Alcohol consumption and cancer: there's more to the story - a perspective from Australia

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The Alcohol Policy Coalition published a position statement entitled Cancer, Cardiovascular Disease and Alcohol Consumption on 19 September 2011, which sought to provide rationale for alcohol policy reform in Australia[1]. This position statement provided some of the story, and the rest of the story is provided here.

It is well documented and cannot be disputed that the consumption of alcohol above the Australian National Health and Medical Research Council's (2009)[2] recommendations of not more than two standard drinks(10g)/day for both men and women is associated with adverse health effects. These can be short-term effects such as accidents, drowning and suicides generally associated with binge drinking patterns, that is, a large amount consumed in a small period of time. These can also be long-term effects associated with continuous heavier consumption, over many years, such as alcohol-related cardiovascular disease, cancers, liver cirrhosis and pancreatitis.

It is also well documented, however, in peer-reviewed published data over more than three decades that light-to-moderate alcohol consumption, that is, approximately corresponding with the recommended not more than two standard drinks/day for both men and women, is associated with a reduced risk of developing and dying from cardiovascular diseases, selected cancers, diabetes, and cognitive function disorders such as dementia[1,2,3,4,5,6,7,8]. This equates to a reduced risk of dying from all or any causes including cardiovascular diseases and cancers, and is in comparison to both abstainers and heavy consumers. These relationships are best described as j-shaped and are most relevant for individuals aged over 40-45 years, that is, in particular for those who are at greater risk of cardiovascular disease[9].

Alcohol and cardiovascular disease

The j-shaped relationship between the amount of alcohol consumed (g/day) and the relative risk of developing cardiovascular diseases has probably been most publicised[10,11,12]. Light-to-moderate drinking is considered as 10 to 20 g alcohol/day or 1 to 2 standard drinks/day, and is associated a reduced risk of atherosclerosis (hardening and rigidity of the artery wall), high blood pressure, heart attacks, heart failure and ischaemic strokes from blockages of brain blood vessels.

For example, blood pressure increases after approximately two standard drinks/day for women and three standard drinks/day for men. High and high-normal blood pressure is having a systolic pressure of 130 to 139 mm Hg and/or diastolic pressure of 85 to 89 mm Hg[13]. The relationship between blood pressure and amount of alcohol consumed is then linear, an approximate 1 mmHg increase in blood pressure for each standard drink consumed. Another cardiovascular risk factor is arrhythmias or atrial fibrillation, also referred to as 'holiday heart syndrome' as they often occur with binge drinking heavy or excessive amounts on a long weekend or during holidays. This is a changed or disturbed sequence of electrical impulses causing your heart to beat either too slowly or too fast and/or irregularly, which can cause your heart to pump less effectively. The symptoms are dizziness, palpitations, shortness of breath, and chest discomfort or pain, as well as sudden death.

Eighty per cent of strokes are diagnosed as ischaemic and 20% are diagnosed as haemorrhagic (bleeding of the brain blood vessels). Drinking heavy or excessive amounts of alcohol can increase the risk of both forms of stroke. Heavy drinking can actually increase the formation of blood clots via alcohol's effects on heart muscle and on heart beats and which can block an artery in the brain. Conversely, the increased blood pressure from heavy drinking can cause an artery in the brain to rupture where the bleeding into the brain is greater due to the decreased formation of blood clots and the increased breakdown of blood clots.

The risk of all these adverse effects on the cardiovascular system reduces and reverses when alcohol consumption is reduced from heavy to light-to-moderate[14,15,16,17,18]. Indeed, light-to-moderate alcohol consumption is associated with reduced cholesterol or fat deposits in arteries (atherosclerosis), protection against the formation of blood clots, and promotion of the break down of formed blood clots, all of which protect against heart attacks and ischaemic strokes. The alcohol component of all alcoholic beverages, combined with wine-derived phenolic compounds, are responsible for these biological effects.

This j-shaped relationship is acknowledged by the World Health Organisation[9,19] and its recommendations specifically refer to harmful or heavy alcohol consumption. While the impact of alcohol consumption on health varies between individuals, on a global level, the protective effects of light-to-moderate alcohol consumption outweigh the adverse effects of heavy alcohol consumption on cardiovascular disease. For example, as moderate alcohol consumption reduces the risk of cardiovascular disease by approximately 25% [20,21], all alcohol consumption combined actually accounts for - 4.7% of the total cardiovascular disease burden in Australia.

