National Institute for Health and Clinical Excellence

Alcohol use disorders – clinical management
Guideline Consultation Comments Table
17 September – 12 November 2009

Comment No.	Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
1.	SH	Alder Hey Children's NHS Foundation Trust	6		General	General	CAMHS LAC figures on referrals where a Looked After Child has a parent with a drug or alcohol problem since Jan 09 averages at 64%	Thank you for your comment.
2.	SH	Alder Hey Children's NHS Foundation Trust	7		General	General	Very adult centred document – need to have figures re: gender breakdown – importance in terms of how males and females respond to alcohol physiologically.	Thank you for your comment. The literature was searched for information pertaining children as well as adults although there was a paucity of data. While males and females respond differently to alcohol and have different susceptibilities to the harmful effects, this impacts on sensible limits and not the clinical management of the end organ damage.
3.	SH	Alder Hey Children's NHS Foundation Trust	8		General	General	Need more information on age as it appears some of these physical consequences are being manifested in much younger clients. Figures form A&E of admission of children/young people for alcohol related problems – CAMHS LAC at least 2 in last nine months	Thank you for your comment. We considered age throughout the discussions and have made comment when the clinical management of the patient is different because of the age.
4.	SH	Alder Hey Children's NHS Foundation Trust	9		General	General	Cost analysis needs to consider hidden costs like family breakdown and Tran generational alcohol abuse Social return on Investment Analysis (www.nef-consulting.co.uk) No mention of this in the document.	Thank you for your comment. We used a UK NHS and PSS perspective. The methodology advocated by NICE for the cost-effectiveness analyses excludes patient-level costs, considering only direct medical costs.

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							Actuarial statistics – having an alcoholic parent makes you x times more likely to be an alcoholic yourself ???	
5.	SH	Alder Hey Children's NHS Foundation Trust	10		General	General	I couldn't find anything in it about possible increase in Foetal Alcohol syndrome(it's called something else now) I've heard that there is an increase in Learning disability that can be linked with maternal alcohol increase!	Thank you for your comment. The scope of the guideline excluded women who are pregnant.
6.	SH	Royal Pharmaceutical Society of Great Britain	1		General	General	Community Pharmacy – pharmacists, as part of the public health component of the new community pharmacy contractual framework, provide information and advice and participate in health promotion campaigns which could include alcohol. They provide medicine checks with patients on repeat dispensing and, if accredited, medicine usage reviews all of which provide an opportunity to raise the issues around alcohol usage and its effects on medicines and health in general. Certain PCTs have commissioned community pharmacies to provide enhanced services to target alcohol users. These generally involve screening and brief interventions. (E.g. Wirral, Leeds, Lincolnshire and Westminster PCTs). More recently Isle of Wight PCT has developed an enhanced service involving a pilot hepatitis screening and vaccination service in pharmacies using suitably trained staff.	Thank you for your comment. The role of screening and brief intervention is being covered by the Public Health guidance.
7.	SH	Royal	2		Genera	Gene	Pharmacist Specialists – pharmacists	Thank you for your comment.

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		Pharmaceutical Society of Great Britain			l	ral	specialising in addictions such as alcohol are now moving into advanced practice in areas of high addiction such as Glasgow and Clyde. Such post holders will develop the role of pharmaceutical care in relation to alcohol, provide professional support to pharmacies engaged in alcohol services and liaise on pharmacy issues with other health, social and voluntary care organisations involved in alcohol services.	
8.	SH	South Asian Health Foundation	14			Gene ral	Congratulations to the Guideline Development Group for an excellent and thorough document in this important area. SAHF believes that the treatment of alcohol-related disorders is important, not just for ethnic minority groups where problems can present differently, but for the whole population. We also think closer working between different medical groups, eg, gastroenterologists, psychiatrists, alcohol liaiso, public health, needs to be encouraged and resourced.	Thank you for your comment.
9.	SH	The British Association for Parenteral & Enteral Nutrition	3	Appen dices			It is stated that the full scope is at Appendix A but it isn't	Thank you for your comment. The scope has been added to the appendix.
10.	PR	NETSCC, Referee 1	1	Full	general	gene ral	**1.1 Are there any important ways in which the work has not fulfilled the declared intentions of the NICE guideline (compared to its scope – attached)** None	Thank you for your comment.
11.	PR	NETSCC, Referee 1	2	Full	general	gene ral	**2.1 Please comment on the validity of the work i.e. the quality of the methods and**	Thank you for your comment.

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							their application (the methods should comply with NICE's Guidelines Manual available at http://www.nice.org.uk/page.aspx?o=guidelinesmanual). In general, I thought the methods were of good quality, I have a few minor comments on the health economic methods that are listed in the next section.	
12.	PR	NETSCC, Referee 1	10	Full	general	general	**3.1 How far are the recommendations based on the findings? Are they a) justified i.e. not overstated or understated given the evidence? b) Complete? i.e. are all the important aspects of the evidence reflected?** I found the recommendations to be appropriate and justified by the evidence presented.	Thank you for your comment.
13.	PR	NETSCC, Referee 1	11	Full	general	general	**3.2 Are any important limitations of the evidence clearly described and discussed?** Yes. The group has been careful to describe the limitations of the evidence presented.	Thank you for your comment.
14.	PR	NETSCC, Referee 1	12	Full	general	general	**4.1 Is the whole report readable and well presented? Please comment on the overall style and whether, for example, it is easy to understand how the recommendations have been reached from the evidence.** The report is extremely clear, very well presented and easy to read.	Thank you for your comment.

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15.	PR	NETSCC, Referee 1	16	Full	general	general	**4.2 Please comment on whether the research recommendations, if included, are clear and justified.** The research recommendations made are clear and well justified. There were however a few instances when I felt research recommendations could have value, but where none were made.	Thank you for your comment. The GDG are limited to five research recommendations in the NICE guidance.
16.	PR	NETSCC, Referee 2	1	Full	general	general	**1.1 Are there any important ways in which the work has not fulfilled the declared intentions of the NICE guideline (compared to its scope – attached)** No comments given	Thank you for your comment.
17.	PR	NETSCC, Referee 2	2	Full	general	general	**2.1 Please comment on the validity of the work i.e. the quality of the methods and their application (the methods should comply with NICE's Guidelines Manual available at http://www.nice.org.uk/page.aspx?o=guidelinesmanual)** Overall I felt the quality of existing evidence or lack of it sometimes was lost by the time recommendations were made. This have to be clear but sometimes seemed over simplistic	Thank you for your comment.
18.	PR	NETSCC, Referee 2	13	Full	general	general	**4.2 Please comment on whether the research recommendations, if included, are clear and justified.** Given the paucity and quality of research found I was surprised not to find a more general recomendation	Thank you for your comment. All research recommendations are made in accordance with the NICE Technical Manual 2009 and therefore must be written in PICO format. Where a lack of evidence has been found in specific areas the GDG formulated research recommendations.
19.	SH	Alder Hey Children's NHS Foundation	2	Full			[Relates to point 6 – in terms of hidden	This guidance was written taking in the costs of treating the patient. The wider

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		Trust					social costs] Need to consider family issues – where parents have an alcohol or drug problem issues over who is caring for the children needs to be considered as part of a treatment package otherwise a care episode for the children can result. Think Family Policy driver	family was not considered. This may be of more relevance when dealing with the management of dependence rather than the management of acute alcohol withdrawal
20.	SH	Alder Hey Children's NHS Foundation Trust	3	Full			Interaction of these drug treatments for pregnant women and for younger adults (esp. as they discuss 16 year olds)	Thank you for your comment. It is unclear which drugs treatments you refer to. Pregnant women were not in our scope.
21.	SH	Alder Hey Children's NHS Foundation Trust	4	Full			No alternative treatments offered – such as robust nutrional supplementation	Thank you for your comment. We assume best supportive care and consider nutrition as a separate treatment issue when there is evidence of it's effect as a treatment per se.
22.	SH	College of Mental Health Pharmacists	9	Full		Appendices	Could not see the forest plots, too small.	Thank you for your comment. This has been amended.
23.	SH	Lundbeck Ltd	1	Full	General	General	Lundbeck has no comments for this consultation at this stage.	Thank you.
24.	SH	NHS North of Tyne encompassing: Newcastle PCT, North Tyneside PCT, Northumberland Care Trust	1	Full	General	General	In addition to the Comments forwarded on by BALANCE (North East Regional Alcohol office) which are fully supported, the NHS North of Tyne has a number of additional comments which have come in from professionals across the 3 PCO areas which are outlined below. Whilst the NHS North of Tyne supports the publication of the draft guidance 'Alcohol-	Thank you for your comment. Although this comment pertains to the Public Health guidance.

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							use disorders: preventing the development of hazardous and harmful drinking', it would be good in the overview/intro to comment on the impact and possible consequences specific to young people including anti-social behaviour, teenage pregnancy, STIs and health consequences in relation to extensive use and immature liver.	
25.	SH	NHS North of Tyne encompassing: Newcastle PCT, North Tyneside PCT, Northumberland Care Trust	11	Full	General	Overall commentary	Overall, the guidance appears more focussed around health and criminal justice and should be more inclusive of education and other partners. We need to be more transparent about inferences derived from the evidence but not be reticent about using this in practice, as we can be fairly sure that the benefits of using brief interventions with younger people and in a range of settings will be more likely to have positive effects and at the very least, will do no harm, alongside the usual course of action. Therefore, the undertaking of a brief advice approach in a range of settings with a range of age-groups need to be supported, providing it is underpinned by training and support at a local level.	Thank you for your comment. We agree that these issues are important, but pertain to the Public Health guidance.
26.	SH	Royal College of Nursing	7	Full	General	General	In general, there is no reference to the effect of alcohol misuse in the workplace. The majority of people with early alcohol misuse problems are in employment. Although this document is covering the acute and clinical issues for treatment,	Thank you for your comment but the developers believe this pertains to the Public Health guidance.

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							some patients may well be 'in work' and a reference to this and a link to occupational health support should be included. This could include reference to the clinical teams working with the Occupational Health Team and other members of the primary & public health care teams to provide ongoing support.	
27.	SH	Royal College of Paediatrics and Child Health	2	Full	General	General	The College notes that, while this guideline is more relevant for the adult population, alcohol use is alcohol use is increasing in the paediatric population. We think the guideline should cover adolescents and children more specifically, and include studies that discuss a link between early age of alcohol drinking with later alcohol dependency.	Thank you for your comments. Where data was available pertaining to the paediatric population it was reported. The correlation between early age of alcohol intake with later alcohol dependency is being covered by the Mental Health guidance.
28.	SH	Royal College of Paediatrics and Child Health	3	Full	General	General	The interpretation of the evidence by the guideline development group is good.	Thank you for your comment.
29.	SH	Royal College of Paediatrics and Child Health	4	Full	General	General	The College notes that excessive drinking habits and alcohol related illness of parents and carers may negatively affect children within the family.	Thank you for your comment.
30.	SH	Royal College of Paediatrics and Child Health	5	Full	General	General	The College notes that this guideline deals exclusively with the management of physical symptoms. We do note that appropriate psychosocial care should be provided to any child admitted with alcohol poisoning or any alcohol use disorder. We note that these children sometimes fall through the gap between self-harm services and substance misuse services. It therefore should be clear in each ward/department	Thank you for your comment. NICE does not issue guidance on service delivery. The psychosocial care of the child will be covered by the Mental Health guidance.

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							how this group will be managed.	
31.	SH	Royal College of Paediatrics and Child Health	1	Full	General	General / 2	The College notes that the guideline does not cover the identification and effective interventions for alcohol drinkers who are pregnant. (Neither the words pregnancy or pregnant appear in the document.) Pregnant women are a small subsection of the total sum of alcohol misuse, but the effects on the fetus are lifelong and can be devastating. Effective intervention can potentially reduce and even prevent these possibilities. Fetal alcohol spectrum disorder (FASD) is the commonest form of preventable mental disability. (We do note that fetal damage comes bottom of the table on page 2 of damage from chronic alcohol misuse.) The College notes a BMA report on FASD. See British Medical Association Board of Science. Fetal alcohol spectrum disorders: a guide for health care professionals. June 2007 (may be downloaded from http://www.bma.org.uk/images/FetalAlcoholSpectrumDisorders_tcm41-158035.pdf). We recommend that the guideline consider: 1) strategies for identifying pregnant women who are problem drinkers (TWEAK, T-ACE and AUDIT) 2) effective interventions We note there is good clinical evidence for	Thank you for your comment. The scope of the guideline excludes pregnant women. The developers acknowledge this is an area of great concern and have previously referred it to the NICE topic selection committee.

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							both of these. References include: Burd L, Martsolf J, Klug MG, O'Connor E, Peterson M. Prenatal alcohol exposure assessment: multiple embedded measures in a prenatal questionnaire. Neurotoxicology and Teratology. 2003;25(6):675-679. Chang G, Wilkins-Haug L, Berman S, Goetz MA, Behr, Hiley A. Alcohol use and pregnancy: improving identification. Obstetrics & Gynecology. 1998 91(6): 892-898. Dawson DA, Das A, Faden VB, Bhaskar B, Krulewitch CJ, Wesley B. Screening for high- and moderate-risk drinking during pregnancy: a comparison of several TWEAK-based screeners. Alcoholism: Clinical & Experimental Research. 2001;25(9):1342-1349. Russell M, Martier SS, Sokol RJ, Mudar P, Jacobson S and Jacobson J. Detecting risk drinking during pregnancy: a comparison of four screening questionnaires. American Journal of Public Health. 1996 86(10): 1435-1439. An additional reference looks at interventions once an issue is identified with screening: Psychological and/or educational interventions for reducing alcohol consumption in pregnant women and	

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							women planning pregnancy. Cochrane Database of Systematic Reviews. 2009;2. CD004228. doi: 10.1002/14651858.CD004228.pub2 (may be downloaded from http://mrw.interscience.wiley.com/cochrane/clsysrev/articles/CD004228/frame.html)	
32.	SH	Royal College of Physicians	11	Full	General		Overall, the guideline includes an extremely comprehensive literature review. The cost analyses provide an essential background to the evidence of clinical effectiveness or lack of effectiveness of the treatments discussed. This is important as alcohol related health problems are so common and consume so much health resource.	Thank you for your comment.
33.	SH	Royal College of Physicians	2	Full	General	General	The section on liver disease contains no mention of the clinical and cost-effectiveness of betablockers in preventing variceal bleeding, or in screening for hepatomas in patients with cirrhosis. The clinical and cost effectiveness of these are discussed in the review by Kaner E, et al in 2008. http://www.ncl.ac.uk/ihs/assets/pdfs/liverreview.pdf	Thank you for your comment. Due to finite time and budgetary resources, the guidance does not cover all aspects of the care pathway. The GDG prioritised areas for inclusion within the confines of the scope. It was decided that the generic management of end-stage liver disease, regardless of aetiology, would not be covered. The GDG recognise the importance of these issues and have referred it to the NICE topic selection committee.
34.	SH	Royal College of Physicians	3	Full	General	General	The discussion regarding the treatment of alcohol withdrawal, delirium tremens and seizures needs to be set in the modern clinical context. Most detoxifications occur in non-specialist wards in District General Hospitals. They are mainly conducted out of	Thank you for your comment. As NICE do not offer guidance on service delivery the developers are prohibited from recommending the employment of alcohol nurse specialists and alcohol misuse lead consultants. Where applicable the GDG

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							hours. There is a vital need for training of medical and ward nurse staff if there is to be any meaningful discussion of the various dosing regimens. The key people involved in training of staff and in supervision of detoxifications are the alcohol specialist nurses. Research recommendation 3 on page 56, for assessing the clinical and cost-effectiveness of alcohol specialist nurses in acute hospital settings, is laudable. However, there is already good evidence from the Liverpool studies as to their effectiveness, especially in reducing length of stay. It is also manifest that the longer the delay between discharge following in-patient detoxification and follow-up in the community, then the higher the relapse rate. We urge the PDG to recommend: That every acute hospital should have two Alcohol Nurse Specialists (to cover extended hours – remembering problems of alcohol misuse are worse in the evenings and at week-ends). That every acute hospital (i.e. with an A&E) should have a nominated Lead Consultant for combating Alcohol Misuse with 5 Programmed Activity (20 hours) allocated for this role.	have specified the competencies required to carry out a procedure/task rather than the role of the person required to undertake it.
35.	SH	Royal	6	Full	Genera		RPSGB & PharMAG welcomes this and	Thank you for your comment.

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		Pharmaceutical Society of Great Britain			l		related NICE guidance.	
36.	SH	The British Association for Parenteral & Enteral Nutrition	1	Full	General		I read this document in relation to its coverage of nutritional issues and was pleased to see they were included. However, I was surprised to find that there is very little about the management of patients with established cirrhosis with or without decompensation beyond the referral for transplantation issue. I believe that this is an important omission not least because there are important nutritional issues in such patients including questions on optimal amounts and types of nutrient provision.	Thank you for your comment. The developers acknowledge that nutritional issues are important, particularly in relation to the optimal management of patients with decompensated cirrhosis. However, due to finite time and budgetary resources the generic management of cirrhosis was not prioritised for inclusion in the guidance.
37.	SH	The British Association for Parenteral & Enteral Nutrition	2	Full	General		Both Alcoholic hepatitis and Alcoholic pancreatitis are labelled as section 3	Thank you for your comment. This has been amended.
38.	SH	The Society for Acute Medicine	6	Full	General	General	The guidance mentions the need for trained staff, but fails to emphasise the importance of specific alcohol support services in hospitals. Ward et al (2009) found that 58% of hospitals had no formal services. This is despite evidence suggesting that such services are necessary. For example, a randomized controlled trial showed that even screening and referral for brief intervention in an Emergency Department lowered alcohol consumption and reduced reattendance. As stated in the paper by Ward et al (2009), nationally, we are	Thank you for your comment. As NICE do not provide guidance on service delivery the GDG are not able to recommendation the implementation of specific alcohol support services. The use of screening tools and brief interventions are being addressed by the Public Health guidance.

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							missing an opportunity to support this group of patients by failing to provide services, which are proven to benefit them and reduce attendance rates. NICE should not miss this opportunity. [Crawford MJ, Patton R, Touquet R, Drummond C, Byford S, Barrett B, et al. Screening and referral for brief intervention of alcohol misusing patients in an emergency department: a pragmatic randomised controlled trial. Lancet 2004; 364:1334–39.]	
39.	SH	The Society for Acute Medicine	7	Full	General	General	The guidance in general leaves the opportunity to support continued variation in practice and requires more focussed recommendation. Our concern is the guideline in areas lacks focus (see above) and in place sis contradictory which will confuse or hinder frontline practice in what is an epidemic problem. We understand the need for more research but will this be funded and how will this guidance support this vital area.	Thank you for your comment. NICE are unable to guarantee that funding will follow all research recommendations but five of the research recommendations made as part of each NICE clinical guideline go direct to the Priority Strategy Group of the National Institute for Health Research which directs NHS research funding (thereby removing 8-9 months of the scrutiny stages of this organisation). In this way, research priorities are identified based on the gaps identified as part of the reviews of clinical evidence conducted as part of NICE guidance.
40.	SH	Welsh Assembly Government	1	Full	General	General	Thank you for giving the Welsh Assembly Government the opportunity to comment on the above. We have no comments to make	Thank you for your comment.

