The clinical consequences of alcohol use and abuse

HCC Webinar, December 6th, 2019

Professor Simon Anderson
The George Alleyne Chronic Disease Research Centre
Alcohol and health

3 million deaths from harmful use of alcohol every year

Harmful use of alcohol causes

- 100% of alcohol use disorders
- 18% of suicides
- 18% of interpersonal violence
- 27% of traffic injuries
- 13% of epilepsy
- 48% of liver cirrhosis
- 26% of mouth cancers
- 26% of pancreatitis
- 20% of tuberculosis
- 11% of colorectal cancer
- 5% of breast cancer
- 7% of hypertensive heart disease
Harmful use of alcohol

• Harmful use of alcohol is accountable for 7.1% and 2.2% of the global burden for males and females respectively.

• Alcohol is the leading risk factor for premature mortality and disability among those aged 15 to 49 years, accounting for 10 percent of all deaths in this age group.

• Disadvantaged and especially vulnerable populations have higher rates of alcohol-related death and hospitalization.

https://www.who.int/health-topics/alcohol#tab=tab_1
Conceptual causal model of alcohol consumption and health outcomes

Alcohol consumption
- Volume
- Patterns

Health outcomes
- Chronic
- Acute

Societal vulnerability factors
- Level of development
- Culture
- Drinking context
- Alcohol production, distribution, regulation

Individual vulnerability factors
- Age
- Gender
- Familial factors
- Socioeconomic status

Mortality by cause
Socioeconomic consequences
Harm to others

Nature Reviews | Gastroenterology & Hepatology

Gilmore, W. et al. (2016) Alcohol: taking a population perspective
Nat. Rev. Gastroenterol. Hepatol. doi:10.1038/nrgastro.2016.70
Global status report on alcohol and health 2018
Estimates from 2016

• Alcohol caused an estimated 0.4 million of the 11 million deaths globally in 2016 from communicable, maternal, perinatal and nutritional conditions.

• Harmful use of alcohol caused some 1.7 million deaths from noncommunicable diseases in 2016, including deaths from digestive, cardiovascular diseases and from cancers.

• Globally an estimated 0.9 million injury deaths were attributable to alcohol, including deaths due to road injuries due to self-harm and interpersonal violence.

• Of the road traffic injuries, 187 000 alcohol-attributable deaths were among people other than drivers.
# Causes of death and disability causally related to alcohol consumption

## Diseases and injuries included in the analysis

### Detrimental

- Communicable, maternal, perinatal and nutritional conditions
  - Tuberculosis, HIV/AIDS, lower respiratory infections
- Noncommunicable diseases
  - Lip and oral cavity, pharyngeal cancers (excluding nasopharyngeal), oesophagus cancer, colon and rectum cancers, liver cancer, breast cancer, larynx cancer, alcohol use disorders, epilepsy, hypertensive heart disease, haemorrhagic stroke, alcoholic cardiomyopathy, cirrhosis of the liver, pancreatitis
- Injuries
  - Unintentional injuries
    - Road injury, poisonings, falls, fire, heat and hot substances, drowning, exposure to mechanical forces, other unintentional injuries
  - Intentional injuries
    - Self-harm, interpersonal violence

### Beneficial (at low levels of alcohol consumption*)

- Noncommunicable diseases
  - Diabetes mellitus, ischaemic heart disease, ischaemic stroke

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*WHO. Global status report on alcohol and health 2018*
Percentage of alcohol-attributable deaths, by broad disease category, 2016

- Intentional injuries: 7.8%
- Infectious diseases: 12.9%
- Unintentional injuries: 20.9%
- Malignant neoplasms: 12.6%
- Alcohol use disorders: 4.9%
- Epilepsy: 0.5%
- Digestive diseases: 21.3%
- Cardiovascular diseases and diabetes: 19.0%

Net total = 3.0 million deaths

WHO. Global status report on alcohol and health 2018
Alcohol, GBV, and infectious disease are closely correlated

Harmful use of alcohol

- lowers inhibitions and increases risk-taking behaviour;
- increases the risk of sexual violence against women, girls, and men

