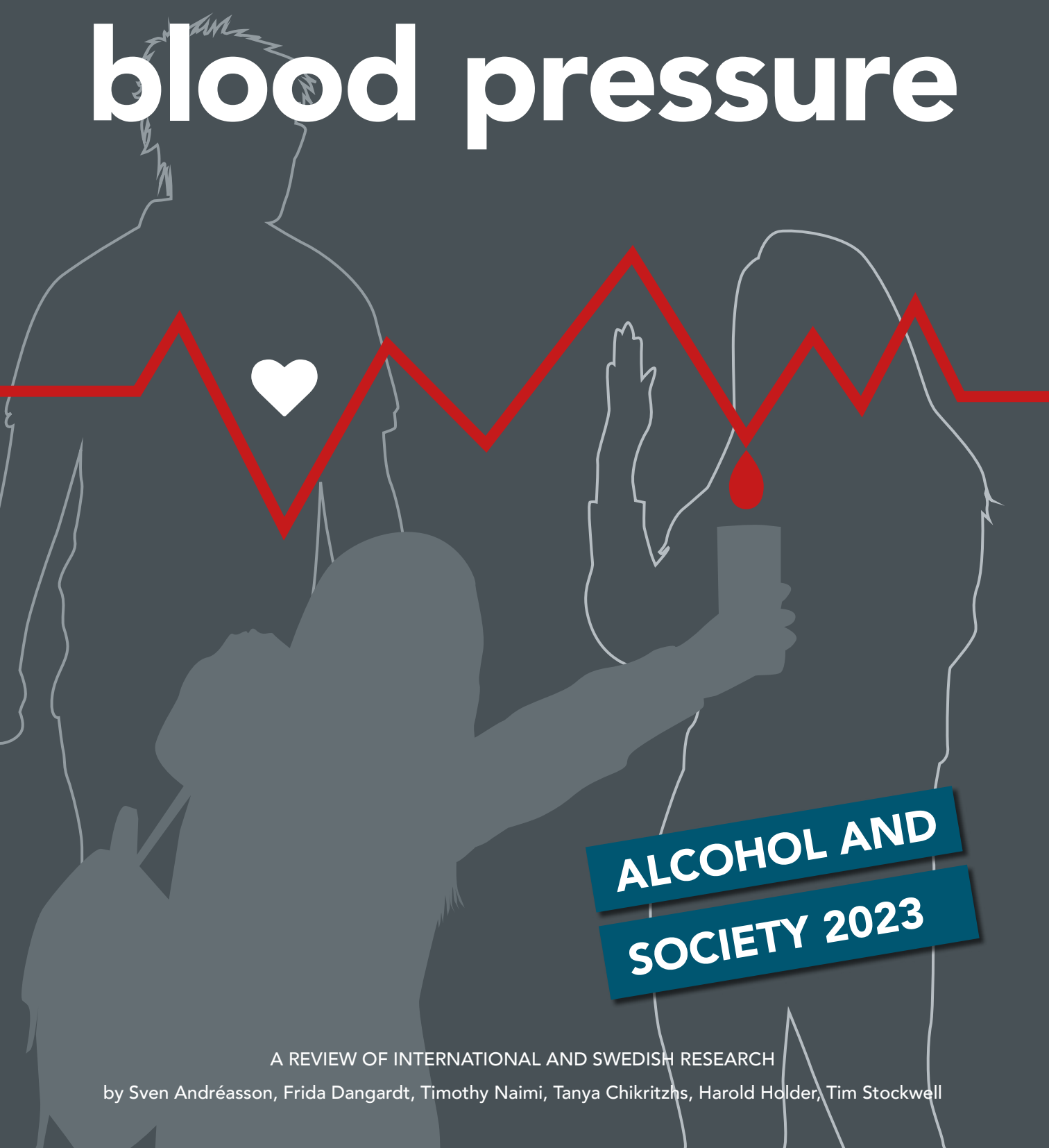
Alcohol and blood pressure



ALCOHOL AND SOCIETY 2023

A REVIEW OF INTERNATIONAL AND SWEDISH RESEARCH

by Sven Andréasson, Frida Dangardt, Timothy Naimi, Tanya Chikritzhs, Harold Holder, Tim Stockwell

Organisations initiating this report are voluntary or academic organisations independent of commercial interests.

SFAM is the professional and scientific college of general practitioners (family physicians) in Sweden with continuing professional development, training of future GPs, assessment of competence, quality improvement and research in general practice/family medicine as main areas of interest.

The Swedish Society of Nursing is a nonprofit organization and a forum for discussing and developing nursing care by promoting nursing research, ethics, education and quality in nursing.

IOGT-NTO focuses on the effects of alcohol and narcotics on individuals and society, but is also engaged in broad social and club activities.

The foundation **Stiftelsen Ansvar För Framtiden** aim to further Nordic cooperation and scientific research regarding sober life styles, public opinion in this regard, as well as care of children. The foundation have eight member organisations in three Nordic countries.

CERA is an interdisciplinary and collaborative centre for education and research into hazardous use, abuse and addiction at Gothenburg University – which works to strengthen and develop research and education in the field of addiction, and to disseminate scientific expertise to people working professionally in the field of abuse and addiction, and other interested parties.

The **Swedish Society of Addiction Medicine** works to promote research and education in the addiction medicine field, and professional development in all specialist care professions.

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Introduction

This report about Alcohol and Hypertension marks the 9th report produced by an international group of medical and public health researchers from Canada, Australia, United States, and Sweden. This group convenes each year without compensation to produce a report about a unique topic concerning alcohol. This report and all of its predecessors have the goal to evaluate the most relevant published scientific research from around the world and to provide a summary of the best knowledge on that topic.

One key goal of this work is to ensure not only that best evidence is presented but that summaries and discussions are readable and understandable by a non-scientific audience. In short, it is important to our group that we make our summaries of scientific knowledge understandable and practically usable. This goal is to ensure that science has an ongoing valid role in and contribution to civil society.

This report as with all others is undertaken in two major steps. First, an extensive search is completed to identify relevant published science. Second, the search results are reviewed and summarized. This is done by in-person discussions and evaluation of the strength of scientific methods of studies by the group as well as opportunity to discuss each written draft in total as a group. In the end, all authors contribute writing, reviews, and edits to all sections of the report. The result is truly a group product extending over several months.

Such an intention to summarize the best scientific research in a useable form is a personal value shared by all members of the group as a means to support evidence-based approaches and policies concerning alcohol as a practical means to contribute to better public health in Sweden as well as all other countries. This collaborative work affords an opportunity for each of us to participate in the preparation of such a report but especially so with an international group of our colleagues. We look forward to coming together this year to work on our next topic: "Alcohol and the Brain".

Harold D. Holder
PhD Chair

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Executive summary

- The focus of this report is alcohol's neglected role as a contributing cause of hypertension, itself the leading cause of heart disease, stroke, type 2 diabetes and dementia.
- Alcohol's causal role in hypertension is supported by (i) physiological research considering effects on the heart and blood vessels (ii) epidemiological research describing associations over time between alcohol use, blood pressure and hypertension.
- High quality clinical and experimental studies show that alcohol intake increases blood pressure, especially in the hours and days after consumption and for higher levels of consumption.
- High quality epidemiological studies show alcohol intake aggravates mechanisms that lead to hypertension, such as inelasticity and thickness of arteries. Such effects are most evident with the common patterns of binge drinking, whether occasional or regular.
- High quality studies with randomization find no evidence that low level alcohol use has beneficial effects on blood pressure or hypertension. Mendelian randomisation studies compare outcomes for people with and without genetic intolerance to alcohol and so minimize confounding and reverse causation. These find strong positive relationships between alcohol use and blood pressure, with no protection from low or moderate levels of consumption.
- Observational studies also find consistent evidence of alcohol's negative impact on hypertension, especially for people with binge drinking.
- There is increasing scientific scepticism for the once widely held belief that low or moderate levels of consumption can provide protection from cardiovascular diseases. Biases in uncontrolled, observational studies can create the appearance of such protection. However, studies with stronger designs (e.g. with Mendelian randomisation) find only negative relationships between alcohol use and risk of ischaemic heart disease and stroke, for example.

- Recognition of alcohol's substantial causal role in the genesis of hypertension and related disease is belatedly being recognised in clinical guidelines for the management of high blood pressure.
- General guidelines on alcohol consumption and health have been lowered in many countries reflecting growing scepticism of health benefits and evidence of harm at even low levels of consumption.
- While screening and appropriate interventions for those identified with hazardous alcohol use may work in some cases, practitioners need more incentives, training, and specialist support for these to be implemented more widely and effectively.
- Alcohol is often neglected in primary prevention and is viewed by practitioners and their patients as less important than regular exercise, diet and not smoking for prevention of hypertension and other diseases.
- The most cost-effective means of reducing hypertension and related health harms in a population are policies which reduce overall population alcohol consumption.
- We therefore recommend governments introduce policies to reduce the affordability, availability and acceptability of alcohol to reduce consumption and improve health.
- We recommend that risks posed by alcohol consumption to elevated blood pressure and hypertension be highlighted in clinical guidelines, on alcohol warning labels and in primary care interventions.
- We recommend individuals reduce their consumption to no more than one Swedish standard drink per day on most days and avoid more than two drinks on a single occasion.

High quality clinical and experimental studies show that alcohol intake increases blood pressure, especially in the hours and days after consumption and for higher levels of consumption.

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Sven Andréasson is senior professor in social medicine at the Department of Global Health, Karolinska Institutet, Stockholm. He is also senior consultant at the health center Riddargatan 1 at the Stockholm Center for Dependency Disorders.

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She has qualifications in epidemiology and biostatistics, some 20 years experience in alcohol research and a national profile as an expert in her field. Her research covers many areas of alcohol policy and alcohol epidemiology, such as alcohol consumption, alcohol related harms, alcohol taxation, liquor licensing, alcohol and heart disease, and alcohol and cancer.

She has received many awards including the prestigious Commonwealth Health Ministers Award for Excellence in Health and Medical Research and an NHMRC Achievement Award (1st ranked in Population Health).

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Harold Holder, Ph.D., is a Senior Research Scientist Emeritus and the former Director of the Prevention Research Center (PRC) of the Pacific Institute for Research and Evaluation, a national center for prevention research, located in Berkeley, California, USA.

Dr. Holder holds a doctorate in communication science and mathematical sociology from Syracuse University. He has explored two major alcohol research areas: the prevention of substance abuse, and the cost and benefits of alcoholism and drug abuse treatment and published work on the impact of changes in retail sales of wine and spirits on drinking and alcohol-involved traffic crashes. His policy studies also include assessments of the prevention potential of alcohol server liability, mandated server training, and environmental strategies as part of comprehensive approaches to prevention. Dr. Holder

has undertaken a series of collaborative studies in the Nordic Countries to study the effects of public policies. These collaborations with researchers from Sweden, Norway, and Finland concern the role and changes in alcohol policy resulting from membership or association in the European Union. In addition, Dr. Holder has participated with prevention scientists from a dozen countries in international projects to document the effects of alcohol policy. The projects have produced three books in which he was a co-author, Alcohol Policy and the Public Good (1994), Alcohol: no ordinary commodity – Research and public policy (2003) and Alcohol: no ordinary commodity, second edition (2010). His most recent professional work has entailed working with a number of U.S. states and local communities on the application of prevention science to practice.

Recently Dr. Holder chaired an international research group in an evaluation of Swedish research on alcohol, narcotics, doping, tobacco and gambling for the Swedish Council for Working Life and Social Research. The evaluation report was published in 2012.

Dr. Holder has received the 1995 Jellinek Memorial Award, awarded for distinction gained by advancing knowledge about alcoholism or fostering its study, treatment, or prevention.

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Tim Stockwell is scientist at, and was Director from 2004 to 2020 of, the Canadian Institute for Substance Use Research (formerly the Centre for Addictions Research of BC), University of Victoria, BC, Canada. He was previously Director of Australia's National Drug Research Institute and Director of Australia's Alcohol Education and Research Foundation. He is member of Canada's National Alcohol Strategy Advisory Committee and of WHO's Technical Advisory Groups on a) alcohol and drug epidemiology b) alcohol labelling.

Tim Stockwell holds degrees from Oxford University (MA Hons, Psychology and Philosophy), University of Surrey (MSc Clinical Psychology) and the University of London (PhD Institute of Psychiatry). His research has covered many aspects of substance use policy, prevention, treatment methods, liquor licensing issues, taxation and the measurement of drinking patterns and their consequences.

He is a Fellow of the Royal Society of Canada and past recipient of the 2013 international E.M. Jellinek Memorial Award for Outstanding Research on Alcohol Policy.

PHOTO: THIRDMAN/PEXELS

1 Introduction

In this report we explore a neglected topic in the prevention of ill-health and premature mortality globally: alcohol use as a contributing cause of high blood pressure. High blood pressure is, in itself, a leading cause of a host of serious illnesses and fatal conditions (e.g. heart disease, stroke, type 2 diabetes, dementia). As a consequence of its wide-ranging ill effects on the human body, high blood pressure is one of the most significant and pressing challenges faced by public health today.

We review evidence regarding physiological mechanisms and disease risk whereby alcohol use at different levels affects blood pressure both in the short and longer term and discuss implications for the prevention of related diseases. The role that alcohol consumption can play in the development of high blood pressure is not well understood by the general public, by healthcare providers or by health policymakers. We also discuss untapped potential for improved clinical practices and broad-based population-wide policies to prevent ill-health and prolong life.

1.1 What is blood pressure?

Put simply, blood pressure is a measure of the maximum force on artery walls created by the pumping of blood around the body. Blood pressure is vital to life, it is the means by which blood is able to circulate and support all essential physiological functions (e.g. oxygen, nutrient delivery, hormone transport, waste and toxin removal).

Maximum blood pressure varies as the heart beats to maintain circulation. Standard measurement of blood pressure at a point in time therefore incorporates two components referred to as, 'systolic' blood pressure and 'diastolic' blood pressure. Systolic blood pressure measures force while the heart beats and diastolic blood pressure is the force between beats as the heart rests. Normal, healthy blood pressure is usually defined as less than 120 millimetres of mercury (mmHg) systolic pressure and 80 millimetres of mercury (mmHg) diastolic pressure, i.e. 120/80. Millimetres of mercury simply refers to the number of millimetres that a column of mercury would rise in response to a particular pressure.

1.2 What is high blood pressure (hypertension)?

Blood pressure is considered elevated and in a state of 'prehypertension' when systolic pressure is 120–129 mmHg and diastolic pressure is less than 80 mmHg. High blood pressure or 'hypertension' is present when systolic blood pressure exceeds 130 mmHg and diastolic blood pressure exceeds 80 mmHg,[1,2] although other limits can be used when treating hypertension.

In order to study effects of blood pressure it should be measured in a standardised way. Check-lists for blood pressure measurements typically include making sure the individual is comfortably seated at least five minutes before reading, with the arm resting on a table at chest height (e.g. https://www.cdc.gov/bloodpressure/measure.htm).

As a consequence of its wide-ranging ill effects on the human body, high blood pressure is one of the most significant and pressing challenges faced by public health today.

Globally, hypertension is the single largest preventable risk factor for morbidity and premature death. It is the largest risk factor for premature deaths in all the four world regions.

1.3 Importance of high blood pressure globally

The magnitude of human ill-health attributable to high blood pressure (hypertension) is truly remarkable. Globally, hypertension is the single largest preventable risk factor for morbidity and premature death. It is the largest risk factor for premature deaths in all the four world regions.[3] Hypertension is a leading cause of common cardiovascular diseases such as ischaemic heart disease and stroke as well as a contributing cause for common non-vascular conditions e.g. type 2 diabetes.[4–6]

One of the global targets for noncommunicable diseases as stated by the World Health Organisation (WHO) is to reduce the prevalence of hypertension by 33% by 2030.[7] Global trends, however, appear to be moving in the opposite direction and according to the Global Burden of Disease Study[3], from 2010 to 2019 prevalence of high blood pressure increased in all regions of the world. A longer estimation of global trends from 1990 to 2019[8] found that the number of people aged 30–79 years with hypertension doubled; 331 (95% credible interval 306–359) million women and 317 (292–344) million men in 1990 to 626 (584–668) million women and 652 (604–698) million men in 2019. These increases are largely due to population growth skewed towards older populations over time, as global age-standardised prevalence has remained stable. Nonetheless, two-thirds of the 1.28 billion adults with high blood pressure live in low- and middle-income countries where treatment and control rates are generally much lower than for high-income countries.[7]

Reflecting the enormity of the burden of disease due to high blood pressure, costs of treatment and control that accrue to both individuals and national health budgets are staggering (e.g.[9–13]). In the USA for example, average total annual cost of hypertension over 2012 and 2013 exceeded 51 billion USD.[11] Ischaemic heart disease, for which high blood pressure is the lead cause, has been described as "…a major cause of catastrophic health expenditure."[14, p.51] with healthcare costs in the USA projected to increase by more than 40% from 2010 to 2040.[15]

In 2012 the global economic cost of heart failure on healthcare systems, premature mortality and lost productivity was estimated at $108 billion annually and is set to increase rapidly as populations age.[16] As such, ongoing efforts aimed at improving effectiveness of clinical practice, health systems, guidelines, and global policy have been considerable (e.g.[17]). Likewise, investment in research focused on pathophysiology, genetics and new pharmacological treatments has been extraordinary.[18]

1.4 Physiology of high blood pressure and consequences for health

When the heart contracts, blood inside the left ventricle is forced out into the aorta and arteries. The blood then enters small vessels with muscular walls, called arterioles. The tone in the muscular walls of the arterioles determines how relaxed or constricted they are. If narrowed, they resist flow. Reduced flow of blood is detected in the brain, the kidneys and elsewhere. Nerve reflexes are stimulated and hormones are then produced. The heart is induced to beat more forcefully so that blood pressure is maintained at a higher level, to overcome the restricted flow through the arterioles. The achievement of good flow (now at high pressure) is important to maintain normal function in several body organs, especially the brain and kidneys. These adjustments occur normally. However, in some people adjustments become fixed and high blood pressure persists. These people have developed hypertension.