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							at this stage.	
41.	SH	Alder Hey Children's NHS Foundation Trust	1	Full		5	Page 5 – Safeguarding concerns should override patient's consent. Very little of mention of Safeguarding issues throughout document.	Thank you for your comment. We agree that safeguarding vulnerable children and adults is of great importance. The principles of safeguarding should be adhered to when dealing with these patient populations, but we did not feel that discussion of these principles added to the specific recommendations for the management of the clinical conditions we were referring to.
42.	SH	NHS North of Tyne encompassing: Newcastle PCT, North Tyneside PCT, Northumberland Care Trust	2	Full	Section on cost of alcohol-use disorders	7	It would be helpful to view NI39 data in the context of adults and young people	Thank you for your comment. While the variable rates of admission with alcohol are of interest, the guidance for management of the clinical conditions associated with harmful and hazardous drinking are the same.
43.	SH	NHS North of Tyne encompassing: Newcastle PCT, North Tyneside PCT, Northumberland Care Trust	2a	Full	Section on cost of alcohol-use disorders	7	There needs to be an improved understanding of 'hot spots' which can be masked by data reporting at whole county level and does not clearly identify those areas with significant alcohol related health and social harms	Thank you for your comment. We acknowledge the variation in resource use related to alcohol consumption across the country however we used 'NHS reference costs' to cost interventions which give an average estimate across England and Wales. This is the source preferred by NICE.
44.	SH	Alcohol Use Disorders: Alcohol dependence and harmful alcohol use Guideline Development Group	27	Full		29 line 34	Street homelessness, lack of social support and psychiatric comorbidity are also usually indications for admission.	Thank you for your comment. The question looked at the following possible indicators for admission age, history of a seizure, history of DT, history of severe withdrawal, previous drinking history and breath or blood alcohol level.

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45.	PR	NETSCC, Referee 1	15	Full	A1	178	**4.1 Is the whole report readable and well presented? Please comment on the overall style and whether, for example, it is easy to understand how the recommendations have been reached from the evidence** The figures are not visible	Thank you for your comment. This has been amended.
46.	SH	South Asian Health Foundation	13	Full		178	The pdfs do not appear to have the Forrest plots for the meta-analyses quoted	Thank you for your comment. This has been amended.
47.	SH	Royal Pharmaceutical Society of Great Britain	3	Full	1	7	"prescribed medication may be needed to alleviate symptoms. It can be carried out at home, or in a hospital or other inpatient facility". This is too restrictive and will prevent innovation. For example, many community substance misuse teams will carry out community detoxes with patients attending daily at the community service. (i.e. neither as inpatient or at home). In addition, some areas have local arrangements where daily dispensing of chlordiazepoxide (already possible with diazepam) is possible and patients attend the local community pharmacy to collect their daily dose of the benzodiazepine and the patient can be monitored by the pharmacist (eg BP, symptom control) – liaising in a shared care arrangements with a specialist key worker.	Thank you. This has been corrected. Our guidance excludes planned medically assisted withdrawal so the amendment is to the introduction and reads 'a variety of settings'.
48.	PR	NETSCC, Referee 2	10	Full	1.1	xv	**4.1 Is the whole report readable and well presented? Please comment on the overall style and whether, for example, it is easy to understand how the**	Thank you for your comment. The glossary spans all three pieces of NICE alcohol guidance and those not relevant to this guideline have been removed. The

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							recommendations have been reached from the evidence. Some of the terms were not well defined e.g. brief intervention (17-20) – this didn't seem to feature in guidance and could be omitted, brief counseling could be seen as an alcohol treatment Clinically significant improvement – this was not a definition and could be omitted Incremental cost – this was very briefly defined and not very useful – is this standard NICE?	definition of incremental cost has been amended also.
49.	SH	South London and Maudsley NHS Foundation Trust	1	Full	1.1	pxiii	The definition of "acute alcohol withdrawal" omits the fact that individuals only experience alcohol withdrawal if they are alcohol dependent. This is an extremely basic but important concept. Alcohol withdrawal is not an "all or nothing" phenomenon but is a cluster of signs and symptoms occurring across a continuum from mild to very severe, and correlates with the continuum of dependence severity. Thus individuals with an alcohol dependence syndrome of mild to moderate severity experience a mild to moderate alcohol withdrawal syndrome, and so on. An alcohol withdrawal syndrome of marked severity can be life-threatening.	Thank you for your comment. This definition has been amended.
50.	SH	South London and Maudsley NHS Foundation Trust	2	Full	1.1	xiii	The definition of "alcohol dependence" used here states that someone who is alcohol-dependent will keep drinking despite harmful consequences. In fact alcohol dependent individuals keep drinking to	Thank you for your comment. The definition for alcohol dependence was taken from the internationally accepted DSM-IV and ICD-10.

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							maintain a steady blood alcohol concentration and to offset the emergence of alcohol withdrawal symptoms. The alcohol withdrawal syndrome develops as a result of neuroadaptation in the alcohol dependent brain.	
51.	SH	Institute of Psychiatry	1	Full	1.1	xvii line 32/33	Indicates that both men and women are recommended to have alcohol free days – my reading of the 1995 DoH sensible drinking guidelines is that this was only recommended following dinking more than the daily recommended limit.	Thank you for your comment. The developers note the department of health policy states: '10.21 After an episode of heavy drinking it is advisable to refrain from drinking for 48 hours to allow tissues to recover. This is a short term measure and people whose pattern of drinking places them at significant risk should seek professional advice. Such breaks are not required on health grounds for people drinking within the recommended benchmarks (para 10.20).' This definition has been amended.
52.	SH	South London and Maudsley NHS Foundation Trust	3	Full	1.2	1 Lines 12/13	In the section on "Background" mention should be made of the proportion of drinkers who are alcohol dependent (about 6% in England: Alcohol Needs Assessment Research Project). Dependent drinkers are admitted to the general hospital as well as hazardous and harmful drinkers. Hazardous drinkers will not be identified unless some sort of screening procedure is used (see Canning et al, 1999. Substance misuse in a general hospital setting Quarterly Journal of Medicine 92, 319-326). Harmful and dependent drinkers are usually identified, but only the latter group will develop	Thank you for your comment. The issue of screening for hazardous, harmful and dependent drinkers is being covered by the Public Health guidance.

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							withdrawal symptoms. Tolerance can occur in heavy drinkers before the evolution of the full dependence syndrome so this sentence should be reworded (lines 12-14).	
53.	SH	Institute of Psychiatry	2	Full	1.2	1 line 20	The BMA have produced a publication reporting 60 conditions related to alcohol misuse that may be worth citing	Thank you for your comment.
54.	SH	South London and Maudsley NHS Foundation Trust	4	Full	1.3 1.3.1	3-5	The scope of this guideline is unclear. Does it relate exclusively or mainly to alcohol dependent individuals admitted to the general hospital? These individuals will also present in the community either to primary care or to addiction services and community presentations are likely to be influenced by the in-patient experience. Also the alcohol dependent patient undergoing an unplanned episode of withdrawal in the general hospital is often discharged after a day or two, to complete their withdrawal unsupervised in the community. It is not practical to consider in-patient treatment separately from community treatment as there is a continuum between the two. Patients who are discharged midway through a "detox" will often prefer to continue on the drug they were receiving in the inpatient unit. Any drug prescribed in the general hospital setting should therefore be safe enough to prescribe in the community. However this guidance is not considered despite the statement in 1.3.1, that the aim of the guideline is to offer "best clinical advice for the management and treatment of people with alcohol use disorders". This	Thank you for your comment. This has been one of the challenges of writing this guideline and reflects difficulties in clinical practice. The guideline does not cover all areas of management or all populations but has a defined scope. Within that scope we have attempted to ask, and give recommendations on, areas where there is great variability in clinical practice. We did not assess all drugs for withdrawal but did not exclude any on the basis of not being safe in the community. If there had been evidence that a drug was more effective and cost effective than the others, but needed to be used as an inpatient for acute alcohol withdrawal, we would have recommended it with that caveat.

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							is a much wider remit than that presented in the document.	
55.	SH	Derbyshire Mental Health Services NHS Trust	1	full	1.2.1.2	10	If the diagnosis is certain, there is anecdotal evidence to suggest that continuing beyond five days will continue to have a beneficial effect if the pt is not able to tolerate substantial oral diet.	Thank you for your comment. We found this area very difficult because of the lack of good evidence and the abundance of opinion and anecdote. We have now changed the recommendation to read, at least five days.
56.	SH	Alcohol Use Disorders: Alcohol dependence and harmful alcohol use Guideline Development Group	1	Full	2	General	Clinical practice would suggest that the severity of withdrawal symptoms (seizures and DTs) are significantly correlated with severity of dependence yet there is little guidance in this document related to the assessment of the severity of dependence. We realise that the "other GDG" is addressing this, however, if severity of dependence predicts severe withdrawal symptoms, or predicts the relative risk of developing severe withdrawal symptoms, as assumed in clinical practice – severity of alcohol dependence should also be an indicator for treatment setting (e.g. severe alcohol dependence indicates inpatient settings)	Thank you for your comment. We agree that an assessment of the severity of dependence is a very useful clinical tool prior to considering treatment for acute withdrawal or when assessing a patient for an elective medically assisted withdrawal however this was not within our scope. The mental health guidance will be addressing this area.
57.	SH	Alcohol Use Disorders: Alcohol dependence and harmful alcohol use Guideline Development Group	7	Full	2	General	There is no real description as to how community alcohol withdrawal regimes should "look" and how these may differ from inpatient settings; should this be in this guidance as many patients present in acute withdrawal in practices, services and departments?	Thank you for your comment. Community withdrawal regimens were not in this guideline's scope but are being covered by the mental health guidance.
58.	SH	Alcohol Use Disorders: Alcohol dependence and	8	Full	2	General	Much information has been reviewed for chapter 2 'Acute alcohol withdrawal' which is clearly written. Evidence from studies that	Thank you for your comment. The aim of the developers was to cover the management of acute alcohol withdrawal

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		harmful alcohol use Guideline Development Group					met their entry criteria (p17 – "studies that applied multivariate, covariate, regression or discriminant function analyses were included.. Studies only with a sample size of 50 or fewer were excluded") was often lacking to guide the Guideline group in determining their recommendations. Their aim is to cover inpatient detox and not community detox. Therefore how to do an outpatient detox is not covered and will need to be addressed by the Alcohol use disorder CDG.	whether it be in an inpatient or outpatient setting. The mental health guidance will cover the planned situation where alcohol intake is reduced or stopped under medical supervision in an in patient or outpatient setting.
59.	SH	Alcohol Use Disorders: Alcohol dependence and harmful alcohol use Guideline Development Group	9	Full	2	General	In the narrative part of the chapter, the discussion describes how difficult it was to reach conclusions (eg 2.1.6) however this is not reflected, even absent, from the bold one-line recommendations eg R5, R6. Consequently whilst efficacy may be equal between different drugs, risk is not. The setting and context is also important and the	Thank you for your comment. The recommendations are written as guidance based on the best evidence and opinion. We have now amended recommendation #5 to read 'Offer pharmacotherapy to treat the symptoms of acute alcohol withdrawal; benzodiazepine[1], clomethizole (in-patient settings only)[2] or carbamezepine[3] are

[1] 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.

[2] 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.

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							recommendations do not make this clear enough ie that these are aimed at unplanned inpatient detox in a medical unit and not a planned detox in the community with limited support.	equally efficacious. (see sections 1.1.4 and 1.1.5 for treatment of delirium tremens and alcohol withdrawal seizures).' Our guidance for the use of medication for acute withdrawal was not setting specific except where stated.
60.	SH	Alcohol Use Disorders: Alcohol dependence and harmful alcohol use Guideline Development Group	10	Full	2	General	In the full guidance, the recommendations eg R5 do not appear to consider relative risks whilst in the summary guidelines, there a number of crucial footnotes that outline risks involved in using particular medications. We are concerned therefore	Thank you for your comment. Recommendation #5 has been amended to read 'Offer pharmacotherapy to treat the symptoms of acute alcohol withdrawal; benzodiazepine[4], clomethizole (in-patient settings only)[5] or carbamezepine[6] are

[3] 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.

[4] 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.

[5] 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.

[6] 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.

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							that without reading both parts of their guidance, practitioners new to the field of alcohol detox will follow a course of action which may not be appropriate given risks associated with some medications whilst those familiar with the field may have their prescribing altered by commissioners using NICE to define what they think is acceptable treatment and translating this advice for inpatient unplanned to planned outpatient detox.	equally efficacious. (see sections 1.1.4 and 1.1.5 for treatment of delirium tremens and alcohol withdrawal seizures).'
61.	SH	Alcohol Use Disorders: Alcohol dependence and harmful alcohol use Guideline Development Group	11	Full	2	General	In the chapter, 'no evidence was found' is used (eg p28, line 31) however we would suggest that there is 'absence of or limited evidence' rather than 'no evidence to support' the statement that follows. This is particularly likely given their entry criteria for studies looked at.	Thank you for your comment but the developers are unable to locate the sentence in question with the reference quoted.
62.	SH	Alcohol Use Disorders: Alcohol dependence and harmful alcohol use Guideline Development Group	17	Full	2	General	The 'Alcohol dependence and harmful use' guideline has been referenced in relation to planned withdrawal, e.g. p29 'As such, the GDG emphasised the need to direct people presenting with withdrawal towards alcohol addiction services and encourage them to undergo planned withdrawal (to be covered in 'Alcohol use disorders…)', and p32 'During a planned medically-assisted withdrawal (to be covered in 'Alcohol use disorders…)'. Might have to be more specific when referring to the dependence guideline to avoid confusion for the reader.	Thank you for your comment. The guideline has been amended.
63.	SH	Alcohol Use	15	Full	2		Issue of medicated vs non-medicated	Thank you for your comment. The GDG

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		Disorders: Alcohol dependence and harmful alcohol use Guideline Development Group					withdrawal. Does this make a difference – since many animal models do not treat the alcohol withdrawal. Could this be made a research recommendation?	are not able to look at the literature for aspects of acute alcohol withdrawal and prioritised those with greatest variability in practice were prioritised for inclusion.
64.	SH	Greater Manchester West Mental Health NHS Foundation Trust	14	Full	2	General	The guidance seems to neglect the topic of best practice and evidence base for community detoxification Most of the guidance relates to inpatient management The majority of assisted alcohol withdrawals will take place in the community where recommendations such as symptom triggered prescribing will not be practical Further review of the evidence base for the management of assisted withdrawal in the community is essential to include. As a group of specialist addiction psychiatrists in the North west we have reviewed the literature and developed a consensus statement on best practice in community detoxification if this would be useful for the GDG I am happy to send this through	Thank you for your comment. The recommendation regarding the treatment regimens have been modified. The mental health guidance will be addressing the specifics of community detoxification.
65.	SH	South London and Maudsley NHS Foundation Trust	5	Full	2	15	The clinical introduction discusses alcohol withdrawal without mentioning that this occurs in the context of alcohol dependence. In fact, symptoms of alcohol withdrawal can develop as early as 3-6 hours after cessation of alcohol. What is the source of the evidence that most patients manifest a "minor symptom complex"? This is unlikely to be the case in individuals admitted to the general hospital who require a medically supervised	

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							withdrawal. The word "fits" is used on line 10 and again on line 28 (p15). The term alcohol withdrawal seizures is preferred. What is lacking is clear guidance on how to assess the alcohol dependence syndrome, and how to quantify its severity (using scales such as the Severity of Alcohol Dependence Questionnaire; SADQ), as this has relevance for the starting doses of alcohol withdrawal medication to be used. This information is set out in a number of accessible texts including: (1) Edwards et al (2003) The Treatment of Drinking Problems 4th edition. Cambridge: Cambridge University Press (5th edition in press) and (2) Conigrave et al (2009) The Oxford Handbook of Addiction Medicine. Oxford: Oxford University Press.	The assessment of dependence is being covered by the Mental Health guidance.
66.	SH	South London and Maudsley NHS Foundation Trust	6	Full	2	16 RR1	The severity of the alcohol dependence syndrome has a bearing on whether someone should be admitted to hospital for treatment of their alcohol withdrawal syndrome. Individuals at the severe end of the alcohol withdrawal spectrum have higher rates of alcohol- related problems (i.e there is a correlation between the severity of the dependence syndrome and the level of alcohol-related problems) and are therefore more likely to experience a more complicated withdrawal syndrome. Individuals in mild to moderate alcohol withdrawal can be treated in the community. There is no need to admit them to the	Thank you for your comments. The developers agree that the severity of the withdrawal is important in making the decision about admission. The assessment of community detoxification programmes is outside the scope of the guidance.

Comment No.	Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
							general hospital unless there is a persuasive medical reason. What about testing the effectiveness and feasibility of community withdrawal programmes based in the general hospital (either in OPD or the A& E Department).	
67.	SH	Alcohol Use Disorders: Alcohol dependence and harmful alcohol use Guideline Development Group	26	Full	2	16 and 29	"specialist alcohol treatment services" is a better term for 'follow-up services'	Thank you for your comment. The developers kindly disagree with this suggested change as the follow-up of these patients can made be at many levels and does not necessarily need to involve or be restricted to Tier 4 services.
68.	PR	NETSCC, Referee 1	3	Full	1.3.8	8	**2.2 Please comment on the health economics and/or statistical issues depending on your area of expertise.** On what basis were the economic evaluations appraised?	Thank you for your comment. We appraised the health economist evidence using the checklist from the NICE Guideline manual (2009). We amended the guideline to reference this in the correct manner.
69.	PR	NETSCC, Referee 1	4	Full	1.3.8	11	**2.2 Please comment on the health economics and/or statistical issues depending on your area of expertise.** Why an NHS perspective, given the NICE requirement of an NHS/personal social services perspective?	Thank you for your comment. This has been amended.
70.	PR	NETSCC, Referee 2	3	Full	1.3.8	11	**2.2 Please comment on the health economics and/or statistical issues depending on your area of expertise.** The perspective taken is restricted to the NHS. This is in my opinion a valid position given that for most of the guidance only short term consequences to the drinker are considered. However, hazardous and	Thank you for your comment. We have added information in the guideline.

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							harmful use has in the CMO England's terms "passive" drinking impacts both on the health service and other public sectors. Illicit drug guidance has used a wider perspective. This should be mentioned at least in the economic model appendix.	
71.	SH	Alcohol Use Disorders: Alcohol dependence and harmful alcohol use Guideline Development Group	24	Full	2.1	15	The AUD diagnosis and clinical management of harmful drinking and alcohol dependence will be looking at "identification and diagnosis" of dependence rather than "screening".	Thank you for your comment. The guideline has been amended accordingly.
72.	SH	Alcohol Use Disorders: Alcohol dependence and harmful alcohol use Guideline Development Group	25	Full	2.1	16 Line 5	Patients often present in this way to emergency mental health services as well.	Thank you. The guideline has been amended.
73.	SH	Alcohol Use Disorders: Alcohol dependence and harmful alcohol use Guideline Development Group	19	Full	2.2		For the clinical question for this section, studies were restricted to systematic reviews/ meta-analysis of RCTs or individual RCTs. One Cochrane systematic review on benzodiazepines for alcohol withdrawal was identified and appraised. The list of studies included from the Cochrane review is not clear from description p 32-33 - were some excluded? Were all in inpatients? All published studies of clomethiazole are from inpatients. Why offer carbamazepine and not one of	Thank you for your comment. The section below is from the clinical methods introduction and explains why some studies were excluded from the Cochrane: 'The Cochrane systematic review included studies on patients who were not in acute alcohol withdrawal. In addition, some studies were on pharmacological interventions that were not relevant for the clinical question under consideration here. In addition, the drug clomethiazole was classified as an anticonvulsant in the Cochrane and re-classified as a hypnotic

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							other anticonvulsants? Why exclude other anticonvulsants when clinicians have reported issues with using carbamazepine (eg side effect of ataxia that could be emerging WE instead)? For instance, oxcarbazepine has a better side effect profile than carbamazepine. In Germany where clomethiazole is used widely for inpatient detox, it is not used for outpatient. One important clinical issue regarding recommending clomethiazole is that patients are often discharged from hospital before their medication regimens for detox are completed. Therefore people will be given a bottle of clomethiazole and in addition have (greater) access to alcohol. With no-aftercare generally in place, they are at risk of resuming drinking and therefore of dangerous interaction and risk of respiratory depression. Issues for consideration are 1. what is relative risk between clomethiazole or a benzodiazepine when taken with alcohol when taking for alcohol detox 2. increase in amount of clomethiazole prescribed and availability and who has access to it In the RCP draft guidelines there is limited critical discussion of side-effects or risks of	(other agents) for the meta-analysis presented. After these studies had been removed, 21 out of the 56 studies were included in the meta-analysis. However, not all studies reported on the outcomes reported here. The follow-up period ranged from eight hours to 14 days.' Recommendation #5 has now been changed to say clomethiazole should only be used in an in-patient setting.

