Dried fruit consumption and cardiometabolic health: a randomised crossover trial

Valerie K. Sullivan, Kristina S. Petersen and Penny M. Kris-Etherton

Department of Nutritional Sciences, The Pennsylvania State University, University Park, PA 16802, USA

Abstract

Fruit intake is associated with lower risk of cardiometabolic diseases. However, effects of dried fruits on cardiometabolic health are not well researched. We investigated the effect of daily dried fruit consumption compared with a carbohydrate-rich snack on cardiometabolic disease risk factors in adults with increased cardiometabolic risk. A two-period randomised crossover trial was conducted in adults (*n* 55) with elevated BMI and at least one additional risk factor for cardiometabolic disease to compare the effects of consuming 3/4 cup/d mixed dried fruits (plums, figs, dates and raisins) or an energy- and carbohydrate-matched control snack for 4 weeks. The primary outcome was LDL-cholesterol; secondary outcomes included other lipids and lipoproteins, glucose and insulin, C-reactive protein, blood pressure and vascular stiffness. Linear mixed models were used for data analysis. Lipid and lipoprotein concentrations did not differ between conditions; however, dried fruit increased LDL-cholesterol (0·10 mmol/l, 95 % CI 0·01, 0·20) compared with baseline. Compared with the control, dried fruit increased mean fasting glucose (0·08 mmol/l, 95 % CI 0·005, 0·16; *P* = 0·038). Vascular outcomes, fasting insulin and C-reactive protein did not differ between conditions. Mean weight changes did not differ (*P* = 0·55) but tended to increase after both conditions (dried fruit 0·3 kg, 95 % CI –0·09, 0·65; control 0·4 kg, 95 % CI 0·01, 0·75). Thus, short-term daily consumption of a large portion of mixed dried plums, figs, dates and raisins, without structured dietary guidance, did not improve cardiometabolic risk factors, compared with carbohydrate-rich snacks, in adults with increased baseline cardiometabolic risk.

Key words: Dried fruit: Cardiometabolic risk: Fasting glucose: Cholesterol: Vascular health: Sugar: Phenolic compounds

Suboptimal fruit intake is a leading dietary contributor to cardiometabolic diseases worldwide[1]. Substantial observational evidence shows that greater fruit consumption is associated with lower risk of CVD[2,3], type 2 diabetes[4,5] and the metabolic syndrome[6], and increasing fruit and vegetable intake improves risk factors such as blood pressure and lipids/lipoproteins[7,8]. Strategies to increase fruit intake are needed to reduce the burden of cardiometabolic diseases.

Optimal fruit intakes, associated with the lowest risk of mortality, range from 200 to 300 g/d for most diseases[1]. This range is consistent with dietary guidelines in many countries[9–11], which encourage selection of various whole, non-juice forms of fruit including fresh as well as frozen, cooked, canned and dried fruits. Dried fruits are shelf-stable forms of fruit that are widely available and can be eaten without preparation as a snack or included in a meal, thereby overcoming some common barriers to adequate fruit intake[12,13]. Traditional dried fruits are dried by sun or thermal processing, without addition of sugar or juice[14], and largely retain the nutrients and bioactives in their fresh counterparts, excluding heat- and light-sensitive vitamin C[15]. Most dried fruits are good sources of dietary fibre and K[16], which

have been associated with lipid-lowering and vascular benefits, respectively[17,18]. Although dried fruits are concentrated sources of simple sugars, the sugars in traditional dried fruits are intrinsic to the fruits and are excluded from recommended limits for added sugar consumption[19]. Compared with fresh fruits, carotenoid contents of dried fruits are generally reduced, while the effect of drying on phenolic contents varies, with increases in some types and decreases in others reported[15]. Authoritative dietary guidelines recognise dried fruits as acceptable alternatives to fresh fruits[9–11]. Though dried fruit consumption is low in Western countries[14,20–22], encouraging consumption could be a strategy to improve fruit intake and, thereby, benefit cardiometabolic health.

Few randomised trials have assessed the cardiometabolic effects of consuming dried fruits[23–28]. Single fruit interventions were used in previous studies, which limits the generalisability of findings and contrasts with the recommendation to consume a variety of fruits[9]. Furthermore, most trials have utilised a parallel design with small sample sizes, making it difficult to distinguish within-person from between-person variation[25,26,28,29]. Therefore, we conducted a randomised crossover trial to determine the

effect of daily consumption of mixed dried fruits, compared with energy- and carbohydrate-matched snacks, on cardiometabolic risk factors in adults with elevated baseline risk. The primary endpoint was LDL-cholesterol, an established causal factor in the development of CVD[30]. We hypothesised that inclusion of 3/4 cup of mixed dried fruits as part of habitual dietary intake would decrease LDL-cholesterol due to the fibre content, compared with the processed low-fibre snacks. We further hypothesised that dried fruits would lower brachial and central blood pressure and improve arterial stiffness compared with the control group, due to the phenolic compounds[31] and K[18] provided by dried fruits. Markers of glycaemic control, C-reactive protein and other lipids/lipoproteins were also assessed.

Methods

Study design

A two-period randomised crossover trial was conducted to determine the effect of daily dried fruit consumption on cardiometabolic risk factors, compared with an energy- and carbohydrate-matched control. A computer-generated randomisation scheme (www.randomization.com) was used to assign the condition order for enrolled participants; each condition was followed for 4 weeks. After a 2- to 4-week compliance break, subjects crossed over to the alternate condition. The Metabolic Diet Study Center manager kept the randomisation code, and the personnel responsible for endpoint measurement and analysis were blinded to condition allocation until study completion. Participants were not blinded to the condition allocation.

The primary outcome was LDL-cholesterol. Secondary outcomes included concentration, size and particle number of major lipid and lipoprotein classes, fasting glucose, fasting insulin, high-sensitivity C-reactive protein, brachial systolic and diastolic blood pressure, central systolic and diastolic blood pressure, central augmentation pressure, augmentation index, carotid-femoral pulse wave velocity and blood pressures assessed by 24-h continuous blood pressure monitoring. Serum proprotein convertase subtilisin/kexin type 9 (PCSK9) concentration was an exploratory outcome. This study was conducted according to the Declaration of Helsinki Ethical Principles for Medical Research, and all procedures involving human subjects were approved by the Institutional Review Board of the Pennsylvania State University, STUDY00004871. Written informed consent was obtained from all subjects. All data were collected at the Pennsylvania State University Clinical Research Center. This trial is registered at ClinicalTrials.gov, identifier NCT03020758.

