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Coffee consumption and Type 2 Diabetes - An Extensive Review

Review article

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Abstract: Coffee is a complex mixture of potentially active chemicals. It contains significant amounts of phenolic polymers, chlorogenic acid and also caffeine. Agricultural factors, roasting, blending, and brewing determine coffee's chemical composition. Recent epidemiological studies suggest that habitual coffee consumption may help to prevent some chronic diseases including type 2 diabetes. Despite reports from the clinical trials of the effect of caffeine on decreasing insulin sensitivity, long-term prospective studies revealed that coffee may improve fasting glucose, glucose tolerance and insulin sensitivity as well. In the most recent publication habitual coffee drinkers have a lower total and cardiovascular mortality rate among diabetic subjects.

Keywords: *Coffee • Type 2 diabetes • Glucose tolerance*

1. Introduction

Type 2 diabetes, formerly known as non-insulin-dependent diabetes (NIDDM), is the most common form of diabetes and is a major health problem associated with excess morbidity and mortality, which results in substantial health care costs. The total number of people with diabetes is projected to rise from 171 million in 2000 to 366 million in 2030 [1]. In Europe their number will increase from approximately 16 million in1994 to 24 million in 2010 [2].

Type 2 diabetes is caused by complicated interplay of genes and environment. Genetic factors play an important role in type 2 diabetes, but the pattern is complicated, since both impairment of beta cell function and abnormal response to insulin are involved. Dramatic changes in the prevalence or incidence of type 2 diabetes have been observed in communities where there have been major changes in the type of diet consumed, from a traditional indigenous diet to a typical western diet, e.g. Pima Indians in Arizona, Micronesians in Nauru and Aborigines in Australia [3-5]. Changing disease rates are almost explained by changes in several dietary factors as well as by changes in other lifestyle related factors (obesity and sedentary lifestyle). This may be particularly important in triggering the genetic elements that cause this type of diabetes.

Evidence increasingly indicates that healthy lifestyle and dietary habits can prevent most cases of type 2 diabetes. The prevention of type 2 diabetes has become a major issue from the public health perspective [6]. Coffee with its large number of consumers and numerous constituents has provided good grounds on this issue.

Coffee is a complex mixture of more than a thousand chemicals and significant amounts of caffeine and chlorogenic acid. The psychoactive effects of caffeine have been well documented, and most „folk knowledges" attributes the effects of coffee to be

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Table 1. Adjusted linear regression analysis of the association between coffee consumption and glucose and insulin levels among non-diabetic men and women [53].

Coffee consumption, cups/day	Regression coefficient (95% CI)		
	Fasting glucose	2-hour glucose	Fasting insulin
Men			
Adjustment for age and study year	-0.18 (-0.39 to 0.03)	-0.55 (-1.14 to 0.04)	-0.14 (-0.24 to -0.03) [c]
Multivariate adjustment[a]	-0.33 (-0.56 to -0.10)[c]	-0.64 (-1.28 to -0.01) [c]	-0.22 (-0.33 to -0.12) [c]
Women			
Adjustment for age and study year	-0.10 (-0.35 to 0.15)	-1.34 (-1.99 to -0.68) [c]	-0.10 (-0.23 to 0.03)
Multivariate adjustment[a]	-0.26(-0.50 to -0.01) [c]	-1.77 (-2.43 to –1.12) [c]	-0.26 (-0.38 to -0.14) [c]
Men and women combined[b]			
Adjustment for age and study year	-0.15 (-0.31 to 0.01)	-0.89 (-1.33 to -0.45) [c]	-0.12 (-0.21 to -0.04) [c]
Multivariate adjustment[a]	-0.29 (-0.45 to -0.12) [c]	-1.16 (-1.61 to -0.70) [c]	-0.24 (-0.31 to -0.16) [c]

