

Alcohol, Other Drugs, and Health: Current Evidence

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Health Outcomes

Marijuana Smoking and Pulmonary Complications

The impact of marijuana smoking on pulmonary function and respiratory complications is not clearly understood. Therefore, researchers conducted a systematic review and summarized the findings of 34 studies.

- Short-term marijuana smoking was associated with improved airway response in 10 of 11 challenge studies.* However, the results of 1 challenge study suggested a reversal of this effect after 1.5 to 2 months of marijuana smoking.
- Longer-term** marijuana smoking was inconsistently associated with airflow obstruction. Results from pulmonary function tests (FEV₁, FVC, FEV₁/FVC, DL_{CO}) were worse in marijuana smokers than in controls in 8 of 14 studies.
- Longer-term marijuana smoking was associated with an increased risk of various respiratory complications (e.g., cough, sputum production, wheezing, dyspnea, pharyngitis, worsening of asthma symptoms) in 14 of 14 studies.
- The overall quality of studies varied. Many failed to control for tobacco

smoking, and none defined a standardized measure of marijuana dose.

Comments: Although short-term marijuana exposure may cause bronchodilation, longer-term exposure may obstruct airflow. Physiologic data that can describe the relationship between marijuana smoking and airway hyperreactivity are currently inconclusive. Nonetheless, long-term marijuana smoking appears to increase the risk of respiratory symptoms and complications.

Julia H. Arnsten, MD, MPH

*Studies that experimentally administered marijuana and assessed its effects immediately or shortly after (e.g., 15 minutes, 1 hour) administration

**Defined variably across studies

Reference: Tetrault JM, et al. Effects of marijuana smoking on pulmonary function and respiratory complications: a systematic review. *Arch Intern Med.* 2007;167(3):221-228.

Patients on Methadone With Unhealthy Alcohol Use Have Poor Quality of Life

Excessive alcohol consumption is prevalent among patients receiving methadone treatment for opioid dependence and may be associated with poor quality of life. In this cross-sectional study of 192 outpatients receiving methadone, researchers in England assessed the association between unhealthy alcohol use (measured with the Alcohol Use Disorders Identification Test [AUDIT]) and health-related quality of life (measured with the SF-12 Health Survey).

- Thirty percent of patients had current unhealthy alcohol use (i.e., score of ≥ 8

on the AUDIT); 10% did not have current unhealthy alcohol use but reported past alcohol problems.

- The mean SF-12 score was 56 (a score < 67 indicates poor health).
- Health-related quality of life was significantly lower in patients with current unhealthy alcohol use (mean difference in SF-12 scores, 10.4) or with past alcohol problems (mean difference, 12.5) than in patients with neither current unhealthy alcohol use nor past alcohol problems.

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Patients on Methadone With Unhealthy Alcohol Use (continued from page 1)

Comments: Because these findings are from a cross-sectional survey, they should be confirmed in other studies. However, addressing comorbid drinking problems should improve quality of life for patients receiving methadone treatment.

Julia H. Arnsten, MD, MPH

Reference: Senbanjo R, et al. Excessive alcohol consumption is associated with reduced quality of life among methadone patients. *Addiction*. 2007;102(2):257–263.

Persistent Pain Increases Risk of Relapse

Persistent pain is prevalent among people with substance use disorders. It is not known, however, whether such pain increases the risk of relapse following periods of abstinence.

Researchers assessed data on pain and substance use in 397 adults who, as part of a larger randomized trial, had been interviewed periodically in the 24 months after their discharge from an urban, residential alcohol and drug detoxification unit. Pain was measured with the pain item on the SF-36 Health Survey. Analyses were adjusted for potential confounders (e.g., demographics, addiction severity, depressive symptoms).

Sixteen percent of subjects reported persistent pain (moderate-to-higher levels of pain at all available interviews) in the 24 months after detoxification. Subjects reporting persistent pain were significantly more likely than those with mild or no pain to have used the following in the past 30 days at the 24-month follow-up:

- heroin/opioids not prescribed for

pain (odds ratio, 5.4);

- heavy amounts of alcohol (≥ 3 drinks on at least 1 day or intoxication; odds ratio, 2.2).

Comments: Persistent pain is common among alcohol and drug users who have undergone detoxification and increases the likelihood of relapse. This study suggests that clinicians must be careful to screen for pain symptoms in patients with substance dependence. When persistent pain is present, thoughtful management is required to minimize risks associated with under-treatment while not fostering opioid abuse.

