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## A review of the relationship between pulse consumption and reduction of cardiovascular disease risk factors

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## ABSTRACT

Pulses are valuable dry grains from leguminous crop with excellent nutritional properties and numerous bioactive compounds, including phytochemicals, bioactive peptides, and fermentable fibres. Pulses reduce cardiovascular disease (CVD) risk, primarily by altering plasma lipid composition, and several meta-analyses conclude that ~2/3 cup pulses daily significantly lowers total and LDL cholesterol. Pulses also lower CVD risk by other mechanisms, including increased satiety, thereby reducing food intake and the accumulation of excessive adipose tissue; through improvements in glycemic control; and by reducing blood pressure and inflammation. Pulse based functional foods can support efforts to increase pulse consumption; however, few clinical trials have examined the effect of processing on the cardio-protective properties of pulses, making it unclear whether pulse fractions are also effective in reducing CVD risk. Overall, available evidence suggests that whole pulse consumption lowers CVD biomarkers and supports a role for pulses as part of a dietary strategy for CVD prevention.

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*Abbreviations:* ACE, angiotensin converting enzyme; CVD, cardiovascular disease; CHD, coronary heart disease; CRP, C-reactive protein; DPP-IV, dipeptidyl peptidase; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; MetS, metabolic syndrome; MUFA, monounsaturated fatty acids; RCT, randomized controlled trial; SCFA, short-chain fatty acids; T2D, type 2 diabetes; TG, triglycerides.

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## 1. Cardiovascular disease and the role of pulses in the diet

Pulses are a subgroup of legumes, defined as the dry seeds harvested from one of twelve leguminous crops; excluded from this definition are crops used for oil extraction (e.g. soybeans), sowing (e.g. clover, alfalfa), or consumed as a green vegetable (FAO, 1994). Hundreds of varieties of pulses exist; however, pea (*Pisum sativum* L.), lentil (*Lens culinaris*), bean (*Phaseolus vulgaris*) and chickpea (*Cicer arietinum* L.) are among the most commonly known and frequently consumed pulses worldwide (FAO, 2016). Together, these four crops represent approximately 70% of the estimated total global output of pulses (77.3 million tonnes), of which beans account for approximately 30%, followed by chickpeas (17%), peas (15%) and lentils (7%) (FAO, 2015). In addition to their nutritional and agricultural importance, pulses are recognized as an ecologically sustainable food source as their ability to fix atmospheric nitrogen reduces fertilizer demand, and their increased water efficiency (compared to animal-derived protein) results in less water utilized per kg produced (FAO, 2016). Recently, pulses have received attention for their role in promoting cardiovascular health, primarily by altering the ratio of plasma lipids. Cardiovascular diseases (CVD) describe a spectrum of disorders affecting the vasculature of the heart, brain, and peripheral tissue (WHO, 2011). The most common CVD is coronary heart disease (CHD), which is caused by the accumulation of cholesterol-rich deposits in the coronary arteries (NIH, 2014) and has a genetic predisposition, but is strongly associated with unhealthy lifestyle behaviours such as smoking, lack of exercise, and poor diet. Further, CVD is often accompanied by comorbidities such as type 2 diabetes (T2D) and hypertension (WHO, 2011). CVD is the leading cause of death globally, attributed mostly to CHD, which claims over 7 million lives each year (WHO, 2011). The absolute and relative concentrations of the plasma lipids LDL cholesterol (LDL-C), HDL-cholesterol (HDL-C), and triglycerides (TG) are integral to defining CVD risk. Indeed, elevated LDL-C is a well-established CVD risk factor and a target for CVD risk reduction involving pharmaceutical and lifestyle interventions (Ray et al., 2014). Although pharmacological therapy remains the primary mode of CVD prevention among high-risk individuals, dietary modifications make significant contributions toward reducing CVD risk (Whelton, Chow, Ashen, & Blumenthal, 2012). For example, the Mediterranean-style eating pattern, which emphasizes pulses, is a successful cardio-protective diet that appears to reduce CVD risk by a magnitude similar to that of statin medications used to reduce cholesterol levels (Dalen & Devries, 2014). The Diet Portfolio, which substitutes meat products high in saturated fats with vegetarian alternatives such as soy, pulses, almonds, and other plants containing viscous fibres is also effective in reducing biomarkers of CVD risk (Jenkins et al., 2005). The emphasis of pulses in these eating patterns underscores their beneficial role in diets targeting CVD risk. An accumulating body of evidence also suggests that pulses can be useful in the dietary management of persons with T2D, which further mitigates the risk of developing CVD (Ramdath, Renwick, & Duncan, 2016).

In recognition of the agricultural, economical and nutritional importance of pulses, the Food and Agriculture Organization of the United Nations has decided to promote the culinary and agricultural uses of pulses by declaring 2016 the International Year of Pulses (FAO, 2016). Traditionally, pulses have been featured prominently in the diets of developing countries as economical, vegetarian alternatives to animal protein (Hayat, Ahmad, Masud, Ahmed, & Bashir, 2014). Pulses are becoming increasingly recognized as an important component in the Western diet, in part because of the associated health benefits such as reduced CVD risk (Ros & Hu, 2013). Indeed, many national dietary and clinical practice guidelines recommend regularly consuming pulses; however,

domestic consumption in North America is still low and global consumption levels are declining (Kearney, 2010). Therefore, it is important to review the available evidence on the effectiveness of pulses on CVD risk reduction and suggest new evidence-based approaches to incorporating pulses into the regular diet. This review aims to provide a summary on the role of commonly consumed dietary pulses (beans, chickpeas, lentils, peas) in reducing CVD risk, with particular focus given to the modifying effect of pulses on the plasma lipids profile. Several bioactive components of pulses and their proposed mechanisms of action are reviewed, and the effect of food processing on the activity of these components is discussed. Finally, the effect of pulses on other traditional and emerging CVD biomarkers is also considered.