Alcohol and cancer

Specifically, the ethanol component of all alcoholic beverages and its primary breakdown product, acetaldehyde, are toxic to the cells, organs and tissues of the body[22]. They are also carcinogens in humans as defined by the International Agency for Research on Cancer (IARC) in 1988 and in 1998. For example, both ethanol and acetaldehyde initiate, promote and progress cancer by directly mutating critical cells and stimulating their growth. The occurrence of malignant tumours of the oral cavity, pharynx, larynx, oesophagus (collectively known as the upper aero-digestive tract) and liver is causally related to the consumption of alcoholic beverages, as well as of the colon and rectum in men where the mucosal lining of the tract comes in direct contact with ethanol and acetaldehyde to mutate cells, and malignant tumours of the breast in women indirectly due to the alcohol-stimulated liver metabolism of estrogen. Indeed, alcohol consumption is associated with an increased risk of selected cancers, but not of all cancers.

Data suggest that in 2003 alcoholic beverages accounted for approximately 3.1% of the total cancer burden in Australia (that is, 3.1% of the years of life lost due to premature death from cancer and years of healthy life lost due to disability from cancer)[23,24]. This figure was increased to 3.5% in 2005 and the Cancer Council of Australia suggests that this figure is now 5% when cancers of the colon and rectum are included in calculations.

It is also known that the cumulative effect of other lifestyle choices with alcohol also contributes to the occurrence of cancer. Of all lifestyle factors related to cancer, the attributable risk for tobacco is approximately 20%, that for diet is 20-50%, that for physical inactivity is 5.6% and that for alcohol is 4-6%[25,26,27].

Unlike cardiovascular disease, the overall relationship between alcohol consumption and cancer is linear, where the risk increases as the consumption of an alcoholic beverage increases[28]. The relationship, however, is complex. Low consumption hence suggests relatively low risk. In addition, there may be threshold effects in the relationship between alcohol consumption and the risk of cancers as well as other contributing factors. For cancers of the upper aero-digestive tract, liver, colon and rectum, the risk only increased when more than 25 g alcohol/day was consumed[29]. It has also been suggested that the risk of developing a cancer of the aero-digestive tract is less when alcohol is consumed with food[30]. A recent comprehensive review of more than 7,000 peer-reviewed papers on the association of lifestyle factors and cancer undertaken by the World Cancer Research Fund, in cooperation with the American Institute for Cancer Research (2007)[31], reports that there are alcohol threshold effects for cancers of the colon and rectum. The review reports that an increased risk for cancers of the colon and rectum is only apparent above a threshold of 30 g alcohol/day for both men and women. The fact that not all heavy drinkers develop cancer and that some light-to-moderate drinkers develop cancer, suggests that an individual's genetics also influences their risk of developing cancer. A recent analysis of 27 cohort and 34 case–control studies by Fedirko et al. (2011)[32] also suggested that there is an increase in risk (21%) for consumers averaging up to 49.9 g alcohol/day, but that the increase in risk was significantly greater (52%) for consumers of more than 50 g alcohol/day or five standard drinks/day. In addition, only approximately 10 to 15% of alcohol dependent drinkers develop cirrhosis of the liver and, of those, only 10% develop liver cancer[33].

Recent case-control analyses by Anantharaman et al. (2011)[34] and Szymańska et al. (2011)[35] of alcohol and the risk of cancers of the upper aero-digestive tract (UADT) also suggest that 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. An important observation was that among former alcohol consumers and former smokers, the increased risks associated with alcohol and tobacco use

decreased steadily as the time since quitting increased. For example, from Anantharaman et al. (2011)[34] concurrent tobacco use and alcohol consumption accounted for 73% of total UADT cancer burden in the European Union. This can be broken down to tobacco use alone accounted for 28.7%, alcohol consumption alone accounted for only 0.4%, but the combination of smoking and drinking accounted for 43.9% of the population attributable risk.

