



PinotFile

The First Wine Newsletter Exclusively Devoted to Pinotphiles

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A sip of Pinot is worth a thousand words

The Debate as to the Health Benefits of Wine Continues in 2011

“Alcohol makes breast cancer more likely but cuts heart attack risk. It could drive one to drink.”

Jill U. Adams, *Los Angeles Times*, 2011

The heated argument as to the health benefits of wine and other beverage alcohol as part of a healthy lifestyle continued in 2011. A focus of the controversy in 2011 was breast cancer as new studies were reported confirming a long-suspected link between some forms of breast cancer and alcohol. Unfortunately, selected press releases sensationalized the research results causing some unjustified panic. The concern among women was heightened by publications that failed to present the implications of the research accurately. With little access to or inadequate understanding of the research findings, women were left to wonder what to do.

I can sympathize with the public's confusion. As a medical doctor, I have read all the medical literature and research on the relationship between alcoholic beverages and health, yet I find it increasingly exasperating trying to decipher the conflicting reports. Practically every published research study ends with the disclaimers such as, “Further study is necessary,” “More research is needed to explain the results,” and “The results may be explained by biases and confounding.” The word “suggestive” or the two word “interpret cautiously” are often employed.



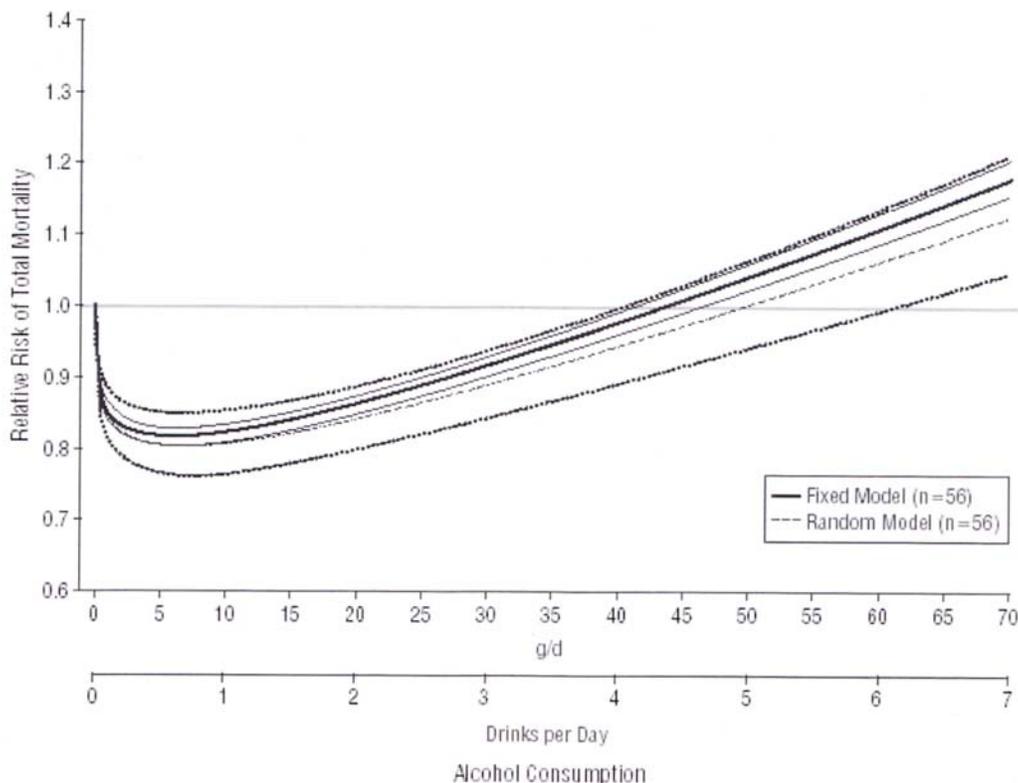
The uncertainty stems primarily from the fact that all the research to date has been performed either in vitro on lower life forms (rats, yeast, worms), or in vivo with cohort and case-control analyses. There have been no well-executed, randomized, double-blinded, intervention trials controlled for all confounding variables. As noted American researcher Arthur L. Klatsky, M.D., has reported, “The major issue is residual confounding by diet, smoking and other traits, problematic statistical modeling, and under estimation of drinking amount which

lowers the apparent threshold of risk. The association of a behavioral trait such as alcohol drinking with a health outcome in any study could be due to chance, due to bias (confounding), or causal. While a chance relation is always possible, statistical evaluation can render the likelihood vanishingly small. The accepted standard for elimination of confounding and establishment of likely causality is the double-blinded randomized controlled trial. Problems in blinding and prescription of long-term behavior, plus the perceived risk of harmful effects have so far precluded this type of long term study with chronic disease endpoints. As a result, the issue of how well we can infer causality from observational data remains a formidable challenge. While even well performed observational studies cannot completely exclude possible genetic or environmental predilections to health outcomes....criteria exist that can establish a very high probability of causality in these data.”

Man has been consuming wine for over 10,000 years and the link between wine and health has been recognized for over 5,000 years. The use of wine as a sedative, antiseptic and vehicle for other medicines was described in the Old and New Testament: “Use a little wine for thy stomach’s sake and thy frequent infirmities, St. Paul, Timothy 5:23. Hippocrates, the Father of Western Medicine, advocated the use of wine to treat practically every illness he had identified. “Wine is fit for man in a wonderful way, provided that it is taken with good sense by the sick as well as the healthy.” Another Greek physician, Pliny the Elder, described wine as a medicine in “Naturalis Historia,” and said, “Nothing is more useful than wine for strengthening the body and also more detrimental to our pleasures if moderation be lacking.” Paracelsus was a German physician in the Middle Ages who is considered the father of modern pharmacology. He stressed the tonic value of wine and invented the word alcohol. “Whether wine is nourishment, medicine or poison, is a matter of dosage.”

It is clear from the quotes of the ancients that they knew that there was a boundary between the health benefits of wine and hazardous imbibing. The term, hormesis, applies here, meaning a biological phenomenon in which the favorable effect of moderate dosage of a substance is toxic in higher doses.

Since the first report of the effect of moderate alcohol consumption and the relationship between alcohol intake and mortality in 1926 by biologist and researcher Raymond Pearl (*Alcohol and Longevity*), validation has come from Arthur Klatsky, M.D., and others through extensive epidemiological studies that a J-shaped curve exists for the composite alcohol-total mortality relationship: **abstinence** is an adverse health risk, **moderate** drinking enhances health and lengthens life, and **excessive** drinking is the most dangerous to health and life. This curve also holds true for cardiovascular disease, some cancers, and cognitive dysfunction as well. The J-shaped curve is widely accepted whenever health and alcohol consumption is debated.



In interpreting the graph above or any study on the relationship between alcoholic beverages and health, it is important to understand the definition of “moderate drinking” which is frequently referenced in research articles. A few key definitions must be understood. In the United States, a standard drink (or unit) contains 17.7 ml of ethanol (about 14 grams of pure alcohol) which is equivalent to 12 ounces of beer (about 5% alcohol), 5 ounces of table wine (about 12% alcohol) and a shot of 80-proof distilled spirits (about 40% alcohol). A full bottle of wine (750 ml) contains about 5 to 7 drinks depending on the alcohol percentage. To determine the number of standard drinks in a bottle of wine, multiple 750 ml by the alcohol percentage and divide by 17.7.

STANDARD DRINK EQUIVALENTS	APPROXIMATE NUMBER OF STANDARD DRINKS IN:
BEER or COOLER	
12 oz.  ~5% alcohol	<ul style="list-style-type: none"> • 12 oz. = 1 • 16 oz. = 1.3 • 22 oz. = 2 • 40 oz. = 3.3
MALT LIQUOR	
8-9 oz.  ~7% alcohol	<ul style="list-style-type: none"> • 12 oz. = 1.5 • 16 oz. = 2 • 22 oz. = 2.5 • 40 oz. = 4.5
TABLE WINE	
5 oz.  ~12% alcohol	<ul style="list-style-type: none"> • a 750 mL (25 oz.) bottle = 5
80-proof SPIRITS (hard liquor)	
1.5 oz.  ~40% alcohol	<ul style="list-style-type: none"> • a mixed drink = 1 or more* • a pint (16 oz.) = 11 • a fifth (25 oz.) = 17 • 1.75 L (59 oz.) = 39 <p>*Note: Depending on factors such as the type of spirits and the recipe, one mixed drink can contain from one to three or more standard drinks.</p>

It is important to note that many drinkers do not understand the concept of a standard drink and according to an article in *Current Drug Abuse Review* (2008), they often believe a standard drink is of greater volume than it is. This is termed the “over-sizing effect” and leads to a false sense of drinking within the confines of moderation. According to *BBC News* (October 7, 2011), the Office of National Statistics in the UK found that 82% of adults claim to know what a unit of alcohol is, but 77% don’t know how many units are in a typical large glass of wine and only 13% kept a check on the number of units they drank.



Moderate drinking is defined in the *Dietary Guidelines for Americans* as no more than 1 standard drink per day for women and no more than 2 standard drinks per day for men. This definition is referring to the amount consumed on any single day and is not intended as an average over several days. A bottle of 16% alcohol wine will contain 6.8 drinks or about 1 more drink than a bottle with 13% alcohol indicating alcohol percentage in wine does make a difference when you are looking to drink in moderation. Obviously, one would want to scale back the volume of drinking when imbibing a wine with a higher alcohol percentage or reach for a lower alcohol wine to insure that you are drinking moderately.

Michael Apstein, M.D. in a report to *SFGate.com* (August 7, 2011) emphasized that the alcoholic content of wine can make a big difference. He published a table showing the blood alcohol concentration (BAC) for an average 130-pound woman who consumes two 5-ounce glasses of wine over 1½ hours. The results were: 12% (0.065% BAC), 13% (0.073% BAC), 14% (0.081% BAC), and 15% (0.088% BAC). As the alcohol content of the wine rose 25% (from 12% to 15%), the BAC went up 35% to above the legal California driving limit of 0.08%. Refer the blood alcohol calculator at www.globalrph.com.

Perhaps the most important well-publicized verification of the health benefits of wine came this year when a new study by the United States Centers for Disease Control and Prevention (CDC) showed that moderate alcohol consumption was one of four “low-risk lifestyle behaviors” that can reduce mortality significantly. People who practiced the four behaviors (never smoking, eating a healthy diet, getting adequate exercise, and consuming alcohol in moderation) studied in the National Health and Nutrition Examination Survey III mortality study had a 63 percent less mortality rate than people who did not participate in the four behaviors. Both abstention from alcohol and heavy drinking raised mortality rates. People who practiced any of the lifestyle behaviors alone had a significant reduced mortality, but moderate alcohol use had a larger effect than either diet or physical activity, and the greatest benefit was accrued when moderate alcohol consumption was combined with the other three behaviors

Despite the significance of the government’s admission that alcohol in moderation is healthy, there were no recommendations offered for drinking. Although the revised 2010 Dietary Guidelines for Americans includes information on the benefits of moderate drinking, neither the United States government nor most medical professionals currently advise abstainers to begin drinking for health reasons. That said, if there are no contraindications to drinking alcohol, light-to-moderate wine drinking is considered a healthy habit. There is absolutely no added health benefit to drinking more than moderate amounts of wine daily.

It cannot be overemphasized that the moderate intake of wine by itself is not a health panacea. Regular exercise and weight control are also important as part of a healthy lifestyle. If wine is consumed, it should be drunk regularly with meals and the meals should include non-starchy vegetables and low glycemic index fruits, whole-grain foods, fish, lean meats, low-fat dairy products, limited portions of saturated, trans-fat and cholesterol and high levels of fats from fish and vegetable oils, and minimal salt intake. Smoking should be avoided. A study published in the journal *PLoS Medicine* (October 2011) found that a healthy diet rich in raw fruits and vegetables was able to mitigate the risk of cardiovascular disease and heart attack conferred by the DNA sequence variation on chromosome 9p21. The authors of the study noted, “This is eye-opening because it says that even if you have a predisposition to a disease, lifestyle makes a big difference. The effect can be overcome by having a good diet.”

Another study that appeared in the *Archives of Internal Medicine* conducted by the National Institutes of Health and AARP found important health benefits for dietary fiber. Men and women who ate the highest amount of fiber were 22 percent less likely to die from any cause compared to those who ate the lowest amount. Fiber was linked to a lower risk of cancer deaths in men but not women (men are more likely to die from cancers related to diet such as esophageal cancer), with the strongest benefit from diets high in fiber from grains as opposed to fruits, vegetables and beans. Fiber is thought to improve cholesterol levels, reduce inflammation and decrease blood sugar levels.

The frequency of moderate drinking seems to matter. Many knowledgeable researchers recommend a daily glass of wine with dinner, but in the *BBC News* (January 6, 2012) a report by the UK Commons Science and Technology Committee that suggests two to three alcohol free days a week. The recommendation was based on data indicating an increased risk of liver disease for those who drank daily or near daily compared with those who drank periodically.

