



SCIENTIFIC REVIEW

BEER AND HEALTH

MODERATE CONSUMPTION AS PART OF A HEALTHY LIFESTYLE

5TH EDITION

Scientific Committee

Prof Arne Astrup | Dr Ramon Estruch | Dr Henk Hendriks | Prof Frans Kok
Prof Ascensión Marcos | Dr Vincenzo Solfrizzi | Dr Corina-Aurelia Zugravu



SCIENTIFIC REVIEW

BEER AND HEALTH
MODERATE
CONSUMPTION AS PART
OF A HEALTHY LIFESTYLE

2016

Scientific Committee

Prof Arne Astrup | Dr Ramon Estruch | Dr Henk Hendriks | Prof Frans Kok
Prof Ascensión Marcos | Dr Vincenzo Solfrizzi | Dr Corina-Aurelia Zugravu

INDEX

	From the Editor	6
	From the Scientific Committee	8
	Key Messages	10
	Infographic: Beer and a healthy lifestyle	12
1	Basics on beer and health	14
2	Components of beer	22
	Interview: Prof Frans Kok	28
	Infographic: Basics of beer	30
3	Beer and body weight	32
	Infographic: Beer and body weight	40
4	Health aspects of non-alcoholic beer	42
5	Beer and cardiovascular disease	48
	Interview: Dr Ramon Estruch	56
	Infographic: Beer and cardiovascular disease	58
6	Beer and diabetes	60
	Interview: Prof Arne Astrup	70
	Infographic: Beer and type 2 diabetes	72
7	Beer and cancer	74
	Infographic: Beer and cancer	84
8	Beer and the brain	86
9	Beer and other health effects	94
10	Beer and health: making up the balance	100
	Abbreviations	107
	Colophon	109
	References	110

FROM THE EDITOR

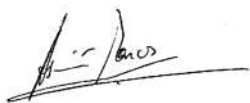
Beer has been a staple part of European diets for thousands of years, and through the ages it has become deeply ingrained in our traditions and culture. Hundreds of different types of beer are brewed across Europe. Made from natural raw materials, beer can play an important part in healthy adult diets and lifestyles, provided that it is consumed in moderation. This booklet provides an overview of the current state of scientific knowledge on the potential benefits and risks of moderate beer consumption. Together with the other members of the Scientific Committee, I have reviewed all sections for scientific soundness, and the many peer-reviewed publications from which the information has been drawn are listed at the end.

Excessive versus responsible alcohol consumption

Beer usually contains alcohol and it must be stressed that the health risks associated with inappropriate and excessive alcohol consumption are well established. Excessive alcohol consumption exerts deleterious effects on the human body, with increased potential for harm to many organs, primarily the liver, as well as on the cardiovascular and central nervous systems. In addition, there are associated social problems such as increased risks of accidents, violence and crime. Besides those well known adverse effects of excessive alcohol consumption, findings presented here also indicate that there is strong evidence for certain benefits from responsible beer drinking.

To drink or not to drink?

The information in this booklet is not intended to encourage people who abstain from drinking alcohol, for whatever reason, to begin consuming beer on health grounds. The purpose is to inform and reassure those who already enjoy drinking beer, that when consumed in moderation, beer can play a role in a healthy diet. However, it is not intended as nutritional advice for individuals. Decisions and recommendations about beer consumption, and alcohol consumption in general, must consider the full range of potential benefits and negative impacts for each individual and society as a whole, according to the recommended limits, and after consulting a general practitioner.



Prof Ascensión Marcos
Editor



FROM THE SCIENTIFIC COMMITTEE

We, the Scientific Committee of the Beer and Health booklet, have reviewed the content and conclude that all relevant scientific literature has been consulted and addressed. The booklet is an accurate presentation of the current state of knowledge on moderate beer consumption and health.

Prof Arne Astrup

Department of Nutrition, Exercise and Sports, University of Copenhagen, Denmark

Expertise: Obesity, energy metabolism, metabolic syndrome, diabetes, dietary fats, appetite

Dr Ramon Estruch

Hospital Clinic, CIBER Obesity and Nutrition, University of Barcelona, Spain

Expertise: Mediterranean diet, wine, beer, cardiovascular disease, atherosclerosis, inflammation

Dr Henk Hendriks

Consultant, the Netherlands

Expertise: Nutrition intervention studies, functional food evaluation, metabolic diseases, weight management

Prof Frans Kok, chair

Emeritus Professor of Nutrition and Health, Wageningen University, the Netherlands

Expertise: Diet in disease prevention, energy balance and body composition

Prof Ascensión Marcos, editor

Immunonutrition Research Group, Institute of Food Science, Technology and Nutrition, Spanish National Research Council, Madrid, Spain
Expertise: Immunonutrition and lifestyle

Dr Vincenzo Solfrizzi

Geriatric Medicine and Memory Unit, University of Bari, 'A. Moro', Italy
Expertise: Mediterranean diet, cognitive decline, pre-dementia, Alzheimer's disease and other dementias

Dr Corina-Aurelia Zugravu

University of Medicine and Pharmacy Carol Davila, Romania
Expertise: Public health nutrition, health promotion and dietary intake evaluation

On behalf of the Scientific Committee

A handwritten signature in black ink, appearing to be 'F. Kok', with a checkmark-like flourish at the end.

Prof Frans Kok
Chair, Scientific Committee

KEY MESSAGES

- ⬡ Beer is a versatile drink with a relatively low alcohol percentage that, when drank in moderation, can be part of an adult's healthy lifestyle.
- ⬡ There are two sides to beer consumption because of the alcohol it contains. There is no doubt that heavy drinking can cause damage in the short and the long term. On the other hand, moderate drinking can have beneficial effects on health.
- ⬡ People who do not drink alcoholic beverages are not encouraged to start drinking them (even in moderation) for health reasons. Alcohol consumption may in some cases lead to excessive use and addiction which is harmful to health.
- ⬡ People who do drink beer or other alcoholic beverages are encouraged to do so in moderation as part of a healthy lifestyle.
- ⬡ For some groups and in some circumstances, such as for those under the legal purchasing age, when driving, when operating machinery, before physical activity such as sports, when taking certain medication, for women during pregnancy or who are trying to conceive or are breastfeeding, for patients with past alcoholism or liver, gastrointestinal or pancreatic disease, it is better not to drink any alcoholic beverages at all.
- ⬡ Years of relevant scientific research from around the world suggests that regular consumption of beer up to two drinks per day for adult men and up to one drink per day for adult women, may have a beneficial effect on health. This is associated with a lower risk of all-cause mortality, mainly because of a lower risk of cardiovascular

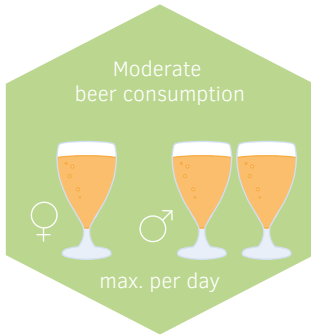
disease, type 2 diabetes, and probably dementia (see Chapters 5, 6, 8 and 10). However, moderate alcohol consumption should always be considered as a supplement and not as an alternative to other healthy lifestyle choices that lower the risks of chronic diseases such as coronary heart disease and type 2 diabetes.

- ⬡ Consumption of all alcoholic beverages, including beer, can contribute to the risk of cancers of the breast, colorectum, head and neck, liver and oesophagus, sometimes at low levels (see Chapter 7). As such, consumers with an already increased susceptibility to such cancers should consider reducing their alcohol consumption.
- ⬡ There is no such thing as ‘a standard drink’, though this booklet defines ‘a drink’ as one that contains 10 grams of alcohol, which equals for example 250 ml of 5% beer (see Chapter 1).
- ⬡ Beer is made from the natural ingredients: water, cereals, hops and yeast. It usually contains alcohol, and contains small amounts of B vitamins, minerals, polyphenols and fibre (see Chapter 2).
- ⬡ The relationship between body weight and beer consumption is complex, but it appears that weight gain may be associated with higher consumption of all alcoholic beverages, including beer (see Chapter 3).
- ⬡ Non-alcoholic beer can be a good alcohol-free alternative. Some studies have looked at the mostly positive effects of alcohol-free beer on hydration, breastfeeding, anxiety, sleep and cardiovascular biomarkers, but more research is needed (see Chapter 4).



BEER AND A HEALTHY LIFESTYLE

Moderate beer consumption can be part of an adult's healthy lifestyle and can have health benefits.



Moderate beer consumption can fit in a healthy lifestyle.

Moderate drinking may lower the risk of cardiovascular disease, type 2 diabetes and dementia.



For people who don't want to consume alcohol, non-alcoholic beer can be a good alternative.

Don't drink if you are:



underaged



driving



pregnant or trying to conceive



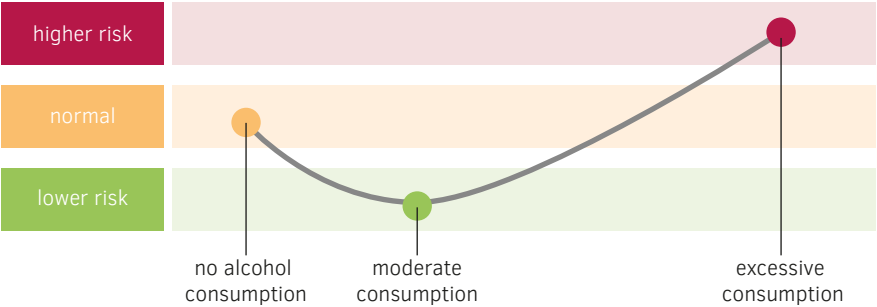
breastfeeding

There is no doubt that heavy drinking can cause damage in the short and the long term.



Potential health effects only apply to moderate beer consumption by adults. This is defined in this infographic as no more than two 25 cl drinks of 5% beer (or two 33 cl drinks of 3.8% beer, or two 10 cl drinks of 13% wine) daily for men and one for women. This may vary for one's age, size and overall health. An otherwise healthy lifestyle is ►

Moderate alcohol consumption reduces the risk of all-cause mortality.



strongly advised. For personal guidance, check with your general practitioner. Please note this does not constitute a drinking guideline. All statements from this infographic are backed-up by science that can be retrieved on www.beerandhealth.eu. ■



1



BASICS ON BEER AND HEALTH

This booklet summarises the relevant scientific literature on moderate beer consumption in relation to health, but there are some aspects you have to take into consideration while reading it.

KEY MESSAGES

- ⬡ Generally, beer usually contains alcohol and this is responsible for some beneficial health effects provided that it is consumed in moderation, i.e. up to two drinks per day for adult men and up to one drink per day for adult women.
- ⬡ There is no such thing as a standard drink, though this booklet defines 'a drink' as one that contains 10 grams of alcohol.
- ⬡ For some groups and in some circumstances, such as for those under the legal purchasing age, when driving, when operating machinery, before physical activity such as sports, when taking certain medication, for women during pregnancy or who are trying to conceive or are breastfeeding, for patients with past alcoholism or liver, gastrointestinal or pancreatic disease, it is better not to drink any alcoholic beverages at all.
- ⬡ When in doubt, it is recommended that you check with your general practitioner for personal guidance on drinking.

1.1 Beer versus alcohol

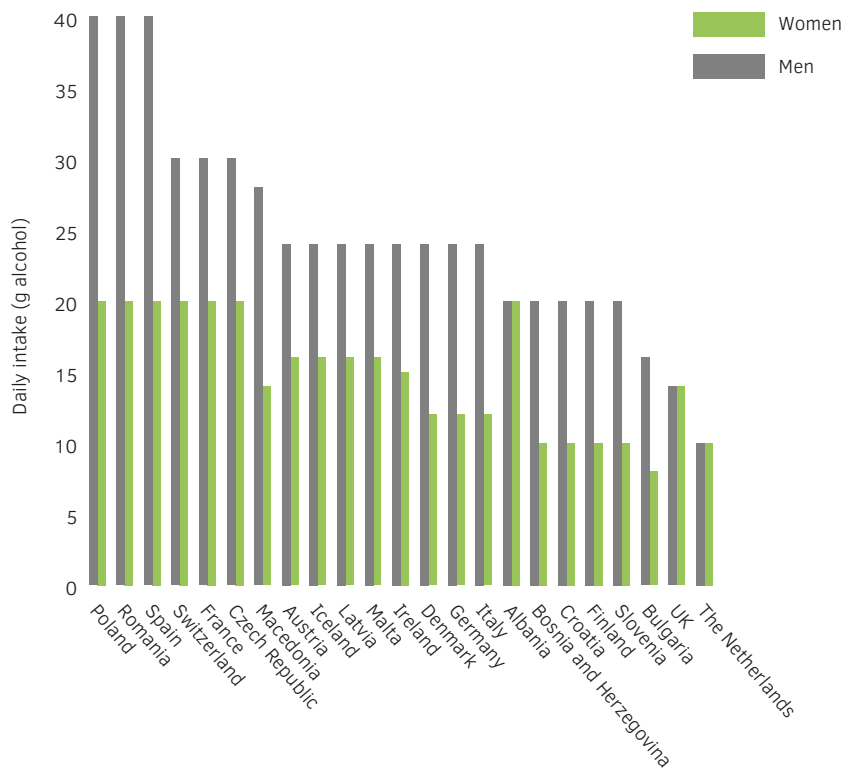
Beer usually contains alcohol, and alcohol is responsible for some positive health effects provided that it is consumed in moderation. Therefore, some of the chapters in this booklet are about the consumption of alcohol in general, and the effects of alcoholic beverages other than beer are also mentioned. Of all alcoholic beverages, beer is a beverage with a relatively low alcohol percentage (on average 4–5%). Other

chapters thus focus on the potential health effects of beer as derived from the natural raw materials from which it is brewed.

1.2 Interpretation of scientific research on beer and health

Years of scientific research suggests that the regular consumption of beer, up to two glasses per day for adult men and up to one glass per day for adult women (while avoiding excessive drinking) can have a ►

Figure 1. Drinking guidelines in Europe



Sources: national guidelines and www.iard.org (April 2016)

The strength of scientific research

In health science, different types of studies are used to analyse and understand the patterns, causes and effects of health and disease conditions in defined populations. Figure 2 shows the strength of conclusions from different studies.

Population studies (observational)

In a population study, for example a cohort study or case control study, a large group of people is followed over a long period of time to try and identify any common (lifestyle) factors that people who get a certain disease may have. However, as scientists cannot control all factors during such studies, some may be overlooked or incorrectly linked to certain disease risks, and so proof of causality cannot be proven with a population study.

Intervention studies (experimental)

In an intervention study, for example randomized controlled trials, (life-

style) factors are deliberately varied in subjects to see if these cause any effect. Intervention studies may provide insight into the biological mechanisms by which selected (lifestyle) factors affect a disease.

Systematic reviews

A systematic review is a thorough, comprehensive and explicit means of integrating and analysing the existing scientific literature in order to try to identify stronger associations.

Meta-analyses

A meta-analysis is a statistical approach to combine data derived from a systematic review, though not all data from systematic reviews are suitable for meta-analysis. ■

Figure 2. Hierarchy in scientific evidence



protective effect on health. However, this statement may not be generalised to the overall population since some individuals may have a family or medical history or a certain lifestyle which counters the general trend. That is why in the text, words like 'may' and 'potential' are often used. When in doubt, it is recommended that you check with your general practitioner for personal guidance on drinking. A characteristic of scientific research is that the results of new studies can change insights, but only when there is enough evidence advice will change. In this booklet, the current state-of-the-art insights based on the most recent evidence are presented.

1.3 How much is moderate?

Recommendations on the safe limits of alcohol consumption vary from one country to another (see Figure 1), and range from a maximum of 8–40 g per day. Also, the amount of alcohol in any one 'standard' drink varies considerably depending on the size of the glass and the strength of the beverage, differing across Europe according to historic traditions and customs from 8–20 g per drink. To be specific about the amount

of alcohol that is responsible for certain health effects, grams of alcohol are used in this booklet.

Definition of moderate alcohol consumption

In this booklet, moderate alcohol consumption is defined as the regular consumption of alcohol up to 20 grams of alcohol per day for adult men and up to 10 grams of alcohol per day for adult women (while avoiding excessive drinking) (see Chapter 10), taking into account a range around the optimal moderate consumption levels.

Communicating to the public

Individuals often consider alcohol consumption in terms of 'drinks' rather than grams of alcohol consumed, but there is no such thing as a 'standard drink'. The sizes and strengths of drinks vary from country to country, from drink to drink, and from consumer to consumer. To be as objective and informative as possible, this booklet uses the term 'a drink' to describe one that contains 10 grams of alcohol. Table 1 shows the size of different drinks containing different levels of alcohol by volume. ►

Table 1. Volume of different drinks, each containing 10 grams of alcohol

Beverage	Volume [ml]
Beer 3.8% alc.	330
Beer 5% alc.	250
Wine 13% alc.	100
Spirits 40% alc.	30

Understanding relative risk

In this booklet you can read about beer consumption lowering or increasing the risk of suffering from certain diseases. It is important to understand that these numbers present relative risks. For example, someone can have a 20% risk of getting a disease, and moderate beer consumption may lower the risk by 10%. This means that the risk is reduced by 2% (10% of 20), i.e. from 20% to 18% when drinking beer in moderation, and not that the risk is reduced to 10%. Equally, when talking about increased risk it is important to know what the existing risk is in order to understand the scale of the issue. ■

Cultural differences in drinking habits

There used to be very clear differences in drinking habits in Northern and Eastern Europe as compared to Southern Europe. But today, we see that cultural differences in drinking habits are changing.^{1,2}

Current drinking preferences

Traditional beer drinking cultures such as Germany have experienced a decrease in beer consumption and an increase in wine consumption. In traditional wine drinking cultures such as France, Italy and Spain, a beer culture has also emerged.² These shifts in drinking habits are accompanied by changes in drinking patterns. Binge drinking used to occur predominantly in Northern and Eastern Europe, but is now seen, though often nowhere near to the same extent, in younger populations throughout Europe.^{2,3}

No 'typical' European consumer

Although nowadays beer and wine are consumed in all countries and both excessive and moderate consumers are found in all countries, drinking cul-

tures do still vary from one country to another. So it remains impossible to talk about the European consumer as one homogenous type of drinker.

Drinking environments

Drinking alcohol occurs mostly in social settings. Traditionally in Southern Europe, drinking of alcohol was embedded in everyday social events, like during meals. In Northern and Central Europe, people used to consume alcohol frequently when going out. These drinking patterns are becoming more and more intertwined, combining alcohol consumption during meals and drinking in other contexts.⁴ Special happenings such as birthdays or weddings may also provide occasions to drink alcohol.^{2,5}

Implications for health

Blood alcohol concentration does not increase as quickly when drinking alcohol during a meal as compared to drinking alcohol on an empty stomach (see Chapter 2). A shift from drinking moderate amounts of alcohol during meals to a pattern of drinking intoxicating amounts even occasionally does not benefit health, and would, for example, counter the positive effects of moderate alcohol consumption on cardiovascular health.⁶ ■

1.4 Moderate is not always responsible

For some groups and on some occasions, it is better to drink no alcoholic beverages at all. This applies in the following circumstances.

- When under the legal purchasing age*
- During pregnancy or when trying to conceive
- Women who are breastfeeding
- When driving
- When operating machinery
- Before physical activity such as sports
- When taking certain medication
- Patients with past alcoholism, or liver, gastrointestinal or pancreatic disease

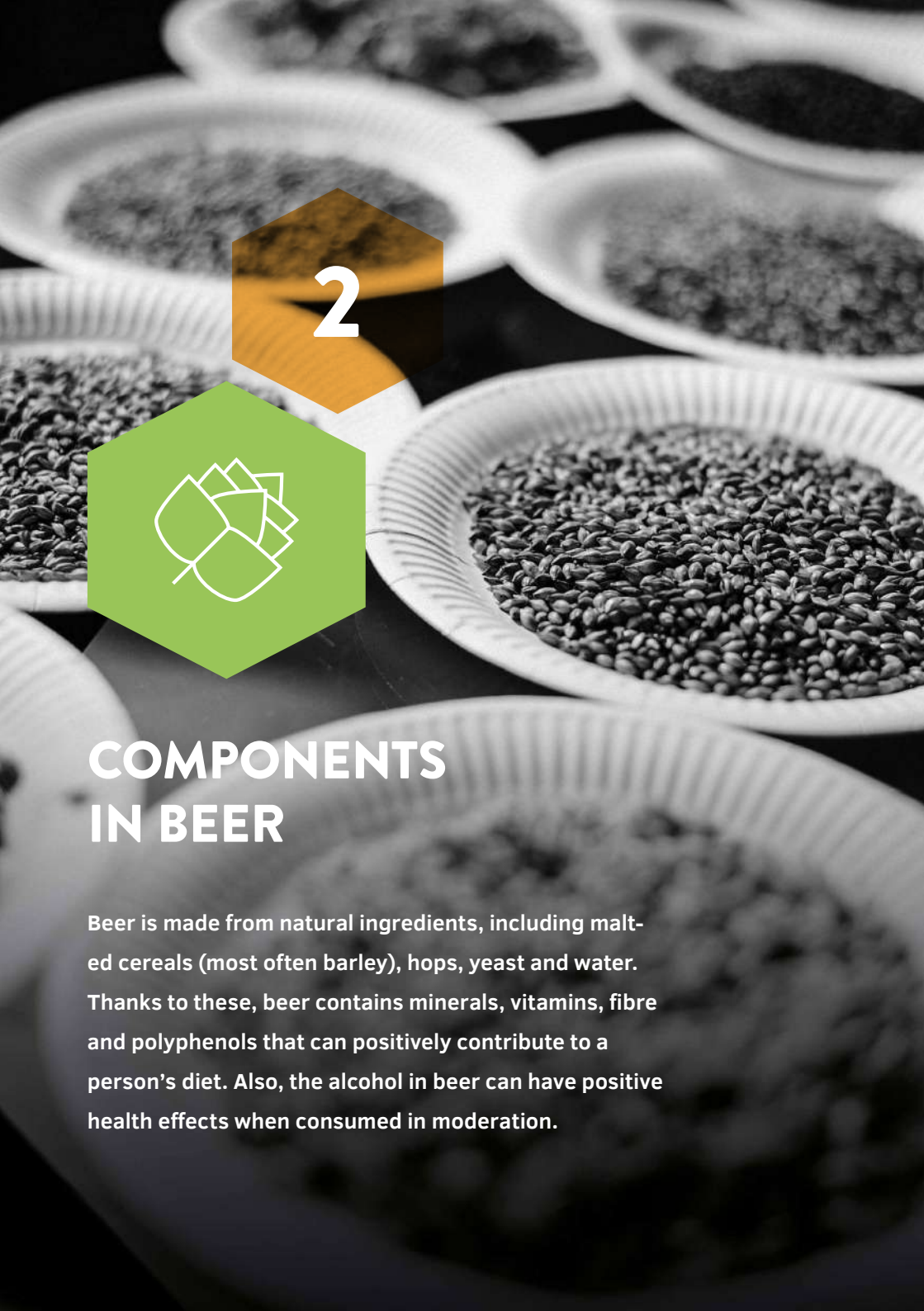
Also, people who do not drink alcoholic beverages are not encouraged to start drinking them (even in moderation) for health reasons. Alcohol consumption can in some cases lead to addiction and excessive use which is harmful to health.

**The legal purchasing age for beer is between 16 and 18 years old in different European countries. ■*

REMEMBER

Saving your drinks only for the weekend is unhealthy

Most health effects of alcohol consumption are attributed to a pattern where drinking is evenly spread out over the week. Research suggests that a pattern including high alcohol consumption ('binge drinking', defined as five or more drinks on a single occasion for men and four or more drinks for women)⁷ can negatively affect health, even when consumption over a week is moderate. Binge drinking must always be discouraged.^{6,8-11} ■



2



COMPONENTS IN BEER

Beer is made from natural ingredients, including malted cereals (most often barley), hops, yeast and water. Thanks to these, beer contains minerals, vitamins, fibre and polyphenols that can positively contribute to a person's diet. Also, the alcohol in beer can have positive health effects when consumed in moderation.



KEY MESSAGES

- ⬡ Beer is made of natural ingredients: water, cereals, hops and yeast.
- ⬡ Thanks to these natural ingredients, beer can make a positive contribution to the diet, especially by providing B vitamins, minerals, polyphenols and fibre.
- ⬡ By eating a balanced diet, most people obtain enough nutrients from food without consuming beer.
- ⬡ If you drink beer, keep in mind that you should drink in moderation as part of a balanced diet.

2.1 What is in a beer?

In addition to the positive effects of moderate alcohol consumption (see Chapters 5, 6, 8 and 9), beer can also make a small contribution to diets by providing certain B vitamins, minerals, polyphenols and fibre. The actual composition of different beers range considerably depending on the raw materials used and the way it is made. Table 2 shows the average composition of regular pilsner/lager beers relative to recommended daily dietary intakes, and the nutritional highlights are discussed in this chapter. Gluten, which people having celiac disease have to avoid, will also be discussed. By eating a balanced diet, most people will get enough nutrients, though beer can also play a role in a balanced diet as long as it is consumed in moderation.

2.2 Vitamins

Small quantities of many B vitamins are available in beer, and their bioavailability has been confirmed by intervention research that has shown an increased absorption level of B vitamins with moderate beer consumption (330 ml per day for women and 660 ml per day for men).^{17,18}

Folate and homocysteine levels

An experimental and a population study have demonstrated that beer consumption may help to maintain homocysteine levels in the normal range due to the high folate content,^{17,19} whereas wine, vodka and whiskey contain no detectable levels of folate.²⁰ High homocysteine levels are found in people having cardiovascular or Alzheimer's disease, though meta-analyses show that lowering homocysteine levels by using B vitamins did not have a significant effect on cardiovascular events, cognitive aging or mortality.^{21,22}

2.3 Minerals

Cereals, water, hops, yeast and processing conditions can all contribute to the mineral content of beer.²³ About 75% of the minerals in beer come from the malt, with the remaining 25% originating from the water.²⁴

Some important minerals for health effects include silicon, potassium and sodium.

Silicon

Many biological roles of silicon remain unknown, and consequently, the recommended daily silicon intake has not yet been set.²⁵ Beer is a substantial source of silicon in the diet, in the range of 6.4–56.5 mg/l²⁶ with an average of ~19 mg/l. After drinking beer, serum and urinary silicon levels increase significantly, confirming that beer is a readily bioavailable source of silicon,²⁷ and beers made from barley tend to contain more silicon than those made from wheat. Hops contain substantially more silicon than cereals, but quantitatively, hops make a much smaller contribution to beer than malt. In comparison, wines and spirits have lower levels of silicon.¹³ A review shows that the accumulated evidence over the past 30 years indicates that silicon plays an important role in bone formation and in bone and connective tissue health,¹³ and it is suggested that the silicon component of beer may contribute to some of these positive effects.²⁸ However, more research is needed to investigate whether the dietary silicon provided by moderate beer consumption actually reduces the risks of developing osteoporosis (see Chapter 9).

Potassium to sodium ratio

Beer has a relatively high potassium to sodium ratio (typically 4:1), which is beneficial in keeping blood pressure at normal and healthy levels.²⁹

2.4 Polyphenols

In the past decade, there has been increased interest in the potential health benefits of dietary plant polyphenols, due to their observed antioxidant and anti-inflammatory effects. Epidemiological studies and associated meta-analyses suggest that the long term consumption of diets rich in plant polyphenols offer protection against the development of cancers, cardiovascular diseases, diabetes, osteoporosis and neurodegenerative diseases.³⁰ ►

Table 2. The average composition of a Pilsner style, lager beer in Europe relative to recommended dietary intakes

Component	Unit	Average in beer Per 100 ml	Daily requirements for adults (19–50 years old) ¹⁴⁻¹⁶	
			Male	Female
Water	g	93	3700	2700
Alcohol	%	4.4	-	-
Carbohydrate	g	2.9	130	130
Protein	g	0.34	56	46
Energy	kcal	39	2550	1940
Fibre ¹²	g	0.2	38	25
Vitamins				
Thiamin (B1)	mg	0.01	1.0	0.8
Riboflavin (B2)	mg	0.03	1.3	1.1
Niacin (B3)	mg	0.65	17	13
Pantothenic acid (B5)	mg	0.06	5	5
Pyridoxine (B6)	mg	0.04	1.4	1.2
Folate	µg	5.25	200	200
Cobalamin (B12)	µg	0.05	1.5	1.5
Minerals				
Calcium	mg	4.90	700	700
Copper	mg	0.01	1.2	1.2
Iron	mg	0.09	8.7	14.8
Potassium	mg	35.33	3500	3500
Magnesium	mg	7.54	300	270
Manganese	mg	0.02	3	3
Silicon ¹³	mg	1.92	ND	ND
Sodium	mg	4.51	1600	1600
Phosphorus	mg	19.42	550	550
Selenium	µg	0.31	75	60
Zinc	mg	0.03	9.4	6.8

ND = not determined

Sources:

Composition of beer: Derived from the Food composition data of 16 European countries via www.EuroFIR.org (except for data on fibre and silicon).

