# Substance Use Disorders and Primary Health Care: Addressing the Gap

## PRISM Systematic Reviews and Papers

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If scientists discovered a previously unrecognized, but potentially treatable pathogen accounting for a substantial number of misdiagnoses, treatment failures and medical costs in several chronic medical illnesses, this would initiate preventive action throughout the healthcare system. In fact, there is a class of agents – alcohol and other drugs of abuse - that has this type of broad impact across the spectrum of acute and chronic medical illnesses. Alcohol and drug use - even at levels below the threshold of addiction - regularly lead to misdiagnoses, poor adherence to prescribed care, interference with commonly prescribed medications, greater amounts of physician time, unnecessary medical testing, poor outcomes and increased costs – particularly in the management of chronic illness. This situation can be improved. The health and cost implications of ignoring substance use problems among patients in treatment for chronic illness are substantial. The good news is that these currently unrecognized, untreated problems can be addressed in standard clinical settings, easily and at very low cost.

The Program of Research to Integrate Substance Use Issues into Mainstream Health Care (PRISM) was co-founded in 2002 by Barbara Turner, M.D. of the University of Pennsylvania School of Medicine and A. Thomas McLellan, Ph.D. of the Treatment Research Institute. PRISM commissioned systematic research reviews evaluating alcohol's effects on common chronic clinical conditions including diabetes, sleep disorders, hypertension, depression, and bone disease. PRISM has also commissioned systematic reviews exploring the impact of illicit drug use on common conditions such as back pain (opioids) and lung disease (marijuana). Several reviews and papers have been published and are summarized on the following pages.

PRISM is premised on the well-founded belief that physicians will consider and address alcohol and illicit drug impacts if given sound evidence and appropriate educational programs, quality standards, and practice designs. Through its collaboration with four medical societies, PRISM is developing a model of care that integrates clinically relevant, evidence-based information about the effects of alcohol and illicit drug use on common chronic conditions.

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# Systematic Reviews

**Howard AA, Arnsten JH, Gourevitch MN. Effect of alcohol consumption on diabetes mellitus: A systematic review. *Ann Intern Med.* 2004;140:211-9.**

## Abstract

BACKGROUND: Both diabetes mellitus and alcohol consumption are prevalent in the United States, yet physicians are poorly informed about how alcohol use affects risk for or management of diabetes.

PURPOSE: To conduct a systematic review assessing the effect of alcohol use on the incidence, management, and complications of diabetes mellitus in adults.

DATA SOURCES: English-language studies in persons 19 years of age or older that were identified by searching the MEDLINE database from 1966 to the third week of August 2003 and the reference lists of key articles.

STUDY SELECTION: Two independent assessors reviewed 974 retrieved citations to identify all experimental, cohort, or case-control studies that assessed the effect of alcohol use on diabetes risk, control, self-management, adverse drug events, or complications.

DATA EXTRACTION: Two independent reviewers extracted data and evaluated study quality on the basis of established criteria.

DATA SYNTHESIS: Thirty-two studies that met inclusion criteria were reviewed. Compared with no alcohol use, moderate consumption (one to 3 drinks/d) is associated with a 33% to 56% lower incidence of diabetes and a 34% to 55% lower incidence of diabetes-related coronary heart disease. Compared with moderate consumption, heavy consumption (>3 drinks/d) may be associated with up to a 43% increased incidence of diabetes. Moderate alcohol consumption does not acutely impair glycemic control in persons with diabetes.

CONCLUSIONS: Moderate alcohol consumption is associated with a decreased incidence of diabetes mellitus and a decreased incidence of heart disease in persons with diabetes. Further studies are needed to assess the long-term effects of alcohol consumption on glycemic control and noncardiac complications in persons with diabetes.

**McFadden CB, Brensinger CM, Berlin JA, Townsend RR. Systematic review of the effect of daily alcohol intake on blood pressure. *Am J Hypertens.* 2005;18:276-286.**

## Abstract

Numerous epidemiologic investigations have found an association between moderate intake of alcohol and increased blood pressure (BP). However, in controlled clinical studies that directly tested the effects of alcohol intake on BP, findings are inconsistent, perhaps because of differences in duration of alcohol use and the timing of BP measurements. In this setting, we performed a systematic review of trials that measured BP after a period of sustained alcohol intake (defined as daily intake of at least one alcoholic drink daily) in one group and that also had a control group of individuals who consumed no alcohol. Nine studies met the entrance criteria. The review demonstrated a significant rise in systolic blood pressure (SBP) and diastolic BP (DBP) of 2.7 mm and 1.4 mm Hg, respectively, after alcohol intake. An early effect of alcohol leading to a reduction BP (in the hours after exposure) and a later effect (next day) of raising BP led to smaller differences in the net effect of alcohol on BP when ambulatory BP monitoring measurements were compared with casual office- or clinic-based measurements. Our findings may have important implications for interpreting studies measuring the effect of alcohol on BP as well as for regular clinical care. These findings indicate that the timing of BP measurements after alcohol intake has a substantial effect on the magnitude and perhaps even the direction of BP change.

**Brien SE, Ronksley PE, Turner BJ, Mukamal KJ, Ghali WA. Effect of alcohol consumption on biological markers associated with risk of coronary heart disease: systematic review and meta-analysis of interventional studies.** ***BMJ*****. 2011 Feb 22;342:d636.**

## Abstract

OBJECTIVE: To systematically review interventional studies of the effects of alcohol consumption on 21 biological markers associated with risk of coronary heart disease in adults without known cardiovascular disease.

DESIGN: Systematic review and meta-analysis.