Participants

Adults (aged 25–60 years) with a BMI 25–36 kg/m² and at least one additional cardiometabolic risk factor were recruited in State College, PA from January 2017 to November 2018. Subjects were recruited using posted flyers, mailed and online advertisements, and direct communication with previous study participants who consented to be contacted. An initial telephone screening was conducted to ascertain eligibility based on key inclusion and exclusion criteria. Individuals who were eligible based on the telephone screening attended a screening visit at the Clinical Research Center. Participants were instructed to fast for 12 h (no food or beverage consumption other than water); refrain from strenuous activity for 24 h; and avoid taking anti-inflammatory medications for 48 h prior to the screening visit. Weight was assessed to the nearest 0·1 kg using a digital scale, with participants dressed in light clothing with shoes removed. Height was assessed to the nearest 0·5 cm using a mechanical stadiometer. Blood pressure was measured in triplicate using a manual sphygmanometer following a 5-min rest period; the average of the last two measurements was used. Waist circumference was measured by two nurses to the nearest 0·1 cm using a tape measure positioned in a horizontal plane around the abdomen at the level of the iliac crest; two measurements within 0·5 cm were taken and averaged. Blood samples drawn by venepuncture were processed to separate serum and plasma and then immediately refrigerated. Blood was analysed for lipids, lipoproteins, glucose, blood chemistry and complete blood count (Quest Diagnostics). Qualifying risk factors included elevated blood pressure (systolic 120–159 mmHg, diastolic 80–99 mmHg); increased waist circumference (men ≥ 94 cm, women ≥ 80 cm); fasting glucose ≥ 100 mg/dl (5·55 mmol/l) and <126 mg/dl (6·99 mmol/l); fasting TAG >150 mg/dl (1·69 mmol/l) and <350 mg/dl (3·95 mmol/l); low HDL-cholesterol (men < 40 mg/dl (1·03 mmol/l), women < 50 mg/dl (1·29 mmol/l)) and LDL-cholesterol > 116 mg/dl (3·00 mmol/l; mean LDL-cholesterol in US adults[32]). Exclusion criteria included the following: allergy to study foods, tobacco use, alcohol consumption >14 drinks/week, use of lipid-, glucose- or blood pressure-lowering medications or supplements, lactation or pregnancy, diagnosed inflammatory disease, diabetes, CVD, kidney disease, untreated thyroid disease and reported weight loss ≥10 % body weight in the past 6 months.

Composition and nutrient profile of study foods

In the dried fruit condition, participants were given individually pre-packaged portions of equal parts dried plums (California Dried Plum Board), Black Mission figs (California Fig Advisory Board), Deglet Noor dates (California Date Commission) and raisins (California Raisin Marketing Board) for each day of the study period. These types were selected because they are commonly consumed unsweetened dried fruits in the USA and globally[33]. The daily portion provided was 3/4 cup total (112 g), composed of 28 g of each fruit. Animal crackers (43 g; Stauffer's) and fruit snack gummies (51 g; Welch's, The Promotion In Motion Companies, Inc.) were selected as control snacks based on their low fibre and K contents and were portioned to match the energy and carbohydrate content of the fruits. Average daily portions of dried fruits deviated slightly from planned due to variation in the fruit weights. The nutrient profiles of study foods are presented in Table 1. All study foods were stored at room temperature, which is consistent with consumers' usual storage practices.

Sugar, carotenoid and phenolic contents of study foods were chemically analysed according to previously published methods to verify the study foods had levels comparable with published values. Method details and modifications are described further

Table 1. Nutrient profiles and bioactive contents for daily portions of dried fruits and control snacks*

	Control	Dried fruit (planned)	Dried fruit (actual)
	43 g animal crackers 51 g fruit gummies	28 g dried plums 28 g dried figs 28 g dried dates 28 g raisins	30·7 g dried plums 18·6 g dried figs 22·9 g dried dates 28·7 g raisins
Energy (kcal)†	332	300	270
Total fat (g)	2·5	0·5	0·5
Saturated fat (g)	0	0	0
Cholesterol (mg)	0	0	0
Na (mg)	170	11	10
K (mg)	42	787	715
Total carbohydrate (g)	76	79	71
Dietary fibre (g)	1·4	8·2	7·1
Sugars (g)	35‡	60	55‡
Sucrose (g)	26‡	7	7‡
Glucose (g)	5‡	28	22‡
Fructose (g)	3‡	25	21‡
Sorbitol (g)	–	–	5‡
Protein (g)	3	3	3
Total phenolics by UPLC (mg)	4·9‡		40·9‡
Total carotenoids (µg)	40·6‡		414·7‡

UPLC, ultra-performance liquid chromatography.
* Nutrient information obtained from FoodData Central[16] and manufacturers of control snacks. Planned nutrient profile for dried fruit calculated based on equal portions of dried fruits (28 g each) totalling 3/4 cup. Actual nutrient profile calculated as 7-d weighted average of pre-packaged fruit portions used in study.
† To convert energy values from kcal to kJ, multiply by 4·184.
‡ Sugar, carotenoid and phenolic profiles of study foods measured by chemical analysis.

in Supplementary materials. Sucrose, fructose and glucose were determined by LC with refractive index detection as described by Fall *et al.*[34]. Carotenoids were determined by LC with photo-diode array detection, according to methods described by Kean *et al.*[35] with minor modification. Detailed phenolic profiles and quantitation of individual phenolic species were accomplished by ultra-performance LC coupled with tandem MS using methods adapted from Li *et al.*[36] and Shahnazari *et al.*[37]. Total phenolic content was also assessed by the modified Folin-Ciocalteu assay as described by Waterhouse[38], and results expressed as gallic acid equivalents. Carotenoids and phenolic content totals for the dried fruits and control snacks are presented in Table 1. Subtypes are detailed in online Supplementary Tables S1 and S2.

Participants were informed of the energetic value of study foods and were instructed to incorporate the foods into their usual diets, substituting them for other foods they were already consuming. No specific or personalised guidance was provided for which foods to substitute. Participants could consume the study foods whenever and however they preferred as long as the entire portion was consumed daily. In addition, participants were instructed to consume one serving of fresh fruit daily during both conditions; avoid other dried fruits throughout the trial; and otherwise maintain their usual diets and physical activity to support weight maintenance. Compliance with assigned study food consumption was self-reported in weekly written logs. Compliance was quantified as the percentage of days that participants consumed the entire portion of study foods.

Outcome assessment

All data were collected at the Clinical Research Center on two consecutive days at baseline and at the end of each study period. Participants were instructed to fast for 12 h and avoid alcohol and anti-inflammatory medications for 48 h prior to clinic visits. Pre-menopausal women were tested within a week of starting their menstrual period to minimise variability due to hormone fluctuations.

Blood sample collection

Whole blood samples were drawn into serum separator, EDTA-coated and heparin-coated tubes. Serum separator tubes were allowed to clot at room temperature for 30–60 min prior to centrifugation. EDTA- and heparin-coated tubes were immediately centrifuged. Tubes were centrifuged for 15 min, and aliquots of serum and plasma were stored at –80°C until analysis.

Lipids, lipoproteins and PCSK9. Serum lipid and lipoprotein concentrations were measured on two consecutive days at each time point and an average used for data analysis (Quest Diagnostics). Total and HDL-cholesterol and TAG were measured by spectrophotometry. LDL-cholesterol was calculated using the Friedewald equation (in mg/dl: LDL-cholesterol = total cholesterol − HDL-cholesterol − TAG/5)[39]. Concentration, size and particle number of major plasma lipoprotein classes and subclasses were measured on 1 d at each time point by NMR spectroscopy (LabCorp). Serum PCSK9 was assessed in a subset of participants (*n* 45) by solid-phase sandwich ELISA (Penn State Biomarker Core Lab).

