



# coffee&health

from the institute for scientific information on coffee

## Good things in life: Can coffee help in type 2 diabetes risk reduction?

November 2014

### Contents

	Page
1 Introduction	2
2 Epidemiological evidence	3
3 Clinical intervention trials	4
4 Clinical parameters	5
5 Underlying mechanisms	6
6 Conclusions	7



## Institute for Scientific Information on Coffee (ISIC)

The Institute for Scientific Information on Coffee (ISIC) is a not-for-profit organisation, established in 1990 and devoted to the study and disclosure of science related to “coffee and health.” Since 2003 ISIC has also supported a pan-European education programme, working in partnership with national coffee associations in nine countries to convey current scientific knowledge on “coffee and health” to healthcare professionals.

ISIC respects scientific research ethics in all its activities. ISIC’s communications are based on sound science and rely on evidence and scientific studies derived from peer-reviewed scientific journals and other publications.

[www.coffeandhealth.org](http://www.coffeandhealth.org)

## 1. INTRODUCTION

More than 380 million people worldwide have diabetes, making it one of the world’s most significant health problems. By 2035 it is projected that this will have risen to 592 million people. \$548 billion were spent globally as a result of diabetes during 2013 (11% of total health spend on adults)<sup>1</sup>. The World Health Organisation predicts that deaths caused by diabetes will double between 2005 and 2030<sup>2</sup>.

In Europe there are approximately 60 million people with diabetes, which amounts to 10.3% of men and 9.6% of women aged 25 years and over. Of this, an estimated 50% of cases may remain undiagnosed, which means that 30 million Europeans are unaware that they have diabetes. It is predicted that by 2030 the number of people with diabetes in the EU will rise to 64 million<sup>2</sup>.

Once a disease of old age, type 2 diabetes is now increasingly affecting younger people and the highest increase is in the 30-40 year old age group<sup>3</sup>.

The twin epidemics of obesity and type 2 diabetes already represent the biggest public health challenge of the 21st century. It is estimated that at least half of all type 2 diabetes cases would be eliminated if weight gain in adults could be prevented<sup>4</sup>.

Type 2 diabetes is characterised by high blood glucose, together with insulin resistance and relative insulin deficiency. Type 2 diabetes is primarily influenced by lifestyle factors such as diet, physical activity, obesity and age.

Coffee is a widely consumed beverage and research suggests that coffee consumption may help to reduce the risk of developing type 2 diabetes.

This summary of up to date research into coffee and type 2 diabetes is based on a report from the World Congress on Prevention of Diabetes held in 2012, updated to include the latest research in this area.



## 2. EPIDEMIOLOGICAL EVIDENCE

Epidemiological evidence shows that drinking three to four 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 two cups per day<sup>5</sup>.

An early study, published more than ten years ago<sup>6</sup>, investigated the association between coffee consumption and risk of type 2 diabetes in a cohort of 17,111 adults aged 30-60. Over the follow up period, 360 new cases of type 2 diabetes were identified and after adjusting for potential confounders, individuals who drank at least seven cups of coffee a day were half as likely to develop type 2 diabetes than those who drank two cups or fewer. A more recent study among a population-based cohort of middle-aged Chinese people<sup>7</sup>, also found coffee intake to be inversely associated with type 2 diabetes.

Furthermore, two review papers, both published in 2012, add to the existing body of evidence suggesting that habitual coffee consumption is associated with a lower risk of type 2 diabetes<sup>8,9</sup>. The first systematic review<sup>8</sup> concluded that habitual coffee consumption is associated with a lower risk of type 2 diabetes. Participants who drank four to six cups and more than six to seven cups of coffee per day had a lower risk of type 2 diabetes compared with those who drank less than two cups per day. The authors concluded that more detailed studies of coffee consumption, including appropriate measures of postprandial hyperglycemia and insulin sensitivity, are required. A second review<sup>9</sup> discussed the strength of this relationship and assessed the possible mechanisms by which coffee components might affect diabetes development, especially in light of the paradoxical effect of caffeine on glucose metabolism (see section 5 for more information on underlying mechanisms).

