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Is black tea consumption associated with a lower risk of cardiovascular disease and type 2 diabetes?

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Summary

Type 2 diabetes mellitus and cardiovascular disease represent major causes of morbidity, which impact greatly on healthcare expenditure. Clinical studies suggest that ingestion of black tea, which contains a range of bioactive compounds, can inhibit oxidative damage and improve endothelial function. The objectives of this review are to: (1) evaluate observational evidence linking black tea consumption with the prevalence of cardiovascular diseases and type 2 diabetes; (2) consider the mechanisms by which black tea may have a protective effect; and (3) examine the potential role of tea drinking in relation to public health.

The findings from epidemiological studies suggested a significant association between regular black tea consumption and a reduced risk of coronary heart disease at around three or more cups per day. For diabetes risk, the data are restricted to a few large cohort studies that suggested a beneficial association at one to four cups daily. These findings need to be confirmed by intervention trials. While some studies suggest that drinking black tea may reduce the risk of stroke, likely mechanisms remain unclear, highlighting the need for more human intervention studies. Disparities found involving studies may have been influenced by variations in reported tea intakes, limited sample sizes in intervention trials and inadequate control of confounders. In conclusion, drinking black tea may have a role in lowering the risk of coronary heart disease and type 2 diabetes. Future research should focus on controlled trials and studies to elucidate likely mechanisms of action.

Keywords: cardiovascular disease, public health, stroke, tea, type 2 diabetes mellitus

Introduction

Tea is a widely consumed beverage, containing a host of bioactive compounds that reputedly offer a range of potential health benefits (Sharma & Rao 2009). Worldwide, the average consumption of tea is second only to that of water (Hodgson & Croft 2010), with the most popular type being black tea. Of the tea produced worldwide, 78% is black, 20% is green and 2% is oolong (Siddiqui *et al*. 2004), although all teas originate from the plant *Camellia sinensis*. Black tea, which is the focus of this review, is consumed primarily in western regions (International Tea Committee 2010), while green tea is drunk mainly in China, Japan, India and some North African and Middle Eastern regions (Mukhtar & Ahmad 2000). Tea is drunk by 77% of

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adults and is more popular among older people and females (Taylor Nelson Sofres 2007), although findings from the latest UK National Diet and Nutrition Survey have shown a rise in tea drinking among children of all age groups (Bates *et al*. 2010). In adult consumers, tea intakes have remained stable at around 2.3 servings per day (Henderson *et al*. 2003) or 2.07-kg leaf tea per person per annum (International Tea Committee 2010).

A substantial literature base of mostly observational studies has built up over the last few decades linking black tea consumption with a reduced risk of chronic diseases, particularly cardiovascular disease (CVD) (Stangl *et al*. 2006; Gardner *et al*. 2007). Black teas are manufactured by promoting the enzymatic oxidation of tea flavonoids from the leaves of *Camellia sinensis*, leading to the formation of condensed flavonoids, such as theaflavins and thearubigins (Hodgson & Croft 2010). Flavonoids are a class of plant metabolites from the polyphenol group, which have been shown during *in vitro* experiments, and some human interventions, to have antioxidant, anti-inflammatory and anti-proliferative properties (Ruxton 2009; Mulvihill & Huff 2010). Of these flavanols (subclasses of flavonoids), the theaflavins, thearubigins and catechins are thought to be the key bioactive components within black tea (Luczaj & Skrzydlewska 2005). Tea is also a moderate source of caffeine – around 50 mg per serving – which has been associated with cognitive and physical benefits when consumed in amounts of 38–400 mg per day (Ruxton 2008).

Surveys indicate that rates of CVD are reaching pandemic proportions across the globe, with more than 70% of adults having multiple risk factors for the condition (Dahlof 2010). This has significant implications for healthcare costs. In the UK alone during 2007, more than 2.7 million adults developed some form of coronary heart disease (CHD), including angina, while 1.2 million adults had a stroke (Scarborough *et al*. 2010). Stroke is the second most common cause of death in developed countries and a major cause of disability in older people. The incidence of stroke is predicted to rise considerably over the next 20 years because of an increase in life expectancy and thus average age in western populations (Donnan *et al*. 2008). Around 54% of stroke cases worldwide may be attributed to high blood pressure (Lawes *et al*. 2008), a condition that could be ameliorated with simple dietary changes. It may be that regular tea consumption has a role to play in helping to maintain normal blood pressure, according to studies that have examined the impact of tea flavonoids on vascular tone (Jochmann *et al*. 2008; Grassi *et al*. 2009).

Equally, the prevalence of type 2 diabetes mellitus (T2DM) has risen considerably in past decades and worldwide cases are projected to double from 171 million to 366 million by 2030 (Wild *et al*. 2004; Setacci *et al*. 2009). The prevalence of diabetes in the UK has doubled since 1991 and is now 6% in men and 4% in women, with T2DM representing around 90% of cases (Scarborough *et al*. 2010). Further rises in prevalence rates are expected across Europe (Passa 2002), particularly in view of the high obesity levels among young people.

