British Journal of Nutrition (2020), 124, 241–246
doi:10.1017/S000711452000121X

Effects of strawberry intervention on cardiovascular risk factors: a meta-analysis of randomised controlled trials

Qi Gao[1], Li-Qiang Qin[2], Ahmed Arafa[1,3], Ehab S. Eshak[1,4] and Jia-Yi Dong[1]*

[1]*Public Health, Department of Social Medicine, Osaka University Graduate School of Medicine, Osaka, Japan*
[2]*Department of Nutrition and Food Hygiene, School of Public Health, Soochow University, Suzhou, People's Republic of China*
[3]*Department of Public Health, Faculty of Medicine, Beni-Suef University, Beni-Suef, Egypt*
[4]*Department of Public Health, Faculty of Medicine, Minia University, El-Minya, Egypt*

(Submitted 13 December 2019 – Final revision received 26 February 2020 – Accepted 24 March 2020 – First published online 2 April 2020)

Abstract

We conducted a meta-analysis of randomised controlled trials (RCT) to examine the effects of strawberry interventions on cardiovascular risk factors. We searched multiple databases including PubMed, Web of Science and Scopus to identify eligible studies published before 19 May 2019. The endpoints were blood pressure, total cholesterol (TC), HDL-cholesterol, LDL-cholesterol, TAG, fasting blood glucose, endothelial function and inflammatory factors. Pooled analyses were performed using random- or fixed-effects models according to a heterogeneity test. We also conducted sub-group analyses by baseline endpoint levels. We included eleven RCT in this meta-analysis (six for blood pressure, seven for lipid profile, seven for fasting blood glucose and six for C-reactive protein (CRP)). Overall, the strawberry interventions significantly reduced CRP levels by 0·63 (95 % CI −1·04, −0·22) mg/l but did not affect blood pressure, lipid profile or fasting blood glucose in the main analyses. Our analysis stratified by baseline endpoint levels showed the strawberry interventions significantly reduced TC among people with baseline levels >5 mmol/l (−0·52 (95 % CI −0·88, −0·15) mmol/l) and reduced LDL-cholesterol among people with baseline levels >3 mmol/l (−0·31 (95 % CI −0·60, −0·02) mmol/l). There was little evidence of heterogeneity in the analysis and no evidence of publication bias. In summary, strawberry interventions significantly reduced CRP levels and may improve TC and LDL-cholesterol in individuals with high baseline levels.

Key words: **Strawberries: Flavonoids: Cardiovascular risk factors: Interventions: Randomised controlled trials: Meta-analyses**

CVD is the leading cause of morbidity and mortality worldwide[1]. Annually, more than 17 million deaths are attributable to CVD, with these deaths anticipated to increase by 30 % over the next decade[2]. Most CVD are potentially preventable, and it is important to design and implement effective strategies to prevent CVD.

Observational studies have shown fruit consumption was associated with a lower risk for developing total CVD, CHD and stroke[3]. Among kinds of fruits, strawberries are well known for being rich in polyphenol, vitamins and minerals[4,5]. In fact, strawberries have been ranked as a top source of polyphenol and antioxidant capacity among foods consumed in the USA[6]. Strawberry polyphenols have been shown to have direct and indirect antimicrobial, anti-allergy and antihypertensive properties, inhibit the activities of some physiological enzymes and receptors and protect from oxidative stress-related diseases[4].

The biological and functional properties of strawberries have been studied in animal models[4] and extended to humans in a few epidemiological studies[7–9]. In the past decade, emerging interventional trials have been conducted to examine the health effects of strawberries in humans[10–20]. However, most of these trials had small sample sizes, which might have resulted in insufficient statistical power. Additionally, the results varied across studies, with some showing strawberries had a beneficial effect on cardiovascular risk factors whereas others did not. Therefore, we aimed to evaluate the treatment effects of strawberry interventions on cardiovascular risk factors by conducting a meta-analysis of randomised controlled trials (RCT).

Methods

Literature search

This meta-analysis was conducted and reported according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guideline for reporting meta-analyses of RCT[21]. Two authors (Q. G. and J.-Y. D.) independently searched PubMed, Web of Science and Scopus for relevant studies published before 19 May 2019. The search was updated on

Abbreviations: CRP, C-reactive protein; HR, hazard ratio; RCT, randomised controlled trial; TC, total cholesterol.