Glucose, insulin and C-reactive protein. Blood samples collected on 1 d at baseline and after each condition were used for analysis of glucose, insulin and high-sensitivity C-reactive protein. Fasting glucose was assessed from heparinised plasma by spectrophotometry (Quest Diagnostics). Serum insulin was assessed by immunoassay (Quest Diagnostics). Insulin resistance was estimated by homeostatic model assessment of insulin

resistance (HOMA-IR), calculated using the following formula: fasting plasma glucose (mg/dl) × fasting serum insulin (mU/l)/ 405[40]. Serum high-sensitivity C-reactive protein was measured by immunoturbidimetry (Quest Diagnostics). Values exceeding 10 mg/l were assumed to be acute elevations unrelated to study conditions and were excluded from analysis.

Blood pressure and arterial stiffness assessment

Brachial blood pressure was assessed by a nurse using a manual sphygmomanometer after a 5-min seated rest. Subsequently, a cuff was placed on the upper left arm for central arterial wave-form analysis using the SphygmoCor XCEL (AtCor). Participants were then rested in a supine position for assessment of carotid-femoral pulse wave velocity using the SphygmoCor XCEL. An automated cuff placed on the upper right thigh inflated to record femoral pulse, while the right carotid pulse was concurrently recorded by applanation tonometry. For all blood pressure and vascular assessments, three measurements were taken. The second and third measurements were averaged for analysis.

Twenty-four-hour blood pressure. Participants wore an ambulatory blood pressure monitor on the non-dominant arm for a 24-h period at baseline and after each condition (Mortara Instrument Inc.). The monitor was programmed to automatically capture a reading every 20 min during the day and every 30 min overnight. Averages of SBP and DBP readings were computed for the entire period worn as well as separately for readings taken while awake *v.* during sleep.

Weight

Weight was measured at every clinic visit using a digital scale with participants dressed in light clothing and shoes removed. Weights were averaged over the two clinic visits at each time point for analysis.

Statistical analysis

Statistical analyses were performed using SAS software, version 9.4 (SAS Institute). For all variables, normality of the residuals was assessed using univariate analysis to quantitatively evaluate skewness and to visually inspect the distribution and normal probability (Q–Q) plots. Variables with skewed residuals were transformed for analysis. The linear mixed model procedure (PROC MIXED) was used to test the effect of the conditions on end-of-condition means and changes from baseline for all outcomes. Condition was included in the model as a fixed effect, and subject was a repeated effect. Interactions between condition and sex or condition sequence were tested for all outcomes. There was no indication for different responses by sex or condition sequence, and there was no deviation from results of the primary analysis. Therefore, these were removed from the model. Significance level for all statistical tests was set at $P = 0.05$. A per-protocol analysis was conducted to evaluate whether condition response differed in participants who reported ≥90 % compliance with assigned conditions; the between-condition results were unchanged. Therefore, results presented are from the intent-to-treat analysis. A sensitivity analysis was conducted to determine whether weight change explained the observed effects.
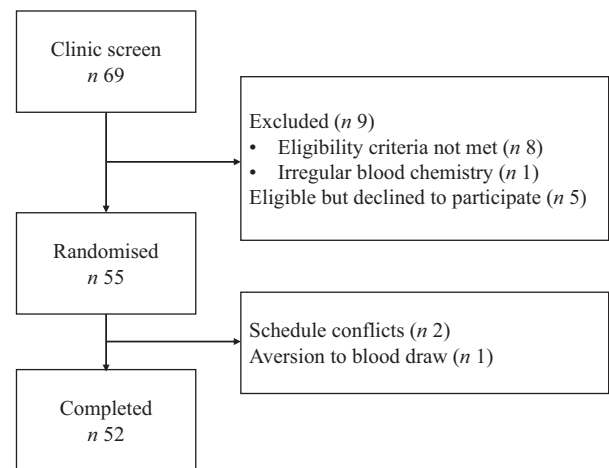

Fig. 1. Consolidated Standards of Reporting Trials 2010 flow diagram.

For endpoints where a significant between-condition difference was detected, analyses were repeated after excluding data from participants who lost or gained 2.0 kg or more of body weight in a study period.

A power calculation estimated that fifty subjects were required to detect a 12 mg/dl (0.31 mmol/l) difference in between-condition LDL-cholesterol, assuming a standard deviation of 30 mg/dl (0.78 mmol/l) at a 5 % significance level with 80 % power[28]. Anticipating a 10 % dropout rate, we enrolled fifty-five participants.

Results

Participants

Fifty-five participants were enrolled and randomised, and fifty-two completed the trial (Fig. 1). One withdrew at the first baseline appointment and two withdrew during the first condition due to schedule conflicts. Most participants (87 %) had elevated waist circumferences (Table 2). Mean BMI was 28.5 kg/m², and mean LDL-cholesterol was above optimal (2.94 (sd 0.94) mmol/l) at baseline. Baseline characteristics did not differ by randomisation sequence (data not presented). Self-reported compliance in participants who returned completed compliance forms for all study days was 98.9 % for dried fruit (*n* 37) and 98.4 % (*n* 39) for the control. Participants gained weight during both conditions (control 0.4 kg, 95 % CI 0.01, 0.75, $P = 0.043$; dried fruit 0.3 kg, 95 % CI –0.09, 0.65, $P = 0.14$) with no between-condition difference in weight change detected ($P = 0.55$).

Lipids, lipoproteins and PCSK9

There were no significant between-condition differences in endpoint-to-endpoint comparison of means or change from baseline for lipid, lipoprotein or PCSK9 concentrations (Table 3). Following the dried fruit condition, LDL-cholesterol (0.10 mmol/l, 95 % CI 0.01, 0.20) and non-HDL-cholesterol (0.12 mmol/l, 95 % CI 0.01, 0.23) increased from baseline, while HDL-cholesterol decreased (–0.05 mmol/l, 95 % CI –0.09, –0.01) (all $P < 0.05$); no changes in these outcomes were detected following the

Table 2. Baseline characteristics of enrolled participants (n 55)
(Mean values and standard deviations; numbers and percentages)

	Mean	SD	Optimal	Participants with suboptimal values n	%
Female (n)	26				
Age (years)	40·5	10·7			
BMI (kg/m²)	28·5	2·7	<25	55	100
Waist circumference (cm)	98·2	8·2	<94 men, <80 women	48	87
SBP (mmHg)	111	9	<120	8	15
DBP (mmHg)	77	8	<80	23	42
Glucose (mmol/l)	5·43	0·43	<5·55	23	42
LDL-cholesterol (mmol/l)	2·94	0·94	<2·60	34	62
HDL-cholesterol (mmol/l)	1·27	0·45	≥1·03 men, ≥1·29 women	26	47
TAG (mmol/l)	1·30	0·61	<1·69	10	18

SBP, systolic blood pressure; DBP, diastolic blood pressure.