### 2.1. Dose response

Research has also suggested a dose response effect of drinking coffee and its possible protection against type 2 diabetes. A systematic review with meta-analysis<sup>5</sup> studied the available prospective epidemiological studies on type 2 diabetes and coffee from eight different countries. The results showed a statistically significant inverse association between coffee consumption and subsequent risk of type 2 diabetes, with each additional cup of coffee reducing the relative risk by 7-8%. A 2013 meta-analysis has supported this effect, in a dose-response analysis the researchers found that the incidence of type 2 diabetes decreased by 12% for every 2 additional cups per day of coffee<sup>10</sup>. A further 2014 meta-analysis suggested that consumption of both caffeinated and decaffeinated coffee were inversely associated with the risk of type 2 diabetes in a dose response fashion<sup>11</sup>.

Additionally, a large US prospective cohort study showed that increasing coffee consumption by one cup per day over a 4 year period resulted in an 11% lower risk of type 2 diabetes in the subsequent 4 years. Those who decreased coffee intake by one cup per day had a 17% higher risk of type 2 diabetes<sup>12</sup>.

### 2.2. Coffee and type 2 diabetes risk factors

Observational studies have also shown that coffee consumption can have an impact on risk factors for type 2 diabetes. For instance, research has found that coffee consumption is associated with lower C-peptide, especially in the overweight or obese<sup>13</sup>, with higher levels of adiponectin<sup>11</sup> and with lower levels of inflammatory markers<sup>14</sup>.

### 2.3. Time of consumption

Research has also suggested that the time of coffee consumption could play a distinct role in glucose metabolism. One prospective cohort study of 69,532 French women examined the long-term effects of coffee on type 2 diabetes and found drinking coffee, especially at lunch time, reduced the risk of developing diabetes.



### 2.4. Coffee type

Whilst the majority of research has been conducted on caffeinated filtered coffee, there have also been epidemiological studies that have identified an inverse association between boiled coffee<sup>15,16</sup> and decaffeinated coffee<sup>5</sup>. Research published in 2012<sup>17</sup> supported the earlier work suggesting that both caffeinated and decaffeinated coffee are associated with a lower risk of type 2 diabetes whilst further recent work<sup>8</sup> showed an advantage of filtered coffee over pot boiled, decaffeinated coffee over caffeinated coffee and a stronger inverse correlation in those under 60 years age group. However, recent results from the Hawaii component of the Multiethnic Cohort<sup>18</sup> suggested that regular but not decaffeinated coffee was much more protective against type 2 diabetes in women of all ethnic groups than in men. Additionally, a 2014 meta-analysis suggested that consumption of both caffeinated and decaffeinated coffee is associated with a lower risk of type 2 diabetes<sup>10</sup>. Further research is required in this area to confirm the associations.

## 3. CLINICAL INTERVENTION TRIALS

Whilst studies have clearly illustrated an association between coffee consumption and reduced type 2 diabetes risk, a definite causal relationship is yet to be established. Clinical intervention trials are helping to establish this.

### 3.1. Single dose studies

Studies have investigated the effect of a single dose of coffee on glucose metabolism. These have shown no beneficial effects in oral glucose tolerance tests (OGTT), however some studies have shown a modest increase in insulin resistance, attributed to caffeine. One prospective randomised controlled trial<sup>19</sup>, tested glucose and insulin after an oral glucose tolerance test with 12g decaffeinated coffee, 1g chlorogenic acid, 500 mg trigonelline, or placebo. This study demonstrated that chlorogenic acid, and trigonelline reduced early glucose and insulin responses, and contribute to the putative beneficial effect of coffee.

### 3.2. Longer term coffee consumption

Research assessing longer term coffee consumption in overweight males<sup>20</sup> has suggested that both caffeinated and decaffeinated coffee are associated with a modest decrease in post load glucose levels, with the authors concluding that coffee may be protective against deterioration of glucose tolerance. This is supported by a study<sup>21</sup>, which also found coffee drinking to be protective against glucose intolerance in a cohort of middle-aged Chinese men.

