# Alcohol use disorders: diagnosis and clinical management of alcohol-related physical complications

## NICE guideline Draft for consultation, September 2009

If you wish to comment on this version of the guideline, please be aware that all the supporting information and evidence is contained in the full version.

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#### Introduction

In the UK, it is estimated that 24% of men and 13% of women drink in a hazardous or harmful way<sup>1</sup> (for definitions of harmful and hazardous drinking see page 7). Levels of hazardous and harmful drinking are lowest in the central and eastern regions of England (21–24% of men and 10–14% of women). They are highest in the north (26–28% of men, 16–18% of women)<sup>1</sup>. Hazardous and harmful drinking are commonly encountered among hospital attendees; 12% of accident and emergency (A&E) department attendances are directly related to alcohol<sup>2</sup> while 20% of patients admitted to hospital for illnesses unrelated to alcohol are drinking at potentially hazardous levels<sup>3</sup>.

Continued hazardous and harmful drinking can result in alcohol dependence and increased tolerance. An abrupt reduction in alcohol intake in these people may result in development of alcohol withdrawal syndrome. In addition, persistent drinking at hazardous and harmful levels can result in damage to almost every organ or system of the body. Alcohol-attributable conditions include acute alcohol withdrawal and delirium tremens, liver damage including hepatitis and cirrhosis, acute and chronic pancreatitis, and Wernicke's encephalopathy. Key areas in the investigation and management of these conditions in adults and young people (aged 10 years and older) are covered in this guideline.

This is one of three pieces of NICE guidance addressing alcohol-related problems among people aged 10 years and older. The others are:

 Alcohol use disorders: preventing the development of hazardous and harmful drinking (publication expected March 2010). Public health guidance on the price, advertising and availability of alcohol, how best to detect alcohol misuse in and outside primary care, and brief interventions to manage it in these settings.

<sup>&</sup>lt;sup>1</sup> NHS Information Centre (2009) Statistics on Alcohol: England, 2009. London: Health and Social Care Information Centre

Social Care Information Centre <sup>2</sup> Pirmohamed M, Brown C, Owens L et al. (2000) The burden of alcohol misuse on an innercity general hospital. QJM 93:291-295

<sup>&</sup>lt;sup>3</sup> Royal College of Physicians (2001) Alcohol - can the NHS afford it? Recommendations for a coherent alcohol strategy for hospitals. London: Royal College of Physicians Alcohol use disorders: physical complications: NICE guideline DRAFT (September 2009)

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 Alcohol use disorders: diagnosis and clinical management of harmful drinking and alcohol dependence (publication expected January 2011). A clinical guideline covering identification, assessment, pharmacological and psychological/psychosocial interventions, and the prevention and management of neuropsychiatric complications.

The guideline will assume that prescribers will use a drug's summary of product characteristics to inform decisions made with individual patients.

#### Patient-centred care

This guideline offers best practice advice on the care of adults and young people with alcohol-related physical complications.

Treatment and care should take into account people's needs and preferences. People with alcohol-related physical complications should have the opportunity to make informed decisions about their care and treatment, in partnership with their healthcare professionals. If patients do not have the capacity to make decisions, healthcare professionals should follow the Department of Health guidelines – 'Reference guide to consent for examination or treatment' (2001) (available from <a href="www.dh.gov.uk">www.dh.gov.uk</a>). Healthcare professionals should also follow the code of practice that accompanies the Mental Capacity Act (summary available from <a href="www.publicguardian.gov.uk">www.publicguardian.gov.uk</a>).

If the patient is under 16, healthcare professionals should follow the guidelines in 'Seeking consent: working with children' (available from <a href="https://www.dh.gov.uk">www.dh.gov.uk</a>).

Good communication between healthcare professionals and patients is essential. It should be supported by evidence-based written information tailored to the patient's needs. Treatment and care, and the information patients are given about it, should be culturally appropriate. It should also be accessible to people with additional needs such as physical, sensory or learning disabilities, and to people who do not speak or read English.

If the patient agrees, families and carers should have the opportunity to be involved in decisions about treatment and care.

Families and carers should also be given the information and support they need.

Care of young people in transition between paediatric and adult services should be planned and managed according to the best practice guidance described in 'Transition: getting it right for young people' (available from www.dh.gov.uk).