Dietary recommendations: European Food Safety Authority,¹⁴ British Nutrition Foundation,¹⁵ Food and Nutrition Board¹⁶

Polyphenols in beer

More than 35 phenolic compounds have been identified in beer, with about 80–90% from the malt and 10–20% from the hops.²³ The total amount of polyphenols depends on the type of beer, based on the raw materials and the brewing process. Per drink (of equivalent alcohol content), beer contains more than twice as many polyphenols as white wine and half the amount in red wine.³¹ In beer, xanthohumol and its metabolites isoxanthohumol and phytoestrogen 8-prenylnaringenin provide in vitro health properties such as anticarcinogenic, anti-invasive, anti-inflammatory and antioxidant effects. However, further studies in humans are needed to determine whether the plasma concentrations of such compounds derived from moderate beer consumption have the same bioactivity as observed in vitro.³²

Cardiovascular disease and polyphenols

As can be seen in Chapter 5, the consumption of 10–20 g alcohol per day can have protective effects against cardiovascular disease. Different studies speculate that other factors in beer (and wine) could also be protective; mainly polyphenols,^{32,33} and two studies suggest polyphenols in non-alcoholic beer may also play a part (see Chapter 4). More randomized clinical trials focused on identifying the actual mechanisms behind the action of polyphenols are needed to understand if and how much they contribute to the protective effect.

2.5 Fibre

Although international food composition tables report no dietary fibre in beer, it is evident that lager and dark beers do contain amounts of soluble dietary fibre (1.87–2.02 g/l). Soluble fibre in beer is derived from the cell walls of barley, and the indigestible carbohydrates (β -glucans and arabinoxylans) are the largest constituents of dietary fibre.¹² The European Food Safety Authority (EFSA) concluded that barley β -glucans have been shown to lower blood cholesterol, and at least 3 g of barley β -glucans should be consumed per day in order to obtain

the claimed effect.³⁴ Barley β -glucans are often found in beer, however, the levels vary widely depending on brewing processes, and more research is necessary.

2.6 Gluten

In Europe, an estimated 1% of adults and children have celiac disease, an autoimmune disorder in which the immune system reacts to gluten.³⁵ As beer is usually made from malted barley or wheat, it will therefore contain small quantities of gluten. There is an issue however, regarding the determination of gluten levels in beer, as the current method described by the Codex Alimentarius is not valid for use in hydrolyzed and fermented products.³⁶ For people diagnosed with celiac disease, only beer with the official gluten free logo should be consumed.³⁷ Official gluten-free beers are brewed by using techniques that reduce the level of gluten in barley-based beer, use gluten free cereals, or use fermentable sugars or syrups.³⁸ ■

REMEMBER

It is better to drink alcoholic beverages on a full stomach

If alcohol is consumed on an empty stomach, it is absorbed faster than if the stomach is full. Since elimination of alcohol does not depend on factors that can be directly influenced, peak blood alcohol concentration (BAC) when drinking alcoholic beverages on an empty stomach will be higher than when drinking during or soon after having a meal.³⁹ But the type of alcoholic beverage is also important. When drinking on an empty stomach, more concentrated beverages like spirits will produce a higher peak BAC than when the same amount of alcohol is consumed as beer. When alcohol is consumed with or soon after a meal, the highest peak BAC is seen with more diluted drinks like beer, but this peak is still lower than when drinking beer on an empty stomach.⁴⁰ So to avoid high peak blood alcohol concentrations, it is better to drink alcoholic beverages with or soon after a meal, or to choose more diluted beverages like beer. ■



INTERVIEW

**“BEER CAN BE PART
OF A HEALTHY
LIFESTYLE”**

PROF FRANS KOK

**Emeritus Professor of Nutrition and Health,
Wageningen University, the Netherlands**

**Expertise: Diet in disease prevention, energy
balance and body composition**

How does moderate beer consumption fit in a healthy lifestyle?

“First of all, there is an obvious risk of medical and social harm from alcohol abuse. And you don’t have to drink alcoholic beverages for your health. There are many other ways to stay healthy. Adults who are used to drinking alcoholic beverages are advised to limit their intake to a maximum of two drinks per day for men and a maximum of one drink for women. The most favourable drinking pattern is regular daily or almost daily drinking, while avoiding the clearly harmful binge drinking. Keeping this in mind, beer consumption can be part of a healthy lifestyle.”

If beer is consumed in moderation, how does it affect your health?

“Adults, who limit their beer consumption to one or two drinks per day, benefit from a lower risk of cardiovascular disease, type 2 diabetes and dementia. Furthermore, beer is made only from natural ingredients, in which there are small amounts of B vitamins from the cereal and yeast, and fibre and polyphenols from the cereals and hops which might also have beneficial effects, but further research is needed. And remember that by eating a balanced diet, most people will get enough nutrients from their food.”

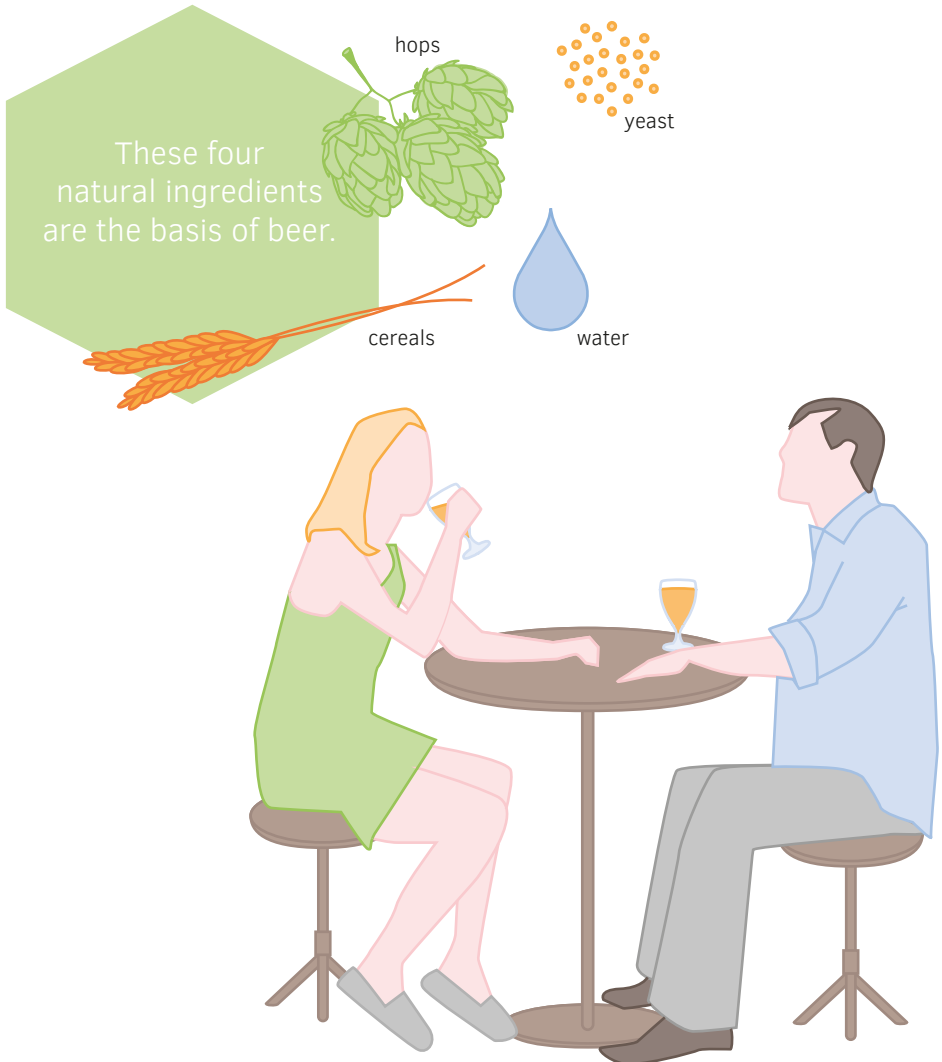
What would you like to study in the area of moderate beer consumption as part of a healthy lifestyle, if you had unlimited funds?

“There are non-alcoholic, low-alcoholic and alcoholic beers. It would be interesting to see whether and how these beverages differ in their influence, for example on rehydration. With increasing life expectancy and the increasing number of elderly people, hydration is an important topic.”



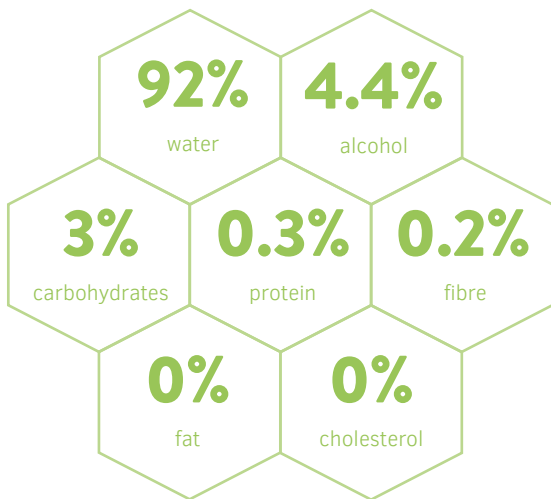
BASICS OF BEER

Beer is a fermented beverage with a relatively low (or no) alcohol percentage, whose natural ingredients contain small amounts of valuable nutrients, minerals and vitamins.

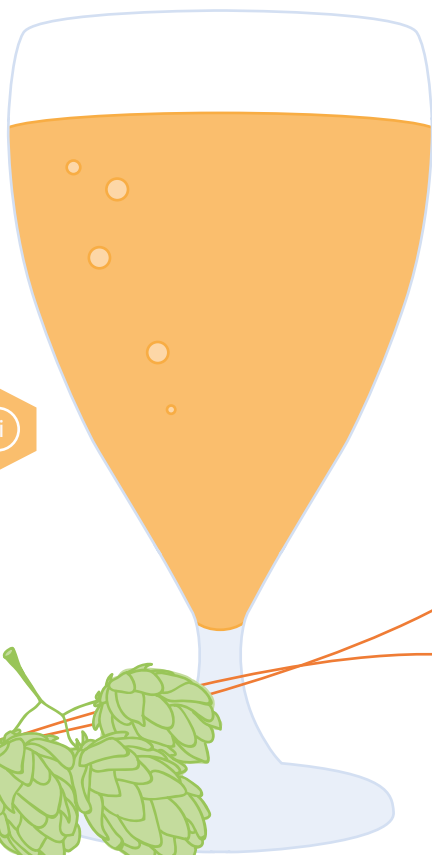
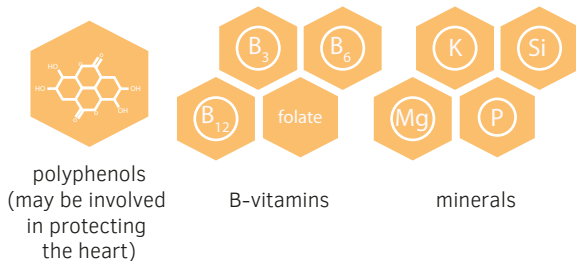


Potential health effects only apply to moderate beer consumption by adults. This is defined in this infographic as no more than two 25 cl drinks of 5% beer (or two 33 cl drinks of 3.8% beer, or two 10 cl drinks of 13% wine) daily for men and one for women. This may vary for one's age, size and overall health. An otherwise healthy lifestyle is ►

The average composition of a Pilsner style, lager beer in Europe.



Beer also contains small amounts of valuable components:



strongly advised. For personal guidance, check with your general practitioner. Please note this does not constitute a drinking guideline. All statements from this infographic are backed-up by science that can be retrieved on www.beerandhealth.eu. ■



3



BEER AND BODY WEIGHT

There is a widespread belief that alcoholic beverages, and beer in particular, lead to weight gain, especially around the abdomen. However, scientific evidence is not clear. Alcoholic beverages certainly contain calories but it seems that weight gain is mostly associated with higher intake levels. Moderate alcohol consumption, particularly in women, seems not to be associated with weight gain.



KEY MESSAGES

- ⬡ In beer, about two thirds of the calories come from the alcohol and about one third from the carbohydrates.
- ⬡ It seems that weight gain is mostly associated with higher levels of drinking beer and other alcoholic beverages, and not with moderate alcohol consumption, particularly in women.
- ⬡ The relationship between body weight and alcohol consumption is complex, involving not only the amount and type of alcohol consumed, but also drinking patterns, gender, beverage type and lifestyle can play a role.
- ⬡ The relationship between alcohol consumption and metabolic syndrome risk seems to be J-shaped, with reduced risk associated with low alcohol consumption and higher risk with heavy drinking.
- ⬡ Obesity is a multi-factorial condition and it is difficult to truly assess the independent influence of alcohol intake on obesity risk.

3.1 Obesity in Europe

In Europe, being overweight or obese (severely overweight) has reached epidemic proportions.⁴² Among the 19 EU member states for which data are available, the proportion of adults (aged 18 years and over) who were considered to be overweight or obese in 2008 varied between 37.0% and 56.7% for women, and between 51.0% and 69.3% for men.⁴³ Obesity is a major contributor to the global burden of chronic diseases and disabilities.⁴⁴ Increased adiposity is a key risk factor for type 2 diabetes, dyslipidemia and cardiovascular disease, and is associated with many other conditions including osteoarthritis, certain types of cancer, mental illness, and increased mortality.⁴⁵⁻⁵¹

3.2 Calories from beer

Beer, as with almost every other food or drink, contains calories. In beer, about two thirds of the calories comes from the alcohol in it, one third from carbohydrates, and a negligible amount from protein, though these proportions can differ depending on the composition and strength of the beer and how it is brewed.⁵²

Calories from alcohol

Alcohol is the richest energy source in beer and has an energy value of 7 kcal per gram. The breakdown of alcohol in the body takes precedence over the breakdown of other nutrients, as the body cannot store alcohol and treats it as a potentially harmful sub-

stance, though small amounts of alcohol with meals may stimulate energy expenditure.^{53,54}

Calories from carbohydrates

By burning carbohydrates, the body metabolises 4 kcal per gram of carbohydrate. In general, carbohydrate levels in beer range from 20–30 g per litre.⁵⁵ A lager beer contains about the same amount of carbohydrates per serving as a sweet white wine, less than a liqueur, but more than a dry white wine.³¹

3.3 Effects of alcohol on appetite, body weight and obesity

If you eat more calories than you burn, you gain weight. Energy from alcoholic beverages is additive to that from other dietary sources. However, data from population studies suggest that moderate alcohol consumption may protect against obesity, particularly in women.⁵⁶ Several studies investigated the influence of alcohol consumption on appetite, body weight and obesity.

Appetite

A brief review of literature clearly shows that energy consumed as alcohol is additive to that from other dietary sources, leading to short term passive overconsumption of energy. Alcohol consumed before or with meals tends to increase food intake, probably through enhancing the short term rewarding effects of food,⁵⁶ and possibly because alcohol increases the rewarding value of food.⁵⁷ ►

Alcohol metabolism

Alcohol is mainly absorbed via the small intestine and is broken down in the liver. Only 5% of alcohol consumed leaves the body directly via excretion, respiration and perspiration, in urine, breath and sweat. The enzymes alcohol-dehydrogenase (ADH) and aldehyde-dehydrogenase (ALDH) in the liver break down about 7 g of alcohol per hour.⁸¹ ADH oxidizes alcohol into acetaldehyde, a carcinogenic compound involved in increased cancer risk. Acetaldehyde is able to bind to and cause mutations in DNA, increasing the risk of uncontrollable cell division. ALDH turns acetaldehyde in the non-toxic compound acetate, and is converted into carbon dioxide (CO₂) or Acetyl CoA, a substrate for energy production in the body (see Figure 3).⁸²

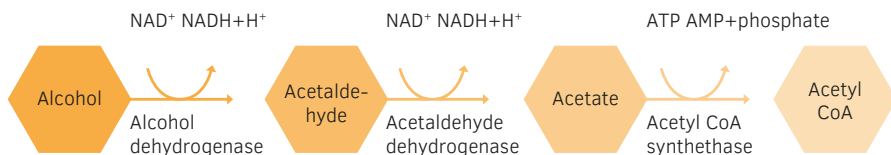
MEOS pathway

When consuming more than 40 g of alcohol per day for at least a week, another mechanism is also activated to break down alcohol, the microsomal ethanol oxidizing system (MEOS). The protein CYP2E1 involved in this system is associated with the activation of carcinogenic reactive oxygen.⁸³

Effect of alcohol on fat oxidation

The human body has no storage capacity for alcohol and aims to eliminate alcohol as soon as it enters the system. When alcohol is consumed, oxidation begins immediately while oxidation of other macronutrients is suppressed. Therefore, alcohol intake decreases fat oxidation during the time that ingested alcohol is being metabolized.^{84,85} ■

Figure 3. Metabolic pathway of alcohol



Body weight and obesity

Overall, it appears that light to moderate alcohol intake is less likely to be a risk factor for obesity than heavy drinking and binge drinking, which have been more consistently linked to adiposity.⁵⁴ A systematic review shows that weight gain is seen with high levels of alcohol consumption. For moderate consumption there is a difference between beverages. Wine seems to protect against weight gain whilst spirits tend to promote weight gain.⁵⁸ But with beer, there is not enough scientific evidence, especially for women,⁴¹ though based on a systematic review it seems that consumption of up to 500 ml per day for men does not contribute to weight gain.

3.4 Other factors that influence the effect of alcohol on body weight

The relationship between body weight and alcohol consumption is complex. Not only are the amount and type of alcohol consumed important, but also drinking patterns, gender, type of beverage and lifestyles may play a role.

Drinking patterns

Drinking patterns may be important in how alcohol consumption influences body weight. A population study shows that among men who consumed moderate amounts (<30 g) or intermediate amounts of alcohol (30–100 g) per week, the ones who drank daily had lower body mass index (BMI) and waist circumference compared

to those who drank on 1–2 days or 3–6 days per week. The results were similar for beer and wine consumption,⁵⁹ and earlier population studies showed similar results. It seems that those who consume the greatest quantity of alcohol and the least frequently (binge drinking) were the most overweight. But frequent light or moderate alcohol consumption is not associated with weight gain.^{60–62}

Gender

Middle aged women who drink moderately might even benefit from lower relative risk of weight gain. A population study found that post-menopausal women of normal weight who consume alcoholic beverages moderately (median intake of 19.4 g per day) have a reduced relative risk of becoming overweight (35%) or obese (88%),⁶³ and these results corroborate those of previously published findings.^{64–70}

Type of beverage and lifestyle

Although some studies suggest that beer may promote obesity more than wine, other studies find similar associations with both.⁴¹ Experimental studies suggest that wine stimulates food intake more than beer,⁷¹ and people who prefer beer may differ from non-drinkers or wine consumers with regard to multiple lifestyle factors related to obesity. Beer drinkers appear to have poorer dietary habits than wine drinkers^{72–74} and beer drinkers are more often smokers.^{72,75,76} ►

Calories in drinks and snacks

On average, men require some 2,500 kilocalories (kcal) a day, while women require 2,000 kcal. If a person consumes more calories than necessary and fails to exercise enough, then weight gain will result. Food and drinks both provide calories (see Table 3). ■

Table 3. Approximate calorie content of food and drinks

Food or drink	Energy (kcal) per 100 ml or g	Serving*	Energy (kcal) per serving**
Cappuccino	35	125 ml - cup	45
Non-alcoholic beer (0.0%)	20	250 ml - glass	50
Beer (5%)	42	250 ml - glass	105
Orange juice	42	250 ml - glass	105
Red Wine (12%)	71	150 ml - glass	105
Banana	90	130 g - average banana	115
Milk	47	250 ml - glass	120
Milk chocolate	542	25 g - small bar	135
Mini pizza	235	100 g	235

* Servings vary across Europe

** Rounded to 5 kcal

Derived from the Food composition data of 16 European countries via www.EuroFIR.org

Physical activity may also be a potential confounding factor, and it is difficult to appropriately adjust for all these factors.⁴¹ Individuals who frequently drink moderate amounts of alcohol may enjoy a healthier lifestyle in general that may protect them from weight gain. Overall, obesity is a multi-factorial condition and it is difficult to truly assess the independent influence of alcohol intake on obesity risk.⁵⁴

3.5 Metabolic syndrome

Metabolic syndrome (MetS) is a clustering of risk factors, including central obesity (high waist circumference), insulin resistance, high blood triglycerides, low high density lipoprotein (HDL) cholesterol, and hypertension, that together result in a fivefold increased risk of type 2 diabetes and a threefold increased risk of cardiovascular disease. Metabolic syndrome might also increase the risk of cancer.⁷⁷ One in six Europeans, and up to one in three in some European countries, suffers from MetS.⁷⁸

Metabolic syndrome and alcohol consumption

Although the level of alcohol consumption for a beneficial effect varies, there seems to be a J-shaped relationship between alcohol consumption and MetS according to two meta-analyses. One showed that alcohol consumption of less than 40 g per day in men and less than 20 g per day in women significantly reduces the prevalence of MetS compared to non-drinkers by 16% and 25%, respectively.⁷⁹ The other showed a significantly reduced relative risk of MetS by 14% with very light alcohol consumption (0.1–5.0 g per day), but a much increased risk by 86% with consumption of more than 35 g of alcohol per day.⁸⁰ ■

REMEMBER

Beer is not always the only cause of a 'beer belly'

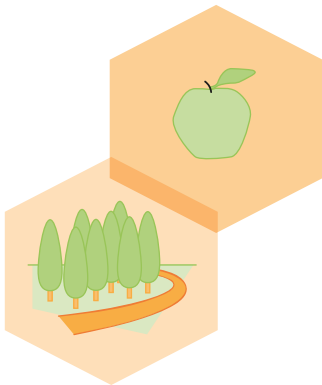
There is a widespread belief that drinking beer causes a fat stomach, a phenomenon popularly referred to as a 'beer belly'. However, there is insufficient scientific evidence to confirm that consuming beer at moderate levels (<500 ml per day) is really responsible for a large waist, although drinking beer at higher levels may be positively associated with getting a bigger belly.⁴¹ If it is not the beer, then where does the 'beer belly' phenomenon come from? It might be at least in part associated with the eating habits and lifestyle of the beer consumer. People who mainly drink beer seem to also eat less healthily than people who prefer wine or who don't drink alcoholic beverages at all. These differences are largely explained by other socio-demographic and lifestyle factors, particularly smoking and a lack of exercise. After adjustment for these factors, the diet of beer and wine drinkers does not seem to differ that much. Thus, it appears most likely that the lifestyle and demographic factors of beer consumers play a more significant role in the formation of 'beer bellies' than the actual consumption of beer per se.⁸⁶ ■



BEER AND BODY WEIGHT

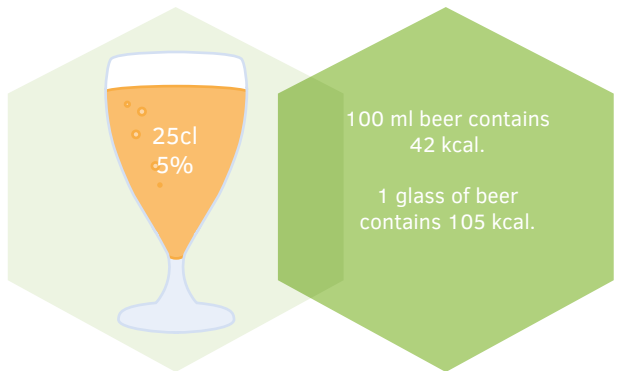
Moderate beer consumption as part of an adult's healthy lifestyle does not lead to weight gain.

Beer can form part of a healthy lifestyle.

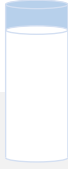


Moderate beer consumption does not make you fat.

Potential health effects only apply to moderate beer consumption by adults. This is defined in this infographic as no more than two 25 cl drinks of 5% beer (or two 33 cl drinks of 3.8% beer, or two 10 cl drinks of 13% wine) daily for men and one for women. This may vary for one's age, size and overall health. An otherwise healthy lifestyle is ►



Calories in beer and other drinks and food.

						
	non-alcoholic beer (250 ml)	beer (250 ml)	red wine (150 ml)	banana (130 g)	milk (250 ml)	mini pizza (100 g)
Kcal per portion (rounded to 5 kcal)*	50	105	105	115	120	235
Kcal per 100 ml/g	20	42	71	90	47	235

Minutes it takes to work off the calories per portion (rounded to 5 minutes).

						
walking	15	25	25	25	25	50
	5	10	10	10	10	25
running						

strongly advised. For personal guidance, check with your general practitioner. Please note this does not constitute a drinking guideline. All statements from this infographic are backed-up by science that can be retrieved on www.beerandhealth.eu. *Source of calories in beer and other drinks and food: Eurofir.org. ■



4

NON
ALCOHOLIC

HEALTH ASPECTS OF NON-ALCOHOLIC BEER

Non-alcoholic beer is increasingly popular in many countries, and this beverage may also influence health. It may be a good alternative to regular beer after sports, may have positive effects when breastfeeding, with evidence from literature suggesting that it may reduce anxiety and help people to sleep better. However, all these health effects require further investigation.



KEY MESSAGES

- ◈ Besides research on the health effects of beer, few studies have been conducted on the health aspects of non-alcoholic beer.
- ◈ 0.0% beer and low-alcoholic beer (<2%) are good alternatives to regular beer (4–5%) especially after exercise for rehydration, but more research is needed.
- ◈ The effects of non-alcoholic beer on breastfeeding need further investigation to confirm any positive effects on breast milk composition and lactation.
- ◈ In depth research is needed to confirm the positive results from early studies on the impacts of hops in non-alcoholic beer on improved sleep and anxiety levels.
- ◈ Although more research is required, non-alcoholic beer appears to be able to influence cardiovascular biomarkers.
- ◈ Non-alcoholic beer may in some countries still contain a small amount of alcohol, due to national definitions. But 0.0% beers exist and are labelled as such.

In some countries, beer labelled as non-alcoholic may still contain a small amount of alcohol due to differing national definitions. However, 0.0% beers also exist and are clearly labelled as such.

4.1 Non-alcoholic beer and sports

It is very common in many team sports to drink beer together after exercise, training or matches.⁸⁷ Beer contains carbohydrates, sodium (see Chapter 2) and fluid, which are important in recovering after physical exercise. However, the alcohol in beer has a diuretic effect, which means that it increases urine output. To rehydrate the body, it is better to choose beer containing 2% alcohol or less. A number of studies have evaluated the diuretic effect and rehydration capacity of beer with different alcohol contents from 0% to 4%. Results from these have generally shown that the stronger the beer, the less it is able to rehydrate the body.^{88,89} However, 2% or less alcohol did not increase urine output or affect blood volume levels after exercise-induced dehydration. Beer with 4% alcohol reduced the recovery rate of blood volume levels compared to 0.0% beer. More fluid was retained when extra sodium was added to a beer with 2.3% alcohol,⁹⁰ or if people could drink as much water as they wanted together with 660 ml of beer (4.5%).⁹¹ A small amount of alcohol (2% or less) may not affect fluid recovery when one is in a dehydrated state, though

drinks containing 4% alcohol can delay the rehydration process. It appears, however, that more research is needed to determine the exact alcohol percentage that influences urine output, relevant blood levels and fluid balance.

4.2 Non-alcoholic beer and breastfeeding

Alcohol and breastfeeding do not go together. The amount of alcohol in the blood stream is equivalent to the amount in the breast milk. Also, after drinking alcohol, lactation may be inhibited by lower milk production and a decreased milk ejection reflex caused by lower production of the hormone oxytocin. The child may still drink enough milk during the whole day, as breastfeeding occurs more frequently 8–12 hours after a mother drinks an alcoholic beverage. If breastfeeding, it is best to note that it takes at least two hours to eliminate 10 g of alcohol, but the long term effects of alcohol consumption on breastfed children are not as yet known and caution is warranted.⁹² Non-alcoholic beer may stimulate secretion of prolactin, a hormone that enhances the production of breast milk. The mechanism behind this is unknown, but could be due to specific compounds derived from barley.⁹³ In addition, non-alcoholic beer consumption may increase the antioxidant capacity of breast milk. An experimental study found an increase after 30 days of drinking 660 ml of 0.0% beer per day. The mothers also

benefited from these effects themselves as oxidative damage in their body decreased, reflected in decreased levels of compounds involved in oxidative stress.⁹⁴ More research is needed, however, to determine the exact effects that non-alcoholic beer consumption may have on the health of both mother and child.