Concerning the relationship between alcohol and breast cancer, it has been suggested that the relationship is linear[36,37,38] or that the relative risk of breast cancer always increases (monotonically increases)[39,40,38] for the average daily amount of alcohol consumed. It has also been suggested that consumption patterns may modify risk[41], such that the consumption of four to five drinks consumed per session may increase/double risk by 50% compared to only one drink consumed per session. Paradoxically, alcohol dependence does not increase the risk of breast cancer[42]. Alcohol consumption is also more strongly associated with hormone sensitive (estrogen receptor positive) breast cancers than those insensitive to hormones (estrogen receptor negative)[43,44,45,46]. The concurrent consumption of alcohol and folate (at least 300 mg/day of folate) has been observed to reduce the relative risk of alcohol-induced breast cancer from 1.24 to 1.05 for women consuming greater than 15 g alcohol/day or one and a half standard drinks, and was reduced to 0.55 for women consuming greater than 600 mg/day of folate. This implies that folate protects against developing breast cancer. Indeed, the concurrent consumption of folate-containing vitamin supplements reduces the relative risk to 0.74 for women consuming greater than 15 g alcohol/day compared to those not using vitamins[47]. The interaction between alcohol and folate has been observed to be primarily limited to estrogen receptor negative breast cancer tumors[43,44,45]. This observation is consistent with an interaction of alcohol and folate on breast tissue tumors being mainly through the primary metabolite of alcohol, acetaldehyde, which is directly carcinogenic as well as indirectly carcinogenic by depleting folate, independent of circulating estrogens medical estrogen receptor-mediated events. Furthermore, a recent multivariable-adjusted analysis of 2,944 invasive breast cancer cases, suggested that alcohol consumption was associated with an increase in the risk of lobular carcinoma (which comprises approximately 15-20% of breast cancers), but was not necessarily associated with the more-common ductal carcinoma[48]. For women consuming up to 12 g alcohol/day, the risk of developing breast cancer was lower for wine consumers than for consumers of other alcoholic beverages.

A relatively recent review of alcohol and cancer stated that drinking, especially heavy drinking, increases cancer risk[49]. It concluded that "Total avoidance of alcohol, although optimum for cancer control, cannot be recommended in terms of a broad perspective of public health, in particular in countries with high incidence of cardiovascular disease."

Concluding thoughts…

Population ageing is occurring on a global scale, with faster ageing projected for the coming decades than has occurred in the past. Globally, the population aged 60 years and over is projected to nearly triple by 2050, while the population aged 80 years and over is projected to experience a more than five-fold increase.

Life expectancy for Australians has also increased significantly, and between now and 2050 the number of older individuals (65 to 84 years) is expected to more than double; and very old individuals (85 and over) are expected to more than quadruple from 0.4 million people today to 1.8 million in 2050[3]. Increased numbers of older individuals may have implications for associated expenditure on income support, housing and health services, although a healthy, independent older population can also form a valued social resource, for example in providing care for others, sharing skills and knowledge and engaging in volunteer activities. Evidence is mounting that older people can also increase the quality of later life.

Established in 1987, the Dubbo Study is Australia's first and longest running longitudinal study of healthy ageing, involving 2,805 non-institutionalised Dubbo residents (1,233 men and 1,572 women). Mean age at entry was approximately 70 years. The study investigated risk factors for mortality, hospitalisation and institutional or nursing home care, including cardiovascular disease and dementia, in order to provide a template for 'healthy ageing'. Interestingly, the study has observed that one alcoholic drink per day may reduce the risk of dementia by 35% for both men and women, and that independent risk factors for mortality include diabetes, very high blood pressure, cholesterol imbalances and zero intake of alcohol[50]. Indeed, managing blood pressure and cholesterol in

older Australians has been shown in clinical studies to reduce the risk of cardiovascular disease and stroke and consequently the risk of all cause mortality. The results showed that alcohol consumption amongst the study subjects was moderate, less than 14 drinks/week, which was found to be associated with significantly longer survival in men up to the age of 74 years and in all elderly women. Men drinking any alcohol lived on average 7.6 months longer, and women on average 2.7 months, compared with non-drinkers. Interestingly, in men there was no evidence of a differential effect between one to two drinks on a given day and an intake of five or more drinks on a given day.

Another, but little publicised, Australian study similarly followed 7,989 individuals aged 65-83 years for five years[51]. One of eight selected low-risk behaviours was having no more than two alcoholic (total 20 g alcohol) drinks/day. Individuals with five or more of the selected low-risk behaviours, including light-to-moderate alcohol consumption had a lower risk of death from any cause within five years compared with those having less than five low-risk behaviours. More importantly, the study showed that while most individuals already have some healthy habits, almost all could make changes to their diet and lifestyle to improve their health.

Consequently, simple dietary measures such as light-to-moderate alcohol and wine consumption to supplement a healthy exercise and nutrition routine, or as an adjunct to prescription medicines when appropriate, may thus be needed to maintain an ageing population.

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