Infectious disease

- reduces women’s ability to negotiate safer sex; leads to extreme stigma and discrimination
- leads to increased alcohol consumption as a coping mechanism for depression or stigma
- leads to HIV, STD transmission through abuse

Gender-based violence

- leads to increased alcohol consumption as a coping mechanism for depression or stigma

THE UNIVERSITY OF THE WEST INDIES | CAIHR www.uwi.edu/caihr
Harmful alcohol use and the Immune System

• Chronic alcohol abuse results in immunodeficiency and liver damage that may also be partly triggered by alcohol-induced autoimmunity
• Higher rates of infectious illnesses, such as pneumonia

Image from: https://sunrisehouse.com/addiction-demographics/infectious-diseases/#1
<table>
<thead>
<tr>
<th>CELL</th>
<th>Moderate Chronic</th>
<th>Heavy Acute</th>
<th>Chronic</th>
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<tr>
<td>Monocyte</td>
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<tr>
<td>Frequency</td>
<td>↓ Frequency</td>
<td>↓ Frequency</td>
<td>↑↑↑ TNF-α</td>
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<td>Phagocytic activity</td>
<td>↓ Frequency</td>
<td>↓ IL-6, IL-12, TNF-α</td>
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<td>IL-6, TNF-α</td>
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<td>↓ Effercytosis</td>
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<td>Dendritic cell</td>
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<td>↑ IL-10</td>
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<td>T lymphocyte</td>
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<tr>
<td>Frequency</td>
<td>↑ Frequency</td>
<td>↓ Frequency</td>
<td></td>
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<tr>
<td>IL-2, IL-4, IL-10, IFN-γ</td>
<td>↑ Frequency</td>
<td>↓ Naive T cells</td>
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<td>IFN-γ/IL-10 ratio</td>
<td>↓ Vaccine responses</td>
<td>↑ Memory T cells</td>
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<tr>
<td>↑ Vaccine responses</td>
<td></td>
<td>↑ Activation</td>
<td></td>
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<td>B lymphocyte</td>
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<tr>
<td>Frequency</td>
<td>↑ Frequency</td>
<td>↓ Frequency</td>
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<tr>
<td>IgA, IgM, IgG</td>
<td>↓ IgA, IgM, IgG</td>
<td>↑ Antigen-specific responses</td>
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<td>↑ Apoptosis</td>
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<td>↑ Apoptosis</td>
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*Opposing Effects of Alcohol Consumption on Immune Cells*

Alcohol and cancer: This is how booze damages DNA inside cells

**ALCOHOL CAN CAUSE 7 TYPES OF CANCER**

- Mouth & Upper throat
- Larynx
- Oesophagus
- Breast in women
- Liver
- Bowel

Larger circles indicate cancers with more UK cancer cases linked to drinking alcohol

**ONE WAY ALCOHOL INCREASES CANCER RISK**

- ETHANOL (ALCOHOL) Enters a stem cell
- ADH ENZYME Converts ethanol to acetaldehyde
- ACETALDEHYDE A toxic chemical that if allowed to build up can cause: Chromosome rearrangements & Mistakes in DNA DAMAGE CAN INCREASE CANCER RISK
- ALDH ENZYME Converts acetaldehyde to acetate
- ACETATE Energy the body can use

Source: Garay-Cochez et al. 2018. Nature. DOI: 10.1038/nature25154
LET'S BEAT CANCER SOONER cruk.org

Alcohol drinking patterns and liver cirrhosis risk: analysis of the prospective UK Million Women Study

Rachel F Simpson, MB BCh  •  Carol Hermon, MSc  •  Bette Liu, DPhil  •  Prof Jane Green, DPhil  •  Prof Gillian K Reeves, PhD  •  Prof Valerie Beral, FRS  •  et al.  •  Show all authors

Open Access  •  Published: November 21, 2018  •  DOI: https://doi.org/10.1016/S2468-2667(18)30230-5  •  Check for updates
Alcohol drinking patterns and liver cirrhosis risk: analysis of the prospective UK Million Women Study

• The Million Women Study is a prospective study that includes one in every four UK women born between 1935 and 1950.

• The women were recruited between 1996 and 2001.