Hypertension is a well-established cause of a wide range of diseases prevalent in human populations. These diseases include vascular conditions, the likes of which most people readily associate with high blood pressure, such as heart attack and stroke, as well as lesser-known non-vascular conditions such type 2 diabetes and dementia.

Of all the health consequences known to arise from hypertension, cardiovascular

diseases are probably the most well-known, and they include conditions such as ischaemic heart disease, ischaemic stroke, intracerebral haemorrhage, cardiomyopathy, aortic aneurysm and chronic kidney disease. A comprehensive review drawing upon data from one million adults across 61 prospective studies[5] found that risk of death from vascular diseases increased as systolic blood pressure rose above 115 mmHg and diastolic above 75 mmHg with no evidence of an age threshold. Section 4 of this report provides a detailed review of evidence in relation to alcohol's role in blood pressure mediated cardiovascular diseases.

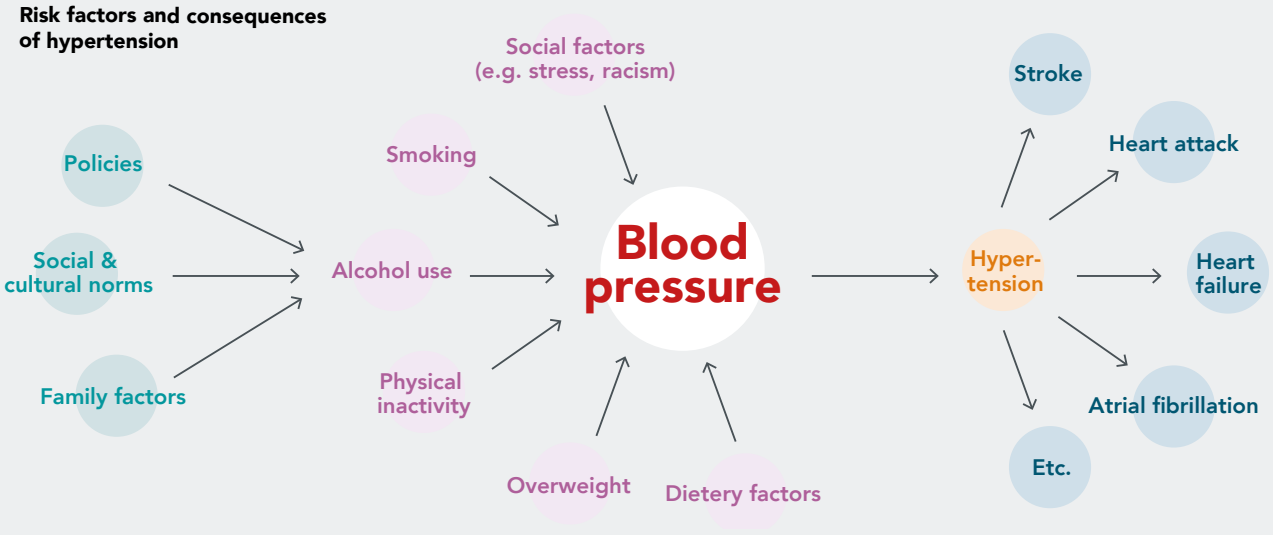
Aggregate mortality from all non-vascular causes is also positively related to blood pressure, although the relationship is much less striking than that for vascular mortality.[5] There is strong evidence summarised in two recent systematic reviews that hypertension is a risk factor for the development of type 2 diabetes.[4,6] Hypertension impairs the body's ability to absorb glucose, increases insulin resistance and impairs vascular function of muscles all of which lead to increased risk of chronic high blood sugar i.e. type 2 diabetes.

Chronic hypertension has been identified as the most prevalent vascular risk factor for Alzheimer's disease and related dementia.[19] Hypertension is associated with brain shrinkage and damage. Causal mechanisms have been identified for this in addition to the effects of chronic high blood pressure alone and include metabolic dysfunction, systemic inflammation and dysrhythmia.

1.5 Why is it important to know about alcohol's effect on blood pressure?

High blood pressure clearly causes extensive morbidity and mortality. Worldwide, high blood pressure is one of the most commonly treated conditions in health care. When a physician makes a diagnosis of hypertension, administration of prescription medication is a common course of action. A range of effective and generally low-cost pharmaceutical drugs are available for the treatment of hypertension.[20]

According to the World Health Organization, however, an estimated 46% of adults with hypertension are not even aware they have the condition. What's more, almost 60% of adults with hypertension go untreated and only an estimated 1 in 5 adults with hypertension have their blood pressure under control.[7] Contrasted against the enormous cost of hypertension-related morbidity and mortality to health systems, the tremendous



Hypertension is largely a preventable disease and many modifiable risk factors have been identified.

resources allocated for research into new pharmaceutical treatments, genomics and pathophysiology and, the intense ongoing efforts poured into implementation of strategies and policies to improve clinical practice, these statistics are notably underwhelming. Some medical commentators have described global progress in addressing hypertension as slow and disappointing and recommend system-wide transformation in research and clinical care approaches. To save the day, much hope appears to be pinned on improved treatment delivery and screening through advancements in digital technologies.[17,18]

It is probably true to say that the value of evidence-informed prevention approaches to reducing individual health and societal burdens from hypertension have not yet been fully realised. Hypertension is largely a preventable disease and many modifiable risk factors have been identified. The World Health Organisation for example recommends reducing salt intake, eating more fruit and vegetables, getting more regular exercise, avoiding tobacco, reducing alcohol intake, limiting saturated fats and eliminating trans fats.[7] Still, in the main, these important health behaviours have not yet been given the attention they deserve in policy, guidelines and clinical practice. This applies especially to alcohol, a widely consumed substance for which an extensive scientific literature points to significant, negative effects on blood pressure that increase with level of consumption.

In sum, given that almost half of all people with hypertension remain unaware of their health status, it seems both obvious and necessary that attention be more pointedly directed towards modifiable and highly prevalent risk factors for hypertension. As highlighted throughout this report, alcohol consumption is one such modifiable risk factor.

This report addresses various ways in which alcohol consumption at different levels affects blood pressure and hypertension in both the short and long-term as well as implications for the prevention of serious illness and premature mortality. We also explore evidence for interventions that can be delivered through healthcare systems and at the general population level through alcohol policies.

FACT DEFINITIONS

Blood pressure is a measure that quantifies the pressure in the large arteries, it is typically measured in millimeters of mercury (Hg). Blood pressure is generally described as 2 numbers (e.g. 138/75), where the top number is the systolic blood pressure and the bottom number is diastolic blood pressure. The systolic blood pressure is the blood pressure while the heart is contracting, and the diastolic blood pressure is when the heart is not contracting. Sometimes a mean arterial pressure is reported, which is a weighted average of the systolic and diastolic pressures.

Hypertension (high blood pressure) refers to the medical condition of having an elevated blood pressure. Conceptually, this would be based on blood pressure levels that are high relative to generally healthy adults, or levels at which risks of related conditions (e.g. strokes) is increased. In the past and for most of the studies reviewed for this report, hypertension was defined as a blood pressure of 140/90 or higher; however the definition of high blood pressure is more commonly defined as that in excess of 130/80, particularly for those with diabetes. Those with blood pressures at lower levels who take antihypertensive medications are also considered to have hypertension.

Mendelian randomization studies are those that rely on genetic variants that are related to alcohol consumption in order to indirectly study effects of alcohol consumption.

Crossover studies assess the effect of a particular intervention within one person over time (for example, checking blood pressure during a 4 week period of alcohol use compared to a 4 week period of non-use).

Randomized controlled trials 'flip a coin' to randomly assign one group or participants to an intervention (e.g. decreasing or increasing alcohol consumption) and another to not partaking of that intervention.

Observational studies are based upon data obtained from self-reported drinkers which is used to investigate the likelihood of various diseases among people who happen to drink.

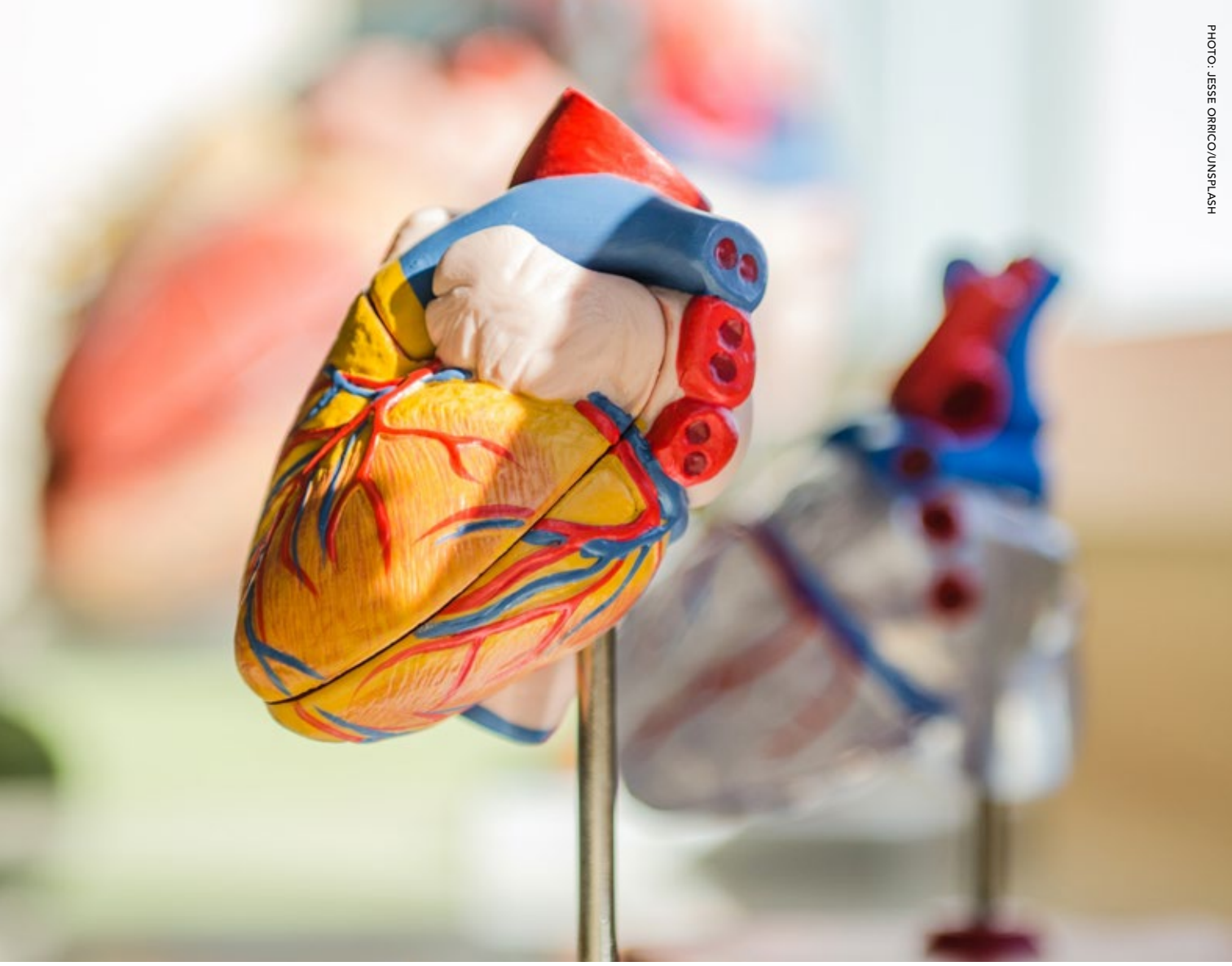


PHOTO: JESSE ORRICO/UNSPLASH

2 Vascular physiology and alcohol

Blood pressure regulation is complex and increased blood pressure is partly caused by less elastic and more constricted blood vessels. Alcohol use has multiple effects on blood vessels including a likely contribution from the sympathetic nervous system, a division of the autonomic nervous system (i.e. functions automatically without conscious control) responsible for 'fight or flight' responses. Alcohol also exerts its effect on blood pressure via hormones from the kidney and liver (renin-angiotensin-aldosterone system), contraction and dilation of blood vessels (myogenic mechanisms), and disruption of blood vessel function through oxidative stress.[21] Each of these mechanisms is discussed in more detail below.

2.1 Constriction and dilatation of blood vessels

The inner layer of the vascular wall, called the endothelium, produces substances that have effects throughout the entire circulatory system. The endothelium reacts to changes in blood flow, blood pressure, inflammation and circulating hormones, so as to continually adjust and optimise muscular tension in the vascular wall.

Animal studies have shown that chronic alcohol consumption increases blood vessel sensitivity to vasoconstrictive agents and impairs vascular relaxation, making the blood vessels more prone to constrict and less prone to relax. Molecular mechanisms include an increase in intracellular calcium, increasing vascular reactivity (an increased sensitivity in the arteries, causing them to contract at a lower threshold) and oxidative stress and a reduction in molecules that relax the arterial wall. In clinical studies on humans increased blood pressure from chronic alcohol consumption has been correlated to increased levels of such vasoconstrictive agents in blood.[21]

There is evidence that the smooth functioning of the endothelium to maintain the capability to dilate the arteries in response to increased blood flow becomes gradually compromised with increased consumption of alcohol, even for light drinkers and especially for those with heavier drinking habits.

There is evidence that the smooth functioning of the endothelium to maintain the capability to dilate the arteries in response to increased blood flow becomes gradually compromised with increased consumption of alcohol, even for light drinkers and especially for those with heavier drinking habits.[22–24]

Oxidative stress is an imbalance between the production of reactive oxygen molecules (free radicals) and the ability to detoxify the reactive intermediates by antioxidants, or to repair the resulting cell damage. This increases the inflammation in the vascular system and is a key mechanism of constriction of blood vessels and reduced blood flow and is associated with increased blood pressure. Alcohol is associated with the development of oxidative stress either directly via stimulating the generation of free radicals or indirectly via reductions in antioxidant systems and increasing the susceptibility of the cell to other stressors. The increase in oxidative stress promoted by ethanol is associated with endothelial dysfunction, vascular inflammation and increased vascular reactivity, as well as with cellular damage in both animals and humans.[21,25]

However, changes in biological markers of oxidative stress from alcohol consumption does not have a direct relation to blood pressure. Studies have shown that acute or short term low-to moderate drinking that reduces the markers of oxidative stress have no effect on blood vessels, neither contracting or relaxing. On the other hand, studies of human binge drinking have found an acute negative effect on blood vessels, including impaired dilation of the microvasculature, through increased oxidative stress. One-time as well as repeated binge drinking induce oxidative stress in both large and small arteries. Long-term heavy alcohol consumption has also been shown to adversely affect vascular function.[25] Low-to-moderate alcohol consumption, however, seems to be associated with a decrease in markers of oxidative stress, although these changes in oxidative markers did not lead to improvement of blood pressure at this level.[25]

Loss of elasticity of blood vessels, or arterial stiffness, can be measured by how fast a blood pressure pulse travels through the blood system as the heart contracts. A fast pulse wave indicates inelastic blood vessels with increased risk for hypertension and heart disease and is closely associated with increased mortality.[26–28] This can be due to several factors, such as an increased muscle tone and vascular constriction through the sympathetic nervous system, an increased thickness of the smooth muscle layer, or more severe remodelling of the arterial wall by inflammatory infiltration, fatty streaks, fibrosis or even calcification.

Two recent and comprehensive reviews of a large literature on this subject show that alcohol consumption can increase arterial stiffness even at low levels such as one drink per week >15 grams/week for women and >30 grams/week for men[29] or more than

8 drinks/week.[26] Binge drinking and higher alcohol consumption have more severe effects. Reductions in arterial stiffness have been observed in individual studies from very low doses of alcohol (e.g. less than 15 grams per week), but this effect has not been found in larger studies and studies covering longer time periods. Even single occasions of binge drinking increases arterial stiffness and there is a definite dose-response effect.[30–36]

It has been shown that even a single occasion of heavy or "binge" drinking can result in increased sympathetic nerve activity and thereby increases arterial stiffness by both acute vasoconstrictive effects and by inducing long-term vascular remodelling, increasing the number of vascular smooth muscle cells (hyperplasia), and deposition of both collagen and elastin increasing the wall thickness as well as stiffness.[26]

2.2 Arterial wall remodelling

Several studies on the effect of alcohol exposure on human cells in the laboratory suggest mechanisms with a protective effect on artery walls. However, similar studies also find that the first metabolite of alcohol, acetaldehyde, has opposing, harmful effects on human tissue.

Contradictory results have been found in human and animal studies regarding the effects of alcohol exposure on carotid artery wall thickness (CIMT). Animal studies have suggested protective effects from alcohol.[37,38]

PHOTO: ISTOCK

Alcohol consumption has also been found to cause calcification in both aortic and coronary arteries, increasing with level or dose of alcohol use. Such effects are especially common and pronounced among binge drinkers.

In human studies, however, alcohol intake has been shown to increase CIMT, independent of age and sex, blood pressure, and a range of other indicators of heart health risk.[39] Particularly significant and harmful effects on CIMT have been demonstrated for alcohol intake above 70 grams/week.[32,40]

Alcohol consumption has also been found to cause calcification in both aortic and coronary arteries, increasing with level or dose of alcohol use. Such effects are especially common and pronounced among binge drinkers.[41–43]

2.3 Heart

There is a mutual dependence between healthy functioning of the heart and healthy functioning of blood vessels, dysfunction of one potentially harming the other. For example, if peripheral blood vessels are constricted, more stress is placed on the heart to pump out blood needed to reach essential organs, thus increasing blood pressure. This may cause the left ventricle of the heart that pumps blood out of the body, to grow more muscle mass (left ventricular hypertrophy). Alcohol use has been found to not only increase this effect,[44] but to also impair relaxation of the heart.[45]

There is also an important feedback system between the autonomic nervous system and the heart, which can be impaired in chronic alcohol use.[46] This is an intricate regulatory system, consisting of nervous control of both vascular tone and heart rate. In the direct blood pressure regulation, receptors in the vascular wall sense changes in blood pressure (due to peripheral vascular constriction or dilatation) and signals to the heart to increase or decrease the heart rate, with the intention of maintaining cardiovascular stability (baroreflex). This system has an "accelerator" (the sympathetic nervous system, SNS) and a "brake" (the parasympathetic nervous system, PNS). Alcohol intake has been shown to increase SNS activity (increase in heart rate, constriction of peripheral arteries), while also impairing PNS function.