The proposed health benefits of wine are thought to result from the combined effects of alcohol and polyphenols found in the skin and seeds of red grapes. Although many studies suggest it is the polyphenols in

wine that give it superior health benefits compared to other alcoholic beverages, this has not been completely proven. Arthur Klatsky, M.D., is considered an authority on wine and health, and he believes it is a scientifically verified truth that wine drinkers are more protected from cardiovascular disease with most of this protection coming from alcohol. He states that death from cardiovascular disease is lowest among red wine drinkers, followed by beer drinkers and spirits drinkers.

However, a study by Italian researchers recently published in the *European Journal of Epidemiology* (November 2011), analyzed about 16 case studies and articles, and found that moderate and regular drinking was good for heart health, but a glass of red wine and a pint of beer (which both contain equivalent amounts of alcohol) were linked equally to good cholesterol and protection against heart disease. Moderate beer and wine consumption reduced the risk of heart disease with maximum protection advantage of 33% at a level of approximately 2 drinks per day by US standards. They found the risk curves (J-shaped relationships) for the two beverages closely overlapped with the risk of cardiovascular disease increasing with increased consumption of either beverage. A J-shaped association was not found for spirits but the pattern of drinking was not included as a confounder in the analyses and spirits drinkers may have different drinking patterns.

Another relevant study appeared recently in the *Journal of Studies on Alcohol and Drugs* (January 2012) titled "Wine Consumption and 20-year Mortality Among Late-Life Moderate Drinkers." This study examined the level of wine consumption and total mortality among older adults ages 55-65 at baseline, controlling for important sociodemographic, behavioral, and health status factors. After adjusting for all co-variables, both high-wine-consumption and low-wine-consumption moderate drinkers showed reduced mortality risks compared with abstainers. Those for whom a low proportion of ethanol came from wine showed a substantially increased 20-year mortality risk of 85%. After controlling for all co-variables, the mortality difference associated with wine consumption was not significant. There are weaknesses in this study (see www.bu.edu/alcohol-forum/critique-065), but it did point out the significant differences in lifestyle habits between low-wine and high-wine groups. Many others have attributed the proposed superior health benefits of wine over other alcoholic beverages to the lifestyle of wine drinkers who often have a higher levels of education and income, a better diet, exercise more frequently, smoke less and overall are healthier.

Alcohol contributes its health benefits through many actions including stimulating the liver to produce HDL (good cholesterol), inhibiting blood clotting and blood vessel inflammation, and extracting polyphenols during fermentation. The polyphenols have many proposed beneficial actions that are very complex and poorly understood at this time. The effects on the cardiovascular system alone are numerous, but the beneficial effects reach beyond cardioprotection to include reduction in carcinogenesis, improved cognitive function, favorable metabolic changes and a number of other health-enhancing effects. It is thought that red wine polyphenols (such as resveratrol, quercetin, lutein, catechins and melatonin) interact with potentially thousands of other wine compounds to produce a wide array of health benefits.

The United States has overtaken Italy and France and now leads the world in volume of wine consumed according to the latest figures from Vinexpo reported in *The Drinks Business.com* (January 11, 2012). Appropriate education of the public about regular, moderate and responsible drinking of wine could dramatically affect the health of this country. It is estimated that 71 million Americans have cardiovascular disease, or 1 in 3, and cardiovascular disease is our country's number one killer. In a small way, perhaps this article will contribute much needed education.

In the following pages, I will summarize peer-reviewed, scientific studies presented in 2011 and very early in 2012 that contribute to our current understanding of the roles that alcohol and particularly wine play in our health. In most cases I have not included the exact publication link since many of these scientific articles are available only to paid subscribers. For those wishing to seek out the articles in their entirety, please visit PubMed which comprises more than 21 million citations for biomedical literature from MEDLINE, life science journals and online books (www.pubmed.gov). A recent listing of relevant medical articles on alcohol and health can be found at www.french-paradox.net. An excellent current review of wine and health was published in December 2011 and is available online in the *American Journal of Enology and Viticulture* (www.ajevonline.org). For general and detailed information consult the websites of the US National Institute on Alcohol Abuse and Alcoholism (www.niaaa.nih.gov), the US Centers for Disease Control and Prevention (CDC) (www.cdc.gov/alcohol/), the UK National Health Service (www.nhs.uk/), and the US Department of Agriculture dietary guidelines (www.cnpp.usda.gov).

Valuable critiques of currently published papers is now being provided by members of the International Science Forum on Alcohol Research, a joint undertaking of the Institute on Lifestyle and Health of Boston University of

Medicine and Alcohol in Moderation (AIM) of the United Kingdom. Its co-directors are R. Curtis Ellison, M.D., Professor of Medicine and Public Health, Boston University School of Medicine, and Helena Conibear, Executive Director, Alcohol in Moderation (AIM), UK. The forum consists of an international group of invited physicians and scientists who are specialists in their fields and committed to balanced and well researched analysis regarding alcohol and health. The forum provides on its open website timely critiques and comments by Forum members on emerging scientific publications and policy statements related to alcohol and health, and **provide an opportunity for all to seek expert opinion on topics related to alcohol and health**. Visit www.bu.edu/alcohol-forum/.

It has been recently reported that a University of Connecticut Health Center researcher has been accused of falsifying data published in eleven scientific journals that have been widely cited in the general media. The red-wine researcher, Dipak K. Das, was reported to have falsified data in 26 journal articles. The exact studies that are implicated have not been reported to the public yet. This disturbing accusation may call into question some research on the health benefits of resveratrol and anthocyanidins, but represents only a tiny fraction of studies that have been published.

Readers should keep themselves informed by reading important scientific publications and policy statements regularly, as well as be advised to follow the lifestyle, diet and drinking advice of their doctors.

Cardiovascular Disease

The ability of wine to reduce cardiovascular disease is thought to be the result of many beneficial effects. Roberto Iermoll, Professor of Internal Medicine at 'Universidad de Buenos Aires' in Argentina spoke to this subject at the 2011 Vinandino seminar held in Mendoza, Argentina in September 2011. He noted that resveratrol in red wines increases nitric oxide levels, keeping potassium channels open in the mitochondria of the heart cells and protecting them from oxygen deficiency consequences. This mechanism causes fewer cells to die and reduces cell mortality to 50% after a heart attack. Also, alcohol stimulates good cholesterol production (HDL) that removes bad cholesterol (LDL) from arteries and veins where it can form plaques. Alcohol helps lessen the stickiness or coagulation of red blood cells, which can cause an embolism and block the blood flow in an artery resulting in a heart attack or stroke. In addition, he pointed out that alcohol has an anti-inflammatory effect that reduces the development of atherosclerosis. **Summary:** Wine has the capacity to reduce cardiovascular disease through several proposed physiological mechanisms.

Probably the most important paper published in 2011 appeared in the *British Medical Journal* (Feb 22, 2011): "Effect of alcohol consumption on biological markers associated with risk of coronary heart disease: systematic review and meta-analysis of interventional studies." Two reviewers independently selected peer-reviewed studies that examined adults without known cardiovascular disease and that compared fasting levels of specific biological markers associated with coronary artery disease after alcohol use with those after a period of no alcohol use (controls). 4690 articles from 1950 to 2009 were screened for eligibility and 63 relevant articles were selected. Favorable changes in several cardiovascular biomarkers (higher levels of high density lipoprotein cholesterol - HDL - and adiponectin and apolipoprotein A1, and significantly lower levels of fibrinogen) provided indirect pathophysiological support for a protective effect of moderate alcohol use on coronary heart disease. The authors of the study also determined that different types of alcoholic beverage had similar effects on biomarkers, but inferences on beverage type should be cautiously considered since most of the studies used wine as the alcohol intervention. Many of the reviewed studies used comparisons with a non-red wine alcohol intervention or with de-alcoholized red wine and it was concluded that the effect observed was most likely due to alcohol rather than to the other components of red wine. The study did have some caveats since potential confounders such as smoking, physical inactivity, body weight and diet could have affected the findings. **Summary:** The results strengthen the case for a casual link between alcohol intake and reduced risk of coronary heart disease.

Alcohol was linked to better survival after heart attack in women in a U.S. study published in the *American Journal of Cardiology* (January 2012). Women who drank anywhere from a few alcoholic drinks a month to more than three a week in the year leading up to a heart attack ended up living longer than women who never drank alcohol. The results of the study indicated a 35 percent lower chance of dying during the ten year follow up period for women who drank, compared to those who didn't. No differences were seen among different beverage types. **Summary:** Adults may not need to stop drinking in moderation once they develop heart disease. One drink a day is a really good target.

A study published in the *Journal of the American Dietetic Association* pooled the results from nine clinical trials and found that grape seed extract reduced systolic blood pressure by about 1.5 points and slowed the user's heart rate by an average of 1.4 beats per minute compared with a placebo pill. These results seem insignificant except that past studies have estimated that a blood pressure reduction of just 3 points can reduce the risk of death among people who have heart disease or have suffered a stroke. There was no effect on cholesterol levels or diastolic blood pressure. Diet changes such as reducing sodium and eating plenty of fruit, vegetables, whole grains and lean protein have shown to have more effect on blood pressure numbers. **Summary:** Grape seed extract is thought to be safe and it is inexpensive but it does have side effects and safety of long-term use is unknown. It does not reduce the risk of heart attacks or strokes. Diet changes such as reducing sodium and eating plenty of fruit, vegetables, whole grains and lean protein have shown to have more favorable effect on blood pressure numbers.

A report in the *Journal of the American College of Cardiology* (February 2011) looked at alcohol consumption and the risk of the cardiac arrhythmia known as atrial fibrillation. A systematic search of Medline from 1966 to 2009 databases was conducted and 14 eligible studies were included in this meta-analysis. The results indicated that even moderate drinking can lead to atrial fibrillation. **Summary:** Results suggest that not consuming alcohol is most favorable for atrial fibrillation risk reduction. The relationship between daily alcohol consumption with the risk of atrial fibrillation is linear and independent of sex. (Most previous studies have found that heavy drinking may increase the risk of atrial fibrillation, but the risk with light to moderate alcohol intake seems unlikely)



A study from Spain published in the *American Journal of Clinical Nutrition* (February 2012) found that ethanol and the nonalcoholic compounds in red wine may cut vascular disease risk. 67 human male volunteers were chosen for study who were considered at high risk for cardiovascular disease on the basis of increased BMI, smoking, diabetes, hypertension, or other risk factors. About half the patients were taking aspirin, statins, oral hypoglycemic drugs and ACE inhibitors. The subjects did not consume any alcohol for a baseline period, then for three one-month periods consumed 30 grams of ethanol per day as red wine or as gin, or an equivalent amount of phenolics from de-alcoholized red wine. The effects of each intervention on a large number of adhesion molecules and chemokines that affect inflammation and relate to cardiovascular disease were evaluated. Both ethanol and nonalcoholic compounds in red wine appeared to have potentially protective effects that may reduce the risk of vascular disease. **Summary:** Both ethanol and polyphenols of red wine may modulate soluble inflammatory mediators and the phenolic content of red wine may modulate leukocyte adhesion molecules in patients at high risk of cardiovascular disease.

Many studies have shown that the effect of alcohol on heart disease is largely attributable to an increase in HDL. A prospective, observational study reported in *Circulation* (October 2011) found that alcohol drinking was associated with a significant decrease in risk of death from coronary artery disease. This well-done analysis suggested that very little of the lower risk of heart disease was due to an increase in HDL from alcohol consumption. **Summary:** This study refutes the results of most other similar studies that shown an increase in HDL is largely responsible for the effect of alcohol on risk of heart disease.

Mice have a similar physiological response to alcohol as humans and have been the subjects of many studies. Research published in *Atherosclerosis* (August 2011) found that mice that drank regularly and moderately (equivalent of two drinks a day) had dramatically better blood lipids, less atherosclerosis (hardening of the arteries), and less inflammation in their arteries than teetotaler mice and weekend binge-drinking mice. **Summary:** Daily moderate alcohol consumption in mice reduces atherosclerotic plaque development.

Researchers in Brazil studied the effect of moderate red wine consumption and physical activity on the cardiovascular system of rats with preexisting high blood pressure. The research was published in *Arquivos Brasileiros de Cardiologia* in 2011. The study found that there was a decrease in cardiovascular disease risk factors for the wine only group and the exercise only group but there was a more significant reduction in systolic blood pressure compared to the control group of the wine only and exercise only groups together. Good cholesterol (HDL) levels in the wine and exercise group were significantly higher than the exercise alone and control group and only slightly higher in the wine only group. **Summary:** Wine and exercise are more beneficial than either wine or exercise alone in rats suggesting red wine and exercise in combination may decrease risk factors for cardiovascular disease.

Neurodegenerative Diseases & Brain

A Swedish paper to be published in the *Journal of Alcoholism: Clinical and Experimental Research* studied men and women over a several years who drank heavily (about 12 bottles of wine a week). Women suffered a 50% decrease in serotonin function in the brain after 4 years and men had the same decrease after 12 years. The damage to serotonin function was equal in the two sexes, but occurred much faster in women. Serotonin is a brain neurotransmitter that is related to the development and treatment of depression and chronic anxiety and is involved in the regulation of impulse control and our ability to fall asleep and stay awake. Heavy drinkers suffered damage to the part of the brain that controls moods, impulses and sleep. **Summary:** Chronic alcohol dependency leads to significantly lower serotonin functions. Women are more vulnerable to the effects of heavy drinking on certain brain functions.