## 2. Bioactive components of pulse legumes and food processing effects

Pulses contain several components with bioactive properties, including fibres, polyphenols, and protein fractions (Rochfort & Panozzo, 2007). The cardio-protective effect of dietary pulses is partially explained by the high content of viscous soluble fibres in these foods (Bouchenak & Lamri-Senhadjji, 2013; Hutchins, Winham, & Thompson, 2012). Soluble fibres lower cholesterol through mechanisms involving increased bile acid/salt excretion in feces; through effects on postprandial insulinemia and, by providing substantial substrate for the colonic bacteria, which undergo fermentation thereby increasing short-chain fatty acid (SCFA) production in the gut (Gunnness & Gidley, 2010). SCFAs are thought to confer cardio-protective effects when they are re-absorbed from the large intestine; in particular, propionate appears to lower serum cholesterol by interfering with endogenous cholesterol production (Slavin, 2013). Different processing techniques can be applied to improve the functional characteristics of pulse fibres. For example, lentils flours were found to contain greater amounts of  $\alpha$ -galactoside, a beneficial prebiotic fibre, and less phytic acid after undergoing an extrusion process (Morales et al., 2015). Also, dry heating (12 h, 60 °C) is shown to preserve antioxidant properties and increase the content of resistant starch in cooked bean flour (Ramírez-Jiménez, Reynoso-Camacho, Mendoza-Díaz, & Loarca-Piña, 2014).

Pulses provide significant quantities of bioactive phytochemicals such as phenolic acids, carotenoids, and tocopherols, which may protect LDL-C from free radical oxidation (Bouchenak & Lamri-Senhadjji, 2013; Ros & Hu, 2013). Recently, 14 polyphenols were identified by HPLC-DAD in cultivars of beans, chickpeas, lentils, and field pea; these included: gallic acid; the anthocyanin glycosides delphinidin 3, 5-diglucoside and cyanidin-3-glucoside; chlorogenic acid; the flavanols (+)- catechin and (–)- epicatechin; caffeic acid; syringic acid; rutin; p-coumaric acid; kaempferol 3-glucoside; ferulic acid; resveratrol; and, quercetin (Giusti, Caprioli, Ricciutello, Vittori, & Sagratini, 2017). Beans were shown to contain primarily catechin, epicatechin, and chlorogenic acids, with significant quantities of kaempferol 3-glucoside noted in some cultivars, while lentil contained primarily catechin, followed by lesser amounts of epicatechin, syringic acid, and in some cultivars anthocyanins. The composition of polyphenols in chickpeas varied widely by cultivar, but was dominated by catechin. Split green peas were found to contain mostly syringic acid, followed by smaller quantities of coumaric acid and ferulic acid (Giusti, Caprioli, Ricciutelli, Vittori, & Sagratini, 2015). Polyphenols, tocopherols, and carotenoids account for the antioxidant capacity of pulses, and *in vitro* free radical scavenging activity has been demonstrated for several varieties of beans, lentils, chickpeas, and peas (Marathe, Rajalakshmi, Jamdar, & Sharma, 2011; Padhi,

Liu, Hernandez, Tsao, & Ramdath, 2016). Industrial food processing techniques can alter the composition, quantity, and bioactivity of pulse phytochemicals. For example, total polyphenol content and antioxidant activity is substantially reduced during roasting (Açar, Gökmen, Pellegrini, & Fogliano, 2009), and during the canning process (Pedrosa et al., 2015), while germination was found to increase total phenolic content (Gharachorloo, Tarzi, & Baharinia, 2013; Limón et al., 2015). Interestingly, although cooking by boiling appears to reduce the quantity of polyphenolic antioxidants, boiling also increases in the content of lipophilic antioxidants (i.e. tocopherol and carotenoids) in chickpeas (Sarmiento, Barros, Fernandes, Carvalho, & Gerreira, 2015) and lentils (Zhang et al., 2014), which effectively preserves the overall antioxidant activity of these foods after cooking.

The protein component of pulses also contributes to its cardio-protective effect. Pulses are a rich source of protein (20–30%, dry weight) and in addition to their role in modulating plasma lipids, they appear to lower CVD risk by displacing dietary saturated fats found in animal-derived protein with plant protein (Rebello, Greenway, & Finley, 2014). Further, bioactive peptides, which are short sequences of amino acids that are released from parent proteins through proteolytic processes occurring during digestion and/or food processing, are receiving attention for their hypotensive activity by angiotensin converting enzyme (ACE) inhibition and antioxidant activity through free radical scavenging (López-Barrios, Gutiérrez-Urbe, & Serna-Saldívar, 2014). Significant peptide sequences capable of ACE inhibition, dipeptidyl peptidase IV (DPP-IV) inhibition, and antioxidant activity were identified in 87.5% of sequenced peptides in bean protein isolates made from 15 cultivars of common bean from Mexico and Brazil (Mojica & González de Mejía, 2015), and hypocholesterolemic and antioxidant properties have been demonstrated in chickpea protein hydrolysate (Yust Mdel, Millán-Linares Mdel, Alcaide-Hidalgo, Millán, & Pedroche, 2012). In rats fed a hypercholesterolemic diet, the administration of pea protein and fibres significantly lowered plasma total cholesterol and hepatic cholesterol content (Parolini et al., 2013), and pea protein hydrolysate reduced blood pressure in both hypertensive rats and human participants compared to unhydrolyzed pea protein, which showed no effect (Li et al., 2011). In addition, glycosylated pea proteins, which resist the degradative effects of digestive enzymes, are able to modify human intestinal gut flora by significantly increasing *Lactobacilli* and *Bifidobacteria* communities, which led to increased acetate, propionate lactate, and butyrate production (Świątecka, Narbad, Ridgway, & Kostyra, 2011). Degradative processes occurring with the application of heat during cooking could alter the bioactive properties of pulse-derived peptides. For example, boiling chickpeas has been shown to alter the composition of chickpeas by reducing the protein and ash content, which may be caused by a loss in total soluble solids (Sarmiento et al., 2015). However, food processing techniques are being developed to preserve bioactive peptides in pulses, such as a “precooking” processing method which involves blanching, the application of high-pressure/heat, followed by oven drying to reduce cooking times; this process does not appear to alter the properties of bioactive peptides in 5 varieties of common bean, and therefore holds promise as a preparation method that could increase bean consumption (and potentially other pulses) in the home (Mojica, Chen, & González de Mejía, 2014).