[a] *Adjusted for age, study year, body mass index, systolic blood pressure, education, occupational and leisure time physical activity, walking or cycling to/from work, cigarette smoking, alcohol and tea consumption.*
[b] *Adjusted also for sex.*
[c] *P value <0.05.*

synonymous with those of caffeine, even though other more abundant components of coffee also have many biological effects but may not have been extensively studied. As it has been said, coffee is a major source of chlorogenic acid in the human diet and may affect glucose metabolism by different mechanisms. Even roasted coffee, where chlorogenic acid has been transformed into the other substances, has been shown to increase insulin sensitivity [7,8]. In addition coffee influences the secretion of gastrointestinal peptides such as glucagon-like peptide-1 (GLP-1) and gastric inhibitory polypeptide (GIP) [9,10]; the other suggested mechanisms are direct stimulation of pancreatic beta-cells by caffeine [11], and the magnesium content of coffee [12-15]. However definite mechanisms for the possible effects of coffee on glucose metabolism are not well known. During the last few decades, research has attempted to clear health benefits or harms received from coffee drinking. Recent population-based studies suggest that coffee consumption may help to prevent several chronic diseases, including type 2 diabetes and its complications. In this state-of-the-art review, we summarize the knowledge regarding the role of coffee consumption on the risks of glucose tolerance, insulin sensitivity, and type 2 diabetes.

2. Mechanisms underlying the protective effects of coffee consumption on type 2 diabetes

Glucose regulation is an important issue in glucose metabolism and development of diabetes, and needs to be investigated in more detail at the intestinal, hepatic and the peripheral delivery stages of glucose metabolism.

Coffee contains many compounds other than well-known caffeine that may have the potential to influence each of these stages. At the intestinal stage, inhibition or retardation of the action of α-Glucosidase by chlorogenic acid is one of the possible mechanisms. The inhibition of this enzyme is an effective approach to control hyperglycemia [16]. It has also been reported that chlorogenic acid inhibits glucose transporters (Na^+-dependent glucose transporters) at the same stage [17]. In addition coffee may also influence the secretion of gastrointestinal peptides such as (GLP-1) and (GIP), both of which are known for their glucose lowering effects [18,19]. At the hepatic stage, reduced Glucose-6-phosphatase (Glc-6-Phase) hydrolysis or its inhibition by chlorogenic acid may reduce plasma glucose output leading to reduced plasma glucose concentration [20-23]. At the peripheral delivery stage, lower fasting insulin values and lower risk of hyperinsulinemia among coffee consumers in this study may be interpreted as an improvement in insulin sensitivity by coffee consumption. The acute effects of caffeine on decreasing insulin sensitivity have also been reported [24]. However we believe these effects might be modified during long periods of coffee consumption as already seen with cardiovascular effects [25] and glucose metabolism may follow different pattern among heavy and chronic coffee consumers. Also the beneficial effects of coffee's components other than caffeine on insulin sensitivity should be considered [7,8]. Ärnlöv and co-workers investigated the association between coffee consumption and both insulin sensitivity and insulin secretion in a cross-sectional study [26]. They determined insulin sensitivity index by hyperinsulinemic euglycemic clamp and found that both coffee and tea consumption improved insulin sensitivity [27].

Table 2. Adjusted odd ratio of the association between coffee consumption and hyperglycaemia and hyperinsulinemia among non-diabetic men and women [53].

Coffee consumption, cups/d	Odd ratios (95% CI)			
	Impaired fasting glucose[a]	Isolated impaired glucose tolerance[a]	Impaired glucose regulation[a]	Hyperinsulinemia
Men	N=978	N=884	N=1051	N=1051
Adjustment for age and study year	0.94 (0.88-1.00)	0.97 (0.89-1.06)	0.95 (0.90-1.01)	0.96 (0.91-1.01)
Multivariate adjustment[b]	0.90 (0.83-0.98)	0.97 (0.87-1.06)	0.92 (0.87-0.99)	0.89 (0.83-0.95)
Women	N=1277	N=1286	N=1383	N=1383
Adjustment for age and study year	0.94 (0.85-1.04)	0.91 (0.83-1.01)	0.92 (0.86-0.99)	0.97 (0.92-1.03)
Multivariate adjustment[b]	0.88 (0.79-0.98)	0.89 (0.80-0.99)	0.89 (0.82-0.96)	0.88 (0.82-0.94)
Men and women combined[c]	N=2255	N=2170	N=2434	N=2434
Adjustment for age and study year	0.94 (0.89-0.99)	0.94 (0.89-1.01)	0.94 (0.90-0.98)	0.96 (0.93-1.00)
Multivariate adjustment[b]	0.90 (0.85-0.96)	0.92 (0.86-0.99)	0.91 (0.87-0.96)	0.89 (0.85-0.93)