#### **Key priorities for implementation**

- Offer admission to hospital for medically assisted withdrawal from alcohol, people with, or who are assessed to be at high risk of developing, alcohol withdrawal seizures or delirium tremens. [1.1.1.1]
- For people in acute alcohol withdrawal, follow a symptom-triggered regimen for drug therapy if 24-hour assessment and monitoring are available. [1.1.3.1]
- Ensure that staff caring for people in acute alcohol withdrawal are trained in the assessment and monitoring of withdrawal symptoms and signs.
   [1.1.6.2]
- Refer for consideration for assessment for liver transplant a person who still
  has decompensated liver disease after best management and 3 months'
  abstinence, if they are otherwise suitable for liver transplantation. [1.3.2.1]
- Refer people with pain from chronic alcohol-related pancreatitis to a specialist centre for multidisciplinary assessment. [1.4.2.1]

#### 1 Guidance

The following guidance is based on the best available evidence. The full guideline ([add hyperlink]) gives details of the methods and the evidence used to develop the guidance.

In this guideline, 'harmful drinking' refers to a pattern of drinking alcohol that causes harm to a person's health or wellbeing. The harm may be physical, psychological or social. 'Hazardous drinking' refers to a pattern of drinking that increases the risk of harmful consequences for the person. 'Alcohol dependence' is defined as a cluster of behavioural, cognitive and physiological factors that typically include a strong desire to drink alcohol and difficulties in controlling its use. Someone who is alcohol-dependent will keep drinking, despite harmful consequences. They will also give alcohol a higher priority than other activities and obligations. 'Medically assisted alcohol withdrawal' refers to the deliberate withdrawal from alcohol by a dependent drinker under the supervision of medical staff. Prescribed medication may be needed to relieve the symptoms. It can be carried out at home or in a hospital or other inpatient facility.

#### 1.1 Acute alcohol withdrawal

#### 1.1.1 Indications for admission to hospital care

- 1.1.1.1 Offer admission to hospital for medically assisted withdrawal from alcohol, people with, or who are assessed to be at high risk of developing, alcohol withdrawal seizures or delirium tremens.
- 1.1.1.2 For people who are alcohol dependent but not admitted to hospital, offer advice to avoid a sudden reduction in alcohol intake and information on how to access appropriate support services.
- 1.1.1.3 Consider a lower threshold for admitting certain vulnerable people for unplanned medically assisted withdrawal (for example, people who are frail, have cognitive impairment or multiple comorbidities,

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- lack social support, have learning difficulties or are aged 16 or 17 years).
- 1.1.1.4 Admit to hospital for physical and psychosocial assessment, young people under the age of 16 years with acute alcohol withdrawal.

#### 1.1.2 Treatment for acute alcohol withdrawal

- 1.1.2.1 Offer a benzodiazepine<sup>4</sup>, clomethiazole<sup>5</sup> or carbamazepine<sup>6</sup> to treat the symptoms of acute alcohol withdrawal.
- 1.1.2.2 Offer hepatology advice to people with decompensated liver disease who are undergoing treatment for alcohol withdrawal.

#### 1.1.3 Dosing regimens

1.1.3.1 For people in acute alcohol withdrawal, follow a symptom-triggered regimen for drug therapy if 24-hour assessment and monitoring are available.

#### 1.1.4 Management of delirium tremens

1.1.4.1 If delirium tremens develops in a person during treatment for withdrawal, review their management.

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<sup>&</sup>lt;sup>4</sup> Benzodiazpines are used in UK clinical practice in the management of alcohol-related withdrawal symptoms. Diazepam and chlordiazepoxide have UK marketing authorisation for the management of acute alcohol withdrawal symptoms. However, at the time of consultation, alprazolam did not have UK marketing authorisation for this indication. In addition, the SPC advises that benzodiazepines should be used with extreme caution in patients with a history of alcohol abuse. Clobazam did not have UK marketing authorisation for this indication. In addition the SPC states that clobazam must not be used in patients with any history of alcohol dependence (due to increased risk of dependence). Lorazepam did not have UK marketing authorisation for this indication. In addition, the SCP advises that use in individuals with a history of alcoholism should be avoided (due to increased risk of dependence). Informed consent on the use of alprazolam, clobazam and lorazapam in these situations should be obtained and documented.