4.3 Non-alcoholic beer and anxiety and sleep

Hops are used for their flavour and preservative capacities in making both alcoholic and non-alcoholic beer. In the human body, the constituents of hops appear to have some sedative effect and thereby may even positively influence sleep and anxiety. The bitter acids and the compounds xanthohumol and myrcenol in hops are probably responsible for this effect, and research suggests that the main mechanism of action of hops is to increase the activity of the neurotransmitter γ -aminobutyric acid (GABA). When the level of GABA increases in the brain, its neural activity decreases. However,

as there are few studies examining the effect of 0.0% beer on sleep and anxiety, more research is needed.

Sleep

Two experimental studies examined the effect of non-alcoholic beer on sleep^{95,96} with some groups drinking 330 ml of 0.0% beer during evening meals for two weeks. In a study with work-stressed nurses, sleep quality improved with reduced sleep latency (the time it takes to fall asleep) and decreased restlessness during the night. Results were compared to one week when the nurses did not consume non-alcoholic beer during evening meals.⁹⁵ Sleep latency also decreased visibly in university students during a stressful exam period, but students rated their overall sleep quality higher than a week before the experiment when they did not consume non-alcoholic beer.⁹⁶ These two studies only examined the effects of non-alcoholic beer on sleep, and more in depth research is needed before conclusions can be drawn. ►

Anxiety

Besides improving the quality of sleep, non-alcoholic beer may also reduce feelings of anxiety. Some experimental studies have examined the effect of 0.0% beer on anxiety levels in a stressed population. Subjects rated their stress levels lower after drinking non-alcoholic beer for two weeks compared to a control period when they did not drink non-alcoholic beer. A decrease in urinary levels of 5-HIAA (high levels of this compound have been found in people having anxiety disorders) was also seen after drinking 0.0% beer for two weeks. All these studies came to the same conclusion: that drinking 330 ml of non-alcoholic beer during evening meals on 14 consecutive days may decrease feelings of anxiety and stress.⁹⁵⁻⁹⁷ These results are promising, but it must be stressed related research is still at an early stage.

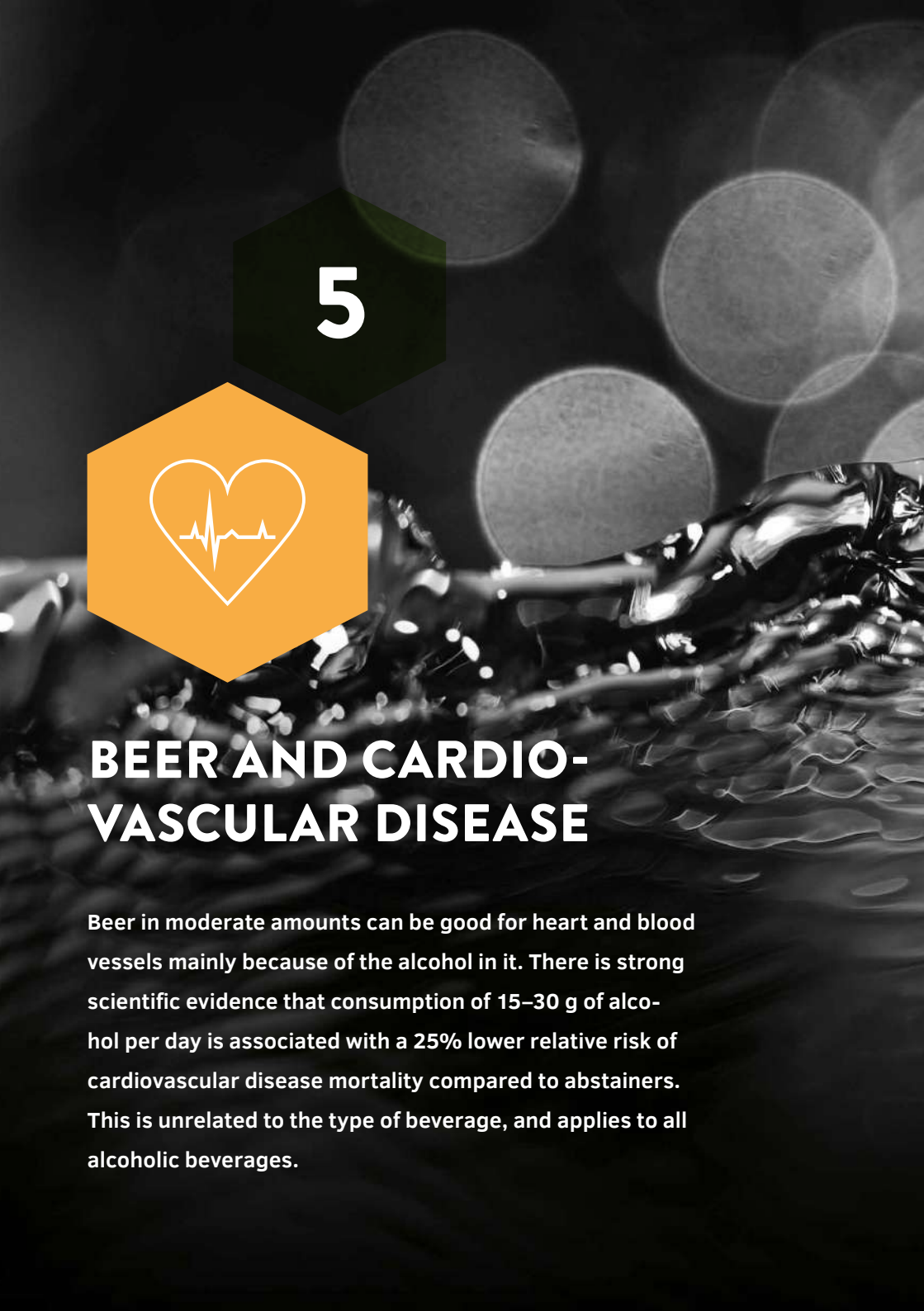
4.4 Non-alcoholic beer and cardiovascular biomarkers

As well as alcohol-containing beers, non-alcoholic beer can also have positive effects on cardiovascular health. Two studies suggest that polyphenols may play a role. In one intervention study with men aged 55–75 years old, a decrease in inflammation factors such as IL-6 was found when consuming 990 ml of non-alcoholic beer (<1 g alcohol) each day for four weeks, with a corresponding decrease in blood pressure of 12–16% and decreased homocysteine levels.⁹⁸ In another study with the same subjects and research design, an increase in endothelial progenitor cells was found (stem cells that repair and maintain endothelial walls of blood vessels). These results are most likely to be caused by hop-derived compounds such as the polyphenol xanthohumol.⁹⁹ However, little research has been conducted on this topic, and more research is needed before conclusions can be made. ■

REMEMBER

No alcohol is the only safe option for pregnant women

The foetus grows and develops during the whole nine months of pregnancy, and it is known that drinking alcohol during this period can lead to neurological disorders, birth defects and mental health problems (see Chapter 8).¹⁰⁰ The exact amount of alcohol that may harm a baby is unknown, so the best advice is not to drink alcoholic beverages at all. Non-alcoholic beer (0.0% alcohol) might be a good alternative, however. ■



5



BEER AND CARDIO- VASCULAR DISEASE

Beer in moderate amounts can be good for heart and blood vessels mainly because of the alcohol in it. There is strong scientific evidence that consumption of 15–30 g of alcohol per day is associated with a 25% lower relative risk of cardiovascular disease mortality compared to abstainers. This is unrelated to the type of beverage, and applies to all alcoholic beverages.



KEY MESSAGES

- ⬡ Beer in moderate amounts may be good for heart and blood vessels mainly because of the alcohol in it.
- ⬡ Consumption of 15–30 g of alcohol per day is associated with a 25% lower risk of cardiovascular disease mortality compared to abstainers. At this level of alcohol intake, coronary heart disease risk is reduced by 34%. The risk for stroke is lowest (20% less) at an intake of up to 15 g of alcohol per day.
- ⬡ Increased HDL cholesterol, improved insulin sensitivity, decreased fibrinogen and reduced inflammation markers are physiological mechanisms that explain this association.
- ⬡ On top of a healthy lifestyle, moderate alcohol consumption may have a cardiovascular protective effect.
- ⬡ People having cardiovascular disease may benefit from moderate alcohol consumption.

5.1 Cardiovascular disease in Europe

Cardiovascular disease (CVD) is the most important cause of death in Europe. Despite a major decline over the last 30 years, approximately four million people died from CVD in 2014, equivalent to 46% of total mortality in Europe. Coronary heart disease (CHD) such as myocardial infarction (heart attack) accounts for almost half, and stroke (brain attack) about a quarter of all cases of CVD.¹⁰²

5.2 Alcohol consumption and cardiovascular disease risk

There is a J-shaped relationship between alcohol consumption and CVD mortality risk. The lowest risk of CVD mortality is seen with alcohol consumption of 15–30 g per day (25% less relative risk), but is still low at intakes of up to 60 g per day compared to non-drinkers.¹⁰³ It seems there are no differences in the beneficial effects of alcoholic beverages. This reduction in risk is comparable to preventive measures such as weight control, exercise, and the use of acetylsalicylic acid (aspirin).^{104,105}

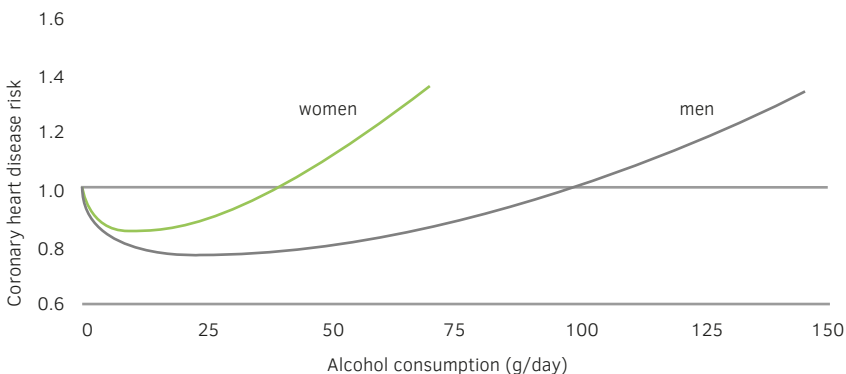
Alcohol consumption and coronary heart disease

With coronary heart disease, there is a J-shaped relationship with alcohol consumption. The lowest relative risk is around 20% less with alcohol consumption of about 25 g per day for men and around 10 g per day for women. Consumption of 25–100 g of alcohol per day is still associated with a lower relative risk of CHD in men (see Figure 4). However, at these levels of consumption there is an increased risk of some cancers and accidents, therefore increasing the risk of overall mortality (see Chapter 10).¹⁰⁶ A more recent meta-analysis showed similar findings, with the lowest relative risk of CHD seen with 15–30 g of alcohol per day (34% less relative risk), and the relative risk of CHD mortality reduced by 20–25% even with consumption of more than 60 g of alcohol per day compared to non-drinkers.¹⁰³

Lifestyle effect

A healthy lifestyle (optimal weight, healthy diet, physically active and non-smoking) lowers the risk of myocardial infarction. ►

Figure 4. Relationship between alcohol consumption and coronary heart disease risk¹⁰⁶



What is cardiovascular disease?

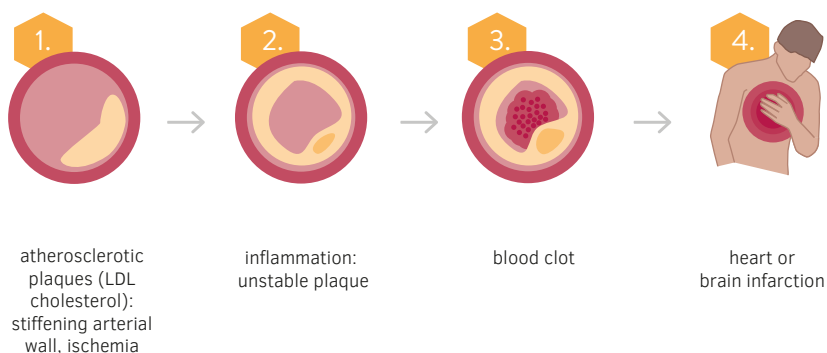
Cardiovascular disease (CVD) is a collective term for diseases of the heart and blood vessels. It is mainly caused by atherosclerosis. During this process, arterial walls harden and become narrow due to the effects of atherosclerotic plaques (see Figure 5). Most of these plaques contain oxidized low density lipoprotein (LDL cholesterol), and plaques can manifest in all arteries. Atherosclerosis is a degenerative disease of the arteries, due mainly to aging, but an unhealthy lifestyle can speed up its development. A stable plaque stiffens the arterial wall and can cause ischemia (shortage of oxygen), but it usually never fully closes an artery. Plaques may become unstable because of inflammation, and an unstable plaque may rupture as it increases in size because of inflammatory reactions. Platelet aggregation can later lead to the formation of a blood clot causing

a local blockage. When this occurs in the coronary arteries and stops oxygen supply to the heart muscle it causes a myocardial infarction. Also, the clot may detach and block arteries causing infarction in a different location such as the brain.^{133,134}

What are the risk factors for cardiovascular disease?

There are multiple factors that can influence the risk of CVD. Lifestyle factors such as a low physical activity level, unhealthy diet, smoking and obesity can speed up the development of atherosclerosis. Some diseases can also increase the risk of CVD. In diabetes mellitus for example, fat and glucose metabolism is disrupted, causing unhealthy lipid and glucose levels in the blood and making such diabetics more susceptible to CVD.¹³⁵ ■

Figure 5. The process of cardiovascular disease



However, even in men with a healthy lifestyle, those consuming 5–30 g of alcohol per day have a lower relative risk than those that do not drink any alcohol (see Figure 6). The finding of this population study indicates that the cardiovascular protective effect of moderate alcohol consumption adds to the beneficial effects of a healthy lifestyle.¹⁰⁷

Alcohol consumption and stroke

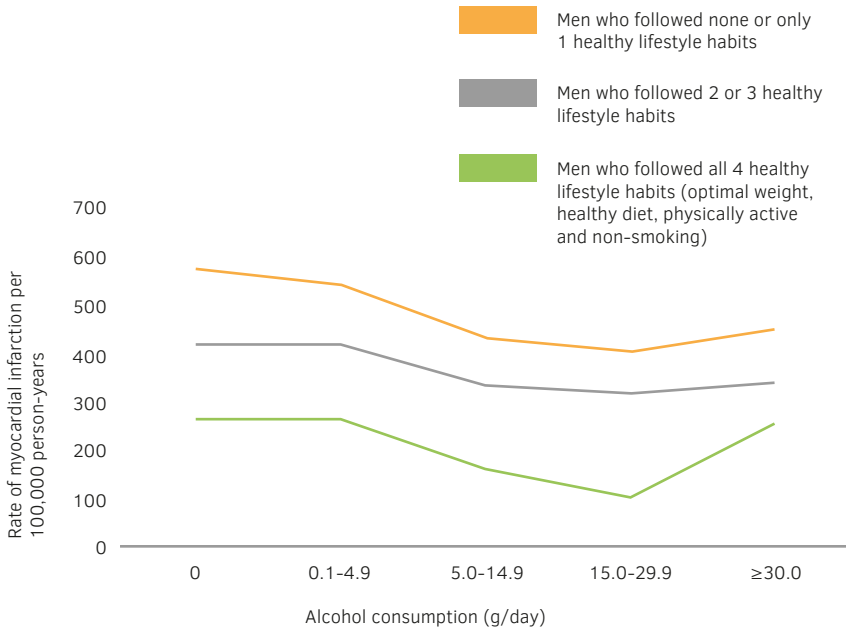
There is a J-shaped relationship between alcohol consumption and the risk of stroke. The relative risk is lowest (20% less risk) with an intake up to 15 g of alcohol per day and increases when consumption is more than 15 g per day.¹⁰³ Ischemic stroke is the most common form of stroke, where a blood clot blocks the blood flow in an artery within the brain. For both men and women the lowest relative risk (around 15% lower than

abstainers) was seen with consumption of around 12 g of alcohol per day. Consumption of more than 35 g per day for men and 44 g per day for women increases the relative risk.¹⁰⁸ In men, there is a positive linear relationship between alcohol consumption and the risk of hemorrhagic stroke. For women, a J-shaped relationship is found with the lowest relative risk at 12 g of alcohol per day (31% less).¹⁰⁸ A hemorrhagic stroke occurs when a blood vessel bursts within or around the brain.

Transient and reversible effects

The effect of alcohol consumption on cardiovascular disease risk may be transient and reversible. Those who started drinking, 14–196 g per week for men and 14–98 g per week for women, were 38% less likely than non-drinkers to have a cardiovascular event during a four-year follow-up period.¹⁰⁹

Figure 6. The risk of myocardial infarction in men according to alcohol intake¹⁰⁷



In another study in men between 40 and 75 years of age, a 12.5 g increase in daily alcohol consumption over a four-year follow-up period was associated with a 22% lower relative risk of myocardial infarction. Conversely, a 12.5 g decrease in daily alcohol consumption was associated with a trend towards a higher relative risk of infarction (10% higher risk).¹¹⁰ A seven-year follow-up study suggested that, among men aged 40 to 84 years with an initially low alcohol consumption of 14 g per week or less, a subsequent moderate increase in alcohol consumption (14–84 g per week) reduced their relative risk of CVD by 29%.¹¹¹

Alcohol consumption and hypertension

Consumption of up to 20 g of alcohol per day modestly lowers the risk of hypertension in women compared to abstainers, whereas higher alcohol consumption significantly increases the hypertension risk. Among men, the relationship is not J-shaped, there is no relative risk reduction with an alcohol intake of <30 g per day, and above 30 g per day the relative risk of hypertension increases. The mechanism by which alcohol affects blood pressure is not clear. However, at least part of the reduction of blood pressure may be related to an increased synthesis of nitric oxide by the arterial endothelium. There may also be an indirect mechanism whereby alcohol alters hormone levels that in turn affect blood pressure. Differences in the pattern of drinking, beverage choices and smoking habits may also contribute to observed variations in individual and gender-related responses.¹¹²

Alcohol consumption and cardiomyopathy

Cardiomyopathy is a heart muscle disease. It can have different causes, but one of them is poisoning of the myocardium (heart muscle) due to chronic alcohol abuse. An observational study showed that people consuming around 240 g of alcohol per day for an average of 16 years developed cardiomyopathy.¹¹³ Therefore it is unlikely that

alcoholic cardiomyopathy could result from moderate drinking.

Alcohol consumption and supraventricular arrhythmias

Atrial fibrillation is the most commonly observed rhythm disturbance of the heart, and observational studies have shown an increased relative risk with consumption of more than 26 g of alcohol per day for women¹¹⁴ and more than 60 g of alcohol per day for men.^{114,115}

5.3 Mechanisms of protective effects of moderate alcohol consumption

Multiple mechanisms by which alcohol consumption affects CVD risk have been identified by intervention studies. These mechanisms support a causal relationship and may explain almost all of the association.⁸

Increase in HDL cholesterol and its key functions

Consumption of 30 g of alcohol per day increases high density lipoprotein (HDL) cholesterol concentration by about 8%.¹¹⁶ A key function of HDL is to promote cholesterol efflux, being the transport of cholesterol from the periphery to the liver for excretion,¹¹⁷ and alcohol consumption increases cholesterol efflux.^{118,119} In addition, paraoxonase activity, another function of HDL, is increased. Paraoxonase is an enzyme entirely complexed to HDL and that may protect against atherosclerosis by protecting LDL cholesterol from oxidation.¹²⁰ The increase in HDL and its functions may explain about half of the risk reduction for CVD from moderate alcohol consumption.¹¹⁶

Improved insulin sensitivity

Moderate alcohol consumption can improve insulin sensitivity (see Chapter 6). Since insulin resistance is linked to CVD, the improvement of insulin sensitivity may be an additional mechanism by which alcohol consumption reduces the risk of CVD. ►

Decrease in fibrinogen

Consumption of about 30 g of alcohol per day can reduce circulating levels of fibrinogen.¹²¹ This protein is the precursor of fibrin, a cofactor for platelet aggregation. By decreasing fibrinogen levels, blood clots are less likely to form and as a result, this might decrease the risk of an infarction.

Reduction of inflammation markers

Alcohol consumption of about 30 g per day has been shown to decrease the plasma concentration of C-reactive protein (CRP) by 35%.^{122,123} CRP is the most commonly studied inflammation marker, active in acute inflammation, but low circulating levels of CRP are not uncommon in people with CVD. CRP may negatively affect the stability of plaques. Other inflammatory markers such as interleukine-6, vascular cell adhesion molecule-1 and intercellular adhesion molecule-1 follow the same trend as with CRP.¹²⁴

5.4 Alcohol consumption in people with cardiovascular disease

People with CVD can benefit from moderate alcohol consumption. Population studies in subjects with hypertension (high blood pressure) show that alcohol consumption of up to 30 g per day may lower their relative risk of CVD by up to 40%.¹²⁵ In those who have already had a myocardial infarction, alcohol consumption of 28–56 g per week can decrease their relative risk of total mortality

by 28%.¹²⁶ After heart surgery, consumption of 50–700 g of alcohol per week has a protective effect against the narrowing of blood vessels and lowers the need for new cardiac surgery.¹²⁷

5.5 Role of genetic variation

Some scientists suggest that the risk reduction of CHD in low to moderate drinkers depends on genetic variation. People with alcohol dehydrogenase polymorphism (ADH1C) resulting in the slow metabolism of alcohol, may have more CHD benefits,¹²⁸ though this finding is not supported by others.¹²⁹ Individuals with yet another genetic variation, the ADH1B polymorphism, were reported to benefit more from drinking less. With low to no alcohol intake, they had a more favourable CVD risk factor profile and fewer CVD events.¹³⁰ However, this allele is very uncommon. Also, people with this polymorphism are unusually sensitive to alcohol, making them more likely to be abstainers than heavy drinkers, and as a result are not representative.¹³¹ In conclusion, the evidence for a genetic role in the health effects of moderate alcohol consumption is still sparse and inconsistent. In addition, there is the question of whether generalised statements about the effects of alcohol on diseases can be made based on results from the analysis of a single nucleotide polymorphism of a gene.¹³² ■

REMEMBER

One to two drinks of beer per day can lower the risk of cardiovascular disease

Despite what scientist at first thought, alcohol is a major factor with respect to lower cardiovascular disease (CVD) risk.¹⁰³ The famous French Paradox study in 1992 found that although French people consume relatively high amounts of saturated fats, they do not suffer as much as expected from CVD. The scientists concluded that this could be due to consumption of red wine.¹³⁶ Although phenolic compounds in wine and in beer may play a role in reducing the risk of CVD^{33,124,137-140}, the largest part of the protective effect of these beverages is still due to the alcohol within them.¹⁰³

Most scientific studies focus on the effect of alcohol on the cardiovascular health of people aged 50 years or older. The reason for this is that young adults have a lower risk of CVD than older people,¹⁴¹ which makes it easier to find significant effects of alcohol consumption in older age. However atherosclerosis is a long-term process that already starts when people are young. A few studies have found decreased incidence of coronary heart disease, decreased arterial stiffness and lower fibrinogen concentration in the 25–50 age groups with the consumption of 0.5–30 g of alcohol per day as compared to abstainers.¹⁴²⁻¹⁴⁴ ■

A black and white portrait of a middle-aged man with a grey beard and glasses, wearing a checkered shirt and a tie. The background is dark. An orange hexagon is on the left side.

INTERVIEW

**“THERE IS NO DIFFE-
RENCE BETWEEN
MODERATE BEER AND
WINE CONSUMPTION
IN PROTECTING THE
HEART”**

DR RAMON ESTRUCH

Hospital Clinic, CIBER Obesity and Nutrition, University of Barcelona, Spain

Expertise: Mediterranean diet, wine, beer, cardiovascular disease, atherosclerosis, inflammation

What is known about specific beer and heart health?

“Some research suggests that regular and moderate consumption of beer and wine seems to provide greater cardiovascular protection than spirits because of the polyphenols in these beverages. However, many more studies show that moderate alcohol consumption in general, irrespective of the type of beverage, reduces cardiovascular morbidity and mortality. So the largest part of the protective effects of beer is due to the alcohol content. Some minor components such as the polyphenols xanthohumol and iso-xanthohumol might contribute to health but play a much smaller role.”

The Mediterranean diet is often associated with wine, but can the wine be replaced by beer?

“The traditional Mediterranean diet includes frequent drinking of moderate doses of especially red wine with meals. But even in ancient times this could also be beer. Thus, some experts have pointed out that beer should be included in the Mediterranean diet pyramid, together with red wine and cider. Even nowadays, several Mediterranean consumers replace wine by beer with the meals, especially in summer. For the protective effect on cardiovascular disease, it makes no difference if you drink wine or beer in this diet.”

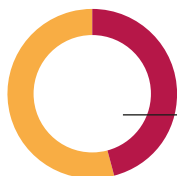
If you had unlimited funds, what would you like to research in the area of moderate beer consumption as part of a healthy lifestyle?

“Although observational studies are already showing strong suggestions, I would like to demonstrate with the highest level of scientific evidence that moderate beer consumption is useful in protecting against cardiovascular events and type 2 diabetes. To do that you need a large group of people from different countries, who consume controlled meals for a long time, with or without beer. The results from this trial would further help the scientific, medical and public health communities in their recommendations to consumers regarding the effects of moderate beer consumption.”



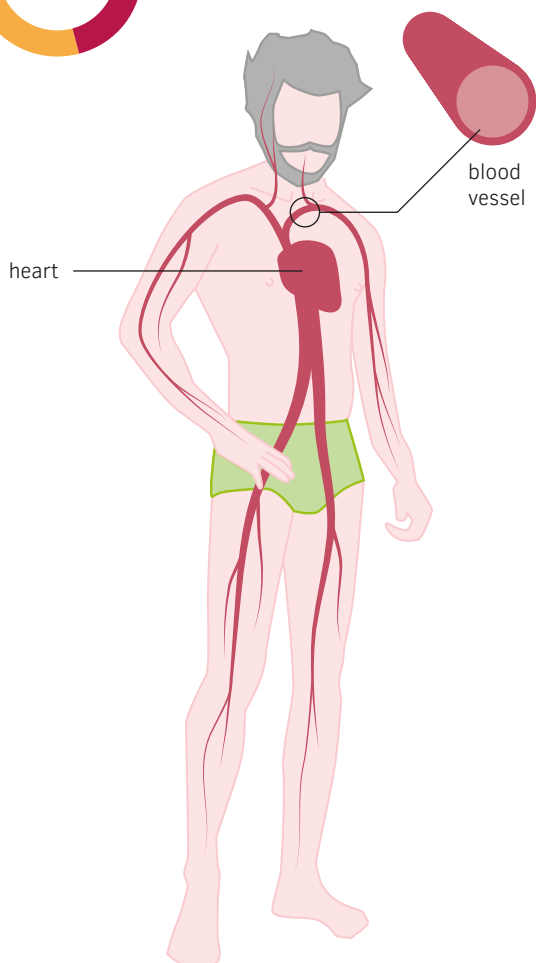
BEER AND CARDIO-VASCULAR DISEASE

Moderate beer consumption can have a positive effect on heart and blood vessels and prevent cardiovascular disease (CVD).

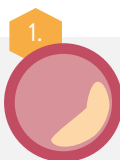


46%

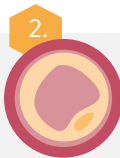
CVD is the main cause of death in Europe.



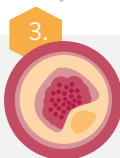
The process of CVD.



1.
plaques (LDL cholesterol - also known as bad cholesterol)



2.
inflammation



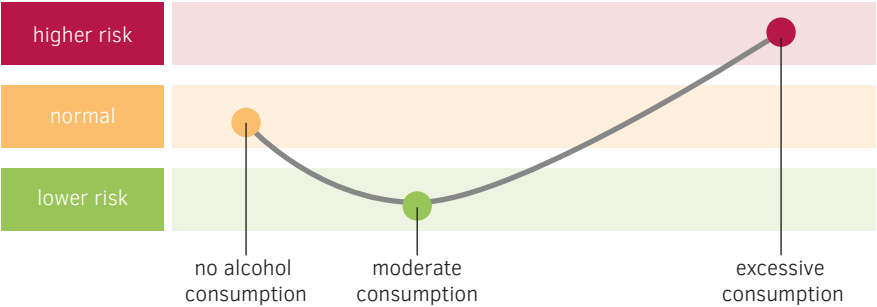
3.
blood clot



4.
infarction

Potential health effects only apply to moderate beer consumption by adults. This is defined in this infographic as no more than two 25 cl drinks of 5% beer (or two 33 cl drinks of 3.8% beer, or two 10 cl drinks of 13% wine) daily for men and one for women. This may vary for one's age, size and overall health. An otherwise healthy lifestyle is ►

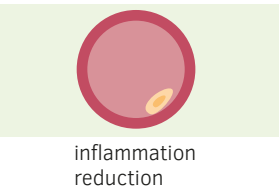
Moderate alcohol consumption reduces the risk of developing CVD.