Another action of alcohol is to activate the kidney-controlled renin-angiotensin-aldosterone system, also very important in blood pressure control. The constriction of the arteries leading to the kidneys result in the release of a hormone cascade causing the blood vessels to constrict and decreases how much fluid the body eliminates from the blood as urine. This combination of higher blood volume in the body and smaller blood vessels increases blood pressure.

3 Research evidence for alcohol's effect on blood pressure

This section reviews the epidemiological research evidence that underpins our understanding of alcohol's effects on the risk of elevated blood pressure. To varying degrees, studies in this area have also shed light on whether; different drinking patterns (e.g. regular use, binge drinking) influence risk, drinker characteristics (e.g. gender, age) may influence associations, and short-and long-term effects differ. Many studies examine not only alcohol's effect on blood pressure per se but also measure drinker risk of developing hypertension (a binary outcome). Among people with hypertension, it is important to understand how alcohol use relates to control of blood pressure among treated and non-treated people, and whether reducing consumption can reduce blood pressure or control hypertension.

An important strength of the research literature concerning alcohol's effect on blood pressure is that researchers have employed a range of study designs and methods including, randomized trials and within-person crossover studies, Mendelian (genetic) randomization (MR) studies, and observational epidemiological studies (e.g. prospective cohort, case-control). As each of these approaches brings their own unique strengths and weakness to bear on the evidence, this section is arranged by study type. Rather than an impediment to understanding causal relationships, when taken as a whole, this variability tends to facilitate a more balanced approach to interpretation, reinforcing our confidence in key conclusions and recommendations.

3.1 Within-person crossover studies and randomized controlled trials

There have been a number of experimental studies on the short-term (i.e., less than one week of exposure, and often just a one-time exposure to alcohol) effects of consuming ethanol in various amounts; most of these studies are within-person crossover studies. It should be noted that short-term effects are distinct from long-term effects of alcohol on blood pressure or long-term effects of blood pressure and related outcomes. A large review of randomised controlled trials[47] found that alcohol may have a biphasic effect on blood pressure, but that this is dose-dependent. Low doses of alcohol, up to 15 grams (approximately 1.3 Swedish standard drinks) had little to no effect on blood pressure in the short-term. Medium-dose (15–30 grams) significantly decreased mean arterial blood pressure within six hours of consumption, was not significantly associated with blood

Among people who drank >24 grams/day, a reduction in alcohol intake significantly reduced blood pressure.

pressure at 6–12 hours, and non-significantly increased blood pressure after 12 hours. High-dose alcohol (>30 grams, >2.5 Swedish standard drinks) was associated with non-significant decreases in mean arterial blood pressure for 12 hours, and significant increases in mean arterial pressure thereafter. There have also been smaller experimental studies pointing in this direction.[48]

A systematic review and meta-analysis of clinical trials lasting at least one week that examined the effect of change in alcohol consumption on blood pressure or hypertension included trials from 1 week to 2 years (median duration 4 weeks). They found that among people who drank >24 grams/day, a reduction in alcohol intake significantly reduced blood pressure, and reductions in BP were greatest among participants who drank six or more drinks per day if they reduced their intake by about 50%. A reduction of alcohol consumption to near abstinence for people who drank 24–35 grams per day (2–3 Swedish standard drinks per day) also resulted in a significant change in BP. Dose-response relationships were generally consistent among healthy participants and people with hypertension or other CVD risk factors; however, there were few studies that assessed reductions among those with hypertension with baseline consumption less than 24 grams/day, and even fewer that changed consumption among those. A reduction in alcohol in this group was not found to be associated with a significant reduction in blood pressure. Results were similar for men and women; however, data for women were sparse. According to the authors, *"Because only three trials reported results for women, we have less confidence in the pooled effect estimates. Similarly, there was only one trial in people with hypertension who consumed three or fewer drinks per day. Because of the public health importance of both alcohol consumption and hypertension, there is an urgent need for additional research to clarify the effect of alcohol intake in people with hypertension at low alcohol intake and in women."*[49]

Other large reviews included additional studies with participants that were mostly heavy drinkers and all studies found decreased blood pressure from reduced alcohol consumption, with a dose-response relationship and where intervention effects were enhanced among drinkers with higher baseline blood pressure. The data is sparse for the lower levels of alcohol consumption, and the evidence for effect of reduction is lower.[50–54]

A longer RCT of alcohol consumption studied 224 patients aged 40–75 with type 2 diabetes mellitus over a 2-year period. Participants were randomly assigned to 14 grams ethanol of mineral water, white wine or red wine with Mediterranean diet dinner. Blood pressure was included as a secondary outcome and was not significantly affected by wine consumption.[55]

Summary

Taken together, findings from randomized or within-person crossover studies lasting one or more weeks find that other than for low average consumption, alcohol use increases blood pressure in men and women, and reductions in consumption among those drinking 24 grams or more per day reduces blood pressure. Moreover, there is no evidence of blood pressure lowering, or protection from hypertension, for any level of alcohol consumption in randomized studies or within-persons crossover trials. There have been too few trials to draw conclusions about effects of alcohol consumption among those consuming 24 grams per day or less with established hypertension; data on this topic are even more limited for women. Short-term (i.e. one-time) administration of ethanol may yield initial blood pressure lowering and subsequent increases after 12 hours; however, this depends on the amount of ethanol consumed, and may not be informative with respect to longer term effects of ethanol on blood pressure and related outcomes.

3.2 Mendelian Randomization (MR) studies

Mendelian Randomization (MR) studies offer a number of strengths compared to RCT studies. Like randomized controlled trials, MR studies can minimise confounding and reverse causation, while more closely reflecting alcohol exposure over the life-course. The relative methodological strength of alcohol studies that use an MR design lies in their ability to capitalise on objective information about participant drinking rather than relying on self-reported alcohol use. MR studies use genetic characteristics randomly present from birth as proxies for alcohol exposure. Established as a cause of drinking level variation in human populations, these genes usually affect consumption throughout one's life. MR studies therefore tend to have naturally stable exposure groups, and, due to the randomness of genetic assignment, group comparisons are less prone to influence by confounders, e.g. socio-economic status, environment.

Genes necessary for alcohol metabolism include aldehyde dehydrogenase 2 (i.e. ALDH2, more common to East Asian populations) and alcohol dehydrogenase 1B (i.e. ADH1B). Some variants of these genes deactivate enzymes necessary for alcohol metabolism, shifting the balance of unpleasurable vs. pleasurable effects of consumption, which results in reduced consumption and a higher likelihood of abstaining. Most MR studies of alcohol and blood pressure have studied Asian populations and used variants of the ALDH2 gene as a proxy for levels of use. This is in large part due to the relatively high prevalence (>30%) and severity of the 'flushing' variant among Asian populations compared to the less common (0.5%–4%) and less severe European population variants (i.e. ADH1B, ADH1C).

A meta-analysis of cross-sectional alcohol and blood pressure/hypertension outcome studies with genetic data on ALDH2 concluded that male alcohol use had a marked linear association with blood pressure. Blood pressure was estimated to increase by around 0.2 mmHg per gram of alcohol (ethanol) per day. Male participants without the flushing gene were also at greater risk of hypertension compared to those with the flushing gene. No association between alcohol and blood pressure or hypertension was found for females. However, the sample was largely Japanese and most females drank at low levels regardless of genotype, i.e. there was insufficient variability in female drinking levels to support exposure level comparisons. The authors' concluded that past observational studies may have underestimated the extent to which even moderate amounts of alcohol elevate blood pressure.[56] A more recent MR study of a South Korean population confirmed these results. They found positive linear associations for alcohol use, blood pressure and risk of hypertension among males but no associations were apparent among the female sample that drank almost exclusively at low levels across all genotypes.[57]

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One study investigated effects of alcohol use risk of hypertension among a multi-national sample of Chinese origin. Although a relatively small sample (no gender-specific estimates were available), the cohort was followed over 5 years. No excess risk of hypertension was found for carriers of the flushing gene who did not drink. However, carriers who drank at moderate/heavy levels were at significantly higher risk of developing hypertension.[58] Au Yeung et al., (2013)[59] sampled 4,500 males from Southern China who either did not drink at all or drank at low/moderate levels (about 13 grams per day on average). Their study did not detect any association between systolic blood pressure and alcohol use, but they did find that low to moderate levels of drinking were positively associated with diastolic blood pressure such that for every 10 grams of ethanol drunk per day, diastolic blood pressure increased by about 0.15 mmHg, on average.

A very large study investigated associations between alcohol use, blood pressure and a range of other cardiovascular conditions among 500,000 males and females over a 10-year period. Taking a novel approach, the authors used both conventional participant self-report and MR methods (including variants of both ALDH2 and ADH1B genes) to measure alcohol use and compared their outcomes. Among males, both conventional and MR methods demonstrated positive linear associations between systolic blood pressure and alcohol consumption level such that systolic blood pressure increased by almost 5 mmHg for every 280 grams of ethanol consumed per week. For women, no associations were found between alcohol use and blood pressure or any other cardiovascular outcomes investigated. Notably, this study suffered a similar limitation as most other MR studies of Asian populations in that few women in the sample drank, severely limiting drinking level variability among gene variant groups (i.e. insufficient inter-group variability to enable detection of differences).[60]

An MR study of alcohol and blood pressure on more than 54,000 white Copenhagen residents of Danish descent used two geno-

types to determine drinker status (ADH1B and ADH1C) and applied multivariable analyses to compare mean blood pressure among drinker groups (12–24 grams ethanol per week as reference group). In keeping with most MR studies of Asian populations, alcohol had a detrimental effect on both systolic blood pressure and diastolic blood pressure with higher levels of alcohol use associated with higher BP. For instance, among participants who drank 108 to 120 grams per week, 180 to 204 grams per week, and 300 grams or more ethanol per week, mean systolic blood pressure estimates were higher by about 0.5, 2, and 4 mmHg respectively compared to those who drank 12 to 24 grams ethanol per week. However, among people who drank between 25 and 96 grams ethanol per week, systolic blood pressure was not significantly different to the reference group. Notably, results for gender-specific models were not provided as alcohol and BP associations were reportedly similar for males and females.[61]

Over 220,000 participants of European decent were investigated for effects of alcohol on a range of cardiovascular conditions including blood pressure. The MR study found that carriers of the gene variant associated with non-drinking (ADH1B), had lower mean alcohol use, fewer episodes of binge drinking, and lower systolic blood pressure on average compared to non-carriers. Both moderate (>0 to <166 grams per week) and heavy drinkers (>= 166 grams per week), were at increased risk of higher blood pressure but only heavy drinkers demonstrated a higher risk of hypertension (12%) compared to non-drinkers.[62]

In the largest MR study of alcohol and cardiovascular outcomes among a European cohort to date, every 12 grams of ethanol ingested per day was found to increase systolic blood pressure by almost 3 mmHg. This relationship held for both males and females although fewer cases and less variability in drinking levels produced weaker effects with wider confidence intervals for women. Alcohol use was also associated with increased risk of atrial fibrillation for which high blood pressure is an established risk factor (see Section 4.4).[63]

Summary

Overall, results from MR studies consistently support a strong positive relationship between alcohol use and blood pressure, and do not find evidence for protective effects. Although supported by MR studies of European populations (e.g.[61,63]), evidence of an association is weaker overall for females but this is likely due to methodological limitations rather than biological differences. The effect of low dose alcohol on risk of hypertension is also not well evidenced by MR studies which tend to have limited capacity for finer grained analysis of drinking levels (e.g. below 100 grams ethanol per week). In summary, this body of evidence suggests that reduced alcohol use is associated with lower blood pressure, even for light to moderate drinkers.

Overall, results from MR studies consistently support a strong positive relationship between alcohol use and blood pressure, and do not find evidence for protective effects.

3.3 Observational studies

For establishing causality, evidence derived from traditional observational studies is comparatively weak due to confounding and selection bias. However, they may offer insights into aspects of alcohol use that are difficult to obtain from RCT and MR studies such as drinking patterns. In addition, observational periods cover longer follow-up periods than is practically possible for randomized clinical trials.

Several reviews of observational studies (i.e. cohort, case-control) find that, for males in particular, regular alcohol consumption increases blood pressure and risk of hypertension in a dose-dependent manner. A relatively recent meta-analysis of cohort studies for instance, found male alcohol consumption, even at low levels (12–24 grams per day), increased hypertension risk. For females, hypertension risk was only increased at heavy levels of use with no association apparent at low to moderate levels.[64] Some older meta-analyses have suggested that low dose alcohol (e.g. <10 grams per day) may have a modest protective effect on female hypertension risk.[65,66] However,

Collectively, these studies suggest that binge drinking in adolescence, young adulthood and middle age predicts higher blood pressure at baseline and several years later.

this is becoming increasingly unlikely given growing evidence from more recent large meta-analyses, randomized trials and MR studies which point to either a linear effect or no association.[67]

Some observational studies also suggest that alcohol consumption may predict onset of hypertension among individuals initially characterised as pre-hypertensive.[68,69] Among a Swedish birth cohort of males, level of alcohol consumption at 40 years of age predicted progression to hypertension three years later and by age 46, was the most important predictor of hypertension.

Several observational studies suggest that binge or 'heavy episodic' (i.e. consumption of 5 or more drinks for men, or 4 or more drinks for women during a drinking occasion) may play a role in the development of higher blood pressure among younger people, especially males (e.g.[69–71]). Collectively, these studies suggest that binge drinking in adolescence, young adulthood and middle age predicts higher blood pressure at baseline and several years later. What's more, compared to non-binge drinkers, both frequent (e.g. weekly) and infrequent (e.g. 1–12 times per year) binge drinkers are more likely to have higher blood pressure or meet criteria for pre-hypertension.

3.4 Summary

Overall, alcohol consumption is a risk factor for increased blood pressure and development of hypertension. This relationship is generally consistent across study designs, and is most pronounced for consumption exceeding 24 grams (about 2 Swedish standard drinks) per day. Nonetheless, MR and cohort studies suggest that increased risk may begin with any consumption. Evidence supporting a causal effect of alcohol on blood pressure and hypertension risk is highly developed for men and although less data are available for women, higher quality evidence is directionally consistent.

From crossover studies and randomized trials there is evidence that reductions in alcohol use lower blood pressure among drinkers with baseline consumption of 24 grams or more per day. Although these studies do not show reduced risk for baseline consumption at lower levels, it should be noted that available data are limited, particularly for drinkers with existing hypertension.

Some past studies, mostly observational, have suggested that low level alcohol use may reduce blood pressure and risk of hypertension among women. Given the current weight of evidence accumulated across all types of studies, the notion that low dose alcohol offers protective effects is unconvincing. It is more plausible that for both men and women, there is either a linear relationship between alcohol and blood pressure and hypertension risk or no significant excess risk at low level drinking.

Findings are consistent for drinkers with and without established hypertension although the scientific literature is less well developed for those with hypertension. Furthermore, existing data are not distinguished on the basis of whether people with hypertension are being treated with anti-hypertensive medications.

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4 Cardiovascular disease

Cardiovascular disease is an umbrella term for a group of conditions affecting the heart and blood vessels. As a group, cardiovascular diseases cause about one-third of all deaths world-wide and ranks first among all causes of premature death and morbidity.[72,73] Cardiovascular disease is also the leading cause of death in Sweden; in 2021, male and female mortality rates were 328 and 214 per 100,000 deaths respectively, which accounts for approximately 30% of all deaths.[74]

Hypertension is quantifiably the most prevalent modifiable risk factor for premature cardiovascular disease and mortality.[75] To address the social, health and economic burdens that cardiovascular disease places on society, it is critically important to identify and understand common risk factors for elevated blood pressure and hypertension. Smoking, lack of exercise and poor diet are easily recognised by health professionals and the general public as hypertension risk factors. Alcohol's role, however, despite many decades of scientific research evidencing strong causal links between hypertension and heavy drinking, appears to be far less widely known or understood (see section 3 and 5). As a highly prevalent and modifiable risk factor for prolonged elevated blood pressure, consumption of alcohol has major implications for prevention of cardiovascular-related premature death and disability.

This section summarises physiological and epidemiological underpinnings for four key cardiovascular conditions where relationships between alcohol, blood pressure and hypertension play an important role in disease risk.

4.1 Ischaemic heart disease

Ischaemic Heart Disease (IHD)[76] refers to a group of heart problems characterised by an imbalance between myocardial blood supply and demand and includes coronary artery disease, heart failure, angina and

Multiple scientific critiques have now been published of the hypothesis that alcohol in low doses can be cardioprotective.

heart attack. When blood flow to the heart muscle is reduced, either by plaque build-up, blood clots or contraction of the coronary arteries – all of which can be affected by alcohol – tissue oxygen levels become too low (ischaemia) and cells begin to self-destruct. If oxygen levels are restored, there will be chest pain, but no lasting damage. If oxygen levels are not restored, heart muscle tissue will be permanently damaged – a life threatening event commonly referred to as a heart attack. IHD makes the single largest contribution to cardiovascular disease burden, accounting for almost 20% of all deaths globally[14] and about one third of all cardiovascular deaths in Sweden.[74]

Hypertension is well-known major preventable risk factor for IHD,[14] and heavy alcohol use is a known risk factor for hypertension. It is important therefore to understand how the scientific literature has addressed and articulated the complex relationship between alcohol and IHD.