<sup>&</sup>lt;sup>5</sup> Clomethiazole has UK marketing authorisation for treatment of alcohol withdrawal symptoms where close hospital supervision is also provided. However, the SPC (September 2009) advises caution in prescribing for individuals known to be addiction prone and to outpatient alcoholics. It also advises against prescribing to patients who continue to drink or abuse alcohol. Alcohol combined with clomethiazole particularly in alcoholics with cirrhosis can lead to fatal respiratory depression even with short term use. Clomethiazole should only be used in hospital under close supervision or, in exceptional circumstances, on an outpatient basis by specialist units when the daily dosage must be monitored closely.

<sup>&</sup>lt;sup>6</sup> Carbamazepine is used in UK clinical practice in the management of alcohol-related withdrawal symptoms. At the time of consultation (September 2009), carbamazepine did not have UK marketing authorisation for this indication. Informed consent should be obtained and documented.

1.1.4.2 Offer oral lorazepam<sup>7</sup> to treat delirium tremens in the first instance. If symptoms persist or oral medication is refused, give parenteral lorazepam, haloperidol<sup>8</sup> or olanzapine<sup>9</sup>.

#### 1.1.5 Treatment for seizures

- 1.1.5.1 If alcohol withdrawal seizures develop in a person during treatment for withdrawal, review their management.
- 1.1.5.2 In patients with alcohol withdrawal seizures, use a quick-acting benzodiazepine (such as lorazepam<sup>10</sup>) to reduce the likelihood of further seizure if needed.

#### 1.1.6 Supportive care

- 1.1.6.1 Assess people in acute alcohol withdrawal immediately on admission to hospital.
- 1.1.6.2 Ensure that staff caring for people in acute alcohol withdrawal are trained in the assessment and monitoring of withdrawal symptoms and signs.
- 1.1.6.3 Assess and monitor patients in acute alcohol withdrawal following locally specified protocols. Consider using a tool (such as the

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<sup>&</sup>lt;sup>7</sup> Lorazepam is used in UK clinical practice in the management of delirium tremens. At the time of consultation (September 2009) lorazepam did not have UK marketing authorisation for this indication. Informed consent on the use of lorazepam in this situation should be obtained and documented. In addition, the SCP advises that use in individuals with a history of alcoholism should be avoided (due to increased risk of dependence).

<sup>&</sup>lt;sup>8</sup> Haloperidol is used in UK clinical practice in the management of delirium tremens. At the time of consultation (September 2009) haloperidol did not have UK marketing authorisation for this indication. Informed consent on the use of haloperidol in this situation should be obtained and documented. In addition, the SCP advises caution in patients suffering from conditions predisposing to convulsions, such as alcohol withdrawal.

<sup>9</sup> Olanzapine is used in UK clinical practice in the management of delirium tremens. At the

Olanzapine is used in UK clinical practice in the management of delirium tremens. At the time of consultation (September 2009) olanzapine did not have UK marketing authorisation for this indication. Informed consent on the use of olanzapine in this situation should be obtained and documented. In addition, the SCP advises that the safety and efficacy of intramuscular olanzapine has not been evaluated in patients with alcohol intoxication.

<sup>&</sup>lt;sup>10</sup> Lorazepam is used in UK clinical practice in the management of alcohol withdrawal seizures. At the time of consultation (September 2009) lorazepam did not have UK marketing authorisation for this indication. Informed consent on the use of lorazapam in this situation should be obtained and documented. In addition, the SCP advises that use in individuals with a history of alcoholism should be avoided (due to increased risk of dependence). Alcohol use disorders: physical complications: NICE guideline DRAFT

Clinical Institute Withdrawal Assessment – Alcohol, Revised [CIWA–Ar] scale) as an adjunct to clinical judgement.

#### 1.2 Wernicke's encephalopathy

- 1.2.1.1 Offer prophylactic oral thiamine to harmful drinkers in any of the following situations:
  - if they are malnourished or at risk of malnourishment
  - if they have decompensated liver disease
  - if they are in acute withdrawal
  - before and during a planned detoxification.
- 1.2.1.2 Give prophylactic parenteral thiamine to harmful or dependent drinkers if they are malnourished or at risk of malnourishment and attend an emergency department or are admitted to hospital with an acute illness.

Give parenteral thiamine to people with suspected Wernicke's encephalopathy. Treatment should continue for 5 days unless the person recovers or an alternative diagnosis is made.