Marc N. Gourevitch, MD, MPH

Reference: Larson MJ, et al. Persistent pain is associated with substance use after detoxification: a prospective cohort analysis. *Addiction*. 2007;(Online Early Articles): doi: 10.1111/j.1360-0443.2007.01759.x.

Alcohol Increases Breast Cancer Risk in Certain Women

The mechanisms by which alcohol may affect breast cancer risk are unclear. Using data from the Women's Health Study, researchers examined the association between moderate drinking and breast cancer according to estrogen receptor and progesterone receptor status.

During an average of 10 years of follow-up, 1484 cases of breast cancer were

documented among 38,454 women who were free of cancer and cardiovascular disease at baseline. Analyses were adjusted for potential confounders (e.g., age, body mass index, family history).

- The risks of all breast cancers (invasive and in situ tumors) and invasive breast cancer were

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Alcohol Increases Breast Cancer Risk in Certain Women (continued from page 2)

modestly higher in drinkers than nondrinkers and increased as drinking amounts increased (e.g., relative risks for all breast cancers, 1.0 for <0.5 drinks per day, 1.1 for about 1 drink per day, and 1.3 for about 2.5 drinks per day; *P* for trend=0.02).

- These risks were limited to estrogen receptor positive and progesterone receptor positive tumors and strongest in women currently taking hormone replacement therapy.
- Risks were similar across beverage type and not affected by folate intake.

Comments: Like many previous reports, this analysis shows

Drinking Levels and Death: How Much Is Safe?

Research indicates that light-to-moderate drinkers have a lower risk of death than nondrinkers and heavy drinkers. The safest level of alcohol intake for men and women, however, remains unclear.

To help determine this safest level, researchers conducted a meta-analysis of 34 prospective studies on alcohol and all-cause mortality. Of these studies, 29 reported adjustment for potential confounders and included a total of 285,490 women and 622,692 men (13,448 and 73,493, respectively, died during follow-up).

- Drinking up to 3 drinks* per day for men and up to 1.5 drinks per day for women decreased the risk of death.
- For both men and women, risk was lowest at 0.5 drinks per day (relative risks, 0.8 for both versus nondrinkers).

Comments: This very large meta-analysis confirms the J-

Cardiomyopathy Is More Common in Methamphetamine Users

The cardiomyopathic effects of methamphetamine have been previously noted only in case series. In this case-control study, researchers examined the relationship between methamphetamine use and cardiomyopathy (CM) in patients discharged from a tertiary care medical center in Honolulu.

Through medical record review of patients aged 45 years or younger, researchers identified 107 cases (i.e., had a discharge diagnosis of CM or congestive heart failure) and 114 controls (i.e., had echocardiographic evidence of normal heart function [i.e., ejection fraction \geq 55% and no wall motion abnormalities]).

- Forty-two percent of cases and 20% of controls had ever used methamphetamine.
- Methamphetamine use was significantly more common in

that alcohol intake is associated with a slight overall increase in the risk of breast cancer. The important findings are that the increase was (1) limited to estrogen receptor and progesterone receptor positive tumors and (2) strongest in current users of postmenopausal hormonal therapy. Unlike previous studies, this study did not show any protective effect of folate intake on breast cancer risk.
R. Curtis Ellison, MD

Reference: Zhang SM, et al. Alcohol consumption and breast cancer risk in the Women's Health Study. *Am J Epidemiol.* 2007;165(6):667–676.

shaped relationship between alcohol use and death. The amount associated with the lowest risk in this study (0.5 drinks per day) is lower than that reported for men in previous research. In addition, the upper limits associated with a protective effect exceed U.S. recommendations for low-risk drinking for men and women. Overall, the available research supports the beneficial effect of low levels of alcohol use on mortality.

Kevin L. Kraemer, MD, MSc

*Based on 12–14 g of alcohol in a standard drink

Reference: Di Castelnuovo A, et al. Alcohol dosing and total mortality in men and women: an updated meta-analysis of 34 prospective studies. *Arch Intern Med.* 2006;166(22):2437–2445.

cases than in controls in analyses adjusted for age, body mass index, and renal failure (odds ratio, 3.7).

Comments: These data—plus a plausible pathophysiological mechanism of injury related to excess catecholamines—support an evolving perspective: methamphetamine use is an important cause of cardiomyopathy in younger heart failure patients in regions where the drug is commonly abused.

Jeffrey H. Samet, MD, MA, MPH

Reference: Yeo K-K, et al. The association of methamphetamine use and cardiomyopathy in young patients. *Am J Med.* 2007;120(2):165–171.

How Much Can Older People Safely Drink?