The University of Missouri College of Arts and Sciences published a study in the *Journal of Abnormal Psychology* (May 2011) that found that people exhibit drunken behavior not because they are not aware of what they are doing, but because they just don't care as much and are not as bothered by the implications of such behavior. **Summary:** Young people (aged 21-35) were less likely to notice mistakes when under the influence of alcohol while performing challenging computer tasks and were less likely to care. More research is needed to understand how alcohol affects the brain.

Researchers in Belgium reported in *the European Journal of Neurology* (November 2011) that patients who had the relapsing form of multiple sclerosis but not progressive onset multiple sclerosis had less progression of disability when they also drank wine, coffee and ate fish. Cigarette smoking was associated with an enhanced risk of disability. The protective effect of wine on symptoms was limited and the mechanism of effect was unclear. **Summary:** More research is needed as the results could indicate reverse causality (people who had less progression of disability due to multiple sclerosis might have felt more comfortable in drinking alcohol, including wine).

There have been a number of studies that support a decreased risk of dementia and Alzheimer's disease among moderate drinkers. Researchers at Loyola University Chicago Strich School of Medicine reviewed 365,000 people who were in studies dating back to 1977. Published in the journal *Neuropsychiatric Disease and Treatment* (August 2011), the paper found that moderate drinkers (2 drinks a day for men and 1 drink a day for women) were 23% less like to develop dementia, Alzheimer's disease and other "cognitive impairment." Heavy drinking (more than 3-5 drinks a day) had a higher risk of dementia and cognitive impairment but the results were not statistically significant. Wine appeared to be more beneficial than beer or spirits in both men and women. The results were statistically significant in 14 out of 19 countries including the United States. **Summary:** The International Scientific Forum on Alcohol Research agreed with the conclusions of the authors that overall, light to moderate drinking did not appear to impair cognition in younger subjects and actually seems to reduce the risk of dementia and cognitive decline in older subjects. Moderate drinking may increase blood flow to the brain and might make brain cells more fit by slightly stressing them. Since there is no randomized clinical study available, the results of this review are only suggestive.

The German Study on Aging, Cognition and Dementia in Primary Care Patients evaluated the association between alcohol consumption and incidence of dementia and Alzheimer's over three years. The daily consumption of alcohol was found to reduce the risk of dementia by near 30 percent compared to nondrinkers in patients 75 and older. The risk was another 30 percent lower for people who drank one to two servings per day of alcohol. No significant differences were found among the different types of alcoholic beverages consumed. **Summary:** Moderate drinking is associated with less dementia and Alzheimer's disease in individuals aged 75 years and older.

Gary Small, M.D., director of UCLA's Longevity Center and co-author of *The Alzheimer's Prevention Program: Keep Your Brain Healthy for the Rest of Your Life*, wrote an update on the relationship between alcohol and Alzheimer's Disease in *Huffpost Healthy Living* (January 19, 2012). He reported on a study that showed a nearly 30 percent lower risk for dementia among light drinkers compared to teetotalers or those who overindulged. This was not a double-blind placebo controlled study so it is not proof that moderate drinking protects the brain but there is a possibility. Other studies suggest that one glass of wine or spirits is brain protective for women and two glasses are the healthy brain limit for men. Some experts believe that light to moderate alcohol consumption may lower the risk of Alzheimer's disease because of associated lifestyle habits and personality. Studies on the effect of wine on experimental lab mice that possess a human Alzheimer's gene showed that when mice ingested moderate amounts of Cabernet Sauvignon wine (a mouse equivalent of 6 ounces), the animals had better memory ability and less of the protein building blocks that lead to amyloid plaques in the brain of the type seen in Alzheimer's. **Summary:** Small amounts of wine, beer and spirits all appear to lower the risk for Alzheimer's disease. Antioxidant effects of alcohol and polyphenols in wine may protect the brain.

Rats treated with resveratrol showed a reversal in diabetes-associated brain damage in a study published in the *American Journal of Physiology* (June 10, 2011). Brain tissue in diabetic rats treated with 10 milligrams of resveratrol per kilogram of weight per day (a very high dose) showed some reversal of damage associated with diabetes. Resveratrol appeared to relax arteries and keep blood flowing in the brain of the treated rats as well as normalizing oxygen levels. The authors of the study speculate that the observed effects of resveratrol may reduce the stress factors that lead to strokes in diabetics and opened the possibility that resveratrol could be a potential agent used to prevent brain dysfunction and reduce stroke risk in diabetics. **Summary:** Even less resveratrol could be as effective for reversal of diabetes-associated brain damage in rats. Much more study is necessary.

A study presented at the American Academy of Neurology's 63rd Annual Meeting in April, 2011, that was performed at the Harvard School of Public Health in Boston, suggested that the flavonoids in plants and fruits may increase dopamine levels in the brain and possibly prevent Parkinson's disease. Of the subjects monitored during the study, men who ate more foods containing flavonoids, such as berries, apples and oranges, were 40 percent less likely to develop Parkinson's disease. In women, there was no relationship between eating general flavonoids and the occurrence of Parkinson's disease, but the flavonoids such as anthocyanins found in berries were found to protect women against the disease. **Summary:** A diet high in fruits and vegetables could be protective against Parkinson's disease risk but the results are still preliminary. Research needs to be done to see what other flavonoid-rich foods such as cacao and red wine do for the risk of Parkinson's and other neurological diseases.

Drinking red wine over a lifetime apparently reduces the risk of essential tremor significantly. In the medical journal *Movement Disorders* (April 2011), researchers found that over a period of approximately 30 years, three glasses of red wine a day led to a 65 percent lower risk of developing tremors and four or five glasses of red wine daily led to an 86 percent lower risk. It was postulated that antioxidants in red wine provide a protective effect. **Summary:** This case-control study was subject to bias and more research is needed to determine the role of alcohol drinking in the development of essential tremor.

A study published in *Alcoholism: Clinical & Experimental Research* (November 2011) by Japanese researchers looked at the effect of alcohol on sleep. 10 healthy male university students were given three different alcohol beverages at three week intervals: 0 alcohol (control), a low dose of alcohol, or a high dose of pure ethanol. A Holter electrocardiogram was attached to each subject for a 24-hour period and the subject was instructed to drink one of the three alcoholic beverages 100 minutes before going to bed. Polysomnography was performed for 8 hours. The team found that alcohol increased the heart rate and interfered with sleep and the more alcohol the participants drank, the greater the effect. The subjects exhibited good sleep quality in the first half of the sleep cycle, but in the second half, the alcohol interfered with sleep quality and the restorative role of sleep. **Summary:** A "nightcap" before bedtime may actually prevent a good night's sleep.

Gastrointestinal

A study reported in the *American Journal of Clinical Nutrition* (October 2011) found that European men, but not women, who drank more than four alcoholic drinks per day had an increased risk of stomach cancer. Men who

averaged more than four drinks per day were twice as likely to develop stomach cancer as light drinkers (a half drink a day or less). Beer, rather than wine or liquor, was associated with the stomach cancer risk. The findings were confirmed regardless of smoking habits (smoking is a risk factor for stomach cancer). **Summary:** One of the metabolic byproducts of alcohol, acetaldehyde, is a human carcinogen and nitrosamines in beer have been shown to cause cancer in animals. The combination of those two carcinogens may explain why beer drinkers are more at risk for stomach cancer.

An analysis of the relationship between alcohol intake and upper aerodigestive cancers was published in *Oral Oncology* (September 2011). Smoking is the most important factor in the risk of these cancers but the risk is increased in those who also consume 2 or more drinks per day. Tobacco use alone explain 28.7% of the aerodigestive cancers in Europe, the combination of smoking and drinking 43.9%, and alcohol use alone only 0.4%. In women, the study suggested that wine may play a role in reducing the risk associated with smoking since in women, the risk of these cancers was higher among abstaining smokers than among those who both smoked and drank alcohol. **Summary:** Aerodigestive cancers are causally related primarily to smoking, with alcohol playing a lesser role. More studies are needed to determine the effects on risk of varying levels of alcohol consumption.

A British study reported in the *British Journal of Surgery* (August 2011) found that drinking wine and beer excessively did not increase the risk of acute pancreatitis but binge drinking spirits did raise the risk. The number of drinks consumed per occasion affected the risk of pancreatitis. **Summary:** Spirits drinkers may experience a greater rise in BAC as a result of a faster rate of drinking and this may be an important factor in the higher risk of pancreatitis.

Moderate alcohol consumption can lead to gastrointestinal symptoms due to bacterial overgrowth in the small intestine. As reported in *Teatro Naturale International* (November 2011), this study at Dartmouth-Hitchcock Medical Center and the Mayo Clinic, is one of the first to look at the relationship between moderate alcohol consumption and small intestinal bacterial overgrowth (SIBO). Patients in the study who drank a moderate amount of alcohol, sometimes less than 1 drink per day, were at high risk for SIBO. SIBO is a potentially harmful condition that leads to abnormally large numbers of bacteria in the small intestine that consume many of the nutrients that otherwise would be absorbed. **Summary:** It has been previously shown that alcoholics have high rates of SIBO, but this study indicates that even light to moderate drinking may predispose to SIBO. Alcohol cessation may be a treatment for this condition.

Considering the recent developments in the reported risks of Lap-Band surgery and the requests for Congress to investigate, a study released by Swedish researchers in 2011 is relevant. Two common procedures used for management of obesity are gastric bypass and Lap-Band surgery. Gastric bypass creates a smaller stomach pouch and bypasses part of the intestine. The Lap-Band procedure is performed by placing an inflatable silicon band around the stomach to decrease food intake, but food continues to pass through the intestine. After examining 12,277 patient records, the researchers found a 2.3 times increased risk of developing alcoholism among those who had gastric bypass compared to the group who got Lap-Band surgery. **Summary:** After gastric bypass surgery, alcohol that normally would be metabolized by stomach enzymes reaches the intestines largely intact. Gastric bypass surgery doubles the risk of developing alcoholism as a result. A prospective observational study published in 2011 found that the LAP-BAND AP system offered a safe and effective therapy to reduce weight in severely obese patients.

Metabolism

The medical journal *Nutrition Reviews* (August 2011) reported a Spanish study that found that moderate drinkers gain less weight than the general population. A meta-analysis was conducted of numerous studies on alcohol and weight between 1984 and March 2010. Theoretically, alcohol adds additional calories to one's diet (one gram of alcohol equals 7.1 kilocalories; a standard 5 ounce glass of red wine contains about 106 calories but this varies with alcohol content), and may lead to weight gain by increasing a person's daily energy intake. Alcohol does contribute to obesity in heavy beer and spirits drinkers. The study found that those who consume 1 to 2 glasses per day of wine, but not those who drink three glasses or more, gain less weight than the general population. Consumption of spirits was positively associated with weight gain. Another study published in *Nutrition* (July-August 2011) found that moderate wine drinkers compared to beer and spirits drinkers showed less yearly weight gain. **Summary:** The reasons why moderate wine drinkers have less

weight gain than beer or spirits drinkers are not clear. Suggested factors include the dietary patterns of wine drinkers and the possibility that resveratrol in red wine inhibits the conversion of sugars into fat.

In the *Annals of Internal Medicine* (September 6, 2011), scientists from the National Heart, Lung and Blood Institute and the National Cancer Institute (both part of the National Institutes of Health) reported that moderate alcohol consumption reduces the chances of developing type 2 diabetes (adult onset), especially in women. Moderate drinking reduced the risk by 19 percent in men and 37 percent in women 50 to 71 years of age. The NIH group looked at a health survey of over 500,000 AARP members. The causes for this effect in moderate imbibers, which included wine drinkers, is speculative and includes enhanced insulin sensitivity, anti-inflammatory effects of alcohol, and elevated triglyceride concentration from alcohol. **Summary:** More research is necessary to elaborate the mechanisms that suggest that moderate alcohol drinking lowers diabetes risk. It is not clear why moderate alcohol consumption was associated with a lower risk for diabetes in women.

Dutch scientists report the first study to show the effects of resveratrol on human metabolism in a paper published in *Cell Metabolism* (November 2011). Either large doses of resveratrol supplements or a placebo were given to 11 obese men and then the groups were switched after 30 days. The effects were small but did show a similar benefit to a low-calorie diet or endurance training such as reduced levels of liver fat, blood pressure, triglycerides and blood sugar, and less insulin resistance. The result was more optimal lowered metabolism. Resveratrol did not lead to weight loss but appeared to slow down the problems associated with obesity. **Summary:** This is the first study in humans to show resveratrol effects on human metabolism that might extend lifespan. Moderate wine drinkers cannot expect the same result as the dose of resveratrol needed for a nutraceutical effect, 150 milligrams a day, would be equal to about 10 liters of red wine. However, that amount of resveratrol could conceivably be incorporated into a food supplement or a daily capsule.