[a] *Using normal glucose tolerance, fasting glucose <110 mg/dl and 2-hour glucose <140 mg/dl as reference group in the analysis of hyperglycaemia; impaired fasting glucose, fasting glucose 110-125 mg/dl; isolated impaired glucose tolerance, 2-hour glucose 140-199 mg/dl and fasting glucose <110 mg/dl; impaired glucose regulation, fasting glucose 110-125 mg/dl and/or 2-hour glucose 140-199 mg/dl; hyperinsulinemia; sex- and study year-specific quartile 4 of fasting insulin.*

[b] *Adjusted for age, study year, body mass index, systolic blood pressure, education, occupational and leisure time physical activity, walking or cycling to/from work, cigarette smoking, alcohol and tea consumption.*

[c] *Adjusted also for sex.*

Despite the relatively good correlation between fasting plasma insulin and insulin sensitivity derived from the hyperinsulinemic euglycemic clamp, measures of fasting plasma insulin explain no more than 50% of the variability in insulin action seen in nondiabetic subjects [28,29]. This is because plasma insulin levels depend not only on insulin sensitivity, but also on a complex interplay between insulin secretion, distribution, and degradation [30]. However the measurement of plasma insulin concentration after an overnight fast seems to be one of the most practical ways to give some estimate of insulin resistance from the clinical perspective [31-33] and very high plasma insulin values usually reflect the presence of insulin resistance. Low or even "normal" insulin values are probably effective on postload glucose concentration.

Homocysteine level has been suggested to explain the observed stronger inverse association of decaffeinated coffee and risk of development of diabetes because there is a dose-response relation between coffee and homocysteine level [34,35], and caffeine may be responsible for the homocysteine raising effect of coffee [36]. Furthermore homocysteine level has been indicated as a potential risk factor for developing diabetes [37,38], and it has been hypothesized that the lack of protective effect of decaffeinated coffee might be due to caffeine-induced hyperhomocysteinemia [39].

It has been suggested that the mechanism of the observed inverse association between coffee consumption and diabetes might be, at least in part, due to the inhibition of iron absorption by polyphenol compounds present in coffee [40]. It has been evidenced that higher body iron stores are associated with an increased risk for diabetes [41]; moreover induction of iron deficiency in impaired glucose tolerant subjects has been shown to improve insulin sensitivity [42].

3. Effects of coffee consumption on glycemic profile (glucose tolerance and insulin sensitivity)

Most of the controlled clinical trials have revealed that acute administration of caffeine will impair glucose tolerance and insulin sensitivity [24,43-45]. The effects of coffee consumption for 2 to 4 weeks on serum glucose and insulin level have been examined in randomized clinical trials. Drinking decaffeinated coffee for 14 days by people who used to consume an average of 560 mg/d of caffeine from coffee or tea caused decreased fasting blood glucose levels significantly [46]. The Hoorn investigators found that high coffee consumption for 4 weeks increased fasting insulin but no effects on fasting glucose level were observed, compared to coffee abstinence [47]. One recent study, which compared the acute effects of caffeine and coffee ingestion on glucose metabolism, found impaired glucose tolerance following both caffeine and regular coffee consumption. While caffeine ingestion resulted in higher glucose, insulin, and C peptide responses compared with both placebo and decaffeinated coffee, regular coffee consumption resulted in an attenuated response only for glucose and insulin when compared with decaffeinated coffee, and no difference was observed when compared with

Table 3. Cohort studies of coffee consumption and risk of type 2 diabetes [63].