Table 3. Mean lipid (n 55), lipoprotein (n 52) and proprotein convertase subtilisin/kexin type 9 (PCSK9) (n 45) concentrations for participants at baseline and after dried fruit and control conditions†
(Mean values with their standard errors)

	Baseline Mean	SEM	Control Mean	SEM	Change from baseline	SEM	Dried fruit Mean	SEM	Change from baseline	SEM	P
Weight (kg)	85·3	1·8	85·8	1·9	0·4*	0·2	85·7	1·9	0·3	0·2	0·55
TC (mmol/l)	4·81	0·14	4·89	0·15	0·05	0·06	4·91	0·15	0·07	0·06	0·84
LDL-cholesterol (mmol/l)	2·94	0·13	3·01	0·13	0·05	0·05	3·06	0·13	0·10*	0·05	0·36
Non-HDL-cholesterol (mmol/l)	3·55	0·14	3·64	0·15	0·07	0·06	3·70	0·15	0·12*	0·06	0·39
HDL-cholesterol (mmol/l)	1·27	0·06	1·26	0·06	−0·03	0·02	1·24	0·06	−0·05*	0·02	0·19‡
TC:HDL-cholesterol	4·1	0·2	4·2	0·2	0·1*	0·1	4·3	0·2	0·2*	0·1	0·18‡
TAG (mmol/l)	1·30	0·08	1·37	0·10	0·07	0·07	1·32	0·10	0·01	0·07	0·97‡
VLDL and chylomicron particles (total) (nmol/l)	55·3	3·4	54·4	3·7	−0·9	2·6	54·0	3·7	−1·3	2·6	0·94‡
Large VLDL and chylomicron particles (nmol/l)	4·1	0·5	4·8	0·6	0·6	0·6	4·4	0·6	0·3	0·6	0·43‡
Medium VLDL particles (nmol/l)	21·6	2·4	20·6	2·2	−1·0	1·9	19·7	2·2	−1·8	1·9	0·83‡
Small VLDL particles (nmol/l)	29·6	1·7	29·1	2·2	−0·5	2·2	29·9	2·2	0·3	2·2	0·82‡
LDL particles (total) (nmol/l)	1102	51	1152	53	50	25	1153	53	51*	25	0·96
IDL particles (nmol/l)	180	14	165	16	−15	17	180	16	−1	17	0·24‡
Large LDL particles (nmol/l)	286	27	288	28	2	20	303	28	16	20	0·48
Small LDL particles (nmol/l)	635	30	699	46	63*	26	671	46	36	26	0·23
HDL particles (total) (µmol/l)	31·2	0·8	31·3	0·8	0·1	0·4	31·0	0·8	−0·2	0·4	0·48
Large HDL particles (µmol/l)	6·9	0·5	6·8	0·5	−0·2	0·2	6·6	0·5	−0·4*	0·2	0·38‡
Medium HDL particles (µmol/l)	8·5	0·7	8·6	0·7	0·1	0·6	9·2	0·7	0·7	0·6	0·07‡
Small HDL particles (µmol/l)	15·8	0·8	16·0	0·8	0·2	0·7	15·3	0·8	−0·5	0·7	0·27
VLDL size (nm)	48·5	0·8	49·0	0·9	0·5	1·0	49·1	0·9	0·6	1·0	0·76‡
LDL size (nm)	20·6	0·1	20·6	0·1	0	0·1	20·6	0·1	0	0·1	0·32
HDL size (nm)	9·3	0·1	9·3	0·1	−0·1	0	9·3	0·1	−0·1	0	0·85
Calculated TAG (total) (mmol/l)	1·33	0·10	1·41	0·11	0·08	0·09	1·36	0·11	0·03	0·09	0·85‡
Calculated VLDL and chylomicron TAG (mmol/l)	0·95	0·07	0·99	0·08	0·04	0·06	0·94	0·08	0	0·06	0·92‡
Calculated HDL-cholesterol (mmol/l)	1·29	0·06	1·27	0·06	−0·02	0·02	1·26	0·06	−0·04	0·02	0·45‡
Lipoprotein insulin resistance score	46	2	48	3	2	2	50	3	4	2	0·31
HOMA-IR	1·5	0·1	1·5	0·1	0	0·1	1·6	0·1	0·1	0·1	0·05‡
Insulin (pmol/l)	41·4	2·6	41·0	3·0	−0·6	3·1	44·0	3·0	2·4	3·1	0·09‡
hsCRP (mg/l)	1·8	0·2	2·0	0·3	0·2	0·2	1·9	0·3	0	0·2	0·44‡
PCSK9 (ng/ml)	168	11	168	12	−1	12	177	12	8	12	0·37‡

TC, total cholesterol; hsCRP, high-sensitivity C-reactive protein; HOMA-IR, homeostatic model assessment of insulin resistance.
* Significant change from baseline (P < 0·05).
† Baseline values presented as unadjusted mean values with their standard errors. Least squared mean values with their standard errors for end-of-condition means and changes from baseline for control and dried fruit. P value for linear mixed model comparing end-of-condition means.
‡ Transformed means used in linear mixed model for variables with non-normally distributed residuals.

control condition. The total cholesterol:HDL-cholesterol ratio increased significantly following both conditions (control 0·13, 95 % CI 0·01, 0·26, P = 0·037; dried fruit 0·20, 95 % CI 0·08, 0·33, P = 0·002). LDL particle number increased from baseline after dried fruit (51 nmol/l, 95 % CI 1, 101; P = 0·045); a similar increase after control was not statistically significant (50 nmol/l, 95 % CI 0, 100). Specifically, small LDL particles increased significantly following the control condition (63 nmol/l, 95 % CI 11, 115;
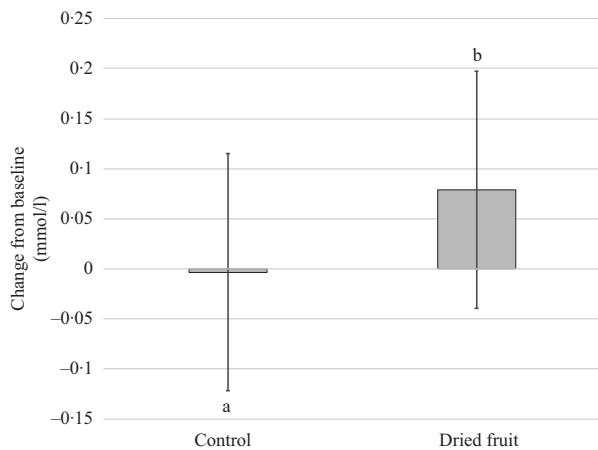
Fig. 2. Changes from baseline for fasting plasma glucose following 4 weeks of consuming dried fruits or the control snacks (n 55). Data are unadjusted mean values and 95 % confidence intervals from linear mixed model comparing changes from baseline. a,b Statistically significant between-treatment effect denoted by unlike letters.

P = 0·018), whereas the increase in total particles with dried fruit was composed of both large and small particles. Large HDL particles decreased from baseline following dried fruit consumption (–0·38 μmol/l, 95 % CI –0·74, –0·01; P = 0·045). After exclusion of participants with substantial weight changes (±2·0 kg within condition v. baseline), all within-condition changes from baseline were attenuated to non-significance with the exception of HDL-cholesterol (online Supplementary Table S3).

Glucose, insulin and C-reactive protein

Mean fasting glucose was significantly greater following the dried fruit condition v. the control condition (mean difference 0·08 mmol/l, 95 % CI 0·005, 0·16; P = 0·038) (Fig. 2). This difference

persisted after exclusion of participants with substantial (±2·0 kg) within-condition weight changes v. baseline. Changes from baseline were not statistically significant for either condition in the intent-to-treat analysis (Table 3). However, the increase in glucose after the dried fruit condition v. baseline was significant in the per-protocol analysis (0·15 mmol/l, 95 % CI 0·01, 0·29; P = 0·038; online Supplementary Table S4) and after exclusions for substantial weight changes (0·12 mmol/l, 95 % CI 0·004, 0·23; P = 0·04; online Supplementary Table S3). The between-condition difference in HOMA-IR approached significance (0·1, 95 % CI –0·3, 0·9; P = 0·054) but was not changed from baseline for either condition. There were no condition effects or changes from baseline for insulin or high-sensitivity C-reactive protein.

