

The Health Benefits of Coffee

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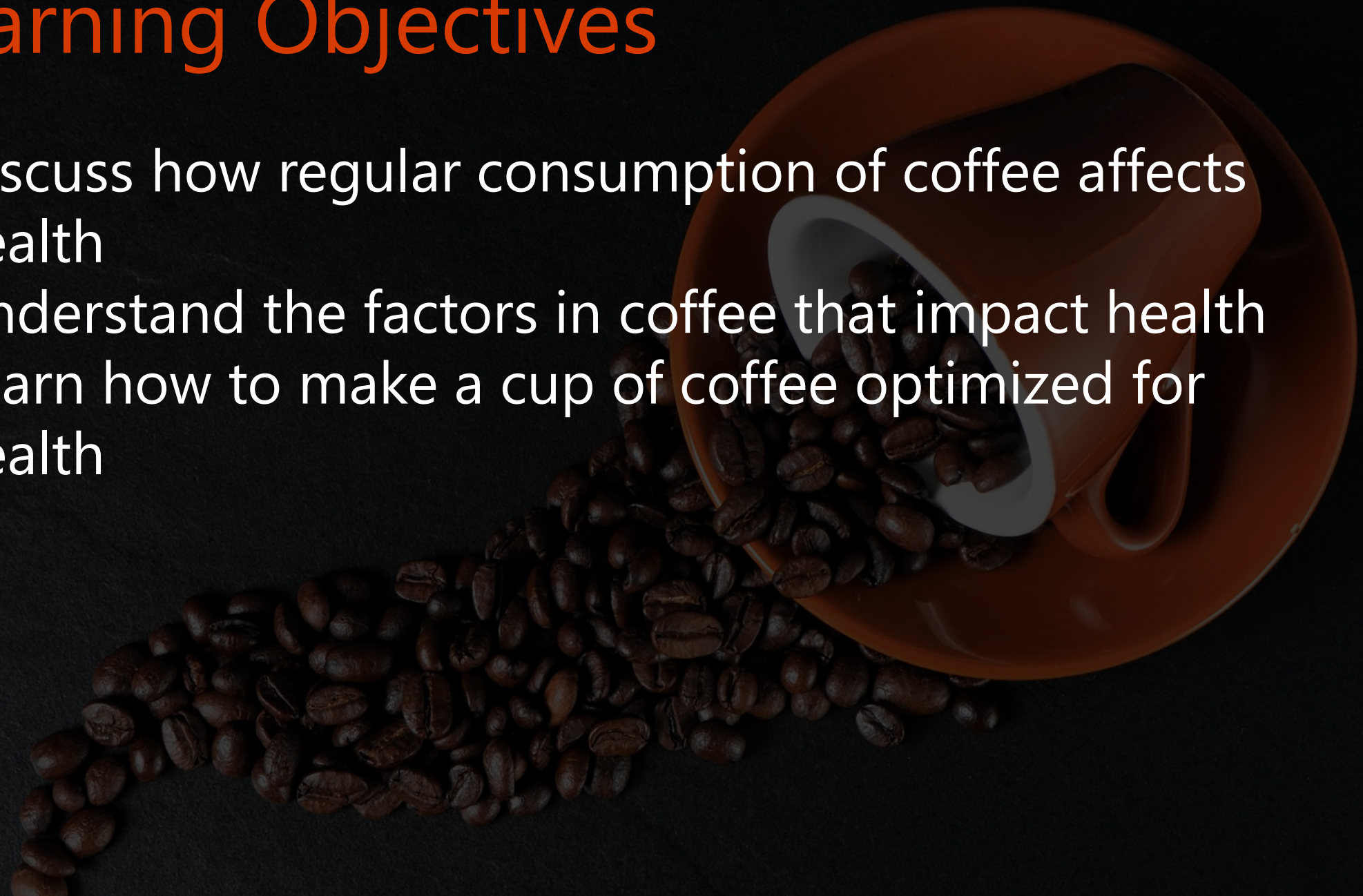
Disclosure

Before We Start: Every effort has been made to make this presentation free from commercial bias. Dr. Thomas owns Umble Coffee Co. No related products or services are discussed in this presentation. Any potential for conflict of interest was resolved through peer review of presentation content.

Learning Objectives

- Discuss how regular consumption of coffee affects health
- Understand the factors in coffee that impact health
- Learn how to make a cup of coffee optimized for health



THE HEALTH BENEFITS OF COFFEE

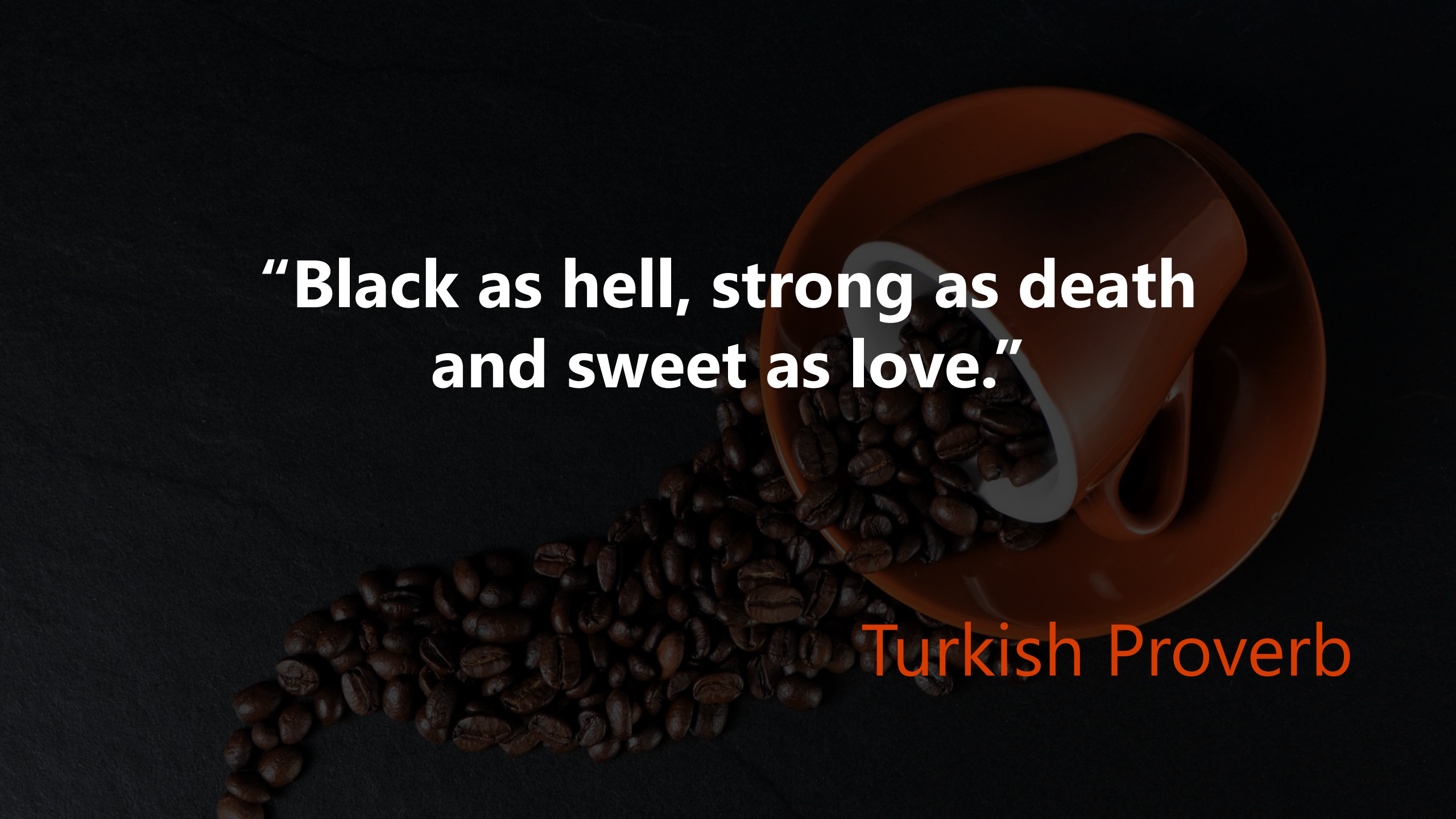
Introduction

- The myth
- What we know
- The process – bean to cup
- Where does health fit in?



The Myth

- Kaldi and his goats
  - Kaldi, a goat herder, one day observed some of his goats eating cherries from coffee trees
  - The goats then proceeded to dance
  - Kaldi decided to chew on some cherries himself and found it gave him more energy
  - He then took them to a local monastery where the monks saw this as a tool of the devil and promptly threw them in the fire
  - Instead of destroying the cherries, it roasted the beans and the first coffee was born!


“Black as hell, strong as death
and sweet as love.”
Turkish Proverb

What We Know

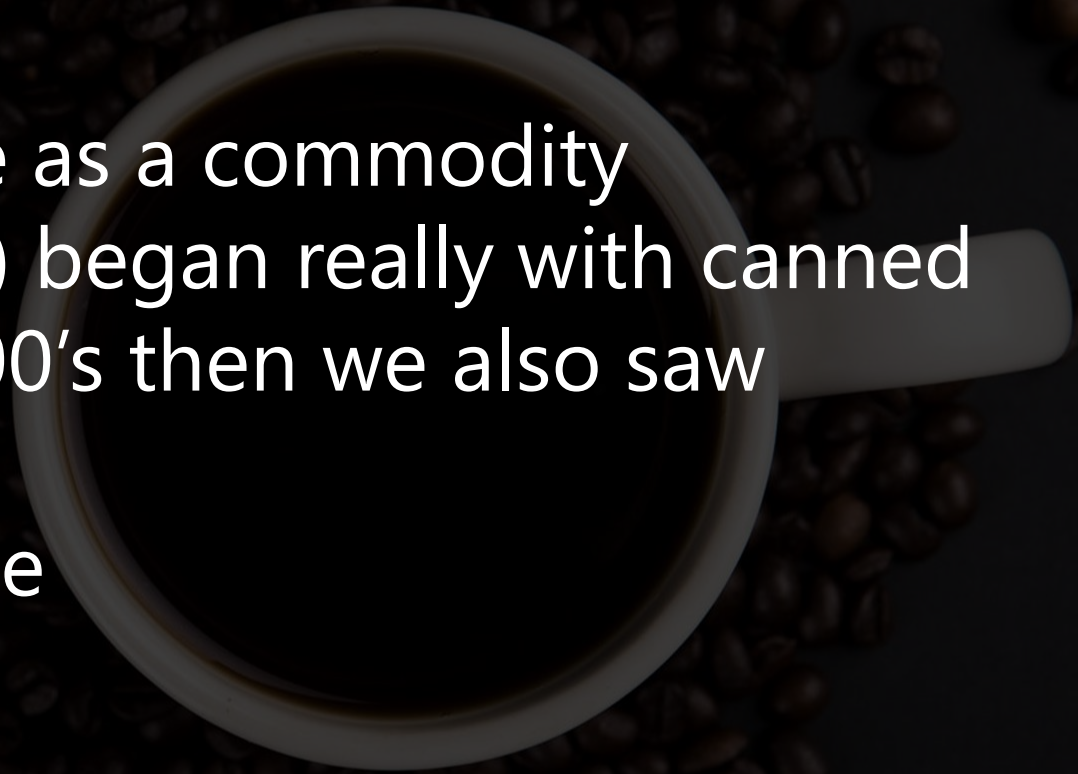
- Coffee likely originated in Ethiopia or Yemen
  - Drank originally around 600 AD as a crushed cherry for nomads before battles and muslim monks before all-night prayer vigils
- First used as a heated beverage around the 10th century in Turkey

What We Know

- The 1500s saw the first coffee houses and it was considered as vital as food and shelter (a Turksh woman could divorce her husband for not being able to provide it for her!)
- 1600s – Europeans loved coffee and, with the explosion of maritime shipping, coffee as an agricultural product began to branch out from it's origin.