DATA SOURCES: Medline (1950 to October 2009) and Embase (1980 to October 2009) without limits.

STUDY SELECTION: Two reviewers independently selected studies that examined adults without known cardiovascular disease and that compared fasting levels of specific biological markers associated with coronary heart disease after alcohol use with those after a period of no alcohol use (controls). 4690 articles were screened for eligibility, the full texts of 124 studies reviewed, and 63 relevant articles selected.

RESULTS: Of 63 eligible studies, 44 on 13 biomarkers were meta-analysed in fixed or random effects models. Quality was assessed by sensitivity analysis of studies grouped by design. Analyses were stratified by type of beverage (wine, beer, spirits). Alcohol significantly increased levels of high density lipoprotein cholesterol (pooled mean difference 0.094 mmol/L, 95% confidence interval 0.064 to 0.123), apolipoprotein A1 (0.101 g/L, 0.073 to 0.129), and adiponectin (0.56 mg/L, 0.39 to 0.72). Alcohol showed a dose-response relation with high density lipoprotein cholesterol (test for trend P=0.013). Alcohol decreased fibrinogen levels (-0.20 g/L, -0.29 to -0.11) but did not affect triglyceride levels. Results were similar for crossover and before and after studies, and across beverage types.

CONCLUSIONS: Favourable changes in several cardiovascular biomarkers (higher levels of high density lipoprotein cholesterol and adiponectin and lower levels of fibrinogen) provide indirect pathophysiological support for a protective effect of moderate alcohol use on coronary heart disease.

**Ronksley PE, Brien SE, Turner BJ, Mukamal KJ, Ghali WA. Association of alcohol consumption with selected cardiovascular disease outcomes: a systematic review and meta-analysis. *BMJ*. 2011 Feb 22;342:d671.**

## Abstract

OBJECTIVE: To conduct a comprehensive systematic review and meta-analysis of studies assessing the effect of alcohol consumption on multiple cardiovascular outcomes.

DESIGN: Systematic review and meta-analysis.

DATA SOURCES: A search of Medline (1950 through September 2009) and Embase (1980 through September 2009) supplemented by manual searches of bibliographies and conference proceedings. Inclusion criteria Prospective cohort studies on the association between alcohol consumption and overall mortality from cardiovascular disease, incidence of and mortality from coronary heart disease, and incidence of and mortality from stroke. Studies reviewed Of 4235 studies reviewed for eligibility, quality, and data extraction, 84 were included in the final analysis.

RESULTS: The pooled adjusted relative risks for alcohol drinkers relative to non-drinkers in random effects models for the outcomes of interest were 0.75 (95% confidence interval 0.70 to 0.80) for cardiovascular disease mortality (21 studies), 0.71 (0.66 to 0.77) for incident coronary heart disease (29 studies), 0.75 (0.68 to 0.81) for coronary heart disease mortality (31 studies), 0.98 (0.91 to 1.06) for incident stroke (17 studies), and 1.06 (0.91 to 1.23) for stroke mortality (10 studies). Dose-response analysis revealed that the lowest risk of coronary heart disease mortality occurred with 1-2 drinks a day, but for stroke mortality it occurred with ≤1 drink per day. Secondary analysis of mortality from all causes showed lower risk for drinkers compared with non-drinkers (relative risk 0.87 (0.83 to 0.92)).

CONCLUSIONS: Light to moderate alcohol consumption is associated with a reduced risk of multiple cardiovascular outcomes.

**Sullivan LE, Fiellin DA, O'Connor PG. The prevalence and impact of alcohol problems in major depression: a systematic review. *Am J Med*. 2005;118:330-341.**

## Abstract

Major depression and alcohol problems are common in primary care, yet little is known about the prevalence of alcohol problems in patients with depression or alcohol's effect on depression outcomes. We strove to answer the following questions: How common are alcohol problems in patients with depression? Does alcohol affect the course of depression, response to antidepressant therapy, risk of suicide/death, social functioning and health care utilization? In which alcohol categories and treatment settings have patients with depression and alcohol problems been evaluated? English language studies from MEDLINE, PsychINFO, and Cochrane Controlled Trial Registry were reviewed. Studies were selected using predefined criteria if they reported on the prevalence or effects of alcohol problems in depression. Thirty-five studies met criteria and revealed a median prevalence of current or lifetime alcohol problems in depression of 16% (range 5-67%) and 30% (range 10-60%), respectively. This compares with 7% for current and 16-24% for lifetime alcohol problems in the general population. There is evidence that antidepressants improve depression outcomes in persons with alcohol dependence. Alcohol problems are associated with worse outcomes with respect to depression course, suicide/death risk, social functioning, and health care utilization. The majority of the studies, 34 of 35 (97%), evaluated alcohol abuse and dependence, and 25 of 35 (71%) were conducted in psychiatric inpatients. We conclude that alcohol problems are more common in depression than in the general population, are associated with adverse clinical and health care utilization outcomes, and that antidepressants can be effective in the presence of alcohol dependence. In addition, the literature focuses almost exclusively on patients with alcohol abuse or dependence in psychiatric inpatient settings, and excludes patients with less severe alcohol problems and primary care outpatient settings.

**Stein MD, Friedmann PD. Disturbed sleep and its relationship to alcohol use.**

***Subst Abuse.*** **2005 Mar;26(1):1-13.**

## Abstract

STUDY OBJECTIVES: To review evidence of an association between disturbed sleep and alcohol use.

