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# Substance Misuse Module

## Diagnosis & Treatment of People with Alcohol Problems

Developing people
for health and
healthcare

www.hee.nhs.uk

# Insert name of the LEP

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## Aims and Objectives (from handbook)

- Assessment, diagnosis and treatment of people with alcohol problems
- To develop awareness of complications associated with alcohol use
- To understand some of the practical aspects of managing people with alcohol problems
- To gain awareness of local provisions and guidelines

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## To achieve this

- Case Presentation
- Journal Club
- 555 Presentation
- Expert-Led Session
- MCQs

- Please sign the register and complete the feedback

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## Expert Led Session

Alcohol Dependence

P Horgan

Consultant in Substance Misuse, Cumbria

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# Overview

- Calculation of units / pharmacology
- Epidemiology
- Health consequences
- Dependence/ harmful use/ hazardous use
- Treatment issues

# Units of alcohol

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- 1 unit of alcohol = 10 ml  = 8 g
- Alcohol usually measured as volume per volume
- Carlsberg 3.8%  v/v (ABV)
- 3.8ml per 100 mls
- 38ml per 1000 mls
- 3.8 units in 1000 mls
- 1.9 units in 1 standard can of 500 mls

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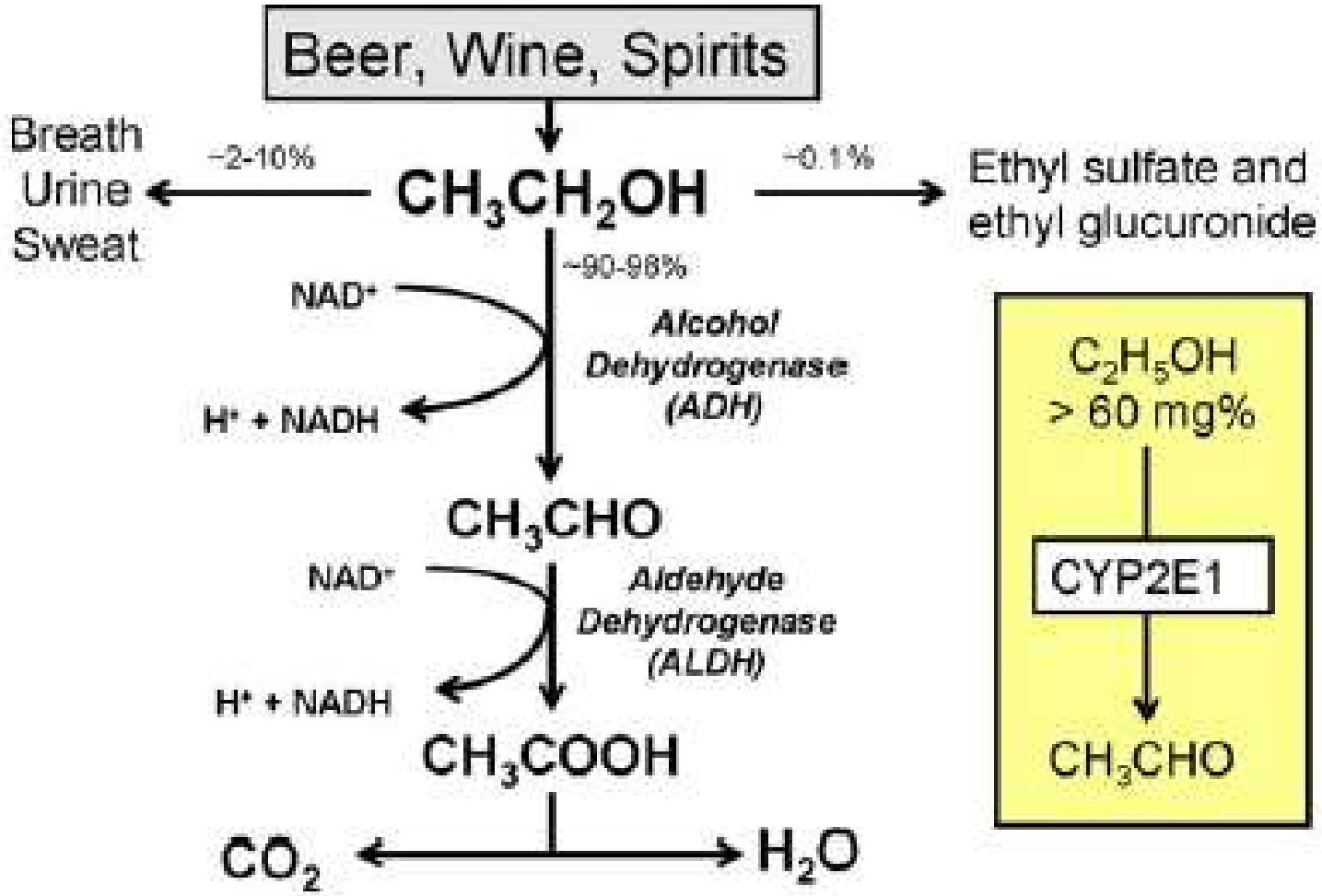
# Formula

$$\frac{\text{Percent alcohol x volume in ml}}{1000} = Units$$

- 1x can (500 mls) of Carlsberg 3.8%
  - (3.8 x 500 )/ 1000 = 1.9 units
- I x bottle (700 mls) bottle of whisky 40%
  - (40 x700)/1000 = 28 units

