

# WineHealth 2017 – Navigating the health effects of alcohol consumption

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***In February, the WineHealth 2017 international wine and health conference was held in Spain, the eighth in a series held since 1996. Approximately 200 delegates debated and discussed the latest data presented on the health effects of alcohol consumption, and considered future research directions. This article provides a summary of the trends discussed at that conference.***

## EFFECTS OF ALCOHOL CONSUMPTION ON NON-COMMUNICABLE DISEASES

Non-communicable diseases (NCD) such as cardiovascular disease (CVD), cancers, diabetes and dementia are major causes of death and disability across the world. The World Health Organisation (WHO) suggests CVD currently accounts for the most NCD deaths, or 17.7 million people annually, followed by cancers (8.8 million), respiratory diseases (3.9 million), and diabetes (1.6 million). As such there is considerable interest in understanding the risk factors for these diseases and any potential preventative measures that can be taken to reduce their incidence and severity. Modifiable behaviours, such as tobacco use, physical

inactivity, unhealthy diet and the harmful use of alcohol, all increase the risk of NCDs.

Numerous population-based studies have investigated the effects of consuming alcoholic beverages on the risk of these NCDs. Heavy alcohol consumption has been consistently shown to be a risk factor for cardiovascular disease, cancers, diabetes and dementia, while the health effects of light to moderate alcohol consumption (approximately 10 to 20g alcohol/day) on the risk of NCDs continue to be considered by public health authorities. In Australia, one standard drink is approximately 10g alcohol (Food Standards Australia New Zealand 2017). Although the majority of population-level

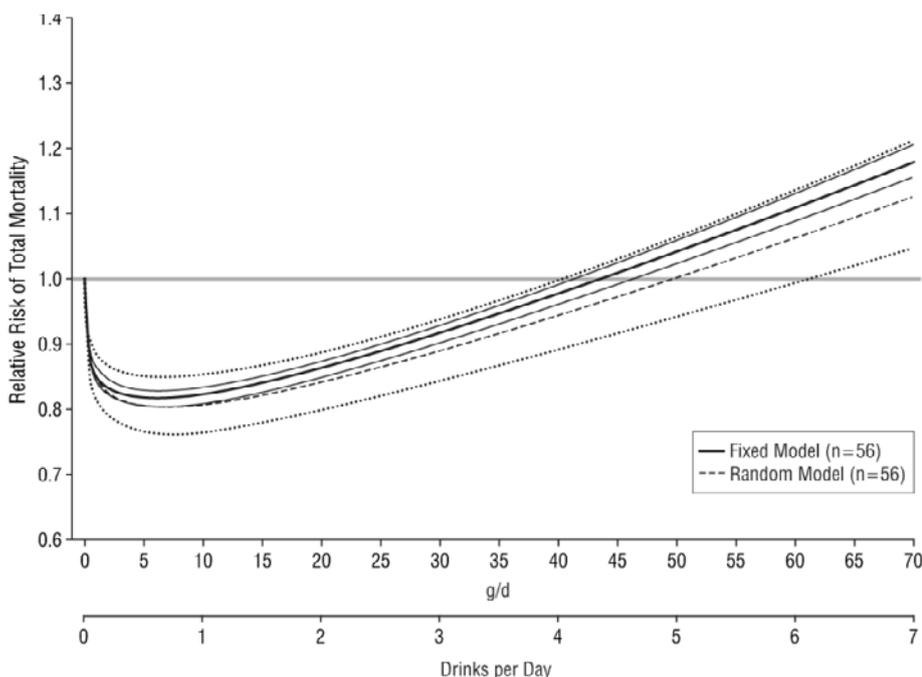
studies have not differentiated between wine, beer and spirit consumption, studies at the individual level have focussed on the different beverages.

Clinical studies are also being conducted to examine the effects of consuming light to moderate amounts of alcohol, and test tube and animal studies are exploring plausible potential biological mechanisms of actions for the effects observed.

### Cardiovascular disease

Cardiovascular disease includes high blood pressure, heart attacks, coronary heart disease, heart failure and stroke, and is currently the leading cause of death (33 percent of all deaths) in Australia. Of the 200 population-based studies conducted over the past 40 years, most have concluded the relationship between the consumption of alcoholic beverages and the risk of CVD is J-shaped for both men and women. Light to moderate alcohol consumers have approximately a 30 percent lower risk of CVD compared with non-drinkers and heavier consumers (Di Castelnuovo *et al.* 2006, Rehm *et al.* 2010).