DESIGN: We searched MEDLINE, PSYCHINFO, ETOH, BIBLIOSLEEP and the Rutgers Alcohol Studies databases between January 1966 and August 2002. Search terms included alcohol-related disorders or alcoholism in combination with sleep, sleep initiation and maintenance disorders, or sleep apnea syndromes. The search produced over 440 citations. We reviewed 107 relevant articles, of which 60 included quantitative measures of both alcohol use and sleep.

MEASUREMENTS AND RESULTS: Behavioral studies suggest that up to 2 to 3 standard drinks before bedtime initially promotes sleep, but these effects diminish in as few as 3 days of continued use. Clinical investigations support a relationship between sleep disturbance and alcohol use, but variability in the definition and measurement of these domains and a preponderance of cross-sectional studies make uncertain the strength and direction of the association.

CONCLUSIONS: The association of insomnia with alcohol use disorders suggests that the clinical evaluation of patients with sleep problems should include a careful assessment of alcohol use. Future studies of this relationship should employ prospective designs with standardized, validated measures of both sleep and alcohol use. Rigorous treatment studies for chronic insomnia in alcohol dependent patients are also needed.

**Berg KM, Kunins HV, Jackson JL, Nahvi S, Chaudhry A, Harris KA Jr, Malik R, Arnsten JH. Association between alcohol consumption and both osteoporotic fracture and bone density Am J Med. 2008;121(5):406-18.**

## Abstract

OBJECTIVE: Alcoholism is a risk factor for osteoporotic fractures and low bone density, but the effects of moderate alcohol consumption on bone are unknown. We performed a systematic review and meta-analysis to assess the associations between alcohol consumption and osteoporotic fractures, bone density and bone density loss over time, bone response to estrogen replacement, and bone remodeling.

METHODS: MEDLINE, Current Contents, PsychINFO, and Cochrane Libraries were searched for studies published before May 14, 2007. We assessed quality using the internal validity criteria of the US Preventive Services Task Force.

RESULTS: We pooled effect sizes for 2 specific outcomes (hip fracture and bone density) and synthesized data qualitatively for 4 outcomes (non-hip fracture, bone density loss over time, bone response to estrogen replacement, and bone remodeling). Compared with abstainers, persons consuming from more than 0.5 to 1.0 drinks per day had lower hip fracture risk (relative risk=0.80 [95% confidence interval, 0.71-0.91]), and persons consuming more than 2 drinks per day had higher risk (relative risk=1.39 [95% confidence interval, 1.08-1.79]). A linear relationship existed between femoral neck bone density and alcohol consumption. Because studies often combined moderate and heavier drinkers in a single category, we could not assess relative associations between alcohol consumption and bone density in moderate compared with heavy drinkers.

CONCLUSION: Compared with abstainers and heavier drinkers, persons who consume 0.5 to 1.0 drink per day have a lower risk of hip fracture. Although available evidence suggests a favorable effect of alcohol consumption on bone density, a precise range of beneficial alcohol consumption cannot be determined.

**Fiellin L, Turner B.J., et al. A Meta-analysis of the efficacy of non-physician brief interventions for unhealthy alcohol use: implications for the patient-centered medical home. Am J Addict, in press.**

A META-ANALYSIS OF THE EFFICACY OF NON-PHYSICIAN BRIEF INTERVENTIONS FOR UNHEALTHY ALCOHOL USE: IMPLICATIONS FOR THE PATIENT-CENTERED MEDICAL HOME L.E. Sullivan1; J.M. Tetrault1; R.S. Braithwaite2; D.A. Fiellin1. 1Yale University, New Haven, CT; 2Yale University, West Haven, CT. (Tracking ID # 205552)

BACKGROUND: Unhealthy alcohol use is common in primary care yet few patients are counseled about their alcohol use by their physician. Physician-based brief interventions are modestly effective at decreasing alcohol consumption but physicians often do not have the time to conduct these interventions. The purpose of this meta-analysis was to examine the efficacy of brief interventions by non-physician clinicians for patients with unhealthy drinking in primary care.

METHODS: We identified English language studies by searching the electronic databases; MEDLINE (1967 to January 2008), PsychInfo (1967-January 2008), the Cochrane Drug and Alcohol Group specialized register (to 1st quarter 2008), CINAHL (1982-January 2008), and the Social Sciences Citation Index (to 1st quarter 2008) and Science Citation Index (to 1st quarter 2008). Studies were included if they had alcohol as their primary focus, were based in primary care, were not solely physician-based, examined drinking outcomes, and consisted of a behavioral intervention. Three reviewers independently abstracted quantitative and qualitative data. Study quality was evaluated according to U.S. Preventive Services Task Force criteria. We combined drinking outcomes at 6 months using the random effects method, performed sensitivity analyses excluding studies that contributed disproportionately to heterogeneity, and conducted the meta-analysis with and without the one study with disproportionate heterogeneity.

RESULTS: 13 randomized clinical trials met initial criteria. All studies had a usual care arm, consisting of brief advice from either a physician or other clinician. Sample sizes ranged from 28–1329 subjects, intensity of intervention ranged from a single 5 minute session to six 90-minute sessions. Seven studies (2633 patients) met criteria for inclusion in the meta-analysis. The interventions lowered the mean drinks per week by 1.7 standard drinks compared with the control arms (95% CI, -0.03–3.5; p=0.054).

CONCLUSION: Non-physician interventions are effective in producing reductions in alcohol consumption at 6 months in unhealthy drinkers in primary care. These findings have implications for their implementation within the patient-centered medical home.