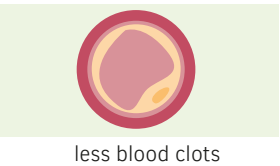
Effects of moderate alcohol consumption on CVD.



Increase of HDL cholesterol - also known as good cholesterol - and insulin sensitivity.



Reduction of inflammatory factors involved in CVD.



Decrease in fibrinogen, which reduces formation of blood clots.

For CVD prevention:
Do not smoke, be active and eat and drink healthily and in moderation.

Not only can moderate beer consumption lower the risk of developing CVD but also people with CVD may benefit from the protective effects of alcohol.

6

BEER AND DIABETES

As beer contains alcohol, it can have an effect on diabetes. There is considerable scientific evidence that alcohol consumption of up to 24 g per day can lower the relative risk of type 2 diabetes by up to 30%. In people with diabetes, moderate alcohol consumption may improve glycaemic control and convey cardiovascular risk reduction and mortality benefits. These effects apply to all alcoholic beverages.



KEY MESSAGES

- ⬡ Moderate beer consumption may lower the risk of developing type 2 diabetes, because of the alcohol in beer.
- ⬡ Alcohol consumption of up to 24 g per day can lower the risk of type 2 diabetes by 30%, and appears to be more pronounced in women than in men.
- ⬡ Increased adiponectin levels, increased insulin sensitivity, reduction of fasting insulin, glycaemic status control, and anti-inflammatory effects, are biological mechanisms that explain this association.
- ⬡ In addition to a healthy lifestyle, moderate alcohol consumption can also protect against type 2 diabetes.
- ⬡ People with diabetes can also benefit from moderate alcohol consumption, with a lower risk of dying from coronary heart disease and a lower risk of microvascular complications.

6.1 Diabetes in Europe

There are about 60 million people with diabetes in Europe (type 1 and type 2, see box on Background of diabetes), and the prevalence of diabetes is increasing, already reaching 10–12% in some countries.¹⁴⁵ In addition, there is a large suspected number of undiagnosed diabetics. In Europe, about one in three people with diabetes do not know they have it.¹⁴⁶ Of those with diabetes, 50% die of cardiovascular disease (primarily coronary heart disease and stroke), and 10–20% die of kidney failure.^{145,147,148}

6.2 Alcohol consumption and type 2 diabetes risk

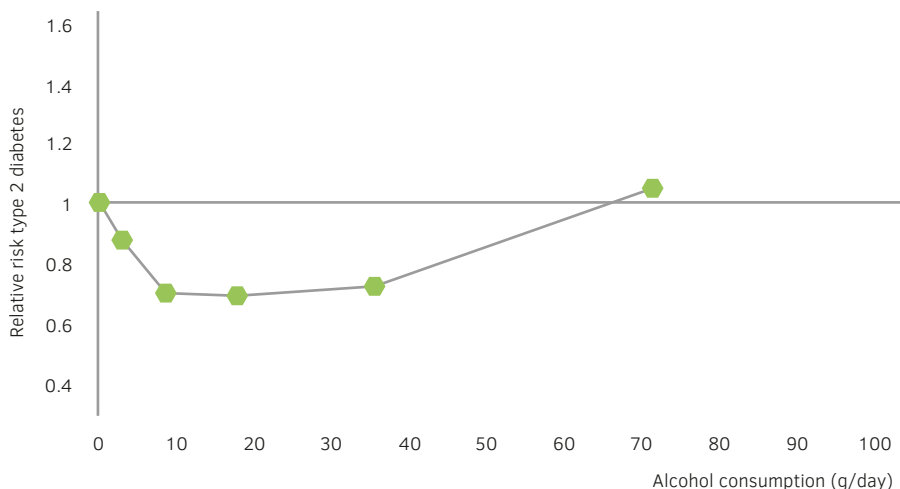
Population studies show a J-shaped relationship between alcohol consumption and risk for type 2 diabetes (see Figure 7). Compared to those who do not consume alcoholic beverages, consumption of up to 24 g of alcohol per day is associated with a 30% lower relative risk for type 2 diabetes on average. There appears to be a marked gender difference, the effect being more pronounced among women than men.

The putative protective effect was found to be up to 25% for men and up to 45% for women.^{149–151} Another meta-analysis found the positive effect to be confined to women and non-Asian populations only.¹⁵² Higher alcohol consumption results in a comparable or higher risk for type 2 diabetes compared to non-consumers.^{149–152} The difference in risk reduction between men and women could be explained in part by body fat distribution¹⁵¹, alcohol metabolism¹⁵³ or drinking patterns.¹⁵⁴

Lifestyle effect

The association between moderate alcohol consumption and type 2 diabetes is not likely to be explained by a healthier lifestyle. In subjects already at lower risk of developing type 2 diabetes based on a favourable lifestyle (low body weight, high physical activity level, non-smoking and healthy diet), alcohol consumption of 5–14.9 g per day for women and 5–29.9 g per day for men is associated with an additional 44% lower relative risk of developing type 2 diabetes (see Figure 9).¹⁵⁶ ►

Figure 7. Relationship between alcohol consumption and type 2 diabetes relative risk¹⁴⁹



What is type 1 diabetes?

Type 1 diabetes accounts for around 10% of all diabetes worldwide. It is characterised by deficient insulin production due to the autoimmune destruction of pancreatic cells. Insulin is a hormone produced by the pancreas that regulates the absorption of glucose from the blood. Type 1 diabetes is not preventable with current knowledge, and treatment requires the daily administration of insulin.

What is type 2 diabetes?

Type 2 diabetes is a disease in which the body first becomes insensitive to insulin (see Figure 8). Then, as a result of insulin insensitivity, insulin production is increased, which may lead to impaired

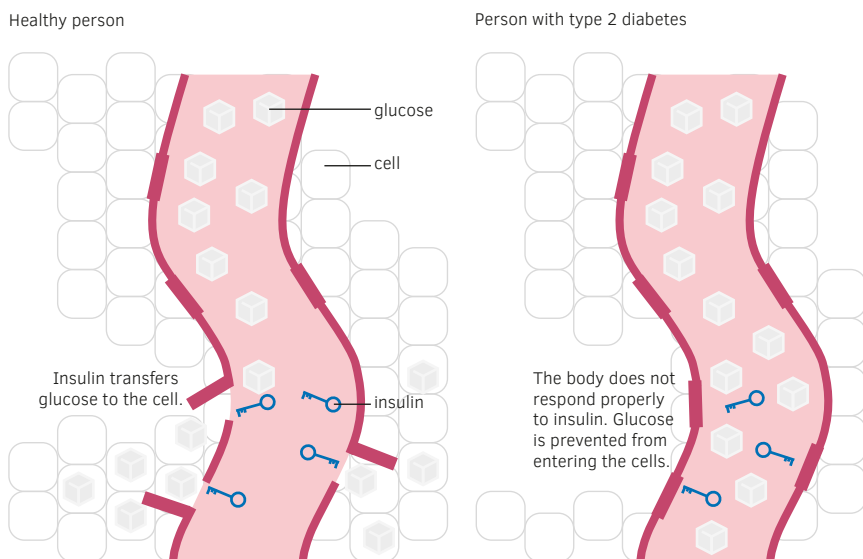
insulin secretion by the pancreas.

This leads to high blood glucose levels (hyperglycaemia), which can result in serious damage to nerves and blood vessels over time.¹⁴⁵

What are the risk factors for type 2 diabetes?

Lifestyle related factors that increase the risk of type 2 diabetes are mainly excess adiposity¹⁴⁷ and insufficient physical activity, the latter may decrease insulin sensitivity and increase adiposity.¹⁷⁵ Other risk factors are a high intake of calories from refined carbohydrates and saturated fats, a low intake of fruit and vegetables, high intake of salt, and smoking.^{147,176} ■

Figure 8. Type 2 diabetes explained



Transient and reversible effect

The effect of alcohol on diabetes risk may be transient and reversible based on data of a four year follow-up epidemiological study. A decrease in alcohol consumption from 5–30 g per day to 0–5 g per day is accompanied by a modest increase in relative risk of type 2 diabetes. On the other hand, an increase of alcohol consumption of 7.5 g per day in those not drinking or those drinking less than 15 g per day lowers the type 2 diabetes relative risk by 10–20%.¹⁵⁵

6.3 Mechanisms explaining the beneficial effect of moderate alcohol consumption

Multiple biological mechanisms that may explain how alcohol consumption affects type 2 diabetes risk have been explored in intervention studies.

Increased adiponectin levels

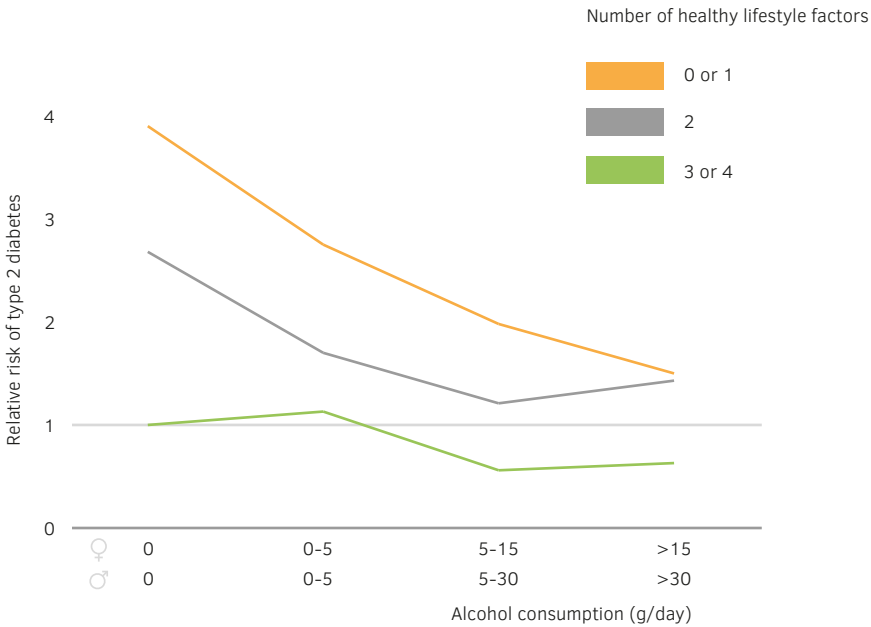
Increased adiponectin levels (10%) have been observed in subjects consuming alcoholic beverages (20–40 g of alcohol per day) compared to abstainers.¹²¹ This increase in adiponectin levels is suggested to be the most important mechanism, explaining about 25–30% of the relationship between moderate alcohol consumption and

lower risk of type 2 diabetes.¹⁵⁷ Adiponectin is a signalling peptide secreted by adipose tissue. It has been shown to increase insulin sensitivity,¹⁵⁸ and higher adiponectin levels have been associated with a lower risk of type 2 diabetes.¹⁵⁹ Furthermore, adiponectin is inversely associated with inflammatory markers related to type 2 diabetes risk.¹⁶⁰ Adiponectin is predominantly secreted in the adipose tissue of the buttocks and legs,¹⁶¹ which may contribute to explaining why alcohol may give better diabetes protection in women compared to men.

Increased insulin sensitivity and reduction of fasting insulin

Alcohol consumption of less than 40 g per day may improve insulin sensitivity and decrease fasting insulin concentrations in women, but not in men. This might also explain the larger risk reduction with moderate alcohol consumption in women compared to men.¹⁶² The biological mechanism by which alcohol consumption improves insulin sensitivity has not been fully elucidated. Alcohol itself strongly affects lipid metabolism,¹¹⁶ and could therefore also influence insulin resistance and risk of type 2 diabetes. ►

Figure 9. The relative risk of type 2 diabetes according to alcohol intake, in relation to the number of healthy lifestyle factors¹⁵⁶



Another possibility is that acetate, the main metabolite of alcohol oxidation, reduces fatty acid release from adipose tissue and inhibits the uptake of circulating fatty acids by muscle.¹⁶³ This reduction in systemic fatty acid availability would be expected to enhance glucose oxidation and insulin sensitivity.^{164,165}

Glycaemic status control

Lower levels of hemoglobin A1c (HbA1c) have been observed in those consuming less than 40 g of alcohol per day as compared to abstainers.¹⁶² The concentration of HbA1c in the blood reflects average glucose levels over the preceding 8–12 weeks and is used as a measure of glycaemic status. A low level of HbA1c indicates a better glucose regulation. The underlying mechanism of glycaemic control by alcohol is not clearly understood, but alcohol may decrease HbA1c by suppressing the acute rise in blood glucose after a meal and increasing the early insulin response.¹⁶²

Anti-inflammatory effects

Alcohol consumption may reduce inflammatory factors involved, like C-reactive protein.^{122,166,167} Low-grade inflammatory changes have been shown to precede type 2 diabetes by many years.¹⁶⁸

6.4 Alcohol consumption in people having diabetes

For people who have diabetes, moderate alcohol consumption may affect blood glucose level and complications related to diabetes.

Hypoglycaemic effect of alcohol

Alcohol has acute effects on carbohydrate metabolism since it inhibits the production of glucose by the liver. When alcoholic beverages are consumed without food, this may result in hypoglycaemia in subjects with diabetes using insulin or insulin stimulating medication (with the exception of GLP-1 analogues).¹⁶⁹ Low blood glucose level after alcohol consumption is specifically ►

Glycaemic response

The glycaemic response (GR) is the blood glucose response after eating food or a meal that contains carbohydrate.

Glycaemic index

The glycaemic index (GI) is the GR after eating a portion of food containing 50 g (or in some cases 25 g) of available carbohydrate measured within a period of two hours. The GI is expressed as a percentage of the GR after 50 g (or 25 g) of the reference carbohydrate (i.e. either a glucose solution or white wheat bread, defined respectively as the glucose scale or the bread scale). Foods having carbohydrates that are digested, absorbed and metabolised quickly are considered high GI foods (GI $\geq$ 70) whereas those that are digested, absorbed and metabolised slowly are considered low GI foods (GI $\leq$ 55).

Glycaemic load

The glycaemic load (GL) expresses the total available carbohydrate content in a given amount of food, multiplied by its GI: (GI $\times$ carbohydrate (g))/100. Foods with a GL $\leq$ 10 are been classified as low GL, and those with a value $\geq$ 20 as high GL.

Effect on type 2 diabetes risk

In population studies, diets with a high GI or GL have been associated with an increased risk of developing type 2 diabetes and coronary heart disease, whereas a low dietary GI or GL reduces the risk. The biological mechanism behind this protective effect is that low GI or GL diets may improve insulin sensitivity, lipid profile and inflammatory markers including C-reactive protein.¹⁷⁷

Beer: High glycaemic index versus low diabetes risk

Beer is classified as a high GI food, with the GI of lager beer around 100^{178,179}, comparable with the GI of potatoes or breakfast cereals.¹⁸⁰ However, the GL of beer is only 7.5 because of the low carbohydrate content (7.5 g carbohydrates per 250 ml*). In comparison with other products, a glass of a regular soft drink has a GI of 63 and a GL of 16, and a boiled potato of 150 g has a GI of 96 and a GL of 24.¹⁸⁰ Although diets high in GI or GL have been associated with an increased risk of diabetes,¹⁸¹ alcohol consumption up to 24 g per day is related to a lower diabetes risk.¹⁴⁹⁻¹⁵¹ This contradiction might be explained because when beer is consumed with or before a carbohydrate meal, beer tends to reduce the blood glucose peak after the meal. The biological mechanism behind this is likely to be alcohol's ability to acutely inhibit glucose production in the liver and so counteracts the blood glucose response as a result of glucose absorption from the food/meal by the gut, and thereby reducing the overall GR (blood glucose peak). This results in more stable blood glucose levels after the food/meal, and that might consequently reduce the risk of type 2 diabetes.¹⁸² As alcoholic beverages are often consumed together with a meal, the GR of beer consumed together with a meal might be more important to consider for diabetes risk than the GI of beer itself.

**Based on an average carbohydrate content of 2.5 g per 100 ml. Some beers will be higher or lower. ■*

a risk when glycogen stores are depleted, which could be the case for people on a low carbohydrate diet or those who are fasting. Therefore, consuming alcohol with a meal is the preferred option for people with diabetes and using insulin or insulin stimulating medication.¹⁷⁰

Risk of coronary heart disease

Individuals with diabetes are at higher risk of coronary heart disease (CHD).¹⁷¹

Consumption of 18 g or more alcohol per day compared with non-drinking lowers the risk of developing CHD in these individuals by 40% and the relative risk of dying of CHD by 66%.¹⁷² In a follow-up study, a CHD relative risk reduction of 61% was observed

with the consumption of 100–200 g of alcohol per week.¹⁷³

Risk of neuropathy, retinopathy and nephropathy

Apart from the macrovascular (large blood vessel) complications resulting in CHD, people having diabetes also have an increased risk of developing microvascular (small blood vessel) complications such as neuropathy (nerve damage), retinopathy (damage to the retina of the eye) and nephropathy (damage/disease of the kidney). Consumption of 30–70 g of alcohol per week may reduce the relative risk of these complications by 40% or more.¹⁷⁴ ■

REMEMBER

Most people with diabetes can safely drink beer, in moderation

The recommendations for alcohol consumption for people with diabetes are the same as for the general population,¹⁸³ whether they are taking medication or not. However, those using insulin or insulin stimulating medication should be aware of the hypoglycaemic effect of alcohol, but when alcoholic beverages are consumed in moderation with food, only minimal acute effects on plasma glucose concentrations are expected.¹⁷⁰ Moderate alcohol consumption may improve glycaemic control and convey cardiovascular risk reduction and mortality benefits in people having diabetes.^{170,172,173} ■

A black and white portrait of a middle-aged man with light-colored hair, smiling slightly. He is wearing a dark suit jacket, a white shirt, and a patterned tie. The background is dark and out of focus.

INTERVIEW

**“MODERATE BEER
CONSUMPTION
CAN LOWER THE
RISK OF TYPE 2
DIABETES”**

PROF ARNE ASTRUP

Department of Nutrition, Exercise and Sports, University of Copenhagen, Denmark

Expertise: Obesity, energy metabolism, metabolic syndrome, diabetes, dietary fats, appetite

Compared to healthy lifestyle habits that lower the risk of type 2 diabetes, how large is the impact of moderate alcohol consumption?

“Excessive body fat and abdominal fatness, i.e. a fat belly, together with physical inactivity, can explain up to 90% of all new cases of type 2 diabetes, but factors such as smoking, diet and drinking habits make an additional though relatively small contribution. Consumption of 1–2 glasses of alcoholic beverage per day has a small but important protective effect on type 2 diabetes – important because many people including health professionals, believe that alcohol increases the risk.”

Beer as with most other drinks, contains calories. How does moderate beer consumption decrease the risk of type 2 diabetes?

“Population studies show a J-shaped relationship between beer intake and risk of type 2 diabetes. Compared to those who do not consume alcoholic beverages, consumption of up to 24 g of alcohol per day decreases the risk of type 2 diabetes by up to 30%. Higher alcohol consumption, however, results in a higher risk of type 2 diabetes. The mechanisms behind this effect might be the stimulation of the insulin-sensitizing hormone adiponectin, and more direct effects on insulin sensitivity and secretion.”

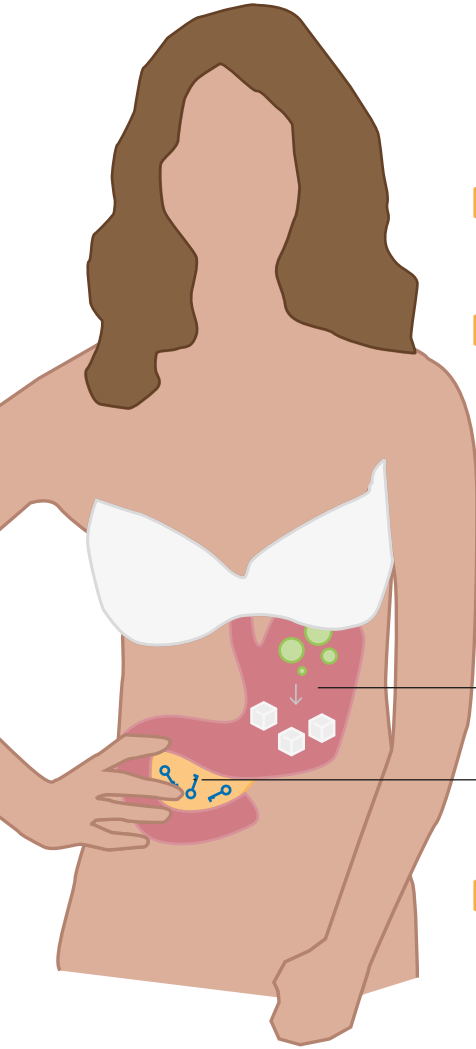
If you had unlimited funds, what would you like to research in the area of moderate beer consumption as part of a healthy lifestyle?

“Moderate beer consumption is likely to reduce stress and anxiety, on top of the effect on type 2 diabetes and cardiovascular disease. However, most of the evidence is based on observational studies, and I would like to conduct a randomized controlled trial to get the final proof.”



BEER AND TYPE 2 DIABETES

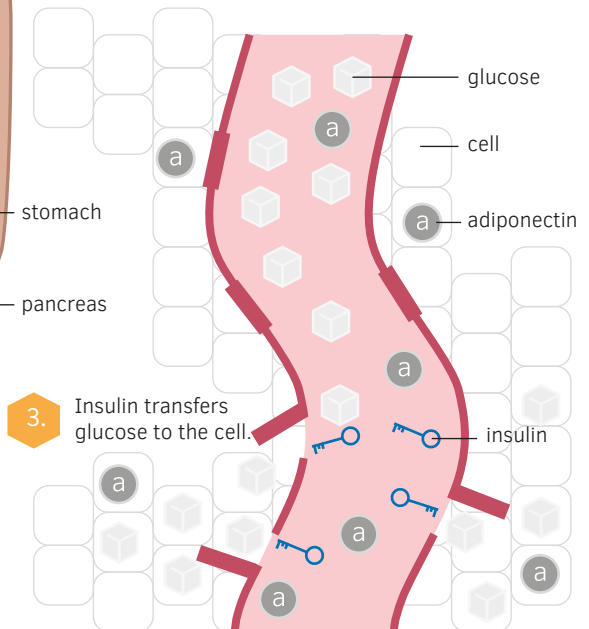
Moderate beer consumption can lower the risk of developing type 2 diabetes.



1. The mouth, stomach and small intestine convert food into glucose, which enters the blood stream.

2. The rising glucose level prompts the pancreas to produce insulin.

Healthy person



Potential health effects only apply to moderate beer consumption by adults. This is defined in this infographic as no more than two 25 cl drinks of 5% beer (or two 33 cl drinks of 3.8% beer, or two 10 cl drinks of 13% wine) daily for men and one for women. This may vary for one's age, size and overall health. An otherwise healthy lifestyle is ►



60 million

type 2 diabetes
patients.



50%

of type 2 diabetes
patients die because of
cardiovascular disease.



1 in 3

people do not
know they have
type 2 diabetes.

Moderate beer consumption can lower risk of developing type 2 diabetes through:

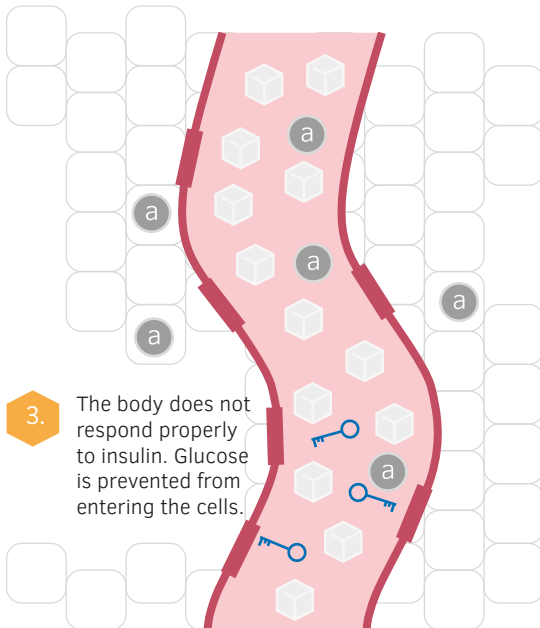


Anti-inflammatory effects,
due to an increase in
adiponectin (= peptide
secreted by adipose tissue).

Low grade inflammation
precedes type 2 diabetes.

Increased insulin sensitivity,
due to an increase in adipo-
nectin and a positive
influence on lipid metabolism.

Person with type 2 diabetes



3.

The body does not
respond properly
to insulin. Glucose
is prevented from
entering the cells.



For type 2 diabetes
prevention: Do not
smoke, be active and eat
and drink healthily and
in moderation.

Not only can moderate
beer consumption lower the
risk of developing type 2
diabetes but also in people
with type 2 diabetes it may
improve blood glucose
regulation and reduce
complications.

7



BEER AND CANCER

Alcohol can increase the risk of breast, colorectal, head and neck, liver, and oesophageal cancer. A substantial part of the alcohol-related cancer cases in Europe is associated with consumption of more than 24 g per day for men and more than 12 g per day for women. In men, about 3% of alcohol-related cancer cases are associated with alcohol consumption of less than 24 g per day, and 1% for women consuming less than 12 g alcohol per day.



KEY MESSAGES

- ⬡ Most alcohol-related cancers are those of the breast, colorectum, head and neck, liver and oesophagus.
- ⬡ Substantial numbers of alcohol-related cancers in Europe are associated with consumption of more than 24 g per day for men and more than 12 g per day for women.
- ⬡ In men, about 3% of alcohol-related cancer cases are associated with consumption of less than 24 g per day. For women only 1% of alcohol-related cases are seen with a consumption of less than 12 g of alcohol per day.
- ⬡ Alcohol can increase cancer risk even at low levels. With breast cancer for example, consumption of 10 g per day is associated with an increased relative risk of 3–9%. In comparison, using the birth control pill is associated with increased relative risk of 24%.
- ⬡ All statements on increased and reduced risk must be put into the context of the absolute lifetime risk of getting such cancers.
- ⬡ There are indications of lower risk for kidney cancer, non-Hodgkin lymphoma and thyroid cancer, associated with moderate alcohol consumption.

7.1 Cancer in Europe

More than 3.4 million new cases of cancer were diagnosed in Europe in 2012.¹⁸⁴ Cancer is a leading cause of death, comprising around 20% of the total number of deaths each year.¹⁸⁵ In 2012, the most common cancer sites were cancers of the female breast (458,337 cases), followed by the colorectum (446,801), lung (409,911) and prostate (399,964). These four cancers represent half of the overall burden of cancer in Europe. The most common causes of death from cancer were cancers of the lung (353,580 deaths), colorectum (214,727), breast (131,259) and stomach (107,313).¹⁸⁶

7.2 Causes of cancer

The majority of the cancers worldwide are due to exogenous causes. Only a minor part

of all cancers are due to endogenous causes such as genetic predisposition.¹⁸⁷ Cigarette smoking is the largest preventable cause of cancer in Europe. Other major risk factors for cancer are an unhealthy diet (low intake of fruit and vegetables, high intake of red and processed meats, high calorie intake), and physical inactivity. Alcohol consumption and environmental issues (exposure to the sun, pollutants, infections, etc.) also contribute to cancer risk.¹⁸⁸ A substantial part of the cancer cases attributable to alcohol consumption in Europe is associated with a daily alcohol consumption of more than 24 g for men and more than 12 g for women.¹⁸⁹

7.3 Alcohol consumption and cancer risk

Population studies have shown that consumption of alcoholic beverages may ►

Table 4. Incidence, mortality, alcohol attribution and cumulative risk, of cancers associated with alcohol consumption in Europe (2012)

Cancer	Incidence ¹⁸⁶		Mortality ¹⁸⁶		Alcohol attributable fraction ^{189*}		Cumulative risk range**	
	Men	Women	Men	Women	Men	Women	Men	Women
Breast (women only)	NA	458,337	NA	131,259	NA	5%	NA	4.2 – 11.6%
Colorectal	241,621	205,180	113,168	101,559	17%	4%	1.1 – 7.4%	0.9 – 4.1%
Head and neck***	109,837	29,694	52,354	11,116			0.7 – 4.7%	0.1 – 0.9%
Oesophagus	35,069	10,785	30,310	9,194	44%	25%	0.1 – 1.2%	0 – 0.4%
Liver and intra-heptic bile ducts	42,783	20,637	39,899	22,253	33%	13%	0.2 – 1.5%	0.1 – 0.7%

NA = not applicable

* See page 78

** The lowest and the highest risk (differs between countries within Europe) of getting a specific cancer up to 75 years old. Data derived from globocan.iarc.fr

*** Lip, oral cavity, pharynx and larynx

What is cancer?