Given the burden of chronic diseases and their impact on quality of life and healthcare costs, there is a need for increased emphasis on simple dietary modifications that are easily communicated (Mohan *et al*. 2010). One example of this could be habitual consumption of black tea. Therefore, the aim of this review is to examine relevant high quality evidence in order to evaluate whether or not black tea consumption may have a role in helping to prevent CVD and type 2 diabetes. Newer evidence reporting links involving black tea consumption, stroke risk and blood pressure control will also be considered. As the remainder of this paper focuses on black tea, the terms 'tea' and 'black tea' will be used synonymously.

Review criteria

Key journals and MEDLINE were searched in February 2011 for epidemiological studies and intervention trials relating black tea consumption to CVD, stroke and diabetes risk. Key search terms were 'black tea' combined with 'CVD', 'stroke', 'heart disease', 'blood pressure' and 'diabetes mellitus'. The review was restricted to black tea as this variety is most commonly consumed in western regions. Previous studies have not always differentiated clearly between black and green tea when investigating health effects, which can lead to a lack of clarity in the conclusions.

Dates of publication were restricted to the last 20 years, and only English-language peer-reviewed papers were included. From the papers identified, large human observational and intervention studies were selected to ensure that the conclusions related more closely to public health. Inclusion criteria were the following: (1) human studies (animal and cell culture research excluded except when discussing likely mechanisms); (2) studies on black tea (green and oolong teas excluded); and (3) intervention trials should be randomised controlled trials (RCTs). In addition, pharmacological-type studies that investigated only the components of black tea (*e.g.* theanine or flavonoids)

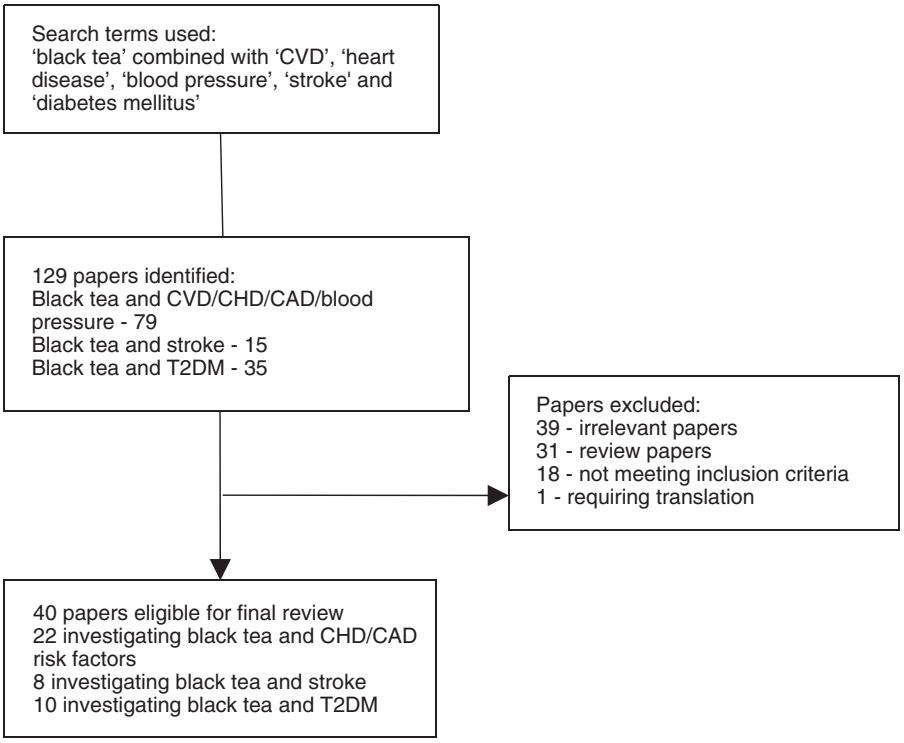

Figure 1 Flow chart of study identification. CVD, cardiovascular disease; CAD, coronary artery disease; CHD, coronary heart disease; T2DM, type 2 diabetes mellitus.

were excluded except when discussing likely mechanisms. Figure 1 provides a flow chart showing how studies were identified.

The quality of included studies was scored by one author (CR) using the Scottish Intercollegiate Guidelines Network (SIGN) 50 (SIGN 2008) in order to determine how much weight should be attributed to the findings when forming conclusions. Thus, meta-analyses and RCT were given a higher score than uncontrolled interventions and epidemiological studies (see Table 1).

Table 1 Ranked levels of evidence adapted from the SIGN grading system (SIGN 2008)

Level	Type of evidence
1	RCT, meta-analyses, systematic reviews of RCT
2	Systematic reviews of case-control or cohort studies, and case-control or cohort studies with a moderate to high probability that the relationship is causal
3	Non-RCT interventions, epidemiology and case reports
4	Expert opinion

RCT, randomised controlled trial; SIGN, Scottish Intercollegiate Guidelines Network.