# Metabolism oxidative and non-oxidative pathways




Jones 2010

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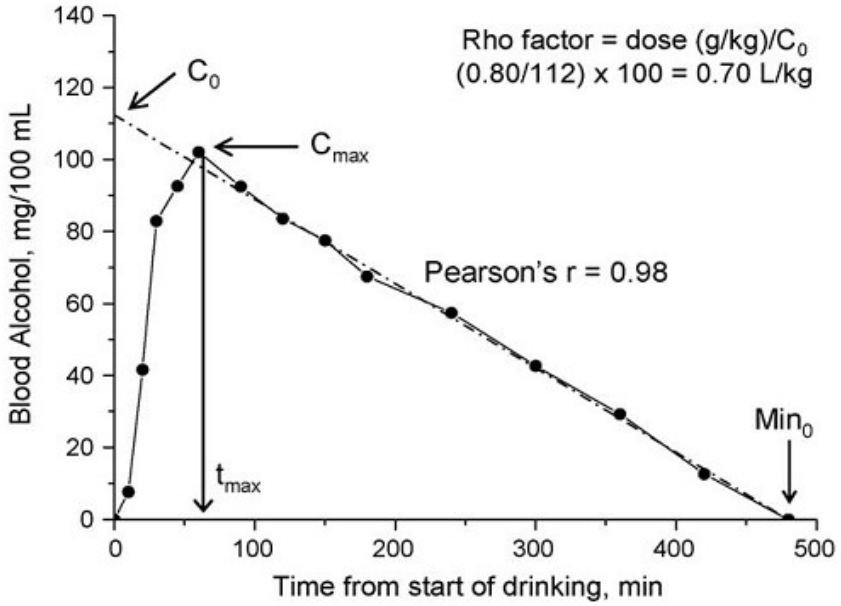
# Alcohol pharmacokinetics




**A typical blood-alcohol curve in a male subject who drank neat whisky (0.80 g ethanol/kg body weight) on an empty stomach. (.8g = .1 unit)**

**Elimination rates from blood is from 10 to 35 mg/100 mL/hour**

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# Blood alcohol and breath alcohol

- Blood alcohol level is mg/100ml
- Limit drink driving 80 mgs/100 mls
- On some breath alcometer machines
  - This will be equivalent to 0.35 micrograms per 100mls
- On other alcometer machines
  - This will be equivalent to 80%

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# Neuropharmacology

- GABA and glutamate
  - Chronic alcohol intake reduce GABA inhibitory function and increase NMDA-glutamatergic activity
  - When alcohol-dependent individual stops drinking this results in brain overactivity after a few hours
    - Results in unpleasant withdrawal symptoms such as anxiety, sweating, craving, seizures and hallucinations
  - Alcohol stimulates endogenous opioids, which are thought to be related to the pleasurable, reinforcing effects of alcohol
  - Opioids in turn stimulate the dopamine system in the brain

NICE 2011

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# ICD 10 Dependence

- A definite diagnosis of dependence should usually be made only if **three or more** of the following have been present together at some time during the previous year:

1. A strong **desire** or sense of **compulsion** to take the substance
2. Difficulties in **controlling** substance-taking behaviour in terms of its onset, termination, or levels of use
3. A **physiological withdrawal** state when substance use has ceased or have been reduced, as evidenced by: the characteristic withdrawal syndrome for the substance; or use of the same (or closely related) substance with the intention of relieving or avoiding withdrawal symptoms

# ICD 10 Dependence

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4. Evidence of **tolerance**, such that increased doses of the psychoactive substance are required in order to achieve effects originally produced by lower doses (clear examples of this are found in alcohol- and opiate-dependent individuals who may take daily doses sufficient to incapacitate or kill non tolerant users)
5. Progressive **neglect** of alternative pleasures or interests because of psychoactive substance use, increased amount of time necessary to obtain or take the substance or to recover from its effects
6. **Persisting** with substance use despite **clear evidence of overtly harmful consequences**, such as harm to the liver through excessive drinking, depressive mood states consequent to periods of heavy substance use, or drug-related impairment of cognitive functioning; efforts should be made to determine that the user was actually, or could be expected to be, aware of the nature and extent of the harm

# ICD 10 Harmful use

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- The diagnosis requires that **actual damage** should have been caused to the mental or physical health of the user
- Harmful patterns of use are often criticized by others and frequently associated with adverse social consequences of various kinds. The fact that a pattern of use or a particular substance is disapproved of by another person or by the culture, or may have led to socially negative consequences such as arrest or marital arguments is not in itself evidence of harmful use
- Acute intoxication, or “hangover” is not in itself sufficient evidence of the damage to health required for coding harmful use
- Harmful use should not be diagnosed if dependence syndrome, a psychotic disorder, or another specific form of drug- or alcohol-related disorder is present

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# ICD 10 Hazardous use

- A pattern of substance use that increases the risk of harmful consequences for the user
- In contrast to harmful use, hazardous use refers to patterns of use that are of public health significance despite the absence of any current disorder in the individual user
- The term is used currently by WHO but is not a diagnostic term in ICD-10

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# Epidemiology

## Dependence

- 4% of people aged between 16 and 65*
  - 6% men
  - 2% women

## Hazardous drinkers

- More than 24% of the English population consume alcohol in a way that is potentially or actually harmful to their health
  - 33% men
  - 16% women

NICE 2011

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# Epidemiology

## Children

- Based on the Adult Psychiatric Morbidity Survey for England
- 595,131 people aged 18 or older identified as alcohol dependent
- 120,419 had children living with them in the household
- 222,007 children living in a household with an adult with alcohol dependence symptoms

