# Substance Use and Women's Health

Abigail Kay, M.D., M.A.
Instructor, Department of Psychiatry and Human Behavior – Division of Substance Abuse,
Medical Director N.A.R.P., Thomas Jefferson University Hospital

Trusandra E. Taylor, M.D., FASAM, M.P.H
JEVS Human Services

Andrea G. Barthwell, M.D., FASAM
CEO, Human Resources Development Institute, Inc.
President, EMGlobal LLC

Request reprints:
Trusandra E. Taylor, M.D., FASAM, M.P.H
JEVS Human Services
5820 Old York Road
Philadelphia, PA 19141
Phone 215-276-8400

**Table of Contents**

## Introduction

Substance use among women is a widespread and costly problem that can lead to a variety of medical complications. In 2006, 571,748 women in the United States were admitted into substance abuse treatment programs that receive public funding[1] – a number significantly higher than the number of new breast cancer cases (182,460) for that same year. Additionally, on an annual basis, $180.9 billion is spent in the U.S. on the associated costs of substance abuse overall.[2] Given the fact that substance abuse contributes to many of the leading threats to women's health, it is essential to understand the relationships between abuse of different substances and the incidence of medical problems in the female population.

## Women's Health Research

Comprehensive research data on the physiological effects of addiction in women has been difficult to obtain prior to the last decade. The recent attention given to and improved understanding of women's health was precipitated by the larger women's social movement beginning in the 1960s, which focused on addressing the social exclusion of women – for example, from traditionally male-dominated careers.[3] This push for inclusion was exemplified in the biomedical field in grass-roots publications such as *Our Bodies, Ourselves*. This work, released in 1973, encouraged women to seek information about their health directly, instead of relying on what the publication called "paternalistic" male medical doctors.[4]

The National Institutes of Health (NIH) is the primary federal agency responsible for funding medical research, with a budget of almost $30 billion annually.[5] It was not until 1994, however, that the NIH officially established guidelines requiring that women be included in federally-funded health studies. At that time, the federal government officially created the NIH Office of Research on Women's Health and specifically requested the inclusion of women into federal research because of concerns that women were underrepresented in medical studies.[6]

Research into the effects of alcohol and smoking on women's health is more available than research into the effects of opioids and stimulants on women's health. Researchers have only recently undertaken studies on the effects of these latter substances on women's health. This delay is due to the aforementioned underrepresentation of women in biomedical research, along with concerns over fetal health and the subsequent legal implications[3] of exposing women who may become pregnant to highly addictive stimulants shown to cause premature birth,[7] lower birth weight,[8] and slow language development.[9,10]

## Female-specific Characteristics of Substance Abuse

Research shows that substance use disorders take a different course in women than in men. Women generally begin using substances later than do men.[11,12] Studies on female substance abuse treatment clients have found that they have lower education levels than male clients, lower rates of employment, and lower average age at admission into treatment.[13,14] In a study of Los Angeles substance abuse treatment clients, Hser et al. found that 39 percent of female clients had

less than a high school education, compared with 19 percent among males.[14] Additionally, substance-dependent females are more likely than substance-dependent males to have spouses or partners who are also substance-dependent.

Additionally, females who are addicted to substances are more likely than their male counterparts to have psychiatric disorders. A study of individuals with opioid abuse disorders found that female users were twice as likely as male users to have a mood or anxiety disorder. Female users are also more likely to have psychiatric disorders that predate their substance use disorders.[15,16]

### *Telescoping*

The telescoping of alcohol addiction has been well established in women – that is, the medical literature confirms that women progress more quickly than men into addiction to alcohol and development of the physiological consequences of alcohol abuse.[17,18] For example, there is considerable evidence that women move quickly from first use to addiction.[19-21] In an analysis of retrospective reports of over 2,000 substance abuse treatment facility clients, Johnson et al. found a faster progression in women from initiation of regular alcohol use to problem use than in men.[21]

A number of studies have also found that medical problems associated with alcohol use progress more swiftly in women.[22-24] Female alcoholics have 50 to 100 percent higher rates of premature death than do male alcoholics. Also, more female alcoholics die from circulatory disorders and cirrhosis of the liver than male alcoholics.[25] Additionally, research has demonstrated that even with shorter durations of heavy drinking than their male counterparts, women have comparable incidence rates of diseases associated with alcoholism (ulcer disease, gastrointestinal hemorrhage, fatty liver, hypertension, obesity, anemia, malnutrition).[24]

Emerging research suggests that this telescoping phenomenon may also occur in women using other substances, such as tobacco, opioids, and stimulants.

## Screening for Substance Use Disorders

Though substance use leads to many social and medical consequences, few seek treatment for substance use disorders. In 2002, the Substance Abuse Mental Health Services Administration (SAMHSA)'s National Survey on Drug Use and Health found that while 26.3 million people had diagnosable chemical abuse disorders, only about six percent of these individuals believed that they should seek treatment.[26] People with substance use disorders may visit a physician to seek treatment for other medical issues, and physicians must use these opportunities to screen patients; users often present with medical ailments that are related to, and may even be caused by, the substance use disorder itself.

While screening tools can be adapted to be gender-specific, it is key that physicians themselves understand the differences in the course of addiction for women, as identifying and treating

substance use can mitigate or prevent many health problems in women, as described below. Medical professionals can thereby help to significantly reduce suffering and health care costs – for both the patient and society as a whole – by addressing an underlying source of medical distress. Through a review of current and past literature, this article will lay out the possible physiological consequences of substance use in women, focusing specifically on the use of alcohol, tobacco, opioids, and stimulants.

## Alcohol

In women who use alcohol, telescoping – the rapid onset of addiction and of the physiological consequences of alcohol abuse – is a result of the way that women's bodies process alcohol. Though this process is not completely understood, it is theorized that the lower average amount of body water in women leads to higher blood alcohol concentrations, even when they consume the same amount of alcohol as men.[27,28] Another possible contributing factor to women's increased susceptibility to alcohol is the fact that women's digestive systems may contain less alcohol dehydrogenase – an enzyme that helps to metabolize alcohol – resulting in reduced metabolizing of alcohol and more alcohol absorption.[29]

Though previous research shows that women tend to begin using substances at later ages than do men,[11,12] more recent research suggests that women are beginning to use alcohol at younger ages.[30,31] Binge drinking among 19- to 22-year-old females has increased from 28 percent to 34 percent between 1995 and 2007.[31] In addition, though men and boys generally have higher rates of alcohol use than women and girls, the gender gap in binge drinking among teenagers has narrowed over the years. One indication of this change is the percentage-point difference between rates of binge drinking among male and female twelfth graders. The difference between the prevalence of 12$^{th}$-grade boys consuming five or more drinks in a row, and the prevalence of 12$^{th}$-grade girls engaging in the same activity, has dropped from 23 points in 1975 to seven points in 2006.[31]

The increased alcohol intake among young adult women is of particular concern in light of the medical complications that alcohol causes, and the more rapid onset of these complications that women face. It is essential, therefore, that physicians screen for alcohol use among these populations.

### Conditions Associated with Alcohol Use

#### *Liver Disease*

Excessive alcohol consumption may lead to a spectrum of liver diseases, including fatty liver, alcoholic hepatitis, and cirrhosis.[32] In the U.S. between 1999 and 2005, deaths resulting from alcoholic liver syndromes among women increased by 15 percent.[33] Various studies have found that the female liver is more susceptible to alcohol than the male liver.[34,35] While cirrhosis mortality rates are twice as high among men compared with women,[36] women develop cirrhosis

faster than do men.[37] Becker et al. studied alcohol consumption and alcohol-related liver disease in a group of more than 13,200 men and women over a 12-year period. The researchers found that the level of alcohol consumption above which women increased their relative risk of developing liver disease (seven to 13 drinks per week) was about half of that for men (14 to 27 drinks per week). In addition, at any level of alcohol intake, women had a significantly higher risk of developing liver disease than did men.[38]

### *Cardiovascular Disease*

In 2006, cardiovascular disease affected 35 percent of women in the U.S.[39] Evidence suggests that, in general, light drinking may be associated with lower risk of cardiovascular complications, whereas heavy drinking is associated with higher risk.[40,41] In a review of key animal and human studies, Saremi and Arora found that while there is evidence that moderate alcohol consumption – especially consumption of red wine – may have a protective effect on cardiovascular health, consumption of three or more drinks a day was associated with hypertriglyceridemia, cardiomyopathy, hypertension, and stroke.[41]

Researchers have also found that both abstaining from alcohol and heavy alcohol consumption increase risk of cardiovascular disease among women. Ikehara et al. surveyed nearly 35,000 men and 49,000 women about lifestyle, medical history, and alcohol. Upon follow up 14 years later, they found that over 1,600 participants had died of stroke, and over 700 had died of heart disease. The researchers also found distinct trends for women versus men.[42] Men who drank greater than or equal to 69 grams of alcohol per day experienced increased risk of coronary heart disease. Meanwhile, women experienced increased risk of mortality from coronary heart disease if they consumed between 23 and 45.9 grams of alcohol per day. This risk was more than tripled in women who drank 46 grams or more of alcohol per day.[42]

This study confirmed that women's risk of cardiovascular disease is increased with use of lower amounts of alcohol than for men. The threshold for increased risk of coronary heart disease among men was found to be 69 grams of alcohol per day, an amount that is three times higher than the 23-gram threshold for increased coronary heart disease risk among the women in this study.[42] Additionally, though light drinking was associated with a reduced risk of mortality from coronary heart disease for both men and women, the amount of alcohol consumption that provided a protective effect for women was significantly less than the amount that had the same effect for men. For men, intake of up to 68.9 grams of alcohol per day was associated with lower risk of coronary heart disease. In contrast, for women, drinking only up to 22.9 grams of alcohol per day had this protective effect.[42]

Despite findings that light drinking reduces risk of cardiovascular disease in men and women, the American Heart Association (AHA) does not recommend drinking alcohol to protect against heart disease, as alcohol may have overall negative consequences on health. Instead, the AHA recommends consulting a doctor about lowering cholesterol and blood pressure, along with making healthy lifestyle choices – such as eating a balanced diet, exercising regularly, and controlling weight – to protect against heart disease.[43]

### *Endocrine Diseases*

Medical research shows that alcohol consumption causes disturbances in endocrine system functioning. Health care providers should be aware of the fact that alcohol consumption can lead to elevated levels of cortisol, as excess levels of cortisol are related to hypertension, impaired immune function, and metabolism disturbances.[44-46] Evidence suggests that alcohol consumption affects the hypothalamic-pituitary-adrenal (HPA) axis, increasing cortisol levels.[47] In one study, Badrick et al. found that, in both men and women, alcohol affected HPA function. In women, heavy drinkers experienced greater cortisol awakening response (a marker of cortisol secretion) than did moderate drinkers.[47]

#### *Obesity*

Excess weight gain and obesity are increasing at an alarming rate among Americans of all ages and both genders. In 2005, 60.5 percent of women were overweight or obese;[48] rates were highest among non-Hispanic black women (79.9 percent) and Hispanic women (68.4 percent).[49] These observations present a significant public health challenge, as being overweight or obese increases the chances of developing heart disease, hypertension, type 2 diabetes, respiratory problems, and certain types of cancers, in both men and women.