Safer drinking recommendations for older people are debated and vary from country to country (e.g., ≤ 1 drink per day in the United States but ≤ 2 drinks per day in England). Researchers addressed this debate by examining data on alcohol use and functional and cognitive disabilities from U.S. and English longitudinal studies including a total of 13,333 people aged 65 years and older. Mortality-related outcomes were also assessed in the U.S. subset. Analyses were adjusted for potential confounders.

Thirty-two percent of English men, 12% of English women and U.S. men, and 3% of U.S. women drank >1 drink per day. At the 4- to 5-year follow-up, subjects who drank at baseline >1 to 2 drinks per day, compared with those who drank >0 to 1 drinks per day, had

- a borderline-significant lower risk of cognitive problems* and difficulties with instrumental activities of daily living** (odds ratios, 0.8 for both);
- similar risks of mortality (unadjusted analyses) and combined mortality-disability outcomes.

Comments: In this study, older people who drank >1 to 2

drinks per day did not develop greater functional or cognitive disabilities than those who drank the U.S. recommended level of ≤ 1 drink per day. The researchers are to be commended for focusing on functional and cognitive outcomes. However, drinking's effect on mortality is unclear in this study because adjusted analyses with mortality as the sole outcome were not reported. The safer drinking limit for older people will most likely remain debated until more evidence is available.

Kevin L. Kraemer, MD, MSc

*Bottom quintile of cognitive function, based on scores on tests that assessed word recall, numeracy, and the ability to correctly specify the date

**Difficulties with one or more of the following: preparing a hot meal, shopping for groceries, making telephone calls, taking medications, and managing money

Reference: Lang I, et al. What level of alcohol consumption is hazardous for older people? Functioning and mortality in U.S. and English national cohorts. *J Am Geriatr Soc.* 2007;55(1):49–57.

Does Moderate Drinking Lower Risk of Heart Failure?

To examine the association between moderate drinking and heart failure, researchers assessed data from 21,601 male participants in the Physicians' Health Study who were free of heart failure at that study's baseline. Analyses were adjusted for potential confounders (i.e., age, smoking, body mass index, and valvular heart disease).

- During an average follow-up of 18 years, 904 incident cases of heart failure occurred.
- The risk of heart failure decreased as drinking increased (hazard ratios, 0.9 for 1–4 drinks per week, 0.8 for 5–7 drinks per week, and 0.6 for >7 drinks per week versus <1 drink per week; P for trend=0.01).
- Drinking was not significantly associated with the risk of heart failure in subjects without antecedent myocardial

dial infarction or coronary artery disease (CAD).

Comments: These results support what many, but not all, recent prospective epidemiological studies have shown: a reduced risk of heart failure among moderate drinkers in comparison with nondrinkers (or, as in this study, occasional drinkers). This lower risk was found primarily in patients with heart failure and CAD, and therefore may result from alcohol's protective effects on myocardial infarction or other consequences of CAD.

R. Curtis Ellison, MD

Reference: Djoussé L, et al. Alcohol consumption and risk of heart failure in the Physicians' Health Study I. *Circulation.* 2007;115(1):34–39.

Assessments and Interventions

Treating Chronic Back Pain With Opioids

Opioids, an effective treatment for acute pain, are sometimes prescribed for chronic back pain. Researchers systematically reviewed the literature to determine the prevalence and efficacy of opioid treatment for chronic back pain. They also assessed the association between this treat-

ment and substance use disorders and prescription medication misuse.

- The prevalence of opioid prescribing for chronic back pain ranged from 3% to 66% across 11 studies.

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Treating Chronic Back Pain With Opioids (continued from page 4)

- Pain decreased nonsignificantly from baseline with opioid treatment in a meta-analysis of data from 5 studies.
- Opioids had better efficacy than placebo or nonopioids in 4 of 6 studies of short-term (<16 weeks) treatment.
- The prevalence of a current substance use disorder in patients receiving opioids for chronic back pain ranged from 3% to 43% across 4 studies, although the studies generally were of poor quality. In the highest quality study, the prevalence was 23%, the same as in a comparison group of patients with chronic back pain who had not received opioid treatment.
- The prevalence of prescription medication misuse in patients receiving opioids for chronic back pain was 5% to 24% across 5 studies, although these studies gener-

ally did not consider whether the misuse might have been due to inadequate pain relief.

Comments: Obviously, we need better treatments for chronic back pain. Opioids seem to be an option at least in the short term. However, their efficacy is not particularly convincing and long-term benefit is unknown. Further, the possibility of a co-existing substance disorder has to be considered and addressed.