Coronary heart disease

Twelve separate publications, relating to 11 epidemiological studies (ten cohorts and one case control), were identified, which investigated associations between black tea consumption and CHD outcomes. Of these, eight suggested a significant protective relationship with tea drinking [odds ratio (OR) 0.30–0.31; relative risk (RR) 0.3–0.57 for higher tea intakes compared with low or no tea consumption], while four reported no associations (see Table 2). The largest cohort carried out to date revealed that high tea intakes (*i.e.* >6 cups per day) were associated with significantly reduced CHD mortality [hazard ratio 0.64; 95% confidence interval (CI) 0.37, 1.11] (Koning Gans *et al.* 2010). Similar reductions in mortality and morbidity were observed in smaller cohort studies, although the strength of the associations appeared to differ depending upon the amount of tea ingested, adjustment for confounders and length of follow-up (Geleijnse *et al.* 2002; Sesso *et al.* 2003; Hakim *et al.* 2003).

The epidemiological evidence also suggests gender- and age-related trends between tea drinking and CHD risk. For example, two studies found protective relationships involving tea drinking: the prevalence of carotid plaques (Debette *et al.* 2008) and risk of severe aortic atherosclerosis (Geleijnse *et al.* 1999) were stronger in women than in men. Equally, findings from the French Etude du Vieillissement Artériel study (women ≥65 years) found that the prevalence of carotid plaques was reduced by ten percentage points when tea intakes exceeded three cups per day (Debette *et al.* 2008). In the

Table 2 Epidemiological studies of black tea, tea constituents and CVD

Study design	Methodology	Outcome variables	Results	Reference
Observational studies, CHD/CAD (12 papers)				
Case-control study	$n = 58$ cases with CAD; 106 controls, men	Dietary factors, lipid profile	Tea consumption found to have a significant protective effect on CAD (OR 0.3; 95%CI 0.15–0.65)	Amani *et al.* (2010).
Cross-sectional, cohort study (Scottish Health Survey)	$n = 10\,359$ men and women	CHD risk	No association between tea intake and CHD after adjustment for confounders	Brown *et al.* (1993)
Two cross-sectional, cohort studies combined (Three-City Study, EVA study)	$n = 6597$ ≥65 years old French women (1) $n = 1123$ French (2)	CCA-IMT, carotid plaques	Daily tea consumption associated with a lower prevalence of carotid plaques in female: 44.0%, 42.5% and 33.7%, respectively, in female drinking no tea, one to two cups/day, vs. ≥3 cups/day ($P = 0.0001$). No associations found in male	Debette *et al.* (2008)
Prospective, longitudinal study (Rotterdam study)	$n = 3454$ men and women (>55 years) free of CVD at baseline; calcified plaques measured at baseline and at 2–3 years	Aortic atherosclerosis	Tea intake significantly associated with lower risk of severe aortic atherosclerosis. OR of 0.54 for drinking one to two cups vs. 0.31 for drinking >4 cups/day. Associations strongest in female	Geleijnse *et al.* (1999)
Prospective, longitudinal study (Rotterdam study)	$n = 4806$ men and women (>55 years) with no history of MI	MI risk	Lower risk of MI in tea drinkers ingesting >375 ml (RR 0.57). Association with tea drinking stronger for fatal events (RR 0.30)	Geleijnse *et al.* (2002)
Cross sectional (Saudi CAD study)	$n = 3430$ men and women, 30–70 years	CHD prevalence	>6 cups of tea/day (>480 ml) associated with a significantly lower prevalence of CHD ($P < 0.001$)	Hakim *et al.* (2003)
Prospective study with 14-year follow-up (Welsh Caerphilly study)	$n = 1900$ Welsh men, 45–59 years	IHD risk	No effect of black tea on outcome variable	Hertog *et al.* (1997)
Prospective study with 13-year follow-up	$n = 40\,008$ men and women, 20–69 years	CVD mortality and morbidity risk	High tea consumption (>6 cups/day) significantly associated with lower risk of CHD (HR 95% CI 0.46–0.90; $P = 0.02$)	Koning Gans *et al.* (2010)
Prospective study	1 010 787 person-years of follow-up, men and women	CVD mortality risk	Tea intake not associated with CVD mortality risk	Mineharu *et al.* (2010)
Prospective study with 20-year follow-up	$n = 5115$ men and women	Markers of atherosclerosis	Tea intake significantly associated with less plaque calcification but not with the degree of atherosclerosis	Reis *et al.* (2010)
Prospective study with 15-year follow-up (College Alumni Health study)	$n = 17\,228$ US men and women, mean 59.5 years	CVD, CHD and stroke risk	No effect of black tea on outcome variables	Sesso *et al.* (2003)
Observational studies, stroke (8 papers)				
Cross sectional	$n = 14\,214$ Chinese men and women, 30–65 years	Stroke prevalence	Tea drinking significantly associated with reduced risk of stroke ($P < 0.05$)	Chen *et al.* (2004)
Cohort study with 6.1-year follow-up	$n = 26\,593$ healthy male smokers, 50–69 years	Stroke risk	RR of subarachnoid haemorrhage lower in males drinking ≥1 cup of tea/day but NS	Hirvonen *et al.* (2000)
Cohort with 15-year follow-up	552 men, 50–69 years	Flavonoid intake, stroke risk	Black tea provided 70% flavonoid intake. The RR for stroke was 0.31 (95% CI 0.12– 0.84) for ≥4.7 cups/day vs. <2.6 cups/day	Keli *et al.* (1996)
Cohort study with 13.6-year follow-up	$n = 26\,556$ male Finnish smokers, 50–69 years	Stroke risk	Tea drinking significantly inversely associated with the risk of cerebral infarction. RR of 0.79 in those drinking ≥2 cups/day compared with non-consumers ($P = 0.002$)	Larsson *et al.* (2008)

