Association between caffeine consumption and nonalcoholic fatty liver disease: a systemic review and meta-analysis

Huafeng Shen, Andrea C. Rodriguez, Ashok Shiani, Seth Lipka, Ghulamullah Shahzad, Ambuj Kumar and Paul Mustacchia

Ther Adv Gastroenterol

2016, Vol. 9(1) 113–120

DOI: 10.1177/
1756283X15593700

© The Author(s), 2015.
Reprints and permissions:
[http://www.sagepub.co.uk/
journalsPermissions.nav](http://www.sagepub.co.uk/journalsPermissions.nav)

Abstract

Objectives: Caffeine consumption is reported to be associated with reduced hepatic fibrosis in patients with chronic liver diseases. We performed a systematic review and meta-analysis to assess the association between caffeine consumption and prevalence or hepatic fibrosis of nonalcoholic fatty liver disease (NAFLD) in observational studies.

Methods: We searched the literature of all languages from PubMed, EMBASE, and the Cochrane library from 1 January 1980 through 10 January 2015. Total caffeine consumption was defined as the daily intake of caffeine (mg/day) from all caffeine-containing products. Combined and subgroup analyses stratified by study designs, study locations, and type of caffeine intake were performed.

Results: Four cross-sectional and two case control studies with a total of 20,064 subjects were included in the meta-analysis. Among these, three studies with 18,990 subjects were included in the analysis for prevalence of NAFLD while the other three studies with 1074 subjects were for hepatic fibrosis. Total caffeine consumption (mg/day) was not significantly associated with either the prevalence [pooled mean difference (MD) 2.36; 95% confidence interval (CI) –35.92 to 40.64] or hepatic fibrosis [higher *versus* lower stages; pooled MD –39.95; 95% CI –132.72 to 52.82] of NAFLD. Subgroup analyses stratified by study designs and locations were also not significant. However, after stratifying by type of caffeine intake, regular coffee caffeine intake (mg/day) was significantly associated with reduced hepatic fibrosis of NAFLD [pooled MD –91.35; 95% CI –139.42 to –43.27; $n = 2$ studies].

Conclusion: Although total caffeine intake is not associated with the prevalence or hepatic fibrosis of NAFLD, regular coffee caffeine consumption may significantly reduce hepatic fibrosis in patients with NAFLD.

Keywords: coffee, caffeine, non-alcoholic fatty liver disease

Introduction

Caffeine consumption has significantly increased over the last several decades. Coffee continues to be the major source of caffeine, followed by soft drinks and tea for the average consumer in the United States [Frery *et al.* 2005]. Current estimates suggest 85% of the US population consume at least one caffeinated beverage daily, mainly sought out for its properties to improve mental alertness, concentration, and fatigue [Mitchell *et al.* 2014; Heckman *et al.* 2010]. Coffee consumption has been associated with a

decrease in all-cause mortality, and multiple studies have highlighted the beneficial effects for several medical conditions including diabetes mellitus type II, Parkinson's disease, hepatitis C virus, hepatocellular carcinoma (HCC), and non-alcoholic fatty liver disease (NAFLD) [Mitchell *et al.* 2014; Bambha *et al.* 2014; Freedman *et al.* 2012; Ruhl and Everhart, 2005; Molloy *et al.* 2012; Anty *et al.* 2012; Bircerdinc *et al.* 2012; Catalano *et al.* 2010; Gutierrez-Grobe *et al.* 2012; Paynter *et al.* 2006; Bravi *et al.* 2007; Wilson *et al.* 2011; Liu *et al.* 2012].

Correspondence to:
Huafeng Shen, MD, MPH
Department of Medicine,
Nassau University Medical
Center, 2201 Hempstead
Turnpike, East Meadow,
NY 11554, USA
hshen@numc.edu;
huafengshen@gmail.com

Andrea C. Rodriguez, MD
Ashok Shiani, MD
Departments of Internal
Medicine, Morsani College
of Medicine, University
of South Florida, Tampa,
FL, USA

Seth Lipka, MD
Digestive Diseases and
Nutrition, Morsani College
of Medicine, University
of South Florida, Tampa,
FL, USA

Ghulamullah Shahzad, MD
Division of Gastroenterology
and Hepatology, Nassau
University Medical Center,
East Meadow, NY, USA