While the inclusion of ex-drinkers in the non-drinking reference groups in many of these early studies may have increased the risk of disease for 'current abstainers' (Stockwell *et al.* 2016), a J-shaped curve has almost always been seen in more recent studies when only lifetime abstainers comprised the non-drinking category (Klatsky and Udaltsova 2007, Midlov *et al.* 2016, Ronksley *et al.* 2011). As of 2017, the vast majority of population-based studies show a J-shaped curve for the relationship between alcohol consumption and CVD and mortality. Protection against CVD and



**Figure 1. Relative risk of total mortality (95 percent confidence interval) and alcohol consumption extracted from 56 studies using fixed- and random-effects models (Di Castelnuovo *et al.* 2006).**

**AT A GLANCE**

- Consumers of light to moderate amounts of alcoholic beverages have lower risk of cardiovascular disease, type 2 diabetes, dementia and all-cause mortality than non-drinkers or heavy drinkers.
- The relationship between alcohol consumption and the risk of cancer is more complex. For some cancers, any alcohol consumption increases the risk. For other cancers, heavy drinking increases the risk and for some cancers there is a reduced risk or no association with alcohol consumption.
- Polyphenolic compounds present in wine, fruits and vegetables have many positive effects in the human body and may act in synergy with other dietary components, including alcohol.
- Consuming alcohol as part of a Mediterranean-style diet combined with other healthy behaviours (non-smoking, healthy weight, regular exercise) provides the greatest protection against the major non-communicable diseases.
- The next WineHealth conference will be held in 2019 at UC Davis, California.



mortality is not seen for drinking levels beyond 30 to 40g alcohol/day or for binge drinking patterns.

Dose effects vary for the different cardiovascular outcomes, with the lowest risk of mortality from coronary heart disease and heart attacks occurring with 10 to 20g alcohol/day, but the lowest risk of mortality from ischaemic stroke occurring with less than 10g alcohol/day (Ronksley *et al.* 2011). When alcoholic beverages are broken down by type, no statistically significant association is found between spirits consumption and CVD risk. However, both wine and beer show a similar J-shaped curve to that for alcohol overall. This may be reasonably explained by a combined effect of the alcohol present in both and of the different but similarly beneficial phenolic compounds in the two beverages (Costanzo *et al.* 2010).

In addition to the established biomarkers for CVD risk such as cholesterol concentration, blood flow and blood pressure, low grade inflammation was recently recognised as another risk factor for CVD as well as for cancer and neurodegenerative diseases. Wine-derived phenolic compounds can act to reduce low grade inflammation (Bonaccio *et al.* 2017, Gresele *et al.* 2011) as well as positively influence the other key biomarkers for CVD risk.

**Diabetes**

Diabetes mellitus is a set of related diseases in which the body cannot regulate the amount of glucose in the blood. Diabetics either do not produce any or enough insulin to regulate their blood glucose level (type 1 diabetes) or their body is less sensitive to the effects of insulin and increasingly ineffective at regulating their blood glucose levels (type 2 diabetes). Type 2 diabetes accounts for more than 85 percent of all incidences of diabetes and is currently the fifth highest cause of death in Australia (Australian Bureau of Statistics 2016). High blood glucose levels promote the development of atherosclerosis (build-up of lipid deposits inside the arteries), high blood pressure and high blood lipid levels, which increase the risk of a heart attack or stroke.

Similar to that for CVD, a J-shaped curve is seen for the relationship between the consumption of alcoholic beverages and risk of type 2 diabetes (Koppes *et al.* 2005, Tresserra-Rimbau *et al.* 2016). A 30 percent reduction in the risk of type 2 diabetes occurs with light to moderate alcohol consumption, as well as for the risk of heart attacks among type 2 diabetics. Reduced risk is also associated with a high intake of phenolic compounds, which are found in wine as well as in fruits and vegetables (Chiva-Blanch *et al.* 2013, Tresserra-Rimbau *et al.* 2013).