Although there is clear consensus among researchers that heavy alcohol use is a cause of IHD, controversy exists as to the role of low level alcohol use on IHD risk. Many older observational studies have concluded that low and/or moderate levels of alcohol consumption protect against IHD. These studies have generated and sustained the belief, held widely among the general public and health professionals, that drinking in moderation improves heart health. Over the past decade or so, however, an increasing number of new studies, particularly those with MR designs, suggest that low dose protective effects demonstrated by observational studies have been exaggerated due to problematic study designs. These new studies have also concluded that either alcohol is not protective for IHD at any level or that protection may be present at very low levels of use (e.g. less than half a drink per day).[77–82]

Much of the diversity in scientific thought about this critically important subject can be explained by the fact that most studies of the association between alcohol and IHD have been observational in nature. As such, these studies are subject to a wide range of problems that limit their ability to draw reliable conclusions about causal relationships (e.g. reverse causation, misclassification error, response bias, confounding by lifestyle, socio-economic and demographic characteristics). There is a long history of observational studies leading to conclusions that have eventually been disconfirmed by studies with stronger designs. Nonetheless, many commentators have drawn confident conclusions about low dose alcohol being beneficial even while alluding to the possibility of confounding affecting their results.[83] Many clinical and experimental studies also find that low dose alcohol protects against IHD purportedly though its beneficial effects on certain biological markers or risk factors for IHD, e.g. by increasing 'good fats'.[84] Again, however, more recent randomised controlled trials and MR studies have cast doubt on whether supposed mechanisms for cardiovascular protection from low level alcohol consumption are in fact reliable risk markers for IHD.[85–90]

Multiple scientific critiques have now been published of the hypothesis that alcohol in low doses can be cardioprotective. It has been pointed out for instance, that IHD is a disease primarily of older populations and that with advancing age individuals tend to cut down or quit drinking as they become frail and receive medication.[91] It should not be surprising then that most observational studies of IHD also enrol cohorts of older people, many of whom have stopped drinking or reduced their drinking over time for health reasons. Most of these studies also operate on the assumption that 'current' (e.g. last month, last year) non-drinkers are the ideal group against which current low or 'moderate' level drinkers are to be compared on health outcomes.[82] Unfortunately, few observational studies can accurately account for entire drinking histories of their participants, so they become highly prone to misclassify older ex-drinkers as non-drinkers. For the vast majority of observation studies therefore,[92] non-drinker

groups are in actuality, comprised mostly of ex-drinkers with markedly poorer health and socio-economic profiles than their current drinker counterparts. When the non-drinker group (compromised with ex-drinkers) is compared to the low-level drinker group it appears as if they are in worse health due to an absence of alcohol consumption. However, when ex-drinkers and poorer health profiles of non-drinker groups are accounted for, the apparent protective effect of low to moderate drinking dissipates.[62,82,93] In other words, drinking into older age is probably a marker of good health rather than a cause of good health.

In conclusion, the strong evidence reviewed in this report that alcohol use leads directly to elevated blood pressure in the short-term and hypertension in the longer term without any safe level or protective effects, contributes to growing doubts that alcohol use protects against death and illness caused by IHD. There is complete consensus, however, that alcohol use at higher levels greatly increases the risk of this highly prevalent disease.

4.2 Stroke

Hypertension has been estimated to account for over 50% of all strokes globally.[94] Blood supply to the brain is dependent on steady blood flow through the arteries. When blood flow is adversely affected, brain cells will be damaged – we call this a stroke. There are two main types of stroke, ischaemic and haemorrhagic. An ischaemic stroke occurs when blood clots form, reducing blood flow and damaging brain cells. Haemorrhagic stroke arises from a weakened artery that ruptures and bleeds into the brain, as blood accumulates and compresses surrounding brain tissue, brain cells are injured.

There is strong scientific evidence and consensus that alcohol use increases risk of both ischaemic and haemorrhagic stroke, especially at high levels of consumption.[95,96] As with IHD, however, observational studies have generated apparent evidence for alcohol's protective effect on stroke risk at low levels of use. This has generated ongoing debate about the veracity of protective effect findings.

As described in detail above (Section 4.1), limitations inherent to observational studies (e.g. life-time selection bias, misclassification error, confounding) generally make them ill-suited to study effects of life-time alcohol use on chronic disease.[97] Like IHD, ischaemic stroke is a degenerative disease that tends to be a more common among older people. Also, it is often the case that older people who self-report as abstainers were in fact drinkers in their early adult to middle aged years who stopped drinking due to health problems. Observational studies of older cohorts are rarely able to adequately account for past drinking behaviours and often contaminate their non-drinker groups with ex-drinkers.[91,92] However, in one Spanish study of alcohol consumption and all-cause mortality among older adults, ex-drinkers were removed from the abstainer group and were classified according to their life-time intake. Results showed that in comparison with never-drinkers, risk of death was slightly higher (Hazard Ratio of 1.05) for light drinkers but was not significantly different.[98]

Studies of alcohol and cardiovascular diseases (i.e. heart disease and stroke combined) with stronger designs employing some form of Mendelian Randomisation plus controls for lifestyle confounding consistently find increased risk with no safe or protective level. A large UK Biobank cohort study[99] (2006–2010, follow-up until 2016), looked for confounding in observed associations between alcohol intake and cardiovascular diseases using Mendelian Randomization. They found that light to moderate alcohol consumption was associated with healthier lifestyle factors. Adjusting for these factors in risk analyses not only diminished evidence for protective effects of low-level alcohol use, it also produced exponentially increased risks for higher levels of intake. The authors concluded that "no amount of alcohol is

protective against cardiovascular disease" and adverse effects of alcohol "unduly affect those who consume heavily".

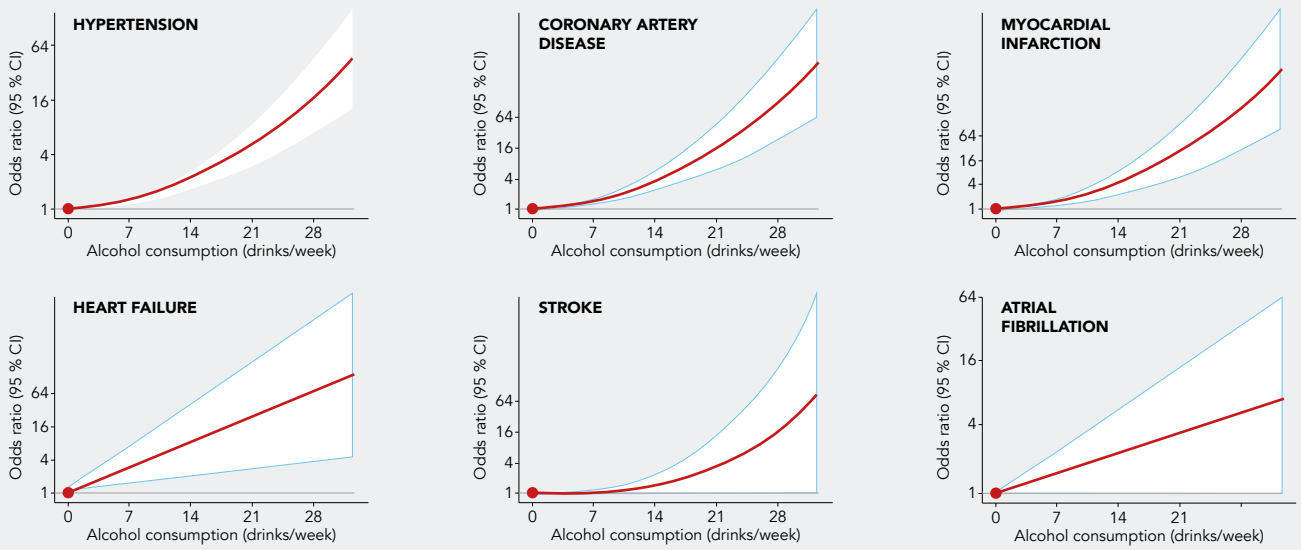
4.3 Cardiomyopathy

Cardiomyopathy refers to a group of conditions which affect the heart muscle's ability to pump blood to the body. Left untreated, cardiomyopathy can lead to heart failure and death. Alcohol causes both structural and functional changes in the heart wall muscle (i.e. myocardium) and its effects are complex. These detrimental effects can be direct and/or indirect. It is the indirect effects that occur as a result of alcohol's ability to elevate blood pressure.

Alcohol (i.e. ethanol) is directly toxic to heart muscle cells (myocites). Animal studies have shown that ethanol causes both programmed cell death and decreased cell function (e.g.[100,101]). This presents as reduced ability of the heart to contract and relax, greater volume of the left ventricle, and eventually, left ventricular wall thinning.[102] It is well established that heavy drinking (≥80 grams per day) over several years presents a high risk of developing cardiomyopathy, and that as lifetime alcohol exposure increases, so too does risk (i.e. risk is dose-dependent).[102] When cardiomyopathy occurs in conjunction with a clinical history of heavy alcohol use over a period of years, *alcoholic* cardiomyopathy may be diagnosed. Alcoholic cardiomyopathy is one of the most well-known cardiovascular complications of heavy drinking and physicians have known of the relationship for almost two centuries.

In addition to alcohol's toxic effect on heart muscle cells, it can increase drinker risk of cardiomyopathy by raising blood pressure and/or causing hypertension. When alcohol use elevates blood pressure it causes increased peripheral vascular resistance to blood flow. Over time, this can cause the heart muscle to grow with the effort of pumping out blood against increased peripheral resistance

Odds Ratio of alcohol and 6 cardiovascular disease phenotypes, fractional polynomial nonlinear MR analyses, using number of alcohol-increasing alleles in rs1229984 in the ADH1B gene, excluding abstainers



From Biddinger KJ, Emdin CA, Haas ME, et al. Association of Habitual Alcohol Intake With Risk of Cardiovascular Disease. JAMA Netw Open. 2022;5(3):e223849, supplement, eFigure 8 (IV)

(i.e. left ventricular hypertrophy) and lead to cardiomyopathy. In addition, as blood pressure is a mediator in the development of cardiomyopathy, even moderate drinking has the potential to cause increased thickness of the left ventricular wall. Increased heart wall thickness compromises heart function, especially its ability to relax and fill properly, which often precedes onset of clinical symptoms and development of alcoholic cardiomyopathy.

Interestingly, it was postulated some time ago that alcoholic cardiomyopathy may require daily drinking of 90 grams or more of pure alcohol over 5 or more years to cause such changes to the heart.[103] However, this estimate may be too high for females as it was based almost exclusively on male data. Other studies have shown for instance that prevalence of cardiac problems may be similar for women and men even when average female consumption is half that for males.[104] Some studies also suggest that cardiomyopathy risk may be tied to specific drinking patterns, e.g. binge versus regular drinking or preferred beverage type (e.g. wine, beer, spirits), but evidence is not well developed.[100]

Although it is possible to measure prevalence of alcoholic cardiomyopathy in higher income countries with good quality health records, reliable quantification of the extent to which alcohol use is an underlying cause of cardiomyopathy overall has proved difficult. Rehm et al (2017)[104] noted for instance that there have been too few studies on the dose-response relationship between alcohol and cardiomyopathy risk to support meta-analyses. Combining mortality data across 103 countries, they tentatively estimated that alcohol caused about 5.6% of cardiomyopathy deaths. However, in countries where heavy drinking is highly prevalent, alcohol may be an underlying cause for more than 60% of all cardiomyopathy deaths.[105]

4.4 Atrial fibrillation

Atrial fibrillation is an irregular and often very rapid heart rhythm that may cause blood clots to form in the heart, and eventually lead to heart failure or stroke. An older estimate of the global burden of disease attributed less than 1% of deaths to atrial fibrillation. However, atrial fibrillation tends to coexist with and exacerbate other cardiovascular conditions with high mortality and morbidity indicative and has significant public health implications. Regional analyses show that Nordic countries are among those where the proportion of deaths attributable to atrial fibrillation are highest in the world.[106]

Hypertension is a risk factor for atrial fibrillation through its relationships with ventricular hypertrophy, left atrial enlargement, and reduced atrial electric conduction velocity, all of which may contribute to disease development. Alcohol consumption is also a strong, dose-dependent risk factor for new atrial fibrillation or the recurrence of atrial fibrillation following treatment with ablation; risk begins to increase with any level of consumption compared to none.[107–109] This may partly be due to direct mediating effects of hypertension on the development of atrial fibrillation, but also to direct effects on the electrical regulation of the heart rhythm.

One estimate suggests that for every additional 10 grams of alcohol consumed per day, risk of atrial fibrillation increases by 8%.[107] In addition, regular moderate drinkers (e.g. 120 grams alcohol per week) with atrial fibrillation may reduce symptom recurrence or become symptom-free by abstaining or significantly reducing their alcohol consumption (approx. 80% reduction).

One estimate suggests that for every additional 10 grams of alcohol consumed per day, risk of atrial fibrillation increases by 8%.

PHOTO: ISTOCK

5 Knowledge of drinking and blood pressure

Previously, there has been considerable focus in scientific and healthcare circles on the purported protective effects of low dose alcohol consumption on heart disease events, e.g. strokes and heart attacks. The belief that 'drinking is good for the heart' is mainstream in many societies. However, our review here of latest research support an alternative perspective. We suggest that increasing evidence of negative impacts of alcohol use on blood pressure, and lack of substantiated protective effects, needs to be better reflected in drinking guidelines both for the general population and for physicians in their management of high blood pressure. There is also increasing evidence of the potential effectiveness of routine screening and brief advice on alcohol intake as a preventative measure for hypertension.

Based on a consensus conference informed by systematic reviews, meta-analyses, clinical guidelines and statistical modelling, Rehm et al (2017)[110] concluded that screening and appropriate interventions for hazardous alcohol use and alcohol use disorders could effectively lower blood pressure levels. However, they also noted mostly poor implementation of these measures in European primary healthcare. Their recommendations included: (1) an increase in screening for hypertension (evidence grade: high); (2) an increase in screening and brief advice re hazardous and harmful drinking for people with newly detected hypertension by physicians, nurses, and other healthcare professionals (evidence grade: high); (3) the conduct of clinical management of less severe alcohol use disorders for incident people with hypertension in primary healthcare (evidence grade: moderate); and, (4) screening for alcohol use in hypertension that is not well controlled (evidence grade: moderate). The first three measures were estimated to potentially result in significant decreases in hypertension prevalence, saving of hundreds of lives annually in the countries considered.

In a simulation study, Rehm et al (2018) further estimated potential effects of improved screening and subsequent intervention for alcohol problems on middle-aged Spanish men and women with hypertension. They estimated benefits of variously informing people of their diagnosis, providing routine treatment, screening and providing appropriate interventions for alcohol use and/or use disorders. Overall, such interventions were estimated to help 9% of men control their hypertension with one-third of the benefit being due to the alcohol intervention and by 7% for women with almost half of the effects due to the alcohol intervention. Overall, such interventions could prevent 412 premature CVD deaths (346 in men, 66 in women) annually in the Spanish population.[111]

The belief that 'drinking is good for the heart' is mainstream in many societies. However, our review here of latest research support an alternative perspective.

Physicians' knowledge of lifestyle changes found to be associated with improved health has been shown to be highest for taking regular exercise and reducing body weight and lowest for quitting smoking and reducing alcohol consumption.

Main challenges with implementing such proven interventions are lack of awareness and knowledge both among the general population and primary care health professionals. Surveys of healthcare professionals in Europe find mostly mixed responses to the consideration of drinking in the treatment of hypertension. While alcohol screening among hypertensive patients was largely accepted among general practitioners from five different European countries (France, Germany, Italy, Spain and the United Kingdom), practitioners report barriers to alcohol screening such as time constraints, stigma and underrating of the importance of alcohol.[112] Physicians' knowledge of lifestyle changes found to be associated with improved health has been shown to be highest for taking regular exercise and reducing body weight and lowest for quitting smoking and reducing alcohol consumption, which also corresponds to the lifestyle changes recommended by physicians to their patients.[113]

An internet survey of Spanish general practitioners indicated that alcohol was mostly viewed as a relatively unimportant issue for hypertension treatment as well as being difficult to address. The three main cited barriers for screening for alcohol consumption in hypertensive patients were the lack of time, lack of clinical significance and fear of negative patient reactions.[114]

A survey of beliefs and practices of German physicians dealing with hypertension and cardiovascular diseases elicited responses from physicians including cardiologists, internists and general practitioners.[115] While over 80% of these physicians reported sometimes assessing alcohol consumption in patients with an existing diagnosis, less than one third reported routine screening for alcohol consumption in newly detected or treatment-resistant cases of hypertension. On average, these physicians recommended maximum alcohol intakes of 13 grams/day for women and 20 grams/day for men, in agreement with most modern alcohol and health guidelines. However, some practitioners reported never addressing alcohol use in the treatment hypertension among known heavy drinkers or in cases of alcohol dependence.

A French study[116] of adults with a known diagnosis of hypertension found that over half reported receiving no lifestyle recommendations as part of their treatment plan while the majority received pharmacological treatment. Physical activity was recommended to 1/3 of sedentary participants and weight loss to slightly less of the of participants who were overweight or obese. Only 20% received any dietary recommendations (e.g to reduce salt intake) and only 11% were advised to reduce alcohol intake.

There is growing evidence that an effective strategy for increasing awareness of alcohol as a risk factor for various health conditions is the use of clear, prominent and well-designed labels mandated on all alcohol containers.[117–119] A recent Canadian study, for example, found that informing drinkers alcohol was a risk factor for breast and colon cancer variously increased knowledge of this risk factor up from very low levels, increased conversations about alcohol use and its effects, increase support for effective alcohol policies like price increases, and led drinkers to consider cutting down their alcohol intake.[120,121] Further, analyses of sales data demonstrated a significant reduction in population alcohol consumption associated with the introduction of these warning labels.[122] Alcohol labelling could also be a useful medium for raising population and health care providers awareness of the causal role alcohol consumption can play in the development of hypertension.

6 Guidelines and interventions in health care

Many countries have guidelines on alcohol consumption. In these, alcohol is identified as a risk factor for morbidity and mortality, in many cases building on reports from the World Health Organisation (WHO) which has identified alcohol as a causal factor in more than 200 diseases, injuries and other health conditions. Guideline levels for personal drinking have lowered in several countries in recent years reflecting both increasing concern about health risks at low levels of consumption for prevalent diseases such as cancer[123] as well as mounting scepticism regarding purported health benefits of alcohol use at these low levels (e.g.[78]).

Most of these guidelines recommend some limits on daily and/or weekly consumption. For example, the US dietary guidelines advise men to limit their drinking to no more than 2 drinks during days when alcohol is consumed, and adult women no more than 1 drink per day on days when alcohol is consumed. For guidelines based on average consumption, they often advise limits on drinking occasions, where men should have no more than 4 drinks and women no more than 3 drinks. Drink sizes vary between countries, and need to be described in the guidelines. Many countries define a standard drink as containing 10 grams of pure ethanol, but there is variation from 8 to 14 grams.