Ambuj Kumar, MD, MPH
Evidence Based Medicine
and Research Outcomes,
Morsani College of
Medicine, University of
South Florida, Tampa,
FL, USA

Paul Mustacchia, MD
Division of Gastroenterology
and Hepatology, Nassau
University Medical Center,
East Meadow, NY, USA

As the most common cause of chronic liver disease, NAFLD most notably denotes an accumulation of fat within the liver; however this includes a wide spectrum of pathologic cellular injury including inflammation, hepatic fibrosis, cirrhosis, and HCC [Chen *et al.* 2014]. NAFLD is thought to be a hepatic manifestation of metabolic disorders such as hypertension, dyslipidemia, obesity, and impaired glucose tolerance, which likely contribute to its rapidly escalating prevalence [Chen *et al.* 2014; Shen *et al.* 2014].

Caffeine consumption is reported to be associated with reduced hepatic fibrosis in patients with chronic liver disease [Modi *et al.* 2010]. Multiple studies have since found similar findings but have been unable to clearly differentiate if the effect is from the coffee or caffeine and how these changes influence hepatic fibrosis of NAFLD, which is thought to be a manifestation of metabolic syndrome [Marchesini *et al.* 2001]. Therefore, to provide a synthesis of all evidence, we performed a systematic review and meta-analysis to evaluate the association between caffeine consumption and prevalence or hepatic fibrosis of NAFLD.

Methods

Literature search and inclusion criteria

We searched the literatures of all languages from PubMed, EMBASE, and the Cochrane library from 1 January 1980 through 10 January 2015, using the search terms ('NAFLD' or 'nonalcoholic fatty liver disease' or 'NASH' or 'nonalcoholic steatohepatitis' or 'fatty liver' AND 'caffeine' or 'coffee'). Publications that met the following criteria: (I) observational studies with a comparison (retrospective or prospective cohort or case-control studies); (II) all study participants were over the age of 18; (III) the reported amount of caffeine consumption can be transformed to milligrams per day; (IV) NAFLD patients were diagnosed by elevated liver enzymes, abdominal ultrasound and/or liver biopsy, were included in the systematic review and meta-analysis. Bibliographies of the studies that met these criteria were also searched for potential applicable studies.

Data extraction and quality assessment

Two reviewers independently extracted the following data: first author, publication year, study population's country of origin, study design,

sample size, and findings. The Newcastle–Ottawa Scale (NOS) was utilized to assess the methodological quality of included studies independently by each reviewer. Methodological quality assessment using the NOS is based on selection of study groups, comparability of study groups, and the ascertainment of the exposure/outcome of interest. Any discrepancies regarding the inclusion/exclusion of studies or data extraction were determined by consensus of the reviewers.

Statistical analysis

To assess the association, summary data from individual studies were pooled using a random effect model. All continuous data are summarized as mean difference (MD) along with 95% confidence intervals (CIs). The inconsistency index (I^2) was used to measure heterogeneity, with values of $I^2 > 50\%$ indicating substantial heterogeneity [Higgins *et al.* 2003]. We planned for but did not assess for publication bias as we found less than 10 studies. All analyses were performed using Review Manager 5.2 with a p value < 0.05 considered statistically significant. MOOSE guidelines were followed during the completion and reporting of this meta-analysis [Stroup *et al.* 2000].

Results

Characteristics of the studies

We initially identified a total of 118 studies that met our search criteria. After title and abstract review, 111 studies were excluded, which resulted in seven studies that underwent full-text review. Finally, six (four cross-sectional and two case control) studies were included in the meta-analysis (Figure 1) [Bambha *et al.* 2014; Molloy *et al.* 2012; Anty *et al.* 2012; Binerdinc *et al.* 2012; Catalano *et al.* 2010; Gutierrez-Grobe *et al.* 2012].

Characteristics of the studies included in this meta-analysis are described in Table 1 and demographic characteristics of the cohorts analyzed are described in Table 2. Four cross-sectional and two case-control studies generated a total study population of 20,064 subjects. Among these, three studies with 18,990 subjects were included in the analysis for prevalence of NAFLD while the other three studies with 1074 subjects were used for the analysis of hepatic fibrosis. Measurement of caffeine intake by each study is included in Table 3.

Figure 1. Study flow diagram.

All of the included studies were thought to be of medium to high quality based on their NOS score.