The primary protective effect of alcoholic beverages on the development of type 2 diabetes has been attributed to increasing insulin sensitivity, and reducing the spike in blood glucose (glycaemic response) that occurs after eating (Beulens *et al.* 2008, Joosten *et al.* 2008). Wine produces the greatest effect on blood glucose compared with beer and spirits, reflecting the fact that wine contains compounds other than alcohol that are physiologically relevant (Brand-Miller *et al.* 2007).

Light to moderate alcohol consumers, and particularly wine consumers, also appear to have a lower risk of developing metabolic syndrome which includes abdominal obesity, insulin resistance, low concentration of high density lipoprotein (HDL) cholesterol and high blood pressure (Tresserra-Rimbau *et al.* 2015). Metabolic syndrome is associated with an increased risk of developing both diabetes and CVD.

**Cancers**

The relationship between the consumption of alcoholic beverages and cancer is complex (Breslow *et al.* 2011, Cao and Giovannucci 2016). For example, the consumption of alcoholic beverages appears to linearly increase the risk of cancers of the upper aerodigestive tract (UADT; mouth, pharynx, larynx and oesophagus), colorectum and female breasts, particularly when more than 25

to 30g alcohol/day is consumed (Bagnardi *et al.* 2013, Bagnardi *et al.* 2015, Klarich *et al.* 2015). These cancers are specifically referred to as alcohol-related cancers. Food consumption at the time of drinking may lessen the risk (Dal Maso *et al.* 2002).

There appears to be a threshold (>50g/day) above which alcohol consumption increases the risk of cancers of the stomach, liver, gallbladder, pancreas and lung. The consumption of wine (but not other alcoholic beverages) appears to be inversely associated with a risk of kidney cancer, Hodgkin's and non-Hodgkin's lymphoma.

While the alcohol component of wine is carcinogenic, a Western Australian study suggests that a diet high in flavonoids sourced from tea, chocolate, fruit, vegetables and red wine may be associated with a reduced risk of cancer, as well as that of CVD and overall mortality (Bo *et al.* 2016, Ivey *et al.* 2015). Wine-derived resveratrol as well as catechin, gallic acid and quercetin all appear to have potentially preventative effects, especially for colon cancer, which is the second most common cancer in Australia. With a grant from Cancer Australia, the AWRI is working in partnership with The Royal Melbourne Hospital to investigate the impact of daily consumption of resveratrol-enhanced wine on the risk of colorectal cancer. Potential mechanisms of action for this apparent anti-carcinogenic effect include protection of cells and DNA from damage leading to cancer, preventing damaged DNA replication and damaged cell growth, as well as initiating the death of damaged cells.

Of all lifestyle factors related to cancer, the attributable risk for tobacco use is 20.1 percent, physical inactivity 5.6 percent, body mass 3.9 percent, and alcohol consumption 3.1 percent (Begg *et al.* 2007, Begg *et al.* 2008). Synergies are also observed between alcohol consumption and other lifestyle choices. Recent studies on alcohol consumption and the risk of cancers of the UADT suggest tobacco use is the most important factor in the risk of these cancers, and that the risk is enhanced among those who also consume two or more alcoholic drinks per day. Alcohol consumption alone among non-smokers had little effect on the risk, except for oesophageal cancer (Anantharaman *et al.* 2011, Dal Maso *et al.* 2016, Hashibe *et al.* 2009, Szymanska *et al.* 2011).

For the relationship between alcohol

consumption and breast cancer, consumption patterns may modify risk, with consumption of four to five drinks per session increasing risk by 50 percent compared with only one drink per session. Broadly speaking, increased risk of cancers appears most related to alcohol consumption above low to moderate levels.

### Dementias

The collective scientific word for the mental processes of thinking, remembering, reasoning, judging and learning is 'cognitive function'. Dementia is a form of cognitive change or impairment (dys-function) where a person loses the ability to think, remember and reason due to physical changes in the brain.

Cognitive decline and dementias such as Alzheimer's disease appear to be triggered by a range of factors including depletion of antioxidants and inflammation. Risk factors for vascular dementia also include high blood pressure and coronary heart disease. In the later stages of dementia, the associated cognitive impairment creates total dependency, such that dementias are the single greatest cause of disability in Australians aged 65 years or older, and the third leading cause of disability burden overall. Dementias are also currently the second highest cause of death in Australia. As there is no cure, identification of factors associated with the preservation of cognitive function could lead to substantial improvements in the quality of life in older Australians.