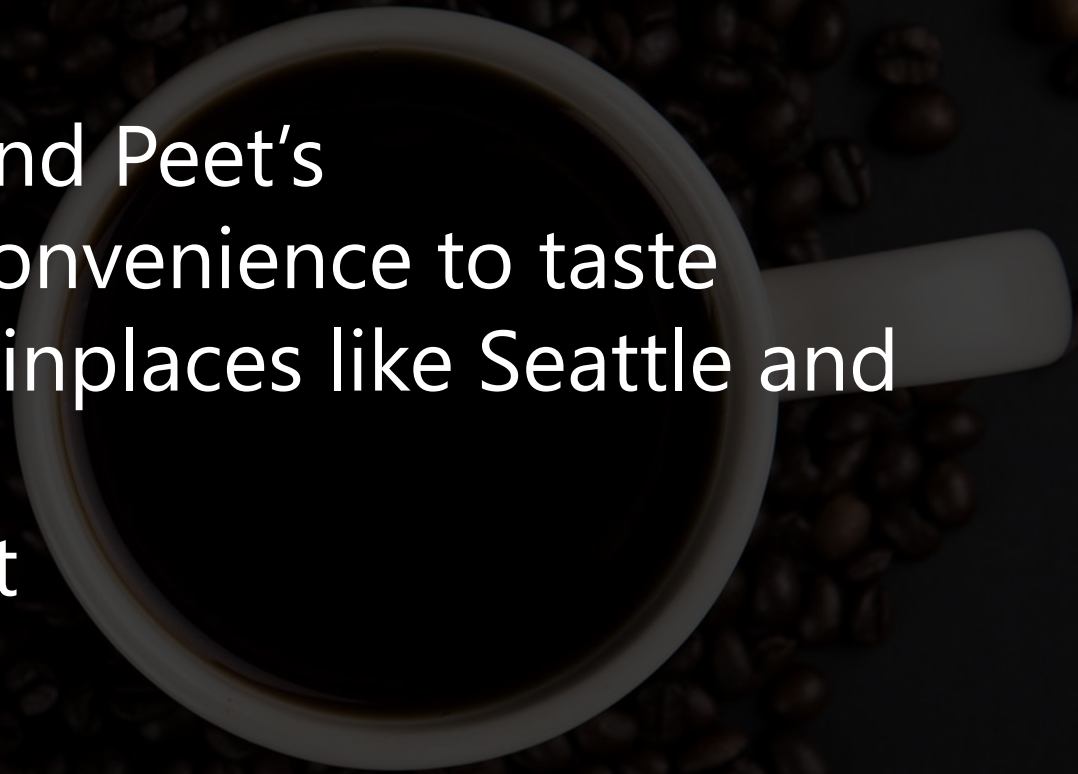
What We Know

- 1st Wave
  - Mass production of coffee as a commodity (convenience over quality) began really with canned coffees as early as the 1800's then we also saw vaccum packed bricks
  - Folgers and Maxwell house



What We Know

- 2nd Wave
  - 1970's – think Starbucks and Peet's
  - Focus shifted back from convenience to taste
  - A coffee culture emerged inplaces like Seattle and Boston
  - Traditionally a darker roast



What We Know

- 3rd Wave
  - Even more focus on craft and quality
  - Direct relationships - farmers, roasters, and shops
  - More focus on the taste qualities of a region rather than taste qualities of the roasting process…this means a lighter roast
  - The whole process, from harvest to roasting to brewing is treated like a fine wine or a craft beer
  - The big three – Counter Culture, Inteligensia, and Stumptown

THE HEALTH BENEFITS OF COFFEE



Picture courtesy of Cafe Imports

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Where Does Health Fit In?

- Especially during the last 20 years, a number of studies suggest that coffee likely exerts beneficial effects on health
- This is of great interest from a public health standpoint due to the high frequency of coffee consumption
  - It's the most widely traded agricultural commodity

Where Does Health Fit In?

- 64% of Americans drink at least 1 cup daily
- For years, doctors warned coffee may stunt growth, increase risk of heart disease, cause ulcers, heartburn etc
- …But turns out coffee wasn't to blame – cofactors including poor health, smoking, drinking and lack of physical activity weren't controlled for.

THE HEALTH BENEFITS OF COFFEE

How does regular coffee consumption impact health?

- Antioxidants
- Microbiome
- Cancer
- Liver Health
- Metabolism
- Cardiovascular Health
- Mental Health
- Detrimental Side Effects or Risks



Antioxidants

- Coffee is a great source of antioxidants and has anti-inflammatory actions
  - This can protect against subclinical inflammation and chronic disease triggered by inflammation like heart disease, stroke, type II diabetes and Parkinson's disease
- Coffee appears to attenuate inflammatory markers like interleukin 6, TNF-a, interferon-gamma, and transforming growth factor-B

Antioxidants

- The main coffee components exerting these effects are phenolic compounds (like chlorogenic acids), caffeine, diterpenes, trigonelline, and melanoidins.
- CGAs decrease production of inflammatory mediators through several mechanisms
- Cafestol and kahweol are naturally occurring diterpenes in coffee.
  - They increase expression of an enzyme used in endogenous synthesis of antioxidants AND increase glutathione production

Antioxidants

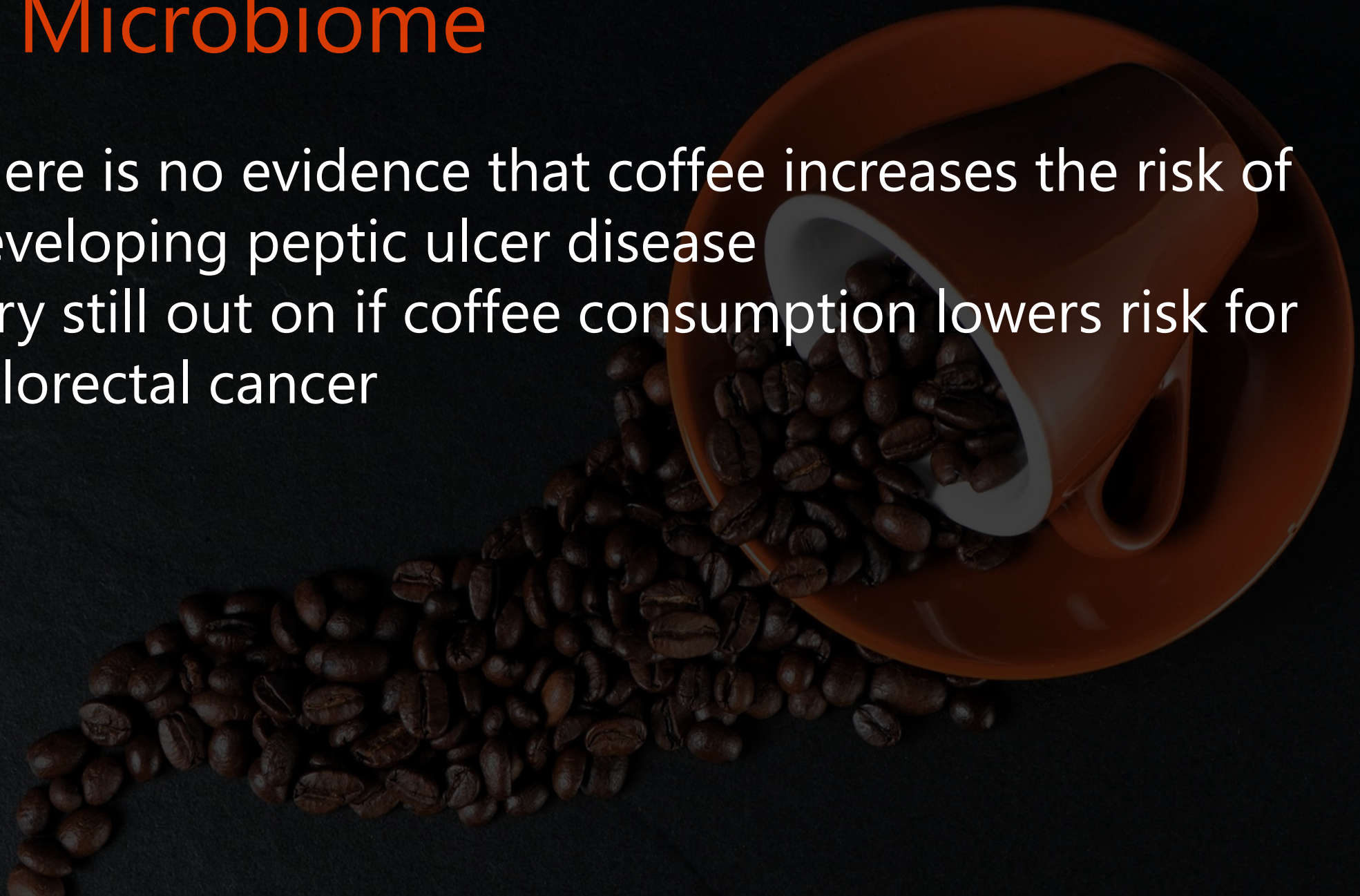
- Trigonelline (a plant alkaloid derivative of vitamin B6) upregulates antioxidant enzyme activity and decreases lipid peroxidation
- Melanoidins (byproducts of the roasting process (partial cause of the brown color) – antioxidant and anti-inflammatory activity through radical scavenging and/or metal chelating attributes