Outcome results

Total caffeine consumption (mg/day) was not significantly associated with either the prevalence [pooled mean difference (MD) 2.36; 95% confidence interval (CI) −35.92 to 40.64] (Figure 2) or hepatic fibrosis (pooled MD −39.95; 95% CI −132.72 to 52.82) of NAFLD (Figure 3). Further subgroup analyses stratified by study designs and locations were also not significant.

Subgroups were then stratified again by type of caffeine intake (Table 4). Regular coffee as the source of caffeine intake was significantly associated with reduced hepatic fibrosis of NAFLD (pooled MD −91.35; 95% CI −139.42 to −43.27; $n = 2$ studies) (Figure 4). However, regular coffee caffeine intake was not associated with prevalence of NAFLD (pooled MD 23.06; 95% CI −8.67 to 54.80; $n = 2$ studies).

Discussion

Previous studies have suggested that caffeine consumption plays a protective role in NAFLD [Bambha *et al.* 2014; Molloy *et al.* 2012; Anty *et al.* 2012; Bircerdinc *et al.* 2012; Catalano *et al.* 2010; Gutierrez-Grobe *et al.* 2012; Modi *et al.* 2010]. To the best of the authors' knowledge this

is the first meta-analysis to investigate this relationship among caffeine consumption and the prevalence or degree of hepatic fibrosis of NAFLD.

The exact role caffeine plays in the prevalence and progression of NAFLD remains unknown. Caffeine has been implicated to have many antifibrotic effects through a series of biochemical processes including stimulation of hepatic stellate cell apoptosis, induction of intracellular F-actin and cAMP expression, inhibition of focal adhesion kinase and actin synthesis, along with inhibition of alpha-smooth muscle actin and procollagen expression [Shim *et al.* 2013]. The difficulty has been trying to tease out the role specific sources such as regular coffee, energy drinks, espresso, tea, etc. may influence these antifibrotic effects.

While this study did not find any significant association between total caffeine consumption and the prevalence or hepatic fibrosis of NAFLD, regular coffee caffeine intake was significantly associated with reduced hepatic fibrosis of NAFLD. Regular coffee consumption was defined as the ingestion of caffeine only from regular coffee, not including other caffeinated beverages such as espresso, tea, soda, etc. The beneficial effect of regular coffee on the liver to reduce liver enzymes (GGT, ALT) has recently been suggested by multiple studies [Molloy *et al.* 2012; Bircerdinc *et al.* 2012; Cadden *et al.* 2007]. As a complex mixture of over one hundred compounds, coffee is considered to be derived

Table 1. Characteristics of studies included in meta-analysis.

Study	Study design	Study location	Cases / subjects	Diagnosis of NAFLD/NASH	Outcome	Confounders controlled	Adjusted OR	NOS*
NAFLD prevalence								
Birerdinc <i>et al.</i> [2012]	Population-based cross-sectional study	USA	1782/18,550	Elevated serum aminotransferases with exclusion of other liver disease and excess alcohol consumption (men >20 g/day, women >10 g/day)	Presence of NAFLD	Age, gender, ethnicity and metabolic syndrome components	0.999319 (0.998955–0.999684)	7
Catalano <i>et al.</i> [2010]	Hospital-based case-control study	Italy	157/310	US with exclusion of other liver disease and excess alcohol consumption (>20 g/day)	Presence of NAFLD	Not available	Not calculated	7
Gutierrez-Grobe <i>et al.</i> [2012]	Hospital-based case-control study	Mexico	57/130	US with exclusion of other liver disease and excess alcohol consumption (>20 g/day)	Presence of NAFLD	Not available	Not calculated	6
NAFLD fibrosis								
Bambha <i>et al.</i> [2014]	Hospital-based cross-sectional study	USA	199/782	Liver biopsy with exclusion of other liver disease and excess alcohol consumption (Men >20 g/day, women >10 g/day)	NASH fibrosis (>stage 2 <i>versus</i> ≤stage 2)	Age, gender, ethnicity, waist circumference, AST, GGT, diabetes, smoking, alcohol, biopsy length, HOMA-IR	0.68 (0.52–0.89)	7
Anty <i>et al.</i> [2012]	Hospital-based cross-sectional study	France	68/195	Surgical liver biopsy with exclusion of other liver disease and excess alcohol consumption (Men >30 g/day, women >20 g/day)	NASH fibrosis (≥stage 2 <i>versus</i> <stage 2)	AST, HOMA-IR, metabolic syndrome, NASH	0.75 (0.58–0.98)	6
Molloy <i>et al.</i> [2012]	Hospital-based cross-sectional study	USA	36/97	US and liver biopsy with exclusion of other liver disease and excess alcohol consumption (>20 g/day)	NASH fibrosis (≥stage 2 <i>versus</i> <stage 2)	Not available	Not calculated	6
*Newcastle-Ottawa scale (NOS) scores of 1–3, 4–6, and 7–9 for low-, intermediate-, and high-quality studies, respectively. NAFLD, nonalcoholic fatty liver disease; NASH, nonalcoholic steatohepatitis; OD, odds ratio.								