Heavy alcohol consumption is linked to disturbances in body weight and nutrition. An eight-year prospective study using multivariate analysis found a non-linear relationship between alcohol consumption and weight gain exceeding five kilograms.[50] Heavy drinking, defined as consumption of alcohol exceeding 30 grams per day, was associated with a slight increase in weight gain among all women. Among women under 35 years of age, heavy drinking was more strongly associated with weight gain. In fact, risk of weight gain among this group was around 68 percent higher than non-drinkers. Additionally, among African-American women, even light drinking was associated with an increased risk of weight gain compared with non-drinkers.[50]

Alcohol consumption may also be associated with abdominal obesity. Schröder et al. found that among men and women, consumption of three or more drinks per day was associated with increased abdominal obesity.[51] Abdominal obesity should be of particular concern to health care providers, as it is a risk factor for type 2 diabetes.[52]

#### *Diabetes*

In the U.S., 9.5 million women have been diagnosed with diabetes,[48] a leading cause of death and disability. An additional 2.5 million women are believed to have undiagnosed diabetes, while another 23 million have been diagnosed with prediabetes.[48] Diabetes is more common in women than in men, and is especially prevalent among non-Hispanic black women. In 2005, diabetes occurred in 106.8 per 1000 in this population compared with 69.1 per 1000 in non-Hispanic white women.[49]

Current research suggests that both abstaining from alcohol and consuming large amounts of alcohol increase risk, whereas light-to-moderate consumption may decrease risk.[53] In a systematic review of literature published between 1963 and August 2003, Howard et al.

concluded that, compared with abstaining from alcohol, moderate consumption (defined as one to three drinks per day) was associated with a 33 to 56 percent lower incidence of diabetes. Meanwhile, heavy consumption of alcohol (more than three drinks per day) was associated with up to a 43 percent increase in diabetes incidence.[53]

Few studies look at this phenomenon specifically in women. In a twenty-year twin cohort study that also investigated alcohol use and diabetes in women, Carlsson et al. found that lean-to-normal weight women who consumed large amounts of alcohol, characterized by prolonged consumption and binge drinking, had an increased incidence of type 2 diabetes.[54] Hu et al. confirmed the finding that low-to-moderate alcohol consumption among women reduces diabetes risk.[55]

Though some studies suggest that alcohol may have a protective effect against type 2 diabetes or its complications, [56,55] the American Diabetes Association (ADA) does not recommend use of alcohol to protect against diabetes. In fact, for people with diabetes, drinking alcohol can cause hypoglycemia. The ADA recommends that people with diabetes practice exercise more caution if consuming alcohol.[57]

*Osteoporosis*

Eight million women in the U.S. are affected by osteoporosis, making up 80 percent of all osteoporosis cases.[58] It is well accepted that use of alcohol is a risk factor for osteoporosis.[60,59] Felson et al. followed participants for 35 years, collecting data on health and alcohol consumption. They found that heavy consumption, defined as seven ounces or more of alcohol per week, caused an increase in risk of hip fracture, especially for women. Women's risk increased by 54 percent, while the risk for men increased by 26 percent.[59] In a more recent analysis of data from three studies, comprising a total of nearly 6,000 men and 11,000 women, Kanis et al. found that found that participants who drank moderate or large amounts of alcohol had increased risk of fracture, osteoporotic fracture, and hip fracture.[60]

Recent research has suggested that light drinking may have a protective effect for women. In a study of twins, Williams et al. found that moderate alcohol consumption did not lead to lower bone density and in fact may be beneficial.[61] In a study of women aged 65 and older, Diaz et al. found that risk of vertebral deformity was reduced significantly in participants who consumed alcohol more than five days per week, especially compared with those who consumed alcohol less than once per week.[62]

Despite these findings, the National Osteoporosis Foundation (NOF) does not recommend consuming alcohol as a preventive measure in its prevention materials for patients. The NOF does, however, acknowledge that heavy drinking increases risk for osteoporosis and recommends no more than two drinks per day.[63]

***Lung Cancer***

Lung cancer affects 219,000 women in the U.S.[64] In a review of literature published between 1966 and 2000, Bandera et al. found that while research is not conclusive, there is some evidence that alcohol, particularly beer, may be associated with lung cancer.[65] In one study, Pollack et al. found that participants who consumed more than 40 ounces of alcohol per month had almost twice the incidence of lung cancer of those who did not drink alcohol.[66] In another study, Djouseé et al. found that consumption of two drinks per day approximately doubled the incidence of lung cancer, controlling for age, smoking history and gender.[67]

***Breast Cancer***

In 2005, nearly 2.5 million women had breast cancer,[64] while over 40,000 women died as a result of breast cancer that year.[68] Studies have consistently shown that alcohol consumption can increase risk for breast cancer.[69-74] One study found that regardless of the specific alcoholic beverage consumed (wine, beer, or liquor), breast cancer rates increase with alcohol consumption. The increased risk of developing breast cancer from consuming three or more drinks per day is roughly comparable to that associated with smoking one pack of cigarettes per day.[75, 76] Various studies have confirmed elevated risk, up to 60 percent higher for heavy drinkers than for non-drinkers (1.19 to 1.6 relative risk). Definitions of heavy drinking varied among these studies, some of which considered 15 grams or more per day to be heavy, while others considered 30 grams or more per day to be heavy. [69-72]

Other studies, however, have found that even light drinking may increase women's risk for breast cancer. In a study of 490,000 males and females with a nine-year follow up, Thun et al. found that mortality from breast cancer was 30 percent higher among women who consumed at least one drink daily compared with non-drinkers (relative risk, 1.3).[73] More recently, Allen et al. followed 1.28 million middle-aged women for an average of seven years, and found that for each 10-gram increase of alcohol per day, risk of breast cancer increased by 12 percent.[77]

Evidence suggests that drinking at later ages also contributes to breast cancer risk in women. Longnecker et al. looked at the influence of age on the relationship between breast cancer and alcohol consumption. Study participants were women with an average age of 58.7 years, who either had breast cancer (6600) or did not (9100). These researchers confirmed a linear relationship between alcohol consumption and breast cancer risk. Women who reported moderate consumption (12 to 18 grams or about one drink per day) had a relative risk of 1.39, compared with a non-drinker, while women who reported heavy consumption (33 to 45 grams or about three drinks per day) had a relative risk of 2.3. They also found, however, that breast cancer risk was not affected by alcohol consumption before the age of 30.[78] In a similar study, Swanson et al. confirmed this finding and also found that heavy drinking during the five-year period leading up to breast cancer diagnosis increased relative risk by 70 percent.[79]

As alcohol consumption, perhaps even light consumption, increases women's risk of breast cancer, reduction of this risk factor is essential. Physicians should emphasize this to female patients, and be sure to assess alcohol use in women, including those who have been diagnosed with breast cancer.

### *Genital/Urinary Cancer*

Endometrial cancer is the most common cancer of the female reproductive tract.[80] An estimated 554,000 women had endometrial cancer as of 2005.[64] Though research is still inconclusive, some studies have found an association between alcohol consumption and endometrial cancer. In a hospital-based study of over 700 endometrial cancer patients and 2100 controls, Parazzini et al. found that as alcohol consumption increased, so did risk of endometrial cancer.[81] Although these findings do not establish a cause-effect relationship, they are consistent with the finding that alcohol use may spur an increase in blood estrogen levels in postmenopausal women.[82]

### *Other Cancers*

Studies have linked alcohol consumption to other cancers as well. In 2009, Allen et al. completed the Million Women Study, in which approximately 1.28 million middle-aged women were surveyed and followed over an average of seven years. During the follow-up period, over 69,700 cancers occurred. Risk for other cancers increased with each 10-gram increase of alcohol per day. Cancer of the rectum increased 10 percent, cancer of the liver increased 24 percent, and cancer of the breast increased 12 percent. There was no significant difference in risk based on type of alcohol consumed.[77]

Allen et al. also found that a 10-gram increase of alcohol per day resulted in increases in risk of cancer of the upper aerodigestive tract (head and neck): Cancer of the oral cavity and pharynx increased 29 percent; cancer of the esophagus increased 22 percent; and cancer of the larynx increased 44 percent. Alcohol-associated risk, however, was restricted to current smokers and did not apply to never- or past-smokers.[77] Other studies[83,84] on the joint effects of smoking and alcohol consumption have found increased risk of cancer for both men and women. Castellsague et al. found an association between simultaneous alcohol drinking and tobacco smoking and esophageal cancer, though smoking alone or alcohol consumption alone did not correlate with esophageal cancer. [83]

## Assessment

Given the evidence of alcohol's harmful effects on women's health, health care providers should address alcohol use among female patients. There are many scales for addressing alcohol use. It is useful to use questions that assess multiple domains, as questions limited to quantity and frequency of alcohol use may not detect alcohol misuse or abuse.

Useful questionnaires include the CAGE (Cut down, Annoyed, Guilty, Eye-opener) questionnaire,[85] the Michigan Alcoholism Screening Test,[86] and the Self-Administered Screening Test.[87] Although these tests are useful, they have limited application to women in terms of quantity, frequency, and consequences. Although they have not had reliability ratings in exclusively female populations, they are, however, better than no instrument. The TWEAK (Tolerance, Worry, Eye-Opener, Amnesia, Cut down), T-ACE (Tolerance, Annoyed, Cut-down,

Eye-opener), and Alcohol Use Disorders Identification Test are more sensitive tools for evaluating women in general.[88]

Studies show that the CAGE questions, taught at most medical schools, are not as sensitive in picking up alcohol disorders in women. The MAST and SAST are lengthy, and responders may require clinical supervision.

In light of the telescoping problem, a physician should use these instruments with a woman who has vague complaints (anxiety, difficulty sleeping, weight loss, depression, fatigue), who is undergoing stressful life events,[89] who lives with an alcohol- or drug-dependent partner, or who uses alcohol as a medication.

**Conclusion**

The medical literature provides sufficient evidence as to the health consequences of alcohol use. As a result of the way the female body metabolizes alcohol, women experience these consequences more quickly than men. Evidence shows that alcohol consumption increases risk of a number of chronic or potentially fatal conditions, including liver disease, coronary heart disease, breast cancer, diabetes, and osteoporosis. In addition, evidence suggests associations between alcohol use and other cancers, such as lung, liver, or rectal cancer. Given the myriad of negative health effects of alcohol consumption, physicians must prioritize addressing alcohol abuse with female patients.

## Tobacco

Tobacco use is known to be a major health hazard, contributing to a broad range of health conditions and disorders. Aside from the established direct causal link between cigarette smoking and lung cancer, tobacco use is also associated with an increased risk of other pulmonary diseases, cardiovascular disease, and many types of cancers, including cancers of the breast, head and neck, esophagus, pancreas, intestinal tract, bladder, and reproductive system. While a direct dose-dependent correlation has not been fully established in some cases for these other illnesses,[90] the literature strongly suggests that these associated risks are not only present but highly significant. Additionally, the telescoping effect described earlier may also occur with smoking in women, hastening many of the adverse health impacts of tobacco use.

Cigarette smoking kills an estimated 178,000 women in the U.S. annually.[91] The three leading smoking-related causes of death in women are lung cancer (claiming 45,000 women's lives per year), heart disease (40,000), and chronic lung disease (42,000).[91] Statistics show that women who smoke more than double their risk of developing coronary heart disease[92] and increase more than tenfold their likelihood of dying from chronic obstructive pulmonary disease.[93, 94] The incidence of these smoking-related deaths and illnesses can only be expected to rise in the future, as global rates of cigarette smoking in women are increasing, making tobacco use an issue of particular concern for women.

## Conditions Associated with Tobacco Use

### *Pulmonary Diseases*

*Lung Cancer*

The causal link between cigarette smoking and lung cancer has been well established, making tobacco use a major cause of death in both men and women. In the year 2000, an estimated 47 percent of lung cancer cases in women in the U.S. were deemed a consequence of tobacco smoking.[95] Moreover, almost 80 percent of all lung cancer deaths in female smokers are attributable to smoking.[96] Since 1950, lung cancer deaths among women have increased by more than 600 percent.[93] By 1987, lung cancer had surpassed breast cancer as the leading cause of cancer-related deaths in U.S. women.[93,97] Studies also show that the incidence of lung cancer in women is steadily increasing worldwide, while lung cancer in men shows signs of stabilization.

Evidence suggests that tobacco use in women also has a telescoping effect with lung cancer. A study of lung cancer patients in Poland revealed that women developed lung cancer at younger ages than did men, despite consuming fewer cigarettes per day and smoking for a shorter duration.[98] The data suggests that women, therefore, have a greater susceptibility to the cancer-causing compounds in cigarette smoke due to a genetic predisposition. This theory is supported by the finding that the gene for the gastrin-releasing peptide receptor is located on the X chromosome. This receptor, when activated, has a demonstrated association with the proliferation of bronchial cells.[99]

*Chronic Obstructive Pulmonary Disease*

Chronic obstructive pulmonary disease (COPD) continues to be the fourth leading cause of death both worldwide[100] and in the U.S.[101] Smoking, particularly heavy smoking, long-term use of tobacco, and smoking of high-tar cigarettes, is a risk factor that is strongly associated with the development of COPD. Figures suggest that 10 to 15 percent of all smokers, and up to 26 percent of heavy smokers, develop COPD.[102,103]

Since the 1970s, as the incidence of tobacco use in the U.S. has increased among women and slightly decreased in men, the percentage of total COPD deaths comprised by women has increased from 19 percent in 1970 to nearly 40 percent in 1993.[104] Female smokers may be at greater risk of COPD-related death than men, as their pulmonary system may be more swiftly compromised by long-term smoking. In a study of the effect of smoking cessation on lung function over five years, women who continued smoking had a proportionately greater decline in lung functioning than men with similar rates of tobacco use.[105] Conversely, women in this study who quit smoking and remained tobacco-free showed greater early improvement in lung functioning than men who also quit.