Cohort study	*n* = 2087 men; 4271 women	Stroke risk	Tea consumption not associated with stroke risk	Tanabe *et al.* (2008)
Case-control study	*n* = 518 MI, 333 haemorrhagic and 1927 ischemic stroke cases; all Chinese men	Stroke risk	Tea consumption significantly associated with reduced risk of haemorrhagic (OR 0.63) and ischemic (OR 0.77) stroke	Wen *et al.* (2008)
Cohort study with 10-year follow-up	*n* = 34 492 post-menopausal women	Flavonoid intake, stroke risk	Tea contributed 36% of flavonoid intake but not associated with CHD/stroke risk	Yochum *et al.* (1999)
Intervention studies, CHD/CAD risk factors (10 papers)				
4-week randomised crossover trial	31 men, 34 women; six mugs of black tea/day or placebo	Blood lipids, blood pressure	No change in LDL, HDL, TAG or blood pressure with tea vs. placebo	Hertog *et al.* (1997)
3-week randomised crossover trial	7 men and 8 women with mild dyslipidaemia; five servings black tea/day vs. placebo + caffeine	Cholesterol and lipoprotein profile	Five servings/day of tea reduced total cholesterol by 6.5%, LDL cholesterol by 11.1%, apolipoprotein B by 5% and lipoprotein(a) by 16.4% compared with placebo	Davies *et al.* (2003)
4-week randomised crossover study	*n* = 66 men and women patients with CAD; drank 900 ml of black tea or water/day	Endothelium-dependent FMD, endothelium-independent nitroglycerin-induced dilation	Short- and long-term black tea consumption reversed endothelial vasomotor dysfunction	Duffy *et al.* (2001)
4-week placebo-controlled parallel design study	*n* = 22 women with mild dyslipidaemia; five cups of black tea/day vs. hot water	Post-ischaemic dilatation of the brachial artery	Three cups/day of tea significantly increased endothelium-dependent dilatation compared with control fluid ($P = 0.03$)	Hodgson *et al.* (2006a)
4-week randomised crossover trial (men and women)	Study 1: 1000 ml/day of black tea vs. hot water + caffeine; *n* = 13 with elevated blood pressure Study 2: 1250 ml/day of black tea vs. hot water; *n* = 22 with raised cholesterol	Urinary F(2)-isoprostane excretion	F(2)-isoprostane excretion unaltered after regular ingestion of black tea compared with control fluid	Hodgson *et al.* (2002b)
4-week randomised controlled crossover study	*n* = 22 men and women; five cups of black tea/day vs. hot water	Platelet aggregation, plasma concentrations of coagulation, fibrinolytic factors and cell adhesion molecules	Black tea resulted in lower soluble P-selectin ($P = 0.01$) compared with control fluid. No impact on other outcome variables	Hodgson *et al.* (2001)
4-week randomised crossover study	*n* = 10 men and women; black tea vs. coffee	Serum lipids, plasma antioxidant capacity, susceptibility to oxidation	No effect of black tea on outcome variables	McAnlis *et al.* (1998)
6-month randomised controlled trial	*n* = 28 men and women at risk of CVD given three servings/day of black tea powder (318 mg/day catechins) vs. water	Lipids, inflammatory markers, blood pressure	No effect of black tea on outcome variables	Mukamal *et al.* (2007)
4-week randomised, placebo-controlled study (men and women)	Smokers given six cups (900 ml) of black or green tea vs. water/day or 3.6 g of green tea polyphenols/day (*n* = 13–16 per group)	LDL and HDL cholesterol, LDL oxidation *ex vivo*, plasma antioxidants	No effect of black tea on outcome variables	Princen *et al.* (1998)
6-week randomised controlled double-blind trial	*n* = 75 men given 1050 mg/day of black tea extract vs. placebo drink	C-reactive protein, inflammatory markers	Black tea significantly reduced platelet activation ($P = 0.02$) and C-reactive protein ($P = 0.05$) compared with placebo	Steptoe *et al.* (2007)
4-week parallel comparison trial	*n* = 45 men and women given 900 ml (six cups) of mineral water, green tea or black tea/day	Resistance of LDL to oxidation *ex vivo* and serum lipid concentrations	No effect of black tea on outcome variables	van het Hof *et al.* (1999)