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							medication cited for use in withdrawal in main document. The risks associated with inpatient vs outpatient use are not the same due to levels of monitoring, access to alcohol etc. Clomethiazole has a narrower safety margin than benzodiazepines, is dangerous in patients who are still drinking, has highly variable bioavailability, and is not licensed for outpatient use unless the administration is closely monitored. It also has a reported addiction potential in alcohol dependent populations. The GDG should therefore consider an additional statement that "chlormethaizole is contraindicated in outpatient assisted alcohol withdrawal", as the guideline covers both inpatient and outpatient settings. Given the limited discussion of the relative risks, we suggest the following studies and points for consideration. There is a risk of dependency with both medications. Clinically it can be very challenging to reduce or even achieve abstinence from either clomethiazole or benzodiazepines. The risks for benzodiazepine are well-known and Reilly, BJPsych 1976, 128 p375-378 and McInnes, BMJ, 1987, 294:592 set out some of the issues for clomethiazole. There is no specific medical treatment for clomethiazole overdose – but is for benzodiazepine overdose eg flumazenil. Houston et al 1983 states that people tend	

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							to die from clomethiazole overdose before get to hospital, particularly when combined with alcohol. Concerning toxicity, Reith et al 2003 (Clinical Toxicology,41:7,975 - 980) found that death rates from clomethiazole were greater than for other benzodiazepines. "The relative rates of death per DDD (95% CI) for alprazolam and clomethiazole compared with the other sedatives / anxiolytics were 6.2 **(1.6-1** 7.0) and 20.9 (2.5-79.8) respectively." Buckley & McManus, 2004 (Drug Saf. 2004;27(2):135-41) state that clomethiazole had greater fatal toxicity index than benzodiazepine based on UK data. However this is not to say that benzodiazepines in the presence of alcohol are completely safe eg Serfaty M, Masterton G. Br J Psychiatry. 1993 163:386-93.	
74.	SH	Alcohol Use Disorders: Alcohol dependence and harmful alcohol use Guideline Development Group	12	Full	2.1.1	15 last para	For the purposes of this guideline, medically-assisted withdrawal from alcohol with (TYPO) be referred to as (i) planned, which as the name implies is an elective process which is usually undertaken in the community or else as part of a planned programme within addiction services; or (ii) unplanned which occurs when patients stop or suddenly reduce their alcohol intake either inadvertently because of an intercurrent illness, because they make a conscious decision to stop or were inadvertently deprived of alcohol, for example, following an accident. These patients may present to their GP or to acute	Thank you. These definitions have now been included in the guideline.

Comment No.	Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
							hospital services.	
75.	SH	Institute of Psychiatry	3	Full	2.1.1	15 line 4	"Misuse alcohol" – is not defined and is not specific	Thank you for your comment. The developers aimed to avoid this term and have amended the guideline.
76.	SH	Institute of Psychiatry	4	Full	2.1.1	15 line 15	"Less than 5% of individuals withdrawing from alcohol" – again this is a very non-specific statement e.g. are they physically dependent etc	Thank you for your comment. By definition a person is physically dependent if they experience withdrawal symptoms when stopping or reducing their alcohol intake.
77.	SH	Royal College of Physicians	5	Full	2.2.	32	Treatment of alcohol withdrawal The authors have reviewed 22 studies of the use of benzodiazepines (predominantly chlordiazepoxide) in the successful treatment of alcohol withdrawal. However, they have produced no evidence for the use of chlormethiazole and there is no reference to the study by Pentikinin & Co. from 1976 with 6 deaths in connection with chlormethiazole infusion. Despite this the recommendations suggest that benzodiazepines, chlormethiazole and carbamazepine are of equal benefit in treating the symptoms of acute alcohol withdrawal. This conclusion is inconsistent with the evidence and clinical view that chlormethiazole should <u>not</u> be used in the treatment of alcohol withdrawal – due to its addictive properties and its narrow margin between efficacy and toxicity. It is especially dangerous when given by non-specialist staff, who supervise most withdrawals. Given the lack of evidence for the benefit of	Thank you for your comment. The recommendation has now been altered. The recommendation here is made on the best evidence available. The GDG took into account the risk of instituting a symptom- triggered regimen in acute hospitals and still recommend this as the optimum clinical and cost-effective therapy.

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							chlormethiazole, the recommendation for its use (beside long-acting benzodiazepines) should be withdrawn. In the comparison between fixed-dose and symptom-triggered drug withdrawal regimes, the panel accept that there was only one study performed in a general medical ward setting as opposed to a specialist addiction setting. We suspect that the number of alcohol withdrawal episodes treated in a general hospital setting far outweigh those of any specialist treatment settings. It is therefore likely that in the vast majority of cases these patients may be treated by medical and nursing staff inexperienced in the diagnosis and treatment of alcohol withdrawal. In this context the recommendation that patients should be treated using a symptom-trigger regime rather than a fixed-dose regime are not consistent with the evidence. This raises concerns about patients being under-treated when managed by inexperienced medical and nursing staff as is probably often the case in the UK.	
78.	SH	Institute of Psychiatry	5	Full	2.1.1	15 line 28	"Previous withdrawal fits …..and DTs clearly indicate dependence" "Clearly" seems to be too strong a phrase – for example individuals with a history of DTs	Thank you. The guideline has been amended accordingly.

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							and fits may not currently be drinking at dependent levels.	
79.	PR	NETSCC, Referee 2	8	Full	2.3		**3.1 How far are the recommendations based on the findings? Are they a) justified i.e. not overstated or understated given the evidence? b) Complete? i.e. are all the important aspects of the evidence reflected?** I was most concerned about the certainty expressed around the recommendation of symptom triggered versus fixed dose schedules because of the link between the symptom based regime and the skill of those monitoring which does not seem to have fully featured in the review.	The GDG debated the wording of this recommendation thoroughly and have amended it make this relationship more clear.
80.	PR	NETSCC, Referee 2	12	Full	2.3		**4.2 Please comment on whether the research recommendations, if included, are clear and justified.** RR3 – this mixes the issue of the person delivering the intervention with the type of care pathway.	Thank you for your comment. The research recommendation has been amended to read: 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 acute hospital setting with no input from a specialist nurse?
81.	SH	Alcohol Use Disorders: Alcohol dependence and harmful alcohol use	13	Full	2.1.2		The clinical question states 'What are the benefits and risks of unplanned 'emergency' withdrawal from alcohol in acute medical settings versus discharge?', and the text	For the clinical question 'What are the benefits and risks of unplanned 'emergency' withdrawal from alcohol in acute medical settings versus discharge"

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		Guideline Development Group					reads 'Studies were included if they reported on individuals admitted for planned or unplanned medically-assisted withdrawals, but restricted to acute, inpatient settings only'. Therefore did the group only look at those in inpatient settings? (the Malcolm study is an outpatient study). Is the 'Alcohol dependence' guideline group specifically needed to look at community detox? There are 2 Malcolm et al 2000 studies – number 10 & 21 in reference list, but only 10 is in Table 2-1. Why were Lechtenberg & Worner (Arch Neurol. 1990 May;47(5):535-8) and Mayo-Smith & Barnard (Alcohol Clin Exp Res. 1995 Jun;19(3):656-9) not included?	studies were included in both inpatient and outpatient settings (including the study by (Malcolm). For the question "what criteria should be used to admit a patient with acute alcohol withdrawal for unplanned emergency alcohol" studies were restricted to acute, inpatient settings only. The 'Alcohol use disorders': management of alcohol dependence guidance is addressing management of alcohol withdrawal in community and residential settings'. This is an error and has been amended. Only one Malcolm study (ref 21) was included in the evidence review. Lechtenberg & Worner was excluded from the evidence review 2.1.2 because the studies used univariate analysis (see exclusion criteria p33) Mayo-Smith was excluded because relevant studies on mortality were included in the Cochrane review and therefore in our evidence review (section 2.2.3). There were no relevant studies for section 2.4 management of delirium (the drug comparisons were not included in our evidence review)
82.	SH	Alcohol Use Disorders: Alcohol	2	Full	2.3		Clinical practice would suggest that there is a relationship between alcohol withdrawal	Thank you for your comment. The developers agree with your comments and

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		dependence and harmful alcohol use Guideline Development Group					symptoms, through severity of alcohol dependence that indicates commencement dose regimens for withdrawal medications. This issue does not appear to have been explored fully. In clinical practice a robust assessment of the patients' alcohol dependence together with SADQ scores appears to provide a useful indicator for the first days medication in a fixed dose schedules that are tailored to this history for "planned withdrawal schedules"	the assessment of a patient's alcohol dependence is being addressed by the mental health guidance. The relationship between the severity of dependence and dosages of medication required for planned withdrawal schedules was not explored by the developers as they focussed on the type of drug and the regimen rather than the dose. We do accept that the level of dependence will influence the dose.
83.	SH	Alcohol Use Disorders: Alcohol dependence and harmful alcohol use Guideline Development Group	4	Full	2.3		The observation that, *If the health-care worker spends longer than four-minutes extra per assessment using the symptom-triggered regimen compared to using the fixed-dosing regimen, then the symptom-triggered option is no longer cost-effective* (pg.54) is vitally important. We know that there is great variability in health care workers attitudes, knowledge base and skills in working with alcohol patients. We are not convinced that training will develop the appropriate skills required across health care staff. Clinical staff do not readily intervene with this patient group therefore there will be great variability in practice, even after training in the assessment, monitoring and care in the provision of symptom triggered schedules. Additionally the health care staff on a ward will be highly variable ranging from unqualified staff (Agenda to Change Band 2-4) and qualified	Thank you for your comment. Please find a discussion about the point you raise in section 2.3.6.

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							staff (Agenda to Change Band 5+). The feasibility of symptom-triggered schedules needs to be questioned as a broad recommendation for the NHS outside specialist services.	
84.	SH	Alcohol Use Disorders: Alcohol dependence and harmful alcohol use Guideline Development Group	33	Full	2.3		In principle a symptom triggered detox is much better for higher risk patients and is used in specialist inpatient units generally based on standardised instruments such as the CIWA-AR. Advantages of symptom triggered: 1. Possibly safer as it forces staff to check and score patients in clearly defined intervals and not just give out medication - no more waking someone up at 2am to give 40mg Librium. 2. Stop dosing after 48 hrs, therefore reducing inpatient time and workload for staff after that period. A massive advantage to the currently accepted UK standard of 10 days for a detox - you can do this in five days! 3. Generally well accepted by clients - though no clear evidence to support this - if done well, less risk of over- or undersedation. However, in a community and general hospital setting a fixed regimen is much more practical, particularly if it includes vitamins as well. Some settings such as the prison environment do afford 24 hour nursing availability but owing to the prison	Thank you for your comment. The GDG discussed this at length. We agree with points 1 to 3. We also agree that in the community there will not be the facilities for a symptom triggered regimen. We accept that the implementation in a general hospital ward may require closer monitoring than has been traditionally provided, but if it means delivering better care we believe that we should promote the best practice. There is no reason why a ST regimen could not include a fixed regimen of the most suitable vitamins.

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							regime and issues with patients being locked behind the cell door and knowledge of the state of service modernisation would not be fit for anything other than fixed regime	
85.	SH	Alcohol Use Disorders: Alcohol dependence and harmful alcohol use Guideline Development Group	5	Full	2.3.		The required frequency of assessment of withdrawal symptoms in the first 24-hours for symptom-triggered schedules would seem difficult to implement without clear, interested and knowledgeable leadership to support such practice. Although these settings (pg54) can demonstrate these approaches as cost-effective - we are concerned such protocols can be implemented successfully in standard care, therefore suggesting fixed-dose as the "safest option" in routine settings?	Thank you for your comment. Please find a discussion of your concerns in section 2.3.6. of the full guideline.
86.	SH	South London and Maudsley NHS Foundation Trust	16	Full	2.3	General	Front-loading is possible in an ICU type setting. It may have been developed in response to insurance constraints in North America.	Thank you .
87.	SH	South London and Maudsley NHS Foundation Trust	11	Full	2.3	39-56	Clinical units in the UK tend to have fixed-dosing (FD) regimes. This is likely to have arisen for a number of reasons: (1) Clinical experience has developed in relation to this type of administration, (2) The dosing schedule is straightforward and uncomplicated (3) It is safer to implement in in-patient settings with relatively low staff: patient ratios.	Thank you for your comment. The GDG have recommended the use of symptom-triggered regimens as it is the most clinical and cost-effective regimen. NICE do not issue guidance on service provision but have considered the cost-impact of this recommendation.
88.	SH	Greater Manchester West Mental Health	1	Full	2.1.2	17	The studies were restricted to acute inpatient settings were there studies in other	Thank you for your comment. Studies on emergency demand for medically assisted

Comment No.	Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
		NHS Foundation Trust					settings that were excluded including emergency demands for medically assisted withdrawals in the community	withdrawals in the community were not considered.
89.	PR	NETSCC, Referee 2	9	Full	2.1.2	18	**3.2 Are any important limitations of the evidence clearly described and discussed?** A comment is made (lines5-6) on the limits of retrospective recording of previous detoxifications but how would this data be accurately recorded. It was an odd comment and brought doubts about potentially other bias assessments.	Thank you for your comment. The GDG consider that evidence obtained from a prospective cohort is of higher quality than that obtained from a retrospective review.
90.	SH	College of Mental Health Pharmacists	1	Full	2.1.2	18	Line 10 should say assessed instead of assesses.	Thank you for your comment. This has been amended.
91.	SH	South London and Maudsley NHS Foundation Trust	7	Full	2.2.1	32, lines 20-22	It would perhaps be helpful to outline the "places" where benzodiazepines, clomethiazole and carbamazepine are used. Treatment in the acute medical setting is implied. Clomethiazole should be reserved for in-patient use (see BNF).	Thank you for your comment. Recommendation #5 has been amended to so clomethiazole is used for inpatient settings only.
92.	SH	College of Mental Health Pharmacists	2	Full	2.2.1	32	Line 29 benzodiazepine written twice.	Thank you. This has been amended.
93.	SH	South London and Maudsley NHS Foundation Trust	17	Full	2.4	56-58	There is no advice in the guideline about symptomatic treatment for DTs: a significant omission. When DTs emerge at about 72 hours post cessation of drinking they typically do so in the early hours of the morning when the ward lights are dimmed. The patient becomes disoriented and distressed. It is important to nurse these patients in a quiet, well-lit room and pay attention to their clinical observations, general hydration and electrolyte levels.	Thank you for your comment. We understand the importance of this, but the purpose of the guideline is not to write a textbook on care, but to provide guidance based on specific clinical questions. The number of questions was strictly limited due to time and budgetary constraints and restricted to areas where there is clinical debate about best practice.

Comment No.	Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
							See Edwards et al, 2003 for a more detailed account of DTs and their management. DTs will not supervene in an appropriately treated alcohol withdrawal syndrome. Thus one of the aims of a medically assisted alcohol withdrawal protocol is to prevent the emergence of DTs (and alcohol withdrawal seizures).	
94.	SH	Greater Manchester West Mental Health NHS Foundation Trust	2	Full	2.1.3	23	Previous detoxifications and incidence of DTs when referring to previous detoxification history does this mean the number of previous detoxifications completed or whether there was a history of DTs in previous detoxifications or both.	Thank you for your comment. The text has been amended to clarify that there is no significant difference for the number of prior inpatient detoxifications or prior incidence of delirium tremens.
95.	SH	Greater Manchester West Mental Health NHS Foundation Trust	3	Full	2.1.3	23	Factors associated with incidence of seizures no studies reported on this however there were studies reporting on an association between prediction of seizures and previous history of seizures as part of kindling	Thank you for your comment. No studies included in the review reported on whether the previous history of a seizure was a predictor of a seizure in the current withdrawal episode.
96.	SH	Greater Manchester West Mental Health NHS Foundation Trust	4	Full	2.1.3	24	No association between alcohol level on admission and incidence of seizures however is there an association between alcohol level on admission with signs of autonomic over activity and the development of seizures?	Thank you for your comment. No studies reported on the whether alcohol level on admission was a predictor of a seizure (p24 line 20). Signs of autonomic over activity were associated with the risk of developing the DTs (p25 line 1). The paper (Palmstieria) reported on a model for predicting alcohol withdrawal delirium not specifically on the development of seizures.
97.	SH	College of Mental Health Pharmacists	3	Full	2.3.1	39	Table 2-3 Doses of medications are high compared to those used in clinical practice – please justify	Thank you. This table was given as an example and has been replaced with a table containing the more commonly used lower doses.