A review of randomised controlled trials (RCTs) investigating the effects of caffeine on blood glucose and/or insulin sensitivity in humans, diagnosed with type 1, type 2 or gestational diabetes mellitus (GDM)<sup>22</sup>, suggested that caffeine has a negative effect on blood glucose control in individuals with type 2 diabetes, but the authors concluded that further work was required.



## 4. CLINICAL PARAMETERS

Drinking coffee is often linked to unhealthier habits, such as smoking and low levels of physical activity, yet counter intuitively it has also been associated with a reduced risk of type 2 diabetes. So how significant are clinical parameters relating to coffee and type 2 diabetes?

### 4.1. Coffee and hormones

Coffee consumption has been demonstrated to increase levels of the hormone adiponectin, which has been shown to increase insulin sensitivity. This effect has been observed in both diabetic and non-diabetic individuals<sup>14</sup>.

### 4.2. Coffee and chronic diseases

In addition to its possible effects on type 2 diabetes, research suggests that coffee does not increase the risk of certain chronic diseases. In fact, it is inversely associated with some cancers, including bladder, breast, colorectal, liver, pancreas, and prostate cancers. This is important to note, as individuals with type 2 diabetes also have an increased risk of developing certain cancers.

### 4.3. Coffee, cholesterol and cardiovascular disease

Some research has shown that unfiltered, but not filtered, coffee increases serum levels of total and LDL cholesterol<sup>23,24</sup>. However, in a small clinical trial, a beneficial effect on HDL cholesterol levels was demonstrated amongst coffee drinkers<sup>25</sup>. Also, despite a high circulating cholesterol being a key risk factor for cardiovascular disease (CVD), other studies have illustrated that coffee consumption is not associated with an increased risk of hypertension, stroke or coronary heart disease<sup>26,27,28</sup>. Research in patients with CVD has also shown that moderate coffee consumption is inversely associated with risk of heart failure, with a J-shaped relationship<sup>29</sup>. Additional support for this is provided by a ten year follow up study<sup>30</sup> in which coffee consumption was associated with a lower risk of coronary heart disease mortality. Furthermore, in diabetic patients coffee consumption was not associated with increased risk for CVD or premature mortality among diabetic women<sup>31</sup>.

### 4.4. Coffee and the liver

A healthy liver helps keep blood glucose within the 'normal range' and protects against diabetic complications. Coffee consumption is also associated with higher levels of fetuin-A, a biomarker for inflammation and liver function. It is a glycoprotein secreted by the hepatocytes with effects on insulin signaling via inhibition of the insulin receptor tyrosine kinase in both liver and skeletal tissue<sup>32,33</sup>. Indeed, a recent randomized control trial<sup>34</sup> concluded that improvements in adipocyte and liver function as indicated by changes in adiponectin and fetuin-A concentrations may contribute to the beneficial metabolic effects of long-term coffee consumption.

Additionally, cross sectional studies have shown coffee consumption to be linked with lower levels of markers of liver damage<sup>5</sup> and a significant reduction in risk of fibrosis among Non Alcoholic Steatohepatitis patients<sup>36</sup>.



## 5. UNDERLYING MECHANISMS

### 5.1. The Coffee Conundrum

Coffee consumption has been associated with a decreased risk of developing type 2 diabetes, however a causal relationship has yet to be established. In order to explain this relationship, there are two key questions that need to be answered:

#### 5.1.1. What is the physiology?

There are a number of potential physiological processes that may lead to the reduced risk of type 2 diabetes. For example, it could be due to energy metabolism, where by coffee consumption causes an increase in calorie burning, or perhaps coffee affects glucose metabolism causing the body to handle glucose differently. A 2014 review<sup>38</sup> suggested that caffeine may cause alterations in glucose metabolism, decreasing glucose uptake and causing elevations in blood glucose. Other effects include potential increases in hormones such as epinephrine, which decreases peripheral glucose disposal. Despite these potential effects the authors concluded that increased coffee intake is associated with a reduced risk of type 2 diabetes.