**Mertens JR, Lu YW, Parthasarathy S, Moore C and Weisner CM. Medical and psychiatric conditions of alcohol and drug treatment patients in an HMO: comparison with matched controls. *Arch Intern Med*. 2003;163:2511-7.**

## Abstract

BACKGROUND: Substance abuse and health problems seem to be inextricably related. Yet, prior research on the health conditions related to substance abuse is largely focused on alcohol and is from patients treated in publicly funded programs, inpatients, and the general population.

METHODS: This study compares the prevalence of medical and psychiatric conditions among 747 substance abuse patients and 3690 demographically matched controls from the same health maintenance organization, and examines whether any heightened prevalence for substance abuse patients (relative to controls) varies according to demographic subgroups and type of substance.

RESULTS: Approximately one third of the conditions examined were more common among substance abuse patients than among matched controls, and many of these conditions were among the most costly. We also found that pain-related diagnoses, including arthritis, headache, and lower back pain, were more prevalent among such patients, particularly those dependent on narcotic analgesics.

CONCLUSIONS: Our findings point to the importance of examining comorbid medical conditions and substance abuse in both primary and specialty care. Our findings regarding pain-related diagnoses among patients dependent on narcotic analgesics highlight the need for linkages between primary care and substance abuse treatment. Moreover, optimal treatment of many common medical disorders may require identification, intervention, and treatment of an underlying substance abuse disorder.

**Martell BA, O'Connor PG, Kerns RD, Becker WC, Morales KH, Kosten TR, Fiellin DA. Systematic review: opioid treatment for chronic back pain: prevalence, efficacy, and association with addiction. Ann Intern Med. 2007 Jan 16;146(2):116-27.**

## Abstract

BACKGROUND: The prevalence, efficacy, and risk for addiction for persons receiving opioids for chronic back pain are unclear.

PURPOSE: To determine the prevalence of opioid treatment, whether opioid medications are effective, and the prevalence of substance use disorders among patients receiving opioid medications for chronic back pain.

DATA SOURCES: English-language studies from MEDLINE (1966-March 2005), EMBASE (1966-March 2005), Cochrane Central Register of Controlled Clinical Trials (to 4th quarter 2004), PsychInfo (1966-March 2005), and retrieved references.

STUDY SELECTION: Articles that studied an adult, nonobstetric sample; used oral, topical, or transdermal opioids; and focused on treatment for chronic back pain.

DATA EXTRACTION: Two investigators independently extracted data and determined study quality.

DATA SYNTHESIS: Opioid prescribing varied by treatment setting (range, 3% to 66%). Meta-analysis of the 4 studies assessing the efficacy of opioids compared with placebo or a nonopioid control did not show reduced pain with opioids (g, -0.199 composite standardized mean difference [95% CI, -0.49 to 0.11]; P = 0.136). Meta-analysis of the 5 studies directly comparing the efficacy of different opioids demonstrated a nonsignificant reduction in pain from baseline (g, -0.93 composite standardized mean difference [CI, -1.89 to -0.03]; P = 0.055). The prevalence of lifetime substance use disorders ranged from 36% to 56%, and the estimates of the prevalence of current substance use disorders were as high as 43%. Aberrant medication-taking behaviors ranged from 5% to 24%.

LIMITATIONS: Retrieval and publication biases and poor study quality. No trial evaluating the efficacy of opioids was longer than 16 weeks.

CONCLUSIONS: Opioids are commonly prescribed for chronic back pain and may be efficacious for short-term pain relief. Long-term efficacy (> or =16 weeks) is unclear. Substance use disorders are common in patients taking opioids for back pain, and aberrant medication-taking behaviors occur in up to 24% of cases.

**Mehra, R, Moore BA, Crothers K, Tetrault J, Fiellin D. The Association Between Marijuana Smoking and Lung Cancer: A Systematic Review. Arch Intern Med. 2006;166:1359-1367**

## Abstract

BACKGROUND: The association between marijuana smoking and lung cancer is unclear, and a systematic appraisal of this relationship has yet to be performed. Our objective was to assess the impact of marijuana smoking on the development of premalignant lung changes and lung cancer.

METHODS: Studies assessing the impact of marijuana smoking on lung premalignant findings and lung cancer were selected from MEDLINE, PSYCHLIT, and EMBASE databases according to the following predefined criteria: English-language studies of persons 18 years or older identified from 1966 to the second week of October 2005 were included if they were research studies (ie, not letters, reviews, editorials, or limited case studies), involved persons who smoked marijuana, and examined premalignant or cancerous changes in the lung.

RESULTS: Nineteen studies met selection criteria. Studies that examined lung cancer risk factors or premalignant changes in the lung found an association of marijuana smoking with increased tar exposure, alveolar macrophage tumoricidal dysfunction, increased oxidative stress, and bronchial mucosal histopathologic abnormalities compared with tobacco smokers or nonsmoking controls. Observational studies of subjects with marijuana exposure failed to demonstrate significant associations between marijuana smoking and lung cancer after adjusting for tobacco use. The primary methodologic deficiencies noted include selection bias, small sample size, limited generalizability, overall young participant age precluding sufficient lag time for lung cancer outcome identification, and lack of adjustment for tobacco smoking.

CONCLUSION: Given the prevalence of marijuana smoking and studies predominantly supporting biological plausibility of an association of marijuana smoking with lung cancer on the basis of molecular, cellular, and histopathologic findings, physicians should advise patients regarding potential adverse health outcomes until further rigorous studies are performed that permit definitive conclusions.