Comment No.	Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
98.	SH	Greater Manchester West Mental Health NHS Foundation Trust	8	Full	2.3.1	39	Examples of the dosing regime for fixed dose treatment i.e. 50-100mg qds would be considered to be at the upper end of the prescribing range and may account for some of the findings in the studies in terms of overall dose and duration of prescribing. We use a lower dose standard regime commencing on 20-30mg qds and use CIWA triggered PRN prescribing for breakthrough	Thank you. This table was given as an example only and did not represent the dosages given in the studies. It has now been replaced with a table containing the more commonly used lower doses.
99.	SH	Greater Manchester West Mental Health NHS Foundation Trust	12	Full	2.4	57	It is not clear from the references whether the GDG reviewed the paper Management of Alcohol Withdrawal Delirium an evidence based practice guideline ref Mayo- Smith et al Arch Int Med (2004) 164 pg 1405-1412 which provides an excellent review of the literature and a consensus statement on management. There is a review of evidence of treatment impact on mortality duration of delirium, time to control agitation. There also needs to be a consideration of the setting for the management of the delirium, the route of administration of the benzodiazepine and the potential use of adjunctive agents e.g. magnesium which have not been included in the guidance There should also be recommendations on the consideration of parenteral vitamin prophylaxis in delirium tremens patients due to the high risk of Wernicke Korsakoffs in this population	Thank you for your comment. The Mayo-Smith study was excluded because relevant studies on mortality were included in the Cochrane review and therefore in our evidence review (section 2.2.3). There were no relevant studies for section 2.4 management of delirium (the drug comparisons were not included in our evidence review). A patient who has, or is assessed to be at high risk of developing delirium tremens, should be offered admission to hospital for medically-assisted withdrawal (recommendation #1) By definition, if a person is in alcohol withdrawal they are dependent on alcohol and so should be given prophylactic parenteral thiamine (recommendation #16). Currently the only thiamine preparation licensed for use within the UK is Pabrinex which contains a mix of water soluble vitamins B and C. We have not included guidance on the

Comment No.	Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
								setting for the management of delirium but there has been a further comment on this added to the introduction on alcohol withdrawal. Similarly with route of administration. We could find no evidence to support the use of magnesium in the management of withdrawal
100.	SH	Institute of Psychiatry	8	Full	2.3.1	39 line 31	The example dosing regimen is very high at "50-100mgs qds" – typically our very severely dependent individuals are mostly managed with 40mg qds with PRN in addition if required – is the example correct?	Thank you. The doses given in table 2-3 were provided as an example only and have now been lowered to more accurately reflect clinical practice.
101.	SH	Alcohol Use Disorders: Alcohol dependence and harmful alcohol use Guideline Development Group	21	Full	2.3.1	57 (or 39)	The table (2.3) is referred to as an example, but does not bear resemblance to the more usual regimens for chlordiazepoxide - neither in initial dose nor in rate of reduction. As written, it appears to suggest 50mg four times a day – as a lower dose! Clearer guidance on the link between severity of withdrawal and dosing should be given, along with examples of more standard doses for each of the three systems or else this table should not be included. The difference between specialist treatment centres and general medical or primary settings should be emphasised. Ditto in-patient settings such as A&E or medical admissions wards.	Thank you for your comment. The doses given in table 2-3 were provided as an example only and have now been lowered to more accurately reflect clinical practice.
102.	SH	Greater Manchester West Mental Health NHS Foundation	9	Full	2.3.2	41	I have concerns about potential bias in the studies comparing fixed dose and symptom triggered prescribing in terms of the	Thank you for your comment. The developers also had concerns about bias in these studies and took these into account

Comment No.	Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
		Trust					exclusions from the trials. Patients at risk of delirium tremens and seizures are often excluded from the trials (e.g. Saitz et al) and at times the trials are on relatively uncomplicated withdrawals when any potential differences in this more risky population are not fully identified.	in GDG discussions.
103.	SH	College of Mental Health Pharmacists	4	Full	2.3.2	42	Table 2-4 please add a note about the medication being used outside the product license as in the NICE guideline might be useful.	Thank you. A footnote has been added to the recommendations in the full guidance.
104.	SH	Institute of Psychiatry	7	Full	2.2.3	36 line 13	I believe that is some evidence to suggest that oxazepam is less effective at preventing fits?	Thank you for your comment. We did not find a significant difference in our searches.
105.	SH	Greater Manchester West Mental Health NHS Foundation Trust	10	Full	2.3.3	46-47	'a seizure in a patient during treatment can be considered as a treatment failure' Quoted from later in the guidance The summary of results identifies 2 cases of withdrawal seizures in the symptom triggered groups and none in the fixed dose groups in those where it was reported. Although this number is small and not statistically significant the concern remains that symptom triggered regimes may not be as effective at preventing the onset of more severe withdrawal phenomena compared with fixed dosing (+PRN) This may be confounded by the finding of significantly more protocol violations in the symptom triggered group. I feel we need further investigation of benefits of symptom triggered against fixed dose prescribing in these high risk detoxifications and this caveat should be included in the	Thank you for your comment. We have made our recommendation based on clinical and cost-effectiveness evidence and clinical experience. We have adapted the recommendation to reflect the importance of close monitoring.

Comment No.	Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
							recommendations. Anecdotally in a unit in Manchester where symptom triggered prescribing was developed there were a number of severe adverse withdrawal events requiring transfer to the general medical unit. The issue of training and adherence to protocols needs to be further emphasised. In high risk detoxifications we use higher starting doses for our fixed dose regimes based on historical and examination findings as per Palmstierna such that patients will commence on 50mg qds of chlordiazepoxide + symptom triggered PRN prescribing for breakthrough symptoms.	
106.	SH	The Alcohol and Drug Service	1	Full	2.6	62	Line 35-37 talks about the benefits of an Alcohol Specialist Nurse (ASN). In relation to 'augmenting medical treatment and co-ordinating follow-up' it may be more effective and cost effective to use an alcohol health worker of alcohol practitioner trained in line with DANOS to deliver interventions and link to community services for aftercare. This links to the NICE version comment below.	Thank you for your comment. NICE does not offer guidance on service provision, but rather wished to highlight the need for healthcare workers specifically trained in the delivery of alcohol support services.
107.	SH	Alcohol Use Disorders: Alcohol dependence and harmful alcohol use Guideline Development Group	14	Full	2.1.6		Kindling- No mention of Ballenger & Post (1978) or Brown et al (1988). Much of the clinical evidence is highly suggestive that kindling does occur – depends on how you define it eg seizure or worsening of symptoms.	Thank you for your comment. In order to make a recommendation based on whether kindling does or does not exist good clinical evidence is required either way. We could not find this and therefore made the recommendation based on other factors.
108.	SH	Archimedes Pharma	1	Full	2.7	Gene	There are a number of significant	Thank you for your comment. We have

Comment No.	Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
		Ltd				ral	contradictions within the guidance which could cause potential confusion for the prescriber. Within the body of the document it is recognised that Wernicke's encephalopathy is difficult to diagnose, and the potentially life-threatening consequences of a misdiagnosis are highlighted (P90 lines 24-27). It is also recognised that oral absorption of thiamine is significantly impaired as a direct consequence of alcohol misuse and/or malnourishment (p78 lines 10-17); and, that in patients at high risk of developing Wernicke's encephalopathy the oral route of thiamine supplementation is inadequate (p90 lines 32-33). Despite these clear statements, in the body of the text the guidance states that in the management of patients at "high risk" of developing Wernicke's encephalopathy, "an adequate diet" would "likely suffice", and that additional prophylaxis should only be provided "in some cases" (p90 lines 6-10). An "adequate diet" is not appropriate management of patients in the acute setting, where they are at high risk of developing potentially irreversible brain damage. This is particularly so for those patients who may be thiamine deficient, and going into planned or unplanned alcohol withdrawal. This section also lacks clarity for	tried to be as clear as possible and amended the recommendations as a result. We are now emphasising the importance of having a low threshold for the diagnosis of Wernicke's within the recommendation.

Comment No.	Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
							the prescriber on how they should decide who to offer prophylaxis to. In addition, the term "likely suffice" is an inappropriately low treatment benchmark to aim for in the prevention of Wernicke's encephalopathy, with its potentially catastrophic medical consequences.	
109.	SH	The British Association for Parenteral & Enteral Nutrition	4	Full	2.7		I have seen a young alcoholic who was well nourished overall develop Wernike Korsakoff syndrome with MRI changes following admission after a drinking bout and the administration of 50% dextrose because he was semi-comatose with a low blood sugar. I am sure there is and never will be relevant evidence on this point but perhaps a warning can be given that IV thiamine should be administered with 50% dextrose whenever a hypoglycaemic patient is also an alcoholic.	Thank you for your comment. We have added a comment about this to the full guideline on page 79.
110.	SH	Greater Manchester West Mental Health NHS Foundation Trust	5	Full	2.1.6	28	When excluding patients who were admitted for co-incident problems this means we cannot investigate the issue of whether a detoxification commenced in these circumstances should be continued if the coincident problem is treated and the patient is ready for discharge before the detoxification is completed. Practice indicates these patients can often be given less than optimal discharge arrangements for the continuation of the detoxification. We need to establish whether it is better to complete a detoxification in the community	Thank you for your comment. We agree that this is an important area for future research but were not able to compare management across these three settings in this guidance.

Comment No.	Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
							started in these circumstances or advise the patient to continue drinking and refer to alcohol services for optimised detoxification or whether the development of the role of specialist nurses within the general hospital setting in the continued optimised management of these patients after discharge	
111.	SH	Greater Manchester West Mental Health NHS Foundation Trust	6	Full	2.1.6	29	I think specific recommendations should be made that an individual should be advised to carry on drinking alcohol, at a similar or slightly reduced level until such time as engaged with alcohol services. In identifying predictors of high risk withdrawal the statement of signs and symptoms of autonomic over-activity needs to be clarified how severe do these signs have to be to identify risk in the Wentworth House protocol we use CIWA scores > 10 with a BAC > 200mg/dl as the identifier of high risk withdrawal and a tachycardia on admission of >100bpm.	Thank you for your comment. This issue was discussed by the GDG and is reflected in recommendation #2. With regard to the risk of DTs, this is discussed in the FETR. Without stronger evidence we did not want to be more specific about what CIWA score and BAC should be the cut off. We have made this clearer in the FETR now and added a footnote to the recommendation.
112.	SH	Royal College of Physicians	4	Full	2.1.6	29	The decision as to whether to admit somebody for treatment of alcohol withdrawal should include the need to treat coexistent medical conditions e.g. alcoholic liver disease. There should also be mention of the window of opportunity to admit and diagnose people who may have unrecognised liver disease for example.	Thank you for your comment. We did not cover the specific area of using the withdrawal episode as an opportunity to uncover other alcohol specific conditions. If these patients have liver disease that does not require admission, it was not felt appropriate to admit them for withdrawal that would also otherwise not require admission. This issue has now been covered in the introduction.
113.	PR	NETSCC, Referee 1	5	Full	2.2.5 &	37	**2.2 Please comment on the health economics and/or statistical issues**	Thank you for your comment. This has been amended.

Comment No.	Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
					2.5.5	61	**depending on your area of expertise.** Statements that medication costs are 'relatively low' and treatment given for a 'short period' are used on a number of occasions in relation to the economic sections (I've listed a couple of examples of sections where I have spotted this, but there may be more). These statements are particularly vague and I would recommend the actual cost (e.g. per day, or even 'few pence per dose' as is stated for a number of medications mentioned in the report) and actual treatment length are reported for clarity.	
114.	SH	Alcohol Use Disorders: Alcohol dependence and harmful alcohol use Guideline Development Group	16	Full	2.1.6	Para starting Line 41	Need to be clearer about what this recommendation is about.	Thank you for your comment. The group did not find enough evidence to support making a recommendation concerning repeated unplanned medically assisted withdrawals.
115.	SH	Institute of Psychiatry	6	Full	2.1.6	29 line 39	1,000mg/L – should there be consistency throughout the document regarding units – e.g. would this be better expressed as 100mg/100ml?	Thank you for your comment. This has been changed to read 100mg/100ml.
116.	SH	Alcohol Use Disorders: Alcohol dependence and harmful alcohol use Guideline Development Group	22	Full	2.7	106 (or 88)	The risk factors that indicate possible need for giving Pabrinex are stated, and the BNF comments that risk of allergic reaction should not preclude the giving of pabrinex to these people, does that statement include giving this via intramuscular form when IV is not possible – eg the confused and agitated patient likely to remove IV line	Thank you for your comment. There are real difficulties with IM injection – it is very painful and an agitated patient might move resulting in a missed injection site or needle breakage. There is also a risk of disturbed clotting or reduced platelets because of haematoma formation with considerable risk of an infected injection

Comment No.	Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
							repeatedly.	site. The GDG therefore intend for thiamine to be given by the parenteral rather than intramuscular route when stated in the recommendation.
117.	SH	Alcohol Use Disorders: Alcohol dependence and harmful alcohol use Guideline Development Group	20	Full	2.2.6	Line 12	"In particular, there was no evidence to support the widely held belief that clomethiazole is less safe than the other agents, although the GDG were concerned about use of this agent outside a closely monitored inpatient setting. The trial evidence available was not sufficient to reassure the GDG regarding the use of this agent outside these circumstances." These cautions are not apparent when looking at recommendation R5 – concern that commissioners and practitioners who are not aware about the potential risks of clomethiazole may read only the recommendation and not the context in which it is made. The guideline group should consider ranking which drug should be offered first. The guideline group should consider be clear that clomethiazole – if it is included, that if it is prescribed, it is only done so when the patient will clearly complete their detox as an inpatient and be monitored. We acknowledge that others (eg Herrán & Vázquez-Barquero**)** have raised the issue that the evidence against clomethiazole may mean that the risks of benzodiazepine are overlooked – however in the absence of	Thank you for your comment. This recommendation has now been amended so use of clomethiazole is reserved for in-patient settings only.

Comment No.	Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
							clomethiazole showing better efficacy than benzodiazepines for treating alcohol withdrawal, the risks of clomethiazole do appear to outweigh those of benzodiazepines. This is particularly so for outpatient detox. Therefore the evidence to support prescribing of clomethiazole is not substantial enough to overturn recommendations in the BNF and SPC.	
118.	NICE	Alcohol harm prevention programme development group	3	Full	2.1.7	30 R2	Thousands of people spontaneously stop drinking and as far as we know do not come to any harm as a result of sudden withdrawal. At present patients attending A and E departments who are noted to be abusing alcohol are advised to continue drinking and attend support services (which they may not do) as advised in this recommendation. Nowhere in the document is the utility or danger of this advice examined. For patients not requiring hospital admission an important opportunity may be being lost to advise alcohol withdrawal and to receive **medical advice to continue drinking is really contradictory** and can easily be misinterpreted by the patient or used as an excuse to continue drinking. I believe this recommendation should be withdrawn and the question passes to the alcohol dependence PDG to be fully considered. Where patients are considered to be at high risk of DT's or seizures, surely the advice (to PCT's) should be ensure that sufficient	Thank you for your comment. It is important to clarify the group of patients that this recommendation covers. What this recommendation covers is the dependent population that present in withdrawal. They have already selected themselves out as people that cannot stop drinking suddenly, unlike the thousands you refer to. We recommend that patients at high risk of seizures and/or DTs should be admitted to hospital for medically-assisted withdrawal. Those deemed to not be in the severe risk population still have *some* level of risk of developing seizures and DTs. Suddenly stopping drinking alcohol will put them at more risk. The public health guidance covers the "therapeutic" advice that can be given to hazardous or harmful drinkers in acute settings that may help them to cut down or stop alcohol. We do not agree, however, to

Comment No.	Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
							facilities are available to enable referral for immediate medically assisted planed withdrawal.	remove this recommendation to dependent drinkers that are in withdrawal but not being admitted to hospital.
119.	SH	South London and Maudsley NHS Foundation Trust	8	Full	2.2.6	38, lines 12-13	"...there was no evidence to support the widely held belief that clomethiazole is less safe that the other agents etc..." I would advocate the word view instead of the word belief here. Clomethiazole is safe in a controlled "closely monitored inpatient setting". However, when it was more widely used in the 1980s patients would typically be admitted briefly to a general hospital, started on a detox, and then, when they were discharged a day or two later, be given the balance of their clomethiazole (chlormethiazole as it was then) to take unsupervised at home. As it has a high dependence potential, patients taking it in an unregulated setting (at home) are at risk of developing a clomethiazole dependence syndrome, and are at further risk of developing withdrawal seizures and status epilepticus if they stop taking it abruptly for any reason. The use of chlormethiazole in the community setting is associated with the risk of respiratory depression when it is taken with alcohol. It should be noted that clomethiazole was never passed by the FDA for use in the United States.	Thank you for your comment. We have amended the text accordingly.
120.	SH	Greater Manchester West Mental Health NHS Foundation Trust	7	Full	2.2.6	38	Perhaps it is outside the scope of the guidance to comment but often decisions about the agent to be used for detoxification are made not just on effectiveness in controlling withdrawal symptoms but on	Thank you for your comment. We have considered these factors and amended the chlomethiazole recommendation so its use is limited to in-patient use only. For those with liver impairment we have

Comment No.	Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
							other factors e.g. abuse potential of chlomethiazole compared to chlordiazepoxide In prescribing to the elderly or those with liver disease again the advice about using shorter acting agents needs to be qualified how severe does the liver impairment have to be, how old and frail. Our practice is to use a lower dose of chlordiazepoxide and monitor for any signs of benzodiazepine toxicity in these patient groups	recommended hepatology advice is sought.
121.	SH	The Society for Acute Medicine	1	Full	2.2.6	38	The commonly used agent is chlordiazepoxide (80%) or diazepam (20%) from a national survey of practice by Ward et al (2009). None of the hospitals in that survey used anything else first line. We would prefer to see that more confusion is not caused by the suggestion of too many more historical alternatives, such as clomethiazole. It is unlikely that any head to head trials will ever be conducted now that practice is so widespread with such cheap and effective medications. [Ward et al (2009) A multi-centre survey of inpatient pharmacological management strategies for alcohol withdrawal. Q J Med; 102:773–780. (doi:10.1093/qjmed/hcp116. Advance Access Publication 20 August 2009)]	Thank you for your comment. As NICE recommendations aim to address variations in practice across various medical settings in the UK, the literature pertaining to a selection of agents was reviewed. The GDG found no evidence to support the widely held belief that clomethiazole is less safe than the other agents, but note its use should be closely monitored in an inpatient setting (consistent with the BNF).
122.	PR	NETSCC, Referee 1	6	Full	2.3.5	50	**2.2 Please comment on the health economics and/or statistical issues**	Thank you for your comment. The time horizons used were the periods the

Comment No.	Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
							depending on your area of expertise. Over what period of time are these models run? Was any post-treatment data available? Can the group comment on whether they considered the longer-term implications, particularly whether costs post treatment/discharge are likely to be higher for those discharged earlier?	patients were hospitalised for treating AAW as reported in clinical trials (see Table 1, Appendix 3, p.188). There is no evidence showing a difference in resource use post treatment/discharge using a symptom-triggered regimen or a fixed-dosing regimen.
123.	PR	NETSCC, Referee 2	5	Full	2.3.5	53	**2.2 Please comment on the health economics and/or statistical issues depending on your area of expertise.** I think this is the most important comment. The model is based on a large number of assumptions. It is true that for the deterministic results there are consistent results. However, the probabilistic results indicate that low confidence can be placed once uncertainty is taken into account – all figures suggest that the probability of being below the NICE threshold of less than £20,000 per QALY is between 59 and 63%. The conclusions must be drawn with a lot more caution. Exploring this uncertainty needs also to be the focus of the research questions. It is vitally important to explore issues of training and fidelity along with true variations in resource costs.	Thanks for your comment. Please note: The 'relatively low' probability of cost-effectiveness is due to the lack of significance in the difference in quality of life scores (Appendix 3, Section 5).
124.	SH	College of Mental Health Pharmacists	5	Full	2.4.4	57	Line 12 the cost of olanzapine is exact but those of lorazepam and haloperidol just a few pence. This may be misleading, can you give an exact cost of lorazepam and	Thank you for your comment. This has been added to the full guideline.