* **Corresponding author:** Jia-Yi Dong, email dongjy@mail3.sysu.edu.cn

20 February 2020. The endpoints of interest were blood pressure, total cholesterol (TC), LDL-cholesterol, HDL-cholesterol, TAG, fasting blood glucose, endothelial function and inflammatory factors. The keywords used for the literature search were 'strawberry', 'hypertension', 'blood pressure', 'lipid', 'cholesterol', 'LDL', 'HDL', 'triglyceride', 'blood glucose', 'endothelial function', 'inflammation' and 'trial'. The search strategy is shown in the online Supplementary material. We also conducted a manual review of reference lists of the identified studies. No effort was made to retrieve unpublished studies, and there was no restriction to publication date.

Study selection

Studies were selected for analysis if they (1) were RCT (either parallel or crossover); (2) used strawberries as the intervention and had a control group; (3) measured blood pressure, lipid profiles, blood glucose, endothelial function or inflammatory factors at baseline and follow-up and (4) had an intervention longer than 1 week. Studies were excluded if they examined the acute effects of a strawberry intervention within several hours, or when the intervention included fruits other than strawberries.

Data extraction

We extracted the characteristics of each trial included in this meta-analysis. The extracted data included: name of first author, study area, publication year, intervention duration, study design, dose of intervention and control group, sample size, mean age or age range, sex, as well as the mean and standard deviation values for each endpoint at baseline and post-intervention. For studies with more than two follow-up measurements, data from the last follow-up were used. Similarly, for studies with more than two intervention groups, data from the highest dose group were used.

Quality assessment

The quality of the included trials was evaluated using the revised tool for assessing risk of bias in randomised trials[22]. Each included trial was judged as 'low risk', 'high risk' or 'some concerns' for six aspects: randomisation process, deviations from the intended interventions, missing outcomes, outcome measurement and selection of reported results. An overall risk of bias judgement was then made. Disagreements during study selection, data extraction and quality assessment were resolved by discussion among the authors.

Statistical analysis

For each endpoint, mean net changes between the baseline and follow-up values in the intervention and control groups/periods were calculated. The standard deviations for the net changes were obtained from the original studies or computed using a standard formula[23]. The effect size of the intervention was calculated as the mean difference in the net changes in the intervention and control groups/periods. Heterogeneity between studies was assessed using Cochran's Q test ($P < 0{\cdot}10$ as statistically significant) and the I^2 statistic, which is considered a measure of the inconsistency between studies[24]. A random-effects model[25] was used to perform the pooled analysis when $P_{\text{for heterogeneity}} < 0{\cdot}10$; otherwise, a fixed-effects model was selected. We conducted pre-specified stratified analyses and meta-regression analyses by baseline endpoint values to examine whether baseline levels could modify the effects of the intervention. Sensitivity analyses were also performed to test whether individual studies had a considerable impact on the overall results. The risk for publication bias was assessed using Egger's test[26]. A 'trim and fill' method[27] was used to correct results when such bias was detected. All analyses were performed using Stata version 12.0.

Results

The flow of the literature search is shown in Fig. 1. The initial search of the electronic databases identified 129 records, but most of these were excluded after scanning the title and abstract. This left twenty-two articles for full-text review. Eleven articles were further excluded because they examined acute effects of a strawberry intervention (n 6), had no outcome of interest (n 2), used cranberries or mixed berries as the intervention (n 2) or had no control group (n 1). Finally, eleven RCT were included in our analysis (blood pressure n 6, lipid profile n 7, blood glucose n 7, C-reactive protein (CRP) n 6). The RCT that used oat bran bread as a control[13] was not included in the analysis for lipid profile because there is a body of evidence supporting a lipid-lowering effect of oat bran[28], and using oat bran as a control may mask the true effect of a strawberry intervention on participants' lipid profile.