Table 2. Demographic characteristics of the cohorts analyzed for each study included in meta-analysis.

Study (year)	Age, years	Male (%)	Caucasian (%)	Black (%)	Hispanic (%)	Other (%)	BMI (kg/m ²)
Birerdinc <i>et al.</i> [2012]	–	53.5	70.0	7.4	17.6	5.0	–
Catalano <i>et al.</i> [2010]	49.7	49	–	–	–	–	32
Gutierrez-Grobe <i>et al.</i> [2012]	44.5	–	–	–	–	–	29.2
Bambha <i>et al.</i> [2014]	48	38	84	2.7	12	1.3	–
Anty <i>et al.</i> [2012]	39.4	17.4	–	–	–	–	42.2
Molloy <i>et al.</i> [2012]	53.8	50.1	62.7	11.1	21.9	4.2	30.6

Table 3. Caffeine consumption measurement by each study included in meta-analysis.

Study (first author and year)	Total caffeine intake (mg/day)
Birerdinc <i>et al.</i> [2012]	Total caffeine intake (mg/day)
Catalano <i>et al.</i> [2010]	Espresso coffee intake (cups/day)
Gutierrez-Grobe <i>et al.</i> [2012]	Total caffeine intake (mg/day)
Bambha <i>et al.</i> [2014]	Coffee (unspecified) intake (cups/day)
Anty <i>et al.</i> [2012]	Total caffeine intake (g/week), caffeine from espresso, regular coffee, tea and chocolate or soda (g/week)
Molloy <i>et al.</i> [2012]	Total caffeine or regular coffee caffeine intake (mg/day)

Figure 2. Forest plot: association between caffeine consumption and prevalence of nonalcoholic fatty liver disease (NAFLD). **Figure 3.** Forest plot: association between caffeine consumption and hepatic fibrosis (advanced versus early stage) of nonalcoholic fatty liver disease (NAFLD).

of three main compounds: caffeine, chlorogenic acids, and diterpenes (cafestol and kahweol) [Gressner, 2009]. While caffeine modifies signaling pathways leading to the decreased activity of connective tissue growth factor (CTGF), considered to be a major stimulator of hepatic fibrosis, many of the cytoprotective antioxidant effects of coffee are thought to be independent of the actual

caffeine [Kalthoff *et al.* 2010]. The various forms of brewing coffee additionally complicate the ability to retain the antioxidant effect as the use of high pressured filtration versus ordinary filtration during preparation have been suggested to contain different levels of cafestol and kahweol [Anty *et al.* 2012]. While the exact mechanism of this effect or the amount of coffee required to provide

Table 4. Subgroup analyses stratified by study designs, study locations, types of caffeine consumption.

Subgroup	Number of studies	Pooled MD (95% CI)	Heterogeneity
NAFLD prevalence			
All studies	3	2.36 [-35.92 to 40.64]	$p = 0.02, I^2 = 76\%$
Study design			
Case-control	2	23.06 [-8.67 to 54.80]	$p = 0.75, I^2 = 0\%$
Population-base cross-sectional	1	-23.10 [-23.41 to -22.79]	—
Regular coffee	2	23.06 [-8.67 to 54.80]	$p = 0.75, I^2 = 0\%$
NAFLD fibrosis			
All studies	3	-39.95 [-132.72 to 52.82]	$p = 0.01, I^2 = 78\%$
Study location			
USA	2	-23.89 [-145.22 to 97.44]	$p = 0.03, I^2 = 79\%$
Europe	1	-81.40 [-174.77 to 11.97]	—
Regular coffee	2	-91.35 [-139.42 to -43.27]	$p = 0.74, I^2 = 0\%$

NAFLD, nonalcoholic fatty liver disease; MD, mean difference.