Reference Study	Population	Cases	Association	Hazard ratio for highest to lowest category
van Dam & Feskens, 2002	17,111 M[a], F[a] (Netherland)	306	Inverse	0.50, >7 cups/d, P<0.002
Saremi et al., 2003	2680 M, F (US)	824	Not Significant	0.92, >3 cups/d, P=0.60
Reunanen et al., 2003	19518 M, F (Finland)	855	Not Significant	0.92, >7 cups/d,
Salazar-Martinez et al., 2004	41,934 M (US)	1333	Inverse	0.46, >6 cups/d, P=0.007
Salazar-Martinez et al., 2004	84,276 F (US)	4085	Inverse	0.92, >6 cups/d, P<0.001
Tuomilehto et al., 2004	6974 M, 7655 F (Finland)	381	Inverse	Men: 045, >10 cups/d, P=0.12
				Women: 0.21, >10 cups/d, P<0.001
Rosengren et al., 2004	1361 F (Sweden)	74	Inverse	0.57, >6 cups/d, P=0.029
Carlsson et al., 2004	10,652 M, F	408	Inverse	0.65, >7 cups/d
Van Dam et al., 2004	1312 M, F (Netherland)	128	Not Significant	0.92, >7 cups/d, P=0.09
van Dam & Hu,[b] 2005	193,473 of 9 cohort M, F	8394	Inverse	0.65, >6, >7 cups/d
Iso, et al., 2006	17,413 M, F (Japan)	444	Inverse	0.58, ≥3 cups/d, P=0.027
Periera et al., 2006	28,812 F (US)	1418	Inverse	0.78, >6 cups/d, P=0.06
Paynter et al., 2006	5,414 M, 6,790 F (US)	1437	Inverse	0.77, >4 cups/d, P=0.02
Van Dam et al., 2006	88,259 F (US)	1263	Inverse	0.53, >4 cups/d, P<0.001
Bidel et al., 2007	10,666 M, 11,160 F (Finland)	862	Inverse	Men: 071, >7 cups/d, P=0.02
				Women: 0.47, >7 cups/d, P<0.0001

[a] *M, Male; F, Female*
[b] *Systematic review*

placebo [48].

Although short-term trials of coffee and caffeine ingestion demonstrated the negative impact on glucose tolerance and insulin sensitivity, epidemiological studies revealed that chronic coffee consumption may help to maintain normal glucose tolerance. Cross-sectional studies from diverse countries have found that coffee consumption is inversely associated with the incidence of impaired glucose tolerance after oral glucose load [49-51]. In addition a prospective cohort study of Dutch men and women found inverse association between habitual coffee consumption and the risk of developing impaired glucose tolerance. There was no association between coffee consumption and impaired fasting glucose in this study, which may be interpreted as effects of coffee consumption on post-load glucose metabolism more than fasting glucose [52]. A study by our group revealed an inverse association between coffee consumption and several markers of glycemia and diabetes. We found that coffee consumption was associated with lower values of fasting glucose, 2-hour glucose and fasting insulin among non-diabetic subjects (Table 1). Coffee consumption was significantly and inversely associated with impaired fasting glucose, impaired glucose regulation, and hyperinsulinemia among both men and women and with isolated impaired glucose tolerance only among women [53] (Table 2).

Figure 1. Relative risk of type 2 diabetes according to joint effects of coffee consumption, physical activity and BMI. Cox proportional hazards model adjusted for age, study year, sex, education, systolic blood pressure, bread consumption, frequency of vegetable consumption, frequency of fruit consumption, frequency of sausage consumption, tea and alcohol consumption, and smoking. Inactivity was defined as low physical activity; activity was defined as moderate or high physical activity. *p <0.05 compared with referent group [63].