GI; Microbiome

- Coffee alters the gut microbiome
  - Induces changes in the structure and function of the gut microbiota, modifying the ratio among major phyla (Proteobacteria, Actinobacteria, Bacteroidetes, and Firmicutes) in favor of an anti-obese profile (i.e., decreased Firmicutes-to-Bacteroidetes ratio)
  - Bifidobacteria have been associated with anti-inflammatory effects, which, in turn, may mitigate local inflammation

GI; Microbiome

- There is no evidence that coffee increases the risk of developing peptic ulcer disease
- Jury still out on if coffee consumption lowers risk for colorectal cancer



Diabetes

- Coffee appears to be protective against type 2 diabetes
- It's not the caffeine that causes this, but we're unsure what does cause it
- That said, there's an 11% lower risk of developing type 2 diabetes compared to non-drinkers
- Suspect related in some way to how coffee affects metabolism

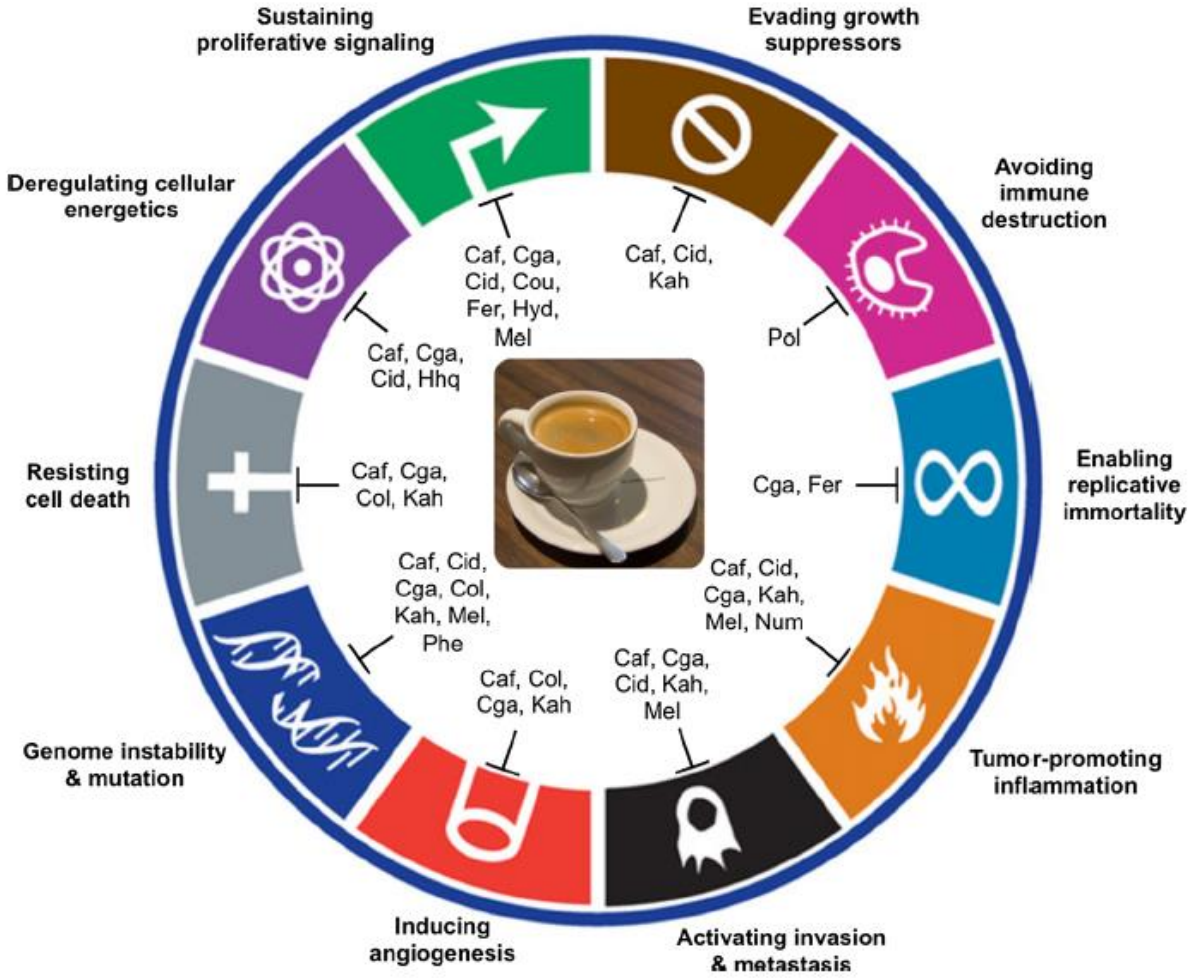
Cancer

- Coffee does NOT increase the risk of breast, ovary, pancreas, or kidney cancer
- The historic thought that coffee might increase the risk of bladder cancer now appears to be no increased risk but rather it was cigarette smoking leading to increased bladder cancer risk
- In one study, an increase in consumption of 1 cup of coffee per day decreased overall cancer risk by 3%

Cancer

- Coffee likely protects against colorectal, male breast, bladder, buccal, pharyngeal, endometrial, esophageal, hepatocellular, leukemic, pancreatic and prostate cancers
  - Part of this lower risk is directly related to caffeine because decaf drinkers in studies don't share the same lowered risk profile
- Suspect lowered risk mainly related to antioxidant and anti-inflammatory effects noted earlier

Natural compounds from coffee targeting the hallmarks of cancer



(Source: Genes Nutr (2015) 10:51)

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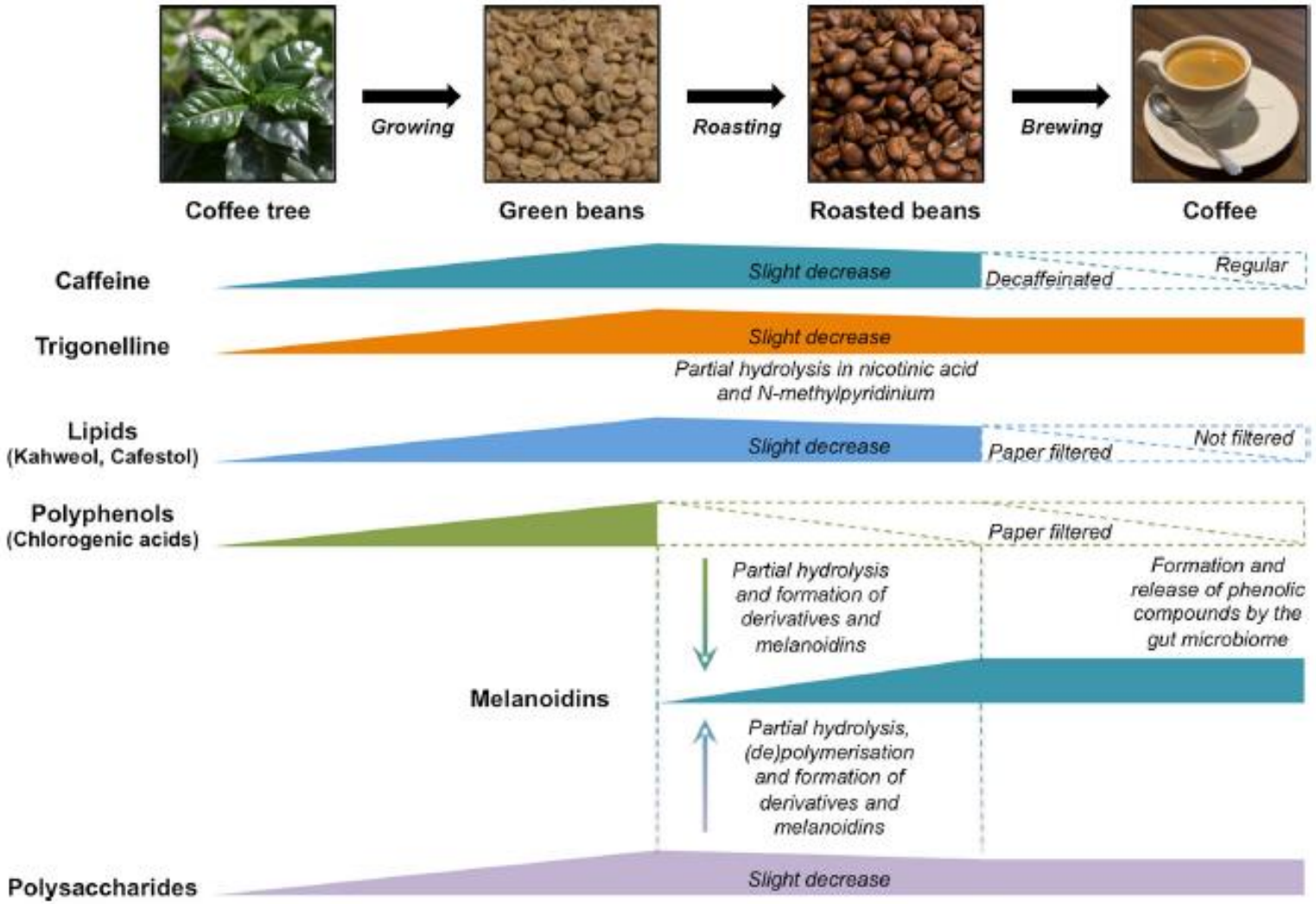

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Bone Health

- In a Korean study on 4,066 postmenopausal women, subjects in the highest quartile of coffee intake had 36% lower odds of osteoporosis compared to those in the lowest quartile

Liver Health

- Coffee protects against gallstone disease
- Coffee consumption is inversely connected with hepatic cirrhosis
- Its consumption has been associated with lower levels of AST, ALT, and GGTP. The effect is even more pronounced in patients with high risk of liver injury – obese, significant alcohol intake, diabetes, viral hepatitis

Liver Health

- Coffee has been shown to inhibit replication of hepatitis C
- Its protective against NAFLD
- Another study showed an association with coffee consumption and lower mortality in chronic liver disease patients

Liver Health

- 2-3 cups of coffee per day reduces risk of hepatocellular carcinoma by 38%
- Men who drank 2 cups of coffee per day had a risk of being affected by symptomatic gallbladder disease that was 60% lower than men who did not rink coffee
- The main mechanism proposed for coffee's hepatoprotection includes caffeine, phenols, and melanoidins

Metabolism & Longevity

- Coffee increases the metabolic rate
- It may help you live longer!
  - Recent study of 208,000 men and women
  - Those who drank coffee regularly were less likely to die prematurely than those who didn't drink coffee
- There's also some evidence coffee may slow some of the metabolic processes that drive aging