Alternatively, coffee could affect insulin sensitivity in the body. For example, a Singapore Prospective Study<sup>37</sup> found an inverse association between coffee consumption and HOMA-IR, a well recognised marker of insulin resistance. A 2014 study of Japanese men using the same marker also suggested that higher coffee consumption may be protective against insulin resistance in normal weight individuals<sup>39</sup>. A further cross-sectional study<sup>40</sup> showed that caffeinated coffee was positively related to insulin sensitivity and decaffeinated coffee was favourably related to measures of beta cell function. Another possibility is that it could simply be an effect of calorie displacement, where choosing coffee over a sugary drink leads to a reduction in calorie consumption.

#### 5.1.2. What coffee compounds are responsible?

The second challenge is to identify the compounds within coffee which are causing the effect. It could be a known bioactive component in coffee, or even a bioactive substance that has yet to be identified. Alternatively it could be a nutrient such as a specific vitamin or mineral. Caffeine has been suggested as the ingredient responsible for the beneficial effects. Again, it is also possible that the effect is the result of the absence of a substance, caused by displacement by drinking coffee in place of other beverages.

Although a consensus has yet to be reached regarding the mechanisms that underlie the association between coffee consumption and type 2 diabetes, a number of plausible theories exist. These include, but are not limited to, the following three hypotheses.

### 5.2. Energy Expenditure Hypothesis

One theory is that caffeine stimulates metabolism and increases energy expenditure. Caffeine acts as an antagonist to adenosine receptors, which play an important role in energy transfer. This effect leads to a build up of cAMP concentration which, in turn, increases the basal metabolic rate – this can lead to a net increase in calories burnt of up to 150 cal/day. However, the limitation of this theory is that experimental data suggests that high levels of caffeine are required, in the region of 600-1200mg/day. This is the equivalent of 6-12 cups of coffee per day.

### 5.3. Carbohydrate Metabolic Hypothesis

Another mechanistic theory has suggested that chlorogenic acid in coffee may play an important role by influencing the glucose balance within the body. This is because chlorogenic acid may inhibit carbohydrate digestion or glucose absorption, which causes glucose concentrations in the liver to decrease. This is thought to modify the responses of certain hormones that cause an increase in the amount of insulin released.



### 5.4. Insulin Sensitivity Hypothesis

There is also a subset of potential mechanisms relating to insulin sensitivity.

#### 5.4.1. Anti inflammation

Coffee contains components that may modulate inflammatory pathways in the body leading to improved insulin sensitivity. Potential components that have been identified include Caffeic acid phenethyl ester, diterpenes or 3-methyl-1,2-cyclopentanedione.

#### 5.4.2. Antioxidants

Coffee contains antioxidants, such as chlorogenic acid and N-methylpyridium, and these have been shown to mediate the oxidative stress of cells and improve insulin sensitivity.

#### 5.4.3. Hormonal effects

Some components found in coffee may interact with cortisol metabolism. One in vitro study found that an undetermined bioactive component in coffee caused a decrease in cellular cortisol concentrations, which could improve insulin sensitivity.

#### 5.4.4. Iron Chelation

Coffee contains phenolics and melanoidins in coffee that may chelate iron. Studies have suggested that a reduction in iron stores may improve insulin sensitivity or cardiovascular health.

## 6. CONCLUSIONS

The research outlined in this report suggests that regular moderate coffee consumption may actually decrease an individual's risk of developing type 2 diabetes. This effect has been linked with higher adiponectin levels, a decrease in inflammatory markers and reduced subclinical inflammation. Furthermore, a dose-dependent, inverse association between both coffee drinking and total mortality has been demonstrated in the general population, as well as among diabetics.

Studies have also found that drinking coffee does not increase cancer risk in the diabetic population, nor does it cause cardiovascular disease, hypertension or stroke. Although more research is needed to make firm conclusions, the findings suggest that coffee in moderation can be safely enjoyed by the healthy as well as by the diabetic population and might even be helpful in type 2 diabetes prevention.