Pryce 2017

# Effects of alcohol

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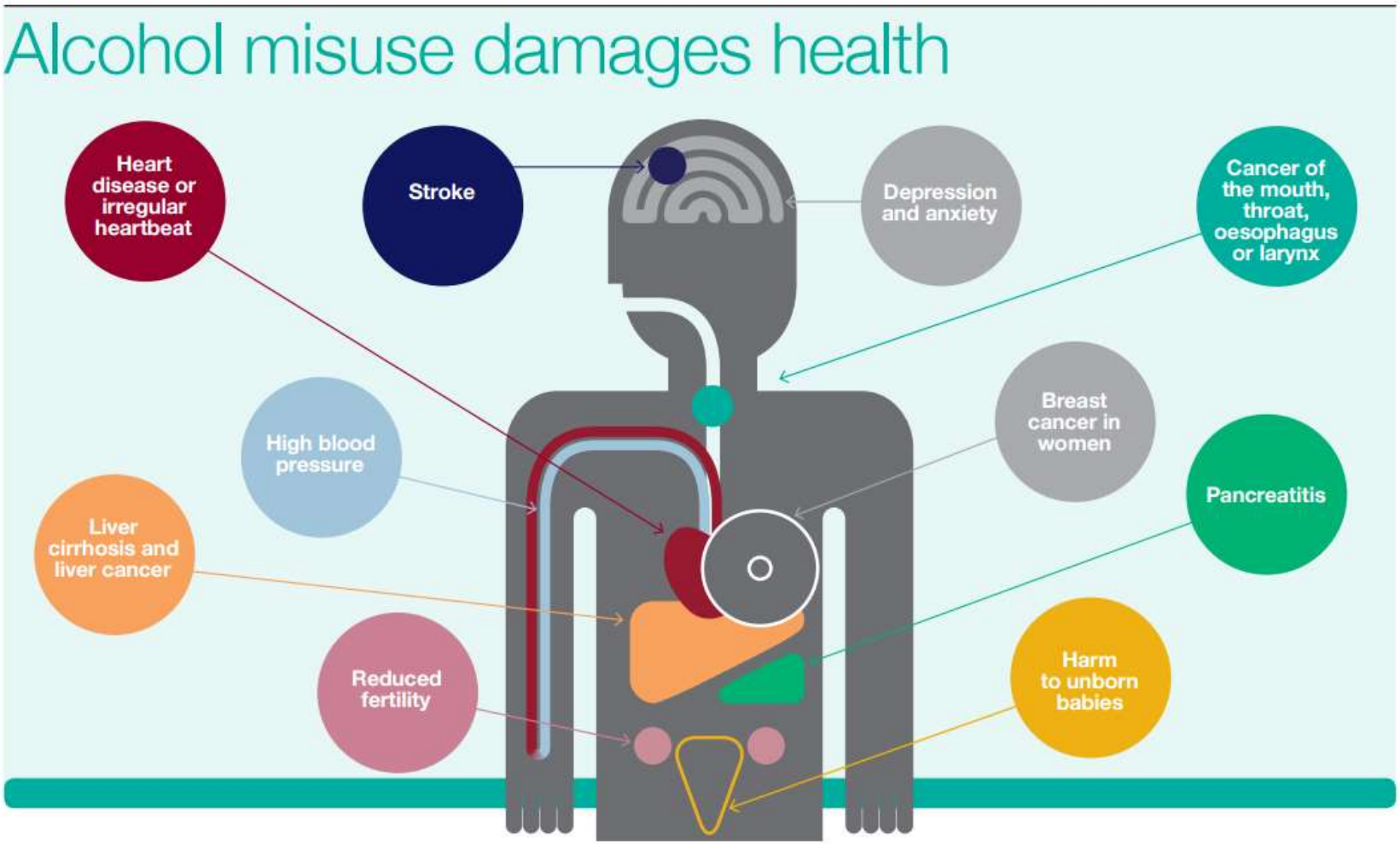


https://publichealthmatters.blog.gov.uk/2015/06/17/alcohol-some-encouraging-trends

# Effects of alcohol

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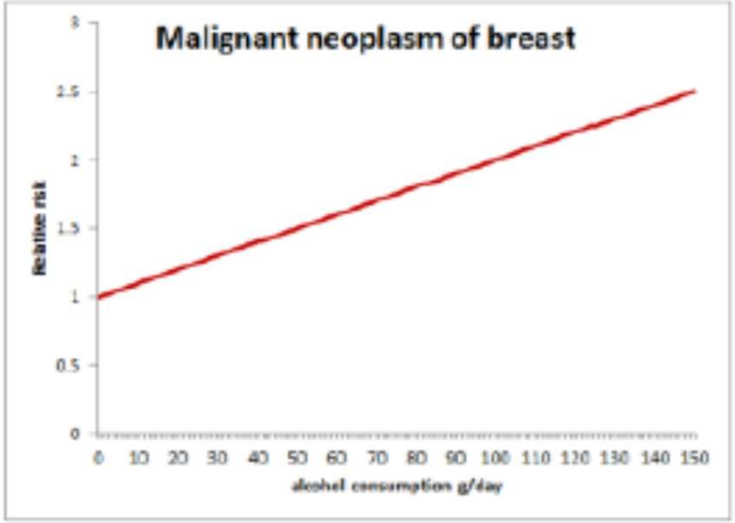