### *Cardiovascular Disease*

Tobacco smoking is generally considered the most important preventable cause of coronary heart disease for both genders.[106,107] Epidemiologic studies have strongly supported a greater

incidence of cardiovascular disease, including fatal coronary artery disease and myocardial infarction, in both men and women who smoke.[108-110] This association appears to be true even when the tobacco is used in different forms; when compared with non-smokers, those using low-tar cigarettes and smokeless tobacco still exhibited an increased risk of cardiovascular events.[111,112] More research is needed on the components of cigarette smoke and the exact mechanisms causing this association.[90]

There have been few studies of factors that predict the occurrence and severity of coronary artery disease (CAD) specifically for women. Research has shown, though, that when women stop smoking, the risk of future coronary events begins to decline within one to two years of the cessation.[113] An Australian study, however, found that the total amount of lifetime cigarette smoking, whether the habit was past or current, was the most relevant quantitative variable to independently predict and prevent premature CAD. Moreover, this study found that the total smoking dose was more predictive for CAD in women than in men.[114]

Research has also shown tobacco use to be a risk factor for sudden death with severe coronary disease in women. The mechanisms leading to sudden coronary death are not fully understood, but components of cigarette smoke are believed to erode coronary plaque, which is a collection of cholesterol, fats, and calcium inside blood vessels.[115] Plaque erosion can cause blockages in blood vessels, leading to a propensity for fatal clotting, especially in women.[116] Indeed, young female smokers without other relevant risk factors (such as high cholesterol or elevated body mass index) account for the majority of fatal acute coronary thrombosis cases caused by plaque erosion in women.[117] Tobacco smoking cessation would, therefore, appear to be the most significant lifestyle change needed in preventing these deaths of young women.[117]

***Breast Cancer***

Breast cancer, as the worldwide leading cause of death from cancer in women (despite being surpassed by lung cancer in the U.S.),[118] is clearly a key health concern for the female population. A direct relationship between cigarette smoking and breast cancer has not been clearly established, as many epidemiologic studies have failed to find that tobacco use is a significant risk factor for the disease.[119] Other evidence, however, suggests that an association may, in fact, exist; in four out of eight case-control studies reviewed in Japan, moderate or strong associations between smoking and breast cancer risk (OR > 2.0) were observed.[120] This and other research supports the plausibility that tobacco smoking has a positive association with the incidence of breast cancer.[121]

Furthermore, experimental studies suggest that genotoxic agents in cigarette smoke are involved in causing breast cancer. In rodents, the genotoxic substances in tobacco smoke were found to be mammary carcinogens.[122] Certain women who smoke may be more susceptible to these carcinogens, depending on their phase of life and genetic characteristics. For example, sensitivity of the female breast to tobacco carcinogens is increased during adolescence and early adulthood, but decreases after first childbirth, when most breast tissue has terminally differentiated.[123]

An example of a specific genetic difference that may put some female smokers at greater breast cancer risk is the speed with which they metabolize a certain gene, NAT2, which encodes an enzyme to activate or deactivate drugs and carcinogens in the body. People fall into three categories: rapid, intermediate, and slow NAT2 acetylators.[124] A 1996 study showed that women who are genetically slow NAT2 acetylators (about 50 percent of the female population) have a significantly elevated risk of breast cancer from smoking. These results held up through 12 similar studies conducted over the next decade.[125,126] While the relative risk is small (~1.5) for NAT2 slow acetylators, the sheer number of breast cancer cases worldwide means attention to these findings and further research into the association with smoking is merited.

### *Cancers of the Reproductive System*

Cervical cancer and other cancers of the reproductive system are also important health concerns for women. Studies have suggested that tobacco use is associated with a higher incidence of both ovarian and cervical cancers. Cigarette smoking, however, also appears to interact with women's systems in unique ways, possibly reducing the risk of endometrial cancer and causing other estrogen-associated effects (please see "Other Female-Specific Consequences of Tobacco Use").

#### *Cervical Cancer*

In studies that controlled for the effect of human papillomavirus (HPV) infection (a recognized cause of the majority of cervical cancers) tobacco use increased the risk of cervical cancer among women who were already HPV-positive.[127] In cross-sectional studies, Human Papilloma Virus (HPV) cervical infection has not been found to be associated consistently with smoking.[128] Research that also investigated other environmental risk factors such as diet, oral contraceptive use, and sexual history, while controlling for HPV infection, found that smoking appears to be the most significant of these factors associated with cancer of the cervix.[129]

These cross-sectional studies conclude that: a) HPV infection cannot explain the association between cervical cancer and smoking; b) the effect of smoking is unlikely to represent only a surrogate marker of a woman's sexual behavior; and c) the association of tobacco smoke with invasive cervical cancer, therefore, indicates a causal relationship.[128] An alarming prediction can be made based on these findings that the increasing rates of smoking in young women may lead to a much greater incidence of cervical cancer in coming years.

#### *Ovarian Cancer*

Compared with other cancers, comparatively little research has been done into the impact of tobacco use on the incidence of ovarian cancer. Some existing studies, however, do point to cigarette smoking as a risk factor for the disease, as the incidence of ovarian cancer was found to be increased even for those women who smoked in the past, but later quit.[130] The findings of Green et al. were especially significant for the incidence of mucinous types of ovarian cancer.[130] Other research suggests that cigarette smoking may only play a role in these mucinous cancers,

but not in ovarian cancers of other cell types.[131] More research is needed to clarify this association.

*Endometrial Cancer*

Interestingly, some studies have found a connection between cigarette smoking and a decreased incidence of endometrial cancer.[132-134] The link appears to be most significant in postmenopausal women.[135,136] Given the myriad adverse and potentially fatal health impacts associated with cigarette smoking, this finding of one reduced risk is not of direct importance from a public health standpoint. It does, however, point to an opportunity to better understand and prevent endometrial cancer through more research into the mechanisms by which tobacco use reduces risk.[136]

***Other Cancers***

Women who smoke tobacco also put themselves at increased risk for other cancers, including cancers of the pancreas, bladder, gastro-intestinal tract, head and neck, and esophagus. Smoking has a significant association with pancreatic carcinoma[137] and bladder cancer,[138] and risks for both these diseases in women may be higher than in men with the same duration and amount of tobacco use. Additionally, a Norwegian study that tracked 26,000 men and women for nearly three decades found that there was a dose-response relationship between cigarette smoking and the risk of cancers of the urinary bladder and upper digestive tract, among other cancers already discussed.[139]

Tobacco use has been found to be a very significant risk factor for head and neck cancers in women, including cancers of the oral cavity, pharynx, and larynx. The overall incidence of squamous (soft-tissue) cancers of the head and neck is roughly three times higher in men than in women. Female smokers, however, have been found in one study to have a higher hazard ratio for developing head and neck cancer when compared with men. Consequently, the authors of that study estimated that cigarette smoking accounts for 75 percent of head and neck cancer in women, compared with 45 percent of these same cancers in men.[140]

Esophageal cancer is one of the least studied cancers,[141, 142] despite being the fifth most common cause of death from cancer in men, and seventh most common in women, worldwide.[118] Studies conducted on the influence of cigarette smoking, and other potential risk factors, on the incidence of esophageal cancer have found that tobacco use is a significant risk factor for the disease. The association was strongest for esophageal adenocarcinomas; smoking was shown to have a strong relationship with the eventual development of these cancers, even 20 years after quitting.[143] This relationship may be caused by the swallowing of carcinogenic material in condensed cigarette, cigar, and pipe smoke.[144]

**Other Female-Specific Consequences of Tobacco Use**

In addition to the increased risk of serious health threats caused by tobacco use in women, smoking has other pervasive effects on the female body. Through mechanisms not fully understood, cigarette smoking is believed to have an anti-estrogenic effect in women. Female

smokers' resulting deficiency of estrogen could explain their reduced incidence of endometrial cancer.[145] A meta-analysis of 12 studies found that the lower hormonal level caused by smoking may also have an impact on fertility in women, leading to difficulty in getting pregnant and possibly even infertility.[146] Decreased estrogen levels associated with smoking may cause earlier menopause as well; a 1999 study showed that on average current smoking decreases the age of natural menopause by two years and past smoking by one year.[147]

Many studies have discovered that postmenopausal women who smoke have lower bone density than women who have never smoked.[148] A meta-analysis of 29 cross-sectional studies on smoking and bone density, and 19 cohort and case-control studies on hip fractures and smoking, found that the cumulative bone loss of smokers over many years is substantially higher than in non-smokers.[149] This finding indicates that women using tobacco after menopause are at increasingly greater risk of bone injury than non-smokers as they age. The authors of this meta-analysis estimated that smoking increases the risk of hip fracture by 17 percent at age 60, 41 percent at age 70, and 71 percent at 80 years of age.

**Conclusion**

The evidence in the literature leaves no doubt that tobacco use has severe and potentially fatal health consequences for women of all ages, from young adulthood through maturity and old age. Moreover, the same risks of cancers, cardiovascular ailments, and pulmonary diseases due to smoking that men experience may be exacerbated in women as a result of their genetic makeup and other physiological mechanisms yet to be revealed. Finally, given the increased risk of preterm delivery, stillbirth, low birth weight, and sudden infant death syndrome (SIDS) in babies born to mothers who smoked during pregnancy,[93] the harmful effects of smoking in women can even extend to impact the chances of survival and health of the next generation.

## Opioids

The incidence of opioid abuse, especially of opioid prescription medications, has been increasing at an alarming rate in the U.S. Rates of prescription drug abuse are especially high among teens, young adults, and those over 60.[150] Over the past decade, the number of people abusing prescription medications has more than doubled,[151] and the majority of this abuse believed to be of pain relievers. According to SAMHSA figures, in 2007 there were 2.1 million new users aged 12 or older of prescription pain relievers.[150]

Heroin use is also on the rise, possibly owing to its connection with the abuse of prescription opioids. This increase may be attributed to the growing number of teens trying prescription opioids such as OxyContin®, which is similar to heroin in chemical composition and produces a similar high. OxyContin® is a synthetic opioid that resembles morphine, the organic substance from which heroin is derived[152,153.] During 2007, 106,000 persons aged 12 or older used heroin for the first time.[150] Recent findings suggest that people who abuse opioid medications may be at risk of graduating to heroin. For example, in 2006, the number of opioid-related deaths (those

comprised of prescription opioid and heroin overdoses) among young people in Massachusetts was five times greater than in 1997.[154]

Opioid use among females of all age groups appears to be on the rise. While levels of cocaine and alcohol abuse among adult women dropped an average of 10 percent between 1992 and 2006, addictions to opioids increased 260 percent in the same time frame.[1] Generally, rates of drug use are higher among men than women. According to SAMHSA, however, females aged 12 to 17 had higher rates of abuse of prescription pain relievers than did males in the same age group (2.8 percent versus 2.5 percent).[150] Additionally, through a review of research published between 1990 and 2006, Simoni-Wastila and Yang concluded that up to 11 percent of older female adults may use prescription medications inappropriately.[155] This research points to opioid abuse as an issue of special and growing concern for women's health.

**Evidence of Telescoping**

Some studies on the patterns of telescoping that pertain to the course of opioid addiction in women, however, have begun to emerge. Researchers have found evidence that women abusing opioids may progress more quickly to addiction.[156,20] In a study of 546 men and women addicted to heroin, Anglin et al. found that women were more likely than men to become addicted to heroin within one month of initial exposure.[156] This study also found that women escalated their use of heroin more rapidly, became addicted in a shorter period of time, and sought treatment earlier in the course of addiction than did men.[156]

Other research conducted more recently supports these findings. A 2004 study of 271 substance-dependent patients found that women entered treatment for heroin addiction sooner after initial exposure to the drug than did men. These researchers also found that, though women had been addicted for less time than men, they reported equal levels of addiction severity.[20] Such findings on the strength and speed of addiction in women make it all the more essential for health professionals to prevent, discover, and treat opioid abuse in female patients.