**Further information on coffee and diabetes can be found on the Coffee and Health website: [www.coffeeandhealth.org](http://www.coffeeandhealth.org)**

## References

- 1 International Diabetes Federation (2013) The Global Burden, Diabetes Atlas, 6th Edition. Available at: [www.idf.org/sites/default/files/EN\\_6E\\_Ch2\\_the\\_Global\\_Burden.pdf](http://www.idf.org/sites/default/files/EN_6E_Ch2_the_Global_Burden.pdf).
- 2 The World Health Organization (2014) European Diabetes Fact Sheet. Available at: [www.euro.who.int/en/health-topics/noncommunicable-diseases/diabetes/data-and-statistics](http://www.euro.who.int/en/health-topics/noncommunicable-diseases/diabetes/data-and-statistics)
- 3 IMAGE (2010) Recommendations launched at the 6th World Congress on Prevention of Diabetes and its Complications, Dresden, Germany. Available at: [www.image-project.eu/Default.aspx?id=0](http://www.image-project.eu/Default.aspx?id=0)
- 4 The International Diabetes Federation (2004) *Diabetes & Obesity: Time to Act*.
- 5 Huxley R. et al. (2009) Coffee, Decaffeinated Coffee, and Tea Consumption in Relation to Incident Type 2 Diabetes Mellitus. *Arch Intern Med* 169:2053-63.
- 6 van Dam R.M. et al. (2002) Coffee consumption and risk of type 2 diabetes mellitus. *Lancet*. 360:1477-8.
- 7 Zhang Y. et al. (2011) Coffee consumption and the incidence of type 2 diabetes in men and women with normal glucose tolerance: The Strong Heart Study. *Nutr Metab Cardiovasc Dis*. 21(6):418-23.
- 8 Muley A. et al. (2012) Coffee to reduce risk of type-2 diabetes?: a systematic review. *Current Diabetes Reviews*. 8:162-8.
- 9 Natella F. & Scaccini C. (2012) Role of coffee in modulation of diabetes risk. *Nutrition Reviews*, 70 (4):207-217.
- 10 Jiang X. et al. (2014) Coffee and caffeine intake and incidence of type-2 diabetes mellitus: a meta-analysis of prospective studies. *European Journal of Nutrition*. 53(1):25-38.
- 11 Ding M. et al. (2014) Caffeinated and Decaffeinated Coffee Consumption and Risk of Type 2 Diabetes: A Systematic Review and a Dose-Response Meta-analysis, *Diabetes Care*. 37(2):569-86.
- 12 Bhupathiraju S.N. et al (2014) Changes in coffee intake and subsequent risk of type 2 diabetes: three large cohorts of US men and women. *Diabetologia*. 57(7):1346-1354.
- 13 Wu J. et al. (2005) Caffeinated Coffee, Decaffeinated Coffee, and Caffeine in Relation to Plasma C-Peptide Levels, a Marker of Insulin Secretion, in U.S. Women. *Diabetes Care*. 28(6):1390-1396.
- 14 Williams C.J. (2008) Coffee consumption is associated with higher plasma adiponectin concentrations in women with or without type 2 diabetes: a prospective cohort study. *Diabetes Care*. 31(3):504-507.
- 15 Sartorelli D.S. et al. (2010) Differential effects of coffee on the risk of type 2 diabetes according to meal consumption in a French cohort of women: the E3N/EPIC cohort study. *Am J Clin Nutr*. 91:1002-12.
- 16 Hjellevik V. et al. (2011) Boiled Coffee Intake and Subsequent Risk for Type 2 Diabetes. *Epidemiology*. 22(3):418-421
- 17 Bhupathiraju S.N. et al. (2012) Caffeinated and caffeine-free beverages and risk of type 2 diabetes, *Am J Clin Nutr*. 97(1):155-6.
- 18 Doo T. et al. (2013) Coffee intake and risk of type 2 diabetes: the multiethnic cohort. *Public Health Nutrition*, 1-9. Epub 2013/02/28. doi: 10.1017/S1368980013000487
- 19 Olthof M.R. et al. (2011) Acute effects of decaffeinated coffee and the major coffee components chlorogenic acid and trigonelline on incretin hormones. *Nutrition & Metabolism*. 8:10 .
- 20 Ohnaka K. et al. (2013) Effects of 16-week consumption of caffeinated and decaffeinated instant coffee on glucose metabolism in a randomized controlled trial, *Journal of Nutrition and Metabolism*, published online ahead of print.
- 21 Lin W.-Y. et al. (2011) Coffee consumption is inversely associated with type 2 diabetes in Chinese, *Eur J of Clin Invest*. 41(6):659-66.