Table 1 shows the characteristics of each included RCT. These eleven trials were published between 2008 and 2017. Seven studies were double-blind RCT, two were single-blind RCT and two were open-label RCT. Six trials used cross-over designs, whereas the others used parallel designs. The interventions

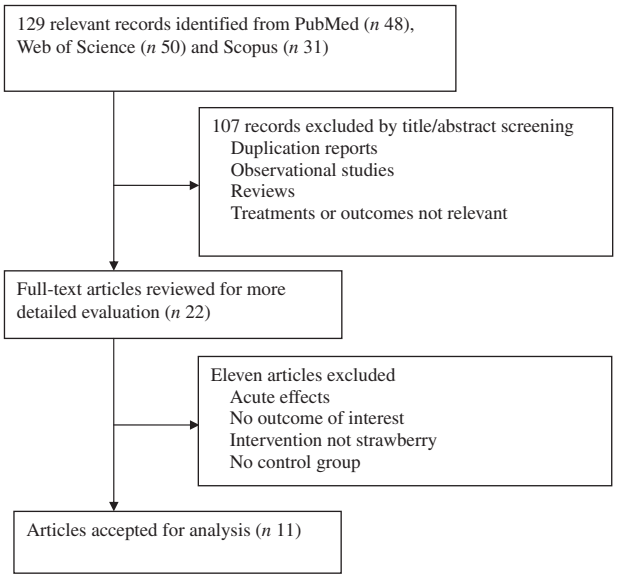

Fig. 1. Flow chart of study selection.

British Journal of Nutrition

Table 1. Characteristics of included randomised controlled trials examining the effects of strawberry intervention on cardiovascular risk factors in men and women (Mean values and standard deviations; ranges)

Author	Year	Design	Treatment	Control	Sample size	Men	Women	Mean	SD	Range	Duration (weeks)
Jenkins *et al.*[13]	2008	Open, X	Fresh strawberries (454 g/d)	Oat bran bread (65 g/d)	28	Not available				38–75	4
Basu *et al.*[18]	2010	Open, parallel	Strawberry beverage (four cups/d)	Four cups water daily	27	2	25	47	3		8
Burton-Freeman *et al.*[17]	2010	SB, X	FDS (10 g/d)	Macro- and micronutrient-matched placebo	24	10	14	50·9	15		6
Ellis *et al.*[15]	2011	SB, X	FDS (10 g/serving)	Flavour- and energy-matched placebo	24	104	14	50·9	15		6
Zunino *et al.*[10]	2012	DB, X	Frozen strawberries (80 g/d)	Flavour-matched placebo	20	7	13			20–50	3
Moazen *et al.*[12]	2013	DB, parallel	FDS beverage (two cups/d)	Macronutrient- and flavour-matched placebo	36	11	25	51·6	10		6
Amani *et al.*[20]	2014	DB, parallel	FDS beverage (two cups/d)	Fibre- and colour-matched drink	36	11	25	51·6	10		6
Basu *et al.*[19]	2014	DB, parallel	FDS beverages (25 and 50 g/d)	Energy- and fibre-matched control	60	5	55	49	10		12
Djurica *et al.*[16]	2016	DB, X	FDS powder (50 g/d)	Energy- and flavour-matched placebo	25	25	0			14–18	1
Feresin *et al.*[14]	2017	DB, parallel	FDS powder (25 and 50 g/d)	Flavour- and colour-matched placebo	60	0	60			45–65	8
Schell *et al.*[11]	2017	DB, X	FDS beverage (50 g/d)	Energy- and macronutrient-matched placebo	17	4	13	57	7		12

X, crossover; SB, single-blind; FDS, freeze-dried strawberries; DB, double-blind.

included freeze-dried strawberry beverage or powder (n 10) or fresh strawberries (n 1). RCT with a single- or double-blind design used a placebo similar in colour and flavour to strawberries as the control, and the two open-label RCT used oat bran bread or water as a control. The sample size of each RCT was 17–60 participants, with a total of 357 participants in the eleven trials. The intervention duration ranged from 1 to 12 weeks, with a median of 6 weeks. All RCT enrolled middle-aged individuals, except for one trial that enrolled adolescents aged 14–18 years[16]. The results of quality assessment of the included RCT are shown in online Supplementary Table S1. In general, most RCT had low risk for overall bias.

The results of the pooled analysis examining the effects of the strawberry interventions on blood pressure, lipid profile, blood glucose and CRP levels are shown in Table 2. The main analyses showed that the strawberry interventions significantly reduced CRP levels by 0·63 (95 % CI −1·04, −0·22) mg/l but did not affect blood pressure, lipid profile or fasting blood glucose. There was little evidence of heterogeneity throughout the analyses. The analysis stratified by baseline endpoint levels showed the strawberry interventions led to a significant decrease in TC levels among those with baseline TC levels >5 mmol/l (weighted mean difference −0·52 (95 % CI −0·88, −0·15) mmol/l) (Fig. 2). Similarly, the strawberry interventions significantly reduced LDL-cholesterol among those with baseline LDL-cholesterol levels >3 mmol/l (weighted mean difference −0·31 (95 % CI −0·60, −0·02) mmol/l) (Fig. 3). Tests for publication bias using Egger's regression showed no evidence of such bias in all endpoints, though the test for TC was borderline significant (Table 2). Correcting the potential bias by the 'trim and fill' method obtained the same results for TC.