**Physiological Effects of Opioid Abuse**

Though there is little research into the effects of opioid abuse on the health of women specifically, some researchers have found increased severity of general health problems in opioid-addicted women versus men. Hernandez-Avila et al. studied male and female substance-dependent patients, utilizing the Addiction Severity Index (ASI) to assess severity of addiction and related problems. This assessment consists of an hour-long interview during which subjects are asked about lifetime and recent severity of problems in several areas of functioning, including medical functioning. Hernandez-Avila et al. found that women addicted to opioids reported slightly more medical issues than did men addicted to opioids.[20] Arfken et al. also conducted a study of substance-dependent patients in which ASI scores were analyzed. Although these researchers did not categorize ASI results by substance of abuse, they found a general trend in which women reported more severe medical issues than did men.[157]

While there is little female-specific research, the literature contains extensive evidence illuminating the medical consequences of opioid use. There is an accepted causal relationship between certain opioids and respiratory depression.158-160**,+ In a 1981 double-blind, placebo-controlled study, six healthy women were administered oral methadone, while six were administered a placebo. In the methadone group, the women's ventilatory response to carbon dioxide, which initiates exhalation, was slowed significantly during and after the half-life of the methadone dose. The significance of this delay lead researchers to conclude that women suffered opioid-induced respiratory depression despite the higher levels of progesterone present during specific menstrual cycles normally regarded as having a regulatory effect on respiration.+158

Methadone and oxycodone overdose has also been linked to specific and sometimes fatal cardiac events, like myocardium or striated muscle damage and depressed heart rate, as measured by prolonged QTc intervals. In a 2009 Danish study, researchers examined one hundred chronic nonmalignant pain patients being treated with methadone and oxycodone, and found that higher doses led to equally long delays in QTc intervals and increases in torsade de pointes, an abnormally fast heart rhythm originating in one or more ventricles. In addition, *in vitro* testing revealed that most opioids can block cardiac potassium channels, possibly leading to other forms of arrhythmia.++161

Furthermore, Toth and Varga found evidence for striated muscle damage in 78 opioid abuse-related deaths. The researchers found that microscopic examinations of individuals' heart muscles in autopsy revealed that all had suffered striated muscle or myocardium damage. The authors suggest that in several cases, undiagnosed striated or myocardium damage may also sometimes be a cause of death.+++162

Additionally, research has found an association between opioid use and a higher incidence of several cancers. It has also been shown that opioids can lead to an increased chance of metastasis and a subsequent decreased survival rate among tumor-bearing animals. A 2008 hospital-based case-control study of 179 patients found that opium users were more likely to develop bladder cancer, a risk that increased six-fold when the user was also a heavy smoker.[163] These findings follow a 2004 study with similar results.[164]

A causal relationship has also been suggested between opioid exposure and esophageal squamous cell carcinoma[165] and laryngeal cancer.[166] Morphine sulfate, the main alkaloid in opium, has been shown to cause an alkylation increase in the esophagus, which can lead to overproduction of diethylnitrosamine and subsequent carcinogenesis, particularly in the esophagus and liver of animals.[167] Research suggests that opioid abuse may have a deleterious effect on the immune system,[168-170] and also that it may increase the risk of bacterial and viral infection in animals.[171,172] More studies are needed to shed further light on the mechanisms of these health impacts, as well as the physiological effects of opioid abuse on specific populations such as women.

***Neurological Consequences of Opioid Abuse***

Opioid abuse can have a number of severe neurological consequences on both men and women. Heroin use, in particular, has been shown to have negative effects on brain function, impacting attention span, memory, and verbal fluency throughout the duration of addiction.[173,174] Trail-making tests, two-back and gambling tasks, and recognition memory tests have been used to show that heroin abusers and methadone-dependent patients alike suffer from deficits in psychomotor speed, working memory, decision-making, and metamemory.[175-177] Studies have also found that heroin abusers exhibit impaired verbal function and visual-spatial analysis,[178] impulse control,[179] and mental planning.[180] Such effects on proper brain functioning may seriously impact an opioid-addicted individual's ability to function in society, care for his or her health, and successfully hold employment.

Though there is a lack of conclusive opioid research specific to female physiology, recent research has suggested that female heroin abusers may experience certain neurological deficits attributed to heroin abuse more acutely than men. In a study of 18 male and 19 female heroin-dependent patients at a detoxification clinic in China, patients were presented with a map on the floor of a room and asked to perform several tasks relevant to navigating the physical space, such as following arrows on the ground and walking to specific points marked by photographs in a particular order. In three out of the four tests, female study participants performed more poorly than both control subjects and male study participants.[181]

The female participants in this same study were also found to be deficient in their ability to perform left-oriented tasks. An earlier study suggested that the capacity to discriminate between left and right was especially impaired in heroin-dependent women, who performed more poorly than control females and heroin-dependent men on all tests. Heroin-dependent males only performed poorly on some of the tests. [182]

**Conclusion**

The escalating rates of opioid abuse, as well as figures that suggest opioids have become the drug of choice for many women, make our understanding of addiction to these substances and its effects critical. Additional studies must be conducted regarding the detrimental health effects of opioid abuse, especially in light of the recently published research linking bladder cancer and other ailments to use of these drugs. Attention must be paid to the physiological and neurological conditions caused by opioid abuse that are specific to, or particularly prevalent among, female patients. Also, more research is clearly needed into female-specific characteristics of addiction to heroin and other opioids, especially prescription pain relievers.

**Stimulants**

In 2007, over 900,000 people aged 12 and older used cocaine for the first time.[150] The number of women seeking treatment for cocaine abuse has slightly decreased since 1992 from 102,076 admissions per year, to 99,380 admissions in 2006. The overall percentage of women who use cocaine admitted into treatment facilities receiving public funding, however, has risen from 37.8 percent to 39.7 percent over the same time frame.[1]

In addition to the danger of fatal overdose from cocaine abuse, behaviors and risks associated with use of the drug can also lead to premature death in both men and women. Marzuk et al. completed a review of data on New York City male and female residents who suffered fatal injury from 1990 to 1992 and found that over 26 percent had used cocaine shortly before their deaths.[183] The researchers detected cocaine in the user's system in almost one out of five fatal-injury cases, which included homicides, suicides, traffic accidents, falls, and other intentional and unintentional incidents. In fact, when compared with leading causes of death, including AIDS, cancer, and heart disease, fatal injuries following cocaine use were the most common cause of death for individuals aged 15 to 24 from all racial and ethnic groups and both genders in New York City, excluding white females. [183]

**Evidence of Telescoping**

Significant evidence exists of telescoping in women abusing cocaine.[184-186] The literature shows that women begin using cocaine earlier in their patterns of concurrent addictions, experience more severe health problems related to cocaine use,[187] and, therefore, seek treatment sooner than men. Women also move more quickly from their introduction to cocaine into abuse.[184,186,188]

In a study of individuals with polysubstance use issues who had been admitted into two Florida drug court programs, Haas et al. found that, while women began using alcohol and marijuana later in life than men, they progressed to using cocaine at an earlier point in the course of addiction. Additionally, in women there was a shorter duration between first cocaine use and cocaine abuse, and they reported more cocaine use-related problems.[186]

**Physiological Effects**

Sweeping physiological changes caused by prolonged abuse of stimulants, including alterations at the molecular, cellular, and tissue levels, can lead to mortality among chronic users. Research in this area is inconclusive and sparse, yet there is some evidence that these changes may affect women more severely than men. In their study of polysubstance-abusing men and women in Florida drug court programs, Haas and Peters found that women reported more current health problems than did men.[186]

Potentially fatal myocardial alterations can occur following chronic cocaine use, including cardiac hypertrophy, myocardial fibrosis, and microangiopathy.[189] In a study of men and women addicted to crack cocaine, Evans et al. found that smoking cocaine produced more prolonged cardiovascular effects and higher cocaine plasma concentrations in women than in men.[190] Additionally, Dudish et al. found that women were more likely to report headaches and trips to the emergency room following crack cocaine use.[191]

Several studies have suggested that cocaine use may broadly suppress the immune system[192,193] and may possibly, as a result, enhance the infectivity of HIV in users.[193] In a study of HIV positive women, Cook et al. found that women who persistently used crack cocaine were three times as likely to die from AIDS. These women were also more likely to develop AIDS-defining illnesses, and to have virologic and immunologic markers of HIV-1 disease progression.[194]

While the link between cigarette smoking and lung cancer has been clearly established after decades of research, studies on the possible association between smoking of illicit drugs and lung cancer are still in their preliminary stages. A 1998 study, however, did suggest that cocaine and marijuana smoking has field cancerization effects on bronchial structures in the lung, potentially putting cocaine users at higher risk of developing lung cancer.[195] The field cancerization theory, first introduced by Slaughter et al., hypothesizes that genetic alterations can occur to whole areas of tissue, developing a "patch" of altered cells and explaining the development of multiple tumors and locally recurring cancers.[196,197] Little to no research has been done on the female-specific incidence of cancer in stimulant users.

### *Effects of Stimulant Use Specific to Female Physiology*

Women's menstrual cycles affect how they experience the subjective effects of cocaine. In one study, women were shown to experience the mood-altering effects of cocaine more strongly during their follicular menstrual cycle (the earliest period of menstruation) when estrogen was high but progesterone was low. Later, in the luteal cycle, when progesterone was higher, the effects of the drug were not felt as strongly. Researchers believe that progesterone played a significant role in dampening the physical reaction to cocaine. The authors did not fully clarify the implications of their research, but these findings demonstrate a clear mechanism specific to women and should be further investigated.[198]

As in cocaine, there is evidence that women experience the euphoric and addictive effects of amphetamines more strongly in the early follicular stages of their menstrual cycle. Of additional concern was that women in one study also reported craving and enjoying the effects of amphetamines more during the early phases of menstruation, particularly in times of high estrogen.[199]

## Psychological Effects

The use of stimulants may exacerbate psychological problems, such as depression, especially in women. Research has established an association between illicit drug use and higher concentrations of cortisol, which may lead to more depressive symptoms.[200] A 2005 study found that among heroin and cocaine users, this association was more pronounced in women, and female users with elevated cortisol concentrations were significantly more depressed than all other participants in the study.[200] This mechanism is not yet fully understood, as it is unknown whether high cortisol levels precede depression or are an associated effect. The "chicken and egg" relationship between depression and illicit drug use may make causative relationships difficult to uncover.

## Conclusion

In future national surveys of persons entering rehabilitation or clinical facilities, more data should be collected regarding the physical condition of subjects in order to better elucidate the

associated health concerns, and determine more accurately the cost to the national economy of drug addiction.

## Social Consequences

### Intimate Partner Violence

In the U.S., women experience 4.8 million instances of intimate partner-related physical assaults and rapes every year.[201] Additionally, during 2005, 1,181 women were murdered by an intimate partner.[202]

Many studies have found an association between alcohol abuse and intimate partner violence.[203-207] Specifically, there is much evidence of an association between intimate partner violence and alcohol use by the perpetrator.[208,203]

Some studies have found a correlation between intimate partner violence and victims' alcohol use.[204,206,209] For example, Miller et al. surveyed alcoholic and non-alcoholic women and found that alcoholic women had higher levels of spouse-to-woman violence in their lives.[206] Additionally, in a study of female welfare recipients, Tolman and Rosen found that women who had experienced intimate partner violence had higher rates of alcohol dependence than did women who had not experienced intimate partner violence.[209] Additionally, an analysis of forensic data from intimate partner related homicides detected alcohol in 45 percent of victims and in 70 percent of suspects.[210] This finding does not suggest a causal relationship. Physicians should be aware of this association so that they can look for signs of possible intimate partner violence in women who abuse alcohol and identify signs of alcohol abuse in women who have experienced intimate partner violence.

### HIV/AIDS and Other Sexually Transmitted Diseases

At the end of 2005, according to the World Health Organization, 17.5 million women worldwide were infected with HIV.[211] HIV disproportionately affects African-American and Hispanic women.[212] Together they represent less than 24 percent of all U.S. women, yet they account for more than 82 percent of AIDS cases in women.[213]

Problems of substance use in women are significantly correlated with high-risk behaviors involving injection drug use, unprotected sexual contact, and multiple sexual partners. Many studies have found a direct relationship between HIV seropositivity and the number of partners with whom injection equipment has been shared, frequency of injection, and frequency of needle sharing.[214-216] Studies have also found that female users have a greater risk of contracting sexually transmitted diseases (STDs) than do male users. In a study of African-American adolescents, Fullilove et al. found that female crack cocaine users were more likely to engage in high-risk activities than non-using females. For example, women who used crack cocaine were more likely to take part in high-risk sexual acts in exchange for money or drugs, and they were less likely to have used a condom during last sexual intercourse than their non-using counterparts.[217] Additionally, there is evidence that women who inject drugs or smoke crack

cocaine have more sex partners than do their male counterparts, further placing them at risk of contracting STDs, including HIV.[218]

Research suggests that women who drink alcohol heavily may have a heightened risk of contracting sexually transmitted diseases, including HIV.[219,220] In a study of STD clinic patients, Hutton et al. found that women who reported binge drinking were twice as likely to report having multiple sex partners, and five times as likely to have gonorrhea, than women who abstained from alcohol.[221]

By screening for and addressing substance use disorders among women, physicians can help women to reduce their risk factors for HIV and other sexually transmitted diseases.