### 3. Epidemiological evidence on pulse consumption and CVD risk

Several observational studies have examined the association between pulse intake and CVD risk; however, some focused on general legume consumption, which could include soy, thereby

making it difficult to dissect the effects of pulses. Regardless, valuable information has come from the National Health and Nutrition Examination Survey (NHANES) that showed men and women ( $n = 9632$ ) consuming  $\geq 4$  servings of pulses/wk experienced a reduction in CVD and CHD risk by 11% and 22%, respectively, compared with those who consumed  $\leq 1$  serving/wk (Bazzano et al., 2001). Further, a longitudinal study that followed survivors of acute myocardial infarction in Costa Rica ( $n = 2119$ ) found that 1 serving (one-third cup, 86 g cooked) of beans daily was associated with a 38% reduction in the risk of subsequent infarction events (Kabagambe, Baylin, Ruiz-Narvarez, Siles, & Campos, 2005). This is consistent with cohort data extracted from the NHANES database, which showed that bean consumers tend to have lower body weight, waist circumference, and systolic blood pressure compared with non-consumers (Papanikolaou & Fulgoni, 2008). Further, sub-analyses of the Japan Collaborative Cohort Study for Evaluation of Cancer Risk, which followed 59,485 men and women for 13 years while tracking fruit, vegetable and bean consumption, found that bean intake was inversely associated with total mortality from CVD (Nagura et al., 2009). The Food Habits in Later Life study, which followed 785 adults  $\geq 70$  yrs in 4 countries (Japan, Sweden, Greece, Australia) for 7 years, found that legume intake significantly predicted survival in the elderly, with an 8% reduction in all-cause mortality for every 20 g increase in daily legume intake irrespective of ethnic background (Darmadi-Blackberry et al., 2004). Most recently, the Ishfan Cohort Study, which followed 6504 individuals without CVD for 7 years and recorded the number of CVD events (fatal and non-fatal myocardial infarction, unstable angina, fatal and non-fatal stroke, sudden cardiac death) found that consuming  $> 3$  servings legumes/wk compared with  $\leq 1$  serving/wk was associated with a 34% lower risk of CVD in older ( $> 55$  yrs) but not middle-aged Iranian adults (35–55 yrs) after adjusting for potential confounding factors such as age, sex, marital status, education status, smoking status, physical activity, and hypolipidemic medications (Nouri, Sarrafzadegan, Mohammadifard, Sadeghi, & Mansourian, 2016). Pulse intake is also associated with a reduced risk of developing atherosclerotic plaque, an important risk factor for stroke (Gardener et al., 2014) and dietary fibres sourced from legumes, in particular, appear to protect against the development of metabolic syndrome (MetS), which is associated with increased CVD risk (Hosseinpour-Niazi, Mirmiran, Sohrab, Hosseini-Esfahani, & Azizi, 2011).

### 4. Meta-analyses of pulse consumption and lipid lowering effects

Convincing evidence suggests that the Mediterranean diet, which is rich in legumes, and coloured fruits and vegetables, offers a cardio-protective effect. A meta-analysis of 11 clinical trials ( $N = 52,044$ ) estimated the effect of the Mediterranean diet on CVD risk, which was defined as including  $\geq 2$  of the following: (1) high monounsaturated fatty acid/saturated fatty acid ratio; (2) low-moderate red wine consumption; (3) high legume intake (including dietary pulses); (4) high grain/cereal intake; (5) high fruit/vegetable intake; (6) low intake of meat/meat products and increased fish consumption; (7) moderate intake of milk/dairy products (Rees et al., 2013). The authors found that consuming a Mediterranean dietary pattern was associated with significant reductions in total cholesterol ( $-0.16$  mmol/L, 95% confidence interval [CI]:  $-0.26$  to  $-0.06$ ) and LDL-C ( $-0.07$  mmol/L, 95% CI:  $-0.13$  to  $-0.01$ ) (Rees et al., 2013). Further, a subgroup analysis found that trials specifically testing the Mediterranean diet (i.e. including all 7 criteria) achieved significantly greater reductions in total cholesterol ( $-0.23$  mmol/L, 95% CI:  $-0.27$  to  $-0.2$ ) (Rees et al., 2013). These findings are supported by a meta-analysis of