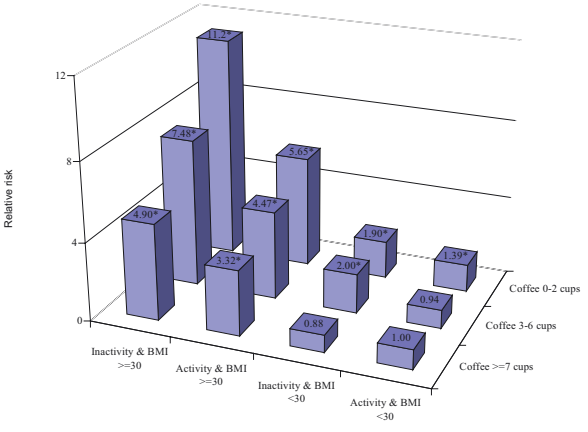

Table 4. Hazard Ratio (95% Confidence Interval) for the Development of Type 2 Diabetes by Volume of Coffee Consumption [63].

	Daily coffee consumption					P Value
	≤2 cups	3-4 cups	5-6 cups	7-9 cups	≥10 cups	
Men						
No. of new cases	41	48	67	28	19	
Person-years	14191	20054	25704	11480	10426	
Adjustment for age and study year	1.00	0.83 (0.54-1.25)	0.88 (0.60-1.30)	0.86 (0.53-1.39)	0.69 (0.40-1.19)	0.735
Further adjustment for other factors[a]	1.00	0.73 (0.47-1.13)	0.70 (0.45-1.05)	0.67 (0.40-1.12)	0.45 (0.25-0.81)	0.116
Women						
No. of new cases	46	68	48	13	3	
Person-years	15821	30367	32036	10523	4980	
Adjustment for age and study year	1.00	0.72 (0.49-1.04)	0.49 (0.32-0.73)	0.47 (0.25-0.87)	0.26 (0.08-0.85)	0.002
Multivariate adjustment[a]	1.00	0.71 (0.48-1.05)	0.39 (0.25-0.60)	0.39 (0.20-0.74)	0.21 (0.06-0.69)	<0.001
Men and women combined[b]						
No. of new cases	87	116	115	41	22	
Person-years	30112	50421	57740	22003	15406	
Adjustment for age and study year	1.00	0.79 (0.59-1.04)	0.67 (0.50-0.88)	0.66 (0.46-0.96)	0.53 (0.33-0.85)	0.016
Multivariate adjustment[a]	1.00	0.76 (0.57-1.01)	0.54 (0.40-0.73)	0.55 (0.37-0.81)	0.39 (0.24-0.64)	<0.001

[a] *Adjusted for age, study year, body mass index, systolic blood pressure, education, occupational physical activity (light, moderate, and active), walking or cycling to/from work (0, 1-29, and ≥30 minutes per day), leisure time physical activity (low, moderate, and high), cigarette smoking (never, past, and current smoking of 1-19 or ≥20 cigarettes per day), alcohol consumption (0, 1-100, 101-300, and >300 g per week), and tea consumption (none, 1-2, and ≥3 cups per day).*

[b] *Also adjusted for sex.*

4. Coffee consumption and Type 2 Diabetes

Although various health effects of coffee have been investigated extensively, until recently the association of coffee consumption and development of type 2 diabetes has not been thoroughly studied. Table 3 summarizes the results of 13 prospective cohort studies of coffee consumption and the risk of type 2 diabetes.