## References


1. U.S. Dept. of Health and Human Services, Substance Abuse and Mental Health Services Administration, Office of Applied Studies. TREATMENT EPISODE DATA SET (TEDS), 1992-2006 (Concatenated) [Computer file]. Prepared by Synectics, Incorporated. ICPSR02184-v8. Ann Arbor, MI: Inter-university Consortium for Political and Social Research [producer and distributor], 2006-12-08.

2. Executive Office of the President. Office of National Drug Control Policy. The Economic Costs of Drug Abuse in the United States 1992-2002.1992-2002. Washington, D.C. December 2004. Available from: http://www.whitehousedrugpolicy.gov/publications/economic_costs/economic_costs.pdf. Accessed March 12, 2009.

3. Blehar MC. Women's Mental Health Research: The Emergence of a Biomedical Field. Annual Review of Clinical Psychology. April 2006;2:135-160.

4. Norsigian J, Boston Women's Health Book Collective. *Our Bodies, Ourselves*. Boston, MA: New England Free Press; 1973.

5. The Nation's Medical Research Agency. National Institutes of Health Web site. Available from: http://www.nih.gov/about/NIHoverview.html. Accessed March 12, 2009.

6. National Institutes of Health. NIH Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research. NIH Guide. 1994;23(11).

7. Frank DA, Jacobs RR, Beeghly M, Augustyn M, Bellinger D, Cabral H, Heeren T. Level of Prenatal Cocaine Exposure and Scores on the Bayley Scales of Infant Development: Modifying Effects of Caregiver, Early Intervention, and Birth Weight Pediatrics. Pediatrics. 2002 December;110(6):1143–1152.

8. Lumeng JC, Cabral HJ, Gannon K, Heeren T, and Frank DA. Pre-natal exposures to cocaine and alcohol and physical growth patterns to age 8 years. Neurotoxicol Teratol. 2007;29(4):446-457.

9. Morrow CE, Bandstra ES, Anthony JC, Ofir AY, Xue L, Reyes MB. Influence of Prenatal Cocaine Exposure on Early Language Development: Longitudinal Findings from Four Months to Three Years of Age. J Dev Behav Pediatr. 2003 February;24(1):39–50.

10. Bandstra ES, Morrow CE, Vogel AL, Fifer RC, Ofir AY, Dausa AT, Xue L, Anthony JC. Longitudinal influence of prenatal cocaine exposure on child language functioning. Neurotoxicol Teratol. 2002;24(3):297–308.

11. Chou SP, Dawson DA. A study of the gender differences in morbidity among individuals diagnosed with alcohol abuse and/or dependence. J Subst Abuse.1994;6:381–392.

12. Gomberg ES. Women and alcohol: use and abuse. J Nerv Ment Dis.1993;181:211–219.

13. Wong CJ, Badger GJ, Sigmon SC, Higgins ST. Examining possible gender differences among cocaine-dependent outpatients. Experimental and Clinical Psychopharmacology. 2002;10:316-323.

14. Hser YI, Huang D, Teruya C, Anglin DM. Gender comparisons of drug abuse treatment outcomes and predictors. Drug and Alcohol Dependence. 2003;72:255-264.

15. Kessler RC, Crum RM, Warner LA, Nelson CB, Schulenberg J, Anthony JC. Lifetime co-occurrence of DSM-III-R alcohol abuse and dependence with other psychiatric disorders in the National Comorbidity Survey. Archives of General Psychiatry. 1997;54:313-321.

16. Grella CE, Karno MP, Warda US, Niv N, Moore AA. Gender and comorbidity among individuals with opioid use disorders in the NESARC study. Addict Behav. 2009 Jan 30..

17. Orford J, Keddie A. Gender differences in the functions and effects of moderate and excessive drinking. Br J Clin Psychol. 1985;24:265–279.

18. Randall CL, Roberts JS, Del Boca FK, Carroll KM, Connors GJ, Mattson ME. Telescoping of landmark events associated with drinking: a gender comparison. J Stud Alcohol. 1999;60:252–260.

19. Diehl A, Croissant B, Batra A, Mundle G, Nakovics H, Mann K. Alcoholism in women: Is it different in onset and outcome compared to men? Eur Arch Psychiatry Clin Neurosci. 2007 Sep;257(6):344-51.

20. Hernandez-Avila CA, Rounsaville BJ, Kranzler HR. Opioid-, cannabis- and alcohol-dependent women show more rapid progression to substance abuse treatment. Drug Alcohol Depend. 2004 Jun 11;74(3):265-72.

21. Johnson PB, Richter L, Kleber HD, McLellan AT, Carise D. Telescoping of drinking-related behaviors: Gender, racial. Subst use Misuse. 2005;40(8):1139-51.

22. Mann K, Ackermann K, Croissant B, Mundle G, Nakovics H, Diehl A. Neuroimaging of gender differences in alcohol dependence: Are women more vulnerable? Alcohol Clin Exp Res. 2005 may;29(5):896-901.

23. HallidayA, Bush B, Cleary P, et al. Alcohol abuse in women seeking gynecologic care. Obstet Gynecol. 1986;68:322.

24. Ashley M, Olin JS, Harding JC, et al. Morbidity in alcoholics: Evidence for accelerated development of physical disease in women. Arch Intern Med. 1977; 137:833.

25. Hill SY. Biological consequences of alcoholism and alcohol-related problems among women. In: Special Populations Issues. National Institute on Alcohol Abuse and Alcoholism. Alcohol and Health Monograph No. 4. DHHS Pub. No. (ADM)82-1193. Washington, DC: Supt. of Docs., U.S. Govt. Print. Off., 1982. pp. 43-73.

26. Coombs RH. Addiction Counseling Review: Preparing for Comprehensive, Certification and Licensing Examinations. Routledge; 2005.

27. Jones BM, Jones MK. Women and alcohol: intoxication, metabolism, and the menstrual cycle. In: Greenblatt M, Schuckit MA, eds. Alcohol problems in women and children. New York: Grne & Stratton, 1976: 103-136.

28. Van Thiel DH, Tarter RE, Rosenblum E, et al. Ethanol, its metabolism and gonadal effects: does sex make a difference? Adv Alcohol Subst Abuse. 1988;3-4:131-169.

29. Frezza M, Di Padoua C, Pozzato G, et al. High blood alcohol levels in women: the role of decreased gastric alcohol dehydrogenase and first-pass metabolism. N Engl J Med. 1990; 322:95-99.

30. Johnston LD, O'Malley PM, Bachman JG, Schulenberg JE. Monitoring the Future national survey results on drug use, 1975-2007. Volume I: Secondary school students (NIH Publication No. 08-6418A). Bethesda, MD: National Institute on Drug Abuse; 2008.707.

31. Johnston LD, O'Malley PM, Bachman JG, Schulenberg JE. Monitoring the Future national survey results on drug use, 1975-2007. Volume II: College students and adults ages 19-45 (NIH Publication No. 08-6418B). Bethesda, MD: National Institute on Drug Abuse; 2008:319.

32. Mann RE, Smart RG, Govoni R. The epidemiology of alcoholic liver disease. Alcoholism, Research and Health. 2003;27:209-219.

33. Centers for Disease Control and Prevention, National Center for Health Statistics. Compressed Mortality File 1999-2005. CDC WONDER On-line Database, compiled from

Compressed Mortality File 1999-2005 Series 20 No. 2K, 2008. Available at: http://wonder.cdc.gov/cmf-icd10.html. Accessed March 12, 2009.

34. Tuyns AJ, Péquignot G. Greater risk of ascitic cirrhosis in females in relation to alcohol consumption. International Journal of Epidemiology 13:53–57,1984.

35. Colantoni A, Idilman R, De Maria N, La Paglia N, Belmonte J, Wezeman F, Emanuele N, Van Thiel DH, Kovacs EJ, Emanuele MA. Hepatic apoptosis and proliferation in male and female rats fed alcohol: Role of cytokines. Alcoholism Clinical Experimental Research. 2003;27:1184-1189.

36. Yoon YH, Yi H, Grant BF, et al. Surveillance Report #57: Liver Cirrhosis Mortality in the United States, 1970–98. Washington, DC: National Institute on Alcohol Abuse and Alcoholism; 2001.

37. Anderson P. Alcohol and risk of physical harm. In: Holder HD, and Edwards G, eds. Alcohol and Public Policy: Evidence and Issues. Oxford: Oxford University Press, 1995. 82–113.

38. Becker U, Deis A, Sorensen TI, Gronbaek M, Borch-Johnsen K, Muller CF, Schnohr P, Jensen G. Prediction of risk of liver disease by alcohol intake, sex, and age: A prospective population study. Hepatology. 1996;23(5):1025–1029.

39. American Heart Association. Heart Disease and Stroke Statistics-2009 Update. Statistics Committee and Stroke Statistics Subcommittee. Circulation. 2008 Dec 15.

40. Foerster M, Marques-Vidal P, Gmel G, Daeppen JB, Cornuz J, Hayoz D, Pécoud A, Mooser V, Waeber G, Vollenweider P, Paccaud F, Rodondi N. Alcohol drinking and cardiovascular risk in a population with high mean alcohol consumption. Am J Cardiol. 2009 Feb 1;103(3):361-8.

41. Saremi A, Arora R. The cardiovascular implications of alcohol and red wine. Am J Ther. 2008 May-Jun;15(3):265-77.

42. Ikehara S, Iso H, Toyoshima H, Date C, Yamamoto A, Kikuchi S, Kondo T, Watanabe Y, Koizumi A, Wada Y, Inaba Y, Tamakoshi A. Alcohol Consumption and Mortality from Stroke and Coronary Heart Disease Among Japanese Men and Women. Stroke. 2008;39:2936-2942.

43. American Heart Association. Alcohol, Wine and Cardiovascular Disease. Available at: http://www.americanheart.org/presenter.jhtml?identifier=4422. Accessed March 12, 2009.

44. Plat L, Leproult R, L'Hermite-Baleriaux M, Fery F, Mockel J, Polonsky KS, Van Cauter E. Metabolic effects of short-term elevations of plasma cortisol are more pronounced in the evening than in the morning. J Clin Endocrinol Metab. 1999;84:3082–3092.

45. Spiegel K, Leproult R, Van Cauter E. Impact of sleep debt on metabolic and endocrine function. Lancet. 1999;354:1435–1439.

46. Whitworth JA, Williamson PM, Mangos G, Kelly JJ. Cardiovascular consequences of cortisol excess. Vasc Health Risk Manag. 2005;1:291–299.

47. Badrick E, Bobak M, Britton A, Kirschbaum C, Marmot M, Kumari M. The Relationship between Alcohol Consumption and Cortisol Secretion in an Aging Cohort. J Clin Endocrinol Metab. 93:750–757;2008.

48. Lloyd-Jones D, Adams R, Carnethon M, De Simone G, FergusonTB, Flegal K, et al., for the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart Disease and Stroke Statistics--2009 Update: A Report From the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Circulation. 2009;119(3): e21-181.

49. U.S. Department of Health and Human Services, Health Resources and Services Administration. Women's Health USA 2007. Rockville, Maryland: U.S. Department of Health and Human Services; 2007.

50. Wannamethee SG, Field AE, Colditz GA, Rimm EB. Alcohol Intake and 8-year Weight Gain in Women: A Prospective Study. Obesity Research. Sept 2004;12(9).

51. Schröder H, Morales-Molina JA, Bermejo S, Barral D, Soler Mándoli E, Grau M, Guxens M, de Jaime Gil E, Domínguez Álvarez M, Marrugat J. Relationship of abdominal obesity with alcohol consumption at population scale. European Journal of Nutrition. 2007;46(7).

52. Hirani V, Zaninotto P, Primatesta P. Generalised and abdominal obesity and risk of diabetes, hypertension and hypertension–diabetes co-morbidity in England. Public Health Nutrition. 2008;11(5):521-527.

53. Howard AA, Arnsten JH, Gourevitch MN. Effect of Alcohol Consumption on Diabetes Mellitus A Systematic Review. Ann Intern Med. 2004;140:211-219.

54. Carlsson S, Hammar N, Valdemar G, Jaakko K. Alcohol Consumption and the Incidence of Type 2 Diabetes – A 20 Year Follow up of the Finnish Twin Cohort Study. Diabetes Care. Oct 2003;23(10)

55. Hu FB, Manson JE, Stampfer MJ, Colditz G, Liu S, Solomon CG, Willett WC. Diet, lifestyle, and the risk of type 2 diabetes mellitus in women. N Engl J Med. 2001 Sep 13;345(11):790-7.