The results of the meta-regression showed that the baseline values of TC and LDL-cholesterol were associated with the magnitude of the treatment effects (online Supplementary Figs. S1 and S2). In the sensitivity analyses, no single RCT showed a substantial impact on the overall pooled results for each endpoint.

Discussion

This meta-analysis of RCT indicated that the strawberry interventions significantly reduced CRP levels but did not affect blood pressure, lipid profile or fasting blood glucose compared with placebo. However, in the sub-group analysis, the strawberry interventions significantly lowered TC and LDL-cholesterol levels in those with high baseline levels. The results of meta-regression indicated that baseline levels of TC and LDL-cholesterol were associated with the treatment effect of strawberry interventions.

The potential cardio-protective effects of strawberry consumption may be attributed to its richness in polyphenols, folate, vitamin C and minerals[5,29]. Anthocyanins are the best-known polyphenolic compounds in strawberries, which have been shown to have antioxidant, anti-inflammation and cardio-protective properties[30]. Studies in animal and cell models showed that gastric lipase[31] and cholesteryl ester transfer protein[32] are necessary for lipid generation. One clinical trial

Table 2. Meta-analysis of randomised controlled trials examining the effects of strawberry intervention on cardiovascular risk factors (Weighed mean differences and 95 % confidence intervals)

	No. of studies	Effect size	95 % CI	I^2	$P_{for\ heterogeneity}$	$P_{for\ publication\ bias}$
Systolic blood pressure (mmHg)	6	−0·26	−2·83, 2·31	0	0·76	0·28
Diastolic blood pressure (mmHg)	6	−0·92	−2·47, 0·64	0	0·91	0·41
Total cholesterol (mmol/l)	7	−0·15	−0·35, 0·05	25·7	0·23	0·08
LDL-cholesterol (mmol/l)	7	−0·11	−0·30, 0·08	1·7	0·41	0·37
HDL-cholesterol (mmol/l)	7	0·00	−0·08, 0·08	0	0·88	0·78
TAG (mmol/l)	7	−0·03	0·25, 0·04	0	0·99	0·11
Fasting blood glucose (mmol/l)	7	0·04	−0·10, 0·18	0	0·78	0·48
C-reactive protein (mg/l)	6	−0·63	−1·04, −0·22	9·7	0·35	0·39