• In 2001 the participants reported their alcohol intake, whether consumption was usually with meals, and number of days per week it was consumed.
Relative risk (RR) of liver cirrhosis by amount of alcohol consumed

Simpson et al.; https://doi.org/10.1016/S2468-2667(18)30230-5
So how does alcohol cause cancer?

• There are three main ways alcohol can cause damage:

• Acetaldehyde - when we drink alcohol, it is turned into a chemical called acetaldehyde which can cause cancer by damaging DNA and stopping our cells from repairing this damage.

• Hormone changes – alcohol can increase the levels of some hormones such as oestrogen and insulin.

• Increased absorption – alcohol can affect the cells between the mouth and throat, which may make it easier for other carcinogens to be absorbed.
Women and alcoholic liver disease — warning of a silent danger

• Alcoholic liver disease (ALD) is a spectrum of liver abnormalities caused by excessive and chronic alcohol use that includes steatosis progressing to steatohepatitis and, over time, to cirrhosis.

• Although ALD can silently lead to cirrhosis, some individuals present with alcoholic hepatitis — a clinically severe form of ALD that carries high mortality.

• In most clinical textbooks ALD is described as a disease of middle-aged and elderly men.

• However, this aspect is rapidly changing due to increased alcohol use by women worldwide.

Factors contributing to increased risk of alcohol-associated liver disease in women.

- substantial gap remains in understanding why women are more susceptible to these diseases
- sex-related differences in the expression and activity of key alcohol-metabolizing enzymes
- an equivalent dose of alcohol results in higher blood ethanol levels in women than in men
Alcohol and cardiovascular disease
Alcohol and cardiovascular disease

• The association between excessive drinking and various forms of cardiovascular disease is well established.

• Significant alcohol consumption is associated with a higher risk of atrial fibrillation and other forms of cardiac arrhythmias, hypertension, left ventricular hypertrophy (LVH), obstructive sleep apnea (OSA) and cardiomyopathy.
Alcohol and cardiovascular disease

• Heavy drinking and binge drinking increase the risks of haemorrhagic types of stroke, such as cerebral haemorrhage and subarachnoid haemorrhage

• Alcohol may be responsible for 16% of hypertensive disease, with the incidence of hypertension increased by 40% if consuming >14 standard drinks/week.
Risk thresholds for alcohol consumption: combined analysis of individual-participant data for 599 912 current drinkers in 83 prospective studies

Angela M Wood, PhD  Stephen Kaptoge, PhD  Adam S Butterworth, PhD  Peter Willeit, MD
Samantha Warnakula, PhD  Thomas Bolton, MMath  et al.

Open Access  Published: April 14, 2018  DOI: https://doi.org/10.1016/S0140-6736(18)30134-X
Risks for subtypes of cardiovascular outcomes in current drinkers, per 100 g per week higher usual alcohol consumption

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Events/participants</th>
<th>Hazard ratio (95% CI)</th>
<th>Heterogeneity P (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All stroke</td>
<td>12090/585588</td>
<td>1.14 (1.10-1.17)</td>
<td>12 (0.05)</td>
</tr>
<tr>
<td>Non-fatal stroke</td>
<td>9910/491050</td>
<td>1.14 (1.10-1.18)</td>
<td>14 (0.04)</td>
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<td>Fatal stroke</td>
<td>2142/532024</td>
<td>1.13 (1.07-1.19)</td>
<td>0 (0.05)</td>
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<tr>
<td>Ischaemic stroke</td>
<td>6256/491204</td>
<td>1.13 (1.09-1.18)</td>
<td>8 (0.37)</td>
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<td>Haemorrhagic stroke</td>
<td>1482/509548</td>
<td>1.17 (1.12-1.23)</td>
<td>0 (0.37)</td>
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<td>Subarachnoid haemorrhage</td>
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<td>1.09 (1.00-1.19)</td>
<td>0 (0.58)</td>
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<td>Unclassified stroke</td>
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<td>1.13 (1.06-1.20)</td>
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<td>All myocardial infarction</td>
<td>14539/594561</td>
<td>0.94 (0.91-0.97)</td>
<td>12 (0.35)</td>
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<td>Non-fatal myocardial infarction</td>
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<td>0.93 (0.90-0.97)</td>
<td>24 (0.45)</td>
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<td>Fatal myocardial infarction</td>
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<td>8 (0.35)</td>
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<td>Coronary disease excluding myocardial infarction</td>
<td>7990/523548</td>
<td>1.06 (1.00-1.11)</td>
<td>26 (0.49)</td>
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<td>Non-fatal coronary disease excluding myocardial infarction</td>
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<td>Fatal coronary disease excluding myocardial infarction</td>
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<td>Heart failure (fatal and non-fatal)</td>
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<td>Death from other types of cardiovascular disease</td>
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<td>Cardiac dysrhythmia</td>
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<td>1.17 (0.86-1.60)</td>
<td>63 (35.79)</td>
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<td>Hypertensive disease</td>
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<td>Sudden cardiac death</td>
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<td>Aortic aneurysm</td>
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<td>1.15 (1.03-1.28)</td>
<td>0 (0.49)</td>
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</table>