A study in *Food & Function* (January 2011) from Vienna tested the chemical composition of two white wines and 10 red wines from Austria. 100 milliliters of a 2003 Blaufränkisch contained four times the recommended daily dose of rosiglitazone, a drug used to treat type 2 diabetes manufactured by GlaxoSmithKline and marketed as Avandia. The researchers also found that red wines contained large amounts of ligands which are molecules that prevent blood clots, reduce inflammation, and promote beneficial cholesterol metabolism. The ligands contain polyunsaturated fatty acids that bind to cholesterol and transport it to the liver for removal. Of the wines studied, not all had equal amounts of the chemicals and white wines had very low measurable amounts. **Summary:** Red wine cannot be considered a treatment for type 2 diabetes, but grape skin or other plant extracts show potential as therapeutic agents.

An article in the *Journal of Nutrition & Metabolism* (August 2010) examined the benefits of grape pomace on type 2 diabetes. Pomace from red grapes (Cabernet Franc) and white grape pomace (Chardonnay) was compared to an extract of red apple pomace as a control. Red grape pomace extract suppressed postprandial hyperglycemia in ST2-induced diabetic mice with a 35% reduction compared to control, while red apple pomace had no effect. **Summary:** This is the first report that grape pomace extract inhibits intestinal α -glucosidase and suppresses postprandial hyperglycemia in diabetic mice. The results suggest a potential for using grape pomace-derived bioactive compounds in the management of diabetes.

Skeletal System

Researchers from the University of East Anglia and King's College London reported in the *American Journal of Clinical Nutrition* (September 2011) that moderate amounts of wine may strengthen bones and reduce the risk of osteoporosis. Other alcoholic drinks such as beer and spirits did not have the same effect. The study assessed more than 1,000 pairs of female twins in their mid-50s by looking at the relationship between diet and risk of bone fracture. Moderate intake of alcohol from wine led to a higher bone mineral density while a diet high in fruit and vegetables had little benefit and a traditional English diet of fish and chips, baked beans, meat pies and cooked meats had damaging effects on bone strength. **Summary:** The study suggests that moderate consumption of wine can improve bone mineral density, supporting a number of previous studies that suggested alcohol might have a protective effect. It is uncertain how wine builds bone strength but previous studies suggest it is polyphenols rather than alcohol that are responsible. Heavy drinking is a major risk factor for osteoporosis.

Skin

Researchers at the University of Barcelona reported in the *Journal of Agriculture & Food Chemistry* (May 2011) that flavonoids in grapes are able to stop the chemical reaction that causes skin cells exposed to UV rays from the skin to die and therefore prevent skin damage. This in vitro study on human keratinocytes showed a protective effect of grape fractions rich in procyanidin oligomers and gallate esters (polyphenols) against UV-induced cell damage and death. **Summary:** Plant-derived polyphenolic extracts may prove valuable as agents for skin photoprotection.

Recent research published in the journal *BMC Complementary and Alternative Medicine* (December 21, 2011) reported that grape seed proanthocyanidins (GSPs) in vitro inhibit the spread of squamous cell skin cancer by preventing cancerous cells from invading healthy cells. The study findings suggest that GSPs could be developed as an alternative medicine for the prevention of invasion and metastases of head and neck squamous cell carcinoma. **Summary:** GSPs are non-toxic agents that may have therapeutic value in inhibiting the metastatic spread of potentially fatal squamous cell carcinomas of the skin.

Teeth

Italian scientists reported in *Molecules* (February 11, 2011) that plant polyphenols can help ward off dental caries. An analysis of the literature supported the anti-bacterial role of polyphenols on cariogenic streptococci. Research in which bacteria typically found in the mouth were exposed to small amounts of red wine with the alcohol removed indicated that bacteria could not cling to the teeth or saliva once they were exposed to red wine. **Summary:** A daily glass of red wine could keep teeth healthy but more studies are needed to establish conclusively that polyphenols can prevent dental caries. White wine, which often has a higher acid content, can erode teeth enamel and lead to tooth decay.

In a 2011 *Wine Spectator* online Q&A report debunks the myth that white wine is healthier for and less likely to stain your teeth. White wine can still stain teeth as badly as red wine when it is consumed with foods and beverages that are high in pigment. A study done by the New York University College of Dentistry looked at cow teeth soaked in black tea alone, and in white wine followed by black tea, and the teeth soaked first in the wine picked up much of the dark tea pigment, while the teeth soaked only in black tea were unstained. **Summary:** Wine erodes enamel, leaving it exposed to staining pigments in food and beverages. To avoid long-term tooth stains and tooth decay, brushing should be performed about an hour after drinking a glass of wine. This enables the saliva to neutralize the layer of acid left on the teeth and prevent damage that can occur if brushing is done in a highly acidic mouth. Gargling with baking soda after drinking wine may have the same effect.

Eyes

A study reported in *Free Radical Biology and Medicine* (December 2011) and funded by the National Eye Institute of the National Institutes of Health and the California Table Grape Commission suggests that eating grapes might slow or help prevent the onset of age related macular degeneration which is thought to be at least partly due to oxidative stress. The study compared the impact of an antioxidant-rich diet on vision using mice prone to developing retinal damage in old age in much the same fashion as humans do. Mice either received a grape-enriched diet, a diet with added lutein, or a normal diet. The grape-enriched diet protected against oxidative damage of the retina and prevented blindness in the mice consuming grapes. Lutein was effective also but less so. **Summary:** The authors suggest that a lifelong diet enriched in natural antioxidants, such as those in grapes, are directly beneficial for retinal health. The three year study showed that eating antioxidant-rich foods should begin before the onset of advanced age, preferably in youth or young adulthood. Mice who receive a grape and lutein-rich diet after the age of the human equivalent of 60 showed little or no improved retinal function. Age related macular degeneration does not seem to be reversible with the institution of a diet rich in antioxidants.

Longevity

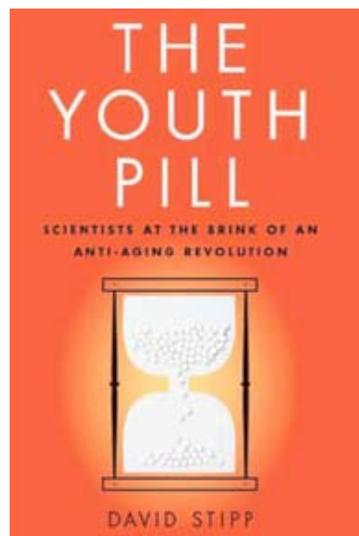
One of the most significant studies to appear in 2011 was titled, "Alcohol consumption at midlife and successful aging in women; a prospective cohort analysis in the Nurses' Health Study." It was published in *PLoS Med* (September 2011). Alcohol consumption at midlife was assessed using a questionnaire administered to 13,894 white registered nurse participants in the Nurses' Health Study who lived to the age of 70 or older and were free of eleven major chronic diseases and had no major cognitive, physical impairment or mental health limitations. The Nurses' Study began in 1976. The study found that light to moderate alcohol consumption at midlife (late 50s) was associated with modestly increased odds of successful aging. Those who drank regularly during the week had better odds of successful aging than those who drank occasionally. Compared to nondrinkers, women who drank less than or equal to 1 drink a day had about a 20% higher chance of successful aging, women who drank 5-7 drinks per week had a 50% greater chance of successful aging, while women who drank little (1-2 drinks per week) had a similar likelihood of successful aging as nondrinkers.

Summary: Light to moderate alcohol consumption at midlife led to modestly increased odds of successful aging in women. This supports earlier studies that indicate successful aging and survival are favorably affected by moderate consumption of alcohol on a regular basis. It also supports the notion that the benefits of moderate drinking outweigh the risks. The results cannot be applied to men or other ethnic groups (most of those in this study were of European ancestry). An important disclaimer is that there may be other lifestyle factors responsible in women who regularly drink a small amount such as an active social life, a healthy appetite, and generally good health.

New research reported in the journal *Nature* (September 2011) calls into question the mechanism by which wine is said to extend life. Studies that began ten years ago suggested that natural proteins called sirtuins could help living things live longer and resveratrol could increase sirtuin production. A team headed by geneticist David Gems at the University College London attempted to replicate earlier experiments with worms and fruit flies but found that they did not live longer. Researchers found that resveratrol did not activate sirtuins. Genetic changes in some of the animals in earlier studies may explain the previous life-extending findings, although researchers on the science advisory board of Sirtris Pharmaceuticals said they repeated the experiments after removing the strain with genetic changes and found sirtuins still produced a life-extending effect, but it was not as impressive as originally reported. **Summary:** The role of resveratrol and sirtuins in prolonging life in humans is in doubt, although sirtuin drugs do show promise in preventing diseases associated with aging like diabetes and heart disease and thereby helping humans to live longer. Sirtris Pharmaceuticals is still working on adapting sirtuins to drugs that could prolong life.

The level of wine consumption and total mortality in 802 adults age 55-65 at baseline was studied with controls for key cofounders. The research appeared in the *Journal of Studies on Alcohol and Drugs* (January 2012). Both high-wine-consumption and low-wine-consumption drinkers showed reduced mortality compared with abstainers but the apparent unique effects of wine on longevity could be explained by confounding factors correlated with wine consumption (see page 5). **Summary:** Wine does not confer longevity over other types of alcoholic drinks when the results are controlled for all co-variates. The study did confirm a lower mortality risk for alcohol consumers than for non drinkers.

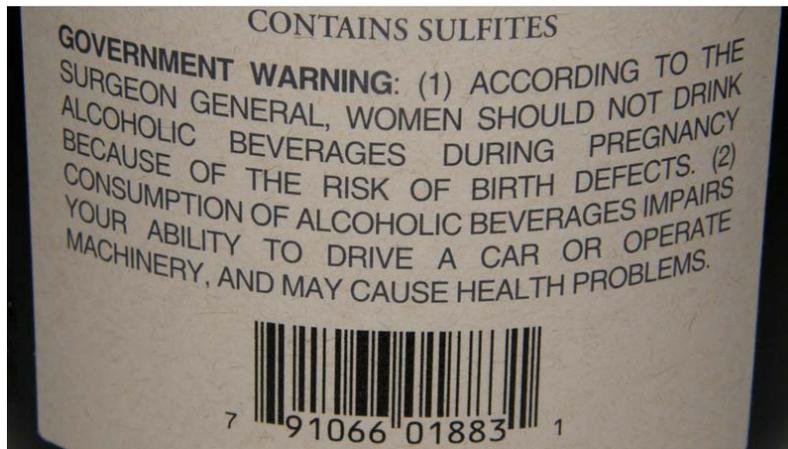
Further entertaining reading on this subject and in particular resveratrol: *The Youth Pill: Scientists at Brink of an Anti-Aging Revolution*, David Stipp (2010).



An article in the *Journal of the American Geriatric Society* (2011) reported a study in which 477 people who were at least 95 years old were identified and completed a survey on their lifestyle habits. The information was compared with surveys from 3,164 people from the general population who were born around the same time but were no longer alive. Overall, there were no significant differences as each group had similar average body mass index, had about the same daily alcohol consumption and had about the same amount of daily exercise. One difference that was noted was the over-95 group were less likely to be obese. **Summary:** The key to longevity may lie in genetics.

Pregnancy

The health risks of moderate drinking in women are extremely low. However, one of the conundrums for women is drinking during pregnancy. Public health officials, the American College of Obstetricians and Gynecologists, the American Academy of Pediatrics and the Surgeon General recommend that pregnant women avoid alcohol entirely. In some countries wine is considered part of a healthy lifestyle even during pregnancy and women feel that an occasional drink is safe. A number of studies have indicated that pregnant women can safely drink a glass or two of wine per week and their children often perform better three years after birth when compared to children of women who abstained. Women who decide to have wine during pregnancy should avoid the first trimester and consume minimal amounts, sipping it slowly with food to avoid a rapid rise in blood alcohol levels. One of the problems with drinking during pregnancy is that women may get pregnant without planning or knowledge and drink both during conception and shortly thereafter.



Findings published in the *Journal of Alcoholism: Clinical and Experimental Research* (January 16, 2012) indicated that any drinking during pregnancy increases the odds of fetal alcohol syndrome (FAS). FAS includes low birth weight, developmental delay, growth deficiencies, abnormal facial features and learning and behavioral problems. It has been the belief that FAS only afflicted children of mothers who were heavy drinkers and not those who had an occasional drink (1 to 2 drinks a week) during pregnancy. This study reported that for every one drink per day increase in alcohol intake during the second half of the first trimester, a woman's baby had a 25 percent increased chance of an abnormally shaped lip, a 12 percent increased risk of a smaller-than-normal head, and a 16 percent increase chance of low birth weight, all of which are signs of FAS. The risk to the fetus was highest if a pregnant woman drank during the second half of the first trimester of pregnancy. An average number of drinks during the third trimester only affected the baby's length at birth. The total number of drinks a woman had while pregnant was most predictive of a baby's risk of FAS. **Summary:** There is no low threshold level below which drinking alcohol doesn't raise the risk of FAS, supporting the Surgeon General's recommendation that drinking be avoided entirely. There are other factors that come into play since not every woman who drinks during pregnancy will have a baby with FAS. These factors include diet, genetic differences, body fat levels and exposure to environmental toxins. Women who are planning a pregnancy, have the potential to become pregnant, or who become pregnant, should not consume alcohol.