#### 1.3 Alcohol-related liver disease

#### 1.3.1 Role of the liver biopsy

- 1.3.1.1 For people with a history of harmful or hazardous drinking, who have abnormal liver function tests, exclude alternative causes of liver disease.
- 1.3.1.2 A clinical diagnosis of alcohol-related liver disease or alcohol-related hepatitis should be confirmed by a specialist experienced in the management of alcohol-related liver disease.
- 1.3.1.3 Take into account the small but definite risks of morbidity and mortality when deciding on the utility of liver biopsy in the

investigation of alcohol-related liver disease or alcohol-related hepatitis. Discuss the benefits and harms of liver biopsy with the patient and ensure informed consent.

1.3.1.4 In people with suspected acute alcohol-related hepatitis, do a liver biopsy to confirm the diagnosis only if the hepatitis is severe enough to require specific therapy such as corticosteroids. Take into account factors such as access and safety.

#### 1.3.2 Referral for consideration of liver transplantation

1.3.2.1 Refer for consideration for assessment for liver transplant a person who still has decompensated liver disease after best management and 3 months' abstinence, if they are otherwise suitable for liver transplantation.

#### 1.3.3 Corticosteroid treatment for alcohol-related hepatitis

1.3.3.1 Treat with corticosteroids<sup>11</sup> people with severe acute alcohol-related hepatitis and a discriminant function of 32 or more.

#### 1.3.4 Nutritional support for alcohol-related hepatitis

1.3.4.1 Provide enteral nutritional support to people with acute alcohol-related hepatitis.

#### 1.4 Alcohol-related pancreatitis

#### 1.4.1 Diagnosis of chronic pancreatitis

1.4.1.1 Use the combination of symptoms, an imaging modality to determine pancreatic structure and tests of pancreatic exocrine and endocrine function to inform a diagnosis of chronic alcohol-related pancreatitis.

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<sup>&</sup>lt;sup>11</sup> Corticosteroids are used in UK clinical practice in the management of severe alcohol-related hepatitis. At the time of consultation (September 2009), prednisolone and methylprednisolone did not have UK marketing authorisation for this indication. Informed consent should be obtained and documented.

1.4.1.2 Use computed tomography as the first-line imaging modality for the diagnosis of chronic alcohol-related pancreatitis.

### 1.4.2 Pancreatic surgery versus endoscopy for chronic pancreatitis

- 1.4.2.1 Refer people with pain from chronic alcohol-related pancreatitis to a specialist centre for multidisciplinary assessment.
- 1.4.2.2 Offer surgery, in preference to endoscopy, to people with pain from large-duct (obstructive) chronic pancreatitis.
- 1.4.2.3 Offer people with poorly controlled pain from small-duct (nonobstructive) chronic alcohol related pancreatitis coeliac axis block, splanchnicectomy or surgery.

#### 1.4.3 Prophylactic antibiotic treatment for acute pancreatitis

- 1.4.3.1 Do not give prophylactic antibiotics to people with mild acute alcohol-related pancreatitis.
- 1.4.3.2 Offer prophylactic antibiotics to people with severe acute alcohol-related pancreatitis.

#### 1.4.4 Nutritional support for acute alcohol-related pancreatitis

- 1.4.4.1 Nutritional support for people with acute alcohol-related pancreatitis should be offered:
  - early (on diagnosis)
  - enterally rather than parenterally where possible.

#### 1.4.5 Enzyme supplementation for chronic pancreatitis

- 1.4.5.1 Offer pancreatic enzyme supplements to improve steatorrhoea and nutritional status in people with exocrine pancreatic insufficiency secondary to alcohol-related chronic pancreatitis.
- 1.4.5.2 Do not prescribe pancreatic enzyme supplements if pain is the only symptom of chronic alcohol-related pancreatitis.

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#### Notes on the scope of the guidance

NICE guidelines are developed in accordance with a scope that defines what the guideline will and will not cover. The scope of this guideline is available from <a href="http://guidance.nice.org.uk/CG/Wave15/77">http://guidance.nice.org.uk/CG/Wave15/77</a>.

#### How this guideline was developed

NICE commissioned the National Collaborating Centre for Chronic Conditions (now the National Clinical Guideline Centre for Acute and Chronic Conditions) to develop this guideline. The Centre established a guideline development group (see appendix A), which reviewed the evidence and developed the recommendations. An independent guideline review panel oversaw the development of the guideline (see appendix B).

There is more information about how NICE clinical guidelines are developed on the NICE website (<a href="www.nice.org.uk/guidelinesprocess">www.nice.org.uk/guidelinesprocess</a>). A booklet, 'How NICE clinical guidelines are developed: an overview for stakeholders, the public and the NHS' (fourth edition, published 2009), is available from NICE publications (phone 0845 003 7783 or email publications@nice.org.uk and quote reference N1739).