A prospective study of about 17000 Dutch man and women found that the risk of developing type 2 diabetes was 50% lower in those who drank 7 cups of coffee daily compared to those who drank 2 cups or less [54]. Two large prospective cohorts, from the US Health Professional Follow-up Study of 41934 men and the Nurses' Health Study of more than 84000 women, revealed that in men who drank at least 6 cups of coffee daily, the risk of developing type 2 diabetes is 54% less than men who are coffee abstainers, and among women with the same amount of coffee consumption they observed a 29% lower risk in habitual coffee consumers compared to coffee abstainers [55]. There was also an observed moderate inverse association between decaffeinated coffee and the risk of type 2 diabetes in those cohorts. In a Finnish twins study there was a 35% risk reduction among those who drank 7 cups of coffee or more compared with those who drank 2 cups or less [56]. In another cohort of Swedish women, those who drank 3 cups of coffee had a 50% lower risk of type 2 diabetes than those who drank 2 cups or less [57]. Another community-based cohort from the US that examined the effect of coffee and sweetened beverages consumption and the risk of type 2 diabetes showed the same inverse association in these community-based US African-American and Caucasian adults, with a 23% decreased risk comparing to the abstainers [58]. An 11-year prospective study of about 29000 postmenopausal women found inverse association between regular and decaffeinated coffee and risk of type 2 diabetes, particularly in the decaffeinated coffee consumers [59]. They used 3 different regression models, each adjusted for a group of confounders. In model 1, which adjusted for age, education and hypertension, there was a 34% risk reduction in women who drank 6 or more cups of coffee compared to coffee abstainers. Adjusting for anthropometric, lifestyle and dietary factors in model 2 attenuated the results and further adjustment for magnesium and phytate in model 3 did not change the results. There was a stronger inverse association with decaffeinated coffee in all these 3 model analyses [59]. The Nurses' Health Study II of 88,259 U.S. women indicated an inverse association between both caffeinated and decaffeinated coffee and the risk of type 2 diabetes [60]. In a recent Japanese study including 17,413 persons, those who drank 3 or more cups of coffee daily had a 42% lower risk of type 2 diabetes than

Table 5. Relationship between coffee consumption and incident diabetes stratified by baseline g-glutamyltransferase level [69].

	Coffee intake (frequency/day)				P for trend
	0-2	3-4	5-6	>=7	
Men	(p of interaction=0.18)				
GGT<75th percentile (40U/L)					
No of cases	38/1335	64/2032	110/2519	73/2049	
Person-years	16019	24992	32838	27181	
Incidence rate/1000 Person-years	2.37	2.56	3.35	2.68	
Age-adjusted RR	1.00	1.06 (0.71-1.58)	1.36 (0.94-1.97)	1.18 (0.80-1.75)	0.22
Multivariate[a] RR	1.00	1.06 (0.71-1.59)	1.14 (0.79-1.66)	0.94 (0.63-1.40)	0.75
GGT>=75th percentile (40U/L)					
No of cases	49/659	53/779	54/756	42/537	
Person-years	6087	7927	7515	6009	
Incidence rate/1000 Person-years	8.05	6.69	7.18	6.99	
Age-adjusted RR	1.00	0.82 (0.56-1.21)	0.93 (0.63-1.37)	0.92 (0.61-1.41)	0.89
Multivariate[a] RR	1.00	0.85 (0.58-1.26)	0.81 (0.55-1.20)	0.68 (0.44-1.05)	0.08
Women	(p of interaction=0.05)				
GGT<75th percentile (21U/L)					
No of cases	33/1452	59/2710	76/2710	30/1322	
Person-years	18390	36692	39428	19615	
Incidence rate/1000 Person-years	1.79	1.61	1.93	1.53	
Age-adjusted RR	1.00	0.82 (0.53-1.25)	0.95 (0.63-1.43)	0.85 (0.52-1.40)	0.85
Multivariate[a] RR	1.00	0.84 (0.55-1.30)	0.86 (0.57-1.30)	0.68 (0.41-1.13)	0.20
GGT>=75th percentile (21U/L)					
No of cases	50/754	72/1139	46/771	13/303	
Person-years	7471	11336	8184	3407	
Incidence rate/1000 Person-years	6.69	6.35	5.62	3.82	
Age-adjusted RR	1.00	0.92 (0.64-1.31)	0.85 (0.57-1.27)	0.67 (0.36-1.24)	0.19
Multivariate[a] RR	1.00	0.75 (0.52-1.09)	0.59 (0.39-0.88)	0.44 (0.24-0.82)	0.002
Men and women[b]	(p of interaction=0.02)				
GGT<75th percentile					
No of cases	71/2787	123/4742	186/5229	103/3371	
Person-years	34409	61684	72266	46796	
Incidence rate/1000 Person-years	2.06	1.99	2.57	2.20	
Age-adjusted RR	1.00	0.95 (0.71-1.27)	1.17 (0.89-1.54)	1.04 (0.77-1.41)	0.38
Multivariate[a] RR	1.00	0.96 (0.71-1.28)	1.01 (0.76-1.33)	0.82 (0.60-1.12)	0.95
GGT>=75th percentile					
No of cases	99/1413	125/1918	100/1527	55/840	
Person-years	13557	19263	15699	9417	
Incidence rate/1000 Person-years	7.30	6.49	6.37	5.84	
Age-adjusted RR	1.00	0.88 (0.68-1.14)	0.89 (0.68-1.18)	0.85 (0.61-1.19	0.51
Multivariate[a] RR	1.00	0.77 (0.59-1.01)	0.70 (0.53-0.93)	0.65 (0.46-0.91)	0.001

