KAFFE & HELBRED

vidensportal for sundhedspersonale

Update September 2020 / Coffee and Type 2 Diabetes Overview

Diabetes is a significant public health concern across the globe and is the subject of much scientific research. It is characterised by high levels of glucose in the blood and there are two main types: type 1 and type 2[1]. Type 1 diabetes is mainly due to genetics, whereas the development of type 2 diabetes is typically associated with diet and lifestyle choices[1]. There have been a number of studies published investigating the possible associations between coffee consumption and type 2 diabetes. This summary provides an overview of the body of research, including the latest findings and presents the potential mechanisms involved.

Scientific research indicates that moderate coffee consumption is associated with a statistically significant reduced risk of developing type 2 diabetes[2-4]. A moderate coffee consumption is typically defined as 3-5 cups per day, based on the European Food Safety Authority's Scientific Opinion on the safety of caffeine[5].

The association has been studied in a number of different populations and the wealth of evidence suggests that a moderate intake of coffee is associated with a lower risk of developing type 2 diabetes, compared to consuming none or less than 2 cups per day[2-4]. Research also suggests a dose response relationship[3,4,6-8]. Interestingly, the association is seen with both caffeinated and decaffeinated coffee[3,6-8].

Currently, a plausible explanation for this association is still lacking. There is no clear consensus on a potential mechanism, although some research suggests coffee components including chlorogenic acids and trigonelline may be key[9-11]. Observations of beneficial effects of coffee consumption on some markers of subclinical inflammation are also interesting[12,13].

The association between coffee/caffeine consumption and diabetes appears to be specific to type 2 diabetes only.

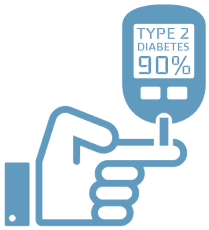
The content in this Topic Overview was last edited in July 2020. Papers in the Latest Research section and further resources are periodically updated.

Diabetes across the globe

Diabetes mellitus is a disease in which the body's ability to produce or respond to the hormone insulin is impaired, resulting in abnormal metabolism of carbohydrates and elevated levels of glucose in the blood. Type 1 diabetes is a condition in which the pancreas produces little or no insulin, whereas type 2 diabetes, the most common type of diabetes, is caused by a combination of inadequate production of insulin and an inability of the body to respond fully to insulin (insulin resistance). A third type of diabetes occurs only during pregnancy – so called gestational diabetes – which causes high blood glucose levels during pregnancy and usually disappears after childbirth[1].

Type 2 diabetes is mostly seen in adults but is increasingly being diagnosed in children and adolescents. Being overweight is a main cause of type 2 diabetes, which is influenced by lifestyle factors such as poor diet, lack of physical activity, and excessive alcohol consumption[1]. The presence of higher blood sugar levels, but not at the level required for diagnosis of type 2 diabetes, is often termed 'pre-diabetes'[14].

In 2019, approximately 463 million people were living with diabetes (type 1 and 2) globally. This is predicted to increase to 700 million by 2045[14]



Type 2 diabetes is the most common type of diabetes, accounting for around 90% of all cases worldwide[14]

8.9%

In Europe, about 59 million people have diabetes (types 1 and 2), representing 8.9% of the population aged 20–79 years: it is estimated that this figure will reach 68.1 million by 2045[14]

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What are the associations between coffee intake and type 2 diabetes?

The body of evidence from epidemiological studies suggests that drinking 3-4 cups of coffee per day is associated with an approximate 25% lower risk of developing type 2 diabetes, compared to consuming none or less than 2 cups per day[2-4,6-8,15-27]. Research also suggests a dose response relationship[3,4,6-8].

Three large data sets are of particular note:

- A 2002 cohort study of 17,111 Dutch men and women suggested that coffee consumption was associated with a substantially lower risk of clinical type 2 diabetes[2].
- A 2009 systematic review with a meta-analysis of 457,922 individuals and 21,897 newly-diagnosed cases of type 2 diabetes from eight different countries showed a statistically significant inverse association between coffee consumption and subsequent risk of type 2 diabetes[3].
- A further meta-analysis published in 2018 with 1,185,210 participants and 53,018 incident type 2 diabetes cases suggested that those in the highest category of coffee consumption (an average of 5 cups per day) had a 29% lower risk of type 2 diabetes compared with those who did not drink coffee[4].