#### 2 Implementation

NICE has developed tools to help organisations implement this guidance (see www.nice.org.uk/CGXX)'.

#### 3 Research recommendations

The Guideline Development Group has made the following recommendations for research, based on its review of evidence, to improve NICE guidance and patient care in the future. The Guideline Development Group's full set of research recommendations is detailed in the full guideline (see section 5).

#### 3.1 Admission to hospital for acute alcohol withdrawal

What is the clinical and cost effectiveness of admitting patients attending hospital in mild or moderate acute alcohol withdrawal for medically assisted withdrawal and follow up compared with no admission and follow-up for abstinence?

#### Why this is important

Patients presenting at a hospital who are at risk of or have alcohol withdrawal seizures or delirium tremens need admission for medical management. Patients with milder withdrawal are not usually admitted, but given advice and provided with information regarding local outpatient alcohol addiction services. One of the concerns with this model is that the opportunity for intervention may be lost and that many of these patients may never contact addiction services. Given that abstinence is the goal, it may be that admission for these patients maximises the likelihood of achieving this goal. The concerns with admission are that it is costly, the patients may not be motivated and there has been no opportunity for psychological input prior to the medically assisted withdrawal from alcohol.

This study aims to compare the two models of treatment with regard to the primary goal of abstinence. Health economic analysis will aim to determine the cost effectiveness of each approach.

#### 3.2 Dosing regimens for acute alcohol withdrawal

What are the safety and efficacy of symptom-triggered, fixed-dosing and front-loading regimens for the management of acute alcohol withdrawal?

#### Why this is important

Traditionally, acute alcohol withdrawal has been managed by administering medication, typically benzodiazepines, according to a predetermined tapered-dosing schedule over a specified number of days (with the option for additional doses for breakthrough symptoms). This is called fixed-dosing. In contrast, medication can be administered in response to a person's individual signs and symptoms (symptom-triggered) or by giving an initial 'loading' dose (front-loading) in conjunction with a symptom-triggered or 'as required' regimen.

The safety and efficacy of symptom-triggered or front-loading regimens in comparison to the 'traditional' fixed-dose regimen needs to be established in patients admitted to acute hospital settings who undergo unplanned acute alcohol withdrawal. Staff and patients' experiences in conjunction with objective measures of acute alchol withdrawal need to be collected.

#### 3.3 Drugs for the management of alcohol withdrawal

What is the efficacy and cost effectiveness of clomethiazole compared to chlordiazepoxide for the treatment of acute alcohol withdrawal with regard to the outcomes of withdrawal severity, risk of seizures, risk of delirium tremens, length of treatment and patient satisfaction?

#### Why this is important

Clomethiazole has powerful, short-acting, sedative, tranquilizing and anticonvulsant properties which are mediated through an indirect effect on gamma-aminobutyric acid (GABA) receptors in the brain. It has fallen out of favour in many units for the management of acute alcohol withdrawal because of reports of dependence and concerns regarding over-sedation. These have been problems in the outpatient use of clomethiazole, but it has now been restricted to the inpatient setting, where clomethiazole may be of great value.

There are limited studies comparing clomethiazole with other agents. As such, an appropriately powered study comparing clomethiazole to the most widely used alternative agent, chlordiazepoxide, with regard to the outcomes

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described above would help to define the role of this potentially very useful drug.

#### 3.4 Supportive care

What is the clinical and cost effectiveness of interventions delivered in an acute hospital setting by an alcohol specialist nurse compared with those managed through usual care pathways with no input from an specialist nurse?

#### Why this is important

Alcohol-related problems are an important public health problem in the UK. Most patients present to acute NHS trusts, where they receive no specific treatment apart from pharmacological detoxification for alcohol withdrawal. There is an urgent need for adequately powered randomised controlled trials (RCTs) of patients with alcohol-related problems that use objective outcome measures and reproducible treatment modalities. A cohort study (unpublished) has shown that an extended form of brief intervention, delivered by an alcohol specialist nurse in an acute hospital setting was effective in reducing alcohol dependence, alcohol consumption and hospital length of stay. The effectiveness of interventions delivered by alcohol specialist nurse in an acute hospital setting should now be tested in an RCT.