Blood pressure and arterial stiffness

No between-condition differences in endpoint-to-endpoint analysis of means or changes from baseline were detected for blood pressure or measures of central arterial stiffness (Table 4). Brachial diastolic pressure and derived central diastolic pressure assessed by the SphygmoCor increased from baseline on the control condition only (diastolic blood pressure 2·1 mmHg, 95 % CI 0·5, 3·7 mmHg; central diastolic blood pressure 2·0 mmHg, 95 % CI 0·4, 3·6; both P = 0·01). Excluding participants with weight changes of 2·0 kg or greater (n for analysis dried fruit = 45, control = 44) attenuated the central diastolic blood pressure change from baseline to non-significance but diastolic blood pressure remained significantly elevated after the control compared with baseline (2·1 mmHg, 95 % CI 0·5, 3·7; P = 0·01). There were no significant changes in clinician-assessed blood pressures, brachial systolic blood pressure, central systolic blood pressure or any central arterial stiffness measures compared with baseline.

Table 4. Vascular outcome means at baseline and after each condition (n 55)†
(Mean values with their standard errors)

	Baseline		Control				Dried fruit				
	Mean	SEM	Mean	SEM	Change from baseline	SEM	Mean	SEM	Change from baseline	SEM	P
Clinician-assessed brachial SBP (mmHg)	111·1	1·3	112·9	1·4	1·8	1·0	112·8	1·4	1·7	1·0	0·99
Clinician-assessed brachial DBP (mmHg)	76·9	1·1	76·7	1·1	–0·5	0·8	76·6	1·1	–0·6	0·8	0·87
Brachial SBP (mmHg)	119·5	1·3	119·7	1·5	0	1·1	120·7	1·5	0·9	1·1	0·31
Brachial DBP (mmHg)	75·9	1·1	78·2	1·2	2·1*	0·8	76·9	1·2	0·8	0·8	0·09
Central SBP (mmHg)	109·0	1·3	109·8	1·3	0·5	1·0	110·1	1·3	0·8	1·0	0·70
Central DBP (mmHg)	76·8	1·2	78·9	1·2	2·0*	0·8	77·6	1·2	0·7	0·8	0·07
Augmentation pressure (mmHg)	7·0	0·6	6·9	0·6	–0·3	0·5	7·6	0·6	0·3	0·5	0·21
Augmentation index (%)	17·5	1·9	18·7	1·8	0·8	1·2	19·7	1·8	1·8	1·2	0·35
Pulse wave velocity (m/s)	6·5	0·1	6·6	0·1	0·1	0·1	6·6	0·1	0·1	0·1	0·90
Combined 24- h SBP	114·4	1·2	115·9	1·4	1·5	1·2	115·2	1·4	0·3	1·2	0·09
Combined 24-h DBP	74·8	0·7	74·8	0·8	0	0·6	75·0	0·8	–0·1	0·6	0·44
Awake SBP	119·7	1·3	120·8	1·4	1·1	1·3	120·7	1·4	0·4	1·3	0·82
Awake DBP	77·6	0·8	77·6	0·8	–0·1	0·7	78·2	0·8	0	0·7	0·04
Asleep SBP	99·4	1·3	100·8	1·4	1·1	1·5	100·5	1·4	1·2	1·5	0·66
Asleep DBP	66·5	0·8	66·1	0·8	–0·6	0·7	66·6	0·8	0·2	0·7	0·19

SBP, systolic blood pressure; DBP, diastolic blood pressure.
* Significant change from baseline (P < 0·05).
† Baseline values presented as unadjusted mean values with their standard errors. Least squared mean values with their standard errors for end-of-condition means and changes from baseline for control and dried fruit. P value for linear mixed model comparing end-of-condition means.

Twenty-four-hour blood pressure

An average of fifty blood pressure readings (thirty-seven during waking hours and thirteen while asleep) was recorded per participant. Mean blood pressure combined across sleeping and wake periods did not differ between conditions (Table 4). When sleeping *v.* awake periods were analysed separately, end-of-condition mean diastolic pressure during waking hours was significantly higher after dried fruit *v.* control condition (mean difference 0·6 mmHg, 95 % CI 0·02, 1·17; *P* = 0·04). Changes from baseline for total, waking, and sleeping SBP and DBP were not significant for either condition and did not significantly differ between conditions.

Discussion

This study aimed to assess the effect of consuming mixed dried fruits, within a self-selected diet, on risk factors for cardiometabolic diseases. Contrary to our hypothesis, consuming a ¾ cup portion of mixed dried plums, figs, dates and raisins daily for 4 weeks did not improve LDL-cholesterol, blood pressure or vascular stiffness in overweight/obese subjects at increased risk of cardiometabolic diseases, compared with a carbohydrate-rich control.

Our findings agree with those of Peterson *et al.*[24], who reported no difference in LDL-cholesterol after adults with above optimal or high LDL-cholesterol (*n* 88; mean baseline LDL-cholesterol 3·49–3·52 mmol/l) consumed 120 g/d of dried Mission figs *v.* their usual diet for 5 weeks. In contrast, two previous trials reported lowering of LDL-cholesterol with dried plum consumption. Tinker *et al.*[23] reported significantly lower LDL-cholesterol after hypercholesterolaemic men (*n* 41; mean baseline LDL-cholesterol 3·89 mmol/l) consumed twelve dried plums (approximately 100 g) daily for 4 weeks compared with an equienergetic daily portion of grape juice (mean difference 0·17 mmol/l, *P* = 0·02). A numerically small increase from baseline (0·03 mmol/l) was observed with plum consumption but, considering the CI of the estimate, was not statistically significant. Likewise, Clayton *et al.*[29] reported 0·63 mmol/l lower LDL-cholesterol after normocholesterolaemic overweight and obese adults (mean baseline LDL-cholesterol 2·03–2·04 mmol/l) consumed two 418 kJ (100 kcal) servings (84 g) of dried plums daily for 8 weeks (*n* 26) *v.* the control group that consumed energy-matched low-fat muffins (*n* 23), though changes from baseline were not significant.

The conflicting results in these studies *v.* ours and that of Peterson *et al.*[24] are not easily explained. Our trial was comparable in duration and fruit dose to Tinker *et al.*[23], and while elevated LDL-cholesterol was not an essential criterion for enrolment in our study, participants' mean baseline LDL-cholesterol was classifiable as 'above optimal' (≥2·6 mmol/l)[41] and exceeded that of participants in the study by Clayton *et al.*[29]. Thus, differences in duration or baseline health of participants do not fully explain why LDL-cholesterol was not reduced by dried fruits in our study. It is possible that cholesterol-lowering was effected by higher soluble fibre content in the dried plum interventions compared with ours, as dried plums contain nearly twice as much soluble fibre as raisins and dates[17].