Cardiovascular Health

- There is no evidence that coffee consumption increases the risk of heart disease
  - Coffee consumption is inversely associated with markers of inflammation and endothelial dysfunction
- Moderate consumption does not increase cardiac arrhythmia risk
- Also, coffee does not relay any long term effect of blood pressure

Cardiovascular Health

- In a large study involving tens of thousands of people, consistent coffee drinkers had a lower risk of stroke
  - Coffee tends to keep blood vessels flexible (lower incidence of atherosclerosis is seen in coffee drinkers)
- Again, coffee's impact on oxidation and inflammation play a role here

Mental Health

- Enhance alertness, concentration, and mental and physical performance
- Protects against Parkinson's disease
- Caffeine and chlorogenic acid appear to protect against the cognitive deterioration or biological features of Alzheimer's disease in the central nervous system

Mental Health

- Coffee improves short term memory
- It improves task-switching performance
- One study showed that repeated intake of 75 mg of caffeine (~1 cup of coffee) every 4 hours led to a pattern of sustained improvement in mood – including in depressed subjects

Mental Health

- Researchers from Sweden, Finland, the UK and Japan conducted a study that showed acute does of caffeine shift nervous system cell expression profiles towards promotion of neuronal projection growth…this research also showed that inhibition on neuronal connectivity is downregulated by caffeine
  - Caffeine seemed to upregulate some neuronal processes
  - This may help us in understanding how caffeine improves memory in the elderly

Mental Health

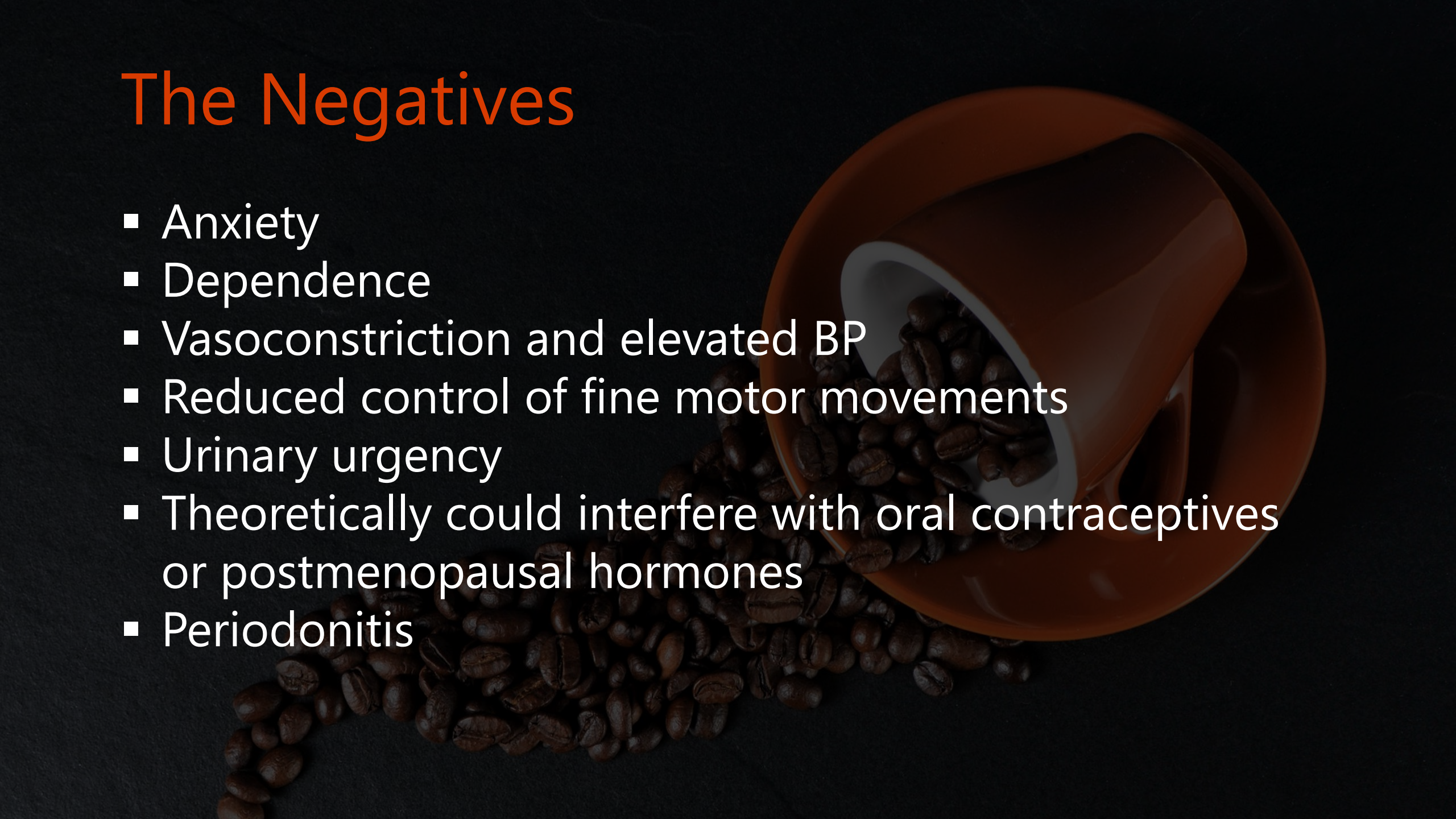
- Coffee's impact on Parkinson's disease
  - Acts as a adenosine receptor antagonist, resulting in release of excitatory transmitters including dopamine
  - Several coffee compounds increase calcium signaling and dopamine release
  - The antioxidant effect of chlorogenic acids have been associated with neurogenesis

The Negatives

- Can increase heartburn but is not significant enough to justify advising patients with GERD against drinking coffee
- There are safe levels in pregnancy, but they're slightly less than the levels recommended for others (conflicting data on spontaneous abortions and impaired fetal growth)
- Can increase cholesterol and homocysteine levels
  - Cafestol and kahweol (coffee lipids)

The Negatives

- Anxiety
- Dependence
- Vasoconstriction and elevated BP
- Reduced control of fine motor movements
- Urinary urgency
- Theoretically could interfere with oral contraceptives or postmenopausal hormones
- Periodonitis



The Negatives

- California's possible labeling coffee as a carcinogen
  - Looking at dietary acrylamide
    - One study – no statistically significant association between dietary acrylamide intake and various cancers
    - You'd have to drink 2,000 cups of coffee per day to get to the level that caused cancer in mice

THE HEALTH BENEFITS OF COFFEE

What factors in coffee impact health?

- Caffeine Content
- Varietals
- Elevation Grown (Bean Density)
- Roast Level
- Whole Bean vs Ground
- Freshness
- Brew Method
- Overall Consumption (Caffeine Intake)
- Quality



Varietals And Geographic Location

- Bourbon, Catuai, Catimor, Carturra, Colombian, Geisha, Maragogipe, Pacamara, Typica
- CGAs and polyphenols can differ geographically – example: CGAs in coffee planted in Mexico and India have higher levels than that grown in China

Elevation Grown (Bean Density)



Papua New Guinea



Sulawesi

Pictures courtesy of Cafe Imports

Elevation Grown (Bean Density)



Brazil



Tanzania

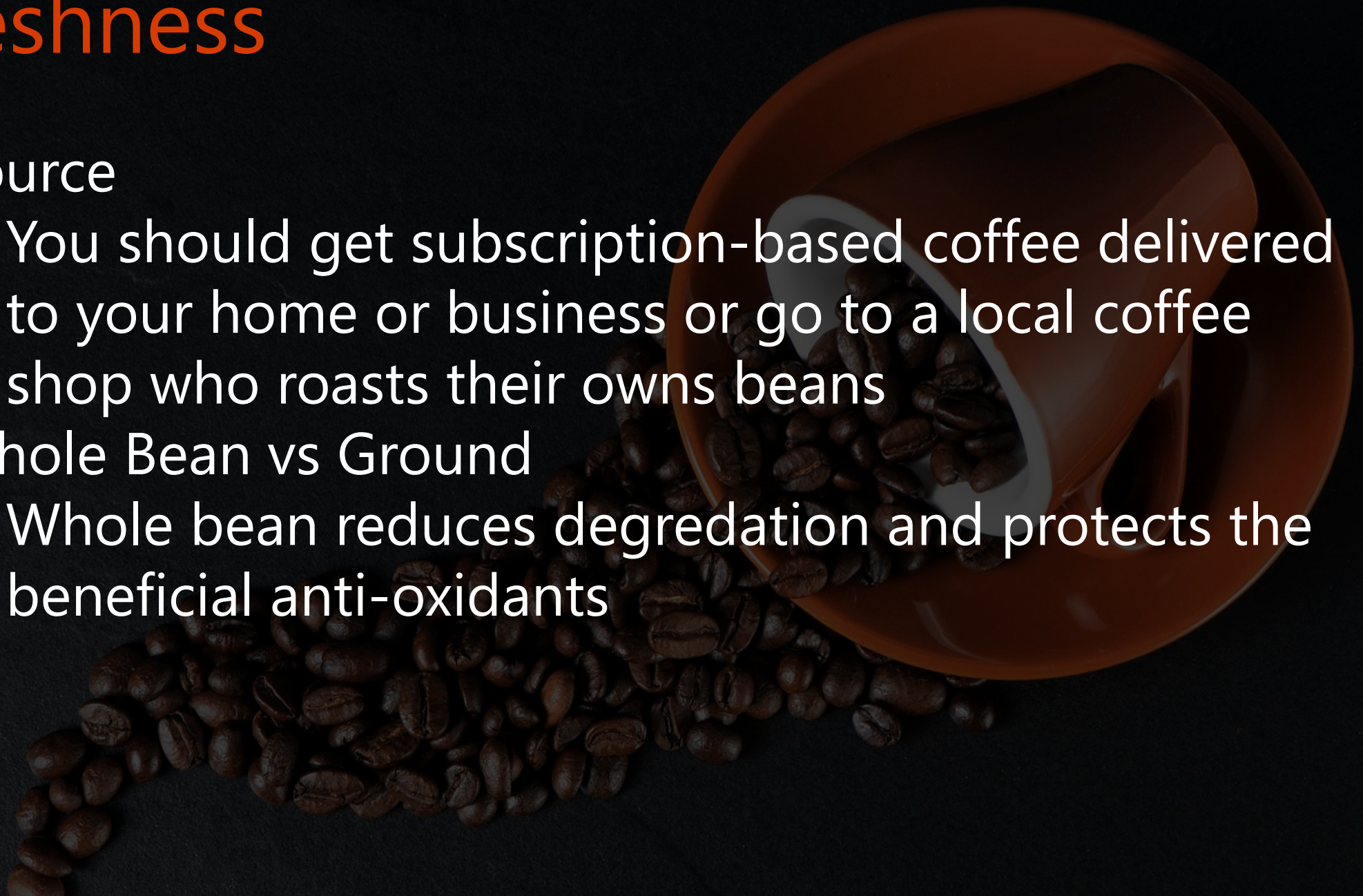
Pictures courtesy of Cafe Imports

Roast Level

- The lighter the roast, the higher the antioxidants
- The darker the roast, the lower the levels of CGAs and polyphenols – this contributes to antioxidant levels decreasing