**Tetrault JM, Crothers K, Moore BA, Mehra R, Concato J, Fiellin DA. Effects of Marijuana Smoking on Pulmonary Function and Respiratory Complications: A Systematic Review. Arch Intern Med. 2007 Feb 12;167(3):221-228**

## Abstract

BACKGROUND: The relationship between marijuana smoking and pulmonary function or respiratory complications is poorly understood; therefore, we conducted a systematic review of the impact of marijuana smoking on pulmonary function and respiratory complications.

METHODS: Studies that evaluated the effect of marijuana smoking on pulmonary function and respiratory complications were selected from the MEDLINE, PsychINFO, and EMBASE databases according to predefined criteria from January 1, 1966, to October 28, 2005. Two independent reviewers extracted data and evaluated study quality based on established criteria. Study results were critically appraised for clinical applicability and research methods.

RESULTS: Thirty-four publications met selection criteria. Reports were classified as challenge studies if they examined the association between short-term marijuana use and airway response; other reports were classified as studies of long-term marijuana smoking and pulmonary function or respiratory complications. Eleven of 12 challenge studies found an association between short-term marijuana administration and bronchodilation (eg, increases of 0.15-0.25 L in forced expiratory volume in 1 second). No consistent association was found between long-term marijuana smoking and airflow obstruction measures. All 14 studies that assessed long-term marijuana smoking and respiratory complications noted an association with increased respiratory symptoms, including cough, phlegm, and wheeze (eg, odds ratio, 2.00; 95% confidence interval, 1.32-3.01, for the association between marijuana smoking and cough). Studies were variable in their overall quality (eg, controlling for confounders, including tobacco smoking).

CONCLUSIONS: Short-term exposure to marijuana is associated with bronchodilation. Physiologic data were inconclusive regarding an association between long-term marijuana smoking and airflow obstruction measures. Long-term marijuana smoking is associated with increased respiratory symptoms suggestive of obstructive lung disease.

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# Papers from PRISM-Funded Studies

**Peppard PE, Austin D, Brown RL. Association of alcohol consumption and sleep disordered breathing in men and women. *J Clin Sleep Med*. 2007 Apr 15;3(3):265-70.**

## Abstract

STUDY OBJECTIVES: Experimental evidence indicates that alcohol use near bedtime may exacerbate sleep disordered breathing (SDB). However, scarce research has examined the relation between moderate habitual alcohol use and objectively assessed SDB, and it is unclear whether patients with SDB, or those at risk for SDB, should be counseled to avoid alcohol regardless of proximity to bedtime. In this population-based epidemiology study, our objective is to measure the association of SDB with usual alcohol consumption habits.

METHODS: Men (N = 775) and women (N = 645)--initially randomly selected from a working population--participating in the Wisconsin Sleep Cohort Study were evaluated for alcohol consumption and SDB. The apnea-hypopnea index (AHI, events/hour) was determined by in-laboratory polysomnography. AHI > 5 defined "mild or worse" SDB and AHI > 15 defined "moderate or worse" SDB. Alcohol consumption (drinks/day) was assessed by questionnaire. Potential confounding or interacting variables such as smoking, body mass index, and medication use, were measured by clinical assessment and questionnaire.

RESULTS: Relative to men who consumed less alcohol, for each increment of one drink per day, men who consumed more alcohol had 25% greater odds of mild or worse SDB (OR = 1.25, 95% CI = 1.07-1.46, p = 0.006). Among women, minimal to moderate alcohol consumption was not significantly associated with increased risk of SDB.

DISCUSSION: In men, increased usual alcohol consumption was associated with increased risk of mild or worse SDB. Persons with SDB might benefit from generally reduced alcohol consumption and not just avoidance near bedtime.

**Vinson DC, Manning BK, Galliher JM, Dickinson LM, Pace WD, Turner BJ.**

**Alcohol and sleep problems in primary care patients: a report from the AAFP National Research Network. Ann Fam Med. 2010 Nov-Dec;8(6):484-92.**

## Abstract

PURPOSE: Hazardous and harmful drinking and sleep problems are common, but their associations among patients seen in primary care have not been examined. We hypothesized that greater levels of alcohol consumption would be associated with several self-reported sleep problems.

METHODS: In a cross-sectional survey in primary care practices, 94 participating clinicians recruited up to 30 consecutive adult patients, and both clinicians and patients completed anonymous postvisit questionnaires. Patients were asked questions on demographics, alcohol consumption, cardinal symptoms of alcohol use disorders, sleep quality, insomnia, sleep apnea, and symptoms of restless leg syndrome. Multivariate analyses explored the associations of drinking status (none, moderate, or hazardous) and sleep problems, adjusting for demographics and clustering of patients within physician.

RESULTS: Of 1,984 patients who responded, 1,699 (85.6%) provided complete data for analysis. Respondents' mean age was 50.4 years (SD 17.4 years), 67% were women, and 72.9% were white. Of these, 22.3% reported hazardous drinking, 47.8% reported fair or poor overall sleep quality, and 7.3% reported a diagnosis or treatment of sleep apnea. Multivariate analyses showed no associations between drinking status and any measure of insomnia, overall sleep quality, or restless legs syndrome symptoms. Moderate drinking was associated with lower adjusted odds of sleep apnea compared with nondrinkers (OR = 0.61; 95% CI, 0.38-1.00). Using alcohol for sleep was strongly associated with hazardous drinking (OR = 4.58; 95% CI, 2.97-7.08, compared with moderate drinking).

CONCLUSIONS: Moderate and hazardous drinking were associated with few sleep problems. Using alcohol for sleep, however, was strongly associated with hazardous drinking relative to moderate drinking and may serve as a prompt for physicians to ask about excessive alcohol use.