CAD, coronary artery disease; CCA-IMT, common carotid artery intima-media thickness; CHD, coronary heart disease; CI, confidence interval; CVD, cardiovascular disease; EVA, Etude du Vieillissement Artériel; FMD, flow-mediated dilation; HDL, high-density lipoprotein; HR, hazard ratio; IHD, ischaemic heart disease; LDL, low-density lipoprotein; MI, myocardial infarction; OR, odds ratio; RR, relative risk; TAG, triacylglycerides, NS, non-significant.

Rotterdam cohort study (adults >55 years), the risk of myocardial infarction (MI) was 43% lower when tea intakes exceeded 375 ml per day (Geleijnse *et al*. 2002). In contrast, three studies in adults who were younger than 60 years old reported no significant associations between tea drinking and CVD risk (Brown *et al*. 1993; Hertog *et al*. 1997). In two of these studies (Brown *et al*. 1993; Hertog *et al*. 1997), socio-economic status may have been a confounder as tea drinking was more frequent in those participants from more deprived areas. In the third study, a trend associating tea consumption with a reduced risk of vascular events just failed to reach significance.

The findings from these epidemiological studies are fairly consistent but cannot prove cause and effect. Thus, intervention trials are required to test the associations under controlled conditions and to shed light on the biological mechanisms by which tea may exert an effect. These should address lipid levels, lipid oxidation, markers of vascular health and markers of inflammation.

To date, six intervention trials (five RCTs and one parallel study) have assessed the effect of tea drinking on blood lipid levels (Table 2). These studies involved ingesting up to six cups/mugs of black tea daily for 4 weeks, finding no significant changes in low-density lipoprotein (LDL) cholesterol, high-density lipoprotein cholesterol, triacylglycerol levels (Bingham *et al*. 1997; Princen *et al*. 1998) or resistance of LDL to oxidation (McAnlis *et al*. 1998; Princen *et al*. 1998; van het Hof *et al*. 1999). Another 4-week randomised crossover trial examined the effects of black tea consumption (1250 ml/day) on urinary F(2)-isoprostane excretion, a marker of lipid peroxidation, but this trial also reported few significant results (Hodgson *et al*. 2002a). In contrast, a crossover trial in 15 adults with mild hypercholesterolemia found that five servings of black tea per day, when consumed over 3 weeks, significantly reduced total and LDL cholesterol by 6.5% and 11%, respectively (Davies *et al*. 2003). It may be that tea flavonoids are more likely to have an effect in people with raised cholesterol levels or perhaps differences in flavonoid absorption at an individual level may account for the differing outcomes reported by these studies.

Turning to vascular health, several RCTs measured endothelial flow-mediated dilation (FMD), an indicator of how vessels dilate in response to blood flow. Two of these recruited patients with pre-existing coronary artery disease (CAD) or mild dyslipidaemia, finding significant improvements to FMD when black tea was consumed at intakes of 900 ml per day (Duffy *et al*. 2001) or at five cups per day (Hodgson *et al*. 2006b). A double-blind crossover RCT in 19 healthy men studied the effects on endothelial function of consuming four different levels of flavonoids from black tea. The results showed a dose-dependent relationship between tea flavonoid intake and FMD, suggesting that black tea may impact favourably on arterial stiffness, a risk factor for CVD (Grassi *et al*. 2009). The proposed mechanism is stimulation of nitric oxide production by tea flavonoids, which enhances vasodilation (Lorenz *et al*. 2009). The few studies that have looked at blood pressure changes after tea consumption have not reported significant effects. This may be because these studies tend to be short-term and performed on normotensive subjects (Hodgson & Croft 2010). In comparison, a meta-analysis of five RCTs, which used flavonoid-rich dark chocolate as the test food, reported significant blood pressure reductions (Taubert *et al*. 2007).

Some studies have examined the impact of black tea consumption on markers of inflammation, another risk factor for CVD. Hodgson *et al*. (2001) found that drinking five cups of black tea per day reduced P-selectin levels (molecules that can bind arterial leucocytes) (Hodgson *et al*. 2001). In addition, a well-designed 6-week double-blind RCT in 75 healthy males showed that daily tea consumption, as 1.05 g black tea extract dissolved in 250 ml of hot water per day, reduced both platelet activation and plasma C-reactive protein, a marker of inflammation (Steptoe *et al*. 2007). The mechanism may involve tea flavonoids suppressing signalling pathways and mediators that can lead to inflammation (Suzuki *et al*. 2009).