Cancer is a collective term for more than 100 different diseases which are all characterised by uncontrollable and abnormal cell growth. This growth is caused by a change in the DNA that controls cell division, and tumours form when abnormal cell growth occurs over a long period of time. Malignant tumours can invade other tissues and spread in the blood and lymphatic system causing metastasis (occurrence of tumours in other parts of the body). Benign tumours do not spread, and eventually stop growing. Only malignant tumours are called cancer.²³⁰ ■

Relative risk tells you nothing about absolute risk

In this chapter you can read about alcohol consumption increasing or lowering the risk of certain types of cancer. It is important to realise that these figures present relative risks. They tell us how much more or less likely the cancer occurs in a group consuming alcohol compared to others not consuming alcohol. This is different from the overall likelihood of getting cancer in your life, i.e. the absolute lifetime risk. The cumulative risk in Table 4 indicates the absolute risk of getting certain types of cancer up to an age of 75 years old. This risk differs between European countries, depending on particular risk factors in each. By knowing the cumulative risks, it is possible to place the relative risks mentioned in this chapter into perspective, as shown in the example below and the breast cancer example

included later. If the cumulative risk is very small, even a huge increase in relative risk due to alcohol consumption may not make much absolute difference. But for a cumulative risk that is quite large already, smaller increases in relative risk can have a large impact.

Example

The highest absolute lifetime risk for European men up to 75 years old contracting colorectal cancer is 7.4% (see Table 4), which occurs in Slovakia. Consumption of 25 g of alcohol per day increases the (relative) risk by 8% (Section 7.3), equivalent to an increase, due to alcohol consumption, in absolute risk from 7.4% to 8.0%, or an increase from 74 to 80 of 1,000 men who develop colorectal cancer.

However keep in mind these are just examples that give an impression of the effect of alcohol consumption on the absolute lifetime risk up to an age of 75 years old. Individual absolute lifetime risk may be higher or lower than these figures depending on particular risk factors such as age and lifestyle. ■

increase the risk of developing cancers of the female breast, colorectum, head and neck, liver and oesophagus.¹⁹⁰ For cancer prevention it is better not to drink alcohol.¹⁸⁸ However, many cancer cases in Europe related to alcohol consumption are associated with daily consumption of more than 24 g of alcohol for men and more than 12 g of alcohol for women.¹⁸⁹ This also partly explains the higher part of the J-shaped curve between alcohol consumption and all cause mortality. With moderate consumption there is a lower risk for all cause mortality (see Chapter 10).

Alcohol attributable fractions

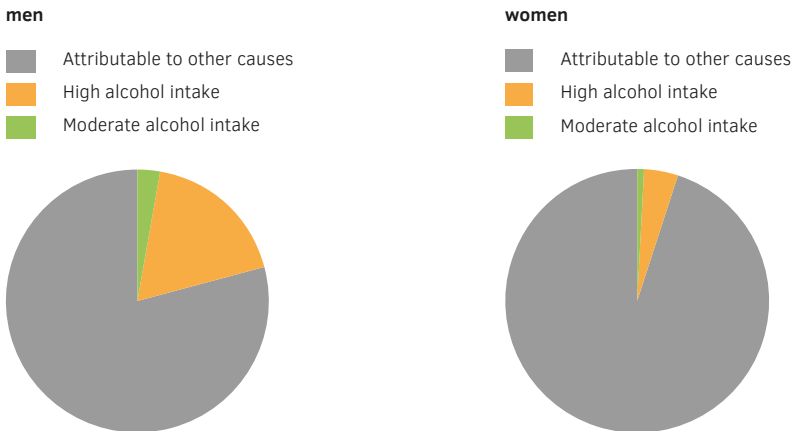
Table 4 gives an overview of the incidence and mortality of alcohol-related cancers in Europe, and the alcohol attributable fractions. This indicates those cases associated with alcohol consumption, or how many cancers could have been prevented if everyone in Europe had always abstained from alcohol. Overall in Europe, cancer cases

attributable to alcohol have been estimated to be about 10% of all cases for men and about 3% for women, varying across countries due to differences in intake and other factors.¹⁸⁹ A substantial part of alcohol-related cancer cases in Europe are associated with consumption of more than 24 g per day for men and 12 g per day for women. In men, about 3% of alcohol-related cancer cases are associated with consumption of less than 24 g of alcohol per day and more than 18% are associated with consumption of more than 24 g alcohol per day. For women consuming less or more than 12 g alcohol per day, the equivalent figures for alcohol-related cancers are 1% and 4%, respectively (see Figure 10).¹⁸⁹

An example of how to interpret the alcohol attributable fraction data in Table 4

The alcohol attributable fraction for breast cancer is 5%. This indicates that of all breast cancer cases in Europe, 5% are associated with alcohol consumption.

Figure 10. Alcohol attributable cancer cases in 8 European countries in 2008¹⁸⁹



The incidence of breast cancer in 2012 was 458,337 cases, and so about 23,000 of these are associated with alcohol consumption. In other words, if all women in Europe had abstained from alcohol during their whole life about 23,000 cases of breast cancer could have been prevented in 2012. Other examples are: if all men in Europe did not consume alcohol during their whole life about 41,000 colorectal cancer and 14,000 liver cancer cases could have been prevented in 2012.

Keep in mind that most alcohol-related cancer cases are associated with high alcohol consumption.

Breast cancer

Female breast cancer is the most prevalent cancer in Europe. Alcohol consumption is one of the factors increasing breast cancer risk, as well as high body weight, physical inactivity and the use of the birth control pill. Relative breast cancer risk increases by 3–9% (compared to existing risk) for every 10 g of alcohol consumed per day.^{191–196} The inconsistency of relative risks found across studies might be partially due to differences in the number of subjects with hormone receptor negative and hormone positive tumours. Non-hormonal pathways such as DNA damage are likely to cause receptor negative tumours. Hormone receptor positive tumours contain receptors for the hormones estrogen and/or progesterone. With alcohol consumption, a higher risk for hor-

mone receptor positive tumours has been reported.^{197–200} The risk effect of alcohol on breast cancer plays a particularly important role in women with a family history of benign mastopathy (diseases of the breast) or other conditions associated with increased breast cancer risk.¹⁹⁴ Although there are indications that there is no relationship with body mass index (BMI) or use of hormones,¹⁹⁶ there are still many other aspects that need to be clarified, such as the effects of the age when drinking started, drinking patterns, menopausal status and genetic polymorphisms.²⁰¹

Colorectal cancer

Colorectal cancer is the second most common cancer in Europe. Red meat consumption, physical inactivity and obesity are risk factors for colorectal cancer, as well as high alcohol consumption. The relative risk of cancers of the colon and rectum appear not to increase with consumption of up to 10 g alcohol per day.^{202–204} With consumption of 25, 50 and 100 g alcohol per day, the relative risk is increased (compared to existing risk) by 8%, 14% and 43%, respectively, in comparison with non-/occasional drinkers.²⁰⁴ It is suggested that the detrimental effect of drinking on colorectal cancer risk is stronger in men than in women.²⁰² The relative risk for colorectal adenoma, the established pre-cancerous lesion for colorectal cancer, is increased by 27% (compared to existing risk) with each 25 g increment of alcohol intake per day.²⁰⁵ ►

Cancers of the head and neck

For cancers of the head and neck, alcohol consumption is a risk factor, particularly in combination with smoking. In Europe, the highest absolute number of cancer cases attributable to alcohol in men is for upper aerodigestive tract cancers (see Table 4), a substantial part being associated with consumption of more than 24 g of alcohol per day.¹⁸⁹ No increase in relative risk for head and neck cancer was found with daily consumption of 12–24 g alcohol, but more than 36 g alcohol per day doubled the relative risk (compared to existing risk) as compared to abstainers.²⁰⁶ Smoking is also a risk factor for cancers of the head and neck, doubling the relative risk with 1–20 cigarettes per day compared to non-smokers. Together, smoking (1–20 cigarettes per day) and high alcohol consumption (more than 36 g per day), have a greater than multiplicative joint effect on the risk of cancers of the head and neck, resulting in a 10 fold increase in relative risk compared to non-drinkers.²⁰⁶

Liver cancer

The incidence and the cumulative risk of liver cancer in Europe is low (see Table 4). Alcohol consumption is a risk factor for liver cancer, and excessive consumption is associated with increased risk. Consumption of 12 g alcohol per day is associated with an increase in the relative risk of liver cancer of 8% (compared to existing risk), and the relative risk is 54% higher with an alcohol consumption of 50 g per day. A separate analysis in people without hepatitis infection indicated that their risk of liver cancer increases when they consume more than 40 g of alcohol per day.²⁰⁷

Oesophageal cancer

The incidence and thus the cumulative risk of oesophageal cancer in Europe is also low (see Table 4). Alcohol consumption is a risk factor for this type of cancer, but the risk is mainly increased with high intake. Alcohol consumption is a risk factor especially for a particular oesophageal cancer

called oesophageal squamous cell cancer. Consumption of less than 12.5 g alcohol per day increases the relative risk by 26% (compared to existing risk),²⁰² the relative risk being doubled with alcohol consumption up to 50 g per day, and increased five fold with more than 50 g per day, as compared to non-drinkers.

7.4 Carcinogenic effects of alcohol

The possible mechanisms by which alcohol consumption increases the risk of certain cancers are complex and not fully understood.

Acetaldehyde and carcinogenic reactive oxygen species

Acetaldehyde, a toxic metabolite of alcohol, plays a major role in cancer risk.²⁰⁸ At higher consumption levels above 40 g alcohol per day for at least a week, the microsomal ethanol oxidizing system (MEOS) is activated. This alcohol breakdown pathway produces carcinogenic reactive oxygen species (for details of the alcohol metabolism, see Chapter 3). Also bacterial microbiota can metabolise alcohol into acetaldehyde. This is mainly the case with high levels of alcohol in the oral cavity and colorectal areas.^{209–211}

Other possible mechanisms

- Alcohol consumption may also stimulate carcinogenesis by inhibiting DNA methylation and by interacting with retinoid metabolism.²⁰⁸
- Alcohol may alter the metabolism of hormones, such as increasing blood sex hormone levels (e.g. oestrogen),^{212,213} which may promote the development of breast cancer.
- Alcohol acts as a dissolvent, making it easier for carcinogenic compounds such as those found in cigarettes, to enter tissues.²⁰⁶
- Alcohol-related malabsorption and deficiency of nutrients like folate are associated with different forms of cancer, which can occur with high alcohol consumption.²¹⁴

Carcinogenic components other than alcohol

Although alcohol is identified as the most important carcinogen in alcoholic beverages, other compounds such as ethyl carbamate and acetaldehyde may also pose risks.²¹⁵ In the 1980s, beer received much attention due to the discovery of high levels of nitrosamines,²¹⁶ identified as potential carcinogenic compounds.²¹⁷ Brewing processes have been optimised since then, and today, there are only negligible amounts of nitrosamines present in beer.²¹⁸

7.5 Alcohol consumption and reduced risk of certain cancers

For certain types of cancers, some risk reduction is seen with alcohol consumption. However, more research is needed to

confirm the findings from these population studies and to find the physiological mechanism explaining the effects.²⁰² The cancers are not the most common cancers. Table 5 provides an overview of the incidence and mortality of these specific cancers, and cumulative risk which indicates the risk of getting that type of cancer up to an age of 75 years. The cumulative risk differs between European countries because of differences in risk factors in each. By knowing this risk, it is possible to put relative risks into perspective (see Box at the start of this chapter). If cumulative risk is very small, even a huge decrease in relative risk due to alcohol consumption may not make much absolute difference. But for a cumulative risk that is quite large already, smaller decreases in relative risk can have a big impact. ►

Table 5. Incidence, mortality and cumulative risk of the cancers that might be reduced by alcohol consumption in Europe (2012)

Cancer	Incidence ¹⁸⁶		Mortality ¹⁸⁶		Cumulative risk range*	
	Men	Women	Men	Women	Men	Women
Kidney including renal, pelvis and urethra	71,739	43,435	31,313	17,678	0.44 – 2.91	0.22 – 1.22
Non-Hodgkin lymphoma	49,533	43,900	20,347	17,553	0.10 – 1.47	0.09 – 1.05
Thyroid	12,283	40,654	2,066	4,270	0.02 – 0.67	0.22 – 2.02
Hodgkin's lymphoma	9,284	8,300	2,621	2,001	0.04 – 0.26	0.05 – 0.23

* The lowest and the highest risk (differs between countries within Europe) of getting a specific cancer up to age of 75 years old. Data derived from globocan.iarc.fr

Kidney cancer

The relative risk of kidney cancer decreases (compared to existing risk) by up to 29% with the consumption of up to 50 g of alcohol per day compared to abstainers.^{202,219,220}

Non-Hodgkin lymphoma

Compared with non-drinkers, those consuming alcohol have a 15% lower relative risk (compared to existing risk) for non-Hodgkin lymphoma. The dose-response relationship indicates the relative risk is significantly reduced by 20% with alcohol consumption of up to 75 g per day.²²³

Thyroid cancer

A significant inverse association is observed between alcohol consumption and thyroid cancer risk. Alcohol consumption of 14–108 g per week decreases the relative risk for thyroid cancer by 17% (compared to existing risk), and consumption of more than 108 g alcohol per week decreases the relative risk by 28% as compared to abstainers.²²¹ Similar findings are observed in a follow-up study where alcohol consumption of 15 g per day or more was associated with a 23% lower relative risk of thyroid cancer compared with those consuming 0.1–4.9 g alcohol per day.²²²

Hodgkin's lymphoma

Hodgkin's lymphoma is a rare cancer in Europe, as also indicated by the low cumulative risks. Compared with non-drinkers, those consuming alcohol have a 30% lower relative risk (compared to existing risk) for Hodgkin's lymphoma. An inverse dose-response relationship has also been indicated, but as it was not significant, caution is required in the interpretation of findings.²²⁴

7.6 Cancer risk after alcohol drinking cessation

It is difficult to estimate how long it takes for such elevated risks to decrease or disappear after someone stops drinking alcoholic beverages. Research is limited and not unequivocal. For mouth and throat cancer it may take more than 35 years to disappear²²⁵ and for oesophageal cancer and liver cancer, 16.5 and 23 years, respectively.^{226,227}

7.7 Alcohol consumption before and after breast cancer diagnosis

Alcohol consumption before and after breast cancer treatment, appears to have limited effects on survival.

Before diagnosis and survival

Based on a large population study of women with breast cancer, there was some indication that consumption of 42–84 g per week modestly improved breast cancer survival by 15% (relative risk) as compared to non-consumers and those who consume more.²²⁸

After diagnosis and survival

Alcohol consumption of more than 140 g per week after breast cancer diagnosis is associated with a reduced relative risk of death from cardiovascular disease (CVD) of 53% and a reduced relative risk of overall mortality of 36%.²²⁸ CVD is an important contributor to mortality among breast cancer survivors, probably because of the cardiotoxic and metabolic effects of some breast cancer treatments.²²⁹ ■

REMEMBER

Each glass of an alcoholic beverage increases the risk of breast cancer

There are multiple risk factors for breast cancer, and alcohol consumption is one of them. The highest lifetime risk of developing breast cancer in Europe up to an age of 75 years old (see Table 4) is 11.6%, as reported from Belgium. Each glass of alcoholic beverage per day (10 g of alcohol) increases the risk by 3–9%,¹⁹¹ meaning the absolute risk increases from 11.6% to 12.0–12.6% (a 0.4–1.0 percentage point increase). This corresponds to an increase from 116 to 120–126 women out of 1,000 who develop breast cancer. To put this in perspective, another risk factor for breast cancer is the birth control pill, and using this pill increases the risk by 24%,²³¹ increasing absolute risk from 11.6% to 14.4% (an increase from 116 to 144 women out of 1,000 who develop breast cancer).

Keep in mind these are just examples that indicate the effects of alcohol consumption and using the birth control pill on the absolute lifetime risk of developing breast cancer up to an age of 75 years old. Absolute lifetime risk may be higher or lower than these figures depending on particular risk factors such as age and lifestyle. This is not intended to discourage use of the birth control pill but rather to put into some context the impact of alcohol consumption. ■



BEER AND CANCER

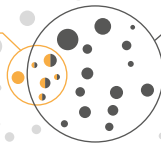
Of over a hundred cancer types there are six related to alcohol and they are mostly associated with heavy alcohol consumption.



> 3 million
new cancer cases
per year in Europe.

There are over 100 types of cancers.

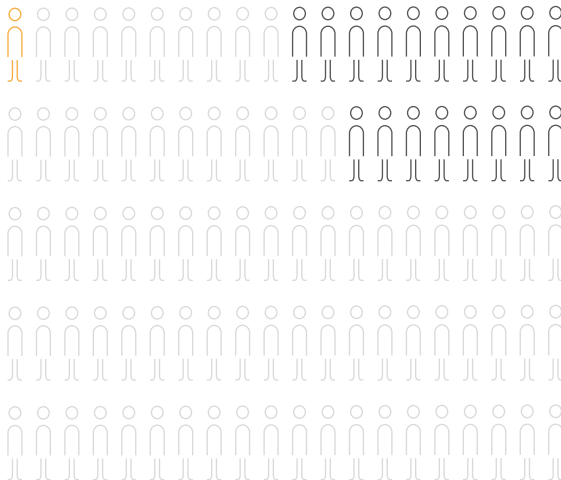
6
There are
alcohol-related
cancers.



17
There are
tobacco-related
cancers.

Only a small number of all cancer cases is associated with alcohol consumption.
(Based on data of 8 West-European countries)

<1%
caused by
moderate
and heavy
alcohol
consumption.

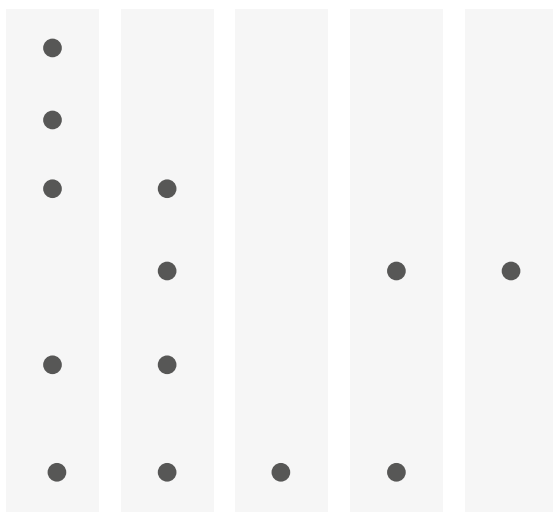
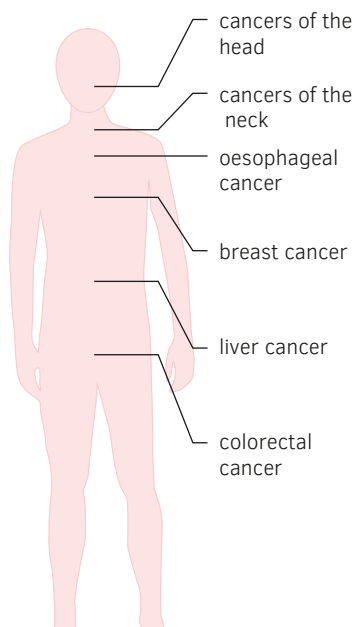
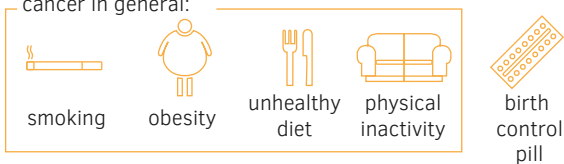


18%
caused by
smoking.

Possible adverse health effects mainly apply to heavy alcohol consumption. A healthy lifestyle is strongly advised. Moderate beer consumption is defined in this infographic as no more than two 25 cl drinks of 5% beer (or two 33 cl drinks of 3.8% beer, or two 10 cl drinks of 13% wine) daily for men and one for women. This may vary for one's ►

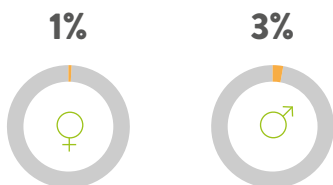
Other lifestyle risk factors for the six alcohol-related cancer types:

The four main lifestyle risk factors for cancer in general:

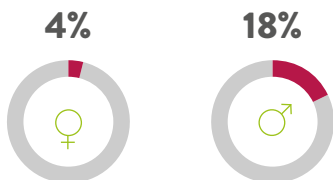


Of these six alcohol-related cancer types the cases associated with alcohol consumption are mostly associated with heavy consumption.

Moderate alcohol consumption:



Heavy alcohol consumption:



age, size and overall health. For personal guidance, check with your general practitioner. Please note this does not constitute a drinking guideline. All statements from this infographic are backed-up by science that can be retrieved on www.beerandhealth.eu. ■

8



BEER AND THE BRAIN

The short term effects of moderate alcohol consumption on the brain are quite clear. Regarding the long term effects however, the body of evidence varies by age range. Below the legal purchasing age and when pregnant, it is not sensible to drink alcohol. During young adulthood (18–25 years of age), the brain is still developing, though it is not yet clear how moderate alcohol consumption affects the brain during this period of life. The risk of mild cognitive impairment and dementia that is more common later in life, might be reduced with moderate alcohol consumption.



KEY MESSAGES

- ⬡ All effects on the brain are due to the alcohol in beer and apply to all alcoholic beverages.
- ⬡ Up to an age of 25 years old, the brain is developing and might be vulnerable to the effects of alcohol.
- ⬡ Until the legal purchasing age and when pregnant, it is not sensible to drink any alcohol.
- ⬡ More research is needed to understand the influence of moderate alcohol consumption on the developing brain after the legal purchasing age (16 to 18 years).
- ⬡ Moderate alcohol consumption may lower risk of dementia by 26% with the consumption of up to 28 drinks per week, and there might also be a lower risk of mild cognitive decline.
- ⬡ Research on the protective effect of alcohol consumption against Parkinson's disease is very limited.

8.1 Alcohol consumption and the developing brain

From conception up to an age of approximately 25 years old, the brain is developing. The total brain size at 6 years old is about 90% of adult size, but the brain continues to undergo dynamic structural changes throughout adolescence and well into young adulthood. During this whole period, the brain may be vulnerable to the effects of alcohol.²³²⁻²³⁴

Foetal stage

Large amounts of alcohol during pregnancy can cause foetal alcohol syndrome (FAS). This is a devastating developmental disorder consisting of structural abnormalities and growth deficits. FAS is associated with a broad spectrum of neurobehavioral abnormalities.²³⁵ The effects of lower doses of alcohol on the foetal brain and other organs are unknown, but whether there exists a safe alcohol dose during pregnancy is uncertain and controversial.²³⁶

Young adulthood

The brain develops up to 25 years of age. More research is needed to understand the influence of moderate alcohol consumption on the developing brain from legal purchasing age* and how this could affect functioning in daily life. Studies conducted to date have mostly focused on adolescents with alcohol use disorder (AUD) (either alcohol

abuse or alcohol dependence). Impairments related to language, attention, learning and memory were found.²³⁷⁻²³⁹ Results of these studies are often generalised to the general public, assuming that findings in this at-risk group can be translated to heavy drinkers in general. However, recent population studies in heavy adolescent drinkers (without diagnosis of AUD) have found only small differences in neurocognitive functioning as compared to abstainers.^{240,241} These preliminary findings need to be confirmed in large prospective studies. Drinking in moderation during adulthood has been associated with improved quality of life (see Chapter 9), and similar benefits have been found in adolescents. The limited literature suggests that moderate alcohol consumption is related to stress response reduction, mood enhancement, improved cognitive performance, reduced clinical symptoms primarily of depression, and improved physical functioning.²⁴²

**The legal purchasing age for beer is between 16 and 18 years old in different European countries.*

8.2 Alcohol consumption and cognitive impairment

Later in life, the brain undergoes changes that influence its functioning. The normal ageing process of the brain results in cognitive decline. Mild cognitive impairment (MCI) is an ageing process of the brain that is ►

The acute effects of alcohol on the brain

Alcohol reaches the brain approximately 5–10 minutes after consumption.²⁵⁹ Depending on the blood alcohol concentration (BAC) there are different effects on the brain (see Table 6). BAC depends on a number of factors including the rate of consumption, gender and body weight. For example, consumption of 10 g of alcohol by a 80 kg man results in a peak BAC of 0.02%, whereas 10 g of alcohol by a 65 kg woman results in a peak BAC of 0.03% (see Chapter 10). At these BACs, the frontal lobe sedates, inducing relaxation, impaired judgement, and increased heart rate.

When BACs rise, the speech and vision centres in the midbrain are affected. At higher concentrations of alcohol in the blood, the cells in the cerebellum responsible for coordination of voluntary muscles are affected, including those used in speech, eye-hand coordination and limb movements. At very high BACs, the conscious brain is completely subdued and the person passes out. Even higher doses of alcohol anesthetize the deepest brain centres that control breathing and heartbeat, causing death.⁸² ■

Table 6. Effects with different blood alcohol concentrations⁸²

Blood alcohol concentration	Effects
0.1%	Impaired coordination, delayed reaction time, exaggerated emotions, impaired peripheral vision, impaired ability to operate a vehicle
0.15%	Slurred speech, blurred vision, staggered walk, seriously impaired coordination and judgement
0.2%	Double vision, inability to walk
0.3%	Uninhibited behaviour, stupor, confusion, inability to comprehend
0.4–0.6%	Unconsciousness, shock, coma, death from cardiac or respiratory failure

beyond what is expected based on age and educational level. People having MCI may retain the ability to be independent, but of those with MCI, 10–15% develop dementia for reasons that still remain unknown. Dementia is a brain disease causing damage and breakdown of nerve brain cells or the connecting tissue between nerves. This results in cognitive deficits that interfere with independence. There is no agreement on the prevalence rates of MCI in Europe. According to the scientific literature, MCI prevalence rates vary from 3% to 42%, depending on the age and definition of cognitive impairment used.²⁴³ In 2015, an estimated 10.5 million of the about 177 million people aged 60 years and over in Europe were suffering from dementia.²⁴⁴ Several population studies have looked at the association between alcohol consumption and cognitive decline, MCI and dementia.

