1	RR 0.48 95%CI 0.21-1.10 Ptrend 0.3	Within family clustering of the diet, childhood family food expenditure, father's social class, district of residence as a child, period of birth, season when studied as a child, and Townsend score for current address or place	Same as above

Author/ Cohort	Country	No of subjects	Characteristics at baseline	Duration	Fruit/ Vegetables	Outcome	Contrast	Result	Adjustments	Funding
									of death	
Ness et al. 2005 Boyd Orr Cohort					Vegetables	Stroke mortality	Q4 vs. Q1	RR 0.40 95%CI 0.19-0.83) Ptrend 0.01	Same as above	Same as above

CRP, C-reactive protein; SBP, systolic blood pressure.

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References

AATOLA, H., KOIVISTOINEN, T., HUTRI-KAHONEN, N., JUONALA, M., MIKKILA, V., LEHTIMAKI, T., VIIKARI, J. S., RAITAKARI, O. T. & KAHONEN, M. 2010. Lifetime fruit and vegetable consumption and arterial pulse wave velocity in adulthood: the Cardiovascular Risk in Young Finns Study. *Circulation,* 122**,** 2521-2528.

AMAGASE, H. & NANCE, D. M. 2008. A randomized, double-blind, placebo-controlled, clinical study of the general effects of a standardized Lycium barbarum (Goji) Juice, GoChi. *J.Altern.Complement Med.,* 14**,** 403-412.

APTEKMANN, N. P. & CESAR, T. B. 2010. Orange juice improved lipid profile and blood lactate of overweight middle-aged women subjected to aerobic training. *Maturitas,* 67**,** 343-347.

BASU, A., BETTS, N. M., ORTIZ, J., SIMMONS, B., WU, M. & LYONS, T. J. 2011. Low-energy cranberry juice decreases lipid oxidation and increases plasma antioxidant capacity in women with metabolic syndrome. *Nutr.Res.,* 31**,** 190-196.

BUSCEMI, S., ROSAFIO, G., ARCOLEO, G., MATTINA, A., CANINO, B., MONTANA, M., VERGA, S. & RINI, G. 2012. Effects of red orange juice intake on endothelial function and inflammatory markers in adult subjects with increased cardiovascular risk. *Am.J.Clin.Nutr.,* 95**,** 1089-1095.

COLLINS, J. K., ARJMANDI, B. H., CLAYPOOL, P. L., PERKINS-VEAZIE, P., BAKER, R. A. & CLEVIDENCE, B. A. 2004. Lycopene from two food sources does not affect antioxidant or cholesterol status of middle-aged adults. *Nutr.J.,* 3**,** 15.

DAVIDSON, M. H., MAKI, K. C., DICKLIN, M. R., FEINSTEIN, S. B., WITCHGER, M., BELL, M., MCGUIRE, D. K., PROVOST, J. C., LIKER, H. & AVIRAM, M. 2009. Effects of consumption of pomegranate juice on carotid intima-media thickness in men and women at moderate risk for coronary heart disease. *Am.J.Cardiol.,* 104**,** 936-942.

DOHADWALA, M. M., HAMBURG, N. M., HOLBROOK, M., KIM, B. H., DUESS, M. A., LEVIT, A., TITAS, M., CHUNG, W. B., VINCENT, F. B., CAIANO, T. L., FRAME, A. A., KEANEY, J. F., JR. & VITA, J. A. 2010. Effects of Concord grape juice on ambulatory blood pressure in prehypertension and stage 1 hypertension. *Am.J.Clin.Nutr.,* 92**,** 1052-1059.

DUFFEY, K. J., GORDON-LARSEN, P., STEFFEN, L. M., JACOBS, D. R., JR. & POPKIN, B. M. 2010. Drinking caloric beverages increases the risk of adverse cardiometabolic outcomes in the Coronary Artery Risk Development in Young Adults (CARDIA) Study. *Am.J.Clin.Nutr.,* 92**,** 954-959.

JAASKELAINEN, P., MAGNUSSEN, C. G., PAHKALA, K., MIKKILA, V., KAHONEN, M., SABIN, M. A., FOGELHOLM, M., HUTRI-KAHONEN, N., TAITTONEN, L., TELAMA, R., LAITINEN, T., JOKINEN, E., LEHTIMAKI, T., VIIKARI, J. S., RAITAKARI, O. T. & JUONALA, M. 2012. Childhood nutrition in predicting metabolic syndrome in adults: the cardiovascular risk in Young Finns Study. *Diabetes Care,* 35**,** 1937-1943.

LYNN, A., HAMADEH, H., LEUNG, W. C., RUSSELL, J. M. & BARKER, M. E. 2012. Effects of pomegranate juice supplementation on pulse wave velocity and blood pressure in healthy young and middle-aged men and women. *Plant Foods Hum.Nutr.,* 67**,** 309-314.

MARUYAMA, C., IMAMURA, K., OSHIMA, S., SUZUKAWA, M., EGAMI, S., TONOMOTO, M., BABA, N., HARADA, M., AYAORI, M., INAKUMA, T. & ISHIKAWA, T. 2001. Effects of tomato juice consumption on plasma and lipoprotein carotenoid concentrations and the susceptibility of low density lipoprotein to oxidative modification. *J.Nutr.Sci.Vitaminol.(Tokyo),* 47**,** 213-221.

MORAND, C., DUBRAY, C., MILENKOVIC, D., LIOGER, D., MARTIN, J. F., SCALBERT, A. & MAZUR, A. 2011. Hesperidin contributes to the vascular protective effects of orange juice: a randomized crossover study in healthy volunteers. *Am.J.Clin.Nutr.,* 93**,** 73-80.

MULERO, J., BERNABE, J., CERDA, B., GARCIA-VIGUERA, C., MORENO, D. A., ALBALADEJO, M. D., AVILES, F., PARRA, S., ABELLAN, J. & ZAFRILLA, P. 2012. Variations on cardiovascular risk factors in metabolic syndrome after consume of a citrus-based juice. *Clin.Nutr.,* 31**,** 372-377.

NESS, A. R., MAYNARD, M., FRANKEL, S., SMITH, G. D., FROBISHER, C., LEARY, S. D., EMMETT, P. M. & GUNNELL, D. 2005. Diet in childhood and adult cardiovascular and all cause mortality: the Boyd Orr cohort. *Heart,* 91**,** 894-898.

PARK, Y. K., KIM, J. S. & KANG, M. H. 2004. Concord grape juice supplementation reduces blood pressure in Korean hypertensive men: double-blind, placebo controlled intervention trial. *Biofactors,* 22**,** 145-147.

PARK, Y. K., LEE, S. H., PARK, E., KIM, J. S. & KANG, M. H. 2009. Changes in antioxidant status, blood pressure, and lymphocyte DNA damage from grape juice supplementation. *Ann.N.Y.Acad.Sci.,* 1171**,** 385-390.

RUEL, G., LAPOINTE, A., POMERLEAU, S., COUTURE, P., LEMIEUX, S., LAMARCHE, B. & COUILLARD, C. 2013. Evidence that cranberry juice may improve augmentation index in overweight men. *Nutr.Res.,* 33**,** 41-49.

SESSO, H. D., LIU, S., GAZIANO, J. M. & BURING, J. E. 2003. Dietary lycopene, tomato-based food products and cardiovascular disease in women. *J.Nutr.,* 133**,** 2336-2341.