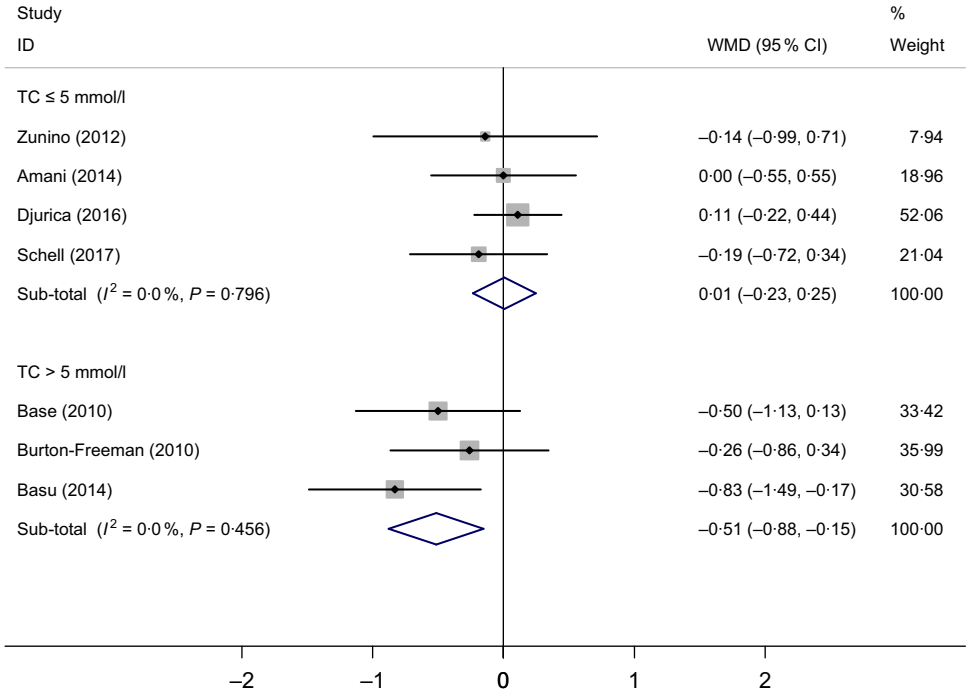

Fig. 2. Meta-analysis on the effects of strawberry intervention on total cholesterol (TC) by the baseline levels. WMD, weighted mean difference.

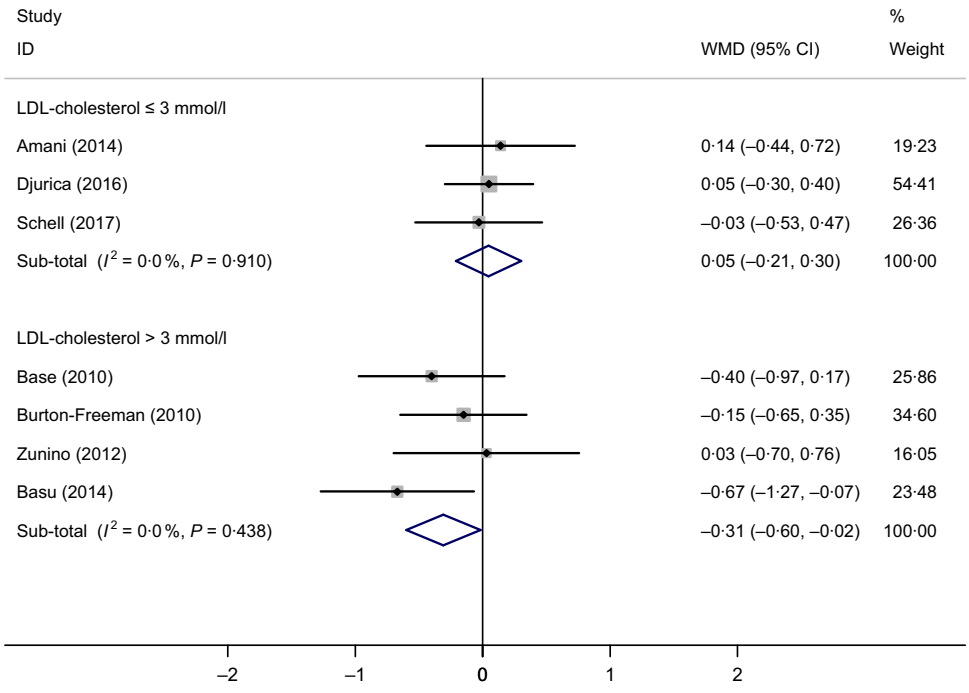

Fig. 3. Meta-analysis on the effects of strawberry intervention on LDL-cholesterol by the baseline levels. WMD, weighted mean difference.

involving 120 patients with dyslipidaemia aged 40–65 years showed that anthocyanins could increase cellular cholesterol efflux to serum and decrease the mass and activity of plasma cholesteryl ester transfer protein[32]. There was also evidence that anthocyanins may enhance ATP-binding cassette transporter A1 (ABCA1)-mediated cholesterol efflux in macrophages, which in turn can improve lipid profiles[33]. Furthermore, a recent meta-analysis of seventeen RCT showed that anthocyanin supplementation led to significant reductions in TAG (−0·10 (95 % CI −0·16, −0·05) mmol/l), LDL-cholesterol (−0·23 (95 % CI −0·29, −0·52) mmol/l) and apoB (−0·14 (95 % CI −0·17, −0·11) μmol/l)[34].

It was uncertain why baseline levels of TC and LDL-cholesterol were associated with the treatment effects of strawberry interventions. One explanation may be that individuals with higher baseline levels of these lipids could have more room for improvement compared with those with lower baseline levels. However, the results of the sub-group analyses should be interpreted with caution because they were based on a limited number of RCT.