Alcohol consumption and cognitive decline

Systematic reviews and meta-analyses did not find a relationship between moderate alcohol consumption and cognitive decline.^{245–247} Results from a recent cohort study suggest that men consuming 36 g of alcohol per day or more in midlife were more likely to experience faster 10-year cognitive decline in all cognitive domains (global cognitive score, executive functioning, and memory), with effect sizes comparable to 1.5 to 5.7 extra years of cognitive decline observed. In women, there was weaker evi-

dence of this effect occurring at more than 9 g per day and in particular for executive functioning.²⁴⁷

Alcohol consumption and mild cognitive impairment

A meta-analysis indicated that moderate alcohol consumption (not specified in grams per day) is associated with a 22% lower relative risk for MCI,²⁴⁸ and results of a recent cohort study are in line with these findings. Compared with abstainers, alcohol consumption of 150–270 g per week is associated with 40% less cognitive impairment 5.7 years later. Although this protective effect was not significant after adjustment for potential confounders, as a group, regular drinkers had lower adjusted odds of cognitive impairment than abstainers or irregular drinkers.²⁴⁸ Patients with MCI who consumed 1.0–14.9 g of alcohol per day had a 85% reduction in the rate of progression towards dementia in comparison to patients with MCI who never consumed alcohol.²⁴⁹ Similar findings were observed in another follow-up study among those with mild cognitive impairment. Patients who consumed more than 20 g of alcohol per day had the highest rate of MCI progression to dementia, those who consumed less alcohol per day had the lowest, while abstainers had an intermediate rate.²⁵⁰ The mechanism by which alcohol intake protects against the progression of MCI to dementia is unknown, though alcohol consumption might have an effect on the cerebral vasculature or is

related to favourable social and lifestyle factors (see Section 8.3).²⁴⁹

Alcohol consumption and dementia

There are suggestions of a J-shaped relationship between alcohol consumption and dementia, with low to moderate drinking levels reducing the risk of overall dementia, but heavy use increasing the risk.²³⁶ Results from a meta-analysis show that light to moderate alcohol consumption (defined in ranges of 1–28 drinks per week) is associated with reductions in relative risk of 28%, 25% and 26%, respectively, of Alzheimer's disease, vascular dementia and any dementia as compared with alcohol abstinence in older adults.²⁴⁵ Similar findings were observed in another review.²⁴⁶ These risk reductions with alcohol consumption are comparable with those observed when following a Mediterranean diet or with high physical activity, for example.²⁵¹ Although some research suggests that wine is better than other alcoholic beverages, this is based on a relatively small number of studies. In addition, studies that made a distinction among different types of alcoholic beverages and dementia risk reported no differences in effects, and effects may be unrelated to the type of beverage.²⁴⁶ It is unclear whether the association between alcohol consumption and dementia is due to an effect of moderate alcohol consumption throughout adulthood, or a specific benefit of moderate alcohol consumption later in life.²⁴⁵

8.3 Mechanisms of effect of moderate alcohol consumption

The mechanism by which moderate alcohol intake could protect against the progression of a normal aging brain to mild cognitive impairment and dementia is, at present, unknown. Mechanisms by which alcohol consumption affects cardiovascular disease risk, increased HDL cholesterol, decreased platelet aggregation, improved glucose tolerance and reduction of inflammation markers (see Chapter 5), might also have an effect on the cerebral vasculature. This also supports the observation that moderate alcohol intake might protect against ischemic stroke (see Chapter 5). It is also possible that moderate alcohol consumption may be an indicator of a complex set of favourable social and lifestyle factors that protect against cognitive impairment.^{249,252}

8.4 Alcohol and Parkinson's disease

Parkinson's disease nerve cells die mostly in the part of the brain called the substantia nigra, which dramatically decreases the amount of the hormone dopamine. A person becomes less and less able to regulate body movements and other normal body functions, as well as emotions. In Europe, 1–2 in every 1000 people have Parkinson's disease,²⁵³ though the exact cause of Parkinson's disease is not yet clear.²⁵⁴ ►

Beer consumption and Parkinson's disease

A meta-analysis found a protective effect against Parkinson's disease by drinking alcohol, and specifically beer. Every 13 g of alcohol per day might be associated with a 5% decrease in Parkinson's disease risk, but more research is needed to confirm this finding,²⁵⁵ and the mechanisms by which alcohol consumption or specifically beer consumption may reduce the risk of Parkinson's disease. Alcohol intake might influence Parkinson's disease risk by the addictive behaviour itself. Smoking and drinking coffee, two common addictive behaviours, have been consistently associated with a reduced risk of Parkinson's disease.²⁵⁴ Beer could have an additional beneficial effect as it contains purine and therefore increases the levels of serum uric acid,²⁵⁶ which is inversely associated with the risk and could delay the progression of Parkinson's disease.²⁵⁷ ■

REMEMBER

It is not advisable to drink alcohol under the legal purchasing age

During adolescence, the brain goes through a number of changes. Brain networks sensitive to social and emotional stimuli and reward processing mature quickly, while cognitive control functions lag behind. Furthermore, adolescence is a period in which individuals need to learn from experience. Both these changes result in adolescents tending to engage in experimental behaviour, including alcohol consumption. Research indicates that if adolescents drink alcohol, they mainly do so in moderation. However, they have a higher risk of binge drinking, which can be explained by findings from animal studies. It seems that the adolescent brain is less sensitive to aversive sedative effects and more sensitive to the rewarding, stimulant effects of alcohol as compared to adults. Such a decreased sensitivity in combination with the rewarding effects of alcohol may lead to loss of control when drinking. The negative consequences of alcohol abuse are ignored, and this leads to binge drinking. Binge drinking may negatively affect social functioning in the short term, and may negatively affect mental and physical health in the long term. In addition, it increases the risk of alcohol dependence in adulthood.²⁴² ■

The background of the entire page is a black and white photograph of a glass filled with beer, with a thick head of foam. Two hexagonal shapes are overlaid on the left side of the image. The top hexagon is green and contains a white number '9'. The bottom hexagon is orange and contains a white medical symbol, specifically a caduceus. The text 'BEER AND OTHER HEALTH EFFECTS' is written in large, bold, white capital letters across the middle of the image, partially overlapping the glass and the orange hexagon. Below this, a paragraph of text in a smaller white font provides context about the health effects of beer.

9



BEER AND OTHER HEALTH EFFECTS

For some diseases such as cancer and cardiovascular disease, the link to beer consumption is already quite clear. Beer can also affect the immune system, bone, joint and kidney health, gallstones, well being and the quality of life. However, more research is needed before strong conclusions can be made on these effects.

KEY MESSAGES

- ⬡ Besides the positive effects of moderate beer consumption on cardiovascular disease, type 2 diabetes and dementia, there might be other health effects, but research is scarce.
- ⬡ Moderate alcohol consumption and bone health appear to be positively related, but the potential beneficial effects of some individual components of beer (such as silicon) need more investigation.
- ⬡ Some research shows moderate alcohol consumption may protect against rheumatoid arthritis, but results are mixed and a mechanism for this protective effect has not been determined.
- ⬡ The risk of gout may increase with alcohol consumption, but the mechanism behind this is not clear, nor is the effect of different types of alcoholic beverages.
- ⬡ Moderate alcohol consumption does not affect kidney functioning.
- ⬡ For protective effects against kidney stones and gallstones, and beneficial effects on the immune system, research is very limited and the optimal amount of beer consumption has not yet been determined.
- ⬡ Well being and the quality of life seem to improve with moderate beer consumption due to the alcohol, but this relationship also needs more research.

9.1 The immune system

Alcohol in small and moderate quantities may have a beneficial effect on the immune system. Some studies reported that moderate alcohol consumption of 10–40 g per day could decrease the risk of the common cold.¹⁶⁷ Others saw a decrease in inflammation and a better response to vaccines.²⁵⁸ Besides alcohol, other components in beer such as polyphenols may influence the immune system.²³ There is very limited research available and more is needed to determine what effects are caused by alcohol and what are caused by the non-alcoholic components in beer.

9.2 Bone health

Light to moderate alcohol consumption (and specifically of beer), might reduce osteoporosis risk by increasing bone mineral density (BMD).

Osteoporosis

Osteoporosis is a disease causing brittle bones, prone to fractures. One in three European women aged 50 years and over and one out of five men of the same age, suffer from osteoporotic fractures. Besides gender, low body mass index (<18.5 kg/m²), older age, lack of physical exercise, previous bone fractures, and smoking, all increase the risk of osteoporosis.²⁵⁹

Alcohol and bones

A high BMD is an indication of strong bones, not brittle ones. Experimental studies show BMD of the hips of men increases 3.4–4.5% with an intake of approximately 10–30 g of alcohol per day. The same amount of alcohol increased hip and spine BMD by 5.0–8.3%

in post-menopausal women.²⁶⁰ However, the BMD of pre-menopausal women may decrease with alcohol consumption above 5 g per day, caused by a difference in hormone composition before and after menopause.^{28,261} However, there is no research available on the effect of alcohol consumption in people who already have osteoporosis.²⁶²

Mechanisms

With light to moderate alcohol consumption, there is limited research on how this affects BMD. One study proposed that 1–30 g of alcohol per day may influence bone remodelling from lower blood levels of osteocalcin. The protein osteocalcin supports the activity of cells that build up bone (osteoblasts), but the size of the impact of this mechanism remains unknown.^{261,262} With more than 30 g of alcohol per day, however, the reverse is true. An increase in bone breakdown cells (osteoclasts) increase oxidative stress, increase the amounts of fat near bone marrow, and decrease calorie intake, which creates a different body composition with lower body fat and muscle mass, and these all seem to be related to low BMD and increases in the risk of osteoporosis.²⁶¹

Beer and bones

The limited available research suggests that specifically beer consumption may be good for bone health. A population study showed an increase in BMD for men and postmenopausal women when they consumed two glasses (around 700 ml) of beer per day, referring to the effect of alcohol but also to another constituent in beer, silicon.²⁶⁰ The involvement of silicon was seen in another

population study where the effect of moderate beer drinking on BMD was compared to non-beer alcoholic beverages. When results were corrected for dietary silicon intake, the magnitude of the effect on BMD decreased for beer, but remained the same with non-beer alcoholic beverages.²⁸ Information on the amount of silicon in beer can be found in Chapter 2.

9.3 Joint health

Alcohol may play a role in decreasing the risk of rheumatoid arthritis, but may increase the risk of gout, another condition of the joints.

Rheumatoid arthritis

Rheumatoid arthritis is an inflammatory disease of the joints. The prevalence in Europe varies from 0.3% in France to 0.8% in the United Kingdom. However, only few countries have available data on the prevalence of rheumatoid arthritis and this makes it unclear how many people suffer from this condition in the EU.²⁶³ Risk factors for getting rheumatoid arthritis are smoking, obesity and being overweight, little physical exercise, and it tends to run in families showing a genetic link.

Alcohol and rheumatoid arthritis

A meta-analysis found a 22% decrease in relative risk of rheumatoid arthritis for both women and men when looking at the results of multiple case-control studies (a type of population study).²⁶⁴ They did not find an effect of alcohol on risk of rheumatoid arthritis in another type of population study (cohort),²⁶⁴ but other researchers did. Women who drank 2–4 glasses of beer (350

ml per glass) per week had a 31% lower relative risk of rheumatoid arthritis than abstaining women.²⁶⁵ No research has been done in men. A mechanism for this effect is not yet established. Also there is no data available on the effect of alcohol in subjects already diagnosed with rheumatoid arthritis.

Gout

Gout is a form of inflammatory arthritis caused by a high amount of uric acid in the blood. It is not clear how many people have gout in Europe, but a recent study from the United Kingdom and Germany shows a stable prevalence of 1.4% in both countries.²⁶⁶

Alcohol and gout

Alcohol consumption can increase the risk of gout. A meta-analysis saw an increase of 16% in relative risk when drinking only one drink (defined as 12.5 g per day). Consumption of 1–3 drinks per day (12.6–37.4 g) caused an increase of 56%.²⁶⁷ In this meta-analysis, no specific beverages were analysed as there are not enough studies that have looked at individual types of beverages, and the mechanism behind the association of gout and alcohol is not clear.

9.4 Kidney health

Moderate alcohol consumption may help to prevent kidney stones and it probably does not harm kidney function.

Kidney stones

As alcohol increases urine output, it could help to prevent kidney stones, hard masses of calcium formed in the kidneys. How many people in Europe have kidney stones is not clear, but it is a common disease ►

that increases in prevalence with obesity, and drinking enough fluids is important in prevention.

Alcohol and kidney stones

A meta-analysis on fluids and kidney stone prevention described a 20% lower relative risk of developing kidney stones with an alcohol intake of 12 g per day. For every extra 10 g of alcohol per day another 20% was added to the total relative risk reduction ($20\% + 20\% = 24\%$). This was the first meta-analysis undertaken, and more research is needed to confirm this finding.²⁶⁸

Chronic kidney disease

Kidney stones may increase the risk of chronic kidney disease (CKD),²⁶⁹ which is defined by a slower filtration rate in damaged kidneys. The main function of the kidneys is to filter waste products from the blood and convert it into urine. In the European population, 5.1–7.0% is at an early stage of CKD and 4.5–5.3% is in a more advanced stage.²⁷⁰

Alcohol and kidney disease

CKD increases the risk of developing heart disease, and heart disease also increases the risk of CKD. There is strong scientific evidence that moderate alcohol consumption has a beneficial effect on the risk of heart diseases (see Chapter 5), but for CKD this cannot be concluded. A meta-analysis shows that alcohol consumption of less than 30 g per day for men and less than 15 g per day for women does not harm kidney function, though no beneficial effects have yet been found.²⁷¹

9.5 Gallstones

Gallstones are hard masses in the gallbladder made largely from cholesterol. They are common in Europe, with prevalence ranging from 5.9% in Italy to 21.9% in Norway.²⁷²

Alcohol and gallstones

The risk of gallstones may decrease with alcohol consumption, but evidence is scarce. In one cohort study, the relative risk

of gallstones decreased by 3% per 7.9 g of alcohol consumed per day for men, though in women no protective effect was found.²⁷³ But in another cohort study, women did benefit from alcohol consumption with a 14% reduction in relative risk with the consumption of 5.0–14.9 g per day.²⁷⁴ As explained in Chapter 5, HDL cholesterol and alcohol are associated. With moderate alcohol consumption, HDL concentrations in the blood can increase, and which may also increase bile acid formation, keeping cholesterol soluble and preventing gallstones from developing.²⁷³ However, to prove this mechanism and the link between alcohol and gallstones, more research will be needed.

9.6 Well being and quality of life

People enjoy the relaxing effect of drinking beer and other alcoholic beverages, but there is limited research on the effects of moderate alcohol consumption on well being and the quality of life.

Well being

One review concluded that consumption of less than 20 g of alcohol per day may reduce stress and tension, and increases sociability and the feeling of well being.²⁷⁵ In an experimental study on social interaction, drinking 1–2 alcoholic drinks (grams not specified) made people more social, friendly and agreeable during a conversation according to the person they were talking to, but what caused these positive changes in mood and well being was not made clear.²⁷⁶

Quality of life

Multiple studies suggest that alcohol consumption of less than 30 g per day positively influences health-related quality of life. On the other hand, excessive alcohol consumption shows the reverse is true in research with adults more than 50 years old.²⁷⁷ In a population study in the USA, people were asked about their alcohol consumption and how they would rate their health. More moderate drinkers (defined as women consuming 42–98 g and men consuming 42–196 g of alcohol per week) rated

their health above average as compared to abstainers and people with a higher alcohol intake.²⁷⁸

Pain management

A review shows that moderate alcohol consumption (stated as less than 7 drinks per week for women and less than 14 drinks per week for men) can also help with pain management and thereby increase the quality of life. Patients with fibromyalgia, rheumatoid arthritis or chronic back pain who drank alcohol moderately, had less pain compared to abstainers. With fibromyalgia patients, a higher quality of life, better physical functioning and fewer symptoms of fibromyalgia were measured. However, excessive alcohol drinking increased the pain. It is not certain if the same effects are achieved with other comparable health problems and diseases, and as such, more research is suggested.²⁷⁹

Social life in the elderly

When ageing, one faces many physical, psychosocial and social changes in life. Depression and loneliness are major problems among the elderly, and research shows elderly people prefer to keep engaged in social activities.²⁸⁰ Multiple cohort studies show an increase in the quality of life (measured by questionnaires on mental, physical, psychological and social functioning) with moderate alcohol consumption among people aged 50 years and over.^{277,281,282}

A group of women aged 70–75 years who drank moderate amounts of alcohol (defined as 1–2 drinks per day, 3–6 days per week) rated their general, physical and mental health and social functioning higher than abstainers and women with a high alcohol consumption.²⁸¹ On the other hand, the quality of life still decreased with moderate drinking as they became older, but less so as compared to abstainers and heavy drinkers.^{281,282} ■



10



BEER AND HEALTH: MAKING UP THE BALANCE

Beer is made from natural ingredients and has relatively low (or zero) alcohol content compared to most other alcoholic beverages. Drinking beer in moderation can have a positive effect on life expectancy, due to the alcohol in it. There is a J-shaped relationship between alcohol consumption and all-cause mortality, with the lowest relative risk (with an approximate 10% decrease) associated with the consumption of around 20 g of alcohol per day for men and 10 g of alcohol per day for women. This effect is the sum of the positive effects on cardiovascular disease risk at moderate intake and the negative effects on certain cancers and accidents with higher consumption. It is unrelated to the type of alcoholic beverage.



KEY MESSAGES

- ⬡ Beer is a versatile drink with a relatively low alcohol percentage, that when drank in moderation, can be part of an adult's healthy lifestyle.
- ⬡ Drinking beer in moderation may have positive effects on life expectancy, mainly due to the presence of alcohol.
- ⬡ In addition to the effects associated with alcohol, other properties of beer arising from the raw materials and brewing processes, may also have positive effects on health.
- ⬡ However, moderate alcohol consumption should always be considered as a supplement to, and not as an alternative to, other healthy lifestyle choices that lower the risk of coronary heart disease, type 2 diabetes and other diseases.
- ⬡ People who do drink beer or other alcoholic beverages are encouraged to drink in moderation as part of a healthy diet.
- ⬡ For people who don't want to consume alcohol, non-alcoholic beer can be a good alternative.

10.1 Alcohol consumption and life expectancy

A population study in 1926 had already shown that moderate drinkers live longer than abstainers and heavy drinkers,²⁸³ and a J-shaped relationship between alcohol consumption and mortality risk has also been seen in numerous other studies performed more recently (see Table 7 and Figure 11). Overall, the lowest mortality relative risk with about a 10% decrease is observed with the consumption of around 20 g of alcohol per day for men and 10 g of alcohol per day for women. The relative risk increases again with a consumption of more than 40 g of alcohol per day for men and 20 g of alcohol per day for women. The net health benefit from moderate alcohol consumption is thought to act primarily through its cardio-protective effect (see Chapter 5), though increased alcohol consumption is also associated with an increased risk of certain cancers (see Chapter 7) and death from accidents.

Some scientists suggest that it is better to measure lifetime alcohol consumption and not only the consumption at study entry (baseline). The reason for this is that alcohol consumption is likely to vary over time.²⁹⁰ Therefore, the association between alcohol and mortality might be underestimated or overestimated when only baseline consumption is considered. However, studies that measured lifetime alcohol consumption also showed similar J-shaped relationships with all-cause mortality risk.^{288,289}

Transient and reversible effect

The effect of alcohol on mortality risk may be transient and reversible based on data from a 5-year follow-up population study. Subjects with a stable pattern of light to moderate alcohol consumption (12–72 g alcohol per week) had the lowest all-cause mortality risk. Those individuals starting to drink less or those starting to drink more had a 29% and 32% higher relative risk during follow-up, respectively.²⁹¹

Table 7. Overview of studies focusing on the relationship between alcohol consumption and mortality risk

Ref no.	Study	# Subjects	Mortality risk reduction (alcohol dose)		Mortality risk increases	
			Men	Women	Men	Women
285	Meta-analysis, 34 studies	1,015,835	17% (6 g alcohol per day)	18% (5 g alcohol per day)	>40 g alcohol per day	>20 g alcohol per day
286	Meta-analysis, 24 studies	2,424,964	8% (25 g alcohol per day)	9% (25 g alcohol per day)	>75 g alcohol per day	>50 g alcohol per day
287	Meta-analysis, 9 studies	62,950	10% (1–29 g alcohol per day)		>40 g alcohol per day	
288	Population study (European Prospective Investigation into Cancer and Nutrition)	380,395	10% (≤24 g alcohol per day)	7% (≤12 g alcohol per day)	>60 g alcohol per day	>30 g alcohol per day
289	Population study (Melbourne Collaborative Cohort Study)	39,577	19% (20–39 g alcohol per day)	15% (>0–9 g alcohol per day)	≥80 g alcohol per day	≥40 g alcohol per day

10.2 Critical appraisal on alcohol research

The J-shaped relationship between alcohol consumption and all-cause mortality is a combined result from many studies. The challenge with these is that residual, unmeasured or confounding results can never be completely excluded. Few epidemiological observations, however, have been scrutinised for bias as thoroughly as the apparent health benefits of moderate alcohol consumption,²⁹² but some uncertainty remains regarding the causal nature of the J-shaped association seen in population studies. Several methodological flaws have been shown in alcohol research that might produce apparent benefits of moderate drinking, as discussed below.

The 'sick quitters' hypothesis

Some studies failed to separate lifelong abstainers from ex-drinkers. The non-drinker reference group might therefore include 'sick quitters', being those who stop drinking alcoholic beverages because of health problems.²⁹³ This may lead to the impres-

sion of benefits from moderate drinking, though studies that separated ex-drinkers from lifelong abstainers have refuted this hypothesis.¹⁰³

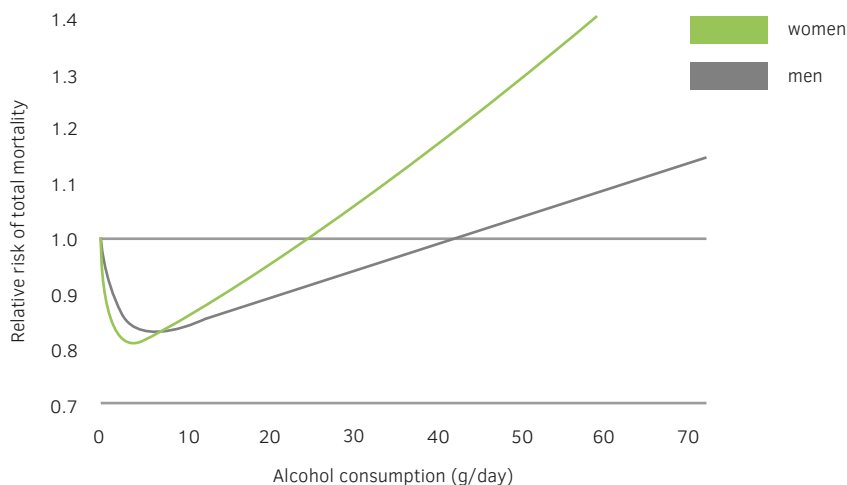
The 'healthy drinker' hypothesis

Another potential source of confounding evidence is the suggested healthier lifestyle of moderate drinkers, or conversely, non-drinkers may show an adverse risk profile.^{294,295} Some studies suggest that the J-shaped relationship between alcohol consumption, cardiovascular disease (CVD) and type 2 diabetes is not likely to be explained by a healthy lifestyle. However, even in those with a healthy lifestyle, moderate alcohol consumption is associated with an additionally lower risk of CVD and type 2 diabetes (see Chapters 5 and 6).

Assessment of actual alcohol consumption

Another concern is the accuracy of alcohol consumption assessments. To date, there is no widely accepted consensus on how to ►

Figure 11. Relationship between alcohol consumption and risk of total mortality²⁸⁵



measure alcohol consumption. Data on alcohol consumption are often based on self-reporting, which can lead to the possibility of misclassification of exposure, and especially the under-reporting of alcohol consumption is a source of potential bias.²⁹⁶ Including heavier drinkers in lower intake categories will lower the threshold of apparent harm, as seen for example in a study showing that the prevalence of hypertension with people reporting to consume 1–2 drinks per day was essentially limited to suspected under-reporters.²⁹⁷

10.3 In conclusion: Beer and health

All the previous chapters in this booklet show us that beer is a versatile drink with relatively low alcohol percentage, that when drank in moderation, can be part of an adult's healthy lifestyle. Due to the natural ingredients there are small amounts of B vitamins, minerals, polyphenols and fibre in beer. And because of the alcohol there may be positive effects on life expectancy. For people who don't want to consume alcohol, non-alcoholic beer can be a good alternative.

Moderate alcohol consumption

There are many adverse effects of heavy alcohol consumption. On the other hand,

moderate drinking may have beneficial effects on health, despite an increased relative risk of certain types of cancer. Mainly, there appears to be a lower risk of cardiovascular disease, type 2 diabetes and dementia that may explain the overall lower relative mortality risk (by around 10%) with the consumption of 10–20 g alcohol per day. This is unrelated to the type of alcoholic beverage. The most favourable drinking pattern is regular daily or almost daily drinking, and avoiding harmful binge drinking.²⁹⁸

Although residual confounding results cannot be excluded, it would be unlikely that they would modify the presented scenarios in any substantial way.²⁸⁵ The consistency and temporal sequence in epidemiological studies and the plausible biological explanations in experimental studies all favour the conclusion that moderate alcohol consumption does have beneficial health effects,²⁹⁹ and the benefits of moderate drinking is relevant for public health.²⁸⁵ However, moderate alcohol consumption should always be considered as a supplement to, and not as an alternative to, other healthy lifestyle habits that also lower the risk of chronic diseases, such as coronary heart disease and diabetes. ■

Table 8. Example of peak blood alcohol concentration in men and women after drinking the same amount of alcohol

	Men	Women
Weight (kg)	80	65
Body fluid (%)	65	55
Body fluid (kg)	52	35
Alcohol (g)	10	10
Peak blood alcohol concentration (%)	0.02	0.03

REMEMBER

A healthy lifestyle is possible with or without drinking beer

Although moderate beer consumption may have health benefits, you do not have to drink beer in moderate amounts for a healthy lifestyle. To ensure a healthy lifestyle, the World Health Organization (WHO) recommends eating lots of fruit and vegetables, reducing fat, sugar and salt intake, and exercising.³⁰¹ What is important, is that if you do drink beer, to do so responsibly and in moderation. ■

Alcohol affects women differently to men

Alcohol affects women differently to men mainly because of their different body composition and lower average body weight. Women have a higher percentage of fat in their body and therefore a lower percentage of body fluid. Since alcohol is water-soluble, it is distributed only in body fluid. Women will therefore have higher peak blood alcohol levels than men when they drink the same amount of alcohol (see Table 8).⁸¹ Other possible mechanisms to explain gender differences in blood alcohol concentration include differences in the relative metabolism of alcohol, the interaction of alcohol dehydrogenase (ADH) with female sex hormones, lower levels of gastric ADH, and more rapid metabolism in the liver by women.³⁰⁰ The difference in blood alcohol concentration between men and women may explain the reason why the inverse association for life expectancy in women disappears at lower alcohol intake compared to that in men, probably due to an increased relative risk of (breast) cancer.²⁸⁴ ■

ABBREVIATIONS

ADH	alcohol-dehydrogenase
ALDH	aldehyde-dehydrogenase
AUD	alcohol use disorder
BAC	blood alcohol concentration
BMD	bone mineral density
BMI	body mass index
CHD	coronary heart disease
CKD	chronic kidney disease
CRP	C-reactive protein
CVD	cardiovascular disease
EFSA	European Food Safety Authority
FAS	foetal alcohol syndrome
GABA	γ -aminobutyric acid
GI	glycaemic index
GL	glycaemic load
GR	glycaemic response
HbA _{1c}	hemoglobin A _{1c}
HDL	high density lipoprotein
kcal	kilocalories
LDL	low density lipoprotein
MCI	mild cognitive impairment
MEOS	microsomal ethanol oxidizing system
MetS	metabolic syndrome
WHO	World Health Organization

COLOPHON

Publisher and author: Kennisinstituut Bier (*The Dutch Beer Institute*),
Wageningen, the Netherlands

Copy editor: Nick Pasiecznik, Cussy en Morvan, France

Design: Studio Lakmoes, Arnhem, the Netherlands

Photos:

Bart Maat (*Frans Kok and Arne Astrup*)

Israel De Lago (*Ascension Marcos*)

Alejandro Caparrós (*Ramon Estruch*)

Kennisinstituut Bier

Nederlandse Brouwers

The Brewers of Europe

Production of this booklet was supported by The Brewers of Europe.

More activities on beer and health can be found at **www.beerandhealth.eu**.

© 2016 Kennisinstituut Bier

www.kennisinstituutbier.nl

REFERENCES

1. Mäkelä P, Gmel G, Grittner U et al. (2006). Drinking patterns and their gender differences in Europe. *Alcohol Alcohol Suppl*, 41(1):i8-18.
2. Gordon R, Heim D, and MacAskill S (2012). Rethinking drinking cultures: A review of drinking cultures and a reconstructed dimensional approach. *Public Health*, 126(1):3-11.
3. Popova S, Rehm J, Patra J et al. (2007). Comparing alcohol consumption in central and eastern Europe to other European countries. *Alcohol Alcohol*, 42(5):465-473.
4. Hughes K, Quigg Z, Bellis MA et al. (2011). Drinking behaviours and blood alcohol concentration in four European drinking environments: a cross-sectional study. *BMC Public Health*, 11:918.
5. Heath DB (1995). An anthropological view of alcohol and culture in international perspective. In *International handbook on alcohol and culture*. Greenwood Pub Group, pp328-347.
6. Roerecke M, and Rehm J (2014). Alcohol consumption, drinking patterns, and ischemic heart disease: a narrative review of meta-analyses and a systematic review and meta-analysis of the impact of heavy drinking occasions on risk for moderate drinkers. *BMC Med*, 12(1):182.
7. Jackson KM (2008). Heavy episodic drinking: determining the predictive utility of five or more drinks. *Psychol Addict Behav*, 22(1):68-77.
8. Mukamal KJ, Jensen MK, Grønbaek M et al. (2005). Drinking frequency, mediating biomarkers, and risk of myocardial infarction in women and men. *Circulation*, 112(10):1406-1413.
9. Mukamal KJ, Maclure M, Muller JE et al. (2005). Binge drinking and mortality after acute myocardial infarction. *Circulation*, 112(25):3839-3845.
10. Roerecke M, and Rehm J (2010). Irregular heavy drinking occasions and risk of ischemic heart disease: a systematic review and meta-analysis. *Am J Epidemiol*, 171(6):633-644.
11. Poli A, Marangoni F, Avogaro A et al. (2013). Moderate alcohol use and health: a consensus document. *Nutr Met Cardiovasc Dis*, 23(6):487-504.
12. Goñi I, Díaz-Rubio ME, and Saura-Calixto F (2009). Dietary fiber in beer: content, composition, colonic fermentability, and contribution to the diet. In *Beer in Health and Disease prevention*, pp299-307.
13. Jugdaohsingh R (2007). Silicon and bone health. *J Nutr Health Aging*, 11(2):99.
14. Dietary reference values and dietary guidelines [Internet]. Cited 26 Oct 2015. Retrieved from: <http://www.efsa.europa.eu/en/topics/topic/drv>
15. Nutrient requirements - British Nutrition Foundation [Internet]. Cited 26 Oct 2015. Retrieved from: www.nutrition.org.uk/nutritionscience/nutrients/nutrient-requirements.html
16. DRI Tables and Application Reports [Internet]. Cited 26 Oct 2015. Retrieved from: <https://fnic.nal.usda.gov/dietary-guidance/dietary-reference-intakes/dri-tables-and-application-reports>
17. van der Gaag MS, Ubbink JB, Sillanauke P et al. (2000). Effect of consumption of red wine, spirits, and beer on serum homocysteine. *Lancet*,

355(9214):1522.