Comment No.	Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
							haloperidol?	
125.	SH	The Society for Acute Medicine	3	Full	2.7.1	78	The report mentions poor absorption in abstinent malnourished alcohol, misusers Line 12 onwards but then advice which poorly correlates with p89/90 in relation to high risk groups and line 7 where good diet may suffice. In other words this appears almost contradictory to the reader	Thank you for your comment. The GDG attempted to establish a balance between prophylaxis against Wernicke's and over-treatment. The reason for this comment in the guideline is that, in spite of reduced absorption, most malnourished heavy drinkers do not go on to develop Wernicke's encepalopathy. This implies that a poor diet usually suffices as prophylaxis and a good one should also. However, the guidance has now been amended and the new recommendations can be found in section 2.7.7.
126.	SH	South London and Maudsley NHS Foundation Trust	9	Full	2.2.6	38, lines 22 and 23	Many clinicians would routinely advocate use of a shorter-acting benzodiazepine in treating alcohol withdrawal in older adults, even when there was no evidence of encephalopathy.	Thank you for your comment. This has been added to the from evidence to recommendation section of the full guideline.
127.	SH	Alcohol Use Disorders: Alcohol dependence and harmful alcohol use Guideline Development Group	18	Full	2.1.8		Research recommendation 1: Suggest consider this compared with no admission and GP / community detox or planning for detox and follow-up for abstinence.	Thank you for your comment. This research recommendation has been amended accordingly.
128.	SH	Alcohol Use Disorders: Alcohol dependence and harmful alcohol use Guideline Development Group	23	Full	2.2.7		Whilst referral to hepatology service (R6) is recommended, referral to or advice from a specialist addiction service is not. Given their concerns expressed about lack of continuity of care to such services, wouldn't a recommendation about this be appropriate?	Thank you for your comment. This guidance is for the management of acute alcohol withdrawal. Do we need specialist addiction services for the acute management? It would be nice, but not realistic. The withdrawing patient with decompensated liver disease is a special situation.

Comment No.	Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
129.	SH	South London and Maudsley NHS Foundation Trust	14	Full	2.3.6	54-56	There is a huge gap between the controlled setting of the efficacy trial on a specialist addiction unit and the real world of alcohol withdrawal management on a busy medical ward, where treatment is unplanned and patients are likely to be admitted in severe withdrawal. Clinical experience would suggest that symptom-triggered regimes are only possible and safe where there is a high staff: patient ratio and may be easier to implement in the treatment of alcohol withdrawal at the lower end of the severity spectrum. One of the studies (no 32, see p 46) reported more protocol errors in the ST group compared with the fixed-schedule dosing group.	Thank you for your comment. The GDG have similar concerns, but there are many medical conditions that require high staff to patient ratios. One of the purposes of the guidance is to improve practice and provide recommendations that are both clinically and cost-effective In this instance the evidence supported the use of symptom-triggered regimens. The NICE implementation team will work to ensure this is in place with the required support.
130.	SH	Royal College of Nursing	3	Full	2.1.8	30-31	It was very positive to read here that the recommendations made are in line with recommendations that any clinician working with people with alcohol problems would like to see, and which would significantly reduce the levels of alcohol related harms on a personal, familial and societal level.	Thank you for your comment.
131.	PR	NETSCC, Referee 2	11	Full	2.1.8	31	**4.2 Please comment on whether the research recommendations, if included, are clear and justified.** It is not clear that this research recommendation could be carried out as it would be very difficult to ethically examine. Should this be refined in some way to make it a researchable and useful question	Thank you for your comment. We think this is a very important research recommendation and one that is ethical as the least interventional arm is current recommended practice.
132.	SH	South London and Maudsley NHS	13	Full	2.3.6	54	The evidence points to the superiority of the symptom-triggered (ST) schedule in terms	Thank you for your comment. Please find a discussion of this issue in section 2.3.6 of

Comment No.	Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
		Foundation Trust					of total cumulative dose, shorter treatment duration and cost-effectiveness. It is of note that the ST option is no longer cost-effective "if the healthcare worker spends longer than four minutes extra per assessment". This is very important and underscores the point that ST regimes require a high level of competence in committed nursing staff. This is not always possible on the busy ward where there may be competing needs, a high turnover of nurses and agency staff. An ST regime is likely to unravel very quickly on a busy ward and is better suited to a specialist unit.	the full guideline.
133.	SH	Greater Manchester West Mental Health NHS Foundation Trust	11	Full	2.3.6	55	Recommendations should include the caveat regarding the use of symptom triggered protocols in high risk detoxifications. Services will vary greatly in the numbers of high risk patients accepted or excluded and thus blanket recommendations regarding the benefits of symptom triggered treatment over fixed dose. In much the same way as there are caveats for the use of symptom triggered protocols in unplanned detoxification in terms of the risk of progression to Dts and seizures	Thank you for your comment. There is now a comprehensive caveat within this recommendation regarding the requirements.
134.	NICE	Health Economist	7	Full	2.4.5	58	The reflection of the GDG discussion and consideration of downstream effects and costs is transparent and comprehensive.	Thank you for your comment.
135.	PR	NETSCC, Referee 2	7	Full	Appendix 3		**2.2 Please comment on the health economics and/or statistical issues**	Thank you for your comment. Results of the cost-effectiveness analysis assume that staff received appropriate training for

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							depending on your area of expertise. CIWA-A scale and its administration seem to be an important issue which was under-explored in the model. It would be expected that the success of monitoring patients is closely linked to training and skills of the practitioners. The higher skills and potentially resources required for the symptom triggered regime in practice could be substantial and the adverse effects of less skilled staff undertaking these regimes could impact on success rates and complications. The baseline assumption of the same costs of assessment between the regimes seems odd, While the one way sensitivity analysis did not make a large impact on the deterministic results, it is less clear whether uncertainty around these parameters contributed to the more uncertain probabilistic results.	using symptom-triggered regimen (and the CIWA-A scale). A different assessment cost was calculated for each regimen in the comparison: 'The cost of staff time was calculated by multiplying the hourly cost of nurse time by the time a nurse is in contact with a patient. The amount of time a nurse is in contact with the patient is determined by the assessment schedule used by the nurse monitoring the patient and the number of minutes required to conduct each assessment' (p.190). The uncertainty around probabilistic results is due to the lack of significance in the difference in quality of life scores (Appendix 3, Section 5).
136.	SH	Alcohol Use Disorders: Alcohol dependence and harmful alcohol use Guideline Development Group	3	Full	2.3.7		Our reading of the summary evidence (2.3.6) is that symptom triggered should by reserved for those competent to provide assessment and monitoring over a 24 hour period – probably only addiction-based services. The narrative describes that more evidence is needed for symptom triggered regimens in the inpatient setting since most comes from specialist inpatient settings. Concerns are also expressed about the suitability of recommending symptom triggered regimen	Thank you for your comment. This recommendation has been amended.

Comment No.	Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
							that requires close monitoring and therefore the need for specialist skills. Despite all this narrative, the recommendation (R7) is that "For people in acute alcohol withdrawal, follow a symptom triggered regimen for drug therapy if 24 hour assessment and monitoring are available". We suggest that specialist or appropriate be added in relation to the assessment and monitoring. In addition, what regimen should be used in their absence needs to be stated.	
137.	SH	South London and Maudsley NHS Foundation Trust	10	Full	2.2.8	RR2 38, lines 42-45	I am amazed that clomethiazole has been judged as meriting a research recommendation when its use, except in the acute clinical setting, has fallen out of favour for sound reasons. Its utility as a pharmacotherapeutic agent for the treatment of alcohol withdrawal in the acute setting is not in doubt.	Thank you for your comment. The research recommendation in this chapter has now been changed. When reviewing the literature on clomethiazole the GDG found no evidence to support the widely held belief that clomethiazole is less safe than other agents when used in a closely monitored inpatient setting.
138.	SH	Royal College of Nursing	4	Full	2.4.6	57-58	This section appears confusing as the panel appears to favour olanzapine due to the reduced side effect risk. Then in the recommendations this is listed third in the medications, which looks as if it is the least favourable option.	Thank you for your comment. The use of olanzapine in the management of delirium tremens is off-label and more expensive than the other two agents. Further olanzapine may not be available for use in all healthcare settings. Therefore, each of the agents are recommended equally based on the consensus opinion of the GDG as there was no robust evidence .
139.	SH	NHS North of Tyne encompassing:	3	Full	3	9	Feedback from our working groups suggests people relate more to the term	Thank you but the developers are unsure what this comment pertains to.

Comment No.	Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
		Newcastle PCT, North Tyneside PCT, Northumberland Care Trust					"increasing risk" and "higher risk"	
140.	SH	NHS North of Tyne encompassing: Newcastle PCT, North Tyneside PCT, Northumberland Care Trust	4	Full	3	13	The wording of this point may be misleading, there is limited evidence on the basis that there have been limited studies in this area, not that studies have been undertaken which have failed to prove efficacy. It would be good to see more commissioned research in these areas, rather than perpetuate the research around health and criminal justice settings.	Thank you but the developers do not understand what this refers to.
141.	SH	South London and Maudsley NHS Foundation Trust	15	Full	2.3.7	56 RR3	Some patients do not experience marked alcohol withdrawal symptoms, and there is a risk that they could be under-medicated on an ST regime and thus deteriorate very quickly, developing severe uncontrolled symptoms/alcohol withdrawal seizures/status epilepticus. Increasing numbers of patients have concurrent cocaine and cannabis use/misuse which complicates the alcohol withdrawal syndrome. Perhaps the safest and most acceptable regimen is a hybrid of the ST and fixed-schedule dosing regimens. This is flexible and offers a tailored withdrawal and merits further investigation.	Thank you for your comment. This guidance does not cover poly drug use. Close monitoring will be required for the symptom-triggered regimen.
142.	SH	The Society for Acute Medicine	2	Full	2.3.7	56	We fully agree that symptom-triggered should be recommended above all other methods of sedation, based on the evidence available.	Thank you for your comment.

Comment No.	Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
143.	SH	Royal College of Nursing	5	Full	2.5.5	61	This is a rather 'picky' point but the text here uses the abbreviation AAW and then the full term acute alcohol withdrawal in some parts of the document – we assume this will be addressed anyway but it can be rather confusing.	Thank you for your comment.
144.	SH	Alcohol Use Disorders: Alcohol dependence and harmful alcohol use Guideline Development Group	6	Full	2.3.7	56, line 9	This statement does not reflect the complexity of the foregoing discussion on symptom triggered versus other regimes. The discussion suggests that most of the evidence is from specialist alcohol units which may not be applicable to the acute hospital or unplanned withdrawal; it relies on having appropriately trained staff with sufficient time to carry out repeated hourly assessments of withdrawal symptoms. It is likely that staff in a busy acute ward will find it difficult to maintain this level of monitoring, particularly at busy times and changeovers of staff. The risk therefore is that the protocol may not be followed correctly and patients will be put at risk of severe complications because of less frequent or ineffective monitoring. It would be more sensible to recommend a fixed does plus prn regime as the default, which is what is provided in most hospitals, and then add "where resources allow, follow a symptom triggered regime….	Thank you for your comment. The recommendation has been changed to reflect the setting in which it is appropriate and the degree of monitoring required.
145.	SH	Alcohol Use Disorders: Alcohol dependence and harmful alcohol use	29	Full	2.3.7	56, line 9	This statement does not reflect the complexity of the foregoing discussion on symptom triggered versus other regimes. The discussion suggests that most of the	Thank you for your comment. The recommendation has been changed to reflect the setting in which it is appropriate and the degree of monitoring required.

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		Guideline Development Group					evidence is from specialist alcohol units which may not be applicable to the acute hospital or unplanned withdrawal; it relies on having appropriately trained staff with sufficient time to carry out repeated hourly assessments of withdrawal symptoms. It is likely that staff in a busy acute ward will find it difficult to maintain this level of monitoring, particularly at busy times and changeovers of staff. The risk therefore is that the protocol may not be followed correctly and patients will be put at risk of severe complications because of less frequent or ineffective monitoring. It would be more sensible to recommend a fixed does plus prn regime as the default, which is what is provided in most hospitals, and then add "where resources allow, follow a symptom triggered regime….	
146.	SH	Alcohol Use Disorders: Alcohol dependence and harmful alcohol use Guideline Development Group	28	Full	2.2.8	38, line 42	It is difficult to see how this can be a priority topic for further research given the demonstrated effectiveness of benzodiazepines.	Thank you for your comment. This research recommendation was made because of the contention about the use of chlormethiazole and its other interesting and potentially important actions such as inhibition of CYP2E1 which are very useful in the withdrawal period.
147.	SH	Alcohol Use Disorders: Alcohol dependence and harmful alcohol use Guideline Development Group	34	Full	2.7.3	82	Table 2-8 (line 3) should read table 2-17, and table 2-9 (line 4) should read table 2-18	Thank you this has been amended.
148.	SH	Alcohol Use	35	Full	2.7.3	85	'Table 2-11' (line 4 should read Table 2-20	Thank you this has been amended.

Comment No.	Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
		Disorders: Alcohol dependence and harmful alcohol use Guideline Development Group						
149.	SH	Alcohol Use Disorders: Alcohol dependence and harmful alcohol use Guideline Development Group	30	Full	2.4.6	57 line 39	While this recommendation appears appropriate from the evidence, it suggests that the management of delirium tremens is simply medication. Such patients need close monitoring, fluids, and bright lighting. These general care elements would be important to mention.	Thank you for your comment. The text in the clinical introduction has been amended to reflect this.
150.	PR	NETSCC, Referee 1	13	Full	3	128	**4.1 Is the whole report readable and well presented? Please comment on the overall style and whether, for example, it is easy to understand how the recommendations have been reached from the evidence** This new section should be numbered 4 not 3.	Thank you this has been amended.
151.	SH	Derbyshire Mental Health Services NHS Trust	3	full	3.1	14	Admission to hospital for acute withdrawal is guaranteed to trigger a withdrawal state that then has to managed. Efforts to reduce alcohol intake should be made in advance along with suitable psychological and vitamin preparation with nutritional monitoring. As long as risk factors are observed, helping pts to manage their own reduction teaches a skill and is based in the usual environment. Follow up and community based skills in essential. The cost of inpatient admission if it can be	Thank you for your comment. We entirely agree with these sentiments. Our recommendations are for those patients in withdrawal and we have limited the indications for admission to hospital.

Comment No.	Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
							avoided is too high. Losing the opportunity for intervention feels intuitively correct but motivational enhancement suggests that motivation to change is not a fleeting moment in time or a whimsical notion that would have been successful. Moreover a responsive and accepting service should be the first experience of a user wishing to stop. This allows for psychological preparation and reduces the chances of alcohol hepatitis induced by sudden cessation.	
152.	SH	Alcohol Use Disorders: Alcohol dependence and harmful alcohol use Guideline Development Group	36	Full	2.7.4	88	Although the published evidence is limited, it would be worth acknowledging the serious long-term implications of developing Korsakoff's psychosis. Short-term memory problems often lead to a requirement for 24 hour supported accommodation. As many individuals develop this at the age of 40 or so, this might mean 30 years of costly accommodation. Seen in this context, prevention with some cheap vitamin preparations becomes extremely cost-effective.	Thank you for your comment. The full guideline has been amended. Please see Section 2.7.5 and Section 2.7.6.
153.	SH	Institute of Liver Studies	4	Full	3.2	General	The section has failed to refer to and encompass the available nationally agreed guidelines for transplantation in the context of alcohol related liver disease. Available at: http://www.uktransplant.org.uk/ukt/about_transplants/organ_allocation/pdf/liver_advisory_group_alcohol_guidelines-november_2005.pdf	Thank you for your comment. Reference to these have now been included.
154.	SH	Derbyshire Mental	2	full	3.2	14	Symptom based treatment relies on	Thank you for your comment. The

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		Health Services NHS Trust					clinicians having the time and training in such measures as the CIWA and excellent observational skills in an inpatient setting. If this is guaranteed then symptomatic treatment is a gold standard. However, As long as initial doses are symptomatically titrated a fixed dosing regime is more reliably administered in a general setting - experience has taught me. Adequate treatment will reduce incidence of violence cause by allowing pts to begin to go into withdrawals and maintain higher degree of treatment conclusions.	evidence reviewed by the GDG supported the use of symptom-triggered dosing regimens when supported by appropriately trained appropriately trained staff.
155.	SH	College of Mental Health Pharmacists	6	Full	2.7.5	32	It would be useful to quote an exact rate of anaphylaxis for pabrinex im and iv.	Thank you for your comment. A reference has been added to the guideline.
156.	SH	Royal College of Physicians	6	Full	2.6.6	77	With relation to R13 'Ensure that staff caring for people in alcohol withdrawal are trained in the assessment and monitoring of withdrawal symptoms and signs' This is a worthy objective but it does not easily translate to reality. There is a need to recognise and understand the pressures on nursing and medical staff in both general medical and other general hospital settings who are treating alcohol withdrawal. This particularly applies in those areas where alcohol withdrawal would not necessarily be expected, notably orthopaedic wards, elderly care wards, maxillofacial wards? Junior medical staff change every few	Thank you for your comment. This recommendation is based on what the GDG considered to be best practice. It also reduces length of stay. There will need to be changes in the delivery of care to this group of patients to accommodate the recommendations which the NICE implementation team will work to introduce.

Comment No.	Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
							weeks and nursing staff also rotate frequently. It is therefore difficult to ensure that staff looking after NHS patients have the full capability to treat the range of general medical, surgical and other problems that they encounter without requiring specific universal training in acute alcohol withdrawal. The key criteria for any alcohol withdrawal regime is that it is extremely simple and relatively easy to follow, and that both regimes should be treatment options.	
157.	SH	Alcohol Use Disorders: Alcohol dependence and harmful alcohol use Guideline Development Group	31	Full	2.6.6	77 line 10	The GDG noted that late identification of withdrawal leads to delay in instituting withdrawal management and a more complicated withdrawal. Prevention of severe withdrawal developing is much more effective. A useful recommendation would be to ask all patients being admitted about recent alcohol consumption to identify those at risk of withdrawal before the symptoms appear. Males drinking more than 15 units a day is at risk of withdrawal (less in women), over 30 units patients are likely to experience severe withdrawal. Alternatively an AUDIT questionnaire score >20 would identify the dependent group. Even better would be a clinical diagnosis and assessment of alcohol dependence (e.g. Severity of Alcohol Dependence Questionnaire) leading to appropriate prophyaxis for alcohol withdrawal. Typically a patient drinking 30 units of alcohol per day	Thank you for your comment. The assessment of the severity of dependence was not in the scope of this guideline. While we accept that an assessment of this nature is important in the management of the patient, we have not reviewed how best to make this assessment.

Comment No.	Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
							for the previous few weeks will have an SADQ score of 30 (out of 60) and require a starting dose of 30mg q.d.s. chlordiazepoxide. The dose can should be titrated to the level of alcohol consumption (e.g. 60 units will typically require 60mg q.d.s.). This provides a simple aide memoire for busy clinical staff and is easier to train staff to deliver than symptom triggered dosing and withdrawal sign recognition or CIWA-Ar scoring.	
158.	SH	Archimedes Pharma Ltd	9	Full	2.7.5	88	Undue emphasis is placed on the risk of anaphylaxis from parenteral thiamine. There have been 9 reported cases of allergic reactions in the UK in the last 10 years, of which 2 were reported as anaphylaxis; during the same period there have been over 7 million pairs of ampoules of Pabrinex prescribed in the UK (Archimedes *data on file*). This is in contrast to other parenteral therapies such as certain antibiotics, which are widely prescribed but have a much higher reported incidence of anaphylaxis.	Thank you for your comment.
159.	SH	Archimedes Pharma Ltd	10	Full	2.7.5	88	It is inappropriate to consider the financial costs related to anaphylaxis in the Health Economic Evidence Statements section (2.7.5). This is a very rare potential side effect with 2 reported cases of anaphylaxis in the last 10 years. During the same period there have been over 7 million pairs of ampoules of Pabrinex prescribed in the UK (Archimedes *data on file*). The potential cost	Thank you for your comment. The Guideline has been amended (Section 2.7.5).