Stroke

Evidence linking black tea with the risk of developing stroke is still emerging, although a number of studies have identified significant inverse associations between regular green tea consumption and stroke risk (Arab *et al*. 2009). Since 1990, eight published observational studies have examined relationships between black tea intake and the incidence of stroke (see Table 2), with six reporting inverse associations, although to varying levels of significance (Keli *et al*. 1996; Hirvonen *et al*. 2000; Chen *et al*. 2004; Larsson *et al*. 2008; Wen *et al*. 2008).

Several Chinese epidemiological studies have reported inverse relationships between black tea consumption and stroke. One cross-sectional study found that higher tea intakes reduced the risk of stroke, reporting an OR of 0.24 for the highest versus the lowest intakes of black tea ($P < 0.05$) (Chen *et al*. 2004). A case-control study found that tea intakes were inversely associated with both haemorrhagic (OR 0.63) and ischaemic (OR 0.77)

stroke, although authors did not give full details about the types of tea consumed (Wen *et al*. 2008).

In Europe, a Finnish cohort study ($n = 26\,556$) found that two or more cups of tea per day significantly reduced cerebral infarction risk in male smokers (RR 0.79; 95% CI 0.68, 0.92) (Larsson *et al*. 2008). Similarly, Keli *et al*. (1996) found that stroke risk was lower among males (50–69 years) drinking nearly five cups of tea daily compared with those drinking less than 2.5 cups.

It is thought that habitual intakes of flavonoids may protect against stroke, with many of the observational studies reporting that tea was the main dietary source of flavonoids (Keli *et al*. 1996; Yochum *et al*. 1999). Animal studies also provide an insight into the possible mechanisms linking tea consumption with a lower risk of stroke. Rat studies have shown that the antioxidant properties of black tea may attenuate the blood pressure of hypertensive rats, speculating that this could translate into a reduced stroke risk in humans (Negishi *et al*. 2004). Indeed, the US National Health and Nutrition Examination Survey found significant associations between drinking four or more cups of tea per day and lower rates of hypertension in men (Choi & Curhan 2007).

Although antioxidant function may be one mechanism by which tea may lower the risk of stroke, other theories have been proposed. *In vivo* studies suggest that black tea constituents can lower blood pressure, regulate nitric oxide production (which improves endothelial function) and increase plasma concentrations of theanine, an amino acid that crosses the blood-brain barrier and which could ameliorate cerebral endothelial damage (Arab *et al*. 2009). In an animal model of stroke, intravenous theaflavins (flavonoid components of black tea) were found to protect neurons from cerebral ischemia-reperfusion injury by limiting leukocyte infiltration and by inhibiting inflammatory-related prooxidative enzymes (Cai *et al*. 2006).

Type 2 diabetes mellitus

Diabetes is also an emerging area of interest in relation to black tea consumption. A search revealed nine observational studies and two intervention trials that met the inclusion criteria (Table 3). With the exception of one 12-year prospective study finding no link between tea intake and T2DM risk (Boggs *et al*. 2010) and the British Whitehall II cohort reporting that moderate intakes of tea and coffee were not individually associated with T2DM risk (Hamer *et al*. 2008), the remaining seven studies showed a potential protective effect (Song *et al*. 2005; Odegaard *et al*. 2008; Polychronopoulos *et al*. 2008; Celik *et al*. 2009; Panagiotakos *et al*. 2009; van Dieren *et al*. 2009), although in one of these, statistical significance was not achieved.

Of these seven, the Singapore Chinese Health Study found that drinking one or more cups of black tea daily reduced T2DM by 14% when compared with non-tea drinkers (Odegaard *et al*. 2008). In the Dutch cohort of the European Prospective Investigation into Cancer and Nutrition study, the RR of developing diabetes was 0.63 (95% CI 0.47, 0.86) for individuals drinking more than five cups of tea per day and diabetes risk was lowered by 42% (van Dieren *et al*. 2009). Similarly, in older individuals, moderate tea consumption (one to two cups daily) was associated with a 70–88% lower odds of having T2DM (Polychronopoulos *et al*. 2008; Panagiotakos *et al*. 2009). Regular tea drinking was also associated with lower fasting blood glucose levels but not in obese individuals (Polychronopoulos *et al*. 2008). Two studies revealed a weaker but suggestive relationship between higher intakes of black tea and reduced diabetes risk in patients with hypertension (Celik *et al*. 2009) and a reduced risk of T2DM in women drinking four or more cups per day, but to a level that just failed to reach statistical significance (Song *et al*. 2005).

Intervention studies were few in number with only two RCTs being identified, which investigated the impact of black tea extract on markers of health in patients with T2DM. In one RCT involving patients with T2DM, total serum antioxidant capacity increased while levels of serum C-reactive protein decreased after consumption of different doses of black tea extract (up to 600 ml) for 4 weeks (Neyestani *et al*. 2010). In contrast, in a 3-month, double-blinded RCT, levels of glycosylated haemoglobin (an indicator of diabetic control) were unaffected by varying doses of black tea extract (up to 750 mg per day) (Mackenzie *et al*. 2007). As these studies used reconstituted black tea extract, rather than the regular brewed beverage, larger doses of polyphenols would have been provided, which may limit the applicability of the results to normal tea drinking habits (Henning *et al*. 2004).