Australia[124], the UK[125] and Canada[126], have recently revised their guidelines down to lower levels following extensive literature reviews. The Australian guidelines recommend no more than 100 grams or 10 drinks per week for men and women alike, and no more than 4 drinks on any day. The Dutch[127,128] (2015) and Danish[129] also have lowered their drinking limits to similar levels. In the latest major review of this field, the Canadian Centre on Substance Use and Addiction[126] has proposed updated guidelines which specify that all drinking involves some risk, with a continuum of risk for a wide range of alcohol-related harms. The risk is described as low or negligible risk up to 2 drinks per week, moderate between 3 and 6 drinks per week, and increasingly high risk at higher levels.

The US dietary guidelines have higher recommended levels for men at no more than 2 drinks in a day (196 grams/week) and for women at 1 drink in a day (98 grams/week).[130] Wood et.al. (2018)[131] estimated that this higher level for men (~200 grams per week) compared with the UK guidelines of 100 grams per week would be responsible for between one and two years of life lost for those drinking to the maximum limit.

There are no official guidelines in Sweden, but in its national guidelines for prevention

A recent policy brief from the World Heart Federation concluded that alcohol has played a major role in the near-doubling of the global prevalence of cardiovascular disease.

and health promotion, the National board for social affairs and health (Socialstyrelsen) still defines hazardous consumption as drinking in excess of 14 drinks per week (168 grams) and 5 drinks at drinking occasions (60 grams) for men; corresponding figures of 9 (126 grams) and 4 (48 grams) for women.[132]

6.1 Guidelines specific to heart disease and hypertension

Recent international clinical guidelines for prevention of heart disease and hypertension, respectively, conclude that alcohol consumption increases the risk of hypertension linearly with no completely safe or reduced risk personal drinking level.

A recent policy brief from the World Heart Federation[78] concluded that alcohol has played a major role in the near-doubling of the global prevalence of cardiovascular disease, including hypertensive heart disease, cardiomyopathy, atrial fibrillation and flutter, and stroke. Further, the widespread message for several decades that alcohol prolongs life, chiefly by reducing the risk of coronary heart disease, is described as a myth by the brief.

Guidelines on the prevention and management of cardiovascular diseases produced by the European Society of Cardiology and other associated medical societies[133] recommend an upper 'safe' level of consumption as being 100g of pure alcohol per week. They base this on epidemiological evidence they interpret as indicating that alcohol increases risk of all stroke subtypes, coronary disease, heart failure, and several less common CVD subtypes but also decreases risk of myocardial infarction. They also cite evidence from genetic studies which greatly reduce confounding effects of lifestyle and environmental factors.

These findings suggest that lifetime abstainers may have the lowest risk of cardiovascular disease (CVD). Further, these studies (using Mendelian Randomisation methods) also indicate uniform increases in blood pressure and body mass index, key risk factors for CVD. Taken together, these findings emphasize that alcohol use, regardless of amount, leads to loss of health across populations with increasing risk at increasing levels of use.

The 2020 International Society of Hypertension Global Hypertension Practice Guidelines[134] also state that high alcohol intake is a risk factor for hypertension and that a positive linear association exists between alcohol consumption, blood pressure, the prevalence of hypertension, and CVD risk.

6.2 Interventions in health care

There is universal recognition that heavy drinking is a risk factor for many diseases and injuries. In many countries there are also guidelines for practitioners in health care to ask patients about their drinking habits and to offer advice when hazardous or harmful drinking is identified, an approach supported by the WHO since the 1980s.[135]

While there is a large research literature on such interventions in health care – screening and brief intervention and referral to treatment (SBIRT) – systematic reviews suggest only modest effects.[136,137] Furthermore, these results are mainly produced in efficacy studies which are not necessarily generalizable to regular health care conditions.

The difficulties involved in integrating screening and brief intervention in practice has now led to rethinking these interventions.[137,138] In particular, the concept of general screening has been questioned by practitioners. An alternative which seems more feasible would be targeted screening, i.e. asking about alcohol when this makes the most clinical sense, as opposed to asking everybody. An obvious example would be hypertension, where alcohol is an accepted risk factor. But, as stated earlier, there are a large number of medical conditions where alcohol can be an important contributor to disease. While general screening identifies more patients with hazardous or harmful drinking than targeted screening,[139] this fact has not been enough to convince practitioners. This illustrates a conflict between a

public health perspective, where health care is seen as an area where a large part of the population can be reached, and a clinical perspective, where the practitioner focuses on the health problem at hand. On the other hand, there is general agreement that inquiries about lifestyle and health habits are a natural part of first visits and general health checks. These should of course not exclude inquiring about alcohol use along with other lifestyle risk factors i.e. smoking, exercise and diet.

Another limitation of the traditional screening and brief intervention approach is uncertainty about how to manage patients who turn out not only to be hazardous or harmful drinkers, but are alcohol dependent. These constitute about one third of the hazardous drinkers. In the SBIRT approach these patients should be referred to addiction specialists. This does not seem to happen. In a meta-analysis no evidence was found that brief alcohol interventions led to an increase in specialist treatment for alcohol use disorders.[140] Most patients with alcohol problems are reluctant to be referred to addiction specialists, largely due to the stigma attached to such treatment.[141] Not knowing how to help these patients contributes to reluctance to ask about alcohol in the first place. The remedy for this reluctance is a combination approach where health care managers require that health behaviours be included in the contracts with health care providers along training in the management of alcohol use disorders. The majority of dependent drinkers have a low or moderate level of dependence, with a good prognosis.[142]

There are simple, but effective approaches that can help general practitioners manage these problems.[143] Patients with severe forms of alcohol dependence, often with psychiatric comorbidity and social problems, may need to be referred to addiction clinics. However, in those clinics which utilize more traditional treatment practices, emphasizing abstinence only, these recommended approaches need to be available and acceptable to referred clients.

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PHOTO: CALEB GEORGE/UNSPLASH

7 Population level intervention

Historically, primary interventions for reducing health risks associated with drinking and blood pressure have included drinking guidelines and brief interventions in health care. Neither of these interventions have been found effective at the population level however.[138,144]

A more cost-effective approach is through the use of policies to reduce overall consumption of alcohol in the wider population, e.g. increased prices, decreased availability and restrictions on alcohol marketing. It has been shown across many countries worldwide that as total alcohol consumption in a population decreases so do numbers of heavier at-risk drinkers and population rates of harm (e.g. alcohol-related chronic illness).[145–147] As discussed earlier, increased risk of hypertension can also occur at quite low levels of consumption but is especially and increasingly enhanced at higher levels of use.

While there is strong general evidence for the effectiveness of alcohol policies in reducing consumption across the spectrum of drinkers and thereby implicitly reducing risks of hypertension, this population association has also been demonstrated in a few studies at the population level. For example, Razvodovsky (2014)[148] explored the relationship over time between total per capita alcohol consumption rates associated with both male and female hypertension mortality rates in Russia. The measurement of total consumption was based upon retail sales plus adjustment for underreported consumption utilizing alcohol psychosis admissions as suggested by Norstrom (2011).[149] The analysis found that alcohol consumption was significantly associated with hypertension mortality rates such that the authors estimated that a 1-litre increase in overall alcohol consumption per year results in a 6.3% increase in the male hypertension mortality rate and in a 4.9% increase in female hypertension mortality rate.

A systematic review and meta-analysis of studies on the association between alcohol consumption and blood pressure in the UK by Roerecke et al, (2017)[49] and Roerecke (2021)[150] found that reduced alcohol consumption was strongly associated with reductions in blood pressure, especially among people consuming more than two drinks per day. These findings have generally been confirmed by other more recent studies (e.g. [50,51]). Modelling from their meta-analysis, Roerecke et al (2018)[64] also estimated that reductions in alcohol use would translate into significant annual reductions in numbers of in-patient hospital admissions and cardiovascular deaths each year.

Important improvements in blood pressure readings can be expected after as little as one month of abstinence from alcohol, with one study demonstrating a 7.2 mmHg reduction in mean blood pressure in previously heavy drinkers. To put the importance of BP control into perspective at a population level, a

Important improvements in blood pressure readings can be expected after as little as one month of abstinence from alcohol.

When discussing population level changes in risks for hypertension, it is important to realise that even small reductions in mean blood pressure levels can translate into substantial reductions in related morbidity and mortality.

2 mmHg increase in mean blood pressure increases mortality from stroke by 10% and from coronary artery disease by 7%.[151]

There have been a number of studies which demonstrate that even modest reductions in per capita alcohol consumption can reduce a variety of alcohol-related harms including cirrhosis mortality, alcohol-related traffic crashes, violent events, and birth-related defects at the population level. Thus, if reductions in overall population level drinking can be achieved via alcohol policy approaches, then there is good reason to advocate for them in reducing the risk of higher blood pressure associated with alcohol consumption. Unfortunately, only about half of hypertension guidelines worldwide recommend a reduction in alcohol consumption to reduce raised blood pressure.[49,154]

There have been some encouraging recent developments. For example, a European Task Force for Cardiovascular Disease Prevention in Clinical Practice, composed of members of the European Society of Cardiology, the European Association of Preventive Cardiology (EAPC) and representatives from 12 cardiology bodies from EU member states, recently recommended restricting alcohol consumption to a maximum of 100 grams per week (about eight Swedish standard drinks) for men and women.[133] They asserted that drinking above this limit lowered life expectancy and that the epidemiological evidence suggested increasing consumption was associated with increased risk for all varieties of cardiovascular disease with the exception of myocardial infarction.

Importantly, the Task Force further recommends population approaches to have the highest level of effectiveness including taxation of alcohol and minimum unit pricing; age limits for sale and serving; drink-driving strategies; government retail monopolies on the sale of alcohol and reducing the hours of sale; and banning alcohol advertising, promotion, and sponsorship of events. They also concluded that alcohol warning labels could add to the effectiveness of these other strategies. Recent studies, however, suggest that of the alcohol warning labels can play special role in encouraging the adoption of more directly effective strategies.[117] Well-designed labels with prominent health messages can both lead to reductions in alcohol consumption.[122]

When discussing population level changes in risks for hypertension, it is important to realise that even small reductions in mean blood pressure levels can translate into substantial reductions in related morbidity and mortality.[155] The author noted that even a 2 mm Hg difference in population systolic pressure was associated with a 4% reduction in heart disease mortality, a 6% reduction in stroke mortality, and a 3% reduction in deaths from all causes.

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8 Summary and recommendations

8.1 Summary

Hypertension is a disorder of the circulatory system that represents the single largest threat to health and longevity globally. It was estimated to be responsible for 10.8 million or 19.2% of deaths worldwide in 20193, largely due to various forms of cardiovascular disease. In this report we discuss evidence for the substantial yet under-appreciated role of alcohol consumption in the causation of high blood pressure and its chronic presentation in the form of hypertension. We also highlight the substantial but mostly untapped potential for the prevention of ill health and mortality through interventions and policies that reduce both individual and population level consumption of alcohol.

We have tried to untangle the considerable complexities in this scientific evidence noting the strengths and weaknesses of different study designs and how the effects of alcohol vary considerably according to dosage, whether BAC is increasing or decreasing and pattern of alcohol intake over time. We have also described the various biological mechanisms responsible for maintaining healthy blood pressure and how alcohol can disrupt these. When making conclusions about causal

associations between risk factors and health it is critical to find consistency between proven biological mechanisms and observed patterns of health in the population. We have attempted this task by considering the results of both clinical and experimental studies alongside many large-scale studies of whole populations and how their health varies according to alcohol consumption across the life course. We have placed particular weight on studies with randomised controlled designs and population level studies using a genetic component to minimise the effects of confounding from lifestyle and demographic factors e.g. Mendelian Randomisation studies. We have placed also particular weight on systematic reviews which summarise the results of all available published high-quality studies.

There is no safe or reduced risk level of consumption of alcohol in relation to risk of hypertension in the longer term and this risk begins to escalate with increased consumption from even a low or moderate level.

There is no safe or reduced risk level of consumption of alcohol in relation to risk of hypertension in the longer term and this risk begins to escalate with increased consumption from even a low or moderate level.

The conclusion that alcohol consumption is causally involved in these observed associations between drinking level and risk of hypertension is supported by high-quality experimental studies on both humans and animals. Such studies have identified a clear role of alcohol consumption in reducing a variety of indicators of the healthy functioning of the circulatory system such as extent of oxidative stress, stiffening of arteries, enlargement of artery walls and blood pressure itself.

We have also considered the full range of both individual and population level strategies to support people reducing their risk of hypertension and the serious associated diseases by reducing their alcohol consumption. This is most readily achieved at the population level provided that governments can be persuaded to implement policies that are effective in reducing population level consumption. Of these the most effective raise or maintain higher prices for alcohol, limit convenience of access and restrict marketing and advertising of alcohol products. Reductions in general population alcohol consumption are primarily achieved through reduced drinking among the heaviest consumers but drinkers across the entire spectrum are known to reduce consumption and hence reduce risk of alcohol-related diseases.

Increasingly, though not universally, guidelines for the specialist management of hypertension include the need for advice that individuals cut down or abstain from drinking alcohol. There is less consensus around the most effective means of primary prevention though we recommend that alcohol is always included in general health screening alongside assessments of other lifestyle risk factors relating to exercise, diet and smoking for example. Physicians and other healthcare providers need training in how best to advise their patients to achieve their health goals. They also need to be supported by specialist advice and readily accessible support services.

Above all else, it is essential for awareness of the causal association between alcohol use, hypertension and related serious diseases to be raised substantially across the population at large, among healthcare providers and among decision-makers responsible for policies that affect the affordability, availability and acceptability of alcohol consumption. There is increasing consensus that requiring compulsory health warnings on all alcohol containers is a necessary first step to encourage less risky use and generate public support for effective population level policies. We provide a number of specific recommendations below that reflect these conclusions.

8.2 Recommendations

Given the strong relationship between alcohol consumption and hypertension, and given the widespread prevalence of hypertension and related diseases such as cardiovascular disease, the following are a series of recommendations intended to: i) increase awareness of this link in the population and among health providers; and, ii) lead to action to prevent and reduce alcohol's contribution to high blood pressure.

Recommendations for Governments and Society

The most effective way to reduce blood pressure in the population is to reduce risk factors at the population level. When it comes to alcohol, the most effective way to reduce consumption, and heavy drinking in particular, is to implement effective alcohol control polices.

- Implement effective policies including those that: maintain or increase alcohol prices (e.g. increased taxes, minimum unit prices), limit the physical availability of alcohol (e.g. restricted trading hours, placing restrictions on home delivery of alcohol, establishing higher minimum drinking age laws), and limit the social appeal of alcohol products (e.g. alcohol advertising restrictions and counter-marketing campaigns, requiring mandatory health warning labels).
- Raise awareness of the links between alcohol and high blood pressure among the general public and health care providers.
- Provide adequate funding and resources to detect and address unhealthy alcohol use.

Recommendations for Health Care Systems and Health Providers

Although it is important to reduce consumption in the population to help prevent hypertension, health care systems and providers are the backbone of treatment for hypertension. Despite this, patients with existing hypertension may not be asked about their alcohol consumption or informed about how this might relate to their hypertension.

- Provide advice on alcohol consumption in hypertension-related practice guidelines.
- Provide adequate incentives, including adequate financial compensation, for counselling and treatment related to alcohol use and/or alcohol use disorders.
- Develop better capacity and evidence-based standards for screening, brief intervention and also treatment of risky drinking and alcohol use disorders within primary care networks.

Recommendations for Individuals

In terms of hypertension, as in terms of overall health, less alcohol is better. People who do not consume alcohol should not start drinking for health reasons. For some, it may be difficult or undesirable to reduce consumption. Nonetheless:

- For all drinkers, it is beneficial to reduce consumption in accordance with national drinking guidelines. For a number of countries, based on the increased risk of hypertension-related diseases and overall risk of death, this would mean reducing maximum weekly consumption to 100g of pure alcohol, not drinking more than 1 Swedish standard drink (12 grams) on most days, and not having more than 2 drinks on a drinking occasion.
- For all drinkers, to minimise alcohol's impact on health (including hypertension) and other social problems, it is especially important to avoid having 4 or more drinks for men or women during a drinking occasion.
- For drinkers with hypertension, particularly when blood pressure is not well controlled with other lifestyle interventions or medications, consider further reductions in alcohol use including a trial of avoiding any use to see if this helps control blood pressure.

The most effective way to reduce blood pressure in the population is to reduce risk factors at the population level.