Comment No.	Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
							of anaphylaxis is therefore inconsequential in this context given the vast numbers of patients treated.	
160.	SH	The Society for Acute Medicine	4	Full	2.7.5	88	BNF 58 ? not 56 What is the incidence of anaphylaxis ? Would guidelines on discussing antibiotics emphsise this risk to this extent SAM members see this as uncommon, much so less antibiotics and appears to be anecdotal rather than based in fact which may discourage high quality care in this vulnerable group of patients.	Thank you for your comment. At the time of reviewing evidence, the BNF no.56 was the latest version available. This information is the same in the BNF no.58.
161.	SH	South London and Maudsley NHS Foundation Trust	18	Full	2.7.6	88-90	The risk factors for thiamine deficiency (p89) are key to any decision to offer thiamine prophylaxis and should be highlighted in the guideline. It is unlikely that alcohol dependent individuals who are admitted to a general hospital will have been "otherwise eating a normal diet and with no other alcohol-related problem" (p89, lines 25, 26) i.e. be "low-risk". The guideline defines the "high-risk" group as "hazardous, harmful or dependent drinkers" with additional risk factors. It is unlikely that this group will be hazardous drinkers. They will be harmful or dependent drinkers. The risk factors should be listed in a coherent way, highlighting the underlying causes of "malnourishment". The guideline, as currently written does not make it clear who should be offered parenteral thiamine, with the attendant risk that a significant proportion of those who need it would not	Thank you for your comment. We have amended the recommendations pertaining to thiamine in an effort to make them more easily understood by the reader.

Comment No.	Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
							qualify as per the guideline.	
162.	SH	South London and Maudsley NHS Foundation Trust	19	Full	2.7.6	89, lines 37-47 and p90 lines 1-4	It might be helpful to list the causes of compromised nutrition in terms of (1) the clinical history (poor diet, weight loss in past year, reduced BMI, recurrent episodes of vomiting in past month); (2) early signs and symptoms of thiamine deficiency (loss of appetite, nausea/vomiting, fatigue, weakness, apathy, diplopia, insomnia) and (3) later signs and symptoms of thiamine deficiency (the classic triad, confusion, confabulation, hallucinations) (as set out in a table in Thomson et al (2008) Alcohol Alcohol 43, 180-186).	Thank you for your comment. Certainly it is possible to list the factors that might compromise a patient's nutritional status e.g. poor dietary intake, unintentional weight loss etc. However, fatigue weakness and apathy are generic symptoms which are not specific for thiamine deficiency while diplopia, if present and not otherwise explained e.g. injury to the orbit, an intracranial lesion, would warrant immediate treatment with thiamine even before the diagnosis is clarified one way or another.
163.	SH	Greater Manchester West Mental Health NHS Foundation Trust	13	Full	2.7.6	90	High risk groups should also include those with evidence of potentially thiamine related physical symptoms such as peripheral neuropathy and cerebellar disorders and beri- beri. Suspected or incipient wernickes should be diagnosed in all cases of confusion during withdrawal including those with obvious features of delirium tremens	Thank you for your comment. If there are new cerebellar signs we think there should be a suspicion of Wernicke's. If there are long-standing cerebellar signs the patient should be treated if they fall into any of the other high risk categories only. For example if a patient with cerebellar signs has stopped drinking and is well nourished, they will not be high risk for WE. This is similar for neuropathy. The recommendation has been amended to emphasise the need for a high index of suspicion for WE.
164.	SH	Institute of Liver Studies	1	Full	3.2.1	109	Use of the word "recidivism" throughout section – defined in Oxford English Dictionary (1989) – "the habit of relapsing to crime" although popular in US text regarding alcohol relapse following liver transplantation. Please see: Webb, K.,	Thank you for your comment. This term is commonly used in the context of this population irrespective of its dictionary meaning.

Comment No.	Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
							Shepherd, L. & Webzell, I. (2008) Time please, gentlemen! *Transplant International.* 21. pp 814-815.	
165.	SH	Institute of Liver Studies	2	Full	3.2.1	109	"No evidence that patients with ALD have a higher frequency of post operative complications". There is reasonable evidence that people with ALD who undergo transplantation experience a higher frequency of post operative acute confusional state e.g. Acute confusional state following liver transplantation for alcoholic liver disease Carlijn I. Buis, Russel H. Wiesner, MD, Ruud A.F. Krom, MD, Walter K. Kremers, PhD and Eelco F.M. Wijdicks, MD). (Belle SH, Beringer KC, Detre KM. Liver transplantation for alcoholic liver disease in the United States: 1988 to 1995. Liver Transplant 1997; 3: 212± 19)	Thank you for your comment. The developers agree with this and the document has been amended.
166.	SH	Alcohol Use Disorders: Alcohol dependence and harmful alcohol use Guideline Development Group	32	Full	2.7.6	90 line 28	Didn't think we were using the term "alcohol abuse"?	Thank you. This has been amended.
167.	SH	South London and Maudsley NHS Foundation Trust	20	Full	2.7.6	90, lines 14, 15	Alcohol withdrawal in itself will use up stores of thiamine, so it is vital that clinicians have an understanding of what constitutes severe alcohol withdrawal. These patients will be poor historians so decisions will often have to be made very quickly on clinical examination alone (Thomson et al, 2008).	Thank you for your comment. The developers are not sure whether this is true. Thiamine requirements relate to carbohydrate intake and if these patients are given unsupported glucose infusion they will need more thiamine. If there is any suspicion of Wernicke's there should be a switch to the treatment recommendation.

Comment No.	Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
168.	SH	South London and Maudsley NHS Foundation Trust	21	Full	2.7.7	R15	Harmful drinkers will not usually be alcohol dependent. Anyone in alcohol withdrawal is a dependent drinker. Some description of the dependent group is required here: mild? moderate? The guideline should have outlined how to identify and assess these patients. More severely dependent drinkers are more at risk of having a compromised diet and of developing thiamine deficiency.	Thank you for your comment. Identification and assessment of dependence are covered by the mental health guidance.
169.	SH	South London and Maudsley NHS Foundation Trust	22	Full	2.7.7	R16	There needs to be clearer guidance as to how to assess alcohol dependent individuals who are malnourished or at risk of malnourishment. It is not always obvious on clinical examination, although clinicians should always look out for proximal myopathy, as from clinical experience this is a helpful marker.	Thank you for your comment. The developers acknowledge this is a difficult area but extensive research has shown that a clinicians observation of the naked or scantily clad patient is as good if not better than anthropometry.
170.	SH	The British Association for Parenteral & Enteral Nutrition	6	Full	3.4		Although I accept that all aspects of care cannot be subject to a full examination of the evidence due to resource constraints, I would have welcomed some general comments, even if only expert opinion/good practice points about the level of nutrition support appropriate for patients with AH, the probable need for some balanced micronutrient supplementation etc. cross reference to the NICE Nutrition support guidance could be used to complete this.	Thank you for your comment. Some additional information has been added to this section of the guideline. The same recommendations are given for nutritional support in patients with decompensated cirrhosis and those with cirrhosis undergoing surgery and liver transplant.
171.	SH	Archimedes Pharma Ltd	2	Full	2.7.7	90-91	The situations listed in R15 present an over-simplified picture. This is unhelpful to the prescriber, particularly as the risk factor would increase where more than one of these situations apply e.g. a malnourished patient presenting with acute or medically	Thank you for your comment. The thiamine recommendations have been amended.

Comment No.	Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
							assisted withdrawal.	
172.	SH	Archimedes Pharma Ltd	3	Full	2.7.7	90-91	It is unclear, but presumably the bullets in R15 are describing situations of patients who are being managed in the primary care setting. If so the guidance should recognise that a sub-set of patients from this group, as assessed on an individual basis, may be more appropriately treated in the secondary care setting.	Thank you for your comments. The thiamine recommendations have been amended and attempt to cover all settings.
173.	SH	Archimedes Pharma Ltd	4	Full	2.7.7	90-91	R15 should recognise that patients undergoing community-based detoxification require the same level of individualised assessment regarding the appropriateness of parenteral or oral thiamine as those undergoing detox in a secondary care setting.	Thank you for your comment. The developers agree with this statement and as such the recommendations pertain to both settings.
174.	SH	Archimedes Pharma Ltd	5	Full	2.7.7	90-91	Taking account of the above comments (2-4) R15 would be better worded as follows: "Offer prophylactic oral thiamine to harmful drinkers, being managed in the primary care setting, in either of the following situations: • if they are malnourished or at risk of malnourishment • if they have decompensated liver disease If the patient is in acute withdrawal, or undertaking planned detoxification, special consideration should be given as to whether:	Thank you for your comment. The developers have amended the thiamine recommendations but did not believe suggested changes make the recommendation clearer.

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							• the use of parenteral thiamine would be more appropriate and/or • the patient would be better managed in the secondary care setting	
175.	SH	Archimedes Pharma Ltd	7	Full	2.7.7	90-91	It would be appropriate to refer the prescriber to the British National Formulary for guidance on the dosage of parenteral thiamine.	Thank you for your comment. The recommendation has been amended. It is noted there is no parenteral thiamine preparation in the BNF – only Pabrinex which is a vitamin cocktail made up of water soluble vitamins B and C.
176.	SH	Archimedes Pharma Ltd	8	Full	2.7.7	90-91	Based upon the points made in the Evidence to Recommendations (2.7.6) it would be appropriate to include the following statement as a lead in to the recommendations in section 2.7.7: "The index of suspicion for considering Wernicke's in these patients should be high and the threshold for considering following the treatment recommendations should be low".	Thank you for your comment. The thiamine recommendations have been amended to include this.
177.	SH	Alcohol Use Disorders: Alcohol dependence and harmful alcohol use Guideline Development Group	37	Full	2.7.7	90	The preceding summary of the evidence presents the limited evidence base very fairly. However, we are concerned by the recommendations given, as taken alone they appear very weak. The introduction to section 2.7 points out that diagnosis of Wernicke's	Thank you for your comment. The thiamine recommendations have now been amended.

Comment No.	Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
							Encephalopathy is difficult, and that the classical triad of symptoms is rarely present. Post Mortem evidence suggests that a high percentage of cases are missed clinically. There is a convincing body of evidence that suggests that oral doses of thiamine are insufficient to get adequate levels of thiamine across the blood brain barrier in the acute situation. Therefore, if there is any suggestion that a patient may be at high risk of Wernicke's, parenteral treatment should be the first line. However, the recommendations on p90/91 imply that parenteral treatment should be reserved for more severe cases. We would argue that malnourished patients in acute withdrawal require parenteral treatment. Surely the threshold for parenteral treatment should be low as the consequences of allowing WKS to develop are so serious.	The body of evidence is old, from patients in very poor socioeconomic groups and not very strong. For this reason we have suggested this as an area for future research. We would also agree that a malnourished patients in acute withdrawal would require parenteral supplementation and this is in line with the recommendations as we have made.
178.	SH	Royal College of Physicians	7	Full	2.7.7	90	The guideline recommends thiamine prophylaxis in patients who are malnourished or at risk of malnourishment. We suspect that the percentage of acute hospital admissions undergoing an adequate assessment of their nutritional status within the few hours after admission (where there is a window of opportunity for prophylactic thiamine treatment) is low. As such, recommendations based on nutritional assessment may put patients in	Thank you for your comment. The developers believe you do not need to make a formal nutritional assessment; a physicians eyeball assessment is all that is required together with some simple questions in relation to recent dietary intake, GI symptoms and unintentional weight loss.

Comment No.	Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
							danger given the safety of thiamine prophylaxis. It is vital to stress that, if in doubt, thiamine should be administered parenterally where malnutrition and alcohol abuse are suspected. This is due to the terrible consequences of missed Wernicke-Korsakoff syndrome.	
179.	SH	Alcohol Use Disorders: Alcohol dependence and harmful alcohol use Guideline Development Group	38	Full	2.7.7	91	The recommendations perhaps need to be stronger in terms of how long parenteral treatment should be continued in cases of suspected Wernicke's Encephalopathy. R17 implies giving treatment for 5 days and then stopping. Experience of working with a working adult dementia services suggests a number of cases where WE was correctly diagnosed in an acute medical setting, parenteral treatment instigated, but then stopped after 3-5 days when improvement was noticed. Such cases then developed a Korsakoff Psychosis, with permanent short-term memory loss. It might be better to say that treatment should continue until improvement stops.	Thank you for your comment. Beyond 5 days it is likely that a patient's stores of thiamine will be saturated and any further thiamine excreted in the urine. Oral supplementation can be continued when parenteral thiamine has been discontinued and the recommendations now reflect this.
180.	SH	Archimedes Pharma Ltd	6	Full	2.7.7	91	In R16 The term "malnourished or at risk of malnourishment" is inappropriate in this context. Not only is it often not feasible to carry out a meaningful nutritional assessment in this group of patients in the acute setting, but the results may also be misleading; Chronic alcohol misusers who are apparently well nourished may be thiamine deficient, due to inadequate dietary intake and/or impaired absorption.	Thank you for your comment. The developers believe you do not need to make a formal nutritional assessment; a physicians visual assessment is all that is required together with some simple questions in relation to recent dietary intake, GI symptoms and unintentional weight loss.

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							It would be more appropriate to word this recommendation as follows: "Give prophylactic thiamine to harmful or dependent drinkers, who may be at risk of thiamine deficiency, if they attend an emergency department or are admitted to hospital with an acute illness. Particular attention should be given to those patients who are malnourished or at risk of malnourishment."	
181.	SH	The British Association for Parenteral & Enteral Nutrition	5	Full	3.4	126, line 23	'Weight' should read 'Weight loss'	Thank you and this has been amended.
182.	SH	The British Association for Parenteral & Enteral Nutrition	7	Full	3.5 (pancreatitis)		Although I do not disagree with the recommendations made regarding EN vs PN, it is important to note that the EN vs PN trials have not compared similar levels of nutrition support. In some PN trials, feeding levels were so high that patients were made hyperglycaemic and if these trials are not included in comparisons, all advantages of EN disappear. I would therefore like to see a Research Recommendation calling for EN vs PN trials in severe pancreatitis restricting maximum levels of feeding to those recommended within the NICE nutrition support guidance.	Thank you for your comment. There would be considerable difficulties with use of parenteral nutrition in this setting as dietary requirements using this route are not clearly delineated.
183.	SH	Derbyshire Mental Health Services NHS Trust	4	full	3.5	16	Oral thiamine has been demonstrated to help patients concentration return in community detoxification settings in my	Thank you for your comment. The recommendations on use of thiamine in Wernicke's encephalopathy have been

Comment No.	Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
							experience. Parenteral thiamine is used usually in hospitals because the crash facilities exist for anaphylaxis. I believe that some GP surgeries should administer as there is anecdotal evidence that this benefit to concentration occurs more rapidly than oral. It would depend if this an important cost effective concern. oral meds also depend on the gastro intestinal tract being intact enough to metabolise the drug. In many cases transit is so rapid that this is doubtful in my experience, therefore multiple oral dosing attempts should be made.	revised.
184.	PR	NETSCC, Referee 1	7	Full	3.2.4	112	**2.2 Please comment on the health economics and/or statistical issues depending on your area of expertise.** I don't necessarily agree that evidence to suggest that transplantation is not cost-effective for patients with alcoholic liver disease precludes the need for the clinical question, since it does not separate out evidence for abstinent versus non-abstinent patients, or for varying lengths of abstinence. Evidence of lack of cost-effectiveness in a general population may hide evidence of cost-effectiveness in sub-groups of this population. It is clear the group have an understanding of this, so I wonder if the sentence could be reworded.	Thanks for your comment. We accept your point. We amended the sentence (changing the word 'would' to 'could'). However, we feel that future discussion in the Guideline is not warranted.
185.	SH	College of Mental Health Pharmacists	8	Full	3.4.3.	Figures	The figures are too small to see	Thank you. This has been amended.
186.	PR	NETSCC, Referee 1	14	Full	3.4.3	151-	**4.1 Is the whole report readable and well**	Thank you. This has been amended.

Comment No.	Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
						152	**presented? Please comment on the overall style and whether, for example, it is easy to understand how the recommendations have been reached from the evidence** The figures are not visible	
187.	SH	Royal College of Physicians	8	Full	3.1.6	108	The suggestions for use of liver biopsy in alcoholic liver disease are reasonable. However, it is usually straight forward to make a clinical assessment of the severity of the liver disease and it is in those patients with alcoholic hepatitis who may need steroids, that biopsy tends to be most hazardous due to poor clotting and ascites. The decision to use steroids rests on the discriminant analysis and does not always need a biopsy. Those who are critically ill with severe acute alcoholic hepatitis, require guidance. In these situations, transjugular liver biopsy is the only safe option. This needs to be performed in specialist centres - usually transplant centres. If all patients with severe acute alcoholic hepatitis were to be transferred to these units for liver biopsy, then they would be no beds to assess patients for liver transplantation. The diagnosis of severe acute alcoholic hepatitis has therefore to be a clinical one, and these patients can only realistically be managed, in the majority of cases, in district general hospitals.	Thank you for your comments. We have changed the recommendation so that liver biopsy is not mandated. This is however, a very contentious area. It is hoped that future trials will answer whether patients with clinical alcoholic hepatitis, a DF > 32 but no features of alcoholic hepatitis on liver biopsy will benefit from steroids or not.

Comment No.	Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
188.	SH	Institute of Liver Studies	3	Full	Table 3.7	109	Incorrectly labelled. Referred to in text as table 3.3	Thank you. This has been amended.
189.	PR	NETSCC, Referee 1	8	Full	3.2.5	112	**2.2 Please comment on the health economics and/or statistical issues depending on your area of expertise.** Did the group consider attempting to model likely cost (and cost-effectiveness) including long-term benefits and modern selection practices? If this was not considered feasible, perhaps that should be noted in the document.	Thank you for your comment. An assessment as you described would not be informative to answer the clinical question (What length of abstinence is needed to establish non-recovery of liver damage, which thereby necessitates referral for consideration for assessment for liver transplant?). The cost-effectiveness analysis from Longworth 2003 was included to inform the group on the influence of this patient selection on resource use and cost.
190.	NICE	Alcohol harm prevention programme development group	4	Full	3.1.7	108 R21	The studies supporting this recommendation are described on pages 101-102 and are concerned with the differentiation of alcoholic hepatitis from cirrhosis. The conclusion given on p 108 is that clinical parameters are sufficient in 80-90% of patients but there is no consideration of any alteration in outcome as a result of biopsy evidence. Is extrapolation here justified?	Thank you for your comment. We feel that a biopsy should be done if it may change practice. If it does not show alcoholic hepatitis in someone that you would otherwise treat with steroids it may change practice. The strength of the recommendation has weakened.
191.	PR	NETSCC, Referee 1	17	Full	3.1.7	108	**4.2 Please comment on whether the research recommendations, if included, are clear and justified.** I wonder if a research recommendation is needed here, particularly in relation to the economics. It is noted that liver biopsy is expensive, but little attention seems to have been paid to this in Section 3.1.6. Given the	Thank you. A research recommendation has been added.