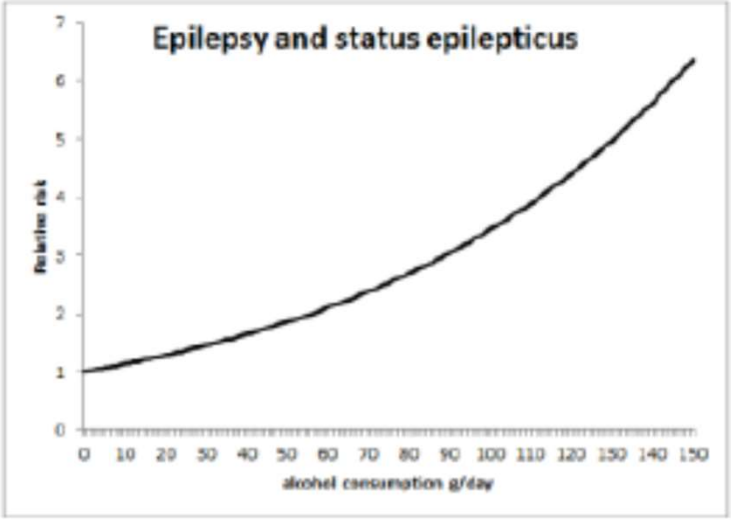


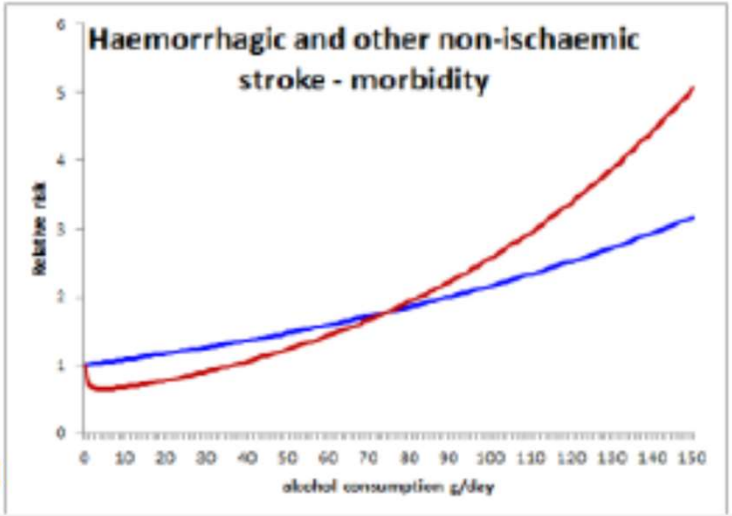


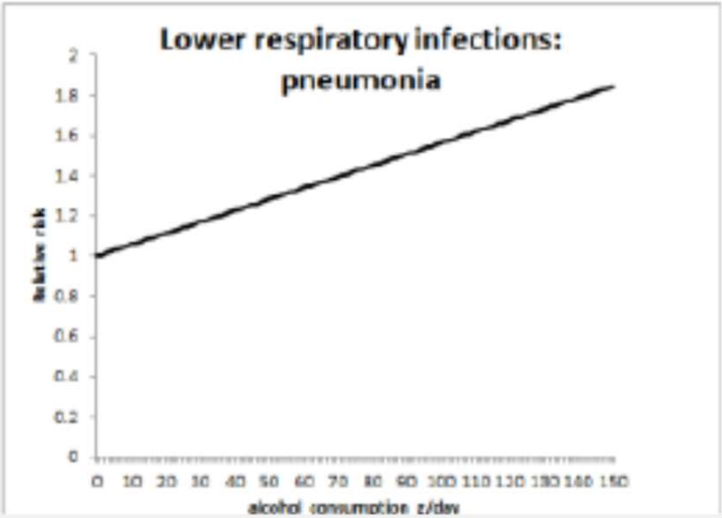


Holmes 2016

# Effects of alcohol

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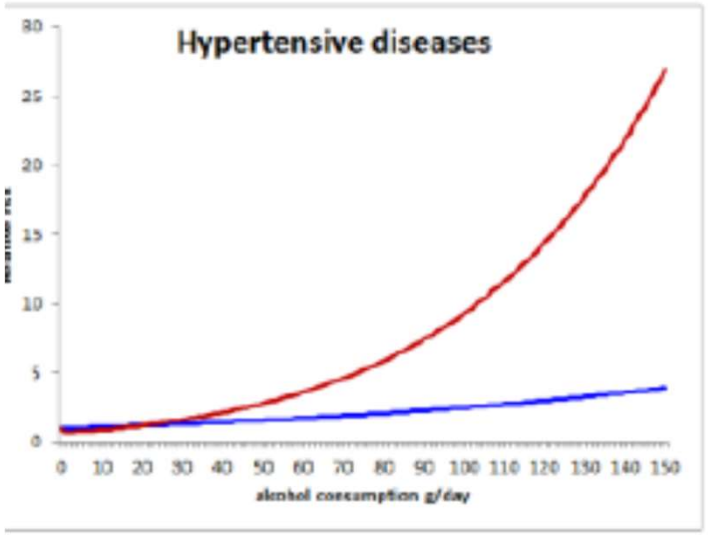