References

1. American Heart Association. (2021). *What is High Blood Pressure?* https://www.heart.org/-/media/Files/Health-Topics/Answers-by-Heart/What-Is-High-Blood-Pressure.pdf
2. Hörnfeldt, E., & Kahan, T. (2021, June). *Hypertoni—Viss.nu* [Text]. Viss.nu, Region Stockholm, Ett kunskapsstöd för dig som arbetar i primärvården. https://viss.nu/kunskapsstod/vardprogram/hypertoni
3. *GBD Compare Data Visualization*. (2020). Institute for Health Metrics and Evaluation (IHME), Seattle, WA: IHME, University of Washington, 2020. http://vizhub.healthdata.org/gbd-compare
4. Ismail, L., Materwala, H., & Al Kaabi, J. (2021). Association of risk factors with type 2 diabetes: *A systematic review. Computational and Structural Biotechnology Journal, 19*, 1759–1785. https://doi.org/10.1016/j.csbj.2021.03.003
5. Lewington, S., Clarke, R., Qizilbash, N., Peto, R., Collins, R., & Prospective Studies Collaboration. (2002). Age-specific relevance of usual blood pressure to vascular mortality: A meta-analysis of individual data for one million adults in 61 prospective studies. *Lancet (London, England),* 360(9349), 1903–1913. https://doi.org/10.1016/s0140-6736(02)11911-8
6. Petrie, J. R., Guzik, T. J., & Touyz, R. M. (2018). Diabetes, Hypertension, and Cardiovascular Disease: Clinical Insights and Vascular Mechanisms. *The Canadian Journal of Cardiology*, 34(5), 575–584. https://doi.org/10.1016/j.cjca.2017.12.005
7. *WHO fact sheet hypertension*. (2021, August 21). World Health Organization, Fact Sheets, Hypertension. https://www.who.int/news-room/fact-sheets/detail/hypertension
8. Zhou, B., Carrillo-Larco, R. M., Danaei, G., Riley, L. M., Paciorek, C. J., Stevens, G. A., Gregg, E. W., Bennett, J. E., Solomon, B., Singleton, R. K., Sophiea, M. K., Iurilli, M. L., Lhoste, V. P., Cowan, M. J., Savin, S., Woodward, M., Balanova, Y., Cifkova, R., Damasceno, A., … Ezzati, M. (2021). Worldwide trends in hypertension prevalence and progress in treatment and control from 1990 to 2019: A pooled analysis of 1201 population-representative studies with 104 million participants. *The Lancet,* 398(10304), 957–980. https://doi.org/10.1016/S0140-6736(21)01330-1
9. Balu, S. (2009). Estimated annual direct expenditures in the United States as a result of inappropriate hypertension treatment according to national treatment guidelines. *Clinical Therapeutics*, 31(7), 1581–1594. https://doi.org/10.1016/j.clinthera.2009.07.010
10. Balu, S., & Thomas, J. (2006). Incremental expenditure of treating hypertension in the United States. *American Journal of Hypertension*, 19(8), 810–816; discussion 817. https://doi.org/10.1016/j.amjhyper.2005.12.013
11. Benjamin, E. J., Blaha, M. J., Chiuve, S. E., Cushman, M., Das, S. R., Deo, R., de Ferranti, S. D., Floyd, J., Fornage, M., Gillespie, C., Isasi, C. R., Jiménez, M. C., Jordan, L. C., Judd, S. E., Lackland, D., Lichtman, J. H., Lisabeth, L., Liu, S., Longenecker, C. T., … American Heart Association Statistics Committee and Stroke Statistics Subcommittee. (2017). Heart Disease and Stroke Statistics-2017 Update: A Report From the American Heart Association. *Circulation,* 135(10), e146–e603. https://doi.org/10.1161/CIR.0000000000000485
12. Davis, K. E. (2013). Expenditures for Hypertension among Adults Age 18 and Older, 2010: Estimates for the U.S. Civilian Noninstitutionalized Population. In *Statistical Brief (Medical Expenditure Panel Survey (US)). Agency for Healthcare Research and Quality (US).* http://www.ncbi.nlm.nih.gov/books/NBK525008/
13. Nakamura, K., Okamura, T., Miura, K., & Okayama, A. (2014). Hypertension and medical expenditure in the Japanese population: Review of prospective studies. *World Journal of Cardiology,* 6(7), 531–538. https://doi.org/10.4330/wjc.v6.i7.531
14. Dai, H., Much, A. A., Maor, E., Asher, E., Younis, A., Xu, Y., Lu, Y., Liu, X., Shu, J., & Bragazzi, N. L. (2022). Global, regional, and national burden of ischaemic heart disease and its attributable risk factors, 1990-2017: Results from the Global Burden of Disease Study 2017. *European Heart Journal. Quality of Care & Clinical Outcomes*, 8(1), 50–60. https://doi.org/10.1093/ehjqcco/qcaa076
15. Odden, M. C., Coxson, P. G., Moran, A., Lightwood, J. M., Goldman, L., & Bibbins-Domingo, K. (2011). The impact of the aging population on coronary heart disease in the United States. *The American Journal of Medicine*, 124(9), 827-833.e5. https://doi.org/10.1016/j.amjmed.2011.04.010
16. Cook, C., Cole, G., Asaria, P., Jabbour, R., & Francis, D. P. (2014). The annual global economic burden of heart failure. *International Journal of Cardiology,* 171(3), 368–376. https://doi.org/10.1016/j.ijcard.2013.12.028
17. Galis, Z. S., Thrasher, T., Reid, D. M., Stanley, D. V., & Oh, Y. S. (2013). Investing in high blood pressure research: A national institutes of health perspective. *Hypertension (Dallas, Tex.: 1979)*, 61(4), 757–761. https://doi.org/10.1161/HYPERTENSIONAHA.111.00770
18. Dzau, V. J., & Balatbat, C. A. (2019). Future of Hypertension. *Hypertension (Dallas, Tex.: 1979)*, 74(3), 450–457. https://doi.org/10.1161/HYPERTENSIONAHA.119.13437
19. Daugherty, A. M. (2021). Hypertension-related risk for dementia: A summary review with future directions. *Seminars in Cell & Developmental Biology, 116*, 82–89. https://doi.org/10.1016/j.semcdb.2021.03.002
20. Derington, C. G., King, J. B., Bryant, K. B., McGee, B. T., Moran, A. E., Weintraub, W. S., Bellows, B. K., & Bress, A. P. (2019). Cost-Effectiveness and Challenges of Implementing Intensive Blood Pressure Goals and Team-Based Care. *Current Hypertension Reports*, 21(12), 91. https://doi.org/10.1007/s11906-019-0996-x
21. Marchi, K. C., Muniz, J. J., & Tirapelli, C. R. (2014). Hypertension and chronic ethanol consumption: What do we know after a century of study? *World Journal of Cardiology*, 6(5), 283–294. https://doi.org/10.4330/wjc.v6.i5.283
22. Goslawski, M., Piano, M. R., Bian, J.-T., Church, E. C., Szczurek, M., & Phillips, S. A. (2013). Binge drinking impairs vascular function in young adults. *Journal of the American College of Cardiology, 62*(3), 201–207. https://doi.org/10.1016/j.jacc.2013.03.049

23. Oda, N., Kajikawa, M., Maruhashi, T., Iwamoto, Y., Kishimoto, S., Matsui, S., Hidaka, T., Kihara, Y., Chayama, K., Goto, C., Aibara, Y., Nakashima, A., Noma, K., Tomiyama, H., Takase, B., Yamashina, A., & Higashi, Y. (2017). Endothelial function is impaired in relation to alcohol intake even in the case of light alcohol consumption in Asian men; Flow-mediated Dilation Japan (FMD-J) Study. *International Journal of Cardiology, 230*, 523–528. https://doi.org/10.1016/j.ijcard.2016.12.065

24. Suzuki, K., Elkind, M. S. V., Boden-Albala, B., Jin, Z., Berry, G., Di Tullio, M. R., Sacco, R. L., & Homma, S. (2009). Moderate alcohol consumption is associated with better endothelial function: A cross sectional study. *BMC Cardiovascular Disorders, 9*, 8. https://doi.org/10.1186/1471-2261-9-8

25. Phillips, S. A., Osborn, K., Hwang, C.-L., Sabbahi, A., & Piano, M. R. (2020). Ethanol Induced Oxidative Stress in the Vasculature: Friend or Foe. *Current Hypertension Reviews, 16*(3), 181–191. https://doi.org/10.2174/1573402115666190325124622

26. Hwang, C.-L., Muchira, J., Hibner, B. A., Phillips, S. A., & Piano, M. R. (2022). Alcohol Consumption: A New Risk Factor for Arterial Stiffness? *Cardiovascular Toxicology, 22*(3), 236–245. https://doi.org/10.1007/s12012-022-09728-8

27. Laurent, S., Boutouyrie, P., Asmar, R., Gautier, I., Laloux, B., Guize, L., Ducimetiere, P., & Benetos, A. (2001). Aortic stiffness is an independent predictor of all-cause and cardiovascular mortality in hypertensive patients. *Hypertension (Dallas, Tex.: 1979)*, 37(5), 1236–1241. https://doi.org/10.1161/01.hyp.37.5.1236

28. Laurent, S., Katsahian, S., Fassot, C., Tropeano, A.-I., Gautier, I., Laloux, B., & Boutouyrie, P. (2003). Aortic stiffness is an independent predictor of fatal stroke in essential hypertension. *Stroke, 34*(5), 1203–1206. https://doi.org/10.1161/01.STR.0000065428.03209.64

29. Del Giorno, R., Maddalena, A., Bassetti, S., & Gabutti, L. (2022). Association between Alcohol Intake and Arterial Stiffness in Healthy Adults: A Systematic Review. *Nutrients, 14*(6), 1207. https://doi.org/10.3390/nu14061207

30. Charakida, M., Georgiopoulos, G., Dangardt, F., Chiesa, S. T., Hughes, A. D., Rapala, A., Davey Smith, G., Lawlor, D., Finer, N., & Deanfield, J. E. (2019). Response to 'Does smoking or alcohol cause early vascular damage in teenage years?' *European Heart Journal, 40*(42), 3497. https://doi.org/10.1093/eurheartj/ehz608

31. El Khoudary, S. R., Barinas-Mitchell, E., White, J., Sutton-Tyrrell, K., Kuller, L. H., Curb, J. D., Shin, C., Ueshima, H., Masaki, K., Evans, R. W., Miura, K., Edmundowicz, D., Sekikawa, A., & ERA JUMP Study Group. (2012). Adiponectin, systolic blood pressure, and alcohol consumption are associated with more aortic stiffness progression among apparently healthy men. *Atherosclerosis, 225*(2), 475–480. https://doi.org/10.1016/j.atherosclerosis.2012.09.015

32. Gonzalez-Sanchez, J., Garcia-Ortiz, L., Rodriguez-Sanchez, E., Maderuelo-Fernandez, J. A., Tamayo-Morales, O., Lugones-Sanchez, C., Recio-Rodriguez, J. I., Gomez-Marcos, M. A., & EVA Investigators. (2020). The Relationship Between Alcohol Consumption With Vascular Structure and Arterial Stiffness in the Spanish Population: EVA Study. *Alcoholism, Clinical and Experimental Research, 44*(9), 1816–1824. https://doi.org/10.1111/acer.14411

33. Hwang, C.-L., Piano, M. R., Thur, L. A., Peters, T. A., da Silva, A. L. G., & Phillips, S. A. (2020). The effects of repeated binge drinking on arterial stiffness and urinary norepinephrine levels in young adults. *Journal of Hypertension, 38*(1), 111–117. https://doi.org/10.1097/HJH.0000000000002223

34. O'Neill, D., Britton, A., Brunner, E. J., & Bell, S. (2017). Twenty-Five-Year Alcohol Consumption Trajectories and Their Association With Arterial Aging: A Prospective Cohort Study. *Journal of the American Heart Association, 6*(2), e005288. https://doi.org/10.1161/JAHA.116.005288

35. Shiina, K., Takahashi, T., Nakano, H., Fujii, M., Iwasaki, Y., Matsumoto, C., Yamashina, A., Chikamori, T., & Tomiyama, H. (2022). Longitudinal Associations between Alcohol Intake and Arterial Stiffness, Pressure Wave Reflection, and Inflammation. *Journal of Atherosclerosis and Thrombosis*. https://doi.org/10.5551/jat.63544

36. Tisdel, D. M., Gadberry, J. J., Burke, S. L., Carlini, N. A., Fleenor, B. S., & Campbell, M. S. (2021). Dietary fat and alcohol in the prediction of indices of vascular health among young adults. *Nutrition (Burbank, Los Angeles County, Calif.), 84*, 111120. https://doi.org/10.1016/j.nut.2020.111120

37. Fitzpatrick, E., Han, X., Liu, W., Corcoran, E., Burtenshaw, D., Morrow, D., Helt, J.-C., Cahill, P. A., & Redmond, E. M. (2017). Alcohol Reduces Arterial Remodeling by Inhibiting Sonic Hedgehog-Stimulated Stem Cell Antigen-1 Positive Progenitor Stem Cell Expansion. *Alcoholism, Clinical and Experimental Research, 41*(12), 2051–2065. https://doi.org/10.1111/acer.13499

38. Liu, W., Harman, S., DiLuca, M., Burtenshaw, D., Corcoran, E., Cahill, P. A., & Redmond, E. M. (2020). Moderate Alcohol Consumption Targets S100ß+ Vascular Stem Cells and Attenuates Injury-Induced Neointimal Hyperplasia. *Alcoholism, Clinical and Experimental Research*, 44(9), 1734–1746. https://doi.org/10.1111/acer.14415

39. J uonala, M., Viikari, J. S. A., Kähönen, M., Laitinen, T., Taittonen, L., Loo, B.-M., Jula, A., Marniemi, J., Räsänen, L., Rönnemaa, T., & Raitakari, O. T. (2009). Alcohol consumption is directly associated with carotid intima-media thickness in Finnish young adults: The Cardiovascular Risk in Young Finns Study. *Atherosclerosis, 204*(2), e93-98. https://doi.org/10.1016/j.atherosclerosis.2008.11.021

40. Britton, A. R., Grobbee, D. E., den Ruijter, H. M., Anderson, T. J., Desvarieux, M., Engström, G., Evans, G. W., Hedblad, B., Kauhanen, J., Kurl, S., Lonn, E. M., Mathiesen, E. B., Polak, J. F., Price, J. F., Rembold, C. M., Rosvall, M., Rundek, T., Salonen, J. T., Stehouwer, C., … Bots, M. L. (2017). Alcohol Consumption and Common Carotid Intima-Media Thickness: The USE-IMT Study. *Alcohol and Alcoholism (Oxford, Oxfordshire), 52*(4), 483–486. https://doi.org/10.1093/alcalc/agx028

41. Mahajan, H., Choo, J., Masaki, K., Fujiyoshi, A., Guo, J., Hisamatsu, T., Evans, R., Shangguan, S., Willcox, B., Okamura, T., Vishnu, A., Barinas-Mitchell, E., Ahuja, V., Miura, K., Kuller, L., Shin, C., Ueshima, H., & Sekikawa, A. (2018). Association of alcohol consumption and aortic calcification in healthy men aged 40-49 years for the ERA JUMP Study. *Atherosclerosis, 268*, 84–91. https://doi.org/10.1016/j.atherosclerosis.2017.11.017

42. Pletcher, M. J., Varosy, P., Kiefe, C. I., Lewis, C. E., Sidney, S., & Hulley, S. B. (2005). Alcohol consumption, binge drinking, and early coronary calcification: Findings from the Coronary Artery Risk Development in Young Adults (CARDIA) Study. *American Journal of Epidemiology, 161*(5), 423–433. https://doi.org/10.1093/aje/kwi062

43. Yun, K. E., Chang, Y., Yun, S.-C., Davey Smith, G., Ryu, S., Cho, S.-I., Chung, E. C., Shin, H., & Khang, Y.-H. (2017). Alcohol and coronary artery calcification: An investigation using alcohol flushing as an instrumental variable. *International Journal of Epidemiology, 46*(3), 950–962. https://doi.org/10.1093/ije/dyw237

44. Yang, Y., Zhang, N., Huang, W., Feng, R., Feng, P., Gu, J., Liu, G., & Lei, H. (2017). The relationship of alcohol consumption with left ventricular mass in people 35 years old or older in rural areas of Western China. *Journal of the American Society of Hypertension: JASH, 11*(4), 220–226. https://doi.org/10.1016/j.jash.2017.02.002

45. Catena, C., Colussi, G., Verheyen, N. D., Novello, M., Fagotto, V., Soardo, G., & Sechi, L. A. (2016). Moderate Alcohol Consumption Is Associated With Left Ventricular Diastolic Dysfunction in Nonalcoholic Hypertensive Patients. *Hypertension (Dallas, Tex.: 1979), 68*(5), 1208–1216. https://doi.org/10.1161/HYPERTENSIONAHA.116.08145

46. Julian, T. H., Syeed, R., Glascow, N., & Zis, P. (2020). Alcohol-induced autonomic dysfunction: A systematic review. *Clinical Autonomic Research, 30*(1), 29–41. https://doi.org/10.1007/s10286-019-00618-8

47. Tasnim, S., Tang, C., Musini, V. M., & Wright, J. M. (2020). Effect of alcohol on blood pressure. *The Cochrane Database of Systematic Reviews, 7*, CD012787. https://doi.org/10.1002/14651858.CD012787.pub2

48. Greenlund, I. M., Cunningham, H. A., Tikkanen, A. L., Bigalke, J. A., Smoot, C. A., Durocher, J. J., & Carter, J. R. (2021). Morning sympathetic activity after evening binge alcohol consumption. *American Journal of Physiology. Heart and Circulatory Physiology, 320*(1), H305–H315. https://doi.org/10.1152/ajpheart.00743.2020

49. Roerecke, M., Kaczorowski, J., Tobe, S. W., Gmel, G., Hasan, O. S. M., & Rehm, J. (2017). The effect of a reduction in alcohol consumption on blood pressure: A systematic review and meta-analysis. *The Lancet. Public Health, 2*(2), e108–e120. https://doi.org/10.1016/S2468-2667(17)30003-8

50. Blalock, D. V., Berlin, S. A., Young, J. R., Blakey, S. M., Calhoun, P. S., & Dedert, E. A. (2022). Effects of Alcohol Reduction Interventions on Blood Pressure. *Current Hypertension Reports, 24*(4), 75–85. https://doi.org/10.1007/s11906-022-01171-y

51. Kabayama, M., Akagi, Y., Wada, N., Higuchi, A., Tamatani, M., Tomita, J., Nakata, Y., Takiuchi, S., Yamamoto, K., Sugimoto, K., Shintani, A., Rakugi, H., & Kamide, K. (2021). A Randomized Trial of Home Blood-Pressure Reduction by Alcohol Guidance During Outpatient Visits: OSAKE Study. *American Journal of Hypertension, 34*(10), 1108–1115. https://doi.org/10.1093/ajh/hpab082

52. Stewart, S. H., Latham, P. K., Miller, P. M., Randall, P., & Anton, R. F. (2008). Blood pressure reduction during treatment for alcohol dependence: Results from the Combining Medications and Behavioral Interventions for Alcoholism (COMBINE) study. *Addiction (Abingdon, England), 103*(10), 1622–1628. https://doi.org/10.1111/j.1360-0443.2008.02317.x

53. Witkiewitz, K., Kranzler, H. R., Hallgren, K. A., O'Malley, S. S., Falk, D. E., Litten, R. Z., Hasin, D. S., Mann, K. F., & Anton, R. F. (2018). Drinking Risk Level Reductions Associated with Improvements in Physical Health and Quality of Life Among Individuals with Alcohol Use Disorder. *Alcoholism, Clinical and Experimental Research, 42*(12), 2453–2465. https://doi.org/10.1111/acer.13897

54. Xin, X., He, J., Frontini, M. G., Ogden, L. G., Motsamai, O. I., & Whelton, P. K. (2001). Effects of alcohol reduction on blood pressure: A meta-analysis of randomized controlled trials. *Hypertension (Dallas, Tex.: 1979), 38*(5), 1112–1117. https://doi.org/10.1161/hy1101.093424