**Klatsky AL, Koplik S, Gunderson E, Kipp H, Friedman GD. Sequelae of systemic hypertension in alcohol abstainers, light drinkers, and heavy drinkers. Am J Cardiol. 2006 Oct 15;98(8):1063-8.**

**Comment in: Am J Cardiol. 2007 Jun 1;99(11):1621**

## Abstract

A link exists between alcohol intake and increased blood pressure (BP), with many studies showing increased hypertension prevalence in heavy drinkers. The harmful and beneficial effects of alcohol can confound the study of the long-term risks of alcohol-related hypertension. We therefore studied cardiovascular sequelae separately in heavy drinkers, light drinkers, and abstainers among 127,212 subjects with BP and alcohol intake ascertained at 1978 to 1985 health examinations. Subsequent cardiovascular end points included mortality risk, hospitalization risk, and outpatient diagnosis of hypertension. Analyses were performed for all subjects and stratified by 5 alcohol-drinking categories (from never drinkers to >or=3 drinks/day). With <120/80 mm Hg as the referent, Cox proportional hazards models were used to estimate relative risks and 95% confidence intervals for 3 higher BP categories (120 to 129/80 to 84, 130 to 139/85 to 89, and >or=140/90 mm Hg). The covariates were age, gender, race, body mass index, education, and smoking. The risk of all outcomes was progressively higher for increasing BP categories, with a similarly increased risk for abstainers, light drinkers, and heavy drinkers. The interaction tests for alcohol and BP were not statistically significant for the mortality and hospitalization outcomes. Interpretation was limited by an inability to separate subjects with increased BP from alcohol consumption from those with other etiologies. In conclusion, the data indicate that the risks of hypertension are similar regardless of the amount of alcohol consumption.

**Klatsky AL, Gunderson EP, Kipp H, Udaltsova N, Friedman GD. Higher prevalence of systemic hypertension among moderate alcohol drinkers: an exploration of the role of underreporting. *J Stud Alcohol.* 2006 May;67(3):421-8.**

## Abstract

OBJECTIVE: Heavy alcohol drinking is associated with increased prevalence of systemic hypertension (HTN), but the relationship between moderate drinking and HTN remains unclear. We explored the possible role of underreporting among moderate drinkers.

METHOD: In a cross-sectional analysis of 105,378 persons, we defined a subset among persons reporting three or fewer drinks per day that was likely to include a disproportionate number of underreporters. This subset included persons who, on another occasion, indicated intake of three or more drinks per day or who ever had a diagnosis of an alcohol-related condition; these persons are called "positive." Persons who never reported three or more drinks per day and who had no alcohol-related diagnosis were called "negative." Logistic regression models estimated the odds ratios (ORs) for prevalent HTN (140/90 mm Hg or greater) in the positive and negative subgroups, compared with lifelong abstainers as referent. All persons and four race-gender groups were studied, and they were controlled for age, education, smoking, and body mass index. We also studied the relationship of blood liver transaminase enzyme levels in the positive and negative subgroups at specific alcohol intake strata.

RESULTS: For persons reporting one to two drinks per day, the OR (95% confidence interval) of HTN was 1.32 (1.21-1.43) for positive persons and 1.16 (1.09-1.25) for negative persons. For those reporting less than one drink per day, the ORs were 0.97 (0.89-1.06) for positives and 0.92 (0.87-0.98) for negatives. For those reporting one to two drinks per day, positive/negative comparisons showed approximately a 75% increased prevalence of high liver transaminase enzymes. For those reporting less than one drink per day, the positive/negative difference was approximately 30%.

CONCLUSION: In these data, increased prevalence of HTN among persons reporting one to two drinks per day appears to be partially due to underreporting of alcohol intake.

**Halanych JH, Safford MM, Kertesz SG, Pletcher MJ, Kim YI, Person SD, Lewis CE, Kiefe CI. Alcohol consumption in young adults and incident hypertension: 20-year follow-up from the Coronary Artery Risk Development in Young Adults Study.Am J Epidemiol. 2010 Mar 1;171(5):532-9**

## Abstract

The relation between alcohol consumption and incident hypertension is unclear, and most observational studies have not accounted for socioeconomic factors. This study examined the association between alcohol consumption in a diverse group of young adults and incident hypertension over 20 years. Participants (n = 4,711) were from the Coronary Artery Risk Development in Young Adults Study cohort, recruited in 1985 (aged 18-30 years) from Birmingham, Alabama; Chicago, Illinois; Minneapolis, Minnesota; and Oakland, California. The 20-year incidence of hypertension for never, former, light, moderate, and at-risk drinkers was 25.1%, 31.8%, 20.9%, 22.2%, and 18.8%, respectively ($P < 0.001$). Race, gender, age, family history of hypertension, body mass index, income, education, and difficulty paying for basics and medical care were associated with hypertension. Adjustment using Cox proportional hazard models revealed no association between baseline alcohol consumption and incident hypertension, except among European-American women in whom any current alcohol consumption was associated with lower risk of incident hypertension. The lack of association between alcohol and hypertension in the majority of this socioeconomically diverse cohort is not definitive. Future studies should include social factors, such as income and education, and consider additional characteristics that may modify or confound associations between alcohol and blood pressure.

**Starrels J.L., Becker W.C., Alford D.P., Kapoor A., Williams R., Turner B.J.**

**Systematic review: Treatment agreements and urine drug testing to reduce opioid misuse in patients with chronic pain. Ann Intern Med; 2010 Jun 1; 152(11):712-20.**

## Abstract

BACKGROUND: Experts recommend opioid treatment agreements and urine drug testing to reduce opioid analgesia misuse, but evidence of their effectiveness has not been systematically reviewed.