Several prospective cohort studies have examined the association of anthocyanin intakes with risk for CVD. Cassidy *et al.* reported that a high intake of anthocyanins was associated with a decreased risk for myocardial infarction among 93 600 women (aged 25–42 years) in the Nurses' Health Study II (hazard ratio (HR) 0·68; 95 % CI 0·49, 0·96)[35]. In addition, those authors detected an 8 % decrease in risk for hypertension (HR 0·92; 95 % CI 0·86, 0·98) in the highest quintile of anthocyanin intake compared with the lowest quintile based on three cohorts: Nurses' Health Study I with 121 700 female nurses aged 30–55 years, Nurses' Health Study II with 116 430 women aged 25–42 years and Health Professionals Follow-Up Study with 51 529 men aged 40–75 years[36]. The inconsistent results of RCT and cohort studies on blood pressure may be due to biases involved in cohort studies, in particular confounding bias and measurement errors. Mink *et al.* showed that dietary intake of anthocyanidins was associated with a reduced risk for mortality from CHD, CVD and all-cause death (for any *v.* no intake: HR 0·88 (95 % CI 0·78, 0·99); HR 0·91 (95 % CI 0·83, 0·99) and HR 0·90 (95 % CI 0·86, 0·95), respectively) in the Iowa Women's Health Study[8]. A recent meta-analysis by Kimble *et al.* showed that intake of dietary anthocyanins reduced the risk for incident CHD (HR 0·91; 95 % CI 0·83, 0·99) and CVD mortality (HR 0·92; 95 % CI 0·87, 0·97)[37]. However, no associations were observed between anthocyanin intake and risk for incident stroke, myocardial infarction or total CVD[37].

Conversely, evidence from observational studies directly examining the association between strawberry consumption and risk for CVD is limited. The Women's Health Study that involved 38 176 middle-aged women showed consuming ≥2 servings/week of strawberries compared with no consumption had a non-significant association with a higher risk for CVD throughout a 10 year follow-up (HR 1·27; 95 % CI 0·94, 1·72)[9]. In addition, a cross-sectional analysis of baseline variables in that study showed a slightly reduced likelihood (14 % lower) of having elevated CRP levels among high strawberry consumers[9]. In the Iowa Women's Health Study (34 489 postmenopausal women aged 55–69 years), higher strawberry consumption was not associated with CHD mortality (HR 0·95; 95 % CI 0·83, 1·08) compared with lower consumption[8]. Among 1299 older adults that participated in the Massachusetts Health Care Panel study, the consumption of ≥1 serving of fresh strawberries or melons per d *v.* an intake of <1 serving per d was not associated with risk for CVD mortality (HR 0·70; 95 % CI 0·10, 4·79); however, it is worth mentioning that only 1·2 % of the participants in that study consumed ≥1 serving of fresh strawberries/melons per d[7]. Given the limited evidence regarding strawberry consumption and risk for CVD, large-scale prospective cohort studies are still warranted.

The main strength of our meta-analysis was that all included studies were RCT, which minimised the risk for confounding and recall biases involved in observational studies. However, limitations of our meta-analysis should also be noted. First, the number of included RCT and the sample size of individual trials were limited. Despite the RCT design, there might have been considerable differences in baseline characteristics between the treatment and control groups in cases with a small sample size. For example, in the study by Amani *et al.*[20], the baseline LDL-cholesterol levels were 2·46 and 3·00 mg/l in the treatment (*n* 19) and control (*n* 17) groups, respectively, although the difference was not significant ($P = 0·13$). Second, the individual trials used various forms of strawberries and different doses as interventions. It remains uncertain whether such differences could result in different treatment effects. However, there was little evidence of heterogeneity across studies for all endpoints. Third, the treatment durations were relatively short (all ≤12 weeks). The long-term effects of the strawberry interventions were therefore not determined. Fourth, publication bias could be a threat to the validity of our findings. Test for such bias in TC was borderline significant, but correcting the bias changed the results little.

In conclusion, the findings of the present meta-analysis of RCT indicated that strawberry interventions significantly reduced CRP levels and may lower TC and LDL-cholesterol in those with higher baseline levels. Because of the limited number of included RCT and small sample sizes, it is premature to recommend strawberries as a dietary therapy for dyslipidaemia. Large-scale RCT are needed to verify our findings.

Acknowledgements

We thank Jennifer Carr for language editing.

This study was supported by Japan Society for the Promotion of Science KAKENHI grant number A18H063910 and T19K214700 to J.-Y. D.