These results are supported by additional studies and reviews.

- Epidemiological studies from different countries have also confirmed the inverse association with coffee consumption[15-27].
- Interestingly, a 10 year follow-up study from Greece, published in 2015, highlighted the significance of habitual coffee drinking in relation to diabetes onset. The authors concluded that habitual coffee drinking, at a level of at least 250 ml/day, versus abstention, was found to exhibit significant protection against diabetes development, decreasing the risk of developing diabetes by more than 50% in this study[13].
- A 2018 study of adults aged 20-70 years with low levels of coffee consumption (the majority consuming 1 cup of coffee per week) suggested that a lower risk of both pre-diabetes *and* type 2 diabetes was observed in coffee drinkers compared to non-drinkers[28].

What have dose response studies shown us?

A number of studies and reviews suggest that the relationship between coffee consumption and type 2 diabetes is dose dependent:

- A dose response analysis, from a 2009 systematic review, concluded that every additional cup of coffee, up to 6-8 cups per day, was associated with a 5-10% lower risk of developing type 2 diabetes; and that drinking 3-4 cups of coffee per day was associated with an approximate 25% lower risk of developing type 2 diabetes, compared to consuming none or less than 2 cups per day[3].
- A meta-analysis of prospective studies suggested a 12% reduction in risk of type 2 diabetes for every additional two cups of coffee per day, and a 14% reduction for every 200mg increment of caffeine per day. This review also suggested that the effect was stronger in women than men[6].
- Another 2014 systematic review and dose response analysis concluded that the risk of diabetes was reduced by a percentage of, respectively: 8, 15, 21, 25, 29 and 33% for 1-6 cups of coffee per day[7].
- A further study in 2014 concluded that participants who increased coffee intake by more than one cup per day over a 4 year period had a 12% lower risk of type 2 diabetes, whilst those who decreased coffee consumption by one cup per day had a 18% greater risk of type 2 diabetes[26].
- And, more recently, a 2018 meta-analysis also suggested that the risk of type 2 diabetes decreased by 6% for each cup-per-day increase in coffee consumption[4].

What effect does decaffeinated coffee have on the risk of developing type 2 diabetes?

Interestingly, as with caffeinated coffee, the majority of published studies that have evaluated the relationship between decaffeinated coffee and risk of type 2 diabetes have reported similar inverse associations[3,6-8].

In fact, a 2014 meta-analysis of prospective studies concluded that in addition to an effect with caffeinated coffee, an 11% reduction for every 2 additional cups of decaffeinated coffee a day was also observed[6].

Two specific studies both published in 2010 – a French study[18] and a large US study with African American women[19] – also looked at the association between type 2 diabetes and decaffeinated coffee. While the French study confirmed an association[18], the US one did not report a correlation[19].

And a multi-ethnic cohort study, in 2014, which also considered the effects of gender on the caffeine/type 2 diabetes association, suggested that caffeinated coffee consumption was much more protective against diabetes in women of all ethnic groups than in men (where the effect was present but smaller); but also that this finding did not apply to decaffeinated coffee[20].

What are the potential mechanisms behind the association between type 2 diabetes and coffee consumption?

Researchers have yet to discover a plausible mechanism to explain the associations between consumption of regular coffee or decaffeinated coffee and a lower risk of developing type 2 diabetes. However, there are a number of potential mechanisms that have been proposed.

Caffeine
Since coffee and tea are the main sources of caffeine in the diet in most countries, it is difficult to separate the potential effect of caffeine from coffee per se. However, since decaffeinated coffee is reported to have a similar size association as regular coffee, it is unlikely that caffeine plays a major role in the inverse association for development of type 2 diabetes[3,6-8].

Paradoxically, research has suggested that an acute (typically short-term, high-level) dose of caffeine intake leads to glucose intolerance and insulin insensitivity, while chronic (typically longer-term, low-level) caffeine intake has only a small effect on glucose metabolism[29,30].