- 22 Whitehead N. & White H. (2013) Systematic review of randomised controlled trials of the effects of caffeine or caffeine drinks on blood glucose concentrations and insulin sensitivity in people with diabetes mellitus, *Journal of Human Nutrition and Dietetics*, 26(2):111-25.
- 23 Jee S.H. et al. (2001) Coffee consumption and serum lipids: a meta-analysis of randomized controlled clinical trials. *Am J Epidemiol* 153:353.
- 24 Cai L. et al. (2012) The effect of coffee consumption on serum lipids: a meta-analysis of randomized controlled trials. *Eur J Clin Nutr.* 66(8):872-7.
- 25 Kempf K. et al. (2010) Influence of insulin resistance on the effect of coffee consumption on subclinical inflammation and lipids. *Am J Clin Nutr.* 91:950-957.
- 26 Lopez E. et al. (2011) Coffee consumption and mortality in women with cardiovascular disease. *Am J Clin Nutr.* 94(1): 218-224.
- 27 Zhang W.H. et al. (2009) Coffee consumption and risk of cardiovascular events and all-cause mortality among women with type 2 diabetes. *Diabetologia.* 52(5):810-817.
- 28 Ahmed H. et al. (2009) Coffee Consumption and Risk of Heart Failure in Men: an Analysis from the Cohort of Swedish Men *Am Heart J.* 158(4):667-672.
- 29 Mostofsky E. (2012) Habitual coffee consumption and risk of heart failure: a dose-response meta-analysis. *Circ Heart Fail.* 5(4): 401-5.
- 30 Greenberg J.A. et al. (2008) Caffeinated coffee consumption, cardiovascular disease, and heart valve disease in the elderly. *Am J Cardiol.* 102(11):1502.
- 31 Lopez E. et al. (2006) Coffee consumption and markers of inflammation and endothelial dysfunction in healthy and diabetic women. *Am J Clin Nutr.* 84(4):888-93.
- 32 Ix J.H. et al. (2008) Fetuin-A and incident diabetes mellitus in older persons. *JAMA.* 300(2):182-188.
- 33 Mori K. et al. (2006) Association of serum fetuin-A with insulin resistance in type 2 diabetic and non-diabetic subjects. *Diabetes Care.* 29(2):468.
- 34 Wedick N.M. et al. (2012) Effects of caffeinated and decaffeinated coffee on biological risk factors for type 2 diabetes: a randomized controlled trial. *Nutr J,* 19;11:86.
- 35 Homan D..J. and Mobarhan S. (2006) Coffee: good, bad, or just fun? A critical review of coffee's effects on liver enzymes. *Nutr Rev.* 64(1):43-46.
- 36 Molloy J.W. et al. (2012) Association of Coffee and Caffeine Consumption with Fatty Liver Disease, Non-alcoholic Steatohepatitis, and Degree of Hepatic Fibrosis. *Hepatology.* 55(2):429-36.
- 37 Rebello S.A. et al. (2011) Coffee and tea consumption in relation to inflammation and basalglucose metabolism in a multi-ethnic Asian population: a cross-sectional study. *Nutrition.* 10:61.
- 38 Zaharieva D.P. & Riddell M.C. (2013) Caffeine and glucose homeostasis during rest and exercise in diabetes mellitus, *Applied Physiology, Nutrition & Metabolism*, Aug;38(8):813-22.
- 39 Otake T. et al. (2014) Linking lifestyle factors and insulin resistance, based on fasting plasma insulin and HOMA-IR in middle-aged Japanese men: A cross-sectional study. *Scandinavian Journal of Clinical & Laboratory Investigation*, Sep;74(6):536-45.
- 40 Loopstra-Masters R.C. et al. (2011) Associations between the intake of caffeinated and decaffeinated coffee and measures of insulin sensitivity and beta cell function. *Diabetologia* 54(2):320-8.