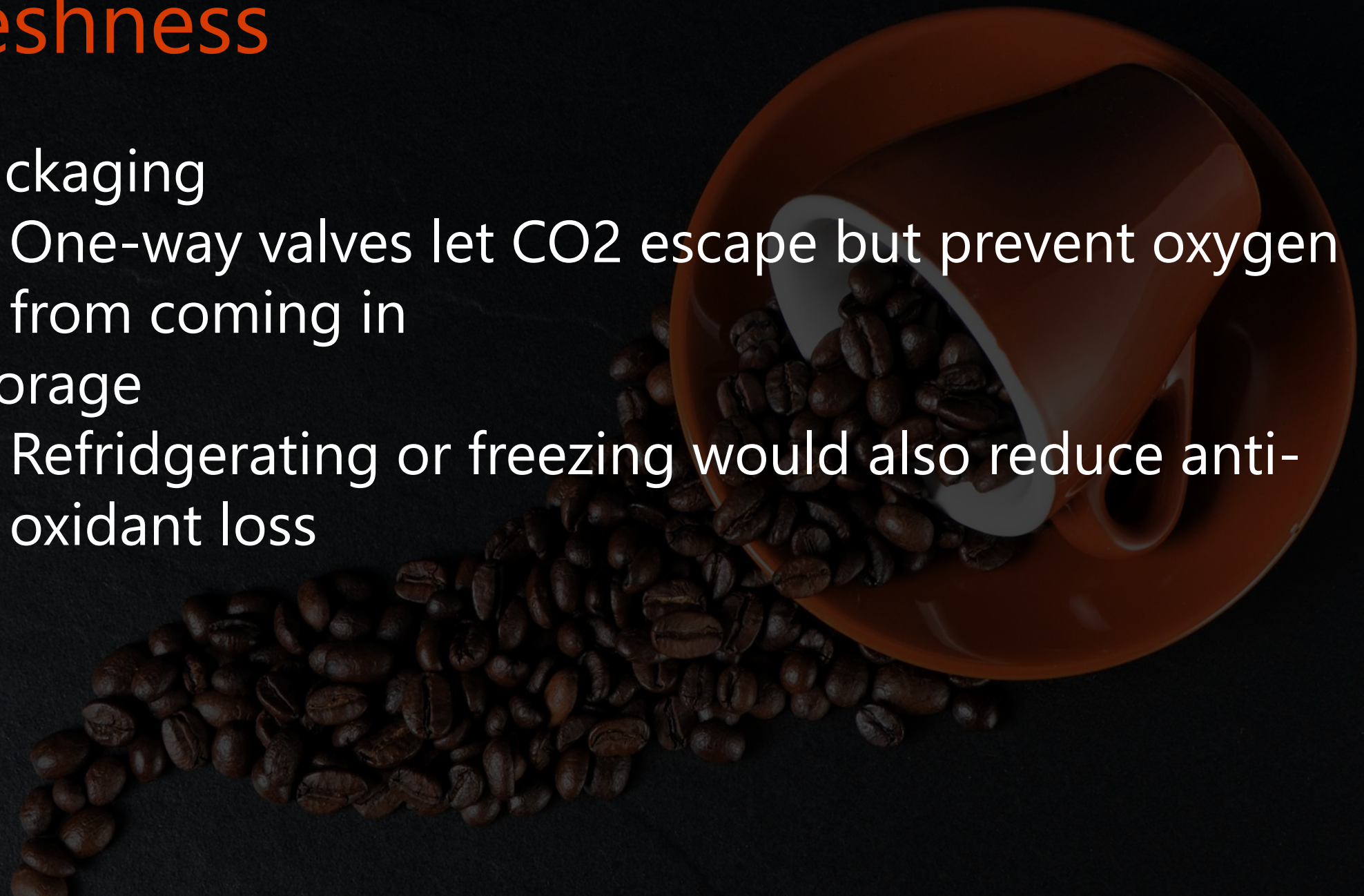
Freshness

- Source
  - You should get subscription-based coffee delivered to your home or business or go to a local coffee shop who roasts their owns beans
- Whole Bean vs Ground
  - Whole bean reduces degredation and protects the beneficial anti-oxidants



Freshness

- Packaging
  - One-way valves let CO2 escape but prevent oxygen from coming in
- Storage
  - Refridgerating or freezing would also reduce anti-oxidant loss



Brew Method

- To filter or not to filter…that is the question
  - Filtered brewing methods filter out diterpenes (cafestol and kaweol) whereas unfiltered methods do not
  - Unfiltered coffee increases cholesterol and homocysteine levels significantly more than filtered coffee

Brew Method

- Filtered
  - Regular pot of coffee
  - Pour over
  - Aeropress
- Unfiltered
  - French Press
  - Instant Coffee
  - Espresso



Caffeine Content

- Four 8-ounce cups of coffee a day is considered safe.
- Another way to put it
  - 400 mg caffeine per day is safe for most adults
  - 300 mg caffeine per day is considered safe for ladies who are pregnant
- These numbers come from a review of over 700 studies conducted between 2001 and 2015

Quality

- A cup of coffee that positively impacts your health is a cup that tastes good black. Ie you shouldn't have to put anything in it take make it 'taste better'!
- If it puts you in a good mood, it has positively impacted your health
- Most of the time, you're not going to find quality in the grocery store.
- Instead of looking at 'best by' dates, try to find 'roasted on' dates

THE HEALTH BENEFITS OF COFFEE

How to Find or Make the Healthiest and Best Cup of Coffee

- In the Community
  - Coffee-stalking
- In Your Home or Office
  - Coffee and Water
  - Equipment
- Caffeine Consumption



In The Community

- Coffee Shop(s) – chains and/or small independents
  - Best place in your community to chance finding the best and healthiest cup
  - Do they roast their own beans? If not, where do they get them from?
  - Do they know the roast date?
  - Pay attention – are they using a scoop or a scale to weight out beans??
  - What do they serve? Is it only dark roasts offered? (the healthiest cup is going to be a lighter roast)

In The Community

- Coffee Shop(s) – chains and/or small independents
  - Do they know the bean importer?
  - Better yet, do they have a relationship directly with the farmer??
  - If you start getting that deer-in-the-headlights look from them, either they have no idea what your asking (not a good sign) or your cover is blown!
  - Remember, coffee-stalking is about being incognito. If you ask too many questions at once, they'll think you're from Yelp and go grab a manager!

In Your Home or Office

- Water:Coffee ratio between 16.1:1 and 18:1
- Coffee
  - Buy from an online subscription or local shop concerned with quality and freshness
  - Be aware of elevation grown (the higher, the more antioxidants etc)
  - The lighter the roast, the better for health benefits but it also has to sit well on your palate! A well roasted coffee, even lighter roasted, can easily (and joyfully) be consumed black

In Your Home or Office

- Coffee cont'd
  - Freshness (look for roast dates as opposed to best by dates)
  - Whole bean
  - Bagged with one-way valve – or keep in an airtight container
  - If you don't consume it all within 3 weeks of the roast date (and I encourage you do!) then store in a cool place – fridge or freezer
  - Brew with a paper (not metal) filter

In Your Home or Office

- Water
  - Makes up 91%-95% of your coffee!
  - If your water at home tastes different than your office which is different than your favorite restaurant, then your coffee will taste different as well!
  - The Specialty Coffee Association has standards
  - Want a fool proof way to get the best tasting coffee?!
    - Distilled water and 3rd Wave Water

In Your Home or Office

- Grinder
  - Blade vs Burr
  - Spend the money and buy a burr grinder
- Kettle
  - Bonavita has a good, reasonably priced gooseneck kettle
  - Really, you're just looking to get water 30 seconds off boiling (195-205 F)

In Your Home or Office

- Scales
  - Use weight (grams) if possible – more accurate than using volume due to progressive water loss during the roasting process and variation in bean densities

In Your Home or Office

- Brew Device
  - The SCA has researched and certified coffee drips machine used for the home and office. This basically means they have good distribution of the water over the ground coffee and the water doesn't start going through until it reaches a temp of 195-205
  - https://sca.coffee/certified-home-brewer/

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THANK YOU!

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References

Critical Reviews in Food Science and Nutrition, 48:464–486 (2008)

Journal of Clinical and Experimental Hepatology | March 2016 | Vol. 6 | No. 1 | 40–46

PLoS ONE 11(1): e0147762. doi:10.1371/journal.pone.0147762

Critical Reviews in Food Science and Nutrition, 46:101–123 (2006)

Mol Nutr Food Res. 2005 Mar;49(3):27484.

Am J Clin Nutr 2006;83:1039–46.

Am J Clin Nutr 2006;84:888-93.

Journal of Clinical and Experimental Hepatology | March 2016 | Vol. 6 | No. 1 | 40–46

Genes Nutr (2015) 10:51

Biol Med (Aligarh) 2015, 7:4

Asian Pacific J Cancer Prev, 14 (3), 1585-1592

Annu Rev Public Health. 2005;26:44567

Genes Nutr (2015) 10:51

Biol Med (Aligarh) 2015, 7:4

PLoS ONE 11(7): e0158845. doi:10.1371/journal.pone.0158845

Am J Clin Nutr 2002;76:1244–8.

Critical Reviews in Food Science and Nutrition, 46:101–123 (2006)

Coffee: Emerging Health Effects and Disease Prevention, First Edition. _C 2012 John Wiley & Sons, Inc. Published 2012 by Blackwell Publishing Ltd

CurrOpinLipidol. 2015 August ; 26(4): 270–275

Journal of Clinical and Experimental Hepatology | March 2016 | Vol. 6 | No. 1 | 40–46

Critical Reviews in Food Science and Nutrition, 46:101–123 (2006)

https://www.quora.com/Does-freshly-ground-coffee-have-any-health-advantages-relative-to-regular-coffee

https://artisancoffeeaccess.wordpress.com/2016/03/04/the-benefits-of-fresh-roasted-coffee

http://ezinearticles.com/?Four-Benefits-of-Fresh-Roasted-Coffee---Enjoy-it-at-Its-Best&id=3672803

http://aurigin.com.au/blog/why-fresh-roasted-coffee-is-miles-ahead-of-instant-coffee

https://artisancoffeeaccess.wordpress.com/2016/03/04/the-benefits-of-fresh-roasted-coffee/

Antioxidants 2013, *2*, 230-245

ClinPharmacolTher. 2010 April ; 87(4): 479–482.