Comment No.	Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
							expense, the uncertainty and the risks in this area, an economic evaluation would be valuable.	
192.	PR	NETSCC, Referee 2	6	Full	3.2.6	112	**2.2 Please comment on the health economics and/or statistical issues depending on your area of expertise.** There is a statement line 26/7 abstinence is linked to resource use which I did not understand	Thank you for your comment. The guideline has been amended.
193.	PR	NETSCC, Referee 1	19	Full	3.1.7	132	**4.2 Please comment on whether the research recommendations, if included, are clear and justified.** Again, would a research recommendation be of value?	If CT is done first line and used with the first recommendation, the developers can't think of a research recommendation that would lead to evidence that would ultimately change this guidance.
194.	PR	NETSCC, Referee 1	18	Full	3.2.7	113	**4.2 Please comment on whether the research recommendations, if included, are clear and justified.** Given the limited evidence available, a research recommendation may be appropriate here.	Thank you for your comment. While it may be interesting to do research on liver transplantation, we believe it may be difficult, ethically, to give a research recommendation here. It would have to be comparing referral after 3 months abstinence with a more prolonged abstinence.
195.	SH	Institute of Liver Studies	5	Full	3.2.7	113	Whilst providing recommendations for referrers to transplant centres it is important to consider patients abstinence in the context of the available guidelines which have not been referred to e.g. people with alcoholic hepatitis or people with a history of drug & alcohol dependence with < 6 months abstinence.	Thank you for your comment. People with drug and alcohol dependence were excluded from the scope of this guideline. Alcoholic hepatitis per se is still a contra-indication to liver transplantation. Those patients that survive 3 months and are abstinent but still have decompensated liver disease may be referred as per the recommendation. This has been made more clear in the 'evidence to

Comment No.	Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
								recommendation' section of the guideline. .
196.	SH	Royal College of Physicians	9	Full	3.2.7	113	R22. This is laudable. However, if patients are to be assessed for liver transplant when they still have decompensated alcoholic liver disease after best management and 3 months abstinence, then there needs to be a major expansion of the hepatology workforce, and more liver transplant units. Reference should be made to the recently published National plan for Liver services, which discusses these recommendations.	Thank you for your comment. NICE do not provide advice on service provision.
197.	SH	College of Mental Health Pharmacists	7	Full	3.3.6	122	Line 2 reference to evidence but the reference is not cited.	Thank you for your comment but the developers have cited all of the studies referenced.
198.	SH	Royal College of Nursing	2	Full	4	15	Referring to people who misuse alcohol here and alluding to the need for them not to stop suddenly is misleading. It is accepted that binge drinkers could be seen to misuse alcohol and yet will often stop after a weekend binge. Referring to mis-users here will further cloud this issue and make the picture even more complicated for clinicians and for people with alcohol issues. The accepted statement is that people who have a physical dependency should not stop suddenly due to the risk of the withdrawals that are mentioned here.	Thank you for your comment. We are referring to dependent patients here. They should not stop suddenly but they can be tapered off and should be directed to an appropriate service as the main intervention.
199.	SH	Royal College of Physicians	10	Full	3.3.7	121	R23 'Treat with corticosteroids people with acute severe alcohol-related hepatitis and discriminant function of 32 or more.'	Thank you for your comment. The meta-analysis undertaken does not leave much doubt that corticosteroids are effective and

Comment No.	Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
							Given the still contentious nature of the use of corticosteroids amongst clinicians it is surprising that no research recommendation is included with the statement. Reference should be made to future research and the forthcoming trial with Pentoxifylline, with or without corticosteroids, in the treatment of acute alcoholic hepatitis.	should be used in patients with a DF > 32. There is only one published paper on pentoxifylline so this drug was not included in the clinical question. As you rightly suggest, we all eagerly await the outcome of the large clinical trial. The 'evidence to recommendation' section has been adapted.
200.	PR	NETSCC, Referee 1	20	Full	3.4.7	151	**4.2 Please comment on whether the research recommendations, if included, are clear and justified.** Would a research recommendation be appropriate for the mild group?	Thank you for your comment. This has already been studied people with mild pancreatitis.
201.	SH	NHS North of Tyne encompassing: Newcastle PCT, North Tyneside PCT, Northumberland Care Trust	5	Full	Recommendation 5	21	We need to be more pragmatic than say just 16 and above, many young people are drinking at increasing and higher risk levels and, in the absence of high levels of specialist capacity to refer all to, professionals in universal settings need the tools to start to address issues around young people's alcohol use	Thank you for your comment. The GDG acknowledge the issues you raise but are not able to provide guidance on service provision. They are working with the NICE implementation team to ensure the recommendations are implemented appropriately.
202.	PR	NETSCC, Referee 2	4	Full	2.2.5 & 2.2.6	36 & 38	**2.2 Please comment on the health economics and/or statistical issues depending on your area of expertise.** Throughout the document it is stated that because the cost of medications are low the intervention is likely to be cost effective. Some caution needs to be put in these statements. This is covered for this first instance further in the text (page 38) when other costs of delivery are mentions but the	Thanks for your comment. The developers believe that the statement is suitably cautious: 'The cost to the NHS for each of the agents was low and no information was available about how any of the agents affects length of hospital stay or other elements of resource use. The cost-effectiveness is therefore uncertain but given the low cost we suspect that these therapies would be considered cost-effective'. (p.38)

Comment No.	Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
							conclusions made are too strong	
203.	SH	NHS North of Tyne encompassing: Newcastle PCT, North Tyneside PCT, Northumberland Care Trust	6	Full	Recommendation 6	23	Not sure what "Routinely assess the ability of these children and young people to consent to alcohol related interventions and treatment" means. Does this mean we can offer a brief advice? We need to know what alcohol related interventions means, but this would suggest it is not brief intervention as that term has not been used. This needs to be clearer and needs to encompass a wider group of professionals. Does not adequately support local needs in managing young people's drinking as the amount of young people drinking at these levels potentially far outweighs the capacity to refer to specialist services or CAF, if we do not engage with the young person using a brief interventions approach, we will potentially miss an opportunity for early intervention, this does not suggest onward referral, CAF etc will not also be used alongside, but will ensure the young person has had the opportunity to discuss their drinking and the non specialist worker is clear about the amount and impact this is having. CAF does not screen for drinking and should only be used if there is a need for CAF. Technically, these guidelines are suggesting that anyone under 16 drinking	Thank you but we believe this comment pertains to the Public Health guidance and this is not one of our recommendations.

Comment No.	Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
							outside the CMO guidelines should have a CAF, realistically, we know that there is a huge percentage locally of young people between 10 and 16 are drinking at varying levels and that onward referral or CAF for all of these would simply swamp the system. We also know that many of these young people will initially be identified in non health or social care settings therefore we need to ensure that areas such as education, have the knowledge to identify the triggers and the confidence to manage the issue in the first instance. Young people under 16 will regularly appear in tutorials, school health drop- ins etc where the issue which brought them there may not be alcohol, but may be related to alcohol use, it is remiss not to use an IBA approach at this point. Recommendation 6 states that the evidence base is IDE (Inference Derived from the Evidence), is this then clear that we can do brief interventions with under 16's? Perhaps we need to be mindful of recommendation 9 which states "work on the basis that offering an intervention is less likely to cause harm than failing to act where there are concerns." This needs to be the same for young people and is certainly what local practitioners and professionals are asking for.	

Comment No.	Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
							IBA gives the worker in any universal setting the opportunity to discuss alcohol in a structured way and will potentially allow the worker to screen more effectively in order to make onward referrals. We need to not take a blanket approach to saying that IBA should not happen with under 16s as this potentially leaves many workers, pastoral staff, teachers, educational welfare etc with limited knowledge of how to deal with these issues in the first instance, reducing the opportunity to impact early. IBA training for this group needs to be sensitive to the fact the person is under 16 but will give workers knowledge and confidence to screen, provide early brief advice and understand referral pathways, alongside their usual course of action. This recommendation should add a brief advice session to the list of what to do. ***School Based Interventions on Alcohol*** also gives, under **recommendation 2**, the guidance to offer one – one brief advice in schools, therefore , this guidance should compliment that advice and offering one-one brief advice should be in the actions, and education settings should be in the section "who should take action"	

Comment No.	Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
204.	PR	NETSCC, Referee 1	9	Full	6.3	190	**2.2 Please comment on the health economics and/or statistical issues depending on your area of expertise.** Did the analysis use cost per hour or cost per hour of face-to-face nurse contact? The former (which is implied), ignores the time spent in preparation, writing notes etc when applied to the time spent in direct patient contact.	Thanks for your comment. We used for base-case analyses the 'cost per hour', assuming the same time for the nurse in compared interventions for preparation, writing notes, etc. We developed an additional sensitivity analysis using the 'cost per hour of face-to-face nurse contact'. Conclusions remained unchanged with this variation of the nurse time cost.
205.	SH	The Society for Acute Medicine	5	Full	2.7.6 and 2.7.7	88-91	We believe that the NICE guidance is a perfect opportunity to give clear guidance to all doctors working with Acute Medical admissions. We are disappointed that it is not clear enough in the current format. Prophylaxis This section emphasises malnourishment as increasing risk. Page 90 minimises the risk to diet may suffice – if we used paracetamol overdose we would not accept a vague treatment recommendation in this regard. Diagnosis and treatment Page 90 in general is confusing as it emphasises risk but line 7-10 are difficult to reconcile with lines 32-37 The paper by Ward et al (2009) highlights that confusion at present is leading to significant variability in the doses of intravenous and oral thiamine prescribed in hospitals (as opposed to the community). At	Thank you for your comments. The Wernicke's recommendations and 'evidence to recommendation' section have now been amended. Lines 7-10 are about patients that DO NOT have Wernicke's encepalopathy but are at risk of getting it. There is no need for rapid absorption. Lines 32-37 are about those with suspected Wernicke's encepalopathy; a very different situation. This is now made clear in the evidence to recommendation section of the guideline.

Comment No.	Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
							times, this can lead to under-treatment of those at risk, and those actually diagnosed with potential Wernicke's Encephalopathy. We endorse the 'if in doubt treat' policy recommended by Thomson et al (2002) and Ward et al (2009) This would avoid the catastrophe of anyone slipping through the net, with no significant risk in anaphylaxis. [Thomson AD, Cook CCH, Touquet R, Henry JA. The Royal College of Physicians report on alcohol guidelines for managing Wernicke's encephalopathy in the accident and emergency department. Alcohol Alcoholism 2002; 37:513–21.] It would be most useful if NICE could recommend an actual regime which could be followed by doctors, similar to that previously recommended by the Royal College of Physicians (2001), but with similar simplifications to those recommended in the paper by Ward et al (2009). This NICE guidance is an opportunity to standardise the dosage for the sake of protecting this vulnerable group of patients. Such guidance would form the basis of a national protocol which could be followed by all doctors as they move around from hospital to hospital. This consistency will save patients from under-treatment.	The developers acknowledge the consequences of a missed diagnosis and current variation in the doses of thiamine that are prescribed. No evidence was found to support recommending a specific dose. The revised recommendation requires that clinicians offer 'doses toward the upper end of the British National Formulary range'. A discussion of the issue can be found in the 'evidence to recommendation' section of this chapter. The need for glucose has been added to the introduction. We could find no evidence for the benefits of magnesium so we have not made a recommendation on this.

Comment No.	Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
							Clearly, the evidence does not suggest an exact dose, due to the absence of dose-ranging, placebo-controlled studies, but there are clear hints at a minimum required dose. The robust studies required to clarify the dose further are unlikely to ever be performed, due to the low cost of intravenous thiamine and the nature of the patients involved. There was also no clear mention of the crucial roles of glucose and magnesium therapy for patients with possible or confirmed Wernicke's. These cannot be ignored and must be included with guidelines regarding the management of Wernicke's. [Alcohol – Can the NHS Afford It? Recommendations for a coherent alcohol strategy for hospitals. A report of a Working Party of the Royal College of Physicians, 2001.]	
206.	SH	NHS North of Tyne encompassing: Newcastle PCT, North Tyneside PCT, Northumberland Care Trust	7	Full	Recommendation 7	24	This misses an opportunity to include higher education and other professional who will have direct contact with this group. Needs to cite education staff as a key group, and could cite attainment as a concern area. There would be of course a need to robustly evaluate to measure impact.	Thank you but the developers are unclear about what section of the guideline this comment refers to.

Comment No.	Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
207.	SH	NHS North of Tyne encompassing: Newcastle PCT, North Tyneside PCT, Northumberland Care Trust	8	Full	Recommendation 9	26	This is limited in its target group, we could include other professionals such as housing and tenancy staff, fire services, Gym staff etc – can we not now be at the point of training any universal staff group where alcohol may be the underlying cause of the difficulty they are trying to manage with the individual. The guidance feels that it is continuing to focus on health and criminal justice setting but we need to be wider in our approach and training of IBA in order to have a bigger impact.	Thank you but the developers are unclear about what section of the guideline this comment refers to.
208.	SH	Royal College of Nursing	6	Full	10	199	Whilst we agree that the symptom triggered treating of patients with acute alcohol withdrawal is cost effective, this is also designed to minimise the distress that people experience when suffering acute alcohol withdrawal. It is also likely to reduce the risk of further complications associated with lack of appropriate prescribing. However staff will need to be trained to recognise the symptoms and be able to plan accordingly. This would also indicate that planned hospital admissions are far more cost effective than waiting until the person has reached crisis point and is admitted as an emergency.	Thanks for your comment. This guidance does not evaluate the cost-effectiveness of planned alcohol withdrawal interventions.
209.	SH	NHS North of Tyne encompassing: Newcastle PCT, North Tyneside PCT,	10	Full	Recommendation 12	30	This directly contradicts recommendation 6. Non NHS professionals working with those over 10 years old will only identify dependence if they have had training and	Thank you for your comment but the developers believe this pertains to the Public Health guidance: 'alcohol-use disorders: preventing the development of

Comment No.	Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
		Northumberland Care Trust					support to do so. Also suggests this is the course of action if they fail to respond to brief advice, however, recommendation 6 does not recommend brief advice under 16 and does not include all non-NHS professionals in the "who should take action" section. There is also no suggestion to use AUDIT for those under 16. UK drinking guidelines – can the guidelines for young people be added here	hazardous and harmful drinking'.
210.	SH	NHS North of Tyne encompassing: Newcastle PCT, North Tyneside PCT, Northumberland Care Trust	9	Full	Recommendation 9 and 10	28	We need to be more inclusive and less focussed around these settings if we want to have maximum impact and build our public health workforce.	Thank you for your comment. The developers agree.
211.	SH	South London and Maudsley NHS Foundation Trust	12	Full version	Table 2-3	39	The example of a FD regime in Table 2.3 here does not reflect clinical practice. Dosing regimens for moderately severe alcohol withdrawal will be lower e.g. starting at 20-30mg qds. As doses are titrated downwards, the qds dosing schedule is usually continued as this is more acceptable to patients. Please refer to the Maudsley Prescribing Guidelines for examples of dosing regimens. Taylor et al (2009). Maudsley Prescribing Guidelines 10th edition. Examples are also given in Edwards et al (2003) and Conigrave et al (2009) (see 5 above for references)	Thank you for your comment. This table was provided as an example only and has now been amended.
212.	NICE	Alcohol harm prevention	1	Full, NICE	General	General	I have examined the report to look for any cross over or conflict with the Alcohol Harm	Thank you. This has now been amended.

Comment No.	Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
		programme development group					Prevention report. None was found except for the definitions of hazardous and harmful drinking. We suggest adoption of our definitions.	
213.	NICE	Alcohol harm prevention programme development group	2	Full, NICE	General	General	The prevention PDG have long debated the role of extrapolation of the evidence in some areas in order to make recommendations in others and the use of the precautionary principal. It is important that where extrapolation and the judgement of the PDG have been used to formulate a recommendation this is made clear.	Thank you. Where the GDG have extrapolated from the evidence they have described this in the 'evidence to recommendation' section of the guidance.
214.	SH	Royal College of Physicians	1	Full, NICE	General	General	The Royal College of Physicians and British Society of Gastroenterology are grateful for the opportunity to comment on the draft guideline. We would like to make the following points.	Thank you.
215.	SH	College of Mental Health Pharmacists	14	General			Please justify why there was no specialist pharmacist on the guidelines development group?	Thank you for your comment. The developers felt the experience of the GDG was sufficient to not warrant the inclusion of a specialist pharmacist.
216.	SH	Dukeries Healthcare Limited	1	General	General	General	Thank you for allowing me the opportunity to comment. The draft has not considered the long term effects of alcohol use, in particular alcohol related brain injury. There are thousands of people who are inappropriately placed in elderly care homes, and the condition (aka Korsakoffs syndrome) is still considered as a dementia rather than a brain injury. The implication being that sufferers are placed in LONG term care homes at a massive cost to the tax payer and the NHS, whereas the condition is known to respond well to	Thank you for your comment. This issue is being addressed by the mental health guidance.

Comment No.	Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
							rehabilitation.	
217.	SH	FASawareUK	1	General	General	General	FASawareUK were the only group to submit information on Foetal Alcohol Spectrum Disorder (FASD) to the UK Alcohol Harm Reduction Strategy in 2003. When the draft document was launched, there was just one small passage on FASD. FASawareUK lobbied to get the UK Government take on board FASD. The awareness has been created, yet we still have women binge drinking. Until all professional sectors embrace the message of informed choice and all agencies giving out the same message of informed choice and work together. Pregnant women are confused with , all the different conflicting messages from different agencies. There is only one safe amount NIL alcohol in pregnancy there are no TWO women the same. We also need to address men's alcohol consumption pre-conception. Men must also be encouraged to support their pregnant partners. What has been observed, many professionals appear to be unsure or uninformed about FASD. If a medical professional is aware of the syndrome and have a history of birth mothers alcohol consumption, they are reluctant to offend the birth family or stigmatise the child. The child usually ends up with an assortment of	Thank you for your comment. The issue of Foetal Alcohol Spectrum Disorder was too large to be covered by this develop group so was referred to NICE topic selection for consideration elsewhere.

Comment No.	Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
							other diagnosis's, the most popular diagnosis is ADHD (Attention Deficit Hyperactive Disorder) What we are observing is a growth in Grandparents who are now bringing up their own children's children. Many of these families have lost the children's birth parents due to alcohol and substance misuse. **How can we make the changes?** We need to start educating children from the age of seven (7) upwards about what is alcohol and how it affects individuals. FASawareUK are not anti alcohol, but feel children should be taught about safe moderate alcohol consumption. Children should also be made aware of Foetal Alcohol Spectrum Disorder. (FASD)	
218.	SH	Royal College of Nursing	1	General	General	General	The RCN welcomes this document. It is comprehensive and timely.	Thank you.
219.	SH	Inclusive Health	4	NICE	General		Given that the guidance for dependence will not come out for a further year, I think this guidance needs to be more explicit in that it does not recommend how alcohol dependence should be treated. It should be clearer that it is dealing with managing the physical consequences of alcohol misuse and is not necessarily recommending hospital admission for medically assisted	Thank you for your comment. A section at the beginning of the guidance details the remit of the mental health guideline development group and this has been amended to clearly outline the difference between these pieces of guidance.

Comment No.	Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
							withdrawal as 'usual' treatment for alcohol misuse, but only if there are DTs or fits. Not to do this risks undermining the work of community based clinicians who are working with drinkers and their families to address their problem in the community. It also risks massively increased and in my view inappropriate demand for medically assisted detoxification on acute wards,	
220.	SH	Inclusive Health	5	NICE	General		NO mention is made of the risk of cross addiction between benzodiazepines and alcohol. It should be made clear that discharge medication should be coordinated with the community medical care giver in order to ensure that benzodiazepines are not released inappropriately into the community.	Thank you for your comment. This is mentioned in the full guideline in the .evidence to recommendation' section.
221.	SH	Inclusive Health	6	NICE	General		No mention is made of the increased incidence of alcohol dependence in the context of other substance misuse / polydrug misuse. Referral of these patients to specialist addiction services for assessment should be considered, as should availability of addiction service advice to acute wards dealing with this kind of patient.	Thank you for your comment. The poly drug use was excluded from the scope of this guideline. Comorbidities will be addressed by the Mental Health guidance.
222.	SH	Inclusive Health	7	NICE	General		No mention is made of the use of gradual alcohol reduction in the management of alcohol dependence. I think this is a significant omission. Although it would not be indicated in someone who required emergency admission for DTs or fits, it does have a role in preparation for planned medical withdrawal from alcohol or indeed	Our scope was the management of acute alcohol withdrawal rather than the management of dependence.