56. Beulens JW, Stolk RP, van der Schouw YT, Grobbee DE, Hendriks HF, Bots ML. Alcohol consumption and risk of type 2 diabetes among older women. Diabetes Care. 2005 Dec;28(12):2933-8.

57. Diabetes Food Pyramid: Alcohol. American Diabetes Association Web site. Available at: http://www.diabetes.org/nutrition-and-recipes/nutrition/alcohol.jsp. Accessed March 12, 2009.

58. Fast Facts on Osteoporosis. National Osteoporosis Foundation Web site. Available at: http://www.nof.org/osteoporosis/diseasefacts.htm#top. Accessed March 12, 2009.

59. Felson DT, Kiel DP, Anderson JJ, Kannel WB. Alcohol consumption and hip fractures: the Framingham study. Am J Epidemiol. 1988 Nov;128(5):1102-10.

60. Kanis JA, Johansson H, Johnell O, Oden A, De Laet C, Eisman JA, Pols H, Tenenhouse A. Alcohol intake as a risk factor for fracture. Osteoporos Int. 2005 Jul;16(7):737-42.

61. Williams FM, Cherkas LF, Spector TD, MacGregor AJ. The effect of moderate alcohol consumption on bone mineral density: a study of female twins. Ann Rheum Dis. 2005 Feb;64(2):309-10.

62. Diaz NM, O'Neill TW, Silman AJ, and the European Vertebral Osteoporosis Study Group. Influence of alcohol consumption on the risk of vertebral deformity. Osteoporosis International. 1997;7:65–71.

63. Prevention. National Osteoporosis Foundation Web site. Available at: http://www.nof.org/prevention/risk.htm#alcoholabuse. Accessed March 12, 2009.

64. Ries LAG, Melbert D, Krapcho M, et al (eds). SEER Cancer Statistics Review, 1975-2005, National Cancer Institute. Bethesda, MD, Available at: http://seer.cancer.gov/csr/1975_2005/. Accessed March 12, 2009.

65. Bandera EV, Freudenheim JL, Vena JE. Alcohol Consumption and Lung Cancer: A Review of the Epidemiologic Evidence. Cancer Epidemiology, Biomarkers & Prevention. 2001;10:813–821.

66. Pollack ES, Nomura AM, Heilbrun LK, Stemmermann GN, Green SB. Prospective study of alcohol consumption and cancer. N Engl J Med. 1984 Mar 8;310(10):617-21.

67. Djoussé L et al. Alcohol Consumption and Risk of Lung Cancer: The Framingham Study. J Natl Cancer Inst. 2002;94:1877-82.

68. Centers for Disease Control and Prevention, National Center for Health Statistics. Compressed Mortality File 1999-2005. CDC WONDER On-line Database, compiled from Compressed Mortality File 1999-2005 Series 20 No. 2K, 2008. Available at: http://wonder.cdc.gov/cmf-icd10.html. Accessed March 12, 2009.

69. Fuchs CS, Stampfer MJ, Colditz GA, Giovannucci EL, Manson JE, Kawachi I, et al. Alcohol Consumption and Mortality among Women. N Engl J Med. 1997;332:1245-1250.

70. Smith-Warner SA, Spiegelman D, Yaun S, van den Brandt PA, Folsom AR, Goldbohm RA, et al. Alcohol and Breast Cancer in Women. A Pooled Analysis of Cohort Studies. JAMA. 1998;279:535-540.

71. Willett WC, Green A, Stampfer MJ, et al. Relative and absolute excess risks of coronary heart disease among women who smoke cigarettes. N Engl J Med 1987;317:1303–9.

72. Gapstur SM, Potter JD, Sellers TA, Folsom AR. Increased Risk of Breast Cancer with Alcohol Consumption in Postmenopausal Women. American Journal of Epidemiology. 136(10): 1221-1231.

73. Thun MJ, Peto R, Lopez AD, Monaco JH, Henley SJ, Heath CW, Doll R. Alcohol Consumption and Mortality among Middle-Aged and Elderly U.S. Adults. N Engl J Med. 1997;337(24):1705-1714.

74. Swanson CA, Coates RJ, Malone KE, Gammon MD, Schoenberg JB, Brogan DJ, et al. Alcohol Consumption and Breast Cancer Risk among Women under Age 45 Years. Epidemiology. May 1997;8(3):231-237.

75. Li Y, Baer D, Friedman GD Md, Udaltsova N, Shim V, Klatsky AL. Wine, liquor, beer and risk of breast cancer in a large population. Eur J Cancer. 2009 Mar;45(5):843-50.
76. European Cancer Conference (2007, September 28). Alcohol Amount, Not Type — Wine, Beer, Liquor —Triggers Breast Cancer. ScienceDaily. Available from: http://www.sciencedaily.com /releases/2007/09/070927083251.htm. Accessed March 12, 2009.

77. Allen NE, Beral V, Casabonne D, Kan SW, Reeves GK, Brown A, Green J. Moderate Alcohol Intake and Cancer Incidence in Women. J Natl Cancer Inst, 2009;101: 296-305.

78. Longnecker MP, Newcomb PA, Mittendorf R, Greenberg ER, Clapp RW, Bogdan GF, et al. Risk of Breast Cancer in Relation to Lifetime Alcohol Consumption. J Natl Cancer Inst. 1995 Jun 21;87(12):923-9.

79. Swanson CA, Coates RJ, Malone KE, Gammon MD, Schoenberg JB, Brogan DJ. Alcohol Consumption and Breast Cancer Risk among Women under Age 45 Years. Epidemiology. May 1997;8(3):231-237.

80. Hill HA, Austin H. Nutrition and endometrial cancer. Cancer Causes Control. 1996;7:19-32.

81. Parazzini F, La Vecchia C, D'Avanzo B, Moroni S, Chatenoud L, Ricci E. Alcohol and endometrial cancer risk: findings from an Italian case-control study. Nutr Cancer. 1995;23:55-62.

82. Purohit V. Moderate Alcohol Consumption and Estrogen Levels in Postmenopausal Women: A Review. Alcoholism: Clinical and Experimental Research. 1998;22(5):994-997.

83. Castellsagué X, Munóz N, De Stefani E, Victora CG, Castelletto R, Rolón PA and Quintana MJ.Independent and joint effects of tobacco smoking and alcohol drinking on the risk of esophageal cancer in men and women. Int J Cancer. 1999;82:657–664.

84. Talamini G, Bassi C, Falconi M, Sartori N, Salvia R, Rigo L, et al. Alcohol and Smoking as Risk Factors in Chronic Pancreatitis and Pancreatic Cancer. Digestive Diseases and Sciences. July 1999;44(7):1303± 1311.

85. Ewing JA. Detecting alcoholism: The CAGE questionnaire. JAMA. 1984;252:1905.

86. Seizes ML: The Michigan Alcoholism Screening Test: A quest for a new diagnostic instrument. Am J Psychiatry. 1971;127:89.

87. Hurt RD, Morse RM, Sorenson WM. Diagnosis of alcoholism with a self-administered alcoholism screening test: Results with 1,002 consecutive patients receiving general examinations. Mayo Clin Proc. 1980;55:365.

88. Zilberman ML, Tavares H, Blume SB, el-Guebaly N. Towards Best Practices in the Treatment of Women with Addictive Disorders. Addictive Disorders and Their Treatment. June 2002;1(2):39-46.

89. Beckman LJ. Women alcoholics: A review of social and psychological studies. J Stud Alcohol. 1975;36:794.

90. Ambrose JA, Barua RS. The pathophysiology of cigarette smoking and cardiovascular disease: An update. Journal of the American College of Cardiology. 19 May 2004;43(10):1731-1737. Available at: http://content.onlinejacc.org/cgi/reprint/43/10/1731.pdf. Accessed March 13, 2009.

91. U.S. Department of Health and Human Services. Women and Smoking: A Report of the Surgeon General. Atlanta, GA: U.S. Department of Health and Human Services, CDC, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health; 2001. Available from: http://www.cdc.gov/tobacco/data_statistics/sgr/sgr_2001/index.htm. Accessed March 13, 2009.

92. Novotny TE, Giovino GA. Tobacco Use. In: Brownson RC, Remington PL, Davis JR (eds). Chronic Disease Epidemiology and Control. American Public Health Association. 1998;117–148.

93. U.S. Department of Health and Human Services. Women and Smoking: A Report of the Surgeon General. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service, CDC, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health; 2001. Available from: http://www.cdc.gov/tobacco/data_statistics/sgr/sgr_2001/index.htm. Accessed March 13, 2009.

94. Centers for Disease Control and Prevention. Perspectives in Disease Prevention and Health Promotion, Smoking-Attributable Mortality and Years of Potential Life Lost—United States, 1984. Morbidity and Mortality Weekly Report [serial online]. 1997;46:444–451. Available at: http://www.cdc.gov/mmwr/preview/mmwrhtml/00047690.htm. Accessed March 13, 2009.

95. Parkin M, Bray F, Ferlay J, Pisani P. Global Cancer Statistics, 2002. Cancer Journal for Clinicians. 2005;55:74-108.

96. Centers for Disease Control and Prevention. Surgeon General's Report: The Health Consequences of Smoking. 2004. Available at: http://www.cdc.gov/tobacco/data_statistics/sgr/sgr_2004/index.htm#lights. Accessed March 13, 2009.

97. Centers for Disease Control and Prevention. Fact Sheet: Women and Tobacco. 2006. Available at: http://www.cdc.gov/tobacco/data_statistics/Factsheets/women_tobacco.htm. Accessed March 13, 2009.

98. Radzikowska E, Glaz P, Roszkowski K. Lung cancer in women: age, smoking, histology, performance status, stage, initial treatment and survival: population-based study of 20,561 cases. Ann Oncol 2002;13:1087–1093.

99. Shriver SP, Bourdeau HA, Gubish CT, Tirpak DL, Davis AL, Luketich JD, et al. Sex-specific expression of gastrin-releasing peptide receptor: relationship to smoking history and risk of lung cancer. J Natl Cancer Inst 2000;92:24–33. Available at: http://jnci.oxfordjournals.org/cgi/content/abstract/92/1/24. Accessed March 12, 2009.

100. World Health Organization. Fact Sheet: The Top Ten Causes of Death. November 2008. Fact Sheet No 310. Available at: http://www.who.int/mediacentre/factsheets/fs310_2008.pdf. Accessed March 12, 2009.

101. Centers for Disease Control and Prevention. National Vital Statistics Reports. April 2008. Deaths: Final Data for 2005. Vol 56, No 10. Available online: http://www.cdc.gov/nchs/data/nvsr/nvsr56/nvsr56_10.pdf. Accessed March 12, 2009.

102. American Thoracic Society. Cigarette smoking and health. Am. J. Respir. Crit. Care Med. 1996. 153:861–865.

103. Fletcher C, Peto R, Tinker C, Speizer FE. The Natural History of Chronic Bronchitis and Emphysema: An Eight-year Study of Early Chronic Obstructive Lung Disease in Working Men in London. Oxford University Press, New York; 1976: 272.

104. Centers for Disease Control. 1996. Mortality patterns—United States, 1993. Morbid. Mortal. Weekly Rep. 45:161–164.

105. Scanlon PD, Connett JE, Waller LA, Altose MD, Bailey WC, Buist AS, et al. Smoking Cessation and Lung Function in Mild-to-Moderate Chronic Obstructive Pulmonary Disease: The Lung Health Study. Am. J. Respir. Crit. Care Med. February 2000;161(2):381-390. Available at: http://ajrccm.atsjournals.org/cgi/reprint/161/2/381. Accessed March 12, 2009.

106. Hennekens CH. Coronary disease: risk intervention. In: Julian DG, Wenger NK, editors, Women and heart disease, 1st ed., London: Martin Dunitz, 1997, 39–48.

107. Roeters van Lennep JE, Westerveld HT, Erkelens DW, van der Wall EE. Risk factors for coronary heart disease: implications of gender. Cardiovasc Res. 2002;53: 538-549. Available at: http://cardiovascres.oxfordjournals.org/cgi/reprint/53/3/538. Accessed March 12, 2009.

108. Jonas MA, Oates JA, Ockene JK, Hennekens CH. Statement on smoking and cardiovascular disease for health care professionals: American Heart Association. Circulation. 1992;86:1664–9.

109. Black HR. Smoking and cardiovascular disease. In: Laragh JH, Brenner BM, editors. Hypertension: Pathophysiology, Diagnosis and Management. 2nd edition. New York, NY: Raven Press Ltd., 1995:2621–47.