25 observational studies and 2 randomized clinical trials ( $N = 501,791$ ) which found an inverse association between legume and nut consumption and incident CHD (Afshin, Micha, Khatibzadeh, & Mozaffarian, 2014). More recently, a meta-analysis of 14 prospective cohort studies published between 2001 and 2016 ( $N = 367,000$ ) among populations in the USA, Japan, Spain, Greece, Finland, and Iran showed that the highest category of dietary legume consumption was associated with a 10% reduction in CVD risk (0.90 RR, 95% CI: 0.84–0.97) (Marventano et al., 2016). It is important to note that these meta-analyses have evaluated all legumes and therefore include clinical trials with soy-based foods whose cholesterol-lowering mechanisms differ from that of pulses (Cho, Juillerat, & Lee, 2007; Tokede, Onabanjo, Yansane, Gaziano, & Djoussé, 2015). However, 3 meta-analyses have specifically assessed the lipid-lowering effect of pulses. An early meta-analysis of 11 randomized clinical trials ( $N = 187$ ) examined the effect of non-soy legumes on plasma lipids and found significant changes in total cholesterol (−7.2%, 95% CI: −5.8% to −8.6%), LDL-C (−6.2%, 95% CI: −2.8% to −9.5%) and triglycerides (−16.6%, 95% CI: −11.8% to −21.5%) with a mean intake of approximately 120 g/d (dry weight) pulses (Anderson & Major, 2002). Another meta-analysis of 10 randomized clinical trials ( $N = 268$ ) published between 1980 and 2009 found that consuming a variety of mixed-pulse dishes significantly reduced total cholesterol (−0.3 mmol/L, 95% CI: −0.4 to −0.2) and LDL-C (−0.2 mmol/L, 95% CI: −0.3 to −0.1), while mean net changes in HDL-C (0.02 mmol/L, 95% CI: −0.04 to 0.08) and triglycerides (−0.2 mmol/L, 95% CI: −0.4 to 0.00) approached significance ( $P = 0.05$ ) (Bazzano, Thompson, Tees, Nguyen, & Winham, 2011). Similarly, an updated analysis that included 26 randomized controlled trials ( $N = 1037$ ) published up to February 2014, found that a median intake of 130 g/d of pulses (beans, chickpeas, lentils, peas) significantly lowered LDL-C (−0.17 mmol/L, 95% CI: −0.25 to −0.09) but did not meaningfully influence HDL-C, non-HDL-C or apolipoprotein B (Ha et al., 2014). Overall, these findings suggest that incorporating pulses into the diet modifies CVD risk by altering the composition of the plasma lipid profile, primarily by lowering lower total- and LDL-C, with little to no effect on HDL-C and other blood lipid components.

### 5. Randomized controlled trials of pulse consumption and CVD risk factors

Large randomized controlled trials have shown that dietary modifications reduce CVD risk, especially when modeled after the Mediterranean-style diet. This is demonstrated in the Omni-Heart study, which tested diets low in saturated fat but with varying macronutrient composition (e.g. high carbohydrate vs. high protein vs. high monounsaturated fatty acids (MUFA)), and measured the relative effect on blood pressure and serum lipids (Appel et al., 2005). This triple crossover study showed that partially replacing carbohydrates with MUFA or protein (approximately half derived from plant sources, including legumes, nuts, grains and seeds) significantly improved these CVD risk factors (Appel et al., 2005). The PREDIMED study, which randomly assigned men and women aged 55–80 yrs ( $n = 7447$ ) at high risk for CVD to either (1) a Mediterranean diet supplemented with either extra-virgin olive oil, (2) a Mediterranean diet supplemented with nuts, or (3) a low-fat diet control, found a 30% reduction in the rate of incident myocardial infarction, stroke or death due to CVD in both Mediterranean diet groups (Estruch et al., 2013). Further, although the risk of developing MetS did not differ between intervention and control, participants with MetS at baseline were more likely to revert to a non-MetS status if assigned to either Mediterranean diet (Babio et al., 2014). Despite strong evidence suggesting

a role for the Mediterranean diet in reducing CVD risk factors, these studies do not examine individual dietary components, making it difficult to discern the relative contribution of pulses toward reducing CVD risk.

Several clinical studies have specifically tested the effect of dietary pulses on CVD risk focusing particularly on plasma lipids (see Table 1) and mainly include interventions with whole cooked pulses (canned or cooked from dry grain). Overall, participants enrolled in randomized controlled trials (RCTs) tend to be overweight (mean  $\pm$  SD BMI:  $29.6 \pm 3.4$  kg/m<sup>2</sup>), middle-aged ( $50 \pm 7$  yrs) and mildly hypercholesterolemic (total cholesterol,  $5.48 \pm 0.19$  mmol/L) at baseline. Three studies included both pulse-based snacks (e.g. biscuits made with pulse flour) and whole pulses as part of the intervention treatment arm (Abeysekara, Chilibeck, Vatanparast, & Zello, 2012; Pittaway, Ahuja, Robertson, & Ball, 2007; Pittaway et al., 2006). One study examined the hypolipidemic effects of a pea protein isolate (Sirtori et al., 2012). In a parallel controlled study, 2 servings daily (250 g, cooked weight) of snacks, salads, soups and meals prepared with green and red split lentils, chickpeas, yellow split peas and a selection of beans (pinto, fava, broad, black and kidney) significantly lowered total and LDL-C in adults ( $\geq 50$  yrs) after 8 weeks, although significant improvements in other CVD risk factors measured were not found, including HDL-C, triglycerides, C-reactive protein (CRP), glucose and insulin (Abeysekara et al., 2012). Another study found that a diet supplemented with chickpeas significantly lowered total cholesterol and LDL-C in adults after 5 weeks (Pittaway et al., 2006).