Bai K, Cai Q, Jiang Y, Lv L. 2016. Coffee consumption and risk of hepatocellular carcinoma: a meta-analysis of eleven epidemiological studies. Onco Targets Ther. 9:4369–75

Bohn SK, Blomhoff R, Paur I. 2014. Coffee and cancer risk, epidemiological evidence, and molecular mechanisms. Mol. Nutr. Food Res. 58:915–30

Botelho F, Lunet N, Barros H. 2006. Coffee and gastric cancer: systematic review and meta-analysis. Cad. Saude Publica 22:889–900

Braem MG, Onland-Moret NC, Schouten LJ, Tjonneland A, Hansen L, et al. 2012. Coffee and tea consumption and the risk of ovarian cancer: a prospective cohort study and updated meta-analysis. Am. J. Clin. Nutr. 95:1172–81

Bravi F, Bosetti C, Tavani A, Bagnardi V, Gallus S, et al. 2007. Coffee drinking and hepatocellular carcinoma risk: a meta-analysis. Hepatology 46:430–35

Bravi F, Bosetti C, Tavani A, Gallus S, La Vecchia C. 2013. Coffee reduces risk for hepatocellular carcinoma: an updated meta-analysis. Clin. Gastroenterol. Hepatol. 11:1413–21

Bravi F, Scotti L, Bosetti C, Gallus S, Negri E, et al. 2009. Coffee drinking and endometrial cancer risk: a metaanalysis of observational studies. Am. J. Obstet. Gynecol. 200:130–35

Bravi F, Tavani A, Bosetti C, Boffetta P, La Vecchia C. 2017. Coffee and the risk of hepatocellular carcinoma and chronic liver disease: a systematic review and meta-analysis of prospective studies. Eur. J. Cancer Prev. In press. http://dx.doi.org/10.1097/CEJ.0000000000000252

Brent RL, Christian MS, Diener RM. 2011. Evaluation of the reproductive and developmental risks of caffeine. Birth Defects Res. B Dev. Reprod. Toxicol. 92:152–87

References

Brown OI, Allgar V, Wong KY. 2016. Coffee reduces the risk of death after acute myocardial infarction: a meta-analysis. Coron. Artery Dis. 27:566–72

Buscemi S, Marventano S, Antoci M, Cagnetti A, Castorina G, et al. 2016. Coffee and metabolic impairment: an updated review of epidemiological studies. NFS J. 3:1–7

Cai L, Ma D, Zhang Y, Liu Z, Wang P. 2012. The effect of coffee consumption on serum lipids: a meta-analysis of randomized controlled trials. Eur. J. Clin. Nutr. 66:872–77

Caini S, Cattaruzza S, Bendinelli B, Tosti G, Masala G, et al. 2016. Coffee, tea and caffeine intake and the risk of non-melanoma skin cancer: a review of the literature and meta-analysis. Eur. J. Nutr. 56:1–12

Caldeira D, Martins C, Alves LB, Pereira H, Ferreira JJ, Costa J. 2013. Caffeine does not increase the risk of atrial fibrillation: a systematic review and meta-analysis of observational studies. Heart 99:1383–89

Cao S, Liu L, Yin X, Wang Y, Liu J, Lu Z. 2014. Coffee consumption and risk of prostate cancer: a meta-analysis of prospective cohort studies. Carcinogenesis 35:256–61

Chen J, Long S. 2014. Tea and coffee consumption and risk of laryngeal cancer: a systematic review meta-analysis. PLOS ONE 9:e112006

Chen LW, Wu Y, Neelakantan N, Chong MF, Pan A, van Dam RM. 2014. Maternal caffeine intake during pregnancy is associated with risk of low birth weight: a systematic review and dose-response meta-analysis. BMC Med. 12:174

Chen LW, Wu Y, Neelakantan N, Chong MF, Pan A, van Dam RM. 2016. Maternal caffeine intake during pregnancy and risk of pregnancy loss: a categorical and dose-response meta-analysis of prospective studies. Public Health Nutr. 19:1233–44

Chen S, Teoh NC, Chitturi S, Farrell GC. 2014. Coffee and non-alcoholic fatty liver disease: brewing evidence for hepatoprotection? J. Gastroenterol. Hepatol. 29:435–41

Cheng J, Su H, Zhu R, Wang X, Peng M, et al. 2014. Maternal coffee consumption during pregnancy and risk of childhood acute leukemia: a metaanalysis. Am. J. Obstet. Gynecol. 210:151.e1–10

Cheng M, Hu Z, Lu X, Huang J, Gu D. 2014. Caffeine intake and atrial fibrillation incidence: dose response meta-analysis of prospective cohort studies. Can. J. Cardiol. 30:448–54

Chiaffarino F, Bravi F, Cipriani S, Parazzini F, Ricci E, et al. 2014. Coffee and caffeine intake and risk of endometriosis: a meta-analysis. Eur. J. Nutr. 53:1573–79

Colussi G, De Ferrari ME, Brunati C, Civati G. 2000. Medical prevention and treatment of urinary stones. J. Nephrol. 13(Suppl. 3):S65–70

Cornelis MC, El-Sohemy A, Kabagambe EK, Campos H. 2006. Coffee, CYP1A2 genotype, and risk of myocardial infarction. JAMA 295:1135–41

Costa J, Lunet N, Santos C, Santos J, Vaz-Carneiro A. 2010. Caffeine exposure and the risk of Parkinson's disease: a systematic review and meta-analysis of observational studies. J. Alzheimers Dis. 20(Suppl. 1):S221–38

Crippa A, Discacciati A, Larsson SC, Wolk A, Orsini N. 2014. Coffee consumption and mortality from all causes, cardiovascular disease, and cancer: a dose-response meta-analysis. Am. J. Epidemiol. 180:763–75

Deng W, Yang H, Wang J, Cai J, Bai Z, et al. 2016. Coffee consumption and the risk of incident gastric cancer—a meta-analysis of prospective cohort studies. Nutr. Cancer 68:40–47

Ding M, Bhupathiraju SN, Chen M, van Dam RM, Hu FB. 2014. Caffeinated and decaffeinated coffee consumption and risk of type 2 diabetes: a systematic review and a dose-response meta-analysis. Diabetes Care 37:569–86

Ding M, Bhupathiraju SN, Satija A, van Dam RM, Hu FB. 2014. Long-term coffee consumption and risk of cardiovascular disease: a systematic review and a dose-response meta-analysis of prospective cohort studies. Circulation 129:643–59

Discacciati A, Orsini N, Wolk A. 2014. Coffee consumption and risk of nonaggressive, aggressive and fatal prostate cancer—a dose-response meta-analysis. Ann. Oncol. 25:584–91

Dong J, Zou J, Yu XF. 2011. Coffee drinking and pancreatic cancer risk: a meta-analysis of cohort studies. World J. Gastroenterol. 17:1204–10

Galarraga V, Boffetta P. 2016. Coffee drinking and risk of lung cancer—a meta-analysis. Cancer Epidemiol. Biomarkers Prev. 25:951–57

Galeone C, Turati F, La Vecchia C, Tavani A. 2010. Coffee consumption and risk of colorectal cancer: a meta-analysis of case-control studies. Cancer Causes Control 21:1949–59

Gan Y, Wu J, Zhang S, Li L, Cao S, et al. 2017. Association of coffee consumption with risk of colorectal cancer: a meta-analysis of prospective cohort studies. Oncotarget 8:18699–711

Giovannucci E. 1998. Meta-analysis of coffee consumption and risk of colorectal cancer. Am. J. Epidemiol. 147:1043–52

Godos J, Pluchinotta FR, Marventano S, Buscemi S, Li Volti G, et al. 2014. Coffee components and cardiovascular risk: beneficial and detrimental effects. Int. J. Food Sci. Nutr. 65:925–36

Greenland S. 1993. A meta-analysis of coffee, myocardial infarction, and coronary death. Epidemiology 4:366–74

References

Greenwood DC, Thatcher NJ, Ye J, Garrard L, Keogh G, et al. 2014. Caffeine intake during pregnancy and adverse birth outcomes: a systematic review and dose-response meta-analysis. Eur. J. Epidemiol. 29:725–34

Grosso G, Micek A, Castellano S, Pajak A, Galvano F. 2016. Coffee, tea, caffeine and risk of depression: a systematic review and dose-response meta-analysis of observational studies. Mol. Nutr. Food Res. 60:223–34

Hernan MA, Takkouche B, Caamano-Isorna F, Gestal-Otero JJ. 2002. A meta-analysis of coffee drinking, cigarette smoking, and the risk of Parkinson's disease. Ann. Neurol. 52:276–84

Higdon JV, Frei B. 2006. Coffee and health: a review of recent human research. Crit. Rev. Food Sci. Nutr. 46:101–23

Higgins LG, Cavin C, Itoh K, Yamamoto M, Hayes JD. 2008. Induction of cancer chemopreventive enzymes by coffee is mediated by transcription factor Nrf2. Evidence that the coffee-specific diterpenes cafestol and kahweol confer protection against acrolein. Toxicol. Appl. Pharmacol. 226:328–37

Huang TB, Guo ZF, Zhang XL, Zhang XP, Liu H, et al. 2014. Coffee consumption and urologic cancer risk: a meta-analysis of cohort studies. Int. Urol. Nephrol. 46:1481–93

Huber WW, Parzefall W. 2005. Modification of N-acetyltransferases and glutathione S-transferases by coffee components: possible relevance for cancer risk. Methods Enzymol. 401:307–41

Huxley R, Lee CM, Barzi F, Timmermeister L, Czernichow S, et al. 2009. Coffee, decaffeinated coffee, and tea consumption in relation to incident type 2 diabetes mellitus: a systematic review with meta-analysis. Arch. Intern. Med. 169:2053–63

Inoue M, Tsugane S. 2012. Insulin resistance and cancer: epidemiological evidence. Endocr. Relat. Cancer 19:F1–8

Jahanfar S, Jaafar SH. 2015. Effects of restricted caffeine intake by mother on fetal, neonatal and pregnancy outcome. Cochrane Database Syst. Rev. 6:CD006965

Je Y, Giovannucci E. 2012. Coffee consumption and risk of endometrial cancer: findings from a large up-to-date meta-analysis. Int. J. Cancer 131:1700–10

Je Y, Giovannucci E. 2014. Coffee consumption and total mortality: a meta-analysis of twenty prospective cohort studies. Br. J. Nutr. 111:1162–73