110. Price JF, Mowbray PI, Lee AJ, Rumley A, Lowe GD, Fowkes FG. Relationship between smoking and cardiovascular risk factors in the development of peripheral arterial disease and coronary artery disease: Edinburgh Artery study. Eur Heart J. 1999;20:344–53.

111. Negri E, Franzosi MG, La Vecchia C, Santoro L, Nobili A, Tognoni G. Tar yield of cigarettes and risk of acute myocardial infarction: GISSI-EFRIM Investigators. BMJ 1993;306:1567–70.

112. Bolinder G, Alfredsson L, Englund A, de Faire U. Smokeless tobacco use and increased cardiovascular mortality among Swedish construction workers. Am J Public Health 1994;84:399–404.

113. Rosenberg L, Palmer JR, Shapiro S. Decline in the risk of myocardial infarction among women who stop smoking. N EngI J Med. 1990;322:213-217.

114. Wang XL, Tam C, McCredie RM, Wilcken DE. Determinants of severity of coronary artery disease in Australian men and women. Circulation 1994;89:1974–81. Accessed 26 February 2009. Available online: http://circ.ahajournals.org/cgi/reprint/89/5/1974.

115. American Heart Association. Gender and Age Differences Found in Clotting Mechanism of Sudden Cardiac Death. 27 Apr 1998. Accessed 9 March 2009. Available online: http://www.eurekalert.org/pub_releases/1998-04/AHA-GAAD-270498.php.

116. E Arbustini, B Dal, P Morbini, A Burke, M Bocciarelli, G Specchia, et al. Plaque erosion is a major substrate for coronary thrombosis in acute myocardial infarction. Heart. 1999 September; 82(3):269–272. Available online: http://www.pubmedcentral.nih.gov/picrender.fcgi?artid=1729173&blobtype=pdf. Accessed March 12, 2009.

117. Burke AP, Farb A, Malcom GT, Liang Y, Smialek J, Virmani R. Effect of risk factors on the mechanism of acute thrombosis and sudden coronary death in women. Circulation 1998;97:2110–6. Available at: http://circ.ahajournals.org/cgi/reprint/97/21/2110. Accessed March 12, 2009.

118. American Cancer Society. Global Cancer Facts & Figures 2007. Available at: http://www.cancer.org/downloads/STT/Global_Facts_and_Figures_2007_rev2.pdf. Accessed March 12, 2009.

119. IARC Monographs on the evaluation of carcinogenic risks to humans. Tobacco smoke and involuntary smoking. Vol. 83. Lyon: IARC; 2004.

120. Nagata,C., Mizoue,T., Tanaka,K., Tsuji,I., Wakai,K., Inoue,M. and Tsugane,S. (2006) Tobacco smoking and breast cancer risk: an evaluation based on a systematic review of epidemiological evidence among the Japanese population. Jpn. J. Clin. Oncol., 36, 387–394. Available online: http://jjco.oxfordjournals.org/cgi/reprint/36/6/387. Accessed March 12, 2009.

121. Morabia A, Ambrosone CB, Baron JA, Phillips DH, Russo IH. What do we currently know about the epidemiological and biological plausibility of the association of smoking and breast cancer? J Womens Cancer 2001;3:5–8.

122. Hecht SS. Tobacco smoke carcinogens and breast cancer. Environ Mol Mutagen 2002;39:119–26.

123. Ha M, Mabuchi K, Sigurdson A, Freedman D, et al. Smoking Cigarettes before First Childbirth and Risk of Breast Cancer. American Journal of Epidemiology. 2007;166(1):55-61.

124. GeneCards. N-acetyltransferase 2. Last updated Jan 2009. Available online: http://www.genecards.org/cgi-bin/carddisp.pl?gene=NAT2. Accessed March 12, 2009.

125. Ambrosone CB, Kropp S, Yang J, Yao S, Shields PG, Chang-Claude J. Cigarette smoking, N-acetyltransferase 2 genotypes, and breast cancer risk: Pooled analysis and meta-analysis. Cancer Epidemiol Biomarkers Prev 2008;17:15–26.

126. Phillips and Garte. Smoking and Breast Cancer: Is There Really a Link? Cancer Epidemiol. Biomarkers Prev. 2008;17:1-2. Available online: http://cebp.aacrjournals.org/cgi/reprint/17/1/1. Accessed March 12, 2009.

127. Plummer M, Herrero R, Franceschi S, Meijer CJ, Snijders P, Bosch FX, et al. Smoking and cervical cancer: pooled analysis of the IARC multicentric case — control study. Cancer Causes Control 2003 ; 14 : 805–14.

128. Vineis P, Alavanja M, Buffler P, Fontham E, Franceschi S, Gao YT, et al. Tobacco and cancer: recent epidemiological evidence. J Natl Cancer Inst. 2004;96:99–106. Available at: http://jnci.oxfordjournals.org/cgi/reprint/96/2/99. Accessed March 12, 2009.

129. Kjellberg L, Hallmans G, Ahren AM, Johansson R, Bergman F, Wadell G, Angstrom T, Dilliner J. Smoking, diet, pregnancy and oral contraceptive use as risk factors for cervical intra-epithelial neoplasia in relation to human papillomavirus infection. Br J Cancer. 2000 Apr;82(7):1332–8.

130. Green A, Purdie D, Bain C, et al. Cigarette smoking and risk of epithelial ovarian cancer (Australia). Cancer Causes Control. 2001;12:713–19.

131. Zhang Y, Coogan PF, Palmer JR, Strom BL, Rosenberg L. Cigarette Smoking and Increased Risk of Mucinous Epithelial Ovarian Cancer. Am J Epidemiol. 2004;159:133-139. Available at: http://aje.oxfordjournals.org/cgi/reprint/159/2/133. Accessed March 12, 2009.

132. Lesko SM, Rosenberg L, Kaufman DW, Helmrich SP, Miller DR, Strom B, et al. Cigarette smoking and the risk of endometrial cancer. N Engl J Med. 1985; 313:593-6.

133. Brinton LA, Barren RJ, Berman ML, Mortel R, Twiggs LB, Wilbanks GD. Cigarette smoking and the risk of endometrial cancer. Am J Epidemiol 1993; 137:281-91.

134. Viswanathan AN, Feskanich1 D, De Vivo1 I, Hunter DJ, Barbieri RL, Rosner B, et al. Smoking and the risk of endometrial cancer: results from the Nurses' Health Study. Int J Cancer. 2005;114:996–1001. Available at: http://www3.interscience.wiley.com/cgi-bin/fulltext/109865074/PDFSTART. Accessed March 12, 2009.

135. Weiderpass E, Baron JA. Cigarette smoking, alcohol consumption, and endometrial cancer risk: a population-based study in Sweden. Cancer Causes Control. 2001;12:239–47.

136. Zhou B, Yang L, Sun Q, Cong R, Gu H, Tang N. Cigarette Smoking and the Risk of Endometrial Cancer: A Meta-Analysis. The American Journal of Medicine. 2008;121:501-508. Available at: http://download.journals.elsevierhealth.com/pdfs/journals/0002-9343/PIIS0002934308001940.pdf. Accessed March 12, 2009.

137. Muscat JE, Stellman SD, Hoffmann D, Wynder EL. Smoking and pancreatic cancer in men and women. Cancer Epidemiol Biomarkers Prev 1997; 6:15–9. Available at: http://cebp.aacrjournals.org/cgi/reprint/6/1/15.pdf. Accessed March 12, 2009.

138. Castelao JE, Yuan JM, Skipper PL, et al. Gender- and smoking-related bladder cancer risk. J Natl Cancer Inst 2001;93:538–45. Available at: http://jnci.oxfordjournals.org/cgi/reprint/93/7/538. Accessed March 12, 2009.

139. Engeland A, Andersen A, Haldorsen T, Tretli S. Smoking habits and risk of cancers other than lung cancer: 28 years' follow-up of 26,000 Norwegian men and women. Cancer Causes & Control. 1996;7:497–506.

140. Freedman ND, Abnet CC, Leitzmann MF, Hollenbeck AR, Schatzkin A. Prospective investigation of the cigarette smoking-head and neck cancer association by sex. Cancer. 2007 Oct 1;110(7):1593-601.

141. Enzinger PC, Mayer RJ. Esophageal cancer. N Engl J Med. 2003;349:2241–2252. Available at: http://www.usagiedu.com/articles/esoca03/esoca03.pdf. Accessed March 12, 2009.

142. Pisani P, Parkin DM, Bray F, Ferlay J. Estimates of the worldwide mortality from 25 cancers in 1990. Int J Cancer 1999;83:18-29. [Erratum, Int J Cancer 1999;83:870-3.]

143. Wu AH, Wan P, Bernstein L. A multiethnic population-based study of smoking, alcohol and body size and risk of adenocarcinoma of the stomach and esophagus (United States). Cancer Causes Control. 2001;12:721-32.

144. De Stefani E, Barrios E, Fierro L. Black (air-cured) and blond (flue-cured) tobacco and cancer risk. III. Oesophageal cancer. Eur J Cancer. 1993;29A:763-6.

145. Baron JA, La Vecchia C, Levi F. The antiestrogenic effect of cigarette smoking in women. Am J Obstet Gynecol. 1990 Feb;162(2):502-14.

146. Augood C, Duckitt K, Templeton AA. Smoking and female infertility: a systematic review and meta-analysis. Hum Reprod. 1998 Jun;13(6):1532-9.

147. Hu FB, Grodstein F, Hennekens CH, et al. Age at natural menopause and risk of cardiovascular disease. Arch Intern Med 1999;159:1061–1066.

148. Hollenbach KA et al. Cigarette smoking and bone mineral density in older men and women. American Journal of Public Health. 1993;83:1265–1270.

149. Law MR, Hackshaw AK. A meta-analysis of cigarette smoking, bone mineral density and risk of hip fracture: recognition of a major effect. BMJ. 1997;315:841–6.

150. Department of Health and Human Services; Substance Abuse and Mental Health Services Administration, Office of Applied Studies. Results from the 2007 National Survey on Drug Use and Health: National Findings [monograph on the Internet]. Rockville (MD): Substance Abuse and Mental Health Services Administration, Office of Applied Studies; 2008 Sept. Available at: http://www.oas.samhsa.gov/NSDUH/2k7NSDUH/2k7results.cfm. Accessed March 12, 2009.

151. Manchikanti L. Prescription drug abuse: what is being done to address the new drug epidemic? Testimony before the subcommittee on criminal justice, drug policy and human resources. Pain Physician. 2006 Oct;9(4):287-321.

152. Educating Voices [homepage on the Internet]. Naperville (IL): Educating Voices, Inc.; [cited 2009 Jan 28]. Oxycontin Facts. Available from: http://www.educatingvoices.org/OXYCONTIN.asp.

153. Educating Voices [homepage on the Internet]. Naperville (IL): Educating Voices, Inc.; [cited 2009 Jan 28]. Heroin Facts. Available from: http://www.educatingvoices.org/HEROIN.asp.

154. Calefati J. Heroin hits the suburbs hard amid wave of drug abuse by teens and 20-somethings. USNews.com. 2008 Dec 5. Available at:

http://www.usnews.com/articles/news/national/2008/12/05/heroin-hits-the-suburbs-hard-amid-wave-of-drug-abuse-by-teens-and-20-somethings.html. Accessed March 12, 2009.

155. Simoni-Wastila L, Yang HK. Psychoactive drug abuse in older adults. Am J Geriatr Pharmacother. 2006 Dec;4(4):380-94.

156. Anglin MD, Hser YI, McGlothlin WH. Sex differences in addict careers. 2. Becoming addicted. Am. J. Drug Alcohol Abuse. 1987;13:59–71.

157. Arfken CL, Klein C, di Menza S, Schuster CR. Gender differences in problem severity at assessment and treatment retention. Journal of Substance Abuse Treatment. 2001; 20(1):53-57.

158. Olsen GD, Wilson JE, Robertson GE. Respiratory and ventilatory effects of methadone in healthy women. Clin Pharmacol Ther. 1981 Mar;29(3):373-80.

159. Nettleton RT, Ransom TA, Abraham SL, Nelson CS, Olsen GD. Methadone-Induced Respiratory Depression in the Neonatal Guinea Pig. Pediatric Pulmonology. 2007;42:1134–1143.

160. Neal RC, Olsen GD. The effects of methadone on respiration and ventilation in Pygmy goats. J Pharmacol Exp Ther.1980;215:45-52.

161. Fanoe S, Jensen GB, Sjøgren P, Korsgaard MP, Grunnet M. Oxycodone is associated with dose-dependent QTc prolongation in patients and low-affinity inhibiting of hERG activity in vitro. Br J Clin Pharmacol. 2009 Feb;67(2):172-9.