Yet, dried figs are higher in soluble fibre than plums and did not lower cholesterol in the study by Peterson *et al.*[24]. Specific bioactives may be responsible for the cholesterol-lowering effect of dried plums that, as part of a dried fruit mixture, may have been consumed in too small a dose or antagonised by other fruits' bioactives[42].

An important distinction between the trials that report LDL-cholesterol-lowering with dried fruit consumption[23,29] *v.* our trial and that of Peterson *et al.*[24] is maintenance of energy balance. In the study by Peterson *et al.*[24], mean energy intake increased by about 837 kJ/d (200 kcal/d) while consuming figs, compared with participants' usual diets. Similarly, we observed modest weight gain (0·3–0·4 kg) after both conditions suggesting daily overconsumption of approximately 314–439 kJ/d (75–105 kcal/d) (approximately 25–30 % of the study foods' daily energetic values), though without dietary records, total energy intakes cannot be estimated. Therefore, our results may be explained by increased sugar intake in the setting of excessive energy intake[43]. Short-term overfeeding with simple carbohydrates increases *de novo* lipogenesis[44], and fructose-containing sugars may be particularly lipogenic as hepatic fructose uptake is not enzymatically regulated[45]. Within a hyperenergetic diet, perhaps even sugars from dried fruits can increase lipogenesis in individuals with elevated cardiometabolic risk. Accordingly, the within-condition increase in LDL-cholesterol following dried fruit consumption was attenuated by omission of data from participants with substantial weight changes, though this *post hoc* analysis should be interpreted with caution due to the loss of statistical power with a reduced sample size (*n* for analysis dried fruit = 45, control = 44). Future investigation into the lipidemic effects of dried fruit under eucaloric and hyperenergetic conditions is required to understand these findings. In addition, comparison with a low-fructose control would further clarify whether energy excess, fructose content or a combination of the two explain the finding.

The K and phenolic compounds in dried fruits were predicted to improve vascular health. However, a 4-week intervention was likely too short to effect structural changes that alter vascular stiffness. Though numerically lower mean DBP was observed after dried fruit consumption, detection of such a small blood pressure-lowering effect would have required hundreds of subjects. Substantial reductions in blood pressure were reported by Anderson *et al.*[25] after daily consumption of raisins (85 g) for 12 weeks. Within-condition changes in SBP at 4, 8 and 12 weeks ranged from –5·4 to –8·3 mmHg, all significantly reduced from baseline (*P* < 0·05). The raisin group had lower DBP at all time points *v.* the control group consuming processed carbohydrate-rich snacks, with a significant reduction from baseline (–5·5 mmHg) reported at week 12. However, a qualifying enrolment criterion for this previous study was elevated blood pressure. In contrast, more than half of our participants had a normal blood pressure at baseline.

Although this study was not specifically designed to investigate the effects of dried fruit on glycaemic control, the increase in fasting plasma glucose observed after dried fruit consumption, compared with the control snack, is intriguing. This increase persisted in both the sensitivity and per-protocol analyses. Dried fruits have a low to moderate glycaemic index, and the acute glycaemic response to carbohydrate-rich meals is attenuated

by replacement of refined starches with dried fruits[46–50]. The lower postprandial glycaemic response is likely due to partial glucose replacement by fructose, which does not contribute substantially to blood glucose and may even stimulate hepatic glucose uptake[51]. However, the longer-term glycaemic effects of dried fruits have been less investigated. Previous studies did not detect changes in fasting glucose in overweight/obese adults consuming raisins (one cup/d) or dried plums (84 g/d) for 6 and 8 weeks, respectively[28,29]. In a randomised parallel study of overweight/obese adults (n 31), a similar dose of dried fruits to what we provided (85 g raisins) for 12 weeks resulted in a non-significant 0.13 ± 0.11 mmol/l ($P = 0.36$) increase in fasting glucose from baseline, which did not statistically differ from the mean change observed in the control arm (n 15) consuming processed snacks (0.03 ± 0.03 mmol/l)[25]. However, this difference is directionally and numerically similar to that observed in our crossover study. Thus, it is possible that differences in study design may explain the inconsistent findings. However, this finding requires further investigation, as glycaemic measures were not the primary focus of our trial.

Many of the hypothesised benefits of dried fruits are attributed to the phytochemicals they contain[52,53]. We assessed the phenolic and carotenoid contents of the provided study foods for comparison with published values. The measured carotenoid contents of our fruits were greater than reference values[16]. Analysed total phenolic contents were greater for dried plums and raisins and lower for dates than previously reported[54], while reported total phenolics in figs were variably higher[54] or lower[55] than ours. Differences in fruit varieties, growing conditions, maturity, drying conditions and analytical methods might contribute to differences in our observed values compared with previous reports. Concentrations of these bioactives were not substantially lower compared with other reports, so it is unlikely that the results of our study are explained by lower bioactive content of the studied dried fruits. However, we did not control how the fruits were consumed (i.e. together v. individually) and, thus, possible antagonism of particular bioactive components by coingestion with the other fruits cannot be excluded[42]. Furthermore, reported contents represent amounts present in the foods, as consumed, but most phenolic compounds are metabolised by gut bacteria prior to absorption, thereby altering their biological activity[56]. Thus, physiological responses to these compounds may depend on composition of the gut microbiome. Substantial interindividual variability in plasma concentrations of individual phenolic compound metabolites has been shown[57,58]. Characterisation of participants' gut microbial populations may help to explain variation in physiological responses to diet.

To our knowledge, this study is the first to assess a wide range of cardiometabolic disease risk factors in free-living subjects consuming mixed dried fruits with minimal guidance as to how or when to consume the fruits. This pragmatic design allowed participants to incorporate study foods into their diets however they preferred, and therefore these results are informative about the cardiometabolic consequences of recommending increased dried fruit consumption as a strategy to improve fruit intakes. In addition to the 3/4 cup/d portion of dried fruit provided, equivalent to 1·5 cup-equivalents of

fruit according to the 2015–2020 Dietary Guidelines for Americans, subjects were instructed to consume one additional fruit serving per d. Thus, total fruit consumption during the dried fruit condition was consistent with recommended fruit intake, and during the control period fruit intake aligned with average US adult intakes[9,59]. While dietary incorporation of dried fruits did assist with meeting recommended fruit intake, the dried fruits were not effectively substituted for other foods in the diet and thereby contributed to weight gain, which may have obscured the expected cardiometabolic benefits. Fully controlling the diet through provision of all foods and beverages could limit the confounding effects of weight changes and other dietary factors and, thereby, determine the efficacy of dried fruits to effect cardiometabolic improvements. However, the health effects observed under these tightly regulated conditions may not readily translate to free-living individuals who incorporate dried fruits into their diets. At minimum, provision of more detailed guidance may be necessary to support maintenance of energy balance in a supplemental dietary trial and may not be unique to dried fruit supplementation[60].