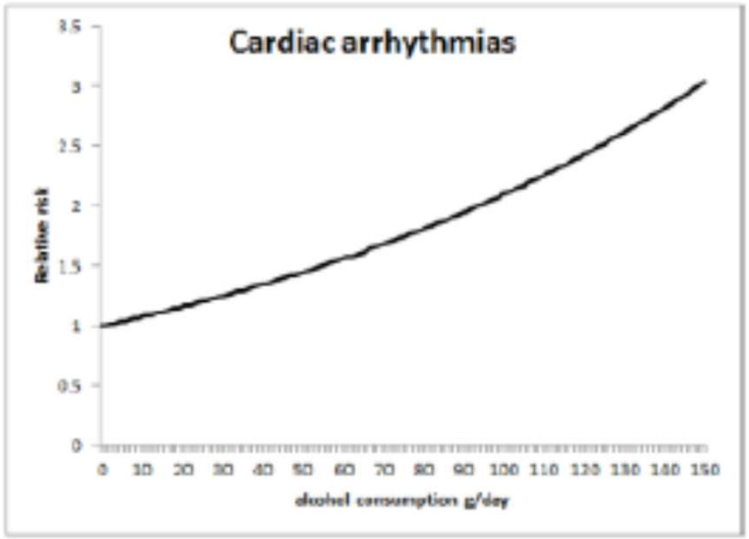


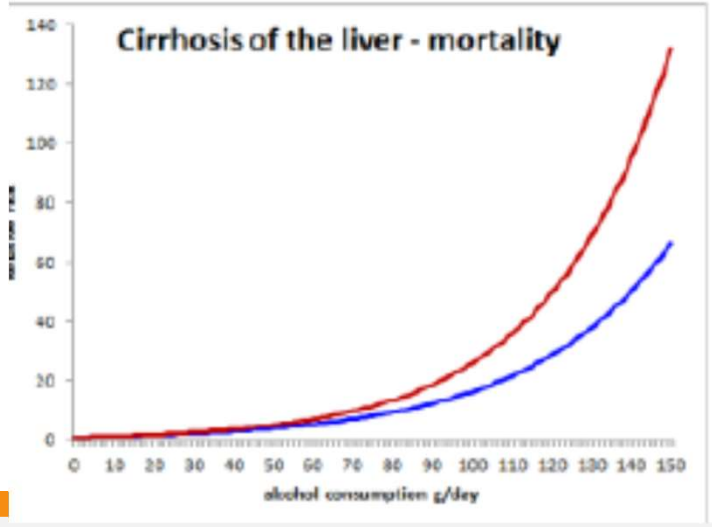


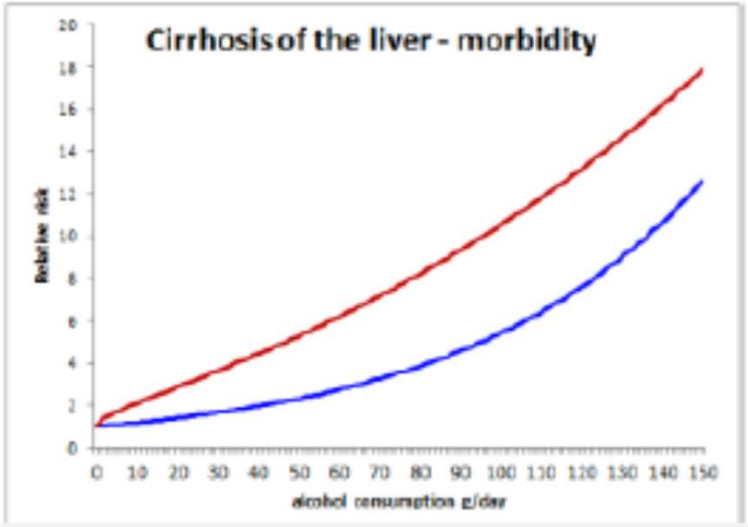


Holmes 2016

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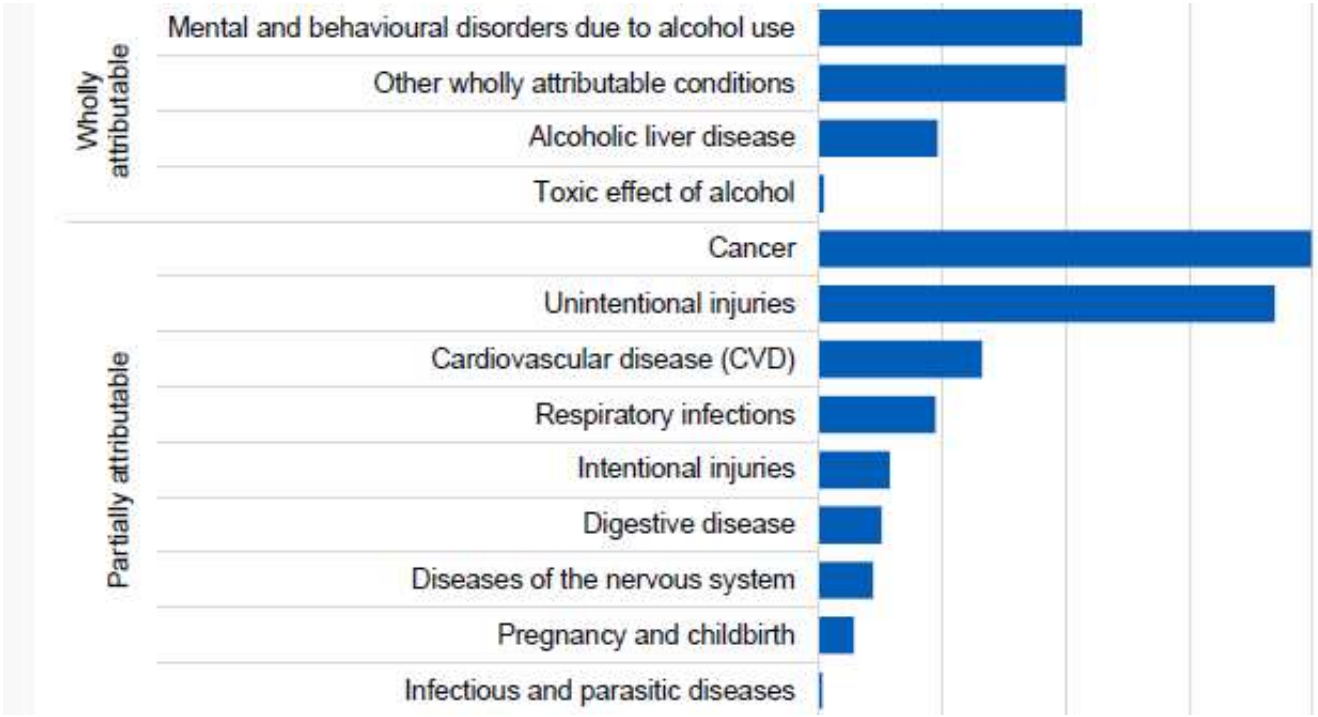
# Alcohol-related hospital admissions for England 2015/2016




339 thousand estimated admissions related to alcohol consumption (Narrow measure). 2.1% of all hospital admissions