55. Gepner, Y., Golan, R., Harman-Boehm, I., Henkin, Y., Schwarzfuchs, D., Shelef, I., Durst, R., Kovsan, J., Bolotin, A., Leitersdorf, E., Shpitzen, S., Balag, S., Shemesh, E., Witkow, S., Tangi-Rosental, O., Chassidim, Y., Liberty, I. F., Sarusi, B., Ben-Avraham, S., … Shai, I. (2015). Effects of Initiating Moderate Alcohol Intake on Cardiometabolic Risk in Adults With Type 2 Diabetes: A 2-Year Randomized, Controlled Trial. *Annals of Internal Medicine, 163*(8), 569–579. https://doi.org/10.7326/M14-1650

56. Chen, L., Smith, G. D., Harbord, R. M., & Lewis, S. J. (2008). Alcohol intake and blood pressure: A systematic review implementing a Mendelian randomization approach. *PLoS Medicine, 5*(3), e52. https://doi.org/10.1371/journal.pmed.0050052

57. Cho, Y., Shin, S.-Y., Won, S., Relton, C. L., Davey Smith, G., & Shin, M.-J. (2015). Alcohol intake and cardiovascular risk factors: A Mendelian randomisation study. *Scientific Reports, 5*, 18422. https://doi.org/10.1038/srep18422

58. Chang, Y.-C., Chiu, Y.-F., Lee, I.-T., Ho, L.-T., Hung, Y.-J., Hsiung, C. A., Quertermous, T., Donlon, T., Lee, W.-J., Lee, P.-C., Chen, C.-H., Mochly-Rosen, D., & Chuang, L.-M. (2012). Common ALDH2 genetic variants predict development of hypertension in the SAPPHIRe prospective cohort: Gene-environmental interaction with alcohol consumption. *BMC Cardiovascular Disorders, 12*, 58. https://doi.org/10.1186/1471-2261-12-58

59. Au Yeung, S. L., Jiang, C., Cheng, K. K., Cowling, B. J., Liu, B., Zhang, W., Lam, T. H., Leung, G. M., & Schooling, C. M. (2013). Moderate alcohol use and cardiovascular disease from Mendelian randomization. *PloS One, 8*(7), e68054. https://doi.org/10.1371/journal.pone.0068054

60. Millwood, I. Y., Walters, R. G., Mei, X. W., Guo, Y., Yang, L., Bian, Z., Bennett, D. A., Chen, Y., Dong, C., Hu, R., Zhou, G., Yu, B., Jia, W., Parish, S., Clarke, R., Davey Smith, G., Collins, R., Holmes, M. V., Li, L., … China Kadoorie Biobank Collaborative Group. (2019). Conventional and genetic evidence on alcohol and vascular disease aetiology: A prospective study of 500 000 men and women in China. *Lancet (London, England), 393*(10183), 1831–1842. https://doi.org/10.1016/S0140-6736(18)31772-0

61. Lawlor, D. A., Nordestgaard, B. G., Benn, M., Zuccolo, L., Tybjaerg-Hansen, A., & Davey Smith, G. (2013). Exploring causal associations between alcohol and coronary heart disease risk factors: Findings from a Mendelian randomization study in the Copenhagen General Population Study. *European Heart Journal, 34*(32), 2519–2528. https://doi.org/10.1093/eurheartj/eht081

62. Holmes, M. V., Dale, C. E., Zuccolo, L., Silverwood, R. J., Guo, Y., Ye, Z., Prieto-Merino, D., Dehghan, A., Trompet, S., Wong, A., Cavadino, A., Drogan, D., Padmanabhan, S., Li, S., Yesupriya, A., Leusink, M., Sundstrom, J., Hubacek, J. A., Pikhart, H., … on behalf of The InterAct Consortium. (2014). Association between alcohol and cardiovascular disease: Mendelian randomisation analysis based on individual participant data. *BMJ, 349*(jul10 6), g4164–g4164. https://doi.org/10.1136/bmj.g4164

63. Lankester, J., Zanetti, D., Ingelsson, E., & Assimes, T. L. (2021). Alcohol use and cardiometabolic risk in the UK Biobank: A Mendelian randomization study. *PloS One, 16*(8), e0255801. https://doi.org/10.1371/journal.pone.0255801

64. Roerecke, M., Tobe, S. W., Kaczorowski, J., Bacon, S. L., Vafaei, A., Hasan, O. S. M., Krishnan, R. J., Raifu, A. O., & Rehm, J. (2018). Sex-Specific Associations Between Alcohol Consumption and Incidence of Hypertension: A Systematic Review and Meta-Analysis of Cohort Studies. *Journal of the American Heart Association, 7*(13), e008202. https://doi.org/10.1161/JAHA.117.008202

65. Briasoulis, A., Agarwal, V., & Messerli, F. H. (2012). Alcohol consumption and the risk of hypertension in men and women: A systematic review and meta-analysis. *Journal of Clinical Hypertension (Greenwich, Conn.), 14*(11), 792–798. https://doi.org/10.1111/jch.12008

66. Taylor, B., Irving, H. M., Baliunas, D., Roerecke, M., Patra, J., Mohapatra, S., & Rehm, J. (2009). Alcohol and hypertension: Gender differences in dose-response relationships determined through systematic review and meta-analysis. *Addiction (Abingdon, England), 104*(12), 1981–1990. https://doi.org/10.1111/j.1360-0443.2009.02694.x

67. Puddey, I. B., Mori, T. A., Barden, A. E., & Beilin, L. J. (2019). Alcohol and Hypertension-New Insights and Lingering Controversies. *Current Hypertension Reports, 21*(10), 79. https://doi.org/10.1007/s11906-019-0984-1

68. Henriksson, K. M., Lindblad, U., Gullberg, B., Agren, B., Nilsson-Ehle, P., & Råstam, L. (2002). Development of hypertension over 6 years in a birth cohort of young middle-aged men: The Cardiovascular Risk Factor Study in southern Sweden (CRISS). *Journal of Internal Medicine, 252*(1), 21–26. https://doi.org/10.1046/j.1365-2796.2002.00996.x

69. Piano, M. R., Burke, L., Kang, M., & Phillips, S. A. (2018). Effects of Repeated Binge Drinking on Blood Pressure Levels and Other Cardiovascular Health Metrics in Young Adults: National Health and Nutrition Examination Survey, 2011-2014. *Journal of the American Heart Association, 7*(13), e008733. https://doi.org/10.1161/JAHA.118.008733

70. Hayibor, L. A., Zhang, J., & Duncan, A. (2019). Association of binge drinking in adolescence and early adulthood with high blood pressure: Findings from the National Longitudinal Study of Adolescent to Adult Health (1994-2008). *Journal of Epidemiology and Community Health, 73*(7), 652–659. https://doi.org/10.1136/jech-2018-211594

71. Wellman, R. J., Vaughn, J. A., Sylvestre, M.-P., O'Loughlin, E. K., Dugas, E. N., & O'Loughlin, J. L. (2016). Relationships Between Current and Past Binge Drinking and Systolic Blood Pressure in Young Adults. *The Journal of Adolescent Health: Official Publication of the Society for Adolescent Medicine, 58*(3), 352–357. https://doi.org/10.1016/j.jadohealth.2015.10.251

72. Khan, M. A., Hashim, M. J., Mustafa, H., Baniyas, M. Y., Al Suwaidi, S. K. B. M., AlKatheeri, R., Alblooshi, F. M. K., Almatrooshi, M. E. A. H., Alzaabi, M. E. H., Al Darmaki, R. S., & Lootah, S. N. A. H. (2020). Global Epidemiology of Ischemic Heart Disease: Results from the Global Burden of Disease Study. *Cureus, 12*(7), e9349. https://doi.org/10.7759/cureus.9349

73. Qureshi, N. Q., Mufarrih, S. H., Bloomfield, G. S., Tariq, W., Almas, A., Mokdad, A. H., Bartlett, J., Nisar, I., Siddiqi, S., Bhutta, Z., Mark, D., Douglas, P. S., & Samad, Z. (2021). Disparities in Cardiovascular Research Output and Disease Outcomes among High-, Middle- and Low-Income Countries – An Analysis of Global Cardiovascular Publications over the Last Decade (2008–2017). *Global Heart, 16*(1), 4. https://doi.org/10.5334/gh.815

74. Socialstyrelsen. (2022). *Statistics on Causes of Death 2021* (p. 6). Socialstyrelsen. https://www.socialstyrelsen.se/globalassets/sharepoint-dokument/artikelkatalog/statistik/2022-6-8021.pdf

75. GBD 2019 Risk Factors Collaborators. (2020). Global burden of 87 risk factors in 204 countries and territories, 1990-2019: A systematic analysis for the Global Burden of Disease Study 2019. *Lancet (London, England), 396*(10258), 1223–1249. https://doi.org/10.1016/S0140-6736(20)30752-2

76. *Ischemic Heart Disease—An overview | ScienceDirect Topics*. (2022). Ischemic Heart Disease - an Overview. https://www.sciencedirect.com/topics/medicine-and-dentistry/ischemic-heart-disease

77. Andréasson, S., Chikritzhs, T., Dangardt, F., Holder, H., Naimi, T., & Stockwell, T. (2014). *The Effects of Low-dose Alcohol Consumption* (Alcohol and Society, pp. 6–23). http://urn.kb.se/resolve?urn=urn:nbn:se:iogt-2014-aos-en

78. Arora, M., ElSayed, A., Beger, B., Naidoo, P., Shilton, T., Jain, N., Armstrong-Walenczak, K., Mwangi, J., Wang, Y., Eiselé, J.-L., Pinto, F. J., & Champagne, B. M. (2022). The Impact of Alcohol Consumption on Cardiovascular Health: Myths and Measures. *Global Heart, 17*(1), 45. https://doi.org/10.5334/gh.1132

79. Griswold, M. G., Fullman, N., Hawley, C., Arian, N., Zimsen, S. R. M., Tymeson, H. D., Venkateswaran, V., Tapp, A. D., Forouzanfar, M. H., Salama, J. S., Abate, K. H., Abate, D., Abay, S. M., Abbafati, C., Abdulkader, R. S., Abebe, Z., Aboyans, V., Abrar, M. M., Acharya, P., … Gakidou, E. (2018). Alcohol use and burden for 195 countries and territories, 1990–2016: A systematic analysis for the Global Burden of Disease Study 2016. *The Lancet, 392*(10152), 1015–1035. https://doi.org/10.1016/S0140-6736(18)31310-2

80. Roerecke, M., & Rehm, J. (2012). The cardioprotective association of average alcohol consumption and ischaemic heart disease: A systematic review and meta-analysis: Alcohol and ischaemic heart disease-a meta-analysis. *Addiction, 107*(7), 1246–1260. https://doi.org/10.1111/j.1360-0443.2012.03780.x

81. Roerecke, M., & Rehm, J. (2013). What is Best Evidence in Epidemiology? A Reply to Stockwell (2012): The journal publishes both invited and unsolicited letters. *Addiction, 108*(2), 427–428. https://doi.org/10.1111/j.1360-0443.2012.04051.x

82. Zhao, J., Stockwell, T., Roemer, A., Naimi, T., & Chikritzhs, T. (2017). Alcohol Consumption and Mortality From Coronary Heart Disease: An Updated Meta-Analysis of Cohort Studies. *Journal of Studies on Alcohol and Drugs, 78*(3), 375–386. https://doi.org/10.15288/jsad.2017.78.375

83. Wallach, J. D., Serghiou, S., Chu, L., Egilman, A. C., Vasiliou, V., Ross, J. S., & Ioannidis, J. P. A. (2020). Evaluation of confounding in epidemiologic studies assessing alcohol consumption on the risk of ischemic heart disease. *BMC Medical Research Methodology, 20*(1), 64. https://doi.org/10.1186/s12874-020-0914-6

84. Brien, S. E., Ronksley, P. E., Turner, B. J., Mukamal, K. J., & Ghali, W. A. (2011). Effect of alcohol consumption on biological markers associated with risk of coronary heart disease: Systematic review and meta-analysis of interventional studies. *BMJ, 342*(feb22 1), d636–d636. https://doi.org/10.1136/bmj.d636

85. Chen, D., Zhang, Y., Yidilisi, A., Xu, Y., Dong, Q., & Jiang, J. (2022). Causal Associations Between Circulating Adipokines and Cardiovascular Disease: A Mendelian Randomization Study. *The Journal of Clinical Endocrinology and Metabolism, 107*(6), e2572–e2580. https://doi.org/10.1210/clinem/dgac048

86. Karjalainen, M. K., Holmes, M. V., Wang, Q., Anufrieva, O., Kähönen, M., Lehtimäki, T., Havulinna, A. S., Kristiansson, K., Salomaa, V., Perola, M., Viikari, J. S., Raitakari, O. T., Järvelin, M.-R., Ala-Korpela, M., & Kettunen, J. (2020). Apolipoprotein A-I concentrations and risk of coronary artery disease: A Mendelian randomization study. *Atherosclerosis, 299*, 56–63. https://doi.org/10.1016/j.atherosclerosis.2020.02.002

87. Richardson, T. G., Sanderson, E., Palmer, T. M., Ala-Korpela, M., Ference, B. A., Davey Smith, G., & Holmes, M. V. (2020). Evaluating the relationship between circulating lipoprotein lipids and apolipoproteins with risk of coronary heart disease: A multivariable Mendelian randomisation analysis. *PLoS Medicine, 17*(3), e1003062. https://doi.org/10.1371/journal.pmed.1003062

88. Sabater-Lleal, M., Huang, J., Chasman, D., Naitza, S., Dehghan, A., Johnson, A. D., Teumer, A., Reiner, A. P., Folkersen, L., Basu, S., Rudnicka, A. R., Trompet, S., Mälarstig, A., Baumert, J., Bis, J. C., Guo, X., Hottenga, J. J., Shin, S.-Y., Lopez, L. M., … O'Donnell, C. J. (2013). Multiethnic Meta-Analysis of Genome-Wide Association Studies in >100 000 Subjects Identifies 23 Fibrinogen-Associated Loci but No Strong Evidence of a Causal Association Between Circulating Fibrinogen and Cardiovascular Disease. *Circulation, 128*(12), 1310–1324. https://doi.org/10.1161/CIRCULATIONAHA.113.002251

89. Voight, B. F., Peloso, G. M., Orho-Melander, M., Frikke-Schmidt, R., Barbalic, M., Jensen, M. K., Hindy, G., Hólm, H., Ding, E. L., Johnson, T., Schunkert, H., Samani, N. J., Clarke, R., Hopewell, J. C., Thompson, J. F., Li, M., Thorleifsson, G., Newton-Cheh, C., Musunuru, K., … Kathiresan, S. (2012). Plasma HDL cholesterol and risk of myocardial infarction: A mendelian randomisation study. *The Lancet, 380*(9841), 572–580. https://doi.org/10.1016/S0140-6736(12)60312-2

90. Ward-Caviness, C. K., de Vries, P. S., Wiggins, K. L., Huffman, J. E., Yanek, L. R., Bielak, L. F., Giulianini, F., Guo, X., Kleber, M. E., Kacprowski, T., Groß, S., Petersman, A., Davey Smith, G., Hartwig, F. P., Bowden, J., Hemani, G., Müller-Nurasyid, M., Strauch, K., Koenig, W., … Morrison, A. C. (2019). Mendelian randomization evaluation of causal effects of fibrinogen on incident coronary heart disease. *PloS One, 14*(5), e0216222. https://doi.org/10.1371/journal.pone.0216222

91. Naimi, T. S., Stadtmueller, L. A., Chikritzhs, T., Stockwell, T., Zhao, J., Britton, A., Saitz, R., & Sherk, A. (2019). Alcohol, Age, and Mortality: Estimating Selection Bias Due to Premature Death. *Journal of Studies on Alcohol and Drugs, 80*(1), 63–68.

92. Fillmore, K. M., Stockwell, T., Chikritzhs, T., Bostrom, A., & Kerr, W. (2007). Moderate alcohol use and reduced mortality risk: Systematic error in prospective studies and new hypotheses. *Annals of Epidemiology, 17*(5 Suppl), S16-23. https://doi.org/10.1016/j.annepidem.2007.01.005

93. Liang, W., & Chikritzhs, T. (2013). The Association between Alcohol Exposure and Self-Reported Health Status: The Effect of Separating Former and Current Drinkers. *PLoS ONE, 8*(2), e55881. https://doi.org/10.1371/journal.pone.0055881

94. Lawes, C. M. M., Vander Hoorn, S., Rodgers, A., & International Society of Hypertension. (2008). Global burden of blood-pressure-related disease, 2001. *Lancet (London, England), 371*(9623), 1513–1518. https://doi.org/10.1016/S0140-6736(08)60655-8

95. Corrao, G., Bagnardi, V., Zambon, A., & La Vecchia, C. (2004). A meta-analysis of alcohol consumption and the risk of 15 diseases. *Preventive Medicine, 38*(5), 613–619. https://doi.org/10.1016/j.ypmed.2003.11.027

96. Piano, M. R. (2017). Alcohol's Effects on the Cardiovascular System. *Alcohol Research: Current Reviews, 38*(2), 219–241.