One study looked more closely at the effect of acute caffeine doses on glucose tolerance in women with or without gestational diabetes mellitus. Caffeine did not affect glucose and insulin levels in the group *without* gestational diabetes, but it did impair insulin sensitivity in women *with* gestational diabetes[31].

Constituents within coffee
Coffee contains many other constituents, such as polyphenols which include chlorogenic acids (CGAs). Research suggests that these components may have an effect on glucose metabolism, and may be associated with a reduced risk of developing type 2 diabetes.

Polyphenols in coffee
- An analytical study of key biomarkers for diabetes suggested that coffee polyphenols may have anti-diabetic effects, but further replications with large samples of both genders were recommended[32].
- Some preliminary human studies and clinical trials have suggested that individual polyphenols in coffee may have specific effects, including improvement of glycemic control in subjects with insulin resistance, reduction of blood glucose and HbA1c levels and the improvement of insulin secretion and resistance. However, further work in this area is required to clarify these effects[33].
- Research suggests that the chlorogenic acids (CGAs), a type of polyphenol, may downregulate fasting glucose and plasma glucose peak in glucose tolerance tests by attenuating intestinal glucose absorption[34].
- One study showed that CGA may reduce early glucose and insulin levels at 15 minutes in oral glucose tolerance tests (OGTT) although decaffeinated soluble coffee showed no effect in this test[9]. Additionally, a further study suggested that coffee intake was positively associated with fasting and the first hour insulin levels and inversely associated with 2nd and 3rd hour plasma glucose levels during the OGTT[35].

- Two literature reviews have also suggested that CGA may have a significant impact on glucose metabolism regulation and, therefore, on related disorders including diabetes[9,10].
- Additionally, researchers have suggested that CGA may be involved in both lipid and glucose metabolism regulation and may be associated with a lower risk of hepatic steatosis, cardiovascular disease, and diabetes. It may also have hepato-protective effects by protecting from chemical or lipopolysaccharide-induced injuries[36].
- A 2020 review of the role of chlorogenic acid and metabolites on glycaemic responses suggested that there is no direct effect of CGAs on post-prandial blood glucose or insulin, but some effects are observed on glucose absorption and utilisation. The study concluded that although chlorogenic acids do not seem to affect carbohydrate digestion directly, they may affect glucose absorption and subsequent utilisation[37].

Antioxidants

- It has been suggested that coffee may also contribute to the total antioxidant load of the diet, and in turn may help to limit oxidative stress and consequently, the development of type 2 diabetes[38,39]. This potential role for coffee is interesting, but the hypothesis has not yet been verified.

What other factors might be behind the association?

A number of additional research papers have tried to answer this question.

- **Genetic polymorphisms**
  The effect of certain genetic polymorphisms (the existence of several alternative DNA states, or alleles, at a defined position in the genome, or locus) on associations between coffee intake and type 2 diabetes was considered in a 2016 review, suggesting that the evidence for a reduced risk of type 2 diabetes in coffee drinkers may be limited when taking into account the genetic profile[40].

- **Additions to coffee**
  Research in a group of pre-diabetic patients concluded that diabetes progression was lowest in patients who drank black coffee three or more times per day. The study also considered the impact that typical additions to coffee, like creamer and sugar, had; and concluded that whilst the risk was lower for the patients who typically consumed black coffee than for those who mixed creamer and sugar into their coffees, the difference was not significant[27].

- **Postprandial effects**
  Research has suggested that coffee could partly inhibit postprandial hyperglycemia, and in turn may prevent the occurrence of type 2 diabetes[41]. A later study suggested that the time of drinking coffee may play a distinct role in glucose metabolism, with the authors reporting the strongest association for coffee consumed at lunchtime[18].

- **Insulin Sensitivity**
  According to a cross-sectional multi-ethnic study amongst 954 non-diabetic adults, the effect of caffeinated coffee was positively related to insulin sensitivity and decaffeinated coffee was favourably related to pancreatic beta-cell function[42]. However, a randomised control study suggested that consuming 4 cups of caffeinated coffee a day for 24 weeks had no significant effect on insulin sensitivity or biological mediators of insulin resistance[43].