With regard to modes of action, it has been postulated that theaflavins in black tea may modulate plasminogen activator inhibitor (PAI-1) function, which is considered to have a role in reducing the risk of chronic disease, including diabetes (Jankun *et al*. 2011). There is also evidence from animal studies, suggesting that black tea extract could help to regenerate the pancreas and protect beta cells against oxidative stress (Manikandan *et al*. 2009).

Table 3 Epidemiological studies of black tea, tea constituents and T2DM

Study design	Methodology	Outcome variables	Results	Reference
Observational studies and T2DM (eight papers)				
Prospective study with 12-year follow-up (Black Women's Health Study)	*n* = 49 906 African American women (30–69 years)	T2DM risk	Tea intake not associated with risk of diabetes	Boggs *et al.* (2010)
Cross sectional (men and women)	*n* = 220 diabetic patients with hypertension; *n* = 230 diabetic patients without hypertension	Blood pressure	Higher intake of black tea related to reduced risk of hypertension (OR = 0.823, $P < 0.001$)	Celik *et al.* (2009)
Prospective study with 11.7-year follow-up (Whitehall II cohort)	*n* = 4044 British men and *n* = 1768 women	T2DM incidence	Moderate intake (>3 cups/day) of tea and coffee not independently associated with incidence of T2DM	Hamer *et al.* (2008)
Prospective study with 6-year follow-up (Singapore Chinese Health Study)	*n* = 36 908 men and women, 45–74 years	T2DM incidence	Intake of ≥1 cup of black tea/day significantly lowered risk of diabetes by 14% (RR 0.86; 95% CI 0.74–1.00)	Odegaard *et al.* (2008)
Cross-sectional study	*n* = 1042 Mediterranean men and women	Fasting blood glucose levels, T2DM incidence	Tea intake inversely associated with lower blood glucose levels. One to two cups of tea/day associated with 70% lower odds of having T2DM	Panagiotakos *et al.* (2009)
Cross-sectional study	*n* = 542 Mediterranean men and women, 65–100 years	Fasting blood glucose levels, T2DM incidence	Tea intake associated with lower blood glucose levels in non-obese only. One to two cups of tea/day associated with 88% lower odds of having diabetes in non-obese only	Polychronopoulos *et al.* (2008)
Prospective study with 8.8-year follow-up	*n* = 38 018 healthy women, ≥45 years	Biomarkers of insulin resistance, systemic inflammation, T2DM incidence	≥4 cups of tea/day vs. none inversely associated with diabetes risk with a borderline significant trend ($P = 0.06$)	Song *et al.* (2005)
Prospective study with 10-year follow-up (EPIC study)	*n* = 40 011 Dutch men and women	T2DM incidence	Total daily intake of ≥3 cups of tea or coffee reduced risk of T2DM by 42%	van Dieren *et al.* (2009)
Intervention trials and T2DM (two papers)				
3-month DB, placebo-controlled, randomised multiple-dose study	*n* = 49 men and women with diabetes not taking insulin, mean age of 65 years; intervention: extract of black and green tea: 0, 375 or 750 mg/day	Glycosylated haemoglobin	No significant differences in HBA1c between tea extract and placebo groups	Mackenzie *et al.* (2007)
4-week RCT	*n* = 46 men and women with T2DM; intervention: 150, 300, 450 and 600 ml of BTE/day during weeks 1, 2, 3 and 4, respectively. Control: 150 ml of BTE/day	Serum total antioxidant capacity, serum malondialdehyde, serum C-reactive protein, serum glutathione	Regular intake of BTE had antioxidative and anti-inflammatory effects in patients with T2DM	Neyestani *et al.* (2010)

BTE, black tea extract; CI, confidence interval; DB, double blind; EPIC; European Prospective Investigation into Cancer; HBA1c, haemoglobin A1c;OR, odds ratio; RCT, randomised controlled trial; RR, relative risk; T2DM, type 2 diabetes mellitus.

Discussion

Many studies have been published on tea and CVD risk, although these have considered a wide range of outcome variables including lipid levels, lipid oxidation, vascular tone, inflammation, development of plaques and platelet aggregation. This makes it more difficult to draw together the findings. The most consistent evidence relates to associations in observational studies between regular tea consumption and risk of MI. A meta-analysis of ten cohort studies reported an 11% reduced risk of MI when three cups of tea were consumed daily (Peters *et al*. 2001). Given the inconsistencies in intervention studies relating to lipid lowering and inhibition of LDL oxidation or inflammation (Sharma & Rao 2009), the likely mechanisms may involve improving endothelial function and reducing platelet aggregation (Hodgson & Croft 2010). In contrast, a review by Wang *et al*. (2011) suggested that black tea intake appeared unrelated to CAD but suggested that many of the studies carried out so far were not designed to properly test associations between black tea and heart disease risk. Clearly, more human interventions are required, particularly longer-term studies on tea drinking.