97. Chikritzhs, T., Stockwell, T., Naimi, T., Andréasson, S., Dangardt, F., & Liang, W. (2015). Has the leaning tower of presumed health benefits from 'moderate' alcohol use finally collapsed?: Editorial. *Addiction, 110*(5), 726–727. https://doi.org/10.1111/add.12828

98. Ortolá, R., García-Esquinas, E., López-García, E., León-Muñoz, L. M., Banegas, J. R., & Rodríguez-Artalejo, F. (2019). Alcohol consumption and all-cause mortality in older adults in Spain: An analysis accounting for the main methodological issues. *Addiction (Abingdon, England), 114*(1), 59–68. https://doi.org/10.1111/add.14402

99. Biddinger, K. J., Emdin, C. A., Haas, M. E., Wang, M., Hindy, G., Ellinor, P. T., Kathiresan, S., Khera, A. V., & Aragam, K. G. (2022). Association of Habitual Alcohol Intake With Risk of Cardiovascular Disease. *JAMA Network Open, 5*(3), e223849. https://doi.org/10.1001/jamanetworkopen.2022.3849

100. Laonigro, I., Correale, M., Di Biase, M., & Altomare, E. (2009). Alcohol abuse and heart failure. *European Journal of Heart Failure, 11*(5), 453–462. https://doi.org/10.1093/eurjhf/hfp037

101. Manzo-Avalos, S., & Saavedra-Molina, A. (2010). Cellular and mitochondrial effects of alcohol consumption. *International Journal of Environmental Research and Public Health, 7*(12), 4281–4304. https://doi.org/10.3390/ijerph7124281

102. George, A., & Figueredo, V. M. (2011). Alcoholic cardiomyopathy: A review. *Journal of Cardiac Failure, 17*(10), 844–849. https://doi.org/10.1016/j.cardfail.2011.05.008

103. Piano, M. R. (2002). Alcoholic Cardiomyopathy. *Chest, 121*(5), 1638–1650. https://doi.org/10.1378/chest.121.5.1638

104. Rehm, J., Hasan, O. S. M., Imtiaz, S., & Neufeld, M. (2017). Quantifying the contribution of alcohol to cardiomyopathy: A systematic review. *Alcohol (Fayetteville, N.Y.), 61*, 9–15. https://doi.org/10.1016/j.alcohol.2017.01.011

105. Leon, D. A., Saburova, L., Tomkins, S., Andreev, E., Kiryanov, N., McKee, M., & Shkolnikov, V. M. (2007). Hazardous alcohol drinking and premature mortality in Russia: A population based case-control study. *The Lancet, 369*(9578), 2001–2009. https://doi.org/10.1016/S0140-6736(07)60941-6

106. Chugh, S. S., Havmoeller, R., Narayanan, K., Singh, D., Rienstra, M., Benjamin, E. J., Gillum, R. F., Kim, Y.-H., McAnulty, J. H., Zheng, Z.-J., Forouzanfar, M. H., Naghavi, M., Mensah, G. A., Ezzati, M., & Murray, C. J. L. (2014). Worldwide epidemiology of atrial fibrillation: A Global Burden of Disease 2010 Study. *Circulation, 129*(8), 837–847. https://doi.org/10.1161/CIRCULATIONAHA.113.005119

107. Kodama, S., Saito, K., Tanaka, S., Horikawa, C., Saito, A., Heianza, Y., Anasako, Y., Nishigaki, Y., Yachi, Y., Iida, K. T., Ohashi, Y., Yamada, N., & Sone, H. (2011). Alcohol consumption and risk of atrial fibrillation: A meta-analysis. *Journal of the American College of Cardiology, 57*(4), 427–436. https://doi.org/10.1016/j.jacc.2010.08.641

108. Larsson, S. C., Drca, N., & Wolk, A. (2014). Alcohol consumption and risk of atrial fibrillation: A prospective study and dose-response meta-analysis. Journal of the American College of *Cardiology, 64*(3), 281–289. https://doi.org/10.1016/j.jacc.2014.03.048

109. Voskoboinik, A., Prabhu, S., Ling, L.-H., Kalman, J. M., & Kistler, P. M. (2016). Alcohol and Atrial Fibrillation: A Sobering Review. *Journal of the American College of Cardiology, 68*(23), 2567–2576. https://doi.org/10.1016/j.jacc.2016.08.074

110. Rehm, J., Anderson, P., Prieto, J. A. A., Armstrong, I., Aubin, H.-J., Bachmann, M., Bastus, N. B., Brotons, C., Burton, R., Cardoso, M., Colom, J., Duprez, D., Gmel, G., Gual, A., Kraus, L., Kreutz, R., Liira, H., Manthey, J., Møller, L., … Zarco, J. (2017). Towards new recommendations to reduce the burden of alcohol-induced hypertension in the European Union. *BMC Medicine, 15*(1), 173. https://doi.org/10.1186/s12916-017-0934-1

111. Rehm, J., Gmel, G., Sierra, C., & Gual, A. (2018). Reduction of mortality following better detection of hypertension and alcohol problems in primary health care in Spain. *Adicciones, 30*(1), 9–18. https://doi.org/10.20882/adicciones.726

112. Hanschmidt, F., Manthey, J., Kraus, L., Scafato, E., Gual, A., Grimm, C., & Rehm, J. (2017). Barriers to Alcohol Screening Among Hypertensive Patients and the Role of Stigma: Lessons for the Implementation of Screening and Brief Interventions in European Primary Care Settings. *Alcohol and Alcoholism (Oxford, Oxfordshire), 52*(5), 572–579. https://doi.org/10.1093/alcalc/agx032

113. Bolbrinker, J., Zaidi Touis, L., Gohlke, H., Weisser, B., & Kreutz, R. (2018). European guidelines on lifestyle changes for management of hypertension: Awareness and implementation of recommendations among German and European physicians. *Herz, 43*(4), 352–358. https://doi.org/10.1007/s00059-017-4575-0

114. Miquel, L., López-Pelayo, H., Nuño, L., Arbesú, J. Á., Zarco, J., Manthey, J., Rehm, J., & Gual, A. (2018). Barriers to implement screening for alcohol consumption in Spanish hypertensive patients. *Family Practice, 35*(3), 295–301. https://doi.org/10.1093/fampra/cmx107

115. Zaidi Touis, L., Bolbrinker, J., Riemer, T. G., & Kreutz, R. (2018). Moderation of alcohol consumption as a recommendation in European hypertension management guidelines: A survey on awareness, screening and implementation among European physicians. *BMJ Open, 8*(10), e022026. https://doi.org/10.1136/bmjopen-2018-022026

116. Vay-Demouy, J., Lelong, H., Neudorff, P., Gabet, A., Grave, C., Blacher, J., & Olié, V. (2022). Underuse of lifestyle recommendations in hypertension management in France: The Esteban study. *The Journal of Clinical Hypertension*, jch.14576. https://doi.org/10.1111/jch.14576

117. Giesbrecht, N., Reisdorfer, E., & Rios, I. (2022). Alcohol Health Warning Labels: A Rapid Review with Action Recommendations. *International Journal of Environmental Research and Public Health, 19*(18), 11676. https://doi.org/10.3390/ijerph191811676

118. *Health warning labels on alcoholic beverages: Opportunities for informed and healthier choices* (Brief No. 4; Snapshot Series on Alcohol Control Policies and Practice). (2021). World Health Organization. https://www.who.int/publications-detail-redirect/9789240044449

119. Kokole, D., Anderson, P., & Jané-Llopis, E. (2021). Nature and Potential Impact of Alcohol Health Warning Labels: A Scoping Review. *Nutrients, 13*(9), 3065. https://doi.org/10.3390/nu13093065

120. Hobin, E., Weerasinghe, A., Vallance, K., Hammond, D., McGavock, J., Greenfield, T. K., Schoueri-Mychasiw, N., Paradis, C., & Stockwell, T. (2020). Testing Alcohol Labels as a Tool to Communicate Cancer Risk to Drinkers: A Real-World Quasi-Experimental Study. *Journal of Studies on Alcohol and Drugs, 81*(2), 249–261. https://doi.org/10.15288/jsad.2020.81.249

121. Schoueri-Mychasiw, N., Weerasinghe, A., Vallance, K., Stockwell, T., Zhao, J., Hammond, D., McGavock, J., Greenfield, T. K., Paradis, C., & Hobin, E. (2020). Examining the Impact of Alcohol Labels on Awareness and Knowledge of National Drinking Guidelines: A Real-World Study in Yukon, Canada. *Journal of Studies on Alcohol and Drugs, 81*(2), 262–272. https://doi.org/10.15288/jsad.2020.81.262

122. Zhao, J., Stockwell, T., Vallance, K., & Hobin, E. (2020). The Effects of Alcohol Warning Labels on Population Alcohol Consumption: An Interrupted Time Series Analysis of Alcohol Sales in Yukon, Canada. *Journal of Studies on Alcohol and Drugs, 81*(2), 225–237. https://doi.org/10.15288/jsad.2020.81.225

123. Shield, K., Manthey, J., Rylett, M., Probst, C., Wettlaufer, A., Parry, C. D. H., & Rehm, J. (2020). National, regional, and global burdens of disease from 2000 to 2016 attributable to alcohol use: A comparative risk assessment study. *The Lancet. Public Health, 5*(1), e51–e61. https://doi.org/10.1016/S2468-2667(19)30231-2

124. Australian Government Department of Health and Aged Care. (2020, December 7). *Australian Alcohol Guidelines revised* [Text]. Australian Alcohol Guidelines Revised; Australian Government Department of Health and Aged Care. https://www.health.gov.au/news/australian-alcohol-guidelines-revised

125. *UK Chief Medical Officers' Low Risk Drinking Guidelines* (p. 11). (2016). UK Department of Health. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/545937/UK_CMOs__report.pdf

126. Paradis, C., Butt, P., Shield, K., Poole, N., Wells, T., Naimi, T., Sherk, A., & the Low-Risk Alcohol Drinking Guidelines Scientific Expert Panels. (2022). *Update of Canada's Low-Risk Alcohol Drinking Guidelines: Final Report for Public Consultation* (p. 65). Canadian Centre on Substance Use and Addiction.

127. *Advies in kort Richtllijnen goede voeding 2015.* (2015). Gezondheidsraad Health Council of the Netherlands. https://www.gezondheidsraad.nl/binaries/gezondheidsraad/documenten/adviezen/2015/11/04/richtlijnen-goede-voeding-2015/Advies+in+kort+RGV2015.pdf

128. *New advice Dutch Health Council: 'Don't drink alcohol or drink no more than one glass daily'.* (2015, November 5). https://www.stap.nl/en/news/news.html/3531/4441/new-advice-dutch-health-council-dont-drink-alcohol-or-drink-no-more-than-one-glass-daily

129. *Sundhedsstyrelsens udmeldinger om alkohol.* (2022, September 19). https://www.sst.dk/da/viden/forebyggelse/alkohol/alkoholforebyggelse/sundhedsstyrelsens-udmeldinger-om-alkohol

130. *Facts about moderate drinking* | CDC. (2022, July 25). https://www.cdc.gov/alcohol/fact-sheets/moderate-drinking.htm

131. Wood, A. M., Kaptoge, S., Butterworth, A. S., Willeit, P., Warnakula, S., Bolton, T., Paige, E., Paul, D. S., Sweeting, M., Burgess, S., Bell, S., Astle, W., Stevens, D., Koulman, A., Selmer, R. M., Verschuren, W. M. M., Sato, S., Njølstad, I., Woodward, M., … Danesh, J. (2018). Risk thresholds for alcohol consumption: Combined analysis of individual-participant data for 599 912 current drinkers in 83 prospective studies. *The Lancet, 391*(10129), 1513–1523. https://doi.org/10.1016/S0140-6736(18)30134-X

132. Socialstyrelsen. (2018). *Nationella riktlinjer för prevention och behandling vid ohälsosamma levnadsvanor: Stöd för styrning och ledning.* Socialstyrelsen. https://www.socialstyrelsen.se/globalassets/sharepoint-dokument/artikelkatalog/nationella-riktlinjer/2018-6-24.pdf

133. Visseren, F. L. J., Mach, F., Smulders, Y. M., Carballo, D., Koskinas, K. C., Bäck, M., Benetos, A., Biffi, A., Boavida, J.-M., Capodanno, D., Cosyns, B., Crawford, C., Davos, C. H., Desormais, I., Di Angelantonio, E., Franco, O. H., Halvorsen, S., Hobbs, F. D. R., Hollander, M., … Williams, B. (2022). 2021 ESC Guidelines on cardiovascular disease prevention in clinical practice. *European Journal of Preventive Cardiology, 29*(1), 5–115. https://doi.org/10.1093/eurjpc/zwab154

134. Unger, T., Borghi, C., Charchar, F., Khan, N. A., Poulter, N. R., Prabhakaran, D., Ramirez, A., Schlaich, M., Stergiou, G. S., Tomaszewski, M., Wainford, R. D., Williams, B., & Schutte, A. E. (2020). 2020 International Society of Hypertension Global Hypertension Practice Guidelines. *Hypertension, 75*(6), 1334–1357. https://doi.org/10.1161/HYPERTENSIONAHA.120.15026

135. Babor, T. F., McRee, B. G., Kassebaum, P. A., Grimaldi, P. L., Ahmed, K., & Bray, J. (2007). Screening, Brief Intervention, and Referral to Treatment (SBIRT): Toward a public health approach to the management of substance abuse. *Substance Abuse, 28*(3), 7–30. https://doi.org/10.1300/J465v28n03_03

136. Kaner, E. F., Beyer, F. R., Muirhead, C., Campbell, F., Pienaar, E. D., Bertholet, N., Daeppen, J. B., Saunders, J. B., & Burnand, B. (2018). Effectiveness of brief alcohol interventions in primary care populations. *The Cochrane Database of Systematic Reviews, 2*(2), CD004148. https://doi.org/10.1002/14651858.CD004148.pub4

137. Saitz, R. (2015). 'SBIRT' is the answer? Probably not. *Addiction (Abingdon, England), 110*(9), 1416–1417. https://doi.org/10.1111/add.12986

138. McCambridge, J. (2021). Reimagining brief interventions for alcohol: Towards a paradigm fit for the twenty first century? : INEBRIA Nick Heather Lecture 2019: This lecture celebrates the work of Nick Heather in leading thinking in respect of both brief interventions and wider alcohol sciences. *Addiction Science & Clinical Practice, 16*(1), 41. https://doi.org/10.1186/s13722-021-00250-w

139. Reinholdz, H., Fornazar, R., Bendtsen, P., & Spak, F. (2013). Comparison of systematic versus targeted screening for detection of risky drinking in primary care. *Alcohol and Alcoholism (Oxford, Oxfordshire), 48*(2), 172–179. https://doi.org/10.1093/alcalc/ags137

140. Glass, J. E., Hamilton, A. M., Powell, B. J., Perron, B. E., Brown, R. T., & Ilgen, M. A. (2015). Specialty substance use disorder services following brief alcohol intervention: A meta-analysis of randomized controlled trials. *Addiction (Abingdon, England), 110*(9), 1404–1415. https://doi.org/10.1111/add.12950

141. Wallhed Finn, S., Bakshi, A.-S., & Andréasson, S. (2014). Alcohol consumption, dependence, and treatment barriers: Perceptions among nontreatment seekers with alcohol dependence. *Substance Use & Misuse, 49*(6), 762–769. https://doi.org/10.3109/10826084.2014.891616

142. Andréasson, S., Danielsson, A.-K., & Hallgren, M. (2013). Severity of alcohol dependence in the Swedish adult population: Association with consumption and social factors. *Alcohol (Fayetteville, N.Y.), 47*(1), 21–25. https://doi.org/10.1016/j.alcohol.2012.10.001

143. Wallhed Finn, S. (2018). Fler kan få beroendebehandling om den integreras i primärvård. *Lakartidningen, 115*, E67P.

144. Holmes, J., Beard, E., Brown, J., Brennan, A., Meier, P. S., Michie, S., Stevely, A. K., Webster, L., & Buykx, P. F. (2020). Effects on alcohol consumption of announcing and implementing revised UK low-risk drinking guidelines: Findings from an interrupted time series analysis. *Journal of Epidemiology and Community Health, 74*(11), 942–949. https://doi.org/10.1136/jech-2020-213820

145. Babor, T. F., Casswell, S., Graham, K., Huckle, T., Livingston, M., Rehm, J., Room, R., Rossow, I., & Sornpaisarn, B. (2022). Alcohol: No Ordinary Commodity-a summary of the third edition. *Addiction (Abingdon, England), 117*(12), 3024–3036. https://doi.org/10.1111/add.16003

146. Kehoe, T., Gmel, G., Shield, K. D., Gmel, G., & Rehm, J. (2012). Determining the best population-level alcohol consumption model and its impact on estimates of alcohol-attributable harms. *Population Health Metrics, 10*, 6. https://doi.org/10.1186/1478-7954-10-6

147. Rossow, I., & Mäkelä, P. (2021). Public Health Thinking Around Alcohol-Related Harm: Why Does Per Capita Consumption Matter? *Journal of Studies on Alcohol and Drugs, 82*(1), 9–17.

148. Razvodovsky, Y. E. (2014). Contribution of alcohol to hypertension mortality in Russia. *Journal of Addiction, 2014,* 483910. https://doi.org/10.1155/2014/483910

149. Norström, T. (2011). The role of alcohol in the Russian mortality crisis. *Addiction (Abingdon, England), 106*(11), 1957–1965. https://doi.org/10.1111/j.1360-0443.2011.03513.x

150. Roerecke, M. (2021). Alcohol's Impact on the Cardiovascular System. *Nutrients, 13*(10), 3419. https://doi.org/10.3390/nu13103419

151. Day, E., & Rudd, J. H. F. (2019). Alcohol use disorders and the heart. *Addiction (Abingdon, England), 114*(9), 1670–1678. https://doi.org/10.1111/add.14703

152. Gonzaga, N. A., do Vale, G. T., Parente, J. M., Yokota, R., De Martinis, B. S., Casarini, D. E., Castro, M. M., & Tirapelli, C. R. (2018). Ethanol withdrawal increases blood pressure and vascular oxidative stress: A role for angiotensin type 1 receptors. *Journal of the American Society of Hypertension: JASH, 12*(7), 561–573. https://doi.org/10.1016/j.jash.2018.03.012

153. Leal, S., Ricardo Jorge, D.-O., Joana, B., Maria, S. S., & Isabel, S. S. (2017). Heavy Alcohol Consumption Effects on Blood Pressure and on Kidney Structure Persist After Long-Term Withdrawal. *Kidney & Blood Pressure Research, 42*(4), 664–675. https://doi.org/10.1159/000482022

154. Chalmers, J., Arima, H., Harrap, S., Touyz, R. M., & Park, J. B. (2013). Global survey of current practice in management of hypertension as reported by societies affiliated with the International Society of Hypertension. *Journal of Hypertension, 31*(5), 1043–1048. https://doi.org/10.1097/HJH.0b013e32835f7eef

155. Stamler, R. (1991). Implications of the INTERSALT study. *Hypertension (Dallas, Tex.: 1979), 17*(1 Suppl), I16-20. https://doi.org/10.1161/01.hyp.17.1_suppl.i16

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