A major strength of our study was its crossover design, which allows separation of between-person from within-person variability. We utilised functional assessments of cardiometabolic health including lipoprotein subclass analysis, pulse wave analysis, carotid-femoral pulse wave velocity measurement and 24-h blood pressure monitoring, in addition to established measurements of CVD risk including lipid profile and brachial blood pressure. We also analysed the phenolic contents of our study foods to more accurately quantify the actual doses provided to participants. However, our inferences regarding the effects of dried fruits are limited by the absence of dietary assessment before or during the intervention, as we were unable to confirm that an isoenergetic substitution occurred in both periods. We made the assumption that participants altered their usual diets similarly to incorporate dried fruits v. the control snacks. Without dietary records, we cannot confirm that background dietary intake was consistent in both periods and cannot determine if, or how, energy content from participants' usual diets were compensated when study foods were consumed. Unmeasured changes in intake of other foods and nutrients, accompanying either the control or dried fruit conditions, may explain the lack of observed cardiometabolic benefits with dried fruit consumption compared with the control. However, with the current diet assessment methods available, we would likely lack the sensitivity to completely understand dietary alterations that occurred in response to the daily consumption of dried fruits. In addition, due to natural variations in the consumer-grade dried fruits, we provided less fruit than planned (approximately 101 v. 112 g), which may have resulted in underestimation of the effects we observed. We did not adjust P values for multiple comparisons, thus the inflation of type I error rate could be responsible for our significant findings. However, we suggest that the observed changes are consistent with metabolic responses to overconsumption of sugars. Finally, given the broad eligibility criteria, participants varied substantially in baseline health status and mean values for most risk factors were within acceptable limits. Individuals

with normal baseline values had little room for improvement, and the absence of changes in these healthier participants may have attenuated improvements in higher-risk participants.

In summary, short-term consumption of 3/4 cup/d of mixed dried plums, figs, dates and raisins within a self-selected diet did not improve risk factors for cardiometabolic disease compared with non-fruit, carbohydrate-rich snacks in adults with increased risk for cardiometabolic diseases. Further research is needed to determine what, if any, dietary guidance regarding portion or pattern of consumption (e.g. with meals) is warranted to support healthful dried fruit consumption. Maintenance of energy balance should be ensured in future studies investigating the efficacy of routine dried fruit consumption to improve health.

Acknowledgements

Supplementary material

For supplementary material referred to in this article, please visit https://doi.org/10.1017/S0007114520002007

References

1. GBD 2016 Causes of Death Collaborators (2017) Global, regional, and national age-sex specific mortality for 264 causes of death, 1980–2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet* **390**, 1151–1210.
2. 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.
3. Bechthold A, Boeing H, Schwedhelm C, *et al.* (2019) Food groups and risk of coronary heart disease, stroke and heart failure: a systematic review and dose–response meta-analysis of prospective studies. *Crit Rev Food Sci Nutr* **59**, 1071–1090.
4. Li M, Fan Y, Zhang X, *et al.* (2014) Fruit and vegetable intake and risk of type 2 diabetes mellitus: meta-analysis of prospective cohort studies. *BMJ Open* **4**, e005497.
5. Schwingshackl L, Hoffmann G, Lampousi AM, *et al.* (2017) Food groups and risk of type 2 diabetes mellitus: a systematic review and meta-analysis of prospective studies. *Eur J Epidemiol* **32**, 363–375.
6. Lee M, Lim M & Kim J (2019) Fruit and vegetable consumption and the metabolic syndrome: a systematic review and dose–response meta-analysis. *Br J Nutr* **122**, 723–733.
7. Appel LJ, Moore TJ, Obarzanek E, *et al.* (1997) A clinical trial of the effects of dietary patterns on blood pressure. *N Engl J Med* **336**, 1117–1124.
8. Toh DWK, Koh ES & Kim JE (2020) Incorporating healthy dietary changes in addition to an increase in fruit and vegetable intake further improves the status of cardiovascular disease risk factors: a systematic review, meta-regression, and meta-analysis of randomized controlled trials. *Nutr Rev* **78**, 532–545.
9. U.S. Department of Health and Human Services & U.S. Department of Agriculture (2015) *2015–2020 Dietary Guidelines for Americans*, 8th ed. https://health.gov/our-work/food-and-nutrition/2015–2020-dietary-guidelines/ (accessed January 2020).
10. Public Health England (2016) *Government Dietary Recommendations*. www.gov.uk/phe (accessed January 2020).
11. National Health and Medical Research Council & Department of Health and Ageing Eat for Health (2013) *Australian Dietary Guidelines*. www.nhmrc.gov.au/guidelines-publications/n55 (accessed January 2020).
12. Nicklas TA, Jahns L, Bogle ML, *et al.* (2013) Barriers and facilitators for consumer adherence to the dietary guidelines for Americans: the HEALTH Study. *J Acad Nutr Diet* **113**, 1317–1331.
13. Haynes-Maslow L, Parsons SE, Wheeler SB, *et al.* (2013) A qualitative study of perceived barriers to fruit and vegetable consumption among low-income populations, North Carolina, 2011. *Prev Chronic Dis* **10**, E34.
14. Sadler MJ, Gibson S, Whelan K, *et al.* (2019) Dried fruit and public health–what does the evidence tell us? *Int J Food Sci Nutr* **70**, 675–687.
15. Kamiloglu S, Toydemir G, Boyacioglu D, *et al.* (2016) A review on the effect of drying on antioxidant potential of fruits and vegetables. *Crit Rev Food Sci Nutr* **56**, Suppl. 1, S110–S129.
16. U.S. Department of Agriculture & Agricultural Research Service (2019) FoodData Central. https://fdc.nal.usda.gov/index.html (accessed April 2019).
17. Dreher ML (2018) Whole fruits and fruit fiber emerging health effects. *Nutrients* **10**, E1833.
18. Blanch N, Clifton PM & Keogh JB (2015) A systematic review of vascular and endothelial function: effects of fruit, vegetable and potassium intake. *Nutr Metab Cardiovasc Dis* **25**, 253–266.
19. Swan GE, Powell NA, Knowles BL, *et al.* (2018) A definition of free sugars for the UK. *Public Health Nutr* **21**, 1636–1638.
20. Bachman JL, Reedy J, Subar AF, *et al.* (2008) Sources of food group intakes among the US population, 2001–2002. *J Am Diet Assoc* **108**, 804–814.
21. Fulgoni VL, Painter J & Carughi A (2017) Association of raisin consumption with nutrient intake, diet quality, and health risk factors in US adults: National Health and Nutrition Examination Survey 2001–2012. *Food Nutr Res* **61**, 1378567.

22. Jesionkowska K, Sijtsema S, Simoneaux R, *et al.* (2008) Preferences and consumption of dried fruit and dried fruit products among Dutch, French and Polish consumers. *J Fruit Ornam Plant Res* **16**, 261–274.

23. Tinker LF, Schneeman BO, Davis PA, *et al.* (1991) Consumption of prunes as a source of dietary fiber in men with mild hypercholesterolemia. *Am J Clin Nutr* **53**, 1259–1265.

24. Peterson JM, Montgomery S, Haddad E, *et al.* (2011) Effect of consumption of dried California mission figs on lipid concentrations. *Ann Nutr Metab* **58**, 232–238.

25. Anderson JW, Weiter KM, Christian AL, *et al.* (2014) Raisins compared with other snack effects on glycemia and blood pressure: a randomized, controlled trial. *Postgrad Med* **126**, 37–43.

26. Bays H, Weiter K & Anderson J (2015) A randomized study of raisins versus alternative snacks on glycemic control and other cardiovascular risk factors in patients with type 2 diabetes mellitus. *Phys Sport* **43**, 37–43.