Several studies have compared the effect of dietary pulses on blood lipids when consumed alongside other targeted interventions. Among older ( $\geq 50$  yrs) hypercholesterolemic women, consuming whole-grain barley products, brown beans and chickpeas significantly improved plasma lipids and other CVD risk factors (apolipoprotein A1 and B, diastolic blood pressure, Framingham 10-yr CVD risk score) than a whole grain wheat control diet (Tovar, Nilsson, Johansson, & Björck, 2014). The effect of pulses on CVD risk in comparison to a low-carbohydrate diet has also been tested. In a parallel controlled trial in which obese adults (BMI: 30–40 kg/m<sup>2</sup>) were recruited to consume either  $\frac{1}{2}$  cup cooked beans with each meal or a low-carbohydrate control diet (meat, egg or vegetable protein, 1–2 servings of non-starchy vegetables, fruit), anthropometric measures (weight, BMI, waist/hip circumference, blood pressure) were significantly improved in all participants after 16 weeks; however, adults consuming the bean-enriched diet also experienced significant reductions in total and LDL-C that were not observed in the control group (Tonstad, Malik, & Haddad, 2014). Diets low in saturated fats have also been compared with pulse-enriched diets. A randomized crossover trial in individuals with type 2 diabetes tested the effect of a Therapeutic Lifestyle Change (TLC) diet (saturated fat <7% total energy, dietary cholesterol <200 mg/d, 25–30 g/d total dietary fibre), with a TLC diet that substituted 2 servings of red meat with  $\frac{1}{2}$  cup (approximately 75–100 g, cooked weight) lentils, chickpeas and peas 3 days/wk (Hosseinpour-Niazi, Mirmiran, Hedayati, & Azizi, 2015). Although total cholesterol was reduced on both diets, the TLC + legume diet group experienced significantly greater reductions in LDL-C (−0.40  $\pm$  0.13 vs. −0.22  $\pm$  0.07 mmol/L,  $P = 0.02$ ) and TG (−0.43  $\pm$  0.07 vs. −0.22  $\pm$  0.07 mmol/L,  $P = 0.02$ ) (Hosseinpour-Niazi et al., 2015).

Currently, there are only a couple of studies that have tested the hypolipidemic effect of pulse-based flours. In one of these studies, although significant reductions in LDL-C were observed when overweight, hypercholesterolemic men and women consumed muffins made with whole pea flour or pea hulls (supplemented with either cellulose or oat fibre); there were no significant differences between treatment and control, which suggests pea flour

**Table 1**Summary of controlled, randomized trials assessing the effect of whole dietary pulses and pulse fractions on LDL-C.<sup>1</sup>

Food <sup>2</sup> (pulse, dose g/d)	Age (y)	Women (%)	Design, Length <sup>3</sup>	N	BMI (kg/m <sup>2</sup> )	Baseline Total-C	ΔLDL-C (95% CI, mmol/L)	Reference
<i>Whole pulses</i>								
<sup>a</sup> Beans, ~50	43 ± 3	56	C, 8	16	27.8 ± 0.9	5.6 ± 0.2	−0.16 (−0.34 to 0.02), p < 0.05	Winham, Hutchins, and Johnston (2007)
Beans, ~50	46 ± 2	56	C, 8	23	27.4 ± 0.9	5.6 ± 0.1	−0.13 (−0.31 to 0.05), p = 0.08	Winham and Hutchin (2007)
Beans, 130	37 ± 11	50	P, 12	40	~23.6 ± 2.9	4.6 ± 0.1	−0.17 (−0.31 to −0.03), p < 0.05	Finley, Burrell, and Reeves (2007) <sup>#</sup>
Mixed, ~90	~37 ± 8	0	P, 8	18	31.8 ± 4.1	NR	−0.88 (−1.17 to −0.59), p < 0.05	Abete, Parra, and Martinez (2009)
Mixed, ~81	52 ± 8	100	P, 16	114	29.6 ± 4.5	5.8 ± 1.0	0.15 (−0.07 to 0.37), NS	Gravel et al. (2010) <sup>#</sup>
Beans, 130	42 ± 10	50	P, 12	40	~33.2 ± 3.8	5.0 ± 0.4	−0.22 (−0.38 to −0.06), p < 0.05	Finley et al. (2007) <sup>#</sup>
Lentils, 50	50 ± 4	NR	C, 6	30	28.9 ± 4.1	5.8 ± 1.5 <sup>§</sup>	0.02 (−0.02 to 0.06), NS	Shams, Tahbaz, Entezari, and Abadi (2008)
<sup>b</sup> Beans, 250	56 ± 8	0	C, 4	28	30.3 ± 3.2	5.3 ± 0.2	−0.21 (−0.41 to −0.01), p < 0.05	Zhang et al. (2010)
<sup>c</sup> Beans, 250	54 ± 8	0	C, 4	36	27.4 ± 3.2	5.0 ± 0.2	−0.26 (−0.46 to −0.06), p < 0.05	Zhang et al. (2010)
Mixed, 2 serv/d <sup>**</sup>	42 ± 11	84	P, 72	108	36.1 ± 6.5 <sup>*</sup>	5.2 ± 1.0 <sup>§</sup>	0.30 (0.10 to 0.60), p < 0.05	Venn et al. (2010) <sup>#</sup>
Beans+, 1 serv/d <sup>x</sup>	43 ± 10	100	P, 8	83	34.2 ± 4.8 <sup>*</sup>	NR	−0.31 (−0.47 to −0.15), p < 0.05	Te Morenga, Levers, Williams, Brown, and Mann (2011)
Mixed, 160–235	36 ± 8	43	P, 8	30	32.5 ± 4.5 <sup>*</sup>	5.6 ± 0.7 <sup>§</sup>	−0.34 (−0.58 to −0.10), p < 0.05	Hermisdorff et al. (2011) <sup>#</sup>
Mixed, 196	60 ± 1	50	P, 12	121	~30.6 ± 0.8	4.2 (3.8–4.5) <sup>4</sup>	−0.06 (−0.20 to 0.08), p < 0.05	Jenkins et al. (2012)
Mixed, 128	46 ± 1	72	P, 8	40	32.8 ± 0.7	5.1 ± 0.2	−0.02 (−0.26 to 0.22), NS	Mollard et al. (2012)
Mixed, 442 <sup>d</sup>	62 ± 1	100	C, 4	46	28.8 ± 1.2	6.4 ± 0.2	−0.50 (−0.58 to −0.42), p < 0.05	Tovar et al. (2014)
Beans/lentils, 225	48 ± 10	78	P, 16	123	36.5 ± 3.8	4.9 ± 0.9	−0.20 (−0.01 to −0.44), p < 0.05	Tonstad et al. (2014)
Mixed, 6 serv/wk <sup>x</sup>	58 ± 6	77	C, 8	31	27.7 ± 0.6	4.5 ± 0.2	−0.40 (−0.66 to −0.14), p < 0.05	Hosseinpour-Niazi et al. (2015)
<i>Pulse Flour</i>								
Pea, ~138	52 ± 11	70	C, 4	23	~30.6 ± 4.4	6.1 ± 0.2	0.13 (−0.18 to 0.44), NS	Marinangeli and Jones (2011)
<i>Whole/flour</i>								
Chickpeas, 140	53 ± 10	60	C, 6	47	27.6 ± 4.1	5.8 (5.4–6.1) <sup>4</sup>	−0.18 (−0.28 to −0.08), p < 0.05	Pittaway et al. (2006)
Chickpeas, 140	51 ± 11	63	C, 5	27	28.8 ± 4.4	NR	−0.20 (−0.36 to −0.04), p < 0.05	Pittaway et al. (2007)
Mixed, 250	60 ± 6	66	C, 8	87	27.5 ± 4.5	4.6 ± 0.9 <sup>§</sup>	−0.23 (−0.43 to −0.03), p < 0.05	Abeysekera et al. (2012) <sup>#</sup>
<i>Protein isolate</i>								
<sup>d</sup> Pea, 35	52 ± 13	44	P, 4	25	25.0 ± 2.1	7.0 ± 0.7	+ 4.6%, NS <sup>5</sup>	Sirtori et al. (2012) <sup>#</sup>
<sup>e</sup> Pea, 35	55 ± 15	68	P, 4	23	25.6 ± 3.2	7.5 ± 1.0	−5.8%, p < 0.05 <sup>5</sup>	Sirtori et al. (2012)
<sup>f</sup> Pea, 35			P, 4	21			−9.2%, p < 0.05 <sup>5</sup>	Sirtori et al. (2012)