A new study has been launched in Australia by the Murdoch Children's Research Institute in Melbourne to determine whether low to moderate levels of alcohol are harmful or not to a fetus. They are recruiting 2,000 pregnant women who will be quizzed throughout their pregnancy about their drinking habits, general health and diets. Their babies will undergo extensive medical examinations at age one and two years to see if there is any

developmental or behavioral affects of alcohol in those women who drank during pregnancy. A study by the University of Newcastle published in 2010 indicated that 80 per cent of Australian women drank during pregnancy.

Reproduction

A study published in *Alcohol* (June 2011) studied the effects of ethanol consumption on chromatin condensation and DNA integrity of epididymal spermatozoa in rats. This experimental study showed for the first time that ethanol consumption disturbs sperm motility and DNA integrity of spermatozoa in rats.

Summary: Ethanol abuse results in the production of spermatozoa with less condensed chromatin, and this may be one possible cause of infertility following ethanol consumption.

Breast Cancer

The relationship of breast cancer and alcohol has drawn more commentary in the press this year than any other subject dealing with health and drinking. After the Harvard-led Nurses' Health Study was published in 2011, panic swept over the country as the study indicated that drinking as little as three glasses of wine or other drinks increased the risk of breast cancer in women compared to abstainers. Published in the *Journal of American Medical Association* (November 1, 2011), this prospective study reviewed the lifetime exposure to alcohol from 1976 to the present in 106,000 women ages 30 to 55 over the 28-year study period. 7,690 women developed breast cancer during the followup. Women who drank as few as three to six drinks a week increased their risk of breast cancer by a modest 15 percent. The risk increased significantly for heavy drinkers with a 51% increased risk of developing breast cancer compared to abstainers during the study period in women who consumed 19 or more drinks per week. The results indicate that there is a dose-response effect that is independent of beverage type. Alcohol intake between the ages of 18 and 40 was linked with higher breast cancer risk later in life regardless of what drinking habits were after the age of 40 indicating that the cumulative amount a woman consumed during all of adulthood was the best predictor of risk. Binge drinking (6 or more drinks at one sitting) led to a 33% increased risk of breast cancer independent of total alcohol intake over time. **Summary:** The seemingly alarming number of a 15% increased risk in light drinkers needs to be clarified. The overall average risk for women nondrinkers for breast cancer over a lifetime is 12% (currently more than 230,000 women a year develop breast cancer in the United States). The 15% increased risk found in this study for light drinkers translates to a 13.8% risk for women. The authors of the study admit that this increased risk was quite small. This was an observational study and cause and effect cannot be linked for certain. Only a controlled clinical trial of the relationship between alcohol and breast cancer could account completely for all confounders. The study's lead author, Wendy Chen, M.D., said, "What I generally tell women is to keep alcohol consumption at a few servings per week."

Discussion

Steven A. Narod, M.D., director of familial breast cancer research at the Women's College Research Institute in Toronto, Canada, offered an authoritative take on drinking and breast cancer risk in an editorial accompanying the Nurses' Health Study research. He pointed out the following. The risk of breast cancer for women in their 50s is 2.4% according to the National Cancer Institute. Using the data from the Nurses' Health Study Research, the 10-year risk rises to 2.8% for women who are light drinkers (less than 1 drink a day), to 3.5% for those who have 1 drink a day (moderate drinkers), and to 4.1% for those that have 2 drinks or more a day. Viewed in these terms, the increased 10 year risk of breast cancer in postmenopausal women is very modest. He remarked, "Some women with other risk factors like a family history of breast cancer or a genetic marker like the BRCA gene may find it prudent to stop drinking. But there is no data to give assurance that giving up alcohol will reduce breast cancer risk. For women without high risk factors who are moderate drinkers, I don't think they need to stop."

It is thought that the higher risk of breast cancer with more than 2 drinks a day is due to an increase in the amount of estrogen and related hormones that circulate in the blood. Alcohol increases the estradiol blood

levels in both pre- and post-menopausal women and may increase the expression of estrogen receptors in breast cells stimulating them to proliferate. This effect appears to be independent of beverage type. The lifetime exposure to reproductive hormones is one of a number of factors that affect the risk of developing breast cancer and is related to number of children, breast feeding, oral contraceptives and hormone replacement drugs, and time of onset of menstruation and menopause. Since breast cancer is a multi-risk factor disease, other factors are important as well and will vary depending on the individual woman. These include age, family history, obesity (particularly weight gain at and after menopause), lack of exercise, smoking, exposure to ionizing radiation (mammograms use low-dose radiation and are thought to be safe), and mutations in the BRCA genes. It is obviously important for women to consult with their physicians to understand what their risk factors are and how to manage them.

The rub is that the decrease risk of heart disease with moderate drinking is significantly greater than the rise in risk of breast cancer. Heart disease is the No. 1 cause of death in females of all ages according to the Centers for Disease Control and Prevention. Women have a 39.2% chance of developing cardiovascular disease in a lifetime. Moderate drinking reduces this risk by 40% to 60% depending on the study. If you consider 40%, the lifetime risk decreases to 23.5%. According to the American Heart Association, one out of every 30 deaths in women is due to breast cancer and one out of every three deaths is attributable to heart disease. Each year 88,000 females age 45 to 64 have a heart attack and 50% will die within 8 years. 63 percent of women who die from a heart attack have no previous symptoms. It has been shown that all the well-known risk factors for heart disease put together (obesity, family history, high blood pressure, high cholesterol, etc.) are not as effective a predictor of heart attack as an EBCT heart scan, which shows the amount of calcium accumulated in the coronary arteries. Doctors refer to EBCT as "the mammogram for the heart." At \$255, the test is inexpensive and is something to consider if there is any significant risk factor for heart disease.

The International Scientific Forum on Alcohol Research emphasized that in the Nurses' Health Study strong effects for the amount of alcohol and the frequency of consumption were not found. Also, the effects of folate intake on the association between alcohol and cancer were not reported although the same investigators had previously shown that folate is a potential moderator of the effects of alcohol on breast cancer risk. The Forum goes on to discuss the dilemma that women face regarding alcohol intake, which may increase slightly the risk of breast cancer but markedly decrease the risk of cardiovascular disease. Forum members and the authors agree, "An individual will need to weigh the modest risks of light to moderate alcohol use on breast cancer development against the beneficial effects on cardiovascular disease to make the best personal choice regarding alcohol consumption."

The mention of folate by the Forum is worth discussing further in the context of breast cancer risk. Linda Prost, a nutritionist who lives and practices in Eugene, Oregon, and is the author of "*Live in the Balance: The Ground-Breaking East-West Nutrition Program*," wrote about the beneficial effects of folate in the *Register-Guard* (December 19, 2011). She points out that back in 2005, a report in the *British Medical Journal* found that Australian women who were moderate to heavy drinkers (2 to 4 or more alcoholic drinks a day) and had low folate intake, had a significantly increased risk of breast cancer compared to light drinkers or abstainers. When moderate or heavy drinkers took 400 micrograms of folate the risk was offset. Other studies have shown that taking extra folate counteracts the risk of breast cancer in women who drink moderately. Diet supplementation with 400 micrograms of folate per day also has been shown to offset the increased risk of colorectal cancer in those men and women who drink two or more alcoholic beverages a day. In addition, studies have shown that increased intake of folate decreases the risk of oral cancer.

Prost notes that excellent sources of folate include liver (the French are known to consume large amounts of foie gras and duck liver pate which are rich sources of folate and may help explain the French Paradox), turnip greens, spinach, asparagus, peanuts, and hummus. Folate can also be taken as a supplement, and folate (L-methylfolate), which is the naturally occurring form found in foods, is a better choice than folic acid. She finishes her report by saying, "If you plan to sip more than a few glasses of libation a week over the holidays, or ever, consider serving up extra chicken livers or duck pate, sauteed greens, asparagus, peanuts and bean dishes. Supplementing with folate is also a good idea. You may be able to protect yourself from breast and colon cancer, reduce your risk of heart disease, and celebrate the holidays all at once."

The effect of alcohol consumption on women who carry a BRCA gene mutation is unclear. BRCA genes function as tumor suppressors, but mutations of these genes, which are hereditary, may be harmful. The mutations can be detected with genetic screening. A case-control study published in the medical journal *Breast* (December 2010) of 1925 matched pairs of predominantly pre-menopausal women who carried a BRCA1 or BRCA2 mutation found that alcohol consumption did not appear to increase breast cancer risk in women

carrying a BRCA gene mutation. Compared to non drinkers, exclusive consumption of wine was associated with a significant reduction in the risk of cancer among BRCA1 carriers.

The same researchers from the Universities of Montreal, Ottawa and Toronto, Canada, will publish another study in early 2012 in *The Breast Journal*. Prepublication information was obtained by winespectator.com. This study found that women with the BRCA1 mutation showed a 62% lower risk of breast cancer than the general population if they drank wine, while women with the BRCA2 mutation showed a 58% greater risk. The researchers attributed the difference to the polyphenol resveratrol found in wine. Resveratrol can bind to estrogen receptors and assist in the regulation of activity of BRCA1-mutated genes, but BRCA2 mutated genes appear to be unreceptive to resveratrol. This theory is speculative as there may be other substances in wine that are decreasing the risk in women with the BRCA1 mutation.

A research report published online in *The FASEB Journal* (October 2011) is relevant. This study showed that resveratrol stops breast cancer cells from growing in vitro by blocking the growth effects of estrogen. A team of American and Italian scientists suggest for the first time that resveratrol is able to counteract the malignant progression by inhibiting the proliferation of hormone resistant breast cancer cells. The authors of the study conclude that resveratrol may prove to be a pharmacological tool to be used in cases when breast cancer becomes resistant to hormonal therapy by therapeutic agents such as tamoxifen. However, they are quick to point out that it does not mean people should start using red wine or resveratrol supplements as a treatment for breast cancer. Gerald Weissmann, M.D., Editor-in-Chief of *The FASEB Journal* said, "What it does mean, however, is that scientists haven't finished distilling the secrets of good health that have been hidden in natural products such as red wine."

It is of note that Americans consume 8.96 liters of wine per capita, while those in France, Portugal and Italy consume 42-45 liters per capita, yet there are no studies from Europe that link alcohol to breast cancer. Could red wine be protective? A new study to be published in an upcoming issue of the *Journal of Women's Health* found that drinking red wine in moderation appears to counter the risks of breast cancer risk associated with alcohol. Researchers at Cedars-Sinai Medical Center and the University of Southern California gave 8 ounces of red wine daily in the evening to 36 women and 8 ounces of white wine to another 36. After a month, the type of wine served was reversed. Blood was collected twice during the women's menstrual cycle to measure hormone levels. The researchers found more favorable lower estrogen and higher testosterone levels when women drank red wine, while white wine did not have the same effect.

The data in this study suggested that substances in the skin and seeds of red grapes act like a class of drugs called aromatase inhibitors (AIs) which have hormone modulating effects and may explain why red wine does not appear to raise breast cancer risk. In other words, red wine acts like a nutritional AI and may work like some of the hormone treatments currently used for cancer. The findings do not mean that white wine raises breast cancer risk. The authors of the study went so far as to suggest that women who drink white wine should consider switching to red wine, but the research does not suggest that women increase their red wine consumption beyond moderation. Obviously, a much larger study is needed to confirm whether red wine can reduce breast cancer risk.

Elaine Schattner, writing in *The Atlantic* online (January 2012), concludes her commentary on the above research with the following pertinent statement. "The underlying problem is that it's hard to prove cause and effect in the context of widespread alcohol use to varying degrees among women in North America today. You can't ethically test the premise that a likely carcinogen is harmful by giving it prospectively to some women and not to others. The correlation is clear enough, but women who drink alcohol tend to be heavier than those who don't. In some communities women who have access to alcohol may also be more affluent, more educated, or more sedentary; these and other potential co-factors aren't easy to dismiss."

Finally, it should be mentioned that lung cancer kills more women than breast cancer. Lung cancer is more lethal and a bigger killer of women than all the other cancers combined. The disease receives little notoriety and has a stigma attached due to its association with smoking. The fact is that most new lung cancers in women are in those who have never smoked or quit many years ago.

Other Cancers

Alcohol (ethanol) has been known to be a carcinogen at several sites in the human body since the 1980s. For most cancers, there is a dose-response curve in that the risk increases with the more alcohol people consume on a regular basis. Years of research have linked alcohol to cancers of the mouth, throat, larynx, esophagus, stomach, colon, pancreas, liver and lung. The highest association of alcohol and cancer is with cancers of the mouth, throat, larynx and esophagus. Many drinkers also smoke and this compounds the risk for these cancers. Generally, the risks of these cancers is related to heavy drinking. The quantity of alcohol matters most for men's cancer risk. The frequency of drinking is more meaningful for women's risk. There is no firm evidence that wine is a healthier drink from the standpoint of cancer risk although at least one study from Spain published in 2004 found that the slight association between consuming white wine and lung cancer disappeared in people who drank red wine and red wine actually had a protective effect.

It is estimated that 90% of the cancer deaths in men world wide could be avoided if drinking was limited to two alcoholic drinks a day and 50% of the cancer deaths in women could be avoided if drinking was limited to no more than one. It is unclear how long it takes for the increased risk associated with heavy drinking to resolve once drinkers cut back.