The funders had no role in the design and conduct of the study; collection, management, analysis and interpretation of the data; preparation, review or approval of the manuscript; or the decision to submit the manuscript for publication.

Q. G. collected the data, analysed the data and wrote the manuscript. L.-Q. Q., A. A. and E. S. E. conducted the technique review and edited the manuscript. J.-Y. D. designed the study, collected the data, analysed the data and edited the manuscript.

The authors declare that there are no conflicts of interest.

Supplementary material

For supplementary material/s referred to in this article, please visit https://doi.org/10.1017/S000711452000121X

References

1. Wang H, Naghavi M, Allen C, *et al.* (2016) Global, regional, and national life expectancy, all-cause mortality, and cause-specific mortality for 249 causes of death, 1980–2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet* **388**, 1459–1544.
2. Smith SC Jr, Collins A, Ferrari R, *et al.* (2012) Our time: a call to save preventable death from cardiovascular disease (heart disease and stroke). *Eur Heart J* **33**, 2910–2916.
3. Aune D, Giovannucci E, Boffetta P, *et al.* (2017) Fruit and vegetable intake and the risk of cardiovascular disease, total cancer and all-cause mortality – a systematic review and dose–response meta-analysis of prospective studies. *Int J Epidemiol* **46**, 1029–1056.
4. Giampieri F, Forbes-Hernandez TY, Gasparrini M, *et al.* (2015) Strawberry as a health promoter: an evidence based review. *Food Funct* **6**, 1386–1398.
5. Giampieri F, Alvarez-Suarez JM & Battino M (2014) Strawberry and human health: effects beyond antioxidant activity. *J Agr Food Chem* **62**, 3867–3876.
6. Halvorsen BL, Carlsen MH, Phillips KM, *et al.* (2006) Content of redox-active compounds (ie, antioxidants) in foods consumed in the United States. *Am J Clin Nutr* **84**, 95–135.
7. Gaziano JM, Manson JE, Branch LG, *et al.* (1995) A prospective study of consumption of carotenoids in fruits and vegetables and decreased cardiovascular mortality in the elderly. *Ann Epidemiol* **5**, 255–260.
8. Mink PJ, Scrafford CG, Barraj LM, *et al.* (2007) Flavonoid intake and cardiovascular disease mortality: a prospective study in postmenopausal women. *Am J Clin Nutr* **85**, 895–909.
9. Sesso HD, Gaziano JM, Jenkins DJ, *et al.* (2007) Strawberry intake, lipids, C-reactive protein, and the risk of cardiovascular disease in women. *J Am Coll Nutr* **26**, 303–310.
10. Zunino SJ, Parelman MA, Freytag TL, *et al.* (2012) Effects of dietary strawberry powder on blood lipids and inflammatory markers in obese human subjects. *Br J Nutr* **108**, 900–909.
11. Schell J, Scofield RH, Barrett JR, *et al.* (2017) Strawberries improve pain and inflammation in obese adults with radiographic evidence of knee osteoarthritis. *Nutrients* **9**, 949.
12. Moazen S, Amani R, Homayouni Rad A, *et al.* (2013) Effects of freeze-dried strawberry supplementation on metabolic biomarkers of atherosclerosis in subjects with type 2 diabetes: a randomized double-blind controlled trial. *Ann Nutr Metab* **63**, 256–264.
13. Jenkins DJ, Nguyen TH, Kendall CW, *et al.* (2008) The effect of strawberries in a cholesterol-lowering dietary portfolio. *Metabolism* **57**, 1636–1644.
14. Feresin RG, Johnson SA, Pourafshar S, *et al.* (2017) Impact of daily strawberry consumption on blood pressure and arterial stiffness in pre- and stage 1-hypertensive postmenopausal women: a randomized controlled trial. *Food Funct* **8**, 4139–4149.
15. Ellis CL, Edirisinghe I, Kappagoda T, *et al.* (2011) Attenuation of meal-induced inflammatory and thrombotic responses in overweight men and women after 6-week daily strawberry (Fragaria) intake. A randomized placebo-controlled trial. *J Atheroscler Thromb* **18**, 318–327.