#### 3.5 Wernicke's encepalopathy

What is the clinical and cost effectiveness for the use of parenteral versus oral thiamine in preventing the first onset of Wernicke's encephalopathy in people undergoing medically assisted alcohol withdrawal?

#### Why this is important

Wernicke's encephalopathy has a devastating effect on the sufferer and can occur when people are withdrawing from alcohol. It is thought to be caused by a lack of thiamine due to poor diet and/or absorption at a time of increased requirement for the vitamin (for cerebral functions in particular). Little is known about the mechanisms involved, although there is some theoretical and trial evidence to suggest that parenteral replacement elevates blood levels more quickly than oral replacement. However, it is not known if this is clinically

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significant, and there is no convincing clinical evidence to suggest which route and dose of thiamine is most effective at preventing Wernicke's encephalopathy. This is important as parenteral dosing uses additional resources, is unpleasant for the patient and has a very small risk of anaphylaxis. Having a placebo arm is probably not acceptable, given the risks of significant brain damage.

#### 4 Other versions of this guideline

#### 4.1 Full guideline

The full guideline, 'Alcohol use disorders: diagnosis and clinical management of alcohol-related physical complications' contains details of the methods and evidence used to develop the guideline. It is published by the National Clinical Guidelines Centre for Acute and Chronic Conditions (formerly the National Collaborating Centre for Chronic Conditions), and is available from www.rcplondon.ac.uk/clinical-standards/ncgc and our website (www.nice.org.uk/CGXXfullguideline). [Note: these details will apply to the published full guideline.]

#### 4.2 Quick reference guide

A quick reference guide for healthcare professionals is available from www.nice.org.uk/CGXXquickrefguide

For printed copies, phone NICE publications on 0845 003 7783 or email publications@nice.org.uk (quote reference number N1XXX). [Note: these details will apply when the guideline is published.]

#### 4.3 'Understanding NICE guidance'

A summary for patients and carers ('Understanding NICE guidance') is available from www.nice.org.uk/CGXXpublicinfo

For printed copies, phone NICE publications on 0845 003 7783 or email publications@nice.org.uk (quote reference number N1XXX). [Note: these details will apply when the guideline is published.]

We encourage NHS and voluntary sector organisations to use text from this booklet in their own information about alcohol-related physical complications.

#### 5 Related NICE guidance

#### **Published**

Interventions in schools to prevent and reduce alcohol use among children and young people. NICE public health guidance 7 (2007). Available from <a href="https://www.nice.org.uk/PH007">www.nice.org.uk/PH007</a>

Community-based interventions to reduce substance misuse among vulnerable and disadvantaged children and young people. NICE public health guidance 4 (2007). Available from <a href="https://www.nice.org.uk/PHI004">www.nice.org.uk/PHI004</a>

Nutrition support in adults: oral nutrition support, enteral tube feeding and parenteral nutrition. NICE clinical guideline 32 (2006). Available from <a href="https://www.nice.org.uk/CG032">www.nice.org.uk/CG032</a>

#### **Under development**

NICE is developing the following guidance (details available from <a href="https://www.nice.org.uk">www.nice.org.uk</a>):

- School, college and community-based personal, social and health education focusing on sex and relationships and alcohol education. NICE public health guidance (publication expected September 2009).
- Alcohol-use disorders in adults and young people: prevention. NICE public health guidance (publication expected March 2010).
- Care of pregnant women with complex social factors. NICE clinical guideline (publication expected June 2010).
- Alcohol-use disorders: the management of alcohol dependence and related brain damage. NICE clinical guideline (publication expected January 2011).

#### 6 Updating the guideline

NICE clinical guidelines are updated so that recommendations take into account important new information. New evidence is checked 3 years after publication, and healthcare professionals and patients are asked for their views; we use this information to decide whether all or part of a guideline needs updating. If important new evidence is published at other times, we may decide to do a more rapid update of some recommendations.

#### **Appendix A: The Guideline Development Group**

#### **Anthony Rudd (GDG Chair)**

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#### **Appendix B: The Guideline Review Panel**

The Guideline Review Panel is an independent panel that oversees the development of the guideline and takes responsibility for monitoring adherence to NICE guideline development processes. In particular, the panel ensures that stakeholder comments have been adequately considered and responded to. The panel includes members from the following perspectives: primary care, secondary care, lay, public health and industry.

#### [NICE to add]

[Name; style = Unnumbered bold heading]

[job title and location; style = NICE normal]

#### **Appendix C: The algorithms**

These are published in a separate file.