Arthur L. Klatsky, M.D., a noted alcohol researcher at the Kaiser Permanente Medical Care Program in Oakland, California, presented a talk at this years Sixth International Wine and Heart Health Summit in Newberg, Oregon, titled, "Alcoholic Beverages and the Risk of Cancer: A Balanced View." He made the following points:

- * Epidemiological evidence shows a strong association of chronic heavy alcohol consumption with cancers of the oral cavity, pharynx, larynx and esophagus. The synergy between alcohol and tobacco is strong. The relationship of moderate drinking is unclear.
- * There is a clear association of heavy drinking with liver cancer.
- * There is a fairly consistent association of heavier alcohol drinking with female breast cancer, but there is considerable debate about the presence and level of a risk threshold.
- * The least consistent alcohol-cancer relationship is the link to the risk of colorectal cancer. Dietary folate deficiency may be an intermediary.
- * The data on many other cancer types is inconclusive.
- * There is a lower risk to alcohol drinkers for hematologic cancers, especially non-Hodgkins lymphoma and kidney cancer.
- * The choice of alcoholic beverage is not shown to be a major factor in alcohol-cancer relationships (but see report above to be published in the *Journal of Women's Health*).

Klatsky points out that there are no randomized controlled trials of the association between alcohol and cancer so a definite cause and effect relationship is difficult to confirm. Results from current cohort and case-control analyses are diminished by residual confounding and problematic statistical modeling as well as underestimation of drinking amount by study participants.

A study published in the *American Journal of Epidemiology* (November 11, 2011) linked alcohol consumption to four types of cancer: breast, colorectal, lung and prostate. This National Health Interview Survey conducted by epidemiologists from the National Institute on Alcohol Abuse and Alcoholism along with Harvard alcohol researcher Kenneth Mukamal had 323,000 American participants. 1 drink a day led to a lower risk of cancer than nondrinkers (13% less). Those who had 2-3 drinks a day had the same risk for the cancers as nondrinkers. People who had more than 3 drinks a day had a 27% higher risk of developing the four cancers (men) or 41% higher risk (women). **Summary:** The research confirms previous studies that link heavy drinking to an increased risk of certain cancers. This study did not eliminate all confounders such as lifestyle choices and did not distinguish between types of alcohol which is unfortunate.

At the American College of Chest Physicians meeting, October 2011, a large study from the Kaiser Permanente health system in Oakland, California, was reported that found that those who drank 3 or more drinks per day regularly, even if they had never smoked cigarettes, had a 30%-40% increased risk of lung cancer with the strongest risk being among beer drinkers.

A study published last year in *Alcoholism: Clinical & Experimental Research* (December 2011), headed by a United States team from the National Institute on Alcohol Abuse and Alcoholism, found that when ethanol is metabolized in the body, the byproducts can lead to DNA damage that may lead to cancerous changes in cells.

Researchers used human cells engineered to produce an enzyme found in liver and breast tissue. The cells were exposed to a concentration of alcohol similar to blood alcohol levels attained after having a few drinks. The results indicated that ethanol was being converted to acetaldehyde, causing DNA damage and switching on the cell's DNA repair genes. **Summary:** The study is consistent with a suspect role for acetaldehyde in alcohol related liver and breast cancer, but more studies on animals and humans are necessary to prove such a role.

Research by the European Prospective Investigation into Cancer and Nutrition (EPIC) cohort looked at alcohol consumption and gastric cancer risk. Published in the *American Journal of Clinical Nutrition* (November 2011), the study found that heavy alcohol consumption (equal to or greater than 6 drinks a day) was association with and increased gastric cancer risk. The association was found for beer, but not wine or spirits. Lower alcohol consumption (less than 6 drinks a day) was not associated with gastric cancer risk. **Summary:** Heavy but not light or moderate primarily beer drinking is association with gastric cancer risk. This was a convenience sample so the transferability of the study results to the general population can be questioned.

In *Nutrition and Cancer* (October 2011), cancer risk and alcohol consumption were studied by reviewing a large number of epidemiological studies. Heavy alcohol consumption (equal to or greater than 4 drinks a day) resulted in a 5 fold increase risk of oral and pharyngeal cancer, and squamous cell cancer of the esophagus. The risk for laryngeal cancer was 2.5 fold. The risk for colorectal cancer was increased by 50% and the risk for breast cancer was increased by 30%. At low doses of alcohol drinking (equal to or less than 1 drink a day) the risk for oral and pharyngeal cancer was increased 20% and the risk of esophageal squamous cell cancer was increased 30%. At this level of drinking there was no increased risk of laryngeal, colorectal or pancreatic cancer. Moderate alcohol intake, especially wine, was inversely associated with distal colorectal cancer and no risk of endometrial cancer. If alcohol consumption was less than 3 drinks a week, there was no increased risk of breast cancer and at 3 to 6 drinks a week, there was a small increased risk. **Summary:** Heavy drinking is associated with a significant increased risk of colorectal, breast, pancreatic, oral, pharyngeal, laryngeal, and esophageal cancers.

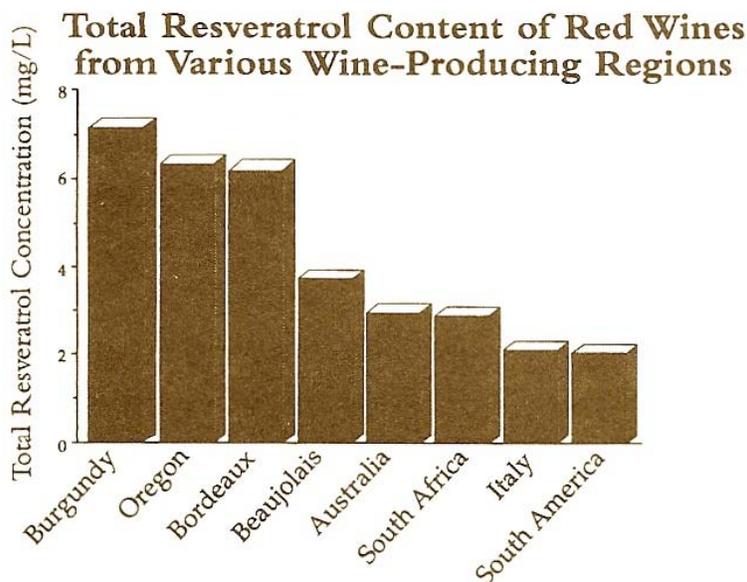
A large Chinese population analysis of all studies involving alcohol consumption and cancer was published in *PLoSOne* (April 2011). Cohort studies indicated that alcohol consumption was not associated with gastric, esophageal and lung cancers. Case-control studies did show an increased risk of gastric, liver, nasopharyngeal and oral cancers and alcohol consumption was protective for female breast cancer and gallbladder cancer. No significant correlations were found with lung, colorectal, pancreatic and prostate cancers. **Summary:** The combined results of case-control and cohort studies reviewed revealed that alcohol consumption was associated with a higher risk of esophageal and gastric cancers.

A large prospective cohort study in eight European countries regarding the alcohol attributable burden of incidence of cancer was reported in the *British Medical Journal* (April 2011). Participants included 109,118 men and 254,870 women, mainly aged 37-70. If causality is assumed, for both men and women, the incidence of total cancer was attributable to former and current alcohol consumption in the eight European countries. For selected cancers the figures were 44% (21 to 56%) and 25% (5 to 46%) for upper aerodigestive tract, 33% (11 to 54%) and 18% (-3 to 38%) for liver, 17% (10 to 25%) and 4% (-1 to 10%) for colorectal cancer for men and women, respectively, and 5% (2 to 8%) for female breast cancer. For all cancers causally related to alcohol consumption, the proportions were 32% in men and 5% in women, with a substantial part (40-98%) being attributable to current alcohol consumption above the recommended limit of two drinks a day in men and one drink a day in women. A substantial part of the alcohol attributable fraction in 2008 was associated with alcohol consumption higher than the recommended upper limit. **Summary:** In western Europe, many cases of cancer can be attributable to alcohol consumption, especially consumption higher than the recommended upper limits.

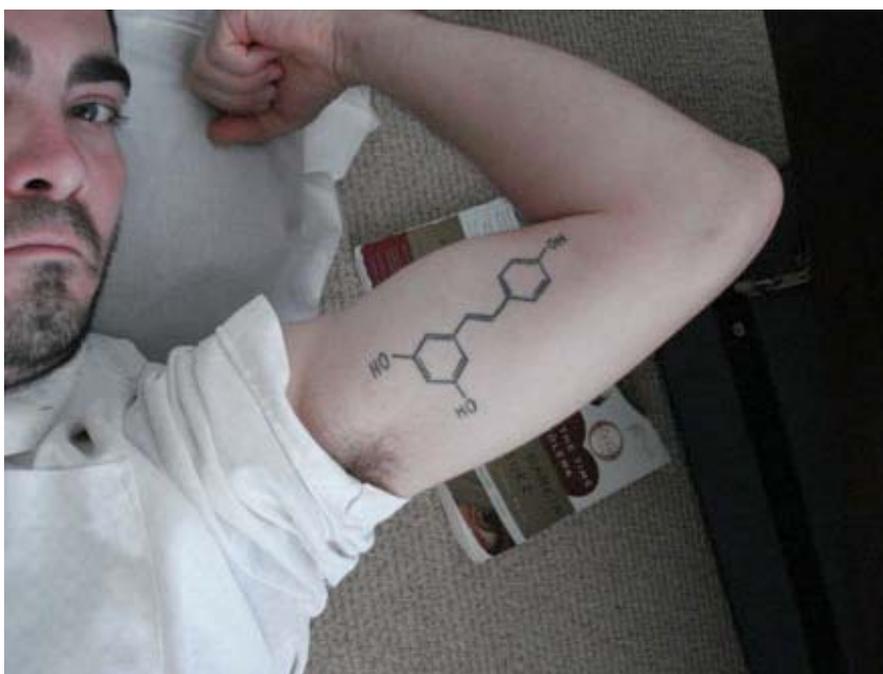
Resveratrol

The bloom is partially off the rose regarding the hype over resveratrol which has been the darling of the media as a panacea for longer life and many other beneficial health effects. Resveratrol was first reported in red wine in 1992 and early on it was thought to explain the French Paradox. Subsequent studies found that resveratrol could extend lifespan in cell culture and animal models and inhibit the development of cancer, diabetes and other life-threatening illnesses. Some recent studies have disputed some of the early research and tempered

some of the optimism (see page 13). There have been a limited number of human trials to date with a substantial body of research on lab animals. Human studies have shown good safety but poor bioavailability. Resveratrol is found not only in grapes, but in grape juice, peanuts and berries including blueberries and cranberries. Resveratrol is but one of many polyphenol flavonoids which are also found in spices and dried herbs, cocoa, some seeds (flaxseed), chestnuts and hazelnuts, and some vegetables including olives and globe artichoke leaves. Resveratrol is found primarily in the skin of red grapes with the amount varying depending on the grape and its geographic origin. The chart below shows published resveratrol content of red wines from various wine-producing regions. There are no significant differences in the polyphenolic composition of wine between wine made from organically grown and conventionally grown grapes. Resveratrol levels in wine can be increased by extending maceration times and by malolactic fermentation and can be decreased by fining and filtration.



Resveratrol is the most researched of the class of compounds known as polyphenols. At the recent 6th International Wine and Heart Health Summit in Newberg, Oregon, Balz Frei, PhD, Director and Endowed Distinguished Professor in the Department of Biochemistry & Biophysics at Oregon State University, presented a paper titled, "Flavonoids; From Antioxidant Capacity to Cardiovascular Functions." This is highly relevant to any discussion of resveratrol and other polyphenols in wine and will be summarized here.

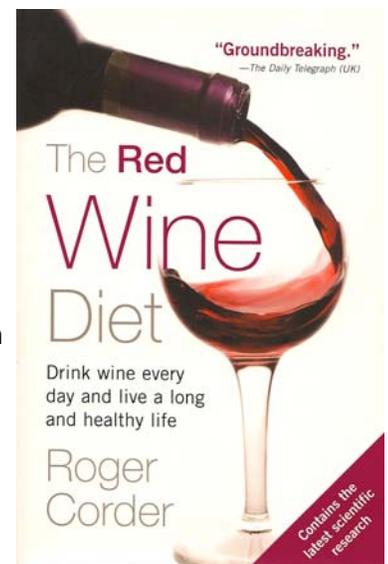


Flavonoids consist of 5,000 plant compounds with a common chemical structure called polyphenol (polyphenols have multiple aromatic rings, that is, six connected carbon atoms who share electrons - see chemical tattoo of resveratrol above). They are found in fruits, vegetables, and beverages such as wine, tea, cocoa and fruit juices. There are seven subclasses of flavonoids: (1) isoflavones (soy products), (2) flavanones (for example naringenin in citrus), (3) flavanols (catechins and condensed tannins or proanthocyanidins in tea, cocoa, red wine and several fruits), (4) flavonols (quercetin in fruits and vegetables), (5) anthocyanidins (in berries and grapes including resveratrol), (6) flavones and (7) flavanones. Flavonoids are poorly absorbed in the digestive tract, rapidly eliminated and have a low bioavailability with their metabolites having often less activity. This has required that studies on flavonoids use high unphysiological amounts and these studies have shown powerful antioxidant activity in vitro but limited effect in vivo. Their beneficial effects have often been attributed to antioxidant actions.