18. Romeo J, Díaz L, González-Gross M et al. (2006). Contribución a la ingesta de macro y micronutrientes que ejerce un consumo moderado de cerveza. *Nutrición Hospitalaria*, 21(1):84-91.
19. Mayer O, Simon J, and Rosolová H (2001). A population study of the influence of beer consumption on folate and homocysteine concentrations. *Eur J Clin Nutr*, 55(7):605-609.
20. Owens JE, Clifford AJ, and Bamforth CW (2007). Folate in beer. *J Inst Brew*, 113(3):243-248.
21. Clarke R, Halsey J, Lewington S et al. (2010). Effects of lowering homocysteine levels with B vitamins on cardiovascular disease, cancer, and cause-specific mortality: meta-analysis of 8 randomized trials involving 37 485 individuals. *Arch Med Res*, 170(18):1622-1631.
22. Clarke R, Bennett D, Parish S et al. (2014). Effects of homocysteine lowering with B vitamins on cognitive aging: meta-analysis of 11 trials with cognitive data on 22,000 individuals. *Am J Clin Nutr*, 100(2):657-666.
23. Sohrabvandi S, Mortazavian AM, and Rezaei K (2012). Health-related aspects of beer: a review. *Int J Food Prop*, 15(2):350-373.
24. Montanari L, Mayer H, Marconi O, Fantozzi P, and Preedy VR (2009). Minerals in beer. In *Beer in Health and Disease Prevention*, pp359-365.
25. Jurkić LM, Cepanec I, Pavelić SK et al. (2013). Biological and therapeutic effects of ortho-silicic acid and some ortho-silicic acid-releasing compounds: New perspectives for therapy. *Nutr Metab*, 10(1):2.
26. Casey TR, and Bamforth CW (2010). Silicon in beer and brewing. *J Sci Food Agric*, 90(5):784-788.
27. Sripanyakorn S, Jugdaohsingh R, Elliott H et al. (2004). The silicon content of beer and its bioavailability in healthy volunteers. *Br J Nutr*, 91(3):403-409.
28. Jugdaohsingh R, Tucker KL, Qiao N et al. (2004). Dietary silicon intake is positively associated with bone mineral density in men and premenopausal women of the Framingham Offspring cohort. *J Bone Miner Res*, 19(2):297-307.
29. Bamforth CW (2002). Nutritional aspects of beer a review. *Nutr Research*, 22(1):227-237.
30. Pandey KB, and Rizvi SI (2009). Plant polyphenols as dietary antioxidants in human health and disease. *Oxid Med Cell Longev*, 2(5):270-278.
31. Suter PM (2001). Alcohol and mortality: if you drink, do not forget fruits and vegetables. *Nutr Rev*, 59(9):293-297.
32. Arranz S, Chiva-Blanch G, Valderas-Martínez P et al. (2012). Wine, beer, alcohol and polyphenols on cardiovascular disease and cancer. *Nutrients*, 4(7):759-781.
33. Chiva-Blanch G, Arranz S, Lamuela-Raventos RM et al. (2013). Effects of wine, alcohol and polyphenols on cardiovascular disease risk factors: evidences from human studies. *Alcohol Alcohol*, 48(3):270-277.
34. Scientific opinion on the substantiation of a health claim related to barley beta-glucans and lowering of blood cholesterol and reduced risk of (coronary) heart disease pursuant to Article 14 of Regulation (EC) No 1924/2006 [Internet]. Retrieved from: www.efsa.europa.eu/sites/default/files/scientific_output/files/main_documents/2471.pdf
35. Mustalhti K, Catassi C, Reunanen A et al. (2010). The prevalence of celiac disease in Europe: results of a centralized, international mass

- screening project. *Ann Med*, 42(8):587-595.
36. Tanner GJ, Colgrave ML, Blundell MJ et al. (2013). Measuring hordein (gluten) in beer - a comparison of ELISA and mass spectrometry. *PLoS One*, 8(2):e56452.
37. Gluten Free Diet [Internet]. Cited Jul 2015. Retrieved from: www.aoecs.org/?q=gluten-free-diet
38. Hager A-S, Taylor JP, Waters DM et al. (2014). Gluten free beer - A review. *Trends Food Sci Technol*, 36(1):44-54.
39. Mitchell MC, Teigen EL, and Ramchandani VA (2014). Absorption and peak blood alcohol concentration after drinking beer, wine, or spirits. *Alcohol Clin Exp Res*, 38(5):1200-1204.
40. Roine RP, Gentry RT, Lim RT et al. (1993). Comparison of blood alcohol concentrations after beer and whiskey. *Alcohol Clin Exp Res*, 17(3):709-711.
41. Bendsen NT, Christensen R, Bartels EM et al. (2013). Is beer consumption related to measures of abdominal and general obesity? A systematic review and meta-analysis. *Nutr Rev*, 71(2):67-87.
42. Berghöfer A, Pischon T, Reinhold T et al. (2008). Obesity prevalence from a European perspective: a systematic review. *BMC Public Health*, 8:200.
43. EC | Overweight and obesity - BMI statistics - Statistics Explained [Internet]. Cited 29 Sep 2015. Retrieved from: http://ec.europa.eu/eurostat/statistics-explained/index.php/Overweight_and_obesity_-_BMI_statistics
44. Swinburn BA, Sacks G, Hall KD et al. (2011). The global obesity pandemic: shaped by global drivers and local environments. *Lancet*, 378(9793):804-814.
45. Mokdad AH, Ford ES, Bowman BA et al. (2003). Prevalence of obesity, diabetes, and obesity-related health risk factors, 2001. *JAMA*, 289(1):76-79.
46. Canoy D, Boekholdt SM, Wareham N et al. (2007). Body fat distribution and risk of coronary heart disease in men and women in the European Prospective Investigation Into Cancer and Nutrition in Norfolk cohort: a population-based prospective study. *Circulation*, 116(25):2933-2943.
47. Pischon T, Nöthlings U, and Boeing H (2008). Obesity and cancer. *Proc Nutr Soc*, 67(2):128-145.
48. Pischon T, Boeing H, Hoffmann K et al. (2008). General and abdominal adiposity and risk of death in Europe. *N Engl J Med*, 359(20):2105-2120.
49. Whitlock G, Lewington S, Sherliker P et al. (2009). Body-mass index and cause-specific mortality in 900 000 adults: collaborative analyses of 57 prospective studies. *Lancet*, 373(9669):1083-1096.
50. Bijlsma JW, Berenbaum F, and Lafeber FP (2011). Osteoarthritis: an update with relevance for clinical practice. *Lancet*, 377(9783):2115-2126.
51. Bradshaw T, and Mairs H (2014). Obesity and serious mental ill health: A critical review of the literature. *Healthcare*, 2(2):166-182.
52. Buiatti S (2009). Beer composition: an overview. In *Beer in health and disease prevention*, pp213-226.
53. Buemann B, and Astrup A (2001). How does the body deal with energy from alcohol? *Nutrition*, 17(7-8):638-641.
54. Traversy G, and Chaput J-P (2015). Alcohol consumption and obesity: an update. *Curr Obes Rep*, 4(1):122-130.

55. Ferreira MPLVO (2009). Beer Carbohydrates. In *Beer in Health and Disease Prevention*, pp291-298.
56. Yeomans MR (2010). Alcohol, appetite and energy balance: is alcohol intake a risk factor for obesity? *Physiology and Behavior*, 100(1):82-89.
57. Schrieks IC, Stafleu A, Griffioen-Roose S et al. (2015). Moderate alcohol consumption stimulates food intake and food reward of savoury foods. *Appetite*, 89:77-83.
58. Sayon-Orea C, Martinez-Gonzalez MA, and Bes-Rastrollo M (2011). Alcohol consumption and body weight: a systematic review. *Nutr Rev*, 69(8):419-431.
59. Dumesnil C, Dauchet L, Ruidavets JB et al. (2013). Alcohol consumption patterns and body weight. *Ann Nutr Metab*, 62(2):91-97.
60. Arif AA, and Rohrer JE (2005). Patterns of alcohol drinking and its association with obesity: data from the Third National Health and Nutrition Examination Survey, 1988-1994. *BMC Public Health*, 5(1):126.
61. Breslow RA, and Smothers BA (2005). Drinking patterns and body mass index in never smokers: National Health Interview Survey, 1997-2001. *Am J Epidemiol*, 161(4):368-376.
62. Tolstrup JS, Heitmann BL, Tjønneland AM et al. (2005). The relation between drinking pattern and body mass index and waist and hip circumference. *Int J Obes*, 29(5):490-497.
63. Thomson CA, Wertheim BC, Hingle M et al. (2012). Alcohol consumption and body weight change in postmenopausal women: results from the Women's Health Initiative. *Int J Obes*, 36(9):1158-1164.
64. Colditz GA, Giovannucci E, Rimm EB et al. (1991). Alcohol intake in relation to diet and obesity in women and men. *Am J Clin Nutr*, 54(1):49-55.
65. Liu S, Serdula MK, Williamson DF et al. (1994). A prospective study of alcohol intake and change in body weight among US adults. *Am J Epidemiol*, 140(10):912-920.
66. Lahti-Koski M, Pietinen P, Heliövaara M et al. (2002). Associations of body mass index and obesity with physical activity, food choices, alcohol intake, and smoking in the 1982-1997 FINRISK Studies. *Am J Clin Nutr*, 75(5):809-817.
67. Wannamethee SG, Field AE, Colditz GA et al. (2004). Alcohol intake and 8-year weight gain in women: a prospective study. *Obes Res*, 12(9):1386-1396.
68. Barry D, and Petry NM (2009). Associations between body mass index and substance use disorders differ by gender: results from the National Epidemiologic Survey on Alcohol and Related Conditions. *Addict Behav*, 34(1):51-60.
69. Wang L, Lee IM, Manson JE et al. (2010). Alcohol consumption, weight gain, and risk of becoming overweight in middle-aged and older women. *Arch Intern Med*, 170(5):453-461.
70. Mozaffarian D, Hao T, Rimm EB et al. (2011). Changes in diet and lifestyle and long-term weight gain in women and men. *N Engl J Med*, 364(25):2392-2404.
71. Buemann B, Toubro S, and Astrup A (2002). The effect of wine or beer versus a carbonated soft drink, served at a meal, on ad libitum energy intake. *Int J Obes Relat Metab Disord*, 26(10):1367-1372.
72. McCann SE, Sempas C, Freudenheim JL et al. (2003). Alcoholic beverage preference and characteristics of drinkers and nondrinkers in western

- New York (United States). *Nutr Metab Cardiovasc Dis*, 13(1):2-11.
73. Ruidavets J-B, Bataille V, Dallongeville J et al. (2004). Alcohol intake and diet in France, the prominent role of lifestyle. *Eur Heart J*, 25(13):1153-1162.
74. Johansen D, Friis K, Skovenborg E et al. (2006). Food buying habits of people who buy wine or beer: cross sectional study. *BMJ*, 332(7540):519-522.
75. Djoussé L, Arnett DK, Eckfeldt JH et al. (2004). Alcohol consumption and metabolic syndrome: does the type of beverage matter? *Obes Res*, 12(9):1375-1385.
76. Paschall M, and Lipton RI (2005). Wine preference and related health determinants in a U.S. national sample of young adults. *Drug Alcohol Depend*, 78(3):339-344.
77. O'Neill S, and O'Driscoll L (2015). Metabolic syndrome: a closer look at the growing epidemic and its associated pathologies. *Obes Rev*, 16(1):1-12.
78. EUFIC | The Metabolic Syndrome epidemic [Internet]. Cited 21 Sep 2015. Retrieved from: www.eufic.org/article/en/diet-related-diseases/diabetes/artid/metabolic-syndrome-epidemic/
79. Alkerwi A, Boutsen M, Vaillant M et al. (2009). Alcohol consumption and the prevalence of metabolic syndrome: a meta-analysis of observational studies. *Atherosclerosis*, 204(2):624-635.
80. Sun K, Ren M, Liu D et al. (2014). Alcohol consumption and risk of metabolic syndrome: a meta-analysis of prospective studies. *Clin Nutr*, 33(4):596-602.
81. Cederbaum AI (2012). Alcohol metabolism. *Clin Liver Dis*, 16(4):667-685.
82. Whitney E, and Rolfes SR (2008). Alcohol and Nutrition. In *Understanding Nutrition*. Eleventh. Thomson Wadsworth, pp242-243.
83. Lieber CS (2004). The discovery of the microsomal ethanol oxidizing system and its physiologic and pathologic role. *Drug Metab Rev*, 36(3-4):511-529.
84. Suter PM, Schutz Y, and Jequier E (1992). The effect of ethanol on fat storage in healthy subjects. *N Engl J Med*, 326(15):983-987.
85. Raben A, Agerholm-Larsen L, Flint A et al. (2003). Meals with similar energy densities but rich in protein, fat, carbohydrate, or alcohol have different effects on energy expenditure and substrate metabolism but not on appetite and energy intake. *Am J Clin Nutr*, 77(1):91-100.
86. Sluik D, Bezemer R, Sierksma A et al. (2015). Alcoholic beverage preference and dietary habits: a systematic literature review. *Crit Rev Food Sci Nutr*, Epub.
87. Maughan RJ (2006). Alcohol and football. *J Sports Sci*, 24(7):741-748.
88. Shirreffs SM, and Maughan RJ (1997). Restoration of fluid balance after exercise-induced dehydration: effects of alcohol consumption. *J Appl Physiol*, 83(4):1152-1158.
89. Hobson RM, and Maughan RJ (2010). Hydration status and the diuretic action of a small dose of alcohol. *Alcohol Alcohol*, 45(4):366-373.
90. Desbrow B, Murray D, and Leveritt M (2013). Beer as a sports drink? Manipulating beers ingredients to replace lost fluid. *Int J Sport Nutr Exerc Metab*, 23(6):593-600.
91. Jiménez-Pavón D, Cervantes-Borunda MS, Díaz LE et al. (2015). Effects

- of a moderate intake of beer on markers of hydration after exercise in the heat: a crossover study. *J Int Soc Sports Nutr*, 12:26.
92. Hastrup MB, Pottegård A, and Damkier P (2014). Alcohol and breast-feeding. *Basic Clin Pharmacol Toxicol*, 114(2):168-173.
 93. Koletzko B, and Lehner F (2000). Beer and breastfeeding. *Adv Exp Med Biol*, 478:23-28.
 94. Codoñer-Franch P, Hernández-Aguilar MT, Navarro-Ruiz A et al. (2013). Diet supplementation during early lactation with non-alcoholic beer increases the antioxidant properties of breastmilk and decreases the oxidative damage in breastfeeding mothers. *Breastfeed Med*, 8:164-169.
 95. Franco L, Sánchez C, Bravo R et al. (2012). The sedative effect of non-alcoholic beer in healthy female nurses. *PLoS One*, 7(7):e37290.
 96. Franco L, Bravo R, Galán C et al. (2014). Effect of non-alcoholic beer on Subjective Sleep Quality in a university stressed population. *Acta Physiol Hung*, 101(3):353-361.
 97. Franco L, Galán C, Bravo R et al. (2015). Effect of non-alcohol beer on anxiety: Relationship of 5-HIAA. *Neurochem J*, 9(2):149-152.
 98. Chiva-Blanch G, Condines X, Magraner E et al. (2014). The non-alcoholic fraction of beer increases stromal cell derived factor 1 and the number of circulating endothelial progenitor cells in high cardiovascular risk subjects: a randomized clinical trial. *Atherosclerosis*, 233(2):518-524.
 99. Chiva-Blanch G, Magraner E, Condines X et al. (2015). Effects of alcohol and polyphenols from beer on atherosclerotic biomarkers in high cardiovascular risk men: a randomized feeding trial. *Nutr Metab Cardiovasc Dis*, 25(1):36-45.
 100. O'Leary CM, and Bower C (2012). Guidelines for pregnancy: what's an acceptable risk, and how is the evidence (finally) shaping up? *Drug Alcohol Rev*, 31(2):170-183.
 101. Regulation (EC) No 1924/2006 of the European Parliament and of the Council of 20 December 2006 on nutrition and health claims made on foods. *OJ L*, 404:9-25.
 102. Nichols M, Townsend N, Scarborough P et al. (2014). Cardiovascular disease in Europe 2014: epidemiological update. *Eur Heart J*, 35(42):2929.
 103. Ronsley PE, Brien SE, Turner BJ et al. (2011). Association of alcohol consumption with selected cardiovascular disease outcomes: a systematic review and meta-analysis. *BMJ*, 342:d671.
 104. Manson JE, Tosteson H, Ridker PM et al. (1992). The primary prevention of myocardial infarction. *N Engl J Med*, 326(21):1406-1416.
 105. Pedersen JØ, Heitmann BL, Schnohr P et al. (2008). The combined influence of leisure-time physical activity and weekly alcohol intake on fatal ischaemic heart disease and all-cause mortality. *Eur Heart J*, 29(2):204-212.
 106. Corrao G, Rubbiati L, Bagnardi V et al. (2000). Alcohol and coronary heart disease: a meta-analysis. *Addiction*, 95(10):1505-1523.
 107. Mukamal KJ, Chiuve SE, and Rimm EB (2006). Alcohol consumption and risk for coronary heart disease in men with healthy lifestyles. *Arch Intern Med*, 166(19):2145-2150.
 108. Patra J, Taylor B, Irving H et al. (2010). Alcohol consumption and the risk of morbidity and mortality for different stroke types - a systematic review and meta-analysis. *BMC Public Health*, 10:258.
 109. King DE, Mainous AG, and Geesey ME (2008). Adopting moderate alco-

hol consumption in middle age: subsequent cardiovascular events. *Am J Med*, 121(3):201-206.

110. Mukamal KJ, Conigrave KM, Mittleman MA et al. (2003). Roles of drinking pattern and type of alcohol consumed in coronary heart disease in men. *N Engl J Med*, 348(2):109-118.
111. Sesso HD, Stampfer MJ, Rosner B et al. (2000). Seven-year changes in alcohol consumption and subsequent risk of cardiovascular disease in men. *Arch Intern Med*, 160(17):2605-2612.
112. Briassoulis A, Agarwal V, and Messerli FH (2012). Alcohol consumption and the risk of hypertension in men and women: a systematic review and meta-analysis. *J Clin Hypertens*, 14(11):792-798.
113. Urbano-Marquez A, Estruch R, Navarro-Lopez F et al. (1989). The effects of alcoholism on skeletal and cardiac muscle. *N Engl J Med*, 320(7):409-415.
114. Conen D, Tedrow UB, Cook NR et al. (2008). Alcohol consumption and risk of incident atrial fibrillation in women. *JAMA*, 300(21):2489-2496.
115. Mukamal KJ, Tolstrup JS, Friberg J et al. (2005). Alcohol consumption and risk of atrial fibrillation in men and women: the Copenhagen City Heart Study. *Circulation*, 112(12):1736-1742.
116. Rimm EB, Williams P, Fosher K et al. (1999). Moderate alcohol intake and lower risk of coronary heart disease: meta-analysis of effects on lipids and haemostatic factors. *BMJ*, 319(7224):1523-1528.
117. Rader DJ, Alexander ET, Weibel GL et al. (2009). The role of reverse cholesterol transport in animals and humans and relationship to atherosclerosis. *J Lipid Res*, 50 Suppl:S189-S194.
118. Sierksma A, Vermunt SH, Lankhuizen IM et al. (2004). Effect of moderate alcohol consumption on parameters of reverse cholesterol transport in postmenopausal women. *Alcohol Clin Exp Res*, 28(4):662-626.
119. Brinton EA (2010). Effects of ethanol intake on lipoproteins and atherosclerosis. *Curr Opin Lipidol*, 21(4):346-351.
120. van der Gaag MS, van Tol A, Scheek LM et al. (1999). Daily moderate alcohol consumption increases serum paraoxonase activity; a diet-controlled, randomised intervention study in middle-aged men. *Atherosclerosis*, 147(2):405-410.
121. Brien SE, Ronksley PE, Turner BJ et al. (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:d636.
122. Imhof A, Froehlich M, Brenner H et al. (2001). Effect of alcohol consumption on systemic markers of inflammation. *Lancet*, 357(9258):763-767.
123. Sierksma A, van der Gaag MS, Kluit C et al. (2002). Moderate alcohol consumption reduces plasma C-reactive protein and fibrinogen levels; a randomized, diet-controlled intervention study. *Eur J Clin Nutr*, 56(11):1130-1136.
124. Estruch R, Sacanella E, Badia E et al. (2004). Different effects of red wine and gin consumption on inflammatory biomarkers of atherosclerosis: a prospective randomized crossover trial. Effects of wine on inflammatory markers. *Atherosclerosis*, 175(1):117-123.
125. Huang C, Zhan J, Liu YJ et al. (2014). Association between alcohol consumption and risk of cardiovascular disease and all-cause mortality in patients with hypertension: a meta-analysis of prospective cohort

- studies. *Mayo Clin Proc*, 89(9):1201-1210.
126. Muntwyler J, Hennekens CH, Buring JE et al. (1998). Mortality and light to moderate alcohol consumption after myocardial infarction. *Lancet*, 352(9144):1882-1885.
 127. Niroomand F, Hauer O, Tiefenbacher CP et al. (2004). Influence of alcohol consumption on restenosis rate after percutaneous transluminal coronary angioplasty and stent implantation. *Heart*, 90(10):1189-1193.
 128. Heidrich J, Wellmann J, Döring A et al. (2007). Alcohol consumption, alcohol dehydrogenase and risk of coronary heart disease in the MON-ICA/KORA-Augsburg cohort 1994/1995-2002. *Eur J Cardiovasc Prev Rehabil*, 14(6):769-774.
 129. Tolstrup JS, Grønbaek M, and Nordestgaard BG (2009). Alcohol intake, myocardial infarction, biochemical risk factors, and alcohol dehydrogenase genotypes. *Circ Cardiovasc Genet*, 2(5):507-514.
 130. Holmes MV, Dale CE, Zuccolo L et al. (2014). Association between alcohol and cardiovascular disease: Mendelian randomisation analysis based on individual participant data. *BMJ*, 349:g4164.
 131. Israel Y. Response: Association between alcohol and cardiovascular disease: Mendelian randomisation analysis based on individual participant data [Internet]. Retrieved from: www.bmj.com/content/349/bmj.g4164/rr/763820
 132. Edenberg HJ (2007). The genetics of alcohol metabolism: role of alcohol dehydrogenase and aldehyde dehydrogenase variants. *Alcohol Res Health*, 30(1):5-13.
 133. Galkina E, and Ley K (2009). Immune and inflammatory mechanisms of atherosclerosis. *Annu Rev Immunol*, 27:165-197.
 134. Finn AV, Nakano M, Narula J et al. (2010). Concept of vulnerable/unstable plaque. *Arterioscler Thromb Vasc Biol*, 30(7):1282-1292.
 135. World Heart Federation | Cardiovascular disease risk factors [Internet]. Cited Apr 2015. Retrieved from: www.world-heart-federation.org/press/fact-sheets/cardiovascular-disease-risk-factors/
 136. Renaud S, and de Lorgeril M (1992). Wine, alcohol, platelets, and the French paradox for coronary heart disease. *Lancet*, 339(8808):1523-1526.
 137. Costanzo S, Di Castelnuovo A, Donati MB et al. (2011). Wine, beer or spirit drinking in relation to fatal and non-fatal cardiovascular events: a meta-analysis. *Eur J Epidemiol*, 26(11):833-850.
 138. Chiva-Blanch G, Urpi-Sarda M, Llorach R et al. (2012). Differential effects of polyphenols and alcohol of red wine on the expression of adhesion molecules and inflammatory cytokines related to atherosclerosis: a randomized clinical trial. *Am J Clin Nutr*, 95(2):326-334.
 139. Chiva-Blanch G, Condines X, Magraner E et al. (2014). The non-alcoholic fraction of beer increases stromal cell derived factor 1 and the number of circulating endothelial progenitor cells in high cardiovascular risk subjects: a randomized clinical trial. *Atherosclerosis*, 233(2):518-524.
 140. Chiva-Blanch G, Magraner E, Condines X et al. (2015). Effects of alcohol and polyphenols from beer on atherosclerotic biomarkers in high cardiovascular risk men: A randomized feeding trial. *Nutr Metab Cardiovasc Dis*, 25(1):36-45.
 141. Stamler J (2005). Established major risk factors: historical overview. In *Coronary heart disease epidemiology - from aetiology to public health*.

2. Oxford Scholarship, pp18-31.
142. van den Elzen AP, Sierksma A, Oren A et al. (2005). Alcohol intake and aortic stiffness in young men and women. *J Hypertens*, 23(4):731-735.
143. Hvidtfeldt UA, Tolstrup JS, Jakobsen MU et al. (2010). Alcohol intake and risk of coronary heart disease in younger, middle-aged, and older adults. *Circulation*, 121(14):1589-1597.
144. Okwuosa TM, Klein O, Chan C et al. (2013). Long-term change in alcohol-consumption status and variations in fibrinogen levels: the coronary artery risk development in young adults (CARDIA) study. *BMJ Open*, 3(7). Epub.
145. WHO Europe | Diabetes [Internet]. Cited Aug 2015. Retrieved from: www.euro.who.int/en/health-topics/noncommunicable-diseases/diabetes/diabetes
146. Tamayo T, Rosenbauer J, Wild SH et al. (2014). Diabetes in Europe: an update. *Diabetes Res Clin Pract*, 103(2):206-217.
147. Hu FB, Manson JE, Stampfer MJ et al. (2001). Lifestyle, and the risk of type 2 diabetes mellitus in women. *N Engl J Med*, 345(11):790-797.
148. Gray SP, and Jandeleit-Dahm K. (2014). The pathobiology of diabetic vascular complications – cardiovascular and kidney disease. *J Mol Med*, 92(5):441-452.
149. Koppes LL, Dekker JM, Hendriks HF et al. (2005). Moderate alcohol consumption lowers the risk of type 2 diabetes: a meta-analysis of prospective observational studies. *Diabetes Care*, 28(3):719-725.
150. Baliunas DO, Taylor BJ, Irving H et al. (2009). Alcohol as a risk factor for type 2 diabetes: A systematic review and meta-analysis. *Diabetes Care*, 32(11):2123-2132.
151. Beulens JW, van der Schouw YT, Bergmann MM et al. (2012). Alcohol consumption and risk of type 2 diabetes in European men and women: influence of beverage type and body size: The EPIC-InterAct study. *J Intern Med*, 272(4):358-370.
152. Knott C, Bell S and Britton A (2015). Alcohol consumption and the risk of type 2 diabetes: A systematic review and dose-response meta-analysis of more than 1.9 million individuals from 38 observational studies. *Diabetes Care*, 38(9):1804-1812.
153. Mumenthaler MS, Taylor JL, O'Hara R et al. (1999). Gender differences in moderate drinking effects. *Alcohol Res Health*, 23(1):55-64.
154. Sieri S, Agudo A, Kesse E et al. (2002). Patterns of alcohol consumption in 10 European countries participating in the European Prospective Investigation into Cancer and Nutrition (EPIC) project. *Public Health Nutr*, 5(6B):1287-1296.
155. Joosten MM, Chiuve SE, Mukamal KJ et al. (2011). Changes in alcohol consumption and subsequent risk of type 2 diabetes in men. *Diabetes*, 60(1):74-79.
156. Joosten MM, Grobbee DE, van der A DL et al. (2010). Combined effect of alcohol consumption and lifestyle behaviors on risk of type 2 diabetes. *Am J Clin Nutr*, 91(6):1777-1783.
157. Beulens JW, Rimm EB, Hu FB et al. (2008). Alcohol consumption, mediating biomarkers, and risk of type 2 diabetes among middle-aged women. *Diabetes Care*, 31(10):2050-2055.
158. Snijder MB, Heine RJ, Seidell JC et al. (2006). Associations of adiponectin levels with incident impaired glucose metabolism and type 2 diabetes

- in older men and women: the hoorn study. *Diabetes Care*, 29(11):2498-2503.
159. Li S, Shin HJ, Ding EL et al. (2009). Adiponectin levels and risk of type 2 diabetes: a systematic review and meta-analysis. *JAMA*, 302(2):179-188.
 160. Hung J, McQuillan BM, Thompson PL et al. (2008). Circulating adiponectin levels associate with inflammatory markers, insulin resistance and metabolic syndrome independent of obesity. *Int J Obes*, 32(5):772-779.
 161. Turer AT, Khera A, Ayers CR et al. (2011). Adipose tissue mass and location affect circulating adiponectin levels. *Diabetologia*, 54(10):2515-2524.
 162. Schrieke IC, Heil AL, Hendriks HF et al. (2015). The effect of alcohol consumption on insulin sensitivity and glycemic status: a systematic review and meta-analysis of intervention studies. *Diabetes Care*, 38(4):723-732.
 163. Siler SQ, Neese RA, and Hellerstein MK (1999). De novo lipogenesis, lipid kinetics, and whole-body lipid balances in humans after acute alcohol consumption. *Am J Clin Nutr*, 70(5):928-936.
 164. Avogaro A, Watanabe RM, Gottardo L et al. (2002). Glucose tolerance during moderate alcohol intake: insights on insulin action from glucose/lactate dynamics. *J Clin Endocrinol Metab*, 87(3):1233-1238.
 165. Kraegen EW, and Cooney GJ (2008). Free fatty acids and skeletal muscle insulin resistance. *Curr Opin Lipidol*, 19(3):235-241.
 166. Hendriks HF (2007). Moderate alcohol consumption and insulin sensitivity: observations and possible mechanisms. *Ann Epidemiol*, 17(5):S40-S42.
 167. Romeo J, Wärnberg J et al. (2007). Moderate alcohol consumption and the immune system: a review. *Br J Nutr*, 98(S1):S111-S115.
 168. Wang X, Bao W, Liu J et al. (2013). Inflammatory markers and risk of type 2 diabetes: a systematic review and meta-analysis. *Diabetes Care*, 36(1):166-175.
 169. Turner BC, Jenkins E, Kerr D et al. (2001). The effect of evening alcohol consumption on next-morning glucose control in type 1 diabetes. *Diabetes Care*, 24(11):1888-1893.
 170. Howard AA, Arnsten JH, and Gourevitch MN (2004). Effect of alcohol consumption on diabetes mellitus: a systematic review. *Ann Intern Med*, 140(3):211-219.
 171. Zhang PY (2014). Cardiovascular disease in diabetes. *Eur Rev Med Pharmacol Sci*, 18(15):2205-2214.
 172. Koppes LL, Dekker JM, Hendriks HF et al. (2006). Meta-analysis of the relationship between alcohol consumption and coronary heart disease and mortality in type 2 diabetic patients. *Diabetologia*, 49(4):648-652.
 173. Beulens JW, Algra A, Soedamah-Muthu SS et al. (2010). Alcohol consumption and risk of recurrent cardiovascular events and mortality in patients with clinically manifest vascular disease and diabetes mellitus: the Second Manifestations of ARterial (SMART) disease study. *Atherosclerosis*, 212(1):281-286.
 174. Beulens JW, Kruidhof JS, Grobbee DE et al. (2008). Alcohol consumption and risk of microvascular complications in type 1 diabetes patients: the EURODIAB Prospective Complications Study. *Diabetologia*, 51(9):1631-1638.