<sup>1</sup> Values are mean ± SE;<sup>#</sup> indicates mean ± SD.<sup>2</sup> Mixed = beans, chickpeas, lentils, peas. Amounts given represent cooked pulses.<sup>3</sup> C = crossover, P = parallel, Length = intervention arm, wks.<sup>4</sup> Mean (95% CI).<sup>5</sup> 95% CI could not be calculated.<sup>†</sup> Daily serving = beans (86 g), chickpeas (82 g), whole grain barley (58 g) and barley kernel bread (216 g).<sup>\*\*</sup> One serving = 1 slice of bread (37 g), 30 g cereal or 90 g pulses.<sup>x</sup> One serving = ½ cup cooked pulses (approximately 75–100 g).<sup>\*</sup> indicates significant weight loss during the trial. ++ other legumes, not specified.<sup>a</sup> Multiple intervention arms combined.<sup>b</sup> Participants were insulin resistant or<sup>c</sup> insulin sensitive.<sup>§</sup> Participants had type 2 diabetes mellitus. NR = not reported. NS = not significant.<sup>d</sup> +cellulose fibre or<sup>e</sup> +oat fibre.<sup>f</sup> +apple pectin. Modified from Ha et al. (2014).

does not lower LDL-C beyond the prescribed background National Cholesterol Education Program Step 1 diet (Marinangeli & Jones, 2011). Similarly, Cryne et al. (2012) found no treatment effect on CVD risk factors among healthy men who consumed 100 g of spray-dried chickpeas, lentils and peas, and a control (50 g of dehydrated potato flakes) for 28 days, with a 28-day washout period.

Other studies have demonstrated that flour derived from lupin seeds (a minor pulse crop that is cultivated and consumed less widely) improves total cholesterol and LDL-C (Belski et al., 2011; Hodgson et al., 2010). In addition, Bähr, Fechner, Kramer, Kiehnopf, and Jahreis (2013) examined the effect of 25 g lupin protein isolate (LPI), incorporated into a beverage, on CVD risk

factors in hypercholesterolemic men and women but did not observe improvements in plasma lipids (Bähr et al., 2013). The findings of RCTs overall suggest that including a variety of whole pulses in the diet results in ~5% reduction in LDL-C in addition to other supplementary targeted dietary interventions; however, evidence supporting the efficacy of fractionated pulse in improving the plasma lipid profile and other CVD risk factors remains limited and, therefore, additional studies are required to elucidate the hypolipidemic effects of whole vs. pulse fractions. Additional clinical studies testing the effect of whole dietary pulses and pulse fractions (e.g. whole pulse flour, pulse hulls, protein isolate) on the LDL-C are summarized in Table 1.