Je Y, Liu W, Giovannucci E. 2009. Coffee consumption and risk of colorectal cancer: a systematic review and meta-analysis of prospective cohort studies. Int. J. Cancer 124:1662–68

Jee SH, He J, Whelton PK, Suh I, Klag MJ. 1999. The effect of chronic coffee drinking on blood pressure: a meta-analysis of controlled clinical trials. Hypertension 33:647–52

Jiang W, Wu Y, Jiang X. 2013. Coffee and caffeine intake and breast cancer risk: an updated dose-response meta-analysis of 37 published studies. Gynecol. Oncol. 129:620–29

Jiang X, Zhang D, Jiang W. 2014. Coffee and caffeine intake and incidence of type 2 diabetes mellitus: a meta-analysis of prospective studies. Eur. J. Nutr. 53:25–38

Kawachi I, Colditz GA, Stone CB. 1994. Does coffee drinking increase the risk of coronary heart disease? Results from a meta-analysis. Br. Heart J. 72:269–75

Kennedy OJ, Roderick P, Buchanan R, Fallowfield JA, Hayes PC, Parkes J. 2016. Systematic review with meta-analysis: coffee consumption and the risk of cirrhosis. Aliment. Pharmacol. Ther. 43:562–74

Kim B, Nam Y, Kim J, Choi H, Won C. 2012. Coffee consumption and stroke risk: a meta-analysis of epidemiologic studies. Korean J. Fam. Med. 33:356–65

Kim J, Oh SW, Myung SK, Kwon H, Lee C, et al. 2014. Association between coffee intake and gastro-esophageal reflux disease: a meta-analysis. Dis. Esophagus 27:311–17

Kim YS, Kwak SM, Myung SK. 2015. Caffeine intake from coffee or tea and cognitive disorders: a meta-analysis of observational studies. Neuroepidemiology 44:51–63

Kua KP, Lee SW. 2017. Systematic review and meta-analysis of clinical outcomes of early caffeine therapy in preterm neonates. Br. J. Clin. Pharmacol. 83:180–191

Larsson SC, Drca N, Jensen-Urstad M, Wolk A. 2015. Coffee consumption is not associated with increased risk of atrial fibrillation: results from two prospective cohorts and a meta-analysis. BMC Med. 13:207

Larsson SC, Orsini N. 2011. Coffee consumption and risk of stroke: a dose-response meta-analysis of prospective studies. Am. J. Epidemiol. 174:993–1001

Larsson SC, Wolk A. 2007. Coffee consumption and risk of liver cancer: a meta-analysis. Gastroenterology 132:1740–45

Lee DR, Lee J, Rota M, Lee J, Ahn HS, et al. 2014. Coffee consumption and risk of fractures: a systematic review and dose-response meta-analysis. Bone 63:20–28

Lee YH, Bae SC, Song GG. 2014. Coffee or tea consumption and the risk of rheumatoid arthritis: a meta-analysis. Clin. Rheumatol. 33:1575–83

Li G, Ma D, Zhang Y, Zheng W, Wang P. 2013. Coffee consumption and risk of colorectal cancer: a meta-analysis of observational studies. Public Health Nutr. 16:346–57

Li J, Zhao H, Song JM, Zhang J, Tang YL, Xin CM. 2015. A meta-analysis of risk of pregnancy loss and caffeine and coffee consumption during pregnancy. Int. J. Gynaecol. Obstet. 130:116–22

References

Li L, Gan Y, Wu C, Qu X, Sun G, Lu Z. 2015. Coffee consumption and the risk of gastric cancer: a meta-analysis of prospective cohort studies. BMC Cancer 15:733

Li S, Dai Z, Wu Q. 2015. Effect of coffee intake on hip fracture: a meta-analysis of prospective cohort studies. Nutr. J. 14:38

Li XJ, Ren ZJ, Qin JW, Zhao JH, Tang JH, et al. 2013. Coffee consumption and risk of breast cancer: an up-to-date meta-analysis. PLOS ONE 8:e52681

Li XL, Xu JH. 2013. Coffee consumption and hip fracture risk: a meta-analysis. J. Nutr. Sci. 2:e23
Medline

Li YM, Peng J, Li LZ. 2016. Coffee consumption associated with reduced risk of oral cancer: a meta-analysis. Oral Surg. Oral Med. Oral Pathol. Oral Radiol. 121:381–89

Li ZX, Gao ZL, Wang JN, Guo QH. 2016. Maternal coffee consumption during pregnancy and neural tube defects in offspring: a meta-analysis. Fetal Pediatr. Pathol. 35:1–9

Lippi G, Mattiuzzi C, Franchini M. 2015. Venous thromboembolism and coffee: critical review and meta-analysis. Ann. Transl. Med. 3:152

Liu F, Wang X, Wu G, Chen L, Hu P, et al. 2015. Coffee consumption decreases risks for hepatic fibrosis and cirrhosis: a meta-analysis. PLOS ONE 10:e0142457

Liu H, Hu GH, Wang XC, Huang TB, Xu L, et al. 2015. Coffee consumption and prostate cancer risk: a meta-analysis of cohort studies. Nutr. Cancer 67:392–400

Liu H, Hua Y, Zheng X, Shen Z, Luo H, et al. 2015. Effect of coffee consumption on the risk of gastric cancer: a systematic review and meta-analysis of prospective cohort studies. PLOS ONE 10:e0128501

Liu H, Yao K, Zhang W, Zhou J, Wu T, He C. 2012. Coffee consumption and risk of fractures: a meta-analysis. Arch. Med. Sci. 8:776–83

Liu J, Shen B, Shi M, Cai J. 2016. Higher caffeinated coffee intake is associated with reduced malignant melanoma risk: a meta-analysis study. PLOS ONE 11:e0147056

Liu QP, Wu YF, Cheng HY, Xia T, Ding H, et al. 2016. Habitual coffee consumption and risk of cognitive decline/dementia: a systematic review and meta-analysis of prospective cohort studies. Nutrition 32:628–36

Liu R, Guo X, Park Y, Huang X, Sinha R, et al. 2012. Caffeine intake, smoking, and risk of Parkinson disease in men and women. Am. J. Epidemiol. 175:1200–7

Lu Y, Zhai L, Zeng J, Peng Q, Wang J, et al. 2014. Coffee consumption and prostate cancer risk: an updated meta-analysis. Cancer Causes Control 25:591–604

Ludwig IA, Clifford MN, Lean ME, Ashihara H, Crozier A. 2014. Coffee: biochemistry and potential impact on health. Food Funct. 5:1695–717

Malerba S, Galeone C, Pelucchi C, Turati F, Hashibe M, et al. 2013. A meta-analysis of coffee and tea consumption and the risk of glioma in adults. Cancer Causes Control 24:267–76

Malerba S, Turati F, Galeone C, Pelucchi C, Verga F, et al. 2013. A meta-analysis of prospective studies of coffee consumption and mortality for all causes, cancers and cardiovascular diseases. Eur. J. Epidemiol. 28:527–39

Martini D, Del Bo C, Tassotti M, Riso P, Del Rio D, et al. 2016. Coffee consumption and oxidative stress: a review of human intervention studies. Molecules 21:979

Marventano S, Salomone F, Godos J, Pluchinotta F, Del Rio D, et al. 2016. Coffee and tea consumption in relation with non-alcoholic fatty liver and metabolic syndrome: a systematic review and meta-analysis of observational studies. Clin. Nutr. 35:1269–81

Meng S, Cao J, Feng Q, Peng J, Hu Y. 2013. Roles of chlorogenic acid on regulating glucose and lipids metabolism: a review. Evid. Based Complement. Altern. Med. 2013:801457

Mesas AE, Leon-Munoz LM, Rodriguez-Artalejo F, Lopez-Garcia E. 2011. The effect of coffee on blood pressure and cardiovascular disease in hypertensive individuals: a systematic review and meta-analysis. Am. J. Clin. Nutr. 94:1113–26

Milne E, Royle JA, Bennett LC, de Klerk NH, Bailey HD, et al. 2011. Maternal consumption of coffee and tea during pregnancy and risk of childhood ALL: results from an Australian case-control study. Cancer Causes Control 22:207–18

Moco S, Martin FP, Rezzi S. 2012. Metabolomics view on gut microbiome modulation by polyphenol-rich foods. J. Proteome Res. 11:4781–90

Moreira AS, Nunes FM, Domingues MR, Coimbra MA. 2012. Coffee melanoidins: structures, mechanisms of formation and potential health impacts. Food Funct. 3:903–15

Mostofsky E, Rice MS, Levitan EB, Mittleman MA. 2012. Habitual coffee consumption and risk of heart failure: a dose-response meta-analysis. Circ. Heart Fail. 5:401–5

Mulak A, Bonaz B. 2015. Brain–gut–microbiota axis in Parkinson's disease. World J. Gastroenterol. 21:10609–20
Myers MG, Basinski A. 1992. Coffee and coronary heart disease. Arch. Intern. Med. 152:1767–72

Nehlig A. 2016. Effects of coffee/caffeine on brain health and disease: What should I tell my patients? Pract. Neurol. 16:89–95

Nie K, Xing Z, Huang W, Wang W, Liu W. 2016. Coffee intake and risk of pancreatic cancer: an updated meta-analysis of prospective studies. Minerva Med. 107:270–78

References

Noordzij M, Uiterwaal CS, Arends LR, Kok FJ, Grobbee DE, Geleijnse JM. 2005. Blood pressure response to chronic intake of coffee and caffeine: a meta-analysis of randomized controlled trials. J. Hypertens. 23:921–28

Ouyang Z, Wang Z, Jin J. 2014. Association between tea and coffee consumption and risk of laryngeal cancer: a meta-analysis. Int. J. Clin. Exp. Med. 7:5192–200

Palatini P, Ceolotto G, Ragazzo F, Dorigatti F, Saladini F, et al. 2009. CYP1A2 genotype modifies the association between coffee intake and the risk of hypertension. J. Hypertens. 27:1594–601

Pan MH, Tung YC, Yang G, Li S, Ho CT. 2016. Molecular mechanisms of the anti-obesity effect of bioactive compounds in tea and coffee. Food Funct. 7:4481–91

Park CH, Myung SK, Kim TY, Seo HG, Jeon YJ, et al. 2010. Coffee consumption and risk of prostate cancer: a meta-analysis of epidemiological studies. BJU Int. 106:762–69

Park KY, Kim HJ, Ahn HS, Kim SH, Park EJ, et al. 2016. Effects of coffee consumption on serum uric acid: systematic review and meta-analysis. Semin. Arthritis Rheum. 45:580–86