175. Wannamethee SG, Shaper AG, and Alberti KG (2000). Physical activity, metabolic factors, and the incidence of coronary heart disease and type 2 diabetes. *Arch Intern Med*, 160(14):2108-2116.
176. WHO Europe | Diabetes - Data and statistics [Internet]. Cited 21 Sep 2015. Retrieved from: www.euro.who.int/en/health-topics/noncommunicable-diseases/diabetes/data-and-statistics
177. Augustin LS, Kendall CW, Jenkins DJ et al. (2015). Glycemic index, glycemic load and glycemic response: An International Scientific Consensus Summit from the International Carbohydrate Quality Consortium (ICQC). *Nutr Metab Cardiovasc Dis*, 25(9):795-815.
178. Hätönen KA, Virtamo J, Eriksson JG et al. (2012). Modifying effects of alcohol on the postprandial glucose and insulin responses in healthy subjects. *Am J Clin Nutr*, 96(1):44-49.
179. Sluik D, Atkinson F, Brand-Miller J et al. (2016). Contributors to dietary glycaemic index and glycaemic load in the Netherlands: the role of beer. *Br J Nutr*, Epub.
180. Glycemic Index [Internet]. Cited 21 Sep 2015. Retrieved from: www.glycemicindex.com/
181. Bhupathiraju SN, Tobias DK, Malik VS et al. (2014). Glycemic index, glycemic load, and risk of type 2 diabetes: results from 3 large US cohorts and an updated meta-analysis. *Am J Clin Nutr*, 100(1):218-232.
182. Brand-Miller JC, Fatema K, Fatima K et al. (2007). Effect of alcoholic beverages on postprandial glycemia and insulinemia in lean, young, healthy adults. *Am J Clin Nutr*, 85(6):1545-1551.
183. Mann JI, De Leeuw I, Hermansen K et al. (2004). Evidence-based nutritional approaches to the treatment and prevention of diabetes mellitus. *Nutr Metab Cardiovasc Dis*, 14(6):373-394.
184. Steliarova-Foucher E, O'Callaghan M, Ferlay J et al. (2015). The European Cancer Observatory: A new data resource. *Eur J Cancer*, 51(9):1131-1143.
185. WHO Europe | Cancer - Data and statistics [Internet]. Cited May 2015. Retrieved from: www.euro.who.int/en/health-topics/noncommunicable-diseases/cancer/data-and-statistics
186. Cancer incidence and mortality in Europe [Internet]. Cited Jul 2015. Retrieved from: <http://eu-cancer.iarc.fr/EUCAN/Country.aspx?ISOCountryCd=968#block-pie-a>
187. Anand P, Kunnumakkara AB, Kunnumakara AB et al. (2008). Cancer is a preventable disease that requires major lifestyle changes. *Pharm Res*, 25(9):2097-2116.
188. Schüz J, Espina C, Villain P et al. (2015). European Code against Cancer 4th edition: 12 ways to reduce your cancer risk. *Cancer Epidemiol*, Epub.
189. Schütze M, Boeing H, Pischon T et al. (2011). Alcohol attributable burden of incidence of cancer in eight European countries based on results from prospective cohort study. *BMJ*, 342:d1584.
190. Scoccianti C, Cecchini M, Anderson AS et al. (2015). European Code against Cancer 4th Edition: Alcohol drinking and cancer. *Cancer Epidemiol*, Epub.
191. Smith-Warner SA, Spiegelman D, Yaun SS et al. (1998). Alcohol and breast cancer in women: a pooled analysis of cohort studies. *JAMA*, 279(7):535-540.
192. Hamajima N, Hirose K, Tajima K et al. (2002). Alcohol, tobacco and

- breast cancer--collaborative reanalysis of individual data from 53 epidemiological studies, including 58,515 women with breast cancer and 95,067 women without the disease. *Br J Cancer*, 87(11):1234-1245.
193. Tjønneland A, Christensen J, Olsen A et al. (2007). Alcohol intake and breast cancer risk: the European Prospective Investigation into Cancer and Nutrition (EPIC). *Cancer Causes Control*, 18(4):361-373.
 194. Seitz HK, Pelucchi C, Bagnardi V et al. (2012). Epidemiology and pathophysiology of alcohol and breast cancer: Update 2012. *Alcohol Alcohol*, 47(3):204-212.
 195. Bagnardi V, Rota M, Botteri E et al. (2013). Light alcohol drinking and cancer: a meta-analysis. *Ann Oncol*, 24(2):301-308.
 196. Romieu I, Scoccianti C, Chajès V et al. (2015). Alcohol intake and breast cancer in the European prospective investigation into cancer and nutrition. *Int J Cancer*, 137(8):1921-1930.
 197. Zhang SM, Lee I-M, Manson JE et al. (2007). Alcohol consumption and breast cancer risk in the Women's Health Study. *Am J Epidemiol*, 165(6):667-676.
 198. Lew JQ, Freedman ND, Leitzmann MF et al. (2009). Alcohol and risk of breast cancer by histologic type and hormone receptor status in postmenopausal women: the NIH-AARP Diet and Health Study. *Am J Epidemiol*, 170(3):308-317.
 199. Li CI, Chlebowski RT, Freiberg M et al. (2010). Alcohol consumption and risk of postmenopausal breast cancer by subtype: the women's health initiative observational study. *J Natl Cancer Inst*, 102(18):1422-1431.
 200. Chen WY, Rosner B, Hankinson SE et al. (2011). Moderate alcohol consumption during adult life, drinking patterns, and breast cancer risk. *JAMA*, 306(17):1884-1890.
 201. Scoccianti C, Lauby-Secretan B, Bello PY et al. (2014). Female breast cancer and alcohol consumption: a review of the literature. *Am J Prev Med*, 46(3 Suppl 1):S16-S25.
 202. Bagnardi V, Rota M, Botteri E et al. (2015). Alcohol consumption and site-specific cancer risk: a comprehensive dose-response meta-analysis. *Br J Cancer*, 112(3):580-593.
 203. Klarich DS, Brasser SM, and Hong MY (2015). Moderate alcohol consumption and colorectal cancer risk. *Alcohol Clin Exp Res*, 39(8):1280-1291.
 204. Wang Y, Duan H, Yang H et al. (2015). A pooled analysis of alcohol intake and colorectal cancer. *Int J Clin Exp Med*, 8(5):6878-6889.
 205. Ben Q, Wang L, Liu J et al. (2015). Alcohol drinking and the risk of colorectal adenoma: a dose-response meta-analysis. *Eur J Cancer Prev*, 24(4):286-295.
 206. Hashibe M, Brennan P, Chuang SC et al. (2009). Interaction between tobacco and alcohol use and the risk of head and neck cancer: pooled analysis in the International Head and Neck Cancer Epidemiology Consortium. *Cancer Epidemiol Biomarkers Prev*, 18(2):541-550.
 207. Chuang SC, Lee YC, Wu GJ et al. (2015). Alcohol consumption and liver cancer risk: a meta-analysis. *Cancer Causes Control*, 26(9):1205-1231.
 208. Seitz HK, and Stickel F (2007). Molecular mechanisms of alcohol-mediated carcinogenesis. *Nat Rev Cancer*, 7(8):599-612.
 209. Seitz HK, Simanowski UA, Garzon FT et al. (1990). Possible role of acetaldehyde in ethanol-related rectal cocarcinogenesis in the rat. *Gastro-*

- enterology, 98(2):406-413.
210. Homann N, Jousimies-Somer H, Jokelainen K et al. (1997). High acetaldehyde levels in saliva after ethanol consumption: methodological aspects and pathogenetic implications. *Carcinogenesis*, 18(9):1739-1743.
 211. Schwabe RF, and Jobin C (2013). The microbiome and cancer. *Nat Rev Cancer*, 13(11):800-812.
 212. Dorgan JF, Baer DJ, Albert PS et al. (2001). Serum hormones and the alcohol-breast cancer association in postmenopausal women. *J Natl Cancer Inst*, 93(9):710-715.
 213. Rinaldi S, Peeters PH, Bezemer ID et al. (2006). Relationship of alcohol intake and sex steroid concentrations in blood in pre- and post-menopausal women: the European Prospective Investigation into Cancer and Nutrition. *Cancer Causes Control*, 17(8):1033-1043.
 214. Hamid A, Wani NA, and Kaur J. (2009). New perspectives on folate transport in relation to alcoholism-induced folate malabsorption--association with epigenome stability and cancer development. *FEBS J*, 276(8):2175-2191.
 215. Lachenmeier DW, Przybylski MC, and Rehm J (2012). Comparative risk assessment of carcinogens in alcoholic beverages using the margin of exposure approach. *Int J Cancer*, 131(6):E995-E1003.
 216. Spiegelhalter B, Eisenbrand G, and Preussmann R (1979). Contamination of beer with trace quantities of N-nitrosodimethylamine. *Food Cosmet Toxicol*, 17(1):29-31.
 217. IARC Working Group on the Evaluation of Carcinogenic Risks of Chemicals to Humans (1978). IARC monographs on the evaluation of carcinogenic risks of chemicals to humans. Some N-nitroso compounds. *IARC Monogr Eval Carcinog Risks Hum*, 17:1-365.
 218. Lachenmeier DW, and FÜgel D (2007). Reduction of nitrosamines in beer: review of a success story. *Brew Sci*, 60:84-89.
 219. Song DY, Song S, Song Y, and Lee JE (2012). Alcohol intake and renal cell cancer risk: a meta-analysis. *Br J Cancer*, 106(11):1881-1890.
 220. Wozniak MB, Brennan P, Brenner DR et al. (2015). Alcohol consumption and the risk of renal cancers in the European prospective investigation into cancer and nutrition (EPIC). *Int J Cancer*, 137(8):1953-1966.
 221. Kitahara CM, Linet MS, Beane Freeman LE et al. (2012). Cigarette smoking, alcohol intake, and thyroid cancer risk: a pooled analysis of five prospective studies in the United States. *Cancer Causes Control*, 23(10):1615-1624.
 222. Sen A, Tsilidis KK, Allen NE et al. (2015). Baseline and lifetime alcohol consumption and risk of differentiated thyroid carcinoma in the EPIC study. *Br J Nutr*, 113(5):840-847.
 223. Tramacere I, Pelucchi C, Bonifazi M et al. (2012). Alcohol drinking and non-Hodgkin lymphoma risk: a systematic review and a meta-analysis. *Ann Oncol*, 23(11):2791-2798.
 224. Tramacere I, Pelucchi C, Bonifazi M et al. (2012). A meta-analysis on alcohol drinking and the risk of Hodgkin lymphoma. *Eur J Cancer Prev*, 21(3):268-273.
 225. Ahmad Kiadaliri A, Jarl J, Gavrilidis G et al. (2013). Alcohol drinking cessation and the risk of laryngeal and pharyngeal cancers: a systematic review and meta-analysis. *PLoS One*, 8(3):e58158.
 226. Jarl J, and Gerdtham UG (2012). Time pattern of reduction in risk of

oesophageal cancer following alcohol cessation--a meta-analysis. *Addiction*, 107(7):1234-1243.

227. Heckley GA, Jarl J, Asamoah BO et al. (2011). How the risk of liver cancer changes after alcohol cessation: a review and meta-analysis of the current literature. *BMC Cancer*, 11:446.
228. Newcomb PA, Kampman E, Trentham-Dietz A et al. (2013). Alcohol consumption before and after breast cancer diagnosis: associations with survival from breast cancer, cardiovascular disease, and other causes. *J Clin Oncol*, 31(16):1939-1946.
229. Doyle JJ, Neugut AI, Jacobson JS et al. (2005). Chemotherapy and cardiotoxicity in older breast cancer patients: a population-based study. *J Clin Oncol*, 23(34):8597-8605.
230. WHO | Cancer [Internet]. Cited Jul 2015. Retrieved from: www.who.int/mediacentre/factsheets/fs297/en/
231. McPherson K, Steel CM, and Dixon JM (2000). ABC of breast diseases. Breast cancer-epidemiology, risk factors, and genetics. *BMJ*, 321(7261):624-628.
232. Riley EP, Infante MA, and Warren KR (2011). Fetal alcohol spectrum disorders: an overview. *Neuropsychol Rev*, 21(2):73-80.
233. Giedd JN, Blumenthal J, Jeffries NO et al. (1999). Brain development during childhood and adolescence: a longitudinal MRI study. *Nature neurosci*, 2(10):861-863.
234. Gulley JM, and Juraska JM (2013). The effects of abused drugs on adolescent development of corticolimbic circuitry and behavior. *Neuroscience*, 249:3-20.
235. Mattson SN, and Riley EP (1998). A review of the neurobehavioral deficits in children with fetal alcohol syndrome or prenatal exposure to alcohol. *Alcohol Clin Exp Res*, 22(2):279-294.
236. Brust JC (2010). Ethanol and cognition: indirect effects, neurotoxicity and neuroprotection: a review. *Int J Environ Res Public Health*, 7(4):1540-1557.
237. Moss HB, Kirisci L, Gordon HW et al. (1994). A neuropsychologic profile of adolescent alcoholics. *Alcohol Clin Exp Res*, 18(1):159-163.
238. Tarter RE, Mezzich AC, Hsieh YC et al. (1995). Cognitive capacity in female adolescent substance abusers. *Drug Alcohol Depend*, 39(1):15-21.
239. Brown SA, Tapert SF, Granholm E et al. (2000). Neurocognitive functioning of adolescents: effects of protracted alcohol use. *Alcohol Clin Exp Res*, 24(2):164-171.
240. Schweinsburg AD, McQueeney T, Nagel BJ et al. (2010). A preliminary study of functional magnetic resonance imaging response during verbal encoding among adolescent binge drinkers. *Alcohol*, 44(1):111-117.
241. Squeglia LM, Schweinsburg AD, Pulido C et al. (2011). Adolescent binge drinking linked to abnormal spatial working memory brain activation: differential gender effects. *Alcohol Clin Exp Res*, 35(10):1831-1841.
242. Hendriks HFJ, and Schrieke IC (2015). Adolescent alcohol consumption: Brain health outcomes. *J Child Adolesc Behav*, 3(5). Epub.
243. Ward A, Arrighi HM, Michels S et al. (2012). Mild cognitive impairment: disparity of incidence and prevalence estimates. *Alzheimers Dement*, 8(1):14-21.
244. World Alzheimer Report 2015. The Global Impact of Dementia. An analysis of prevalence, incidence, cost and trends [Internet]. Cited Jan 2016.

Retrieved from: <http://www.alz.co.uk/research/world-report-2015>.

245. Anstey KJ, Mack HA, and Cherbuin N (2009). Alcohol consumption as a risk factor for dementia and cognitive decline: meta-analysis of prospective studies. *Am J Geriatr Psychiatry*, 17(7):542-555.
246. Neafsey EJ, and Collins MA (2011). Moderate alcohol consumption and cognitive risk. *Neuropsychiatr Dis Treat*, 7:465-484.
247. Sabia S, Elbaz A, Britton A et al. (2014). Alcohol consumption and cognitive decline in early old age. *Neurology*, 82(4):332-339.
248. Almeida OP, Hankey GJ, Yeap BB et al. (2014). Alcohol consumption and cognitive impairment in older men: a mendelian randomization study. *Neurology*, 82(12):1038-1044.
249. Solfrizzi V, D'Introno A, Colacicco AM et al. (2007). Alcohol consumption, mild cognitive impairment, and progression to dementia. *Neurology*, 68(21):1790-1799.
250. Xu G, Liu X, Yin Q et al. (2009). Alcohol consumption and transition of mild cognitive impairment to dementia. *Psychiatry Clin Neurosci*, 63(1):43-49.
251. Scarmeas N, Luchsinger JA, Schupf N et al. (2009). Physical activity, diet, and risk of Alzheimer disease. *JAMA*, 302(6):627-637.
252. Panza F, Frisardi V, Seripa D et al. (2012). Alcohol consumption in mild cognitive impairment and dementia: harmful or neuroprotective? *Int J Geriatr Psychiatry*, 27(12):1218-1238.
253. von Campenhausen S, Bornschein B, Wick R et al. (2005). Prevalence and incidence of Parkinson's disease in Europe. *Eur Neuropsychopharmacology*, 15(4):473-490.
254. Wirdefeldt K, Adami HO, Cole P et al. (2011). Epidemiology and etiology of Parkinson's disease: a review of the evidence. *Eur J Epidemiol*, 26 Suppl 1:S1-S58.
255. Zhang D, Jiang H, and Xie J (2014). Alcohol intake and risk of Parkinson's disease: a meta-analysis of observational studies. *Mov Disord*, 29(6):819-822.
256. Gaffo AL, Roseman JM, Jacobs DR et al. (2010). Serum urate and its relationship with alcoholic beverage intake in men and women: findings from the Coronary Artery Risk Development in Young Adults (CARDIA) cohort. *Ann Rheum Dis*, 69(11):1965-1970.
257. Shen C, Guo Y, Luo W et al. (2013). Serum urate and the risk of Parkinson's disease: results from a meta-analysis. *Can J Neurol Sci*, 40(1):73-79.
258. Barr T, Helms C, Grant K et al. (2015). Opposing effects of alcohol on the immune system. *Prog Neuropsychopharmacol Biol Psychiatry*, Epub.
259. Hernlund E, Svedbom A, Ivergård M et al. (2013). Osteoporosis in the European Union: medical management, epidemiology and economic burden. A report prepared in collaboration with the International Osteoporosis Foundation (IOF) and the European Federation of Pharmaceutical Industry Associations (EFPIA). *Arch Osteoporos*, 8:136.
260. Tucker KL, Jugdaohsingh R, Powell JJ et al. (2009). Effects of beer, wine, and liquor intakes on bone mineral density in older men and women. *Am J Clin Nutr*, 89(4):1188-1196.
261. Maurel DB, Boisseau N, Benhamou CL et al. (2012). Alcohol and bone: review of dose effects and mechanisms. *Osteoporosis Int*, 23(1):1-16.
262. Jugdaohsingh R, O'Connell MA, Sripanyakorn S et al. (2006). Moderate

- alcohol consumption and increased bone mineral density: potential ethanol and non-ethanol mechanisms. *Proc Nutr Soc*, 65(03):291-310.
263. Musculoskeletal health status in Europe version 5 [Internet]. Cited 1 Oct 2015. Retrieved from: www.eumusc.net/workpackages_wp4.cfm
 264. Scott IC, Tan R, Stahl D (2013). The protective effect of alcohol on developing rheumatoid arthritis: a systematic review and meta-analysis. *Rheumatology*, 52(5):856-867.
 265. Lu B, Solomon DH, Costenbader KH et al. (2014). Alcohol consumption and risk of incident rheumatoid arthritis in women: a prospective study. *Arthritis Rheumatol*, 66(8):1998-2005.
 266. Annemans L, Spaepen E, Gaskin M et al. (2008). Gout in the UK and Germany: prevalence, comorbidities and management in general practice 2000-2005. *Ann Rheum Dis*, 67(7):960-966.
 267. Wang M, Jiang X, Wu W et al. (2013). A meta-analysis of alcohol consumption and the risk of gout. *Clin Rheumatol*, 32(11):1641-1648.
 268. Xu C, Zhang C, Wang XL et al. (2015). Self-fluid management in prevention of kidney stones: a PRISMA-compliant systematic review and dose-response meta-analysis of observational studies. *Medicine*, 94(27):e1042.
 269. Rule AD, Krambeck AE, and Lieske JC (2011). Chronic kidney disease in kidney stone formers. *Clin J Am Soc Nephrol*, 6(8):2069-2075.
 270. de Jong PE, van der Velde M, Gansevoort RT et al. (2008). Screening for chronic kidney disease: where does Europe go? *Clin J Am Soc Nephrol*, 3(2):616-623.
 271. Buja A, Vinelli A, Lion C et al. (2014). Is moderate alcohol consumption a risk factor for kidney function decline? A systematic review of observational studies. *J Ren Nutr*, 24(4):224-235.
 272. Shaffer EA (2006). Epidemiology of gallbladder stone disease. *Best Pract Res Clin Gastroenterol*, 20(6):981-996.
 273. Banim PJ, Luben RN, Bulluck H et al. (2011). The aetiology of symptomatic gallstones quantification of the effects of obesity, alcohol and serum lipids on risk. Epidemiological and biomarker data from a UK prospective cohort study (EPIC-Norfolk). *Eur J Gastroenterol Hepatol*, 23(8):733-740.
 274. Leitzmann MF, Tsai CJ, Stampfer MJ et al. (2003). Alcohol consumption in relation to risk of cholecystectomy in women. *Am J Clin Nutr*, 78(2):339-347.
 275. Peele S, and Brodsky A (2000). Exploring psychological benefits associated with moderate alcohol use: a necessary corrective to assessments of drinking outcomes? *Drug Alcohol Depend*, 60(3):221-247.
 276. Aan Het Rot M, Russell JJ, Moskowitz DS et al. (2008). Alcohol in a social context: findings from event-contingent recording studies of everyday social interactions. *Alcohol Clin Exp Res*, 32(3):459-71.
 277. Chan AM, von Mühlen D, Kritiz-Silverstein D et al. (2009). Regular alcohol consumption is associated with increasing quality of life and mood in older men and women: the Rancho Bernardo Study. *Maturitas*, 62(3):294-300.
 278. French MT, and Zavala SK (2007). The health benefits of moderate drinking revisited: alcohol use and self-reported health status. *Am J Health Promot*, 21(6):484-491.
 279. Zale EL, Maisto SA, and Ditte JW (2015). Interrelations between pain and

- alcohol: An integrative review. *Clin Psychol Rev*, 37:57-71.
280. Singh A, and Misra N (2009). Loneliness, depression and sociability in old age. *Ind Psychiatry J*, 18(1):51-55.
281. Byles J, Young A, Furuya H et al. (2006). A drink to healthy aging: The association between older women's use of alcohol and their health-related quality of life. *J Am Geriatr Soc*, 54(9):1341-1347.
282. Kaplan MS, Huguet N, Feeny D et al. (2012). Alcohol use patterns and trajectories of health-related quality of life in middle-aged and older adults: a 14-year population-based study. *J Stud Alcohol Drugs*, 73(4):581.
283. Pearl R (1926). *Alcohol and Longevity*. New York: A.A. Knopf.
284. Corrao G, Bagnardi V, Zambon A et al. (2004). A meta-analysis of alcohol consumption and the risk of 15 diseases. *Prev Med*, 38(5):613-619.
285. Di Castelnuovo A, Costanzo S, Bagnardi V et al. (2006). Alcohol dosing and total mortality in men and women: an updated meta-analysis of 34 prospective studies. *Arch Intern Med*, 166(22):2437-2445.
286. Wang C, Xue H, Wang Q et al. (2014). Effect of drinking on all-cause mortality in women compared with men: a meta-analysis. *J Womens Health*, 23(5):373-381.
287. Jayasekara H, English DR, Room R et al. (2014). Alcohol consumption over time and risk of death: a systematic review and meta-analysis. *Am J Epidemiol*, 179(9):1049-1059.
288. Bergmann MM, Rehm J, Klipstein-Grobusch K et al. (2013). The association of pattern of lifetime alcohol use and cause of death in the European prospective investigation into cancer and nutrition (EPIC) study. *Int J Epidemiol*, 42(6):1772-1790.
289. Jayasekara H, MacInnis RJ, Hodge AM et al. (2014). Alcohol consumption for different periods in life, intake pattern over time and all-cause mortality. *J Public Health*, Epub.
290. Britton A, Ben-Shlomo Y, Benzeval M et al. (2015). Life course trajectories of alcohol consumption in the United Kingdom using longitudinal data from nine cohort studies. *BMC Med*, 13:47.
291. Grønbaek M, Johansen D, Becker U et al. (2004). Changes in alcohol intake and mortality: a longitudinal population-based study. *Epidemiology*, 15(2):222-228.
292. Klatsky AL, and Udaltsova N (2013). Abounding confounding: sick quitters and healthy drinkers. *Addiction*, 108(9):1549-1552.
293. Shaper AG, Wannamethee G, and Walker M (1988). Alcohol and mortality in British men: explaining the U-shaped curve. *Lancet*, 2(8623):1267-1273.
294. Jackson R, Broad J, Connor J et al. (2005). Alcohol and ischaemic heart disease: probably no free lunch. *Lancet*, 366(9501):1911-1912.
295. Naimi TS, Xuan Z, Brown DW et al. (2013). Confounding and studies of 'moderate' alcohol consumption: the case of drinking frequency and implications for low-risk drinking guidelines. *Addiction*, 108(9):1534-1543.
296. Feunekes GI, van 't Veer P, van Staveren WA et al. (1999). Alcohol intake assessment: the sober facts. *Am J Epidemiol*, 150(1):105-112.
297. Klatsky AL, Gunderson EP, Kipp H et al. (2006). Higher prevalence of systemic hypertension among moderate alcohol drinkers: an exploration of the role of underreporting. *J Stud Alcohol*, 67(3):421-428.
298. Holahan CJ, Schutte KK, Brennan PL et al. (2015). Drinking level, drink-

- ing pattern, and twenty-year total mortality among late-life drinkers. *J Stud Alcohol Drugs*, 76(4):552-558.
299. Klatsky AL (2015). Alcohol and cardiovascular diseases: where do we stand today? *J Intern Med*, 278(3):238-250.
300. Thomassen HR (1995). Gender differences in alcohol metabolism: physiological responses to ethanol. *Recent Dev Alcohol*, 12:163-179.
301. WHO Europe | Nutrition - A healthy lifestyle [Internet]. Cited 13 Oct 2015. Retrieved from: www.euro.who.int/en/health-topics/disease-prevention/nutrition/a-healthy-lifestyle