[a] *Adjusted for age, BMI, alcohol consumption, smoking, and physical activity*
[b] *All analyses additionally adjusted for sex.*

Table 6. Hazard ratios (95% CIs) of total, cardiovascular, coronary heart disease, and stroke mortality by volume of coffee consumption among subjects with type 2 diabetes [71].

	Daily coffee consumption, cups				P for trend
	0-2	3-4	5-6	≥7	
Total mortality					
Number of deaths	247	384	529	311	
Person-years	11,772	20,551	29,927	17,406	
Hazard ratios, model 1[a]	1.00	0.79 (0.67-0.93)	0.72 (0.62-0.85)	0.79 (0.67-0.94)	0.001
Hazard ratios, model 1[b]	1.00	0.78 (0.66-0.92)	0.69 (0.59-0.82)	0.72 (0.60-0.87)	<0.001
Hazard ratios, model 1[c]	1.00	0.77 (0.65-0.91)	0.68 (0.58-0.80)	0.70 (0.59-0.85)	<0.001
Cardiovascular mortality					
Number of deaths	146	241	337	185	
Hazard ratios, model 1[a]	1.00	0.81 (0.66-0.99)	0.75 (0.62-0.92)	0.79 (0.63-0.98)	0.04
Hazard ratios, model 1[b]	1.00	0.80 (0.65-0.99)	0.73 (0.59-0.90)	0.74 (0.58-0.94)	0.02
Hazard ratios, model 1[c]	1.00	0.79 (0.64-0.97)	0.70 (0.57-0.86)	0.71 (0.56-0.90)	0.006
Coronary heart disease mortality					
Number of deaths	96	160	231	111	
Hazard ratios, model 1[a]	1.00	0.81 (0.63-1.05)	0.77 (0.61-0.98)	0.71 (0.54-0.94)	0.09
Hazard ratios, model 1[b]	1.00	0.79 (0.61-1.03)	0.73 (0.57-0.95)	0.65 (0.48-0.88)	0.04
Hazard ratios, model 1[c]	1.00	0.78 (0.60-1.01)	0.70 (0.54-0.90)	0.63 (0.47-0.84)	0.01

[a] *Adjusted for age, sex, and study year*
[b] *Adjusted for age, sex, study year, education, alcohol and tea consumption, and smoking status.*
[c] *Adjusted for age, sex, study year, body mass index, systolic blood pressure, total cholesterol, education, alcohol and tea consumption, and smoking status.*

those who drank 1 cup or less per week [61].