PURPOSE: To synthesize studies of the association of treatment agreements and urine drug testing with opioid misuse outcomes in outpatients with chronic noncancer pain.

DATA SOURCES: MEDLINE, PsycINFO, EMBASE, Cochrane Central Register of Controlled Clinical Trials (1966 to 2009), reference lists, and expert contacts.

STUDY SELECTION: Original research addressing opioid medications, chronic pain, and treatment agreements or urine drug testing, with a sample size of 50 participants or more and published in English, Spanish, or French.

DATA EXTRACTION: Two investigators independently identified eligible studies, extracted data, and assessed study quality. The outcome of opioid misuse was defined as drug abuse, drug misuse, aberrant drug-related behavior, diversion, or addiction.

DATA SYNTHESIS: Of 102 eligible studies, 11 met inclusion criteria; 6 were in pain clinics and 5 were in primary care settings. Four primary care studies examined multicomponent strategies that included interdisciplinary support. All studies were observational and rated as poor to fair quality. In 4 studies with comparison groups, opioid misuse was modestly reduced (7% to 23%) after treatment agreements with or without urine drug testing. In the other 7 studies, the proportion of patients with opioid misuse after treatment agreements, urine drug testing, or both varied widely (3% to 43%).

LIMITATIONS: Diversity of interventions and opioid misuse measures precluded meta-analysis. Most studies evaluated combinations of interventions.

CONCLUSION: Relatively weak evidence supports the effectiveness of opioid treatment agreements and urine drug testing in reducing opioid misuse by patients with chronic pain. Further research on effective ways to monitor and reduce opioid misuse is needed, especially in primary care settings.

**Reid M.C., Henderson, C.R. Jr, Papaleontiou,M, Amanfo L, Olkhovskaya Y, Moore AA, Parikh SS, Turner B.J. Characteristics of older adults receiving opioids in primary care: treatment duration and outcomes. *Pain Med.* 2010 Jul; 11(7):1063-71.**

## Abstract

OBJECTIVE: To describe characteristics of older adults who received opioids for chronic non-cancer pain (CP), ascertain types of opioid treatments received, and examine associations between patient characteristics and treatment outcomes.

DESIGN: Retrospective cohort study.

SETTING: Primary care practice in New York City.

PATIENTS: Eligible patients were >or=65 and newly started on an opioid for CP.

OUTCOME MEASURES: Patient characteristics and provider treatments, as well as duration of opioid therapy, proportion discontinuing therapy, and evidence of pain reduction and continued use of opioid for more than 1 year. Other outcomes included the presence and type(s) of side effects, abuse/misuse behaviors, and adverse events.

RESULTS: Participants (N = 133) had a mean age of 82 (range = 65-105), were mostly female (84%), and white (74%). Common indications for opioid treatment included back pain (37%) and osteoarthritis (35%). Mean duration of opioid use was 388 days (range = 0-1,880). Short-acting analgesics were most commonly prescribed. Physicians recorded side effects in 40% of cases. Opioids were discontinued in 48% of cases, mostly due to side effects/lack of efficacy. Pain reduction was documented in 66% of patient records, while 32% reported less pain and continued treatment for >or=1 year. Three percent displayed abuse/misuse behaviors, and 5% were hospitalized due to opioid-related adverse events.

CONCLUSIONS: Over 50% of older patients with CP tolerated treatment. Treatment was discontinued in 48% of cases, mostly due to side effects and lack of analgesic efficacy. Efforts are needed to establish the long-term safety and efficacy of opioid treatment for CP in diverse older patient populations.

**Papaleontiou M, Henderson CR Jr, Turner B.J., Moore AA, Olkhovskaya Y, Amanfo L, Reid MC. Outcomes associated with opioid use in the treatment of chronic noncancer pain in older adults: a systematic review and meta-analysis. J Am Geriatr Soc, 2010 Jul; 58(7):1353-69.**

## Abstract

This systematic review summarizes existing evidence regarding the efficacy, safety, and abuse and misuse potential of opioids as treatment for chronic noncancer pain in older adults. Multiple databases were searched to identify relevant studies published in English (1/1/80-7/1/09) with a mean study population age of 60 and older. Forty-three articles were identified and retained for review (40 reported safety and efficacy data, the remaining 3 reported misuse or abuse outcome data). The weighted mean subject age was 64.1 (mean age range 60-73). Studies enrolled patients with osteoarthritis (70%), neuropathic pain (13%), and other pain-producing disorders (17%). The mean duration of treatment studies was 4 weeks (range 1.5-156 weeks), and only five (12%) lasted longer than 12 weeks. In meta-analyses, effect sizes were -0.557 (P<.001) for pain reduction, -0.432 (P<.001) for physical disability reduction, and 0.859 (P=.31) for improved sleep. The effect size for the Medical Outcomes Study 36-item Health Survey was 0.191 (P=.17) for the physical component score and -0.220 (P=.04) for the mental component score. Adults aged 65 and older were as likely as those younger than 65 to benefit from treatment. Common adverse events included constipation (median frequency of occurrence 30%), nausea (28%), and dizziness (22%) and prompted opioid discontinuation in 25% of cases. Abuse and misuse behaviors were negatively associated with older age. In older adults with chronic pain and no significant comorbidity, short-term use of opioids is associated with reduction in pain intensity and better physical functioning but poorer mental health functioning. The long-term safety, efficacy, and abuse potential of this treatment practice in diverse populations of older persons remain to be determined.