Dr. Frei makes the following important points:

- * There is minimal or no direct antioxidant activity of flavonoids compared to other important antioxidants like Vitamin C and E.
- * Instead, flavonoids modulate cell-signaling pathways, that is, cell growth, cell proliferation, and removal of damaged cells (apoptosis).
- * The concentration need to affect cell-signaling mechanisms is much lower than that need to affect cellular antioxidant activity.
- * Flavonoids may selectively inhibit cell-signaling enzymes called kinases which initiate chronic disease.
- * The modulation of cell-signaling by flavonoids could help prevent cardiovascular disease by (1) decreasing inflammation by lowering c-reactive protein and inhibiting atherosclerosis secondary to inflammation of arterial walls, (2) decreasing vascular endothelial cell adhesion so that inflammatory white blood cells are not allowed to adhere, and (3) increasing vascular endothelial nitric oxide which maintains normal blood vessel relaxation (dilation). Decreasing endothelial-dependent vasodilation is closely related to the risk of cardiovascular disease.
- * Proanthocyanadins are able to suppress endothelin-1 factor which is important in the development of coronary artery disease.
- * Flavonoids decrease platelet aggregation which is one of the first steps in forming a blood clot.
- * Flavonoids can cross the blood-brain barrier and exert a multiplicity of neuroprotective actions in the brain including (1) protecting neurons against injury from neurotoxins, (2) suppressing neurological inflammation which has a crucial role in Alzheimer's and Parkinson's diseases, (3) promoting memory, learning, and cognitive function, and (4) reversing the course of neuronal and behavioral aging.

Also at the International Wine and Heart Health Conference, Roger Corder, PhD and MRPharmS from London's School of Medicine & Dentistry presented a talk on "the Importance of Dietary Polyphenols for Optimal Vascular Health." He noted that the total polyphenol concentration in red wine is between 1 and 3.5 g/L with some wine from Tannat and Sagrantino grapes exceeding 5 g/L. Polyphenol concentration is related to grape variety and the length of maceration of the pips and skins. Other factors are oak aging, vineyard management, ripeness and terroir. The polyphenols contribute to color, flavor and mouth feel of red wines. The importance of the different polyphenols in red wine is the subject of much debate. Corder has shown that the oligomeric procyanidins (OPC - a type of flavanol) have greatest effect on vascular endothelial function at the concentration found in red wine. Resveratrol and quercetin lack biological activity on the vascular endothelium in amounts found in red wine. He plans future clinical trials on OPC-rich products to determine if they could have a future pharmacological role in the prevention and treatment of cardiovascular disease.



I have referenced a number of studies involving resveratrol in previous pages of this issue, but I will summarize additional important research published or presented in 2011 on resveratrol and other polyphenols.

Dr. Andrew Waterhouse, Professor of Enology at University of California at Davis reported on papers presented at the 5th International Conference on Polyphenols & Health in Spain in 2011. His comments were published

in *Wines & Vines* (December 2011). One significant study found that the consumption of wine polyphenols when eating meat results in lower lipid oxidation in the stomach and lower levels of toxic aldehydes circulating in the blood. **Summary:** Drinking red wine with meat has favorable health implications. Note: Dr. Waterhouse points out that since about 2000, the U.S. wine industry has pursued a policy of not funding health related research, and the U.S. government has always avoided supporting any research that might show benefits to alcohol consumption. The reality of this was reflected in the large number of studies reported at the Conference on olive oil, chocolate and juices including grape juices, which all benefit from strong industry funding.

Research presented by the Dutch at the American Heart Association High Blood Pressure Research Meeting in Florida was published in *Health Day News* (September 2011). 61 people who averaged over 61 years of age with borderline high blood pressure were given daily beverages containing red wine polyphenol or a placebo. No difference in blood pressure was found in the two groups after 4 weeks. **Summary:** Polyphenols may be beneficial in reducing heart disease, but it does not seem to be through the mechanism of lowering blood pressure.

A study of red wine polyphenols was reported in *Food Research International* (online July 29, 2011). The researchers studied in vitro the effects of red wine polyphenols on oxidation stability of human plasma fatty acids, particularly those most involved in inflammatory responses. Wine polyphenols conferred increased resistance to peroxidation of omega-3 more than omega-6 fatty acids. **Summary:** Red wine polyphenols may protect omega-3 fatty acids from breaking down in the body. This may be one of the mechanisms to explain the cardiovascular benefits of red wine consumption.

A double-blind randomized placebo-controlled intervention study on 28 male smokers supplemented with 200 mg a day of monomeric and oligomeric flavanols (MOFs) from grape seeds was published in *PLoSOne* (December 2011). All subsequent measured vascular effects at 4 and 8 weeks after instituting supplementation were integrated into a global, so-called vascular health index which revealed a significant improvement of overall vascular health compared to placebo. **Summary:** This integrative multi-biomarker approach unveiled the pleiotropic vascular health benefit of an 8 week supplementation with 200 mg/d of MOF in humans.

A review published this past year did not find that resveratrol could prolong survival or life span of mice. Published in *Heart Failure Reviews* (July 2011), resveratrol was found to induce expression of several longevity genes including Sirt1, Sirt3, Sirt 4, Fox01, Foxo3a, and PBEF and prevent aging related cardiovascular decline function including cholesterol level and inflammatory response but was unable to affect the actual survival of laboratory mice. **Summary:** Resveratrol possesses diverse biochemical and physiological properties, including estrogenic, anti-platelet and anti-inflammatory properties as well as a wide range of health benefits ranging from chemoprevention to cardioprotection. Its life-prolonging ability is controversial and this review disputes its ability to affect actual survival or life span of mice.

A study published in *Nutrition, Metabolism & Cardiovascular Disease* (November 2011) is the first of its kind investigating whether resveratrol can improve flow-mediated dilation (FMD) in a clinical trial setting. This randomized, double-blind, placebo-controlled crossover human intervention trial used obese subjects with high blood pressure. They were given 3 doses (30-90-270 mg) and a placebo using 3 doses a week and the FMD was measured. With increasing doses of resveratrol, there was a proportional increase in the blood plasma resveratrol concentration and FMD was increased for each of the doses. FMD is the loss of endothelial-dependent vascular smooth muscle relaxation and when impaired is a cardiovascular disease risk factor. **Summary:** Oral resveratrol improved endothelial-dependent vasodilation by increasing FMD. There was significant improvement in FMD even at the lowest dose. This effect may contribute to the purported cardiovascular health benefits of grapes and red wine. It is not clear that the amount of resveratrol in a normal diet will have the same effect. Dietary supplements may be the answer.

A comprehensive review of human clinical trials of resveratrol and health was published in *Molecular Nutrition & Food Research* (April 2011). **Summary:** "The emerging data from human clinical trials confirms what the past decade of in vitro and laboratory animal models have suggested: resveratrol has considerable potential to improve health and prevent chronic disease in humans. We believe the evidence is sufficiently strong to conclude that a single dose of resveratrol is able to induce beneficial physiologic responses, and that either weeks or months of resveratrol supplementation produces physiologic changes that are predictive of improved health, especially in clinical populations with compromised health. However, it is not yet certain if long term resveratrol supplementation will maintain these physiologic benefits to ultimately impact the incidence of

chronic disease or extend lifespan, and the small number of human clinical trials remains dwarfed by the thousands of basic science experiments. Nonetheless, we believe it is possible that healthy individuals may still benefit from resveratrol's potential to delay or prevent age and lifestyle induced decrements in health, though considerable research is need on this front.”

Robert Sclafani, a professor of biochemistry and molecular genetics at the University of Colorado School of Medicine and Rajesh Agarwal, a professor in the Department of Pharmaceutical Studies at the School of Medicine have recently found that resveratrol is successful in preventing oral cancer in mice. Their hope is to test the effects of resveratrol in humans with oral cancer. High quantities of concentrated resveratrol could be given to patients with oral cancer as a mouth wash or gel. To date, there are no known side effects of resveratrol. This preliminary report was published online at aurorasentinel.com. **Summary:** Resveratrol is extremely effective in preventing the appearance of oral cancer in mice.

Two interesting studies published in *Food Chemistry* (October and December 2011) looked at which type of cooperage produces wines with the highest polyphenol content. Aging wine in oak barrels changes the sensory characteristics of the wine plus the antioxidant capacity of the wine which is primarily due to polyphenols. The first study on toasting found that wine aged in non-toasted oak barrels had significantly higher antioxidant and total polyphenol levels than wines aged in oak barrels that had been toasted. A second study looked at the origin of the barrel wood and the species of the plant. Aging wine in different species of wood did have influence on the antioxidant capacity of wine due to varying polyphenol composition of different wood species. Theoretically, some woods such as chestnut which are higher in polyphenols could produce healthier wines. **Summary:** The antioxidant capacity and polyphenolic composition of different woods used in cooperage can result in different polyphenolic composition of the resultant wine

I will conclude this section on resveratrol with a few comments on resveratrol supplements which have caught the fancy of many consumers. A word of caution is needed since resveratrol supplements are not regulated by the FDA and the pills vary widely in their purity and actual potency. Many producers are using deceptive marketing to tout the value of resveratrol supplements, yet they have no proven health benefit and long-term effects are yet unknown. The supplements must be made in an oxygen-free environment (single-pill foil wraps) to obtain the active compound and they must be in the trans-resveratrol form. Resveratrol can slow down the speed at which the liver metabolizes certain drugs such as statins and calcium channel blockers and this could affect dosing of these drugs, but otherwise it is thought that the supplements are probably safe if used in moderate doses (100 to 500 mg a day). Many researchers feel it makes more sense to drink red wine and eat foods that contain high amounts of resveratrol naturally than take unproven supplements.

Binge Drinking

A study by the Centers for Disease Control and Prevention (CDC) based on telephone surveys of 450,000 adults was released in January 2012 as part of a new report highlighting the dangers of binge drinking. About one in six adults 18 and older (about 38 million adults total) and one in four adults between the ages of 18 and 34 report binge drinking one or more times within the last 30 days using the definition of four or more drinks within a short period of time or occasion for women and five or more drinks within a short period of time or occasion for men. Binge drinkers engage in this activity on average about four times a month or roughly once a week. Seniors who reported binge drinking (only about 4% of people 65 years of age and over binge drink), did so more frequently, about five times a month, than even younger people which was a surprise to the leaders of the CDC. Also surprising was that binge drinkers reported consuming eight or more drinks on average during at least the largest episodes of binge drinking within the past 30 days. College-age adults average 9 alcoholic beverages when they binge drink. That level of drinking puts the individual binge drinker at an increased risk for a host of problems including long-term issues of cancer, heart disease and liver failure. Binge drinking was more common in men, white non-Hispanics, people who have been to college, those with incomes of \$75,000 or more and residents of the upper midwest with Wisconsin topping the list. Health officials estimate that about 50% of the alcohol consumed in the United States by adults each year is drunk during binge drinking episodes. The CDC study also found that of the 80,000 deaths that alcohol is responsible for in this country every year, half of them are due to binge drinking.

14 colleges and universities have teamed in The Learning Collaborative on High-Risk Drinking, which will examine ways to thwart binge drinking, which affects an estimated 40 percent of college students nationally. For information, visit www.nchip.org/alcohol.

UCLA researchers have discovered a compound that counteracts the effects of alcohol. The report was published in the *Journal of Neuroscience* (January 2012). In vitro experiments on rats involved giving them a strong dose of alcohol and then some rats were also given Dihydromyricetin (DHM) which is from the ancient *Hovenia Dulcis* tree, an ancient herbal treatment. Rats that received the DHM sobered up faster, showed a higher tolerance for alcohol in general, and showed fewer side effects usually associated with hangovers. The research was aimed at finding a treatment for alcohol use disorders, but the hangover resistance was a surprising finding. Rats that were allowed to drink alcohol gradually start consuming more of it, but if they drank DHM-laced alcohol, they did not show a desire to increase consumption. **Summary:** DHM shows promise as a treatment for alcohol use disorders since no alcohol addiction occurs when alcohol is drunk with DHM. DHM may also prove useful in treating hangovers. Human trials are needed to confirm the results.

Anti-Alcohol Forces

The position statement released by the Cancer Council of Australia (CCA) on May 1, 2011 surprised the scientific community. This report was well detailed by Margaret Raber online at winespectator.com (May 13, 2011). The position statement claimed that 5 percent of all cancers in that country were due to long-term alcohol use, arguing that alcohol increased the risk of developing upper aerodigestive tract cancers and colorectal cancers in men and breast cancers in women. The report claimed that 7 percent of male colorectal cancer cases and 22 percent of female breast cancer cases were due to alcohol consumption. The basis for this claim came from data for the United Kingdom, gleaned from the World Cancer Research Fund and the American Institute for Cancer Research. They also stated that alcohol could increase body weight which further increased the risk for cancer. The CCA recommended that people stop drinking alcohol completely or at least stay within the nationally recommended maximums. The CCA went on to say that the current research on the relationship between alcohol and heart health is flawed.