Richard Saitz, MD, MPH

Reference: Martell BA, et al. Opioid treatment for chronic back pain: prevalence, efficacy, and association with addiction. *Ann Intern Med.* 2007;146(2):116–127.

Brief Intervention Is Insufficient for Medical Inpatients With Unhealthy Drinking

Data show that brief intervention reduces consumption and consequences among outpatients with unhealthy, but not dependent, alcohol use. To assess whether brief interventions work among medical inpatients with unhealthy drinking,* researchers randomized 341 of such patients to a 30-minute session of motivational counseling in the hospital or to usual care.

Most subjects had alcohol dependence, were unemployed during the previous 3 months, used other drugs, and had substantial psychiatric symptoms. Almost half were hospitalized for an alcohol-related medical diagnosis.

- At 3 months among subjects with alcohol dependence, similar proportions of the intervention and control groups received alcohol assistance (e.g., specialty treatment) (49% and 44%, respectively).
- At 12 months among all subjects, decreases in alcohol consumption did not significantly differ between the groups (e.g., adjusted mean decreases in drinks per day, 1.5 for intervention subjects and 3.1 for usual care subjects).

Comments: Unlike most brief intervention studies of outpatients, this study enrolled a predominantly alcohol-dependent sample with major comorbidities—a group reflective of the treatment-resistant population identified when screening occurs in inpatient settings. The study suggests that screening, assessment, and brief counseling are necessary but not sufficient to change alcohol consumption in this population. Although the findings are disappointing, this study underscores that alcoholism—like cancer, atherosclerosis and other complex diseases—will not succumb to simple solutions.

Peter D. Friedmann, MD, MPH

*Defined in this study as >14 drinks per week or ≥5 drinks per occasion for men; >11 drinks per week or ≥4 drinks per occasion for women and people ≥66 years old

Reference: Saitz R, et al. Brief intervention for medical inpatients with unhealthy alcohol use: a randomized controlled trial. *Ann Intern Med.* 2007;146(3):167–176.

Video of Patient's Own Delirium Tremens Decreases Relapse Risk

Confrontational approaches to convince patients with alcohol dependence that they are harming themselves tend to be ineffective. Hypothesizing that one such approach might increase patient insight into the disease, researchers assessed whether showing a patient a videotape of his own delirium tremens (DTs) might decrease relapse.

Sixty men hospitalized for alcohol withdrawal delirium were videotaped and randomly assigned to either (1) view

the tape and meet with a psychiatrist who explained the DTs or (2) view the tape, if they chose, at the end of follow-up (controls). Patient and family interviews assessed alcohol use and relapse.*

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*More than 3 periods of drinking lasting less than 1 week, regular consumption of >4.5 drinks (approximately) per day, having an alcohol-related disorder, or receiving inpatient treatment

Video of Patient's Own Delirium Tremens Decreases Relapse Risk (continued from page 5)

At 1 month, none of the intervention subjects but 20% of the control subjects had relapsed. At 6 months, the proportions were 47% and 70%, respectively. Subjects assigned to watch the video, compared with controls,

- had a longer time to relapse (210 versus 109 days);
- drank less (about 25 versus 28 drinks per week at 6 months);
- drank on fewer days (5 versus 6 days per week at 6 months).

Comments: The results from this unusual treatment are surprising and should be confirmed in other studies given the small and selected sample. An editorialist points out that a single intervention that might increase motivation

would not improve self-efficacy or provide skills required to reduce risk of relapse. Nonetheless, these findings should make clinicians rethink a role, in the context of known effective therapies, for showing patients the consequences of their drinking.

Richard Saitz, MD, MPH

References: Mihai M, et al. Viewing videotape of themselves while experiencing delirium tremens could reduce the relapse rate in alcohol-dependent patients. *Addiction*. 2007;102(2):226–231; Bühringer G, et al. Viewing videotapes of one's own delirium tremens: renaissance of alcohol dependence as 'disease of the will'? *Addiction*. 2007;102(2):183–184.

Higher Quality of Primary Care May Lower Addiction Severity

The quality of primary care affects health outcomes in patients with certain chronic disorders. In this study, researchers examined whether patient-reported quality of primary care influenced addiction outcomes in 183 patients who sought primary care after detoxification from alcohol, heroin, and/or cocaine.

Using patient interviews, researchers measured primary care quality at baseline and substance use and addiction severity 6 to 18 months later. Analyses were adjusted for potential confounders (e.g., education, homelessness).