## 6. Pulse consumption, satiety and weight loss

There is good evidence emerging to suggest that pulses may lower CVD risk by increasing satiety, thereby reducing food intake and the accumulation of excessive adipose tissue. A study examining the effect of two hypocaloric diets (pulse-based vs. pulse-restricted) on obese adults found that a pulse-based diet (160–235 g cooked pulses, 4 servings/wk) resulted in greater weight loss compared to control, as well as significant reductions in total cholesterol and LDL-C (Hermsdorff, Zulet, Abete, & Martinez, 2011). Similarly, an 18-month weight loss program that incorporated 2 servings of pulses (180 g) and 4 servings of whole grains daily observed significant reductions in waist circumference (−2.8 cm, 95% CI: −0.4 to −5.1), body weight, and blood pressure values (Venn et al., 2010). Another study found that overweight and obese adults (BMI 27–40 kg/m<sup>2</sup>) consuming either 5 cups/wk (128 g/d) of pulses or a hypocaloric control diet (−500 kcal/d) both had lower food intake, in addition to improvements in risk factors for MetS such as waist circumference, systolic blood pressure, HbA1c, glucose control, and insulin sensitivity (Mollard et al., 2012). Pulse fractions also have beneficial effects on energy intake and body weight; Lambert et al. (2016) recently showed that overweight or obese adults consuming wafers made with 5 g pea fibre 30 min before each of the 3 largest daily meals had modest, but significant improvements in body fat percentage (Lambert et al., 2016). Further, although pea fibre supplementation did not have a significant effect on subjective satiety scores derived from the use of Visual Analog Scales, *ad libitum* food intake was reduced by 16% during test meals (Lambert et al., 2016). These findings are consistent with NHANES data (previously mentioned) which showed that bean consumers have significantly lower waist circumference measures than non-consumers (Papanikolaou & Fulgoni, 2008), and agree with a recent meta-analysis (N = 940) which concluded that consuming a median intake of ~132 g/d dietary pulses was associated with modest reductions in body weight (−0.34 kg, 95% CI: −0.63 to −0.04) when pulses are consumed in complement with energy-restricted diets and during weight maintenance (Kim, de Souza, Choo, Ha, & Sievenpiper, 2016). An accumulating body of evidence suggests that pulses incorporated into energy-restricted diets designed for weight loss exert additional improvements in plasma lipid concentrations that may be independent of body weight reduction, thus defining an additional role for dietary pulses in reducing CVD risk through weight management and reducing adiposity.

## 7. The effect of pulses on other CVD risk biomarkers

### 7.1. Glycemic control

In addition to lowering blood lipids, pulses may also lower CVD risk by improving glycemic control, and by mitigating blood pressure and inflammation (Rebello et al., 2014). Dietary pulses may

reduce CVD risk by aiding in the regulation of postprandial blood glucose, which is important in the prevention and management of T2D, a risk factor for CVD (Younis, Charlton-Menys, Sharma, Soran, & Durrington, 2009). The high soluble fibre content of dietary pulses is digested slowly, which lowers the postprandial blood glucose response, thereby delaying glucose absorption and resulting in an overall lower glycemic index (GI) (Hutchins et al., 2012). A meta-analysis showed that a mean intake of 152 g/d pulses significantly lowered fasting blood glucose (FBG; −0.82, 95% CI: −1.36 to −0.27) and insulin (−0.49, 95% CI: −0.93 to −0.04) when consumed alone (11 trials, N = 253), whereas pulses consumed as part of a low-GI diet (19 trials, N = 762) did not (Sievenpiper et al., 2009). The mechanism behind low-GI diets and reduced CVD risk has not been established and requires further exploration (Hutchins et al., 2012). However, additional sub-analysis of RCTs testing the effect of pulses as part of a high-fibre diet on glycemic control (11 trials, N = 641) found that FBG was significantly reduced (−0.32, 95% CI: −0.49 to −0.15) (Sievenpiper et al., 2009). Recently, the role of pulses in the dietary management of type 2 diabetes has been extensively reviewed, and suggests dietary pulses can make an important contribution toward improving glycemic control (Ramdath et al., 2016).

### 7.2. Hypertension

Chronically elevated blood pressure (i.e. hypertension) increases the likelihood of endothelial injury and is a significant CVD risk factor, defined specifically as systolic pressure values >140 mmHg and/or diastolic blood pressure >90 mmHg (Pujol & Tucker, 2007). A recent meta-analysis of 8 RCTs (N = 554) showed that isocaloric substitution of pulses for non-pulse foods (e.g. white bread, potato flakes) significantly reduced systolic blood pressure (−2.25 mmHg, 95% CI: −4.22 to −0.28) and mean arterial blood pressure (−0.75 mmHg, 95% CI: −1.44 to −0.06) with an average intake of 162 g/d cooked pulses (Jayalath et al., 2014). In terms of the mode of action, preliminary investigations have shown that in a rat model of angiotensin II-induced hypertension, lentil extract, which is rich in polyphenols, was able to prevent hypertension, vascular remodelling and perivascular fibrosis, possibly by decreasing intracellular levels of reactive oxygen species (ROS) (Yao, Sun, & Chang, 2012). Using a metabolomics approach, Hanson, Zahradka, Taylor, and Aliani (2016) found that spontaneously hypertensive rats fed different pulse-based diets developed hypertension except those on the lentil diet, and showed that this effect was associated with the presence of distinct metabolites, which suggests that there may be a unique relationship between lentil consumption and prevention of hypertension (Hanson et al., 2016). Clearly, follow up human studies are needed to confirm this property of lentil.

### 7.3. Inflammation

Inflammation also plays a key role in CVD development by initiating and positively reinforcing the sequence of events that results in the accumulation and transformation of the healthy endothelium into atherosclerotic plaque (Libby, 2006). Mediating this process is obesity, a CVD risk factor which is now recognized to be associated with a heightened state of inflammation. It is evident that excess adipose tissues, particularly visceral adipocytes, secrete inflammatory cytokines and chemokines that initiate or promote a pro-inflammatory state (DeBoer, 2013). Moreover, low levels of the adipokine adiponectin are observed during obesity-associated inflammation, and this is associated with insulin resistance, MetS, and CVD (DeBoer, 2013). Pulse-based diets have an important role in modulating this risk, and much of the available evidence has been derived from interventions using the



Mediterranean diet. Indeed, dietary pulses are substantial sources of polyphenols which could account for the anti-inflammatory effects that are associated with consuming a diet rich in pulses. Polyphenols are potent anti-oxidants and intake is shown to correlate with plasma antioxidant status; it is theorized that these molecules may be capable of donating electrons to stabilize harmful ROS, thereby protecting cells against damage by oxidative stress, and may contribute additional anti-inflammatory effects by targeting pathways involving the production of inflammatory cytokines such as IL-1 $\beta$ , IL-6, and TNF- $\alpha$  (Gothai et al., 2016).