Qi H, Li S. 2014. Dose-response meta-analysis on coffee, tea and caffeine consumption with risk of Parkinson's disease. Geriatr. Gerontol. Int. 14:430–39

Ran HQ, Wang JZ, Sun CQ. 2016. Coffee consumption and pancreatic cancer risk: an update meta-analysis of cohort studies. Pak. J. Med. Sci. 32:253–59

Ranheim T, Halvorsen B. 2005. Coffee consumption and human health–beneficial or detrimental? Mechanisms for effects of coffee consumption on different risk factors for cardiovascular disease and type 2 diabetes mellitus. Mol.
Nutr. Food Res. 49:274–84

Saab S, Mallam D, Cox GA 2nd, Tong MJ. 2014. Impact of coffee on liver diseases: a systematic review. Liver Int. 34:495–504

Sang LX, Chang B, Li XH, Jiang M. 2013. Consumption of coffee associated with reduced risk of liver cancer: a meta-analysis. BMC Gastroenterol. 13:34

Santos C, Costa J, Santos J, Vaz-Carneiro A, Lunet N. 2010. Caffeine intake and dementia: systematic review and meta-analysis. J. Alzheimers Dis. 20(Suppl. 1):S187–204

Shaffer EA. 2006. Gallstone disease: epidemiology of gallbladder stone disease. Best Pract. Res. Clin. Gastroenterol. 20:981–96

Shang F, Li X, Jiang X. 2016. Coffee consumption and risk of the metabolic syndrome: a meta-analysis. Diabetes Metab. 42:80–87

Shen Z, Liu H, Cao H. 2015. Coffee consumption and risk of gastric cancer: an updated meta-analysis. Clin. Res. Hepatol. Gastroenterol. 39:245–53

Sheng J, Qu X, Zhang X, Zhai Z, Li H, et al. 2014. Coffee, tea, and the risk of hip fracture: a meta-analysis. Osteoporos. Int. 25:141–50

Shimamoto T, Yamamichi N, Kodashima S, Takahashi Y, Fujishiro M, et al. 2013. No association of coffee consumption with gastric ulcer, duodenal ulcer, reflux esophagitis, and non-erosive reflux disease: a cross-sectional study of 8,013 healthy subjects in Japan. PLOS ONE 8:e65996

Sofi F, Conti AA, Gori AM, Eliana Luisi ML, Casini A, et al. 2007. Coffee consumption and risk of coronary heart disease: a meta-analysis. Nutr. Metab. Cardiovasc. Dis. 17:209–23

Steevens J, Schouten LJ, Verhage BA, Goldbohm RA, van den Brandt PA. 2007. Tea and coffee drinking and ovarian cancer risk: results from the Netherlands Cohort Study and a meta-analysis. Br. J. Cancer 97:1291–94

Steffen M, Kuhle C, Hensrud D, Erwin PJ, Murad MH. 2012. The effect of coffee consumption on blood pressure and the development of hypertension: a systematic review and meta-analysis. J. Hypertens. 30:2245–54

Tang N, Wu Y, Ma J, Wang B, Yu R. 2010. Coffee consumption and risk of lung cancer: a meta-analysis. Lung Cancer 67:17–22

Tang N, Zhou B, Wang B, Yu R. 2009. Coffee consumption and risk of breast cancer: a metaanalysis. Am. J. Obstet. Gynecol. 200:290.e1–9

Thomopoulos TP, Ntouvelis E, Diamantaras AA, Tzanoudaki M, Baka M, et al. 2015. Maternal and childhood consumption of coffee, tea and cola beverages in association with childhood leukemia: a meta-analysis. Cancer Epidemiol. 39:1047–59

Tian C, Wang W, Hong Z, Zhang X. 2013. Coffee consumption and risk of colorectal cancer: a dose-response analysis of observational studies. Cancer Causes Control 24:1265–68

Timms JA, Relton CL, Rankin J, Strathdee G, McKay JA. 2016. DNA methylation as a potential mediator of environmental risks in the development of childhood acute lymphoblastic leukemia. Epigenomics 8:519–36

Turati F, Galeone C, Edefonti V, Ferraroni M, Lagiou P, et al. 2012. A meta-analysis of coffee consumption and pancreatic cancer. Ann. Oncol. 23:311–18

Turati F, Galeone C, La Vecchia C, Garavello W, Tavani A. 2011. Coffee and cancers of the upper digestive and respiratory tracts: meta-analyses of observational studies. Ann. Oncol. 22:536–44

Vitaglione P, Fogliano V, Pellegrini N. 2012. Coffee, colon function and colorectal cancer. Food Funct. 3:916–22
Wang J, Li X, Zhang D. 2016. Coffee consumption and the risk of cutaneous melanoma: a meta-analysis. Eur. J. Nutr. 55:1317–29

References

Wang L, Shen X, Wu Y, Zhang D. 2016. Coffee and caffeine consumption and depression: a meta-analysis of observational studies. Aust. N. Z. J. Psychiatry 50:228–42

Wang S, Zhang Y, Mao Z, He X, Zhang Q, Zhang D. 2014. A meta-analysis of coffee intake and risk of urolithiasis. Urol. Int. 93:220–28

Wang Y, Yu X, Wu Y, Zhang D. 2012. Coffee and tea consumption and risk of lung cancer: a dose-response analysis of observational studies. Lung Cancer 78:169–70

Welsh EJ, Bara A, Barley E, Cates CJ. 2010. Caffeine for asthma. Cochrane Database Syst. Rev. 1:CD001112

Wu JN, Ho SC, Zhou C, Ling WH, Chen WQ, et al. 2009. Coffee consumption and risk of coronary heart diseases: a meta-analysis of 21 prospective cohort studies. Int. J. Cardiol. 137:216–25

Wu L, Sun D, He Y. 2017. Coffee intake and the incident risk of cognitive disorders: a dose-response meta-analysis of nine prospective cohort studies. Clin. Nutr. 36(3):730–36

Wu W, Tong Y, Zhao Q, Yu G, Wei X, Lu Q. 2015. Coffee consumption and bladder cancer: a meta-analysis of observational studies. Sci. Rep. 5:9051

Xie F, Wang D, Huang Z, Guo Y. 2014. Coffee consumption and risk of gastric cancer: a large updated meta-analysis of prospective studies. Nutrients 6:3734–46

Xie Y, Huang S, He T, Su Y. 2016. Coffee consumption and risk of gastric cancer: an updated meta-analysis. Asia Pac. J. Clin. Nutr. 25:578–88

Xie Y, Qin J, Nan G, Huang S, Wang Z, Su Y. 2016. Coffee consumption and the risk of lung cancer: an updated meta-analysis of epidemiological studies. Eur. J. Clin. Nutr. 70:199–206

Xu C, Zhang C, Wang XL, Liu TZ, Zeng XT, et al. 2015. Self-fluid management in prevention of kidney stones: a PRISMA-compliant systematic review and dose-response meta-analysis of observational studies. Medicine 94:e1042

Yang TO, Crowe F, Cairns BJ, Reeves GK, Beral V. 2015. Tea and coffee and risk of endometrial cancer: cohort study and meta-analysis. Am. J. Clin. Nutr. 101:570–78

Yew YW, Lai YC, Schwartz RA. 2016. Coffee consumption and melanoma: a systematic review and meta-analysis of observational studies. Am. J. Clin. Dermatol. 17:113–23

Yu X, Bao Z, Zou J, Dong J. 2011. Coffee consumption and risk of cancers: a meta-analysis of cohort studies. BMC Cancer 11:96

Zeegers MP, Tan FE, Goldbohm RA, van den Brandt PA. 2001. Are coffee and tea consumption associated with urinary tract cancer risk? A systematic review and meta-analysis. Int. J. Epidemiol. 30:353–62.

Zeng SB, Weng H, Zhou M, Duan XL, Shen XF, Zeng XT. 2015. Long-term coffee consumption and risk of gastric cancer: a PRISMA-compliant dose-response meta-analysis of prospective cohort studies. Medicine 94:e1640

Zhang X, Albanes D, Beeson WL, van den Brandt PA, Buring JE, et al. 2010. Risk of colon cancer and coffee, tea, and sugar-sweetened soft drink intake: pooled analysis of prospective cohort studies. J. Natl. Cancer Inst. 102:771–83

Zhang Y, Lee ET, Cowan LD, Fabsitz RR, Howard BV. 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. 21:418–23

Zhang Y, Wang X, Cui D. 2015. Association between coffee consumption and the risk of oral cancer: a meta-analysis of observational studies. Int. J. Clin. Exp. Med. 8:11657–65

Zhang Y, Yang T, Zeng C, Wei J, Li H, et al. 2016. Is coffee consumption associated with a lower risk of hyperuricaemia or gout? A systematic review and meta-analysis. BMJ Open 6:e009809

Zhang YP, Li WQ, Sun YL, Zhu RT, Wang WJ. 2015. Systematic review with meta-analysis: coffee consumption and the risk of gallstone disease. Aliment. Pharmacol. Ther. 42:637–48

Zhao Y, Wu K, Zheng J, Zuo R, Li D. 2015. Association of coffee drinking with all-cause mortality: a systematic review and meta-analysis. Public Health Nutr. 18:1282–91

Zheng JS, Yang J, Fu YQ, Huang T, Huang YJ, Li D. 2013. Effects of green tea, black tea, and coffee consumption on the risk of esophageal cancer: a systematic review and meta-analysis of observational studies. Nutr. Cancer 65:1–16

Zhong S, Chen W, Yu X, Chen Z, Hu Q, Zhao J. 2014. Coffee consumption and risk of prostate cancer: an up-to-date meta-analysis. Eur. J. Clin. Nutr. 68:330–37

Zhou J, Zhou S, Zeng S. 2013. Experimental diabetes treated with trigonelline: effect on β cell and pancreatic oxidative parameters. Fundam. Clin. Pharmacol. 27:279–87

Zhou Q, Luo ML, Li H, Li M, Zhou JG. 2015. Coffee consumption and risk of endometrial cancer: a dose-response meta-analysis of prospective cohort studies. Sci. Rep. 5:13410

Zhou Y, Tian C, Jia C. 2012. A dose-response meta-analysis of coffee consumption and bladder cancer. Prev. Med. 55:14–22

Zuchinali P, Ribeiro PA, Pimentel M, da Rosa PR, Zimerman LI, Rohde LE. 2016. Effect of caffeine on ventricular arrhythmia: a systematic review and meta-analysis of experimental and clinical studies. Europace 18:257–66

Zulli A, Smith RM, Kubatka P, Novak J, Uehara Y, et al. 2016. Caffeine and cardiovascular diseases: critical review of current research. Eur. J. Nutr. 55:1331–43