27. Chai SC, Hooshmand S, Saadat RL, *et al.* (2012) Daily apple versus dried plum: impact on cardiovascular disease risk factors in postmenopausal women. *J Acad Nutr Diet* **112**, 1158–1168.

28. Puglisi MJ, Vaishnav U, Shrestha S, *et al.* (2008) Raisins and additional walking have distinct effects on plasma lipids and inflammatory cytokines. *Lipids Health Dis* **7**, 14.

29. Clayton ZS, Fusco E, Schreiber L, *et al.* (2019) Snack selection influences glucose metabolism, antioxidant capacity and cholesterol in healthy overweight adults: a randomized parallel arm trial. *Nutr Res* **65**, 89–98.

30. Ference BA, Ginsberg HN, Graham I, *et al.* (2017) Low-density lipoproteins cause atherosclerotic cardiovascular disease. 1. Evidence from genetic, epidemiologic, and clinical studies. A consensus statement from the European Atherosclerosis Society Consensus Panel. *Eur Heart J* **38**, 2459–2472.

31. Bondonno CP, Croft KD, Ward N, *et al.* (2015) Dietary flavonoids and nitrate: effects on nitric oxide and vascular function. *Nutr Rev* **73**, 216–235.

32. Carroll MD, Kit BK, Lacher DA, *et al.* (2012) Trends in lipids and lipoproteins in US adults, 1988–2010. *JAMA* **308**, 1545–1554.

33. International Nut & Dried Fruit Council (2018) *Nuts & Dried Fruits Statistical Yearbook 2018/2019.* https://www.nutfruit.org/files/tech/1553521370_INC_Statistical_Yearbook_2018.pdf

34. Fall LA, Perkins-Veazie P, Ma G, *et al.* (2019) QTLs associated with flesh quality traits in an elite × elite watermelon population. *Euphytica* **215**, 30.

35. Kean EG, Hamaker BR & Ferruzzi MG (2008) Carotenoid bioaccessibility from whole grain and degermed maize meal products. *J Agric Food Chem* **56**, 9918–9926.

36. Li M, Koecher K, Hansen L, *et al.* (2016) Phenolic recovery and bioaccessibility from milled and finished whole grain oat products. *Food Funct* **7**, 3370–3381.

37. Shahnazari M, Turner RT, Iwaniec UT, *et al.* (2016) Dietary dried plum increases bone mass, suppresses proinflammatory cytokines and promotes attainment of peak bone mass in male mice. *J Nutr Biochem* **34**, 73–82.

38. Waterhouse AL (2002) Determination of total phenolics In *Current Protocols in Food Analytical Chemistry*, pp. I1.1.1–I1.1.8 [RE Wrolstad, editor]. New York: John Wiley & Sons, Inc.

39. Friedewald WT, Levy RI & Fredrickson DS (1972) Estimation of the concentration of low-density lipoprotein cholesterol in plasma. *Clin Chem* **18**, 499–502.

40. Matthews DR, Hosker JP, Rudenski AS, *et al.* (1985) Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. *Diabetologia* **28**, 412–419.

41. Grundy SM, Stone NJ, Bailey AL, *et al.* (2019) 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the management of blood cholesterol: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation* **139**, E1082–E1143.

42. Phan MAT, Paterson J, Bucknall M, *et al.* (2018) Interactions between phytochemicals from fruits and vegetables: effects on bioactivities and bioavailability. *Crit Rev Food Sci Nutr* **58**, 1310–1329.

43. Chiavaroli L, de Souza RJ, Ha V, *et al.* (2015) Effect of fructose on established lipid targets: a systematic review and meta-analysis of controlled feeding trials. *J Am Heart Assoc* **4**, e001700.

44. Sevastianova K, Santos A, Kotronen A, *et al.* (2012) Effect of short-term carbohydrate overfeeding and long-term weight loss on liver fat in overweight humans. *Am J Clin Nutr* **96**, 727–734.

45. Samuel VT (2011) Fructose induced lipogenesis: from sugar to fat to insulin resistance. *Trends Endocrinol Metab* **22**, 60–65.

46. Viguiliouk E, Jenkins AL, Blanco Mejia S, *et al.* (2018) Effect of dried fruit on postprandial glycemia: a randomized acute-feeding trial. *Nutr Diabetes* **8**, 59.

47. Esfahani A, Lam J & Kendall CWC (2014) Acute effects of raisin consumption on glucose and insulin responses in healthy individuals. *J Nutr Sci* **3**, e1.

48. Kanellos PT, Kaliora AC, Liaskos C, *et al.* (2013) A study of glycemic response to corinthian raisins in healthy subjects and in type 2 diabetes mellitus patients. *Plant Foods Hum Nutr* **68**, 145–148.

49. Kim Y, Hertzler SR, Byrne HK, *et al.* (2008) Raisins are a low to moderate glycemic index food with a correspondingly low insulin index. *Nutr Res* **28**, 304–308.

50. Zhu R, Fan Z, Dong Y, *et al.* (2018) Postprandial glycaemic responses of dried fruit-containing meals in healthy adults: results from a randomised trial. *Nutrients* **10**, 694.

51. Mirtschink P, Jang C, Arany Z, *et al.* (2018) Fructose metabolism, cardiometabolic risk, and the epidemic of coronary artery disease. *Eur Heart J* **39**, 2497–2505.

52. Ho KKHY, Ferruzzi MG & Wightman JD (2020) Potential health benefits of (poly)phenols derived from fruit and 100 % fruit juice. *Nutr Rev* **78**, 145–174.

53. Arvaniti OS, Samaras Y, Gatidou G, *et al.* (2019) Review on fresh and dried figs: chemical analysis and occurrence of phytochemical compounds, antioxidant capacity and health effects. *Food Res Int* **119**, 244–267.

54. Wu X, Beecher GR, Holden JM, *et al.* (2004) Lipophilic and hydrophilic antioxidant capacities of common foods in the United States. *J Agric Food Chem* **52**, 4026–4037.

55. Ouchemoukh S, Hachoud S, Boudraham H, *et al.* (2012) Antioxidant activities of some dried fruits consumed in Algeria. *LWT Food Sci Technol* **49**, 329–332.

56. Selma MV, Espín JC & Tomás-Barberán FA (2009) Interaction between phenolics and gut microbiota: role in human health. *J Agric Food Chem* **57**, 6485–6501.

57. Feliciano RP, Mills CE, Istas G, *et al.* (2017) Absorption, metabolism and excretion of cranberry (poly)phenols in humans: a dose–response study and assessment of inter-individual variability. *Nutrients* **9**, E268.

58. Manach C, Williamson G, Morand C, *et al.* (2005) Bioavailability and bioefficacy of polyphenols in humans. I. Review of 97 bioavailability studies. *Am J Clin Nutr* **81**, 230S–242S.

59. National Cancer Institute (2019) *Usual Dietary Intakes: Food Intakes, U.S. Population, 2007–10.* https://epi.grants.cancer.gov/diet/usualintakes/ (accessed March 2020).

60. Wibisono C, Probst Y, Neale E, *et al.* (2016) Impact of food supplementation on weight loss in randomised-controlled dietary intervention trials: a systematic review and meta-analysis. *Br J Nutr* **115**, 1406–1414.