- **Caffeine in those with diagnosed diabetes**
  A retrospective study, published in 2018, considered the effect of caffeine consumption in a group of patients already diagnosed with diabetes (both type 1 and type 2). The results suggested that caffeine from coffee was associated with a reduced all-cause mortality in women but not in men. The authors concluded that further research is required to understand the effect of caffeine consumption in men and women with diabetes in more detail[44].

What effect does coffee have on the inflammatory markers associated with type 2 diabetes?

A correlation has been observed between subclinical inflammation, a low level of inflammation, and glycaemic control in patients with type 2 diabetes mellitus, which suggests that such inflammation may play a role in the progress of diabetes. Serum amyloid A is a type of lipoprotein that may be associated with chronic inflammation in the body.

- A Finnish study tested the effects of progressively increasing coffee consumption in obese volunteers in a medium term intervention trial (in the first month, participants abstained from coffee, for the second month 4 cups of coffee were consumed per day and in the third month, participants had 8 cups per day). No effects in the OGTT were seen. Coffee consumption appeared to have beneficial effects on some markers of subclinical inflammation, considered to be risk factors for type 2 diabetes[12].
- And a Greek study, which controlled for oxidative stress and inflammatory biomarkers, suggested that the inverse association between habitual coffee drinking and diabetes was found to be mediated by serum amyloid A levels[13].

Is there an association between coffee drinking and liver function?

A number of researchers have considered associations between coffee consumption, type 2 diabetes, liver function and metabolic syndrome.

- In 2011, researchers at Harvard conducted a randomised controlled trial looking at the effects of caffeinated and decaffeinated coffee on biological risk factors for type 2 diabetes. They compared participants who consumed either 5 cups per day of soluble caffeinated coffee, decaffeinated coffee, or no coffee for 8 weeks. Compared with consuming no coffee, consumption of caffeinated coffee increased adiponectin and interleukin-6 concentrations, possibly reflecting anti-inflammatory and insulin sensitizing effects, whilst consumption of

decaffeinated coffee decreased fetuin-A concentrations, a biomarker for inflammation and liver function. No significant differences were found between treatment groups for measures of glucose tolerance, insulin sensitivity and insulin secretion. The authors concluded that improvements in adipocyte and liver function, as indicated by changes in adiponectin and feutin-A concentrations, may contribute to beneficial metabolic effects of long-term coffee consumption[45].

- Coffee consumption has also been related to a decreased risk of type 2 diabetes mellitus among those with high levels of serum γ-glutamyltransferase, an enzyme found mainly in the liver that is typically used as a marker for liver disease. A 2012 study in a Japanese population examined the association between coffee and glucose tolerance and the effect of modification of serum γ-glutamyltransferase on this association. These authors found coffee drinking to be protective against glucose intolerance. Furthermore, they suggested that the observed possible effect modification of serum γ-glutamyltransferase on the protective association between coffee and type 2 diabetes warrants further research[46].

Have any other potential mechanisms been studied?

A number of other mechanisms, which might explain the association between type 2 diabetes and coffee consumption, have been studied, and whilst the results are not detailed enough to enable firm conclusions to be reached, the insights are varied and fascinating and give hint of the complex nature of systems within our bodies.

- A Japanese study investigated a possible association between psychological factors and diabetes, reporting that the risk of diabetes increased with an increasing stress level, especially among men; and among women who showed an increasing level of type A behaviour (i.e. behaviour patterns linked to competitive drive, speed and impatience, aggressiveness and irritability)[47]. This study also observed an inverse association between coffee consumption and incidence of diabetes. Interestingly, further research has suggested that coffee consumption was inversely associated with depressive symptoms amongst a group of patients with type 2 diabetes. The authors suggested this might be due to biologically active compounds in coffee in addition to caffeine[48].

- A US case-control study on postmenopausal women examined whether plasma levels of sex hormones and sex hormone-binding globulin (SHBG) could account for the inverse association between coffee consumption and type 2 diabetes risk, building on data that implicated the important roles of sex hormones in the development of type 2 diabetes. SHBG may directly mediate intracellular signalling of sex hormones. The study found a correlation between coffee consumption and plasma levels of SHBG. This association was not, however, found for decaffeinated coffee and tea. The authors note that these findings suggest SHBG may account for the inverse association between caffeinated coffee and type 2 diabetes risk[49].

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