162. Tóth AR, Varga T. Myocardium and striated muscle damage caused by licit or illicit drugs. Journal of Legal Medicine. In press.

163. Hosseini SY, Safarinejad MR, Amini E, Hooshyar H. Opium consumption and risk of bladder cancer: A case-control analysis. Urol Oncol. 2008.

164. Aliasgari M, Kaviani A, Gachkar L, Hosseini-Nassab S. Is Bladder Cancer More Common among Opium Addicts? Urol J. 2004 Fall;1(4):253-4.

165. Nasrollahzadeh D, Kamangar F, Aghcheli K, et al. Opium, tobacco, and alcohol use in relation to esophageal squamous cell carcinoma in a high-risk area of Iran. Br J Cancer. 2008;98:1857– 63.

166. Mousavi MR, Damghani MA, Haghdoust AA, et al. Opium and risk of laryngeal cancer. Laryngoscope. 2003;113:1939–43.

167. Ribeiro-Pinto LF, Swann PF. Opium and esophageal cancer: Effect of morphine and opium on the metabolism of N-nitrosodimethylamine and N-nitrosodiethylamine in the rat. Carcinogenesis 1997;18:365–9.

168. Sacerdote P, Limiroli E, Gaspani L. Experimental evidence for immunomodulatory effect of opioids. In: Machelska H, Stein C, editors. Immune Mechanisms of Pain and Analgesia, Advances in Experimental Medicine and Biology. New York: Kluwer Academic Press, 2001; 521,106–12.

169. Sacerdote P. Opioids and the immune system. Palliat Med 2006; 20(Suppl 1):s9 –15.

170. Vallejo R, de Leon-Casasola O, Benyamin R. Opioid therapy and immunosuppression: A review. Am J Ther 2004;11:354–65.

171. Risdahl JM, Khanna KV, Peterson PK, et al. Opiates and infection. J Neuroimmunol 1998;83:4 –18.

172. Wang J, Barke RA, Charboneau R, et al. Morphine impairs host innate immune response and increases susceptibility to Streptococcus pneumoniae lung infection. J Immunol 2005;174:426 –34.

173. Guerra D, Sole A, Cami J, Tobena A. Neuropsychological performance in opiate addicts after rapid detoxification. Drug and Alcohol Dependence. 1987;20:261–270.

174. Kamboj SK, Tookman A, Jones L, Curran HV. The effects of immediate-release morphine on cognitive functioning in patients receiving chronic opioid therapy in palliative care. Pain. 2005;117:388–395.

175. Mintzer MZ, Stitzer ML. Cognitive impairment in methadone maintenance patients. Drug and Alcohol Dependence. 2002;67:41–51.

176. Ornstein TJ, Iddon JL, Baldacchino AM, Sahakian BJ, London M, Everitt BJ, Robbins TW. Profiles of cognitive dysfunction in chronic amphetamine and heroin abusers. Neuropsychopharmacology. 2000;23:113–126.

177. Sjogren P, Christrup LL, Petersen MA, Hojsted J. Neuropsychological assessment of chronic non-malignant pain patients treated in a multidisciplinary pain centre. European Journal of Pain. 2005; 9: 453–462.

178. Prosser J, Cohen LJ, Steinfeld M, Eisenberg D, London ED, Galynker I. Neuropsychological functioning in opiatedependent subjects receiving and following methadone maintenance treatment. Drug and Alcohol Dependence. 2006;84:240–247.

179. Lee TM, Pau CW. Impulse control differences between abstinent heroin users and matched controls. Brain Inj. 2002 Oct;16(10):885-9.

180. Davydov DM, Polunina AG. Heroin abusers' performance on the Tower of London Test relates to the baseline EEG alpha2 mean frequency shifts. Progress in Neuropsychopharmacology and Biological Psychiatry. 2004;28;1143–1152.

181. Wang JH, Liu XF, Chen YM, Sun HY, Fu Y, Ma MX, He J, Wang HY, Wilson FA, Carlson S, Ma YY. Heroin impairs map-picture-following and memory tasks dependent on gender and orientation of the tasks. Behav Neurosci. 2007 Aug;121(4):653-64.

182. Liu N, Li B, Wilson FA, Ma Y, Hu X.Gender effect on the right-left discrimination task in a sample of heroin-dependent patients. Psychopharmacology (Berl). 2005;181(4):735-40.

183. Marzuk PM, Tardiff K, Leon AC, Portera L, Weiner C: Fatal injuries after cocaine use as a leading cause of death among young adults in New York City. N Engl J Med. 1995;332:1753–1757. Available at: http://content.nejm.org/cgi/content/full/332/26/1753. Accessed March 12, 2009.

184. Griffin ML, Weiss RD, Lange U. A comparison of male and female cocaine abuse. Arch Gen Psychiatry. 1989;46:122–6.

185. White KA, Brady KT, Sonne S. Gender differences in patterns of cocaine use. Am. J. Addict. 1996;5:259–261.

186. Haas AL, Peters RH. Development of substance abuse problems among drug-involved offenders. Evidence for the telescoping effect. J Subst. Abuse. 2000;12:241–253.

187. Kosten TA, Gawin FH, Kosten TR, Rounsaville BJ. Gender differences in cocaine use and treatment response. J Subst Abuse Treat 1993;10:63–6.

188. Mendelson JH, Weiss R, Griffin M, Mirin SM, Teoh SK, Mello NK, Lex BW. Some special considerations for treatment of drug abuse and dependence in women. NIDA Res Monogr. 1991;106:313–327.

189. Karch SB. Cocaine Cardiovascular Toxicity. Southern Medical Journal. 2005;98(8):794 .

190. Suzette M. Evans, Margaret Haney, Marian W. Fischman and Richard W. Foltin. Limited sex differences in response to “Binge” smoked cocaine use in humans. Neuropsychopharmacology. 1999;21(3):445-454.

191. Dudish SA, Hatsukami DK. Gender differences in crack users who are research volunteers. Drug Alcohol Depend. 1996 Sep;42(1):55-63.

192. Ou DW, Shen ML, and Luo YD. Effects of cocaine on the immune system of Balb/C mice. Clin. Immunol. Immunopathol. 1989;52:305–312.

193. Baldwin, GC, Roth, MD, Tashkin, DP. Acute and chronic effects of cocaine on the immune system and the possible link to AIDS. Journal of Neuroimmunology. 1998;83 (1-2):123-128.

194. Cook JA, Burke-Miller JK, Cohen MH, Cook RL, Vlahov D, Wilson TE, et al. Crack cocaine, disease progression, and mortality in a multicenter cohort of HIV-1 positive women. AIDS. 11 July 2008;22(11):1355-1363.

195. Barsky SH, Roth MD, Kleerup EC, Simmons M, Tashkin DP. Histopathologic and molecular alterations in bronchial epithelium in habitual smokers of marijuana, cocaine, and/or tobacco. J Natl Cancer Inst 1998;90: 1198–1205. Available online: http://jnci.oxfordjournals.org/cgi/reprint/90/16/1198. Accessed March 12, 2009.

196. Slaughter DP, et al. 'Field cancerization' in oral stratified squamous epithelium; clinical implications of multicentric origin. Cancer. 1953;6:963–968.

197. Braakhuis BJ, Tabor MP, Kummer JA, et al. A genetic explanation of Slaughter's concept of field cancerization: evidence and clinical implications. Cancer Res. 2003;63:1727–1730.

198. Sofuoglu M, Dudish-Poulsen S, Nelson D, Pentel PR, Hatsukami DK. Sex and menstrual cycle differences in the subjective effects from smoked cocaine in humans. Exp. Clin. Psychopharmacol. 1999;7:274–283.

199. Justice AJ, de Wit H. Acute effects of d-amphetamine during the follicular and luteal phases of the menstrual cycle in women. Psychopharmacology (Berl). 1999 Jul;145(1):67-75.

200. Wisniewski AB, Brown TT, Cofranceso JM, Golub ET, Ricketts EP, Wand G and Dobs AS. Cortisol levels and depression in men and women using heroin and cocaine. Psychoneuroendocrinology. 2006;31:250-255.

201. Tjaden P, Thoennes N. Extent, nature, and consequences of intimate partner violence: findings from the National Violence Against Women Survey. Washington (DC): Department of Justice (US); 2000. Publication No. NCJ 181867. Available at: www.ojp.usdoj.gov/nij/pubs-sum/181867.htm. Accessed March 12, 2009.

202. Bureau of Justice Statistics Web site. Intimate Homicide Victims by Gender. Available at: http://www.ojp.usdoj.gov/bjs/homicide/intimates.htm. Accessed March 12, 2009.

203. Caetano R, Schafer J, Cunradi CB. Alcohol-related intimate partner violence among White, Black, and Hispanic couples in the United States. Alcohol Research and Health. 2001;25:58-65.

204. Kantor GK, Straus MA. Substance abuse as a precipitant of wife abuse victimization. American Journal of Drug and Alcohol Abuse. 1989;15:173-189.

205. Leonard KE, Senchak M. Prospective prediction of husband marital aggression within newlywed couples. Journal of Abnormal Psychology.1996;105:369-380.

206. Miller BA, Downs WR, Gondoli DM. Spousal violence among alcoholic women as compared to a random household sample of women. Journal of Studies on Alcohol. 1989;50:533-540.

207. O'Farrell TJ, Van Hutton V, Murphy CM. Domestic violence before and after alcoholism treatment :A two-year longitudinal study. Journal of Studies on Alcohol. 1999;60:317-321.

208. Kyriacou DN, Anglin D, Taliaferro E, Stone S, Tubb T, Linden JA, Muelleman R, Barton E, and Kraus JF. Risk Factors for Injury to Women from Domestic Violence. N Engl J Med. 1999 Dec 16;341(25):1892-8.

209. Toman, RM. Rosen D. Domestic Violence in the Lives of Women Receiving Welfare Mental Health, Substance Dependence, and Economic Well-Being. Violence Against Women. 2001;7(2):141-158.

210. Slade M, Daniel LJ, Heisler CJ. Application of forensic toxicology to the problem of domestic violence. Journal of Forensic Science. 1991;36:708-713.

211. UNAIDS (2006). Annex 2: HIV and AIDS estimates and data, 2005 and 2003. Available at: http://data.unaids.org/pub/GlobalReport/2006/2006_GR_ANN2_en.pdf. Accessed March 12, 2009.

212. AIDSinfo (2008). HIV Infection in Women: Overview 2006. AIDSinfo Web site. Available from: http://www.aidsinfo.nih.gov/. Accessed March 12, 2009.

213. UNAIDS Epidemic Update, Dec. 2007; UNAIDS, Report on the global AIDS epidemic, 2008; Kaiser Family Foundation; U.S. Centers for Disease Control and Prevention, 2008.

214. Curran JW, Jaffe HW, HardyAM, et al. Epidemiology of HIV infection andAIDS in the United States. Science. 1988;239:610-616.

215. Chaisson RE, Moss AR, Onishi R, Osmond D, Carlson JR. Human immunodeficiency virus infection in heterosexual intravenous drug users in San Francisco. Am J Public Health. 1987;77:169-172.

216. Marmor M, DesJarlais DC, Cohen H, et al. Risk factors for infection with human immunodeficiency virus among intravenous drug users in New York City.AIDS. 1987;1:39-44.

217. Fullilove MT, Golden E, Fullilove RE 3rd, Lennon R, Porterfield D, Schwarcz S, Bolan G. Crack cocaine use and high-risk behaviors among sexually active black adolescents. Adolesc Health. 1993 June;4(4):295-300.

218. Booth RE, Watters JK,Chitwood DD. HIV Risk-Related Sex Behaviors among Injection Drug Users, Crack Smokers, and Injection Drug Users Who Smoke Crack. August 1993;83(8).

219. Zenilman JM, Hook EW, 3rd, Shepherd M, Smith P, Rompalo AM, Celentano DD. Alcohol and other substance use in STD clinic patients: relationships with STDs and prevalent HIV infection. Sex Transm Dis. 1994 Jul-Aug;21(4):220-5.

220. Fisher JC, Cook PA, Sam NE, Kapiga SH. Patterns of alcohol use, problem drinking, and HIV infection among high-risk African women. Sex Transm Dis. 2008 Jun;35(6):537-44.

221. Hutton HE, McCaul ME, Santora PB, Erbelding EJ.The relationship between recent alcohol use and sexual behaviors: gender differences among sexually transmitted disease clinic patients. Alcohol Clin Exp Res. 2008 Nov;32(11):2008-15.