Not all recent data have observed an inverse association between coffee consumption and type 2 diabetes. In fact an earlier Finnish cohort study of more than 19000 men and women (1973-1977) with average follow-up of 14 years found no association between coffee consumption and the risk of type 2 diabetes [62]. Until the mid-1970s the coffee consumed in Finland was mostly pot-boiled, and its effect on reducing the risk of type 2 diabetes was less than that of filtered coffee in our more recent analysis [63]. Another study of Pima Indians also found no association between coffee consumption and the risk of type 2 diabetes [64]. Their coffee consumption was very low, and it has been shown that there is a graded inverse effect between the amount of coffee and the risk of diabetes. A systematic review of about 9 cohort studies revealed that the risk of developing type 2 diabetes in participants who drank 4 to 6 cups and more than 6 to 7 cups of coffee per day was 28% and 35% lower respectively compared to those who drank less than 2 cups daily (Table 3) [65]. They found the same inverse association between coffee consumption and impaired glucose tolerance or type 2 diabetes in cross-sectional studies [65]. The association between coffee consumption and risk of developing type 2 diabetes has been examined in several studies by our group. In a large prospective study we followed more than 14000 men and women for about 12 years. We found that the risk of developing type 2 diabetes in Finnish men and women who drank at least 10 cups of coffee were 55% and 79% lower than men and women who drank 2 cups or less [63] (Table 4). We also examined the joint association of coffee consumption and other factors (including physical activity, obesity, and alcohol consumption) with the risk of type 2 diabetes and found that coffee drinking was associated with a reduced risk of type 2 diabetes in both men and women, and this association was observed regardless of the levels of physical activity, body mass index, and alcohol consumption [66] (Figure 1). In larger prospective study we found the same inverse association between coffee consumption and risk of developing type 2 diabetes.

There is a strong association between the serum concentration of gamma-glutamyltransferase (GGT) and the risk of developing impaired fasting glucose or type 2 diabetes [67], and recent results have suggested that GGT may be used as a risk indicator for developing metabolic syndrome and type 2 diabetes [68]. However in a recent study we evaluated the joint association between both coffee consumption and serum GGT levels and the risk of developing type 2 diabetes [69]. We found that the results were influenced by baseline GGT levels. At high GGT levels (≥75% percentile), coffee drinking was inversely associated with type II diabetes in women

and both sexes combined (Table 5). Thus, increased GGT levels may play a role in initiating development of type 2 diabetes; the increasing frequency of the disease in people with high GGT levels may be expected as reported earlier [70]. However in this study we found fewer cases of incident diabetes among habitual coffee consumers with high normal GGT levels which may indicate a stronger protective effect of coffee in these levels [69].

In conclusion the potentially preventable nature of type 2 diabetes has been evidenced by the implementation of lifestyle measures such as weight control and exercise. In many of the borderline cases of type 2 diabetes, the clinical appearance of the disease and its complications may be delayed by diet and exercise for many years. It may show the efficacy of the dietary behaviour in preventing the disease. Even when diabetes has occurred, coffee might have some potential to influence its complication. This has been evidenced by our recent large prospective study in which we evaluated the association between coffee consumption and mortality rate among type 2 diabetic patients [71]. Coffee drinking was associated with reduced total, cardiovascular disease, and coronary heart disease mortality. Patients with type 2 diabetes who drank 7 or more cups of coffee per day had a 21% decrease in total mortality, 21% in cardiovascular disease mortality, and 29% in coronary heart disease mortality rate, as compared to patients who drank 2 cups or less (Table 6).

Coffee has been included to the dietary menu of most people and it seems to be helpful in overall glucose metabolism. However we believe that these protective effects cannot be solely achieved by coffee drinking without considering the other lifestyle measures. In addition many people may end or lessen the effects of coffee drinking through aging, digestive problems or some other health-related reasons and consequently the overall incidental rate has not changed.

Although habitual coffee consumption seems to be a safe and useful lifestyle behaviour with respect to type 2 diabetes, better knowledge of the components of coffee, human consumption and bioavailability is needed in order to properly evaluate the true role of coffee in type 2 diabetes. Eventually research in this area should lead to dietary recommendations optimized for specific population groups at risk for developing type 2 diabetes.

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