1.1 million estimated admissions related to alcohol consumption (broad measure). 7.0% of all hospital admissions

Statistics on Alcohol England, 2017

# Markers of alcohol use

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- ***Gamma*-glutamyl transferase (GGT)**
  - Sensitivity of 50 to 70% in the detection of high levels of alcohol consumption in the last 1 to 2 months and a specificity of 75 to 85%
  - False positive with hepatitis, cirrhosis, cholestatic jaundice, metastatic carcinoma, treatment with simvastatin and obesity
- **Mean corpuscular volume**
  - Sensitivity of 25 to 52% and specificity of 85 to 95% in the detection of alcohol misuse. It remains elevated for 1 to 3 months after abstinence
  - False positives in vitamin B12 and folate deficiency, pernicious anaemia, pregnancy and phenytoin
- **Carbohydrate-deficient transferrin (CDT)**
  - Greater specificity (80 to 98%) than other biomarkers for heavy alcohol consumption
  - Only a few causes of false positive results (severe liver disease, chronic active hepatitis)

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# NICE guidelines monitoring liver disease

- Maddrey's discriminant function* of 32 or more indicate that people with severe alcohol-related hepatitis may need corticosteroid treatment
- Complete Model for End-Stage Liver Disease (MELD**) score every 6 months for people with compensated cirrhosis.
- MELD score of 12 or more indicates that the person is at high risk of complications of cirrhosis

*4.6 x [prothrombin time – control time (seconds)] + bilirubin in mg/dl.

**Includes creatinine / INR/Bilirubin/history of dialysis (www.mdcalc.com)

Alcohol-use disorders: diagnosis and management of physical complications [CG100]
Cirrhosis in over 16s: assessment and management NICE guideline [NG50]

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# Interventions for harmful drinking and mild alcohol dependence

- For harmful drinkers and people with mild alcohol dependence, offer a psychological intervention (such as cognitive behavioural therapies, behavioural therapies or social network and environment-based therapies) focused specifically on alcohol-related cognitions, behaviour, problems and social networks

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# Assessment for assisted alcohol withdrawal

- For service users who typically drink over 15 units of alcohol per day, and/or who score 20 or more on the AUDIT, consider offering:
  - An assessment for and delivery of a community-based assisted withdrawal
  - Assessment and management in specialist alcohol services if there are safety concerns about a community-based assisted withdrawal

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# Consider inpatient if one or more of following present

- Drink over 30 units of alcohol per day
- Have a score of more than 30 on the SADQ
- Have a history of epilepsy, or experience of withdrawal-related seizures or delirium tremens during previous assisted withdrawal programmes
- Need concurrent withdrawal from alcohol and benzodiazepines
- Drink between 15 and 30 units of alcohol per day and have:
  - A significant learning disability or cognitive impairment
  - Significant psychiatric or physical comorbidities (for example, chronic severe depression, psychosis, malnutrition, congestive cardiac failure, unstable angina, chronic liver disease)
- Consider a lower threshold for inpatient or residential assisted withdrawal in vulnerable groups, for example, homeless and older people

SADQ = Severity of Alcohol Dependence Questionnaire

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# Regimes to use

- Fixed-dose or symptom-triggered medication regimens can be used in assisted withdrawal programmes in inpatient or residential settings
- If a symptom-triggered regimen is used, all staff should be competent in monitoring symptoms effectively and the unit should have sufficient resources to allow them to do so frequently and safely
- Prescribe and administer medication for assisted withdrawal within a standard clinical protocol. The preferred medication for assisted withdrawal is a benzodiazepine (chlordiazepoxide or diazepam)
- **Local guidelines will vary in treatments used**

# Typical Chlordiazepoxide regime

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| DATE | 9am | 1pm | 6pm | 10pm | Total |
|---|---|---|---|---|---|
| | 20mg | 20mg | 20mg | 20mg | 80mg |
| | 20mg | 20mg | 20mg | 20mg | 80mg |
| | 20mg | 20mg | 20mg | 20mg | 80mg |
| | 15mg | 15mg | 15mg | 15mg | 60mg |
| | 10mg | 10mg | 10mg | 10mg | 40mg |
| | 5mg | 5mg | 5mg | 5mg | 20mg |
| | Nil | 5mg | Nil | 5mg | 10mg |

# Other medications

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- Ensure that Chlordiazepoxide 10-20mg PRN max QDS is available
- Seizures – Diazepam per rectum 10–20 mg, repeated once after 10–15 minutes if required /Buccal Midazolam (10 mg, repeated once after 10 minutes if necessary)
- Consider Zopiclone 7.5mg nocte PRN for insomnia. This should be for a maximum of 4 days to avoid risk of misuse or dependence
- Medication to treat nausea and vomiting (e.g. Metoclopramide 10mg tds), diarrhoea (Loperamide 2-4mg, max 16mg daily) or skin itching (Loratadine 10mg od) may be required

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# Some potential complications during alcohol detoxification

- Seizures
- Delirium Tremens
- Wernicke encephalopathy-  Korsakoff syndrome

# Seizures

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- Highest risk in first 72 hours after stopping drinking
- Prevention is better than cure so ensure adequate dosing with Chlordiazepoxide and regular monitoring
- Administer appropriate first aid and undertake necessary actions to maintain client's airway and general safety in the event of a seizure
- If the seizure continues for longer than 5 minutes can use Diazepam per rectum 10–20 mg, repeated once after 10–15 minutes if required /Buccal Midazolam (10 mg, repeated once after 10 minutes if necessary)
- If the seizure continues for longer than a further 5 minutes, or there are other concerns call the crash team / ambulance.
- To prevent further seizures review and increase if necessary the dose of Chlordiazepoxide