16. Djurica D, Holt RR, Ren J, *et al.* (2016) Effects of a dietary strawberry powder on parameters of vascular health in adolescent males. *Br J Nutr* **116**, 639–647.
17. Burton-Freeman B, Linares A, Hyson D, *et al.* (2010) Strawberry modulates LDL oxidation and postprandial lipemia in response to high-fat meal in overweight hyperlipidemic men and women. *J Am Coll Nutr* **29**, 46–54.
18. Basu A, Fu DX, Wilkinson M, *et al.* (2010) Strawberries decrease atherosclerotic markers in subjects with metabolic syndrome. *Nutrition Res* **30**, 462–469.
19. Basu A, Betts NM, Nguyen A, *et al.* (2014) Freeze-dried strawberries lower serum cholesterol and lipid peroxidation in adults with abdominal adiposity and elevated serum lipids. *J Nutr* **144**, 830–837.
20. Amani R, Moazen S, Shahbazian H, *et al.* (2014) Flavonoid-rich beverage effects on lipid profile and blood pressure in diabetic patients. *World J Diabetes* **5**, 962–968.
21. Moher D, Liberati A, Tetzlaff J, *et al.* (2009) Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *BMJ* **339**, b2535.
22. Higgins JPT, Sterne JAC, Savovic J, *et al.* (2016) A revised tool for assessing risk of bias in randomized trials. *Cochrane Database Syst Rev*, issue 10, 29–31.
23. Higgins J, Eldridge S & Li T (2019) *Cochrane Handbook for Systematic Reviews of Interventions.* The Cochrane Collaboration. https://training.cochrane.org/handbook/current/chapter-23 (accessed June 2019).
24. Higgins JP, Thompson SG, Deeks JJ, *et al.* (2003) Measuring inconsistency in meta-analyses. *BMJ* **327**, 557–560.
25. DerSimonian R & Laird N (1986) Meta-analysis in clinical trials. *Control Clin Trials* **7**, 177–188.
26. Egger M, Davey Smith G, Schneider M, *et al.* (1997) Bias in meta-analysis detected by a simple, graphical test. *BMJ* **315**, 629–634.
27. Duval S & Tweedie R (2000) Trim and fill: a simple funnel-plot-based method of testing and adjusting for publication bias in meta-analysis. *Biometrics* **56**, 455–463.
28. Hui S, Liu K, Lang H, *et al.* (2019) Comparative effects of different whole grains and brans on blood lipid: a network meta-analysis. *Eur J Nutr* **58**, 2779–2787.
29. Giampieri F, Tulipani S, Alvarez-Suarez JM, *et al.* (2012) The strawberry: composition, nutritional quality, and impact on human health. *Nutrition* **28**, 9–19.
30. Afrin S, Gasparrini M, Forbes-Hernandez TY, *et al.* (2016) Promising health benefits of the strawberry: a focus on clinical studies. *J Agr Food Chem* **64**, 4435–4449.
31. McDougall GJ & Stewart D (2005) The inhibitory effects of berry polyphenols on digestive enzymes. *Biofactors* **23**, 189–195.
32. Qin Y, Xia M, Ma J, *et al.* (2009) Anthocyanin supplementation improves serum LDL- and HDL-cholesterol concentrations associated with the inhibition of cholesteryl ester transfer protein in dyslipidemic subjects. *Am J Clin Nutr* **90**, 485–492.
33. Xia M, Hou M, Zhu H, *et al.* (2005) Anthocyanins induce cholesterol efflux from mouse peritoneal macrophages: the role of the peroxisome proliferator-activated receptor {gamma}-liver X receptor {alpha}-ABCA1 pathway. *J Biol Chem* **280**, 36792–36801.
34. Shah K & Shah P (2018) Effect of anthocyanin supplementations on lipid profile and inflammatory markers: a systematic review and meta-analysis of randomized controlled trials. *Cholesterol* **2018**, 8450793.
35. Cassidy A, Mukamal KJ, Liu L, *et al.* (2013) High anthocyanin intake is associated with a reduced risk of myocardial infarction in young and middle-aged women. *Circulation* **127**, 188–196.
36. Cassidy A, O'Reilly EJ, Kay C, *et al.* (2011) Habitual intake of flavonoid subclasses and incident hypertension in adults. *Am J Clin Nutr* **93**, 338–347.
37. Kimble R, Keane KM, Lodge JK, *et al.* (2019) Dietary intake of anthocyanins and risk of cardiovascular disease: a systematic review and meta-analysis of prospective cohort studies. *Crit Rev Food Sci Nutr* **59**, 3032–3043.