- Of the 9 attributes* of quality primary care that were assessed, all but preventive counseling were significantly associated with lower alcohol addiction severity at follow-up. Three attributes (physician knowledge of the whole person, organizational access, and visit-based continuity) were associated with lower alcohol addiction severity and lower drug addiction severity.
- Whole-person knowledge and patient trust of the provider were associated with a significantly lower likelihood of any drug use or alcohol intoxication (>3 drinks on any occasion) at follow-up (odds ratios, 0.7

for whole-person knowledge and 0.8 for trust).

Comments: In this study, higher quality of primary care was associated with decreased addiction severity (particularly related to alcohol) over time in patients who had completed detoxification. Two characteristics of the patient-physician relationship—trust and whole-person knowledge—were associated with less substance use. These findings support efforts to link patients with substance use disorders to primary care and to cultivate key attributes of patient-physician relationships.

David A. Fiellin, MD

*The 9 attributes, measured by the Primary Care Assessment Survey, included communication, interpersonal treatment, thoroughness of the physical exam, provider knowledge of the whole person, preventive counseling, patient trust of the provider, organizational access, financial access, and visit-based continuity.

Reference: Kim TW, et al. Primary care quality and addiction severity: a prospective cohort study. *Health Serv Res*. 2007;42(2):755–772.

Substance Use Screening Does Not Need to Be Subtle

The Substance Abuse Subtle Screening Inventory (SASSI) was designed to assess substance use disorders in patients who may not answer questions truthfully for various reasons (e.g., denial, wanting to please their clinician). To summarize research on the SASSI, investigators conducted a systematic review of 36 peer-reviewed articles on the instrument's performance in a total of 22,110 patients.

- There was high internal consistency* for the direct but not the indirect (or subtle) components of the SASSI.
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*How consistently questions measure the variable of interest (in this case, substance use disorders)

Subtle Screening for Substance Use (continued from page 6)

- The sensitivity of the SASSI was 70% (weighted mean); the specificity was 62%.*

Comments: Screening for substance use disorders is an initial step in diagnosis and treatment. Clinicians may be concerned that direct questions make it easier for patients to provide socially desirable, rather than honest, answers. This research, however, indicates that subtle screening methods do not necessarily have good operating characteristics and clinical utility. Further, other studies show that

more-direct questions work quite well.

David A. Fiellin, MD

*Sensitivity is the proportion of patients with a disorder that test positive; specificity is the proportion of patients without a disorder who test negative.

Reference: Feldstein SW, et al. Does subtle screening for substance abuse work? A review of the Substance Abuse Subtle Screening Inventory (SASSI). *Addiction*. 2007;102(1):41–50.

Benzodiazepine Use in Patients Receiving Opioid Treatment

Deaths associated with concurrent injection of benzodiazepines and buprenorphine have been documented in Europe. To examine the risk of adverse effects (extreme drowsiness, unconsciousness, or overdose) from concurrent benzodiazepine use, Australian researchers surveyed 250 subjects, recruited from syringe exchange and opioid treatment programs, who had ever received buprenorphine or methadone treatment.

- Subjects who had received both methadone and buprenorphine in the past (n=164) were significantly more likely to report extreme drowsiness (odds ratio [OR], 2.7) and overdose (OR, 10.0) with methadone than with buprenorphine.
- Subjects reporting adverse effects with buprenorphine were significantly more likely than subjects reporting adverse effects with methadone to have injected their treatment (51% versus 21%).
- Of the 193 subjects who had ever received buprenorphine, 67% reported ever concurrently using benzodiazepines (median dose equivalent to 30 mg of diazepam).
- In adjusted analyses, concurrent daily benzodiazepine use in-

creased the odds of adverse effects significantly in subjects receiving methadone (OR, 2.2) and borderline significantly in subjects receiving buprenorphine (OR, 2.1).

Comments: In this study, specific adverse effects were less common in patients receiving buprenorphine than in those receiving methadone. Further, concurrent benzodiazepine use was not associated with a higher risk of adverse effects in subjects receiving buprenorphine than in those receiving methadone. These findings require replication in patients taking the combined formulation of buprenorphine/naloxone. Nonetheless, the results are reassuring to buprenorphine/naloxone prescribers in North America where benzodiazepine use is prevalent but buprenorphine injection is still relatively uncommon.

Peter D. Friedmann, MD, MPH

Reference: Nielsen S, et al. Concurrent buprenorphine and benzodiazepines use and self-reported opioid toxicity in opioid substitution treatment. *Addiction*. 2007;102(4):616–622.

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*Alcohol, Other Drugs, and Health:
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