A systematic review and meta-analysis of the effects of a Mediterranean-style diet on inflammation included 17 RCTs ( $N = 2300$ ) showed that this dietary pattern is associated with lower concentrations of inflammatory markers (CRP, interleukin-6, intracellular adhesion molecule-1) and lower adiponectin concentrations (Schwingshackl & Hoffman, 2014). Similarly, non-soy legume consumption was found to be negatively associated with plasma CRP concentrations in a recent meta-analysis ( $N = 464$ ) (Salehi-Abargouei, Saraf-Bank, Bellissimo, & Azadbakht, 2015). Further, Casas et al. (2014) showed that adherence to a Mediterranean diet significantly reduced markers of atheroma plaque instability, providing a plausible mechanism for the associated cardio-protective effect of this dietary pattern, which involves the consumption of substantial quantities of pulses (Casas et al., 2014). Testing the effect of dietary pulses specifically, participants in the Legume Inflammation Feeding Experiment who consumed a low-GI diet enriched with different bean varieties for 4 weeks experienced greater improvements in biomarkers of insulin sensitivity and inflammation compared to control (Hartman et al., 2010). A meta-analysis of 8 RCTs ( $N = 464$ ) testing the effect of consuming non-soy legumes on systemic inflammation showed a trend toward reduced circulating CRP, but the effect did not reach statistical significance ( $-0.21$ , 95% CI:  $-0.44$  to  $0.02$ ,  $P = 0.068$ ) (Salehi-Abargouei et al., 2015). However, the limited number of trials and substantial heterogeneity between RCTs included in this meta-analysis may limit its interpretation, and thus further studies are required to elucidate the relationship between dietary pulses and systemic inflammation.

#### 7.4. Emerging role of the gut microbiome

It is estimated that approximately 90–95% of ingested polyphenols by-pass absorption in the small intestine and proceed to the large intestine instead, where they are metabolized by the intestinal microbiota into small molecules that can be absorbed into circulation (Amiot, Riva, & Vinet, 2016). The effect of polyphenol metabolites on CVD risk factors will likely be an interesting area for future exploration. Deeper insights into the relationship between metabolic dysfunction and gut microbial density and diversity (or lack thereof) have informed new perspectives on the etiology of several diet-related chronic diseases (Clemente, Ursell, Wegener Parfrey, & Knight, 2012). For example, a novel pathway linking gut-mediated metabolism of dietary lipids with atherosclerosis has been elucidated, which shows that serum metabolites of phosphatidylcholine are correlated with incident CVD and suggests a potential role for therapeutics through pre- and probiotic intervention (Wang et al., 2011). The role of the gut microbiota in short fatty acid metabolism and bile acid regulation may yield additional information on how the intestinal microbiota influences CVD risk (Koopman, Groen, & Nieuwdorpa, 2016). Part of the reason pulses may improve CVD risk may be due to the prebiotic effect of fermentable fibres found in these foods, which have been shown to lower CVD biomarkers such as fasting blood glucose, insulin and circulating inflammatory biomarkers in healthy adults (Nilsson, Johansson, Ekstrom, & Bjorck, 2013). Compared to lean individuals, obese adults have markedly different microbial profiles, repre-

sented by reduced bacterial richness and less diversity (Le Chatelier et al., 2013). It is likely that future studies will investigate the utility of the human gut microbiome as a novel risk factor for predicting CVD risk and the role of whole pulses and pulse fractions in modulating this change.

## 8. Conclusions

Data from observational studies consistently demonstrate that consuming dietary pulses lowers incident CVD and mortality. The mechanism underlying this cardio-protective effect appears to be related to the ability of pulse legumes to attenuate total cholesterol and LDL-C, an effect which has been confirmed by several meta-analyses. However, the effect of dietary pulses on other plasma lipids such as HDL-C and triglycerides, and lipoprotein components (e.g. apolipoproteins) is less clear. Further, few studies have examined the effect of pulse fractions (e.g. pulse flours, hulls, protein isolates) on CVD risk outcomes, and thus, the utility of functional foods made with pulse-based ingredients remains unknown. Overweight and obese individuals appear to reap additional cardiovascular benefits by consuming energy-restricted diets enriched with pulses beyond that which is associated with weight loss; however, this is not uniformly observed in the literature. Further, some RCTs have demonstrated that dietary pulses do not offer additional lipid-lowering effects beyond that which is associated with a diet low in saturated fat or dietary cholesterol, making it unclear to what extent pulses reduce CVD risk. However, the evidence available to date suggests consuming a diet enriched with whole pulses results in a significant and clinically meaningful reduction in total cholesterol and LDL-C, supporting a role for dietary pulses in the management and prevention of CVD. It is likely that future studies will seek to uncover the interaction between pulse components and the human gut microbiome in relation to reduced CVD risk, and that the utility of pulse fractions in comparison to whole pulses will continue to be investigated.

## Author disclosures

All authors declare no conflict of interest.

## Author contributions

All authors contributed substantially to conception, acquisition and interpretation of data. All authors were involved in drafting and revising it critically for important intellectual content. DDR coordinated preparation of the manuscript and prepared the final version. All authors gave final approval of the version to be published.

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