Soon after the report was released, the Winemaker's Federation of Australia responded, emphasizing, "There is currently no research to show a positive relationship between moderate alcohol consumption and cancer risk." Researchers questioned some of the facts contained in the report, including the high rate of risk of breast cancer related to alcohol. Dr. Richard Corder, PhD & MRPharmS, a noted polyphenol researcher from London's School of Medicine and Dentistry commented, "The paper is alarmist, perhaps because too many Australians drink in excess, and so perhaps the message is actually one of moderation to avoid adverse consequences." It is true, that Australians have a notorious reputation for copious social drinking with at least 13.4 percent of Australians drinking at a high risk level of 7 or more drinks per day for men and 5 or more for women (as of the latest National Health Survey statistics in 1995). The typical Australian starts drinking alcohol at the age of 15½ and binge drinking is a serious problem during the teen years.

In August, 2011, the federally funded Alcohol Education & Rehabilitation Foundation in Australia recommended favored warnings for alcoholic beverages that included: "Drinking alcohol increases your risk of developing cancers," and "Drinking alcohol damages the young developing brain." A helpline was set up for people who were concerned about alcohol intake. The Australian Medical Association urged the government to require tough mandatory health warnings on alcoholic beverages. Australia's alcohol industry launched its own voluntary program to label its products with health warnings aimed primarily at teenagers and pregnant women. DrinkWise Australia, headed up the alcohol industry's program, released three principal messages that include, "Kids and Alcohol Don't Mix," "Its Safest Not to Drink While Pregnant," and "Is Your Drinking Harming Yourself or Others."

The Alcohol Policy Coalition of Australia (APC), a group of Australian health organizations, released a position paper in September 2011 titled, "Myth Busted: Red Wine No Magic Remedy for Heart Disease," and published a document entitled *Cancer, Cardiovascular Disease and Alcohol Consumption*. Kathy Bell, CEO of the Heart Foundation and a member of the coalition said, "After reviewing all the scientific evidence it appears any positive effects of alcohol in reducing the risk of cardiovascular disease have been hugely overestimated. In particular, red wine has no special, protective qualities when it relates to cardiovascular diseases. The Heart Foundation does not recommend red wine or other types of alcohol to prevent or treat cardiovascular disease. To reduce your lifetime risk of alcohol related harm, you should drink no more than two standard drinks on any day."

The International Scientific Forum on Alcohol Research responded to the APC's publication in Critique 058. Members of the forum said, "They were disturbed that the coalition statement was limited almost exclusively to

the effects of abusive drinking, was based primarily on extremely limited sources of information, and indicated a strong bias against alcohol." Forum members contended that the Australian report misrepresented the extensive scientific data available on alcohol and health. The full critique can be read at <http://www.bu.edu/alcohol-forum/critique-058-a-misguided-statement-on-alcohol-and-health-from-a-coalition-in-australia-28-september-2011/>.

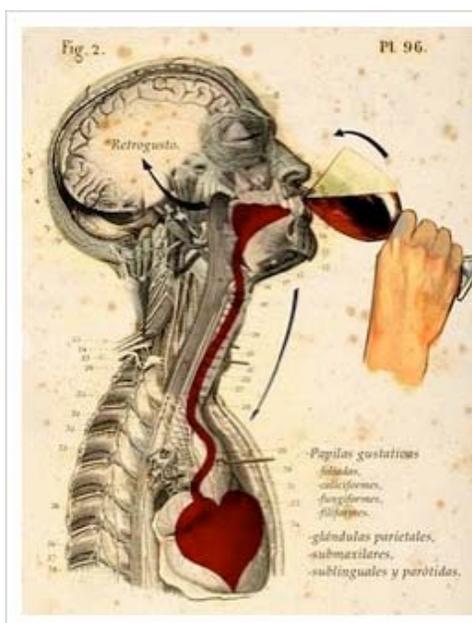
The APC in turn responded to Critique 058 and the argument rages on. The APC's response can be viewed at <http://www.bu.edu/alcohol-forum/a-response-from-the-alcohol-policy-coalition-of-australia-to-critique-058-%E2%80%9Ca-misguided-statement-on-alcohol-and-health-from-a-coalition-in-australia%E2%80%9D/>.

There continues to be significant anti-alcohol sentiment throughout the world. For example, Professor Jennie Connor of the Dunedin School of Medicine in New Zealand, stated to couriermail.com.au, "I feel strongly that there is no scientific justification for the promotion of alcohol as health-enhancing for any subgroup of the population. The potential for harm is great, and the potential for good is unknown." Nicolay Sorenson of Alcohol Concern in the UK told decanter.com, "There is no such thing as risk-free drinking. Every unit of alcohol you drink has a toxic effect as soon as it enters your body."

Postscript

A very conservative, but appropriate view of the alcohol and health discussion is taken by Arthur L. Klatsky, M.D., whose name has appeared throughout this review. He feels confident in making the following generalizations. The increased risk of alcohol related accidents in young men (a 30-year-old for example) outweighs the possible heart related benefits of moderate alcohol consumption. Young women are at low risk for cardiovascular disease so the risk of moderate drinking exceed the benefits. The cardiovascular benefits of moderate consumption increases with age so that a 60-year-old man who drinks one drink a day can expect that the protection afforded against heart disease is likely to outweigh potential harm. A 60-year-old woman is more likely to die from heart disease than breast cancer, so the benefits of light to moderate consumption outweigh the risks, even though women are often afraid of breast cancer. In other words, mature adults benefit potentially most from regular moderate alcohol consumption.

The health benefits from red wine are only obtainable through regular and moderate consumption. Individual ideals will vary considerably depending on a number of factors, but the most widely accepted recommendation is one glass of red wine a day for women and up to two drinks daily for men, assuming no medical contraindications. Consult your physician before altering your alcohol consumption habits.



The words of Hermann Smith-Johannson, a Scandinavian cross-country skier who died at the age of 103, are a fitting conclusion to this discussion. "The secret to a long life is to stay busy, get plenty of exercise, and don't drink too much. Then again, don't drink too little."

Memorable Quotes from 2011

I believe quotes have relevance in a historical context. They tell us about the topics and controversies that are prevalent at a certain time. They also represent a gift that says plenty with few words. I hope you enjoy the quotes that I collected over the past year from the wine literature, many of which were made in the context of a discussion of Pinot Noir. Ted Lemon, the proprietor and winemaker of Littorai, proved to be the most quotable in 2011.

“Burgundy is like the girl from Bennigton who made me miserable my sophomore year at Williams College: She keeps breaking my heart, but I’m obsessed, crazed with lust, spending ridiculous amounts of money on the object of my desire. Because when she’s good, she’s very, very good.”

Jay McInerney, *The Wall Street Journal*

“Burgundy has all the answers if you know to ask the right questions.”

Kevin Harvey, owner of Rhys Vineyards

“Burgundy has the pinnacle all to itself for Pinot Noir.”

Benjamin Lewin MW, *In Search of Pinot Noir*

“Using burgundian techniques doesn’t make the results Burgundy!”

Remington Norman, *Grand Cru*

“There’s no way the average customer understands the legal blending limits. People see ‘Pinot Noir’ on the label and very few would know that could mean a wine that’s only seventy-five percent Pinot,”

Rick Moshin, Moshin Vineyards

“What’s quietly losing favor, then, are those inky, oak-loaded Pinots made for flash and impact, for success with a handful of critics who are slowly fading into the background. These wines have contributed to the de-Pinoting of Pinot as much as the bottom-shelf stuff.”

Jon Bonné, sfgate.com

“I wish people would accept over-oaking as a flaw like they regard Brett as a flaw.”

Jason Lett, winemaker at The Eyrie Vineyards, in *In Search of Pinot Noir*

“Pinot Noir is not about color and tannins.”

Veronique Drouhin, winemaker at Domaine Drouhin Oregon

Pinot Noir is more than just another varietal; it is seductive and ephemeral and attracts a fiercely independent, opinionated breed.”

Lance Cutler, *Wine Business Monthly*

“Its ‘food-friendly’ nature has been well-documented; Pinot makers might as well have coined the phrase.”

Lettie Teague, *The Wall Street Journal*

“Each of us has his or her own Platonic notion of Pinot Noir.”

Doug Frost, *The Kansas City Star*

“The reason there are so many high-alcohol Chardonnays and Pinots is that wineries and their winemakers have a commercial fear of being outside the paradigm of what critics consider fine American Pinot. It’s a style that ignores terroir.”

Ted Lemon, winemaker at Littorai, *The World of Fine Wine*

"I like to see wines that peak at around ten years. I don't want my wines to develop into facsimiles of Burgundy. I just want them to get more interesting."

Ted Lemon, winemaker at Littorai, *The World of Fine Wine*

"Williams Selyem is largely a Dijon clones-free zone."

Bob Cabral, winemaker at Williams Selyem, in *In Search of Pinot Noir*

"In the mouth it carassed my palate like a candied ectoplasm that clung preternaturally until the last bit disappeared."

Miles in *Vertical*, by Rex Pickett

"The day a winemaker dumbs down and makes what everyone wants is the day he should retire."

David Hohnen, founder of Marlborough's Cloudy Bay Winery

"Liquid geography is what we do. All wine is about time and place."

Mike Weersing, winemaker at Pyramid Valley in North Canterbury, New Zealand

"No matter what anyone says, any truly great wine should always have a hint of corruption."

Danny Schuster, New Zealand winemaker and viticulturist

"Wine with flaws that are managed tend to make wines that have a bit more personality."

Erich Bradley, winemaker at Sojourn Cellars

"If you make a wine everyone loves, you've done something wrong."

Jay Somers, J Christopher Winery

"Organic and biodynamic producers considerably overstate the benefits of their approach to wine quality, consumers' health and the environment."

Richard Smart, viticulturist

"It's not a perfect system (biodynamics) but we're moving in the right direction. The 'voodoo' perception is lazy journalism. It's easy to knock something weird."

Monty Waldin, biodynamic winemaker and writer

"At the end of the day, it's all about farming for quality. If you farm for quality - whether you're organic, biodynamic, sustainable or conventional - you're going to make great wine."

Todd Hamina, Biggio Hamina Cellars, *Voodoo Vintners*

"When I buy a bottle of fine wine, I want something more than delicious jam warmed by alcohol. I want something that connects me to a place, that could not be made without that connection, made with such a strong connection that its character can live and develop in the bottle for years."

Joshua Green, *Wine & Spirits*

"I firmly believe that vineyard work is the route to balanced wine."

Jeff Brinkman, winemaker Rhys Vineyards

"I see a site, and somehow it just smells right."

Ted Lemon, winemaker at Littorai

"I think waiting for full physiologic ripeness is too late. Wine doesn't finish on the vine; it is still evolving in the winery, so I try to pick while the flavors and structure are still blossoming."

Jason Drew, Drew Wines

"If the wine is balanced....if you pick the fruit before it's really ripe....I know Sonoma Coast Pinot Noir can age."

Burt Williams, winemaker

"Wine quality is defined like pornography. We don't know what it is, but we know it when we see it."

Francis Percival, *The World of Fine Wine*

“Thankfully, many consumers and winemakers are beginning to favor a more elegant and refined style of wine. It is not that we seek less flavor, texture or depth; it’s simply that we understand abundance and generosity in wine is achievable without excessive extract and alcohol.”

Gary Farrell, winemaker Alysian Wines

“I like wine that sounds good and I like rock ‘n’ roll.”

Michael Browne, Kosta-Browne

“In the absence of any obvious faults, the more you pay for your wine, the better it will taste. Why? In part, because most of us expect more expensive wine to taste better.”

Professor Charles Spence, *The World of Fine Wine*

“The impact of great wine is as much emotional as sensorial and, in any case, at the topmost level one rapidly runs out of distinctive superlatives.”

Remington Norman, *Grand Cru*

“Our wines are made to live full and complete lives. We like to see them blossom, become complex, and then slowly decline into senility.”

Ted Lemon, winemaker at Littorai

“It is probably reasonable to define overripeness as the point when the dark-berry flavors, like blackberries and blueberries, are transformed to flavors of dark chocolate - a flaw that tends to reduce the distinction between wines, regardless of variety or terroir.”

Michel Bettane, *The World of Fine Wine*

“What makes a wine worth drinking is that it is honest and authentic.”

Terry Theise, *The World of Fine Wine*

“There’s a lot of good wines around. But the problem is that people don’t know how to get them to market.”

Stewart Resnick, Fiji water and Landmark Vineyards owner

“It doesn’t make economic sense to buy expensive wine and sit on it. It makes sense to buy wine you want and drink it right away.”

W Blake Gray, *The World of Fine Wine*

“Manipulation isn’t inherently evil, but I have serious reservations about stealthy and dishonest forms of it....The final ‘wine’ is little more than a device - a thing by which a consumer is seduced; a peak at cleavage, but the breasts aren’t real....The next thing you know, you’re drinking the stuff and calling it wine.”

Terry Theise, *The World of Fine Wine*

“Pink wine makes me slutty.”

Zoey Deschanel, singer and actress

My wife says I am busy with Pinot Noir every waking moment. Not true, I also dream about it.”

Rusty Gaffney, Prince of Pinot