Figure 4. Forest plot: association between regular coffee consumption and hepatic fibrosis (advanced *versus* early stage) of NAFLD.

significant benefit remains unclear, it is clear that the potential benefit of coffee needs to be further investigated.

This meta-analysis has several limitations. First, the included studies were quite heterogeneous methodologically. Second, several of our studies diagnosed NAFLD based on ultrasonography without the requirement for pathologic confirmation after liver biopsy. Third, as almost all of the studies measured caffeine intake through the use of a questionnaire at a single point in time, it is difficult to accurately represent caffeine intake over time. Recently, the ability to truly assess adequate intake of coffee accurately and evaluation of the nutritional and lifestyle behaviors of patients included in studies evaluating the role of coffee on NAFLD and hepatic fibrosis have been challenged [Anty *et al.* 2013]. Lastly, several confounders such as cigarette smoking, physical activity, diet, or socioeconomic factors were not included in this analysis.

The inclusion of over 20,000 patients was a significant strength of this meta-analysis. While

cross-sectional and case-controlled studies have their inherent limitations, with the utilization of six studies we were able to generate a much greater statistical power compared with a single study [Mann, 2003]. Lastly, there was a diverse population studied without significant ethnic disparity.

In conclusion, our results suggest regular coffee caffeine consumption is significantly associated with reduced hepatic fibrosis in patients with NAFLD. Further research should be directed at understanding the potential beneficial components of regular coffee and determining the required amount that must be consumed and method of brewing to generate an advantageous effect. Given the potential benefits of regular coffee, patients with NAFLD should be encouraged to consume regular coffee daily.

Authors' contributions

All authors have participated in conception and design, manuscript writing, and final approval of the manuscript.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Conflict of interest statement

The authors report no financial or personal conflicts of interest. This manuscript is not under consideration elsewhere.