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# Delirium Tremens

- Highest risk around 72 hours after stopping drinking
- An acute confusional state and medical emergency therefore refer urgently to medical colleagues for medical admission
- Offer oral Lorazepam in the first instance. If symptoms persist or medication is refused consider parenteral Lorazepam, Haloperidol or Olanzapine (NICE recommended but unlicensed indications for these medications)
- Ensure Pabrinex is given to treat any underlying Wernicke's encephalopathy

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# Wernicke encephalopathy and Korsakoff syndrome

- Wernicke encephalopathy is an acute, potentially reversible neurological disorder
- Deficiency/depletion of thiamine
- Incidence rates in Western countries—up to 12.5% in patients with alcohol problems
- When untreated about 80% of patients with this condition develop Korsakoff syndrome
- Korsakoff syndrome characterised by global amnesia.
  - Patients have severe deficits in memory for new material (despite sparing of general intelligence) and in gait and balance, short-term memory and visuoperceptual implicit learning
  - may also have prefrontal dysfunction – difficulties with problem solving, working memory, cognitive flexibility, perseverative responding, and self-regulation

Zahr et al. 2011

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# Symptoms of Wernicke Encephalopathy

- Classic triad is ocular motor abnormalities, cerebellar dysfunction, and altered mental state
- Only 20% of patients present with the full triad
  - 30% of those only presented with altered mental state
- Altered mental state occurs in 80%
  - mental sluggishness, apathy, impaired awareness of an immediate situation, an inability to concentrate, confusion or agitation, hallucinations, behavioral disturbances mimicking an acute psychotic disorder, or coma
- Ocular motor abnormalities occur in 30%
  - nystagmus or ophthalmoplegia
- Cerebellar dysfunction occur in 25% of patients
  - loss of equilibrium, incoordination of gait, trunk ataxia, dysdiadochokinesia and, occasionally, limb ataxia or dysarthria

Zahr et al. 2011

# Use of thiamine

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- Offer prophylactic oral thiamine to harmful or dependent drinkers:
  - if they are malnourished or at risk of malnourishment **or**
  - if they have decompensated liver disease **or**
  - if they are in acute withdrawal **or**
  - before and during a planned medically assisted alcohol withdrawal.
- Offer prophylactic parenteral thiamine followed by oral thiamine to harmful or dependent drinkers:
  - if they are malnourished or at risk of malnourishment **or**
  - if they have decompensated liver disease
- **and in addition**
  - attend an emergency department **or** are admitted to hospital acutely
- Offer parenteral thiamine to people with suspected Wernicke's encephalopathy
  - Parenteral thiamine should be given for a minimum of 5 days, unless Wernicke's encephalopathy is excluded. Oral thiamine should follow parenteral therapy

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# Wernicke Syndrome followed by Korsakoff Syndrome

A Five stage process of recovery has been described

1. Medical stabilisation and management of the encephalopathy.
2. A few weeks of relatively fast improvement
3. Gradual improvement may take as long as 3 years
4. Strategies are employed to optimise independence in the context of residual cognitive damage
5. Progressive socialisation and relapse prevention

Wilson 2011

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# Interventions for moderate and severe alcohol dependence

- After a successful withdrawal for people with moderate and severe alcohol dependence consider
  - Acamprosate
  - Naltrexone
  - These to be used  with psychological intervention (cognitive behavioural therapies, behavioural therapies or social network and environment-based therapies) focused specifically on alcohol misuse

# Data from animal studies Acamprosate

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- Decreases the withdrawal evoked release of glutamate
- Decreases ethanol-intake behaviour
- Decrease is maintained over repeated cycles of ethanol exposure and withdrawal
- Mutant mice with increased glutamate levels with higher ethanol consumption respond better to Acamprosate than wild mice
- Neurotoxicity in Hippocampal cell cultures obtained during ethanol withdrawal reduced by Acamprosate

Oka 2013

Health Education England

# Use of disulfiram

- After a successful withdrawal for people with moderate and severe alcohol dependence, consider offering disulfiram in combination with a psychological intervention to service users who:
  - have a goal of abstinence but for whom acamprosate and oral naltrexone are not suitable, **or**
  - prefer disulfiram and understand the relative risks of taking the drug

# Disulfiram

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- Irreversible inactivation of liver ALDH and hence the intracellular acetaldehyde concentration rises
- High levels of acetaldehyde account for the symptoms of disulfiram-alcohol reaction
- Disulfiram inhibits the conversion of dopamine to noradrenaline
- Depletion of noradrenaline in the heart and blood vessels facilitates action of acetaldehyde (flushing tachycardia and hypotension)

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# Naltrexone

- Long acting specific opioid antagonist.
- Competitively binds to receptors in CNS and PNS hence blocking effects of (endogenous and exogenous) opioids.
- Assumption is that alcohol leads to stimulation of the endogenous opioid system and naltrexone affects this process
- Nalmefene similar but also partial agonist activity at the κ receptor

# Pharmacological treatments alcohol dependence summary

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| | Lapsing to alcohol consumption | Relapse to heavy drinking | Other Effects |
|---|---|---|---|
| Acamprosate | Significant but small effect (RR 0.83) | Significantly less (RR 0.90) | |
| Naltrexone | No significant effect | Significant but small effect (RR 0.83) | . |
| Disulfiram (Quality of evidence not as good compared to Acamprosate/ Naltrexone) | No significant effect | See descriptions in Other Effects column | (Compared with Acamprosate /Disulfiram)<br>**Increase**<br>Time until first drank any alcohol ( vs A)<br>Time to first heavy drinking day ( vs N)<br>Number of abstinent days ( vs N)<br>**Decrease**<br>The amount of alcohol consumed ( vs A)<br>Number of drinking days ( vs A) |

No clear advantage of combination of Acamprosate and Naltrexone over either drug alone