DOI: [https://doi.org/10.1016/S0140-6736(18)30134-X](https://doi.org/10.1016/S0140-6736(18)30134-X)
Associations of usual alcohol consumption with all-cause mortality and the aggregate of cardiovascular disease in current drinkers

DOI: https://doi.org/10.1016/S0140-6736(18)30134-X
Habitual Alcohol consumption and arrhythmias

ALCOHOL

Atrial Inflammation & Oxidative Stress
Hypertension
OSA
LV remodeling (LVH, cardiomyopathy)

ATRIAL SUBSTRATE
Left atrial remodeling
Left atrial dilation
Elevated left atrial pressure
Left atrial fibrosis

TRIGGER
Acute binge
Cellular effects
Electrophysiological effects
Sympathetic activation
Electrolyte abnormalities ($\downarrow K^+$ and $\downarrow Mg^{2+}$)

Vagal activation

AF

https://doi.org/10.1016/j.jacc.2016.08.074
Summary

Clinical consequences of the harmful use of alcohol
Excessive alcohol use – short term health risks

• Injuries, such as motor vehicle crashes, falls, drownings, and burns
• Violence, including homicide, suicide, sexual assault, and intimate partner violence
• Alcohol poisoning, a medical emergency that results from high blood alcohol levels
• Risky sexual behaviours, including unprotected sex or sex with multiple partners. These behaviours can result in unintended pregnancy or sexually transmitted diseases, including HIV
• Miscarriage and stillbirth or fetal alcohol spectrum disorders among pregnant women

https://www.cdc.gov/alcohol/fact-sheets/alcohol-use.htm
Excessive alcohol use – long term health risks

• High blood pressure, heart disease, stroke, liver disease, and digestive problems.
• Cancer of the breast, mouth, throat, oesophagus, liver, and colon.
• Learning and memory problems, including dementia and poor school performance.
• Mental health problems, including depression and anxiety.
• Social problems, including lost productivity, family problems, and unemployment.
• Alcohol dependence, or alcoholism.

https://www.cdc.gov/alcohol/fact-sheets/alcohol-use.htm
Excessive Alcohol Use and Risks to Women's Health

• Excessive drinking may disrupt the menstrual cycle and increase the risk of infertility.

• Women who binge drink are more likely to have unprotected sex and multiple sex partners. These activities increase the risks of unintended pregnancy and sexually transmitted diseases.

• **Liver Disease**: The risk of cirrhosis and other alcohol-related liver diseases is higher for women than for men.
Excessive Alcohol Use and Risks to Women's Health

• **Impact on the Brain**: women are more vulnerable to the brain damaging effects of excessive alcohol use, and the damage tends to appear with shorter periods of excessive drinking for women than for men.

• **Impact on the Heart**: Studies have shown that women who drink excessively are at increased risk for damage to the heart muscle than men even for women drinking at lower levels.

• **Cancer**: Alcohol consumption increases the risk of cancer of the mouth, throat, oesophagus, liver, colon, and breast among women. The risk of breast cancer increases as alcohol use increases.
Thank you