References

- Anty, R., Marjoux, S., Iannelli, A., Patouraux, S., Schneck, A., Bonnafous, S. *et al.* (2012) Regular coffee but not espresso drinking is protective against fibrosis in a cohort mainly composed of morbidly obese European women with NAFLD undergoing bariatric surgery. *J Hepatol* 57: 1090–1096.
- Anty, R., Marjoux, S., Iannelli, A., Pariente, A. and Tran, A. (2013) Reply to: “regular coffee: a magic bullet or a naked gun? Regular coffee but not espresso drinking is protective against fibrosis in NAFLD”. *J Hepatol* 58: 1265–1266.
- Bambha, K., Wilson, L., Unalp, A., Loomba, R., Neuschwander-Tetri, B., Brunt, E. *et al.* (2014) Coffee consumption in NAFLD patients with lower insulin resistance is associated with lower risk of severe fibrosis. *Liver Int* 34: 1250–1258.
- Birerdinc, A., Stepanova, M., Pawloski, L. and Younossi, Z. (2012) Caffeine is protective in patients with non-alcoholic fatty liver disease. *Aliment Pharmacol Ther* 35: 76–82.
- Bravi, F., Bosetti, C., Tavani, A., Bagnardi, V., Gallus, S., Negri, E. *et al.* (2007) Coffee drinking and hepatocellular carcinoma risk: a meta-analysis. *Hepatology* 46: 430–435.
- Cadden, I., Partovi, N. and Yoshida, E. (2007) Review article: possible beneficial effects of coffee on liver disease and function. *Aliment Pharmacol Ther* 26(1):1–8.
- Catalano, D., Martinez, G., Tonzuso, A., Pirri, C., Trovato, F. and Trovato, G. (2010) Protective role of coffee in non-alcoholic fatty liver disease (NAFLD). *Dig Dis Sci* 55: 3200–3206.
- Chen, S., Teoh, N., Chitturi, S. and Farrell, G. (2014) Coffee and non-alcoholic fatty liver disease: brewing evidence for hepatoprotection? *J Gastroenterol Hepatol* 29: 435–441.
- Frery, C., Johnson, R. and Wang, M. (2005) Food sources and intakes of caffeine in the diets of persons in the United States. *J Am Diet Assoc* 105: 110–113.
- Freedman, N., Park, Y., Abnet, C., Hollenbeck, A. and Sinha, R. (2012) Association of coffee drinking with total and cause-specific mortality. *N Engl J Med* 366: 1891–1904.
- Gressner, O. (2009) Less Smad2 is good for you! A scientific update on coffee’s liver benefits. *Hepatology* 50: 970–978.
- Gutierrez-Grobe, Y., Chavez-Tapia, N., Sanchez-Valle, V., Gavilanes-Espinar, J., Ponciano-Rodriguez, G., Uribe, M. *et al.* (2012) High coffee intake is associated with lower grade nonalcoholic fatty liver disease: the role of peripheral antioxidant activity. *Ann Hepatol* 11: 350–355.
- Heckman, M., Weil, J. and Gonzalez de Mejia, E. (2010) Caffeine (1, 3, 7-trimethylxanthine) in foods: a comprehensive review on consumption, functionality, safety, and regulatory matters. *J Food Sci* 75(3): R77–R87.
- Higgins, J., Thompson, S., Deeks, J. and Altman, D. (2003) Measuring inconsistency in meta-analyses. *BMJ* 327: 557–560.
- Kalthoff, S., Ehmer, U., Freiberg, N., Manns, M. and Strassburg, C. (2010) Coffee induces expression of glucuronosyltransferases by the aryl hydrocarbon receptor and Nrf2 in liver and stomach. *Gastroenterology* 139:1699–1710, 1710.e1–2.
- Liu, R., Guo, X., Park, Y., Huang, X., Sinha, R., Freedman, N. *et al.* (2012) Caffeine intake, smoking, and risk of Parkinson disease in men and women. *Am J Epidemiol* 175: 1200–1207.
- Mann, C. (2003) Observational research methods. Research design II: cohort, cross sectional, and case-control studies. *Emerg Med J* 20(1):54–60.
- Marchesini, G., Brizi, M., Bianchi, G., Tomassetti, S., Bugianesi, E., Lenzi, M. *et al.* (2001) Nonalcoholic fatty liver disease: a feature of the metabolic syndrome. *Diabetes* 50(8):1844–1850.
- Mitchell, D., Knight, C., Hockenberry, J., Teplansky, R. and Hartman, T. (2014) Beverage caffeine intakes in the U.S. *Food Chem Toxicol* 63: 136–142.
- Modi, A., Feld, J., Park, Y., Kleiner, D., Everhart, J., Liang, T. *et al.* (2010) Increased caffeine consumption is associated with reduced hepatic fibrosis. *Hepatology* 51: 201–209.
- Molloy, J., Calcagno, C., Williams, C., Jones, F., Torres, D. and Harrison, S. (2012) Association of coffee and caffeine consumption with fatty liver disease, nonalcoholic steatohepatitis, and degree of hepatic fibrosis. *Hepatology* 55: 429–436.
- Paynter, N., Yeh, H., Voutilainen, S., Schmidt, M., Heiss, G., Folsom, A. *et al.* (2006) Coffee and sweetened beverage consumption and the risk of type 2 diabetes mellitus: the atherosclerosis risk in communities study. *Am J Epidemiol* 164: 1075–1084.

Ruhl, C. and Everhart, J. (2005) Coffee and tea consumption are associated with a lower incidence of chronic liver disease in the United States. *Gastroenterology* 129: 1928–1936.

Shen, H., Lipka, S., Kumar, A. and Mustacchia, P. (2014) Association between nonalcoholic fatty liver disease and colorectal adenoma: a systemic review and meta-analysis. *J Gastrointest Oncol* 5: 440–446.

Shim, S., Jun, D., Kim, E., Saeed, W., Lee, K., Lee, H. *et al.* (2013) Caffeine attenuates liver fibrosis via defective adhesion of hepatic stellate cells in cirrhotic model. *J Gastroenterol Hepatol* 28: 1877–1884.

Stroup, D., Berlin, J., Morton, S., Olkin, I., Williamson, G., Rennie, D. *et al.* (2000) Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. *JAMA* 283: 2008–2012.

Wilson, K., Kasperzyk, J., Rider, J., Kenfield, S., van Dam, R., Stampfer, M. *et al.* (2011) Coffee consumption and prostate cancer risk and progression in the Health Professionals Follow-up Study. *J Natl Cancer Inst* 103: 876–884.

Visit SAGE journals online
<http://tag.sagepub.com>

SAGE journals