**Turner, B.J. Gaps in addressing problem drinking: Overcoming primary care and alcohol treatment deficiencies. Curr Psychiatry Rep. 2009 Oct; 11(5):345-52.**

## Abstract

Despite the high prevalence of problem drinking among Americans, primary care physicians often fail to address this major health threat. In addition, once alcohol use disorders are identified, patients often fail to receive coordinated medical and substance abuse treatment. This article reviews four types of barriers as well as potential facilitators to improving the prevention and management of problem drinking. First, primary care physicians are poorly trained about the clinical relevance of addressing alcohol problems in their daily patient care. Second, primary care physicians are concerned about the stigma and health insurance problems encountered by patients diagnosed with alcohol use disorders. Third, primary care practices have limited organizational and financial support to identify and address alcohol problems. Fourth, primary care and alcohol treatment settings communicate and collaborate poorly in delivering patient care. Opportunities to overcome these challenges are discussed and must be initiated to reduce the myriad of adverse outcomes resulting from problem drinking.

Turner, B.J., McLellan, A.T. Methodological challenges and limitations of research on alcohol consumption and effect on common clinical conditions: evidence from six systematic reviews. J Gen Intern Med, 2009 Oct; 24(10):1156-60.

## Abstract

BACKGROUND: Despite the high prevalence of alcohol consumption in the US, 'mainstream' physicians generally consider it to be peripheral to most patient care. This may be due in part to a dearth of rigorous research on alcohol's effect on common diseases.

METHODS: To evaluate this issue, we examined six systematic reviews, four of which were conducted as part of a research initiative supported by the Robert Wood Johnson Foundation, the Program of Research to Integrate Substance Use Information into Mainstream Healthcare (PRISM). PRISM aimed to assimilate and improve the evidence on the medical impact of alcohol (and other drugs of abuse) on common chronic conditions.

RESULTS: From these reviews, we summarize the methodological limitations of research on alcohol's impact on development and/or clinical course of depression, hypertension, diabetes, bone disease, dementia, and sexually transmitted diseases. The studies included in these reviews were largely fair to good quality, and few were in primary care settings. Syntheses were hampered by the myriad of definitions of alcohol consumption from any/none to seven levels and a plethora of types of alcohol use disorders.

CONCLUSION: We recommend more high-quality observational and experimental studies in primary care settings as well as a more standard approach to quantifying alcohol use and to defining alcohol use disorders.

**McLellan A.T., Turner, BJ. Prescription opioids, overdose deaths, and physician responsibility. [Editorial] JAMA. 2008 Dec 10; 300(22);2672-3.**

The study of overdose deaths in West Virginia by Hall and colleagues in this issue of JAMA[1] revealed that opioid analgesics contributed to 93% of those deaths and most of these potentially avoidable deaths occurred in younger persons (aged 18-44 years). These disturbing findings are certain to raise questions about physician prescribing practices, the safety and adverse effect profiles of opioid medications, and the appropriate management of pain. These findings also raise several important questions for physicians who are trying to balance their duty to relieve pain in individual patients and their obligation to prevent the broader public health problems of addiction and overdose death.

**McLellan AT, Turner BJ. Chronic noncancer pain management and opioid overdose: time to change prescribing practices. [Editorial]. Ann Intern Med. 2010 Jan 19;152(2):123-4.**

At this writing, opioids are the most commonly prescribed class of medication in the United States (1). Prescription of some opioids, such as methadone, has increased more than 800% in the past 10 years (2). This increase in opioid prescribing has caused an increase in overdoses and deaths. Opioid overdose is among the most common causes of accidental death nationwide (3). The increase in deaths due to prescription opioids is a major public health priority and not just a concern for individual physicians and their patients.

It is easy to blame the growing epidemic of opioid overdose and death on manipulative patients who misrepresent pain symptoms to obtain drugs to abuse or sell. A recent report (4) on overdose deaths in West Virginia found that 51% occurred in persons who had never actually been prescribed an opioid (that is, prescription diversion) and that another 20% occurred in persons who had received prescriptions from 5 or more physicians (that is, "doctor shopping"). In an accompanying editorial (5), we acknowledged the role of the patient in adverse events from opioids but also suggested opportunities for physicians to stem the rise in prescription opioid deaths.

## Papers in Progress

Starrels JS, Becker WC, Weiner MG, Li Xuan, Heo M, Turner BJ. Low Use of Opioid Risk Reduction Strategies in Primary Care for High Risk Patients with Chronic Pain, revised and resubmitted.

Grodensky CA, Golin CE. David RA, Turner BJ Systematic Review: Effect of Alcohol Intake on Adherence to Outpatient Medication Regimens

Spitz A, Papaleontiou P, Moore AA, Turner BJ, Olkhovskaya Y, Reid MC. Opioid Use for Chronic Non-Cancer Pain in Older Adults: Understanding Provider and Patient Perspectives.

Brien S, Ronksley P, Turner BJ, Mukamal K, Ghali W. Effect of alcohol consumption on biological markers associated with risk of cardiovascular disease: a systematic review and meta-analysis. Brit Med J. 2011; 342:d636.

Ronksley P, Brien S, Turner BJ, Mukamal K, Ghali W. Association of alcohol consumption with selected cardiovascular disease outcomes: a systematic review and meta-analysis. Brit Med J, 2011;342:d671.

Becker, WC. Starrels JL, Heo, M, Li X, Weiner MG, Turner BJ. Racial differences in primary care opioid risk reduction strategies, Ann Fam Med, in press.

Gannon MA, Qaseem A, Snow V, Turner B. Raising achievement: educating physicians to address effects of at-risk drinking on common diseases. Quality in Primary Care. in press.