NICE 2011

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# Review

- Calculation of units / pharmacology
- Epidemiology
- Health consequences
- Dependence/ harmful use/ hazardous use
- Treatment issues

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# Substance Misuse

## MCQs

1. Which of the following statements about Disulfiram is false:

A. Previous history of CVA is a contraindication

B. Disulfiram use will result in an decrease in accumulation of acetaldehyde in the blood stream

C. A loading dose can be used for initiation

D. Disulfiram may have a role in the treatment of cocaine dependence

E. Hepatic cell damage is a recognised adverse effect of Disulfiram

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# Substance Misuse

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# Substance Misuse

## MCQs

2. The following are true of Wernicke Encephalopathy except:

A. Classic triad is ocular motor abnormalities, cerebellar dysfunction, and altered mental state

B. Only 20% of patients present with the full triad

C. Altered mental state occurs in 40%

D. Altered mental state symptoms include: mental sluggishness, apathy, impaired awareness of an immediate situation, an inability to concentrate, confusion or agitation

E. Ocular motor abnormalities occur in 30%

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# Substance Misuse

## MCQs

2. The following are true of Wernicke Encephalopathy except:

A. Classic triad is ocular motor abnormalities, cerebellar dysfunction, and altered mental state

B. Only 20% of patients present with the full triad

**C. Altered mental state occurs in 40%**

D. Altered mental state symptoms include: mental sluggishness, apathy, impaired awareness of an immediate situation, an inability to concentrate, confusion or agitation

E. Ocular motor abnormalities occur in 30%

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# Substance Misuse

## MCQs

- 3. Which of the following is not based on Nice Guidelines about the need to consider inpatient setting for alcohol detoxification:

  A. Drink over 50 units of alcohol per day

  B. Have a score of more than 30 on the Severity of Alcohol Dependence Questionnaire

  C. Have a history of epilepsy, or experience of withdrawal-related seizures or delirium tremens during previous assisted withdrawal programmes

  D. Need concurrent withdrawal from alcohol and benzodiazepines

  E. Consider a lower threshold for inpatient or residential assisted withdrawal in vulnerable groups, for example, homeless and older people

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# Substance Misuse

## MCQs

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# Substance Misuse

## MCQs

4. Features required for a diagnosis of dependence within ICD 10 include the following except:

A. A strong desire or sense of compulsion to take the substance;

B. Difficulties in controlling substance-taking behaviour in terms of its onset, termination, or levels of use;

C. A physiological withdrawal state when substance use has ceased or have been reduced, as evidenced by: the characteristic withdrawal syndrome for the substance; or use of the same (or closely related) substance with the intention of relieving or avoiding withdrawal symptoms;

D. Evidence of tolerance, such that increased doses of the psychoactive substance are required in order to achieve effects originally produced by lower doses

E. Returning to substance use after a period of abstinence leads to more rapid reappearance of features of dependence than with non-dependent individuals

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# Substance Misuse

## MCQs

4. Features required for a diagnosis of dependence within ICD 10 include the following except:

A. A strong desire or sense of compulsion to take the substance;

B. Difficulties in controlling substance-taking behaviour in terms of its onset, termination, or levels of use;

C. A physiological withdrawal state when substance use has ceased or have been reduced, as evidenced by: the characteristic withdrawal syndrome for the substance; or use of the same (or closely related) substance with the intention of relieving or avoiding withdrawal symptoms;

D. Evidence of tolerance, such that increased doses of the psychoactive substance are required in order to achieve effects originally produced by lower doses

**E. Returning to substance use after a period of abstinence leads to more rapid reappearance of features of dependence than with non-dependent individuals**

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# Substance Misuse

## MCQs

5. The following are correct calculation of units of alcohol (percentages are in vol/vol) corrected to nearest whole number:

A. 750 mls of 11% wine is 8 units

B. 6 Litres of 4.5% cider is 18 units

C. 5 cans of 330 mls of 4.8% lager is 8 units

D. 3 cans of 440 mls of 7.5% strong lager is 10 units

E. 2 bottles of 700 mls of 17% fortified wine is 24 units

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# Substance Misuse

## MCQs

5. The following are correct calculation of units of alcohol (percentages are in vol/vol) corrected to nearest whole number:

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# Substance Misuse EMIs

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*Drugs used in Alcohol Dependence:*

A. Disulfiram

B. Acamprosate

C. Naltrexone

D. Nalmefene

E. Diazepam

F. Oxazepam

G. Lorazepam

H. Vitamin B compound strong

I. Thiamine

J. Baclofen

1a. Which medication may mediates its effect via antagonism of glutamate

1b. Which medication used for detoxification should be avoided in patients with impaired liver function

1c. Which medication acts as a partial agonist on Kappa opioid receptors

# Substance Misuse EMIs

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1b. Which medication used for detoxification should be avoided in patients with impaired liver function

1c. Which medication acts as a partial agonist on Kappa opioid receptors

# Substance Misuse EMIs

NHS
Health Education England

*Investigations for people with alcohol use*

A. Gamma-glutamyl transferase (GGT)

B. Mean corpuscular volume

C. Carbohydrate-deficient transferrin (CDT)

D. Total bilirubin

E. Albumin

F. INR

G. Magnesium

H. Globulin

I. Alkaline phosphatase

J. Platelet Count

2a. This marker has Sensitivity of 50 to 70% in the detection of high levels of alcohol consumption in the last 1 to 2 months but false positive with hepatitis, cirrhosis, cholestatic jaundice, metastatic carcinoma, treatment with simvastatin and obesity

2b. Reduction in this value can result in an increase in a Child Pugh score

2c. A reduction in this can lead to increased risk of seizures and can be related to use of proton pump inhibitors

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# Substance misuse module

Any Questions?

Thank you.