While the six epidemiology papers included in this review concluded that tea drinking might be associated with a reduced risk of stroke risk, only three reported statistically significant findings (Chen *et al*. 2004; Larsson *et al*. 2008; Wen *et al*. 2008). However, the topic is worthy of additional study; a meta-analysis of nine observational studies concluded that daily consumption of three cups of either black or green tea was associated with a 21% reduction in the risk of ischaemic stroke (Arab *et al*. 2009). The authors suggested that tea flavonoids help to maintain normal vascular tone, while theanine (an amino acid found mainly in tea, which crosses the blood:brain barrier) may reduce glutamate-related endothelial damage (Arab *et al*. 2009). However, further studies are needed before firm conclusions can be drawn about the strength of the relationship between black tea consumption and stroke risk, the likely mechanisms involved and the optimal daily intake of tea.

For diabetes, the majority of epidemiology studies show that black tea may have protective effects on T2DM risk (Song *et al*. 2005; Odegaard *et al*. 2008; Polychronopoulos *et al*. 2008; Celik *et al*. 2009; Panagiotakos *et al*. 2009; van Dieren *et al*. 2009). These findings are supported by a meta-analysis, which concluded that higher intakes of tea reduce diabetes risk (Huxley *et al*. 2009). Intervention trials and mechanistic research are now needed to examine dose-response relationships and establish how black tea may mediate its effects. Proposed mechanisms include the suggestion that constituents in black tea may help to maintain normal glycaemic control (Polychronopoulos *et al*. 2008) and protect pancreatic beta cells from oxidative stress (Manikandan *et al*. 2009).

It is difficult to determine optimal intakes of tea given the wide variety of outcome variables. For heart disease, consuming ≥6 cups of tea daily was associated with reduced CHD mortality (Koning Gans *et al*. 2010) and reduced CHD prevalence (Hakim *et al*. 2003), although benefits have been seen with lower daily intakes [*e.g*. consumption of four or more cups has been linked with a reduced risk of aortic atherosclerosis (Geleijnse *et al*. 1999) and vascular events in women (Sesso *et al*. 2003)], while drinking three or more cups has been associated with a reduced risk of MI (Peters *et al*. 2001). For diabetes, as few as one to four cups daily may offer health benefits (Odegaard *et al*. 2008; Panagiotakos *et al*. 2009), although the evidence base is still modest. There are too few studies on stroke to determine an optimal intake of black tea, although the meta-analysis by Arab *et al*. (2009) reported a reduction in stroke risk of 9–66% when three or more cups of tea were consumed daily (compared with non-consumers).

However, there are certain challenges when interpreting the epidemiological evidence, which may help to explain discrepancies among the published findings. These include the use of different dietary assessment methods for estimating tea consumption, failure to specify the actual volume of tea drunk (*i.e*. size of cups/mugs not given) and inadequate control of confounders such as other dietary sources of polyphenols. In addition, it would be useful to gather information on preparation methods, such as brew time, which would influence flavonoid exposure. The addition of milk is another important factor. Some authors have suggested that adding milk to black tea could reduce flavonoid bioavailability and influence antioxidant capacity (Hertog *et al*. 1993), while others have suggested that addition of milk has no clinical impact (Kyle *et al*. 2007).

Given the available evidence, promoting tea drinking may contribute towards dietary strategies designed to protect consumers against CHD and T2DM. For example, in China, tea drinking has been implemented as a public health strategy to lower the risk of stroke (Liang *et al*. 2009). In the United States, the Beverage Guidance Panel advises that tea should be drunk second only to water as a means of ensuring optimal fluid consumption (Popkin *et al*. 2006). Although translating diverse research findings into public health messages is a difficult task, the evidence seems to indicate that drink-

ing one to four cups of black tea daily may help protect against the development of diabetes, while three to six cups per day may contribute to reducing the risk of CHD. Levels of intake required to impact on the risk of stroke are less clear but may be in the region of around three cups per day.

Conclusions

Based on previous meta-analyses and the evidence presented here, regular black tea consumption (three to six cups daily) may offer some protection against CHD. There is consistent epidemiological evidence associating one to two cups of black tea daily with a lower risk of type 2 diabetes, although this needs to be confirmed in long-term controlled trials that use standardised tea drinks and markers of glycaemic control. Future research should also explore the likely mechanisms involved. Finally, there is emerging evidence that regular tea drinking may protect against stroke, but a much larger evidence base, from both longitudinal and intervention studies, is needed before firm conclusions can be drawn. Overall, encouraging the public to drink black tea on a regular basis could be a simple way to contribute towards dietary strategies aimed at lowering the burden of chronic disease.

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Conflict of interest

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