A J-shaped relationship between alcohol consumption and the risk of cognitive decline and development of dementias has been consistently observed (Ilomaki *et al.* 2015). Light to moderate alcohol consumption appears to reduce the risk of cognitive impairment, although heavy consumption is toxic. This relationship is observed for younger, middle-aged and older consumers. There is also a relationship between the effects of alcoholic beverages on the cardiovascular and neurological systems, given that reducing the risk of hardening and narrowing of the arteries and coronary heart disease also lowers the risk of cognitive impairment.

The amount of alcohol generally associated with protection against dementias appears to be up to 30g alcohol daily, where wine may have a greater effect than beer or spirits, although this finding is based on a relatively small number

of studies (Neafsey and Collins 2011, Xu *et al.* 2017). There are also multiple plausible biological mechanisms for wine-derived phenolic compounds to act on the accumulations of protein in the brain which are present in Alzheimer's disease (Pasinetti 2012).

### MORTALITY FROM ALL CAUSES

The J-shaped relationship with the consumption of alcoholic beverages also applies to the risk of death from all causes, with an approximate 20 percent lower risk of death for light to moderate alcohol consumers compared with non-drinkers (Corrao *et al.* 2004, Costanzo *et al.* 2011). Risk increases, however, with consumption over approximately 40-60g alcohol/day (Figure 1). This relationship is evident after controlling for known socio-demographic factors, genetic factors, lifestyle factors such as smoking, diet, and exercise, and diseases such as diabetes and previous coronary heart disease. That is, the observed effect of light to moderate alcohol consumption cannot be attributed to any of these other factors (Behrens *et al.* 2011, Dai *et al.* 2015, Midlov *et al.* 2016).

### WINE AS PART OF DAILY DIET AND LIFESTYLE

A series of large longitudinal studies looking at nutrition and healthy ageing in Australia (Dubbo Study of the Elderly), Italy (Moli-Sani) and Spain (PrediMed) have all shown that the inclusion of moderate alcohol consumption as part of a healthy diet and lifestyle reduces the risk of NCDs. Alcohol and phenolic compounds present in wine and beer may act in synergy with each other and with other dietary components, meaning that total diet may be more important than a single dietary component (Buil-Cosiales *et al.* 2016, Estruch *et al.* 2013).

Subjects in large population studies who are non-smokers, are not obese, eat a Mediterranean-style diet, and get regular exercise have much lower risk of NCDs and total mortality, whether or not they consume alcoholic beverages. Mukamal *et al.* (2006) observed, however, that regardless of other 'healthy' lifestyle factors, moderate consumption of alcoholic beverages provided a greater reduction in the risk of these diseases than was seen for the other factors in isolation (Mukamal *et al.* 2006).

### A MAJOR NEW CLINICAL STUDY

The definitive experiment to determine any clinical association is a double-blind placebo-controlled clinical study. No long-term experimental study of the effects of alcohol consumption on the risk of any chronic disease has been performed. In September 2016, the US National Institute on Alcohol Abuse and Alcoholism received funding to conduct a large, international, randomised but unblinded clinical trial of the effects of alcoholic beverages on cardiovascular diseases and diabetes. Its aim is to better determine the strengths of relationships observed to date in population studies, the results of which will undoubtedly influence subsequent alcohol drinking guidelines (Mukamal *et al.* 2016). Australia is striving to participate in this study.

### LOOKING AT THE BIG PICTURE

The relationships between alcohol consumption and risk of CVD, dementias and diabetes are all J-shaped, with lower risk for low to moderate alcohol consumers than either abstainers or heavy

drinkers. The relationship for alcohol-related cancers is different, with alcohol consumption linearly increasing risk. When all-cause mortality is considered, the J-shaped curve is seen again, with light to moderate alcohol consumers having reduced risk of death from all causes (Chiva-Blanch *et al.* 2013, Ferrari *et al.* 2014, Howie *et al.* 2011). This association is dependent, however, on both the amount and pattern of consumption, and may be modified by patterns such as binge drinking (Bobak *et al.* 2016, Graff-Iversen *et al.* 2013).

In addition to this population-based data, the accumulating experimental evidence continues to support an apparent role for light to moderate alcohol consumption in preventing many NCDs.

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