Comment No.	Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
							as an alternative to planned medical withdrawal from alcohol. It is a very patient centred approach in some cases, and avoids the risks inherent in pharmacoltherapy which are highlighted by the lack of licensed drugs for people who are alcohol dependent. Clinicians using this approach and patient who would prefer this approach would benefit from its mention in NICE Guidance. I have come across cases where staff have been censured for using this approach as unethical (!). Furthermore, in primary care practices which are exposed to high numbers of chaotic individuals who are dependent drinkers, it is not unusual to be approached for 'a detox' because the patient has run out of cash to buy alcohol, but who has no intention of undergoing long term detoxification, merely wishing to be given a script for benzodiazepines to tide them over to the next benefit payment or paycheck. Giving such a prescription is fraught with difficulty due to the risk of drinking on top which will inevitably occur when an associate 'lends' them some alcohol. Many of these patients fit from time to time, and under this guidance, one would be more or less duty bound to admit such a patient to hospital every time, whereas the usual practice is to recommend that the patient 'borrows' enough alcohol to avoid withdrawal. These are difficult real life situations which are managed pragmatically and it would be helpful if these difficulties	

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							were acknowledged and addressed in the guidance.	
223.	SH	Ministry of Defence	1	NICE	GENERAL	GENERAL	The title indicates that the document is about alcohol-related physical problems but the contents relate to only the rarer, most severe physical problems. It may be that another document is planned to deal with the very many problems, such as gastritis, insomnia, accidents and injuries, commonly experienced as a result of alcohol problems. Many of these problems can be managed outside hospital and, with behavioural treatment of the problem, remit without a great deal of medical involvement.	Thank you for your comment but these are not alcohol specific conditions. The management of the accident is not different if it is caused by alcohol than if it were not.
224.	SH	Nottinghamshire Healthcare NHS Trust	17	NICE	General	General	A consistency of terminology should be used within documents relating to alcohol misuse. This guideline uses: alcoholic, alcohol dependence, hazardous, harmful drinking. Other national guidance uses, lower, increasing and higher risk drinking. It would be extremely beneficial to ensure that a definitions section enable the reader to understand exactly what each term means and how the terminology in this guideline relates to that in other current guidance.	Thank you for your comment. A glossary of terms is available in the full guideline and will be added to the NICE version.
225.	SH	Royal College of Physicians	12	NICE	General		Simple, didactic and easy to use. All hospital wards, A&E departments will benefit from having a copy.	Many thanks.
226.	SH	SNDRi	1	NICE	General	General	With reference to this draft guideline consultation we would like to highlight three new SNDRí diet-sheets published this year which are designed to support people with, or at risk from, alcohol-related thiamine deficiency, and are available to all health	Thank you.

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							professionals. Each pack includes staff guidelines for issuing the diet-sheets. They titles available are as follows: **Making Changes** – For people drinking a lot of alcohol who may find it difficult to eat. **Moving On** - For people trying to change by cutting down or cutting out alcohol. **Practical Ways to Help** – information for carers - For people caring for someone who drinks a lot of alcohol.	
227.	SH	South Asian Health Foundation	7	NICE	1.1.1.2/3/4		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; 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, Admit to hospital for physical and psychosocial assessment, young people under the age of 16 years with acute alcohol withdrawal. – as above, agree, community treatment requires resources.	Thank you.
228.	SH	South Asian Health Foundation	8	NICE	1.1.2/3/4/5		Treatment for acute alcohol withdrawal We agree with these suggestions	Thank you.
229.	SH	The National Treatment Agency for Substance Misuse (NTA)	1	NICE	General	General	Please note that the NTA's particular consideration was how the recommendations would affect people dependent on numerous substances, eg alcohol and multiple illicit drugs (hereafter	Thank you for your comment. Poly drug use was excluded from our scope.

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							referred to as poly-drug and alcohol misusers) and drug treatment services.	
230.	SH	The National Treatment Agency for Substance Misuse (NTA)	2	NICE	General	General	The specific needs of poly-drug and alcohol misusers are not acknowledged anywhere in the guidance and consideration should be given to this client group	Thank you for your comment .Poly drug use was excluded from our scope.
231.	SH	South Asian Health Foundation	1	NICE		4	Should some mention be made of high-risk groups eg, men, Scottish/Irish etc.?	Thank you but this is not relevant unless it has an impact on management.
232.	SH	Yorkshire Humberside Improvement Partnership	1	NICE	INTRO	4	Useful to state who the guidelines are aimed at. Eg. My area relates to alcohol use & offenders; are the guidelines aimed at all prescribers, eg. Including within the secure environments (prisons etc), and are they aimed at any other than prescribers?	Thank you for your comment. These guidelines are aimed at all who care for patients with any of the conditions that we give guidance on.
233.	SH	South Asian Health Foundation	2	NICE		5	Patient-centred care – SAHF agrees that this important, especially in the context of health inequalities eg, ethnic minorities	Thank you.
234.	SH	Yorkshire Humberside Improvement Partnership	2	NICE	1 (1.2, 1.4)	10, 11	Useful for brief footnotes explaining some of the key alcohol disorders & medical terms, particularly if the document is aimed at non-clinical, voluntray organisations (as indicated at page 18).	Thank you. A glossary of terms is included in section 1.1 of the guideline.
235.	SH	Nottinghamshire Healthcare NHS Trust	1	NICE	Introduction	3 of 24	There would be a benefit in having a consistency between the terminology in this guidance with that being promoted within the current Alcohol Strategy for England and Wales, that is: lower risk, increasing risk and higher risk – rather than hazardous and harmful.	Thank you for your comment. The developers continued to use the terms hazardous and harmful as these are what are used in the scientific literature reviewed. This decision was taken with the approval of the Department of Health.
236.	SH	Nottinghamshire Healthcare NHS Trust	2	NICE	Patient-centred	5 of 24	There would be a benefit in recommending the role of tier one workforce in relation to alcohol misuse and need for appropriate	Thank you for your comment. NICE do not provide guidance on service provision.

Comment No.	Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
					Care		training to support this role.	
237.	SH	Nottinghamshire Healthcare NHS Trust	3	NICE	1	7 of 24	The statement 'Someone who is alcohol-dependent will keep drinking, despite harmful consequences' could be seen as suggesting that the alcohol dependent person is unable to stop drinking. It needs to be rephrased as follows: 'someone who is alcohol dependent may continue to drink alcohol even if they are aware of actual or potential harmful consequences' The definition of medically assisted alcohol withdrawal should also reflect current practice; as such the wording 'medically assisted alcohol withdrawal will typically be supervised by nursing or other health staff in collaboration with and sometimes direct supervision of medical staff' is a more appropriate definition.	Thank you for your comment. This has definition been amended.
238.	SH	Ministry of Defence	2	NICE	1.1 ALCOHOL WITHDRAWAL	7 - 9	This section refers to in-patient treatment and the infrequent but serious complications of alcohol withdrawal. There is no mention of the more usual detoxification in a community setting and I would refer you to the International Handbook of Alcohol Dependence and Problems edited by Nick Heather, Timothy J. Peters and Tim Stockwell (2001) *Wiley Press,* and also to the article by Duncan Raistrick, Clinical Director of Leeds Addiction Unit, Management of alcohol detoxification in Advances in Psychiatric Treatment (2000) **6: 348-344** wherein he says 'the huge majority of people with an alcohol	Thank you for your comment. The mental health guidance on the assessment and management of dependence are covering detoxification in the community.

Comment No.	Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
							dependence problem that is uncomplicated by serious mental illness or social chaos received treatment in the community'. Whilst the document refers the indications for hospital admission it may, if read as a stand alone guideline, sugges that inpatient detox is the more common route.	
239.	SH	UK Advocates	1	NICE	1.1	7	(Also relates to 3.1, Admissions for acute alcohol withdrawal, p.14 NICE draft for consultation) The experience of UK Advocates suggests standard admission practices to hospital have a tendency to deal with alcohol withdrawal on a reactive rather than proactive basis. Clearly ambulance teams have no other option but to take a severely intoxicated patient to the nearest Accident and Emergency department for observation prior to further decisions about the patient's next steps on a care pathway, including addiction services, which will ideally result in the cessation of alcohol consumption and service exit. Hospitals are not usually configured in such a way that includes the continuum of care needed to help a patient displaying acute or mild withdrawal from alcohol reach a position whereby they are willing to aspire to the 'primary goal' (3.1, 'Why this is important', NICE draft for consultation, p.14) of long-term abstinence by following a clearly defined pathway of care. We submit therefore that neither of the current models	Thank you for your comments. NICE does not offer guidance on service delivery.

Comment No.	Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
							of treatment (outlined in 3.1 of NICE draft for consultation, p.14) are usually cost efficient or effective in providing appropriately structured care for the patient. Given that abstinence is the goal for people presenting at hospital with acute or moderate alcohol withdrawal, where possible dedicated specialist alcohol treatment units could be established or spot purchased from the independent sector. A specialist alcohol unit will be equipped to deal with detoxification, reorientation (from drinking mode to abstinence mode) and stabilisation in a psychiatrist-led nursing home-style environment. Economically, marketing testing carried out by UK Advocates in Nottingham suggests this could achieve savings of up to 50% of the cost of admission to Trust hospitals which, because of their more complex nature, carry a larger overhead burden than those of specialist units within the independent sector. Ideally, patients without illnesses other than alcohol dependency presenting for unplanned detoxification should be diverted to these specialist units prior to admission in an NHS hospital. In this milieu the patient can undergo intensive abstinence-based care, delivered by a team of counsellors working under the supervision of a specialist psychiatrist. This proactive planned model of care would alleviate the concerns set out in p.16, lines	

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							23, 24, 25 of the Full draft for consultation. (The following also relates to 3.4, Supportive Care, p.16 NICE draft for consultation) UK Advocates submit that the proactive rather than the reactive model (above) would restrict the number of detoxifications to those occasions when a patient is expressing a desire to stop drinking and so reduce the impact of what is referred to as the 'kindling effect..where the severity of the withdrawal symptoms increases after repeated withdrawal episodes.' (Full draft for consultation, p16, lines 30, 31). Unplanned multiple detoxing without the clear goal of long-term abstinence is of limited utility and should be carried out only where a patient is in medical danger and with the assistance of an alcohol specialist nurse. Taking this point further, we submit that 'controlled' drinking or so called moderation therapies that characterise many of the treatment pathways patients are currently directed towards following hospitalisation add to the 'kindling effect'. Further drinking amongst this group is considered highly likely to result in relapse in the disorder and increased presentation for multiple detoxes, and should not therefore be considered as appropriate in any subsequent care plan for the patient.	

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							Only an abstinence model takes into account the 'kindling effect' by employing the 'relapse management' approach for those who are unwilling to cooperate with attaining abstinence. These patients can then be kept in contact with addiction services until such time as they have attained a desire to stop drinking. They can then make a planned request for detoxification, reorientation, stabilisation and intensive treatment. Unplanned assisted withdrawal with no prior preparation for abstinence should be viewed solely as a life saving procedure. UK Advocates' experience in this area is similar to that detailed by the GDG on p.29, lines 8, 9, 10 of the Full draft for consultation. These patients should be referred to the dedicated specialist unit, which would include an alcohol specialist nurse, to be prepared for abstinence via a planned and comprehensive programme of treatment. Unpublished data produced by the pilot specialist unit at NHS Nottingham has consistently shown over 70% abstinence at 2 years using the relapse management or Group Abstinence preparation prior to full treatment following withdrawal from alcohol. (Paper documentation containing this data has been sent to the GDG)	
240.	SH	South Asian Health Foundation	9	NICE	1.2		Wernicke's encephalopathy We agree with these suggestions	Thank you.

Comment No.	Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
241.	SH	The National Treatment Agency for Substance Misuse (NTA)	8	NICE	1.2	10	*This section recommends administering prophylactic parenteral thiamine to harmful or dependent drinkers if they are malnourished or at risk of malnourishment.* One practical consideration is that many community alcohol and drug services – who regularly see poly-drug and alcohol misusers at risk of malnourishment – may not be comfortable with parenteral thiamine injection (IM and IV) because of fears about anaphylaxis. The NTA believes that it would be useful if the guidance quantified the risk of anaphylactic complications, so that such services would be more inclined to use parenteral thiamine injection IM and IV.	Thank you for your comment. The rates of anaphylaxis have been added to the health economic section of the full guideline.
242.	SH	Nottinghamshire Healthcare NHS Trust	9	NICE	1.2	10 of 24	There is currently no mention of re-feeding syndrome – this is an error. One of the main risk factors for re-feeding syndrome is 'alcohol dependence', given the potentially devastating consequences of untreated refeeding syndrome this needs to be included within this guidance.	Thank you for your comment. This has be mentioned where nutritional supplementation has been recommended.
243.	SH	Inclusive Health	1	NICE	1.1.1.1		Can be difficult to differentiate alcohol withdrawal seizures from alcohol related seizures due to intoxication	Thank you. The developers agree.
244.	SH	South Asian Health Foundation	3	NICE	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 – we agree	Thank you.
245.	SH	South Asian Health Foundation	10	NICE	1.3		For people with a history of harmful or hazardous drinking, who have abnormal liver function tests, exclude alternative	Thank you.

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							causes of liver disease; 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 – we agree that specialist management is important, as well as educating generalists about referral.	
246.	SH	The National Treatment Agency for Substance Misuse (NTA)	3	NICE	1.1.1.1	p.7	*This section covers admission to hospital for medically assisted withdrawal from alcohol* The NTA was uncertain about and would welcome clarification on the care pathway from primary care and specialist alcohol and drug treatment services into hospital / in-patient care. Referrals at present would not usually be accepted unless the client was in DTs or had had a very recent fit. Otherwise, the referrer is likely to be asked to refer for an outpatient appointment for a future planned admission. At present one could envisage a scenario where such referrals to acute medical inpatient units would be made but declined on the grounds that acute medical units do not usually offer elective alcohol detox.	Thank you for your comment. The guidance pertains to the unplanned emergency medically assisted withdrawal from alcohol. The mental health guidance are covering the assessment and treatment of dependence rather than the treatment of acute alcohol withdrawal. The introduction to the three pieces of guidance has been amended to describe this fact.
247.	SH	Royal Pharmaceutical Society of Great Britain	7	NICE	1.1.1.1	7	Although this statement is to be welcomed, is there a risk of confusion when NHS Trusts work to implement? This NICE guidance is specifically about physical complications and therefore would apply to acute hospital settings where specialist physical treatment can be offered. Mental heath trusts for example trying to implement	Thank you for your comment. This guidance pertains to the management of *acute* alcohol withdrawal.

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							this guidance may have Specialist in-patient beds/ unit eg managed by a consultant psychiatrist but may not have the appropriate resources (eg immediate access to Path lab, nursing staff with appropriate competencies eg if mental health trained) for managing patients with physical complications associated with alcohol. They may only be able to manage planned in-patient detoxes.	
248.	SH	The National Treatment Agency for Substance Misuse (NTA)	4	NICE	1.1.1.1	7	Clients who require treatment for hepatitis C are frequently poly-drug and alcohol users. Alcohol-dependant clients would need to have their alcohol dependency treated first.	Thank you and we agree.
249.	SH	The National Treatment Agency for Substance Misuse (NTA)	5	NICE	1.1.2	8	*This section recommends that benzodiazepines are one of the drugs that may be administered to treat the symptoms of acute alcohol withdrawal.* The NTA would welcome clarification on the appropriate pharmacological management of acute alcohol withdrawal. If chlordiazepoxide and chlormethiazole are equally effective, the risk of clients taking the latter drug in combination with alcohol or other sedative drugs does need emphasising. Even on inpatient units clients may continue to use illicit drugs and leave the hospital to drink alcohol, with potentially fatal consequences. This may be a particular issue for polydrug and alcohol dependent clients. If there is no or in-sufficient evidence about the appropriate	Thank you for your comment. This recommendation has several footnotes explaining the contra-indications and risks of taking these drugs with alcohol.

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							clinical management of this client group. The NTA would welcome a statement in the guidance making this (i.e. the lack of evidence) clear	
250.	SH	Nottinghamshire Healthcare NHS Trust	4	NICE	1.1.1.1	7 of 24	There would be a benefit in defining what is meant by hospital: does this refer to a psychiatric hospital, a general hospital or to a hospital providing planned specialist inpatient detoxification? Are the people being offered admission to hospital those presenting at outpatient / community alcohol services or A&E / GP? This would benefit from being clearer – current wording could be read to suggest that anyone with risk factors for alcohol withdrawal complications could access hospital on their own request; as such this could encourage regular return to drinking and presentation to hospital.	Thank you for your comment. The recommendation pertains to any hospital where staff are trained in the management of acute alcohol withdrawal. Regardless of the circumstance of presentation, admission should be offered in the defined situations.
251.	SH	Nottinghamshire Healthcare NHS Trust	11	NICE	1.3	10 of 24	The section 1.3.1.1 and section 1.3.1.2 is not purely about liver biopsy but fits more appropriately under the sub heading Alcohol Related Liver Disease. The subheading 'role of the liver biopsy' should begin section 1.3.1.3	Thank you for your comment. This has been amended.
252.	SH	Department of Health	1	NICE	1.1.2.1		Thank you for the opportunity to comment on the draft for the above clinical guideline. I have received comments from my colleagues in the Department of Health as follows: "In section 1.1.2.1, the footnote makes clear	Thank you for your comment. This has been amended.

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							the risk of fatal intoxication from alcohol consumption during chlormethiazole treatment. In our view, it would be preferable if this risk could be made explicit in the main body of the text, that is, this section".	
253.	SH	South Asian Health Foundation	11	NICE	1.3.1		Discuss the benefits and harms of liver biopsy with the patient and ensure informed consent. – we agree that this should be offered in the area of diagnostic uncertainty.	Thank you.
254.	SH	College of Mental Health Pharmacists	10	NICE	1.1.2.1	8	It is not clear here that the benzodiazepines should be the first choice in alcohol withdrawal.	Thank you. This has been amended.
255.	SH	Nottinghamshire Healthcare NHS Trust	6	NICE	1.1.2.1	8	Would be useful to indicate minimum standards for how alcohol services should be linked to hepatology / liver disease services.	Thank you for your comment. NICE do not provide guidance on service provision.
256.	SH	Royal Pharmaceutical Society of Great Britain	4	NICE	1.1.2.1	8	Clomethiazole must only be used in in-patient settings (see BNF) – this must be made clear in these guidelines, (it is not sufficient to put it in a footnote which could be missed) it is ambiguous the way it is currently written. PharMAG would question its inclusion at all in NICE. Based on the 80:20 rule of NICE, it is likely that those specialist units that use clomethiazole will fit into the 20% i.e. the minority, there is a risk by including it it will increase its use (NB appreciate that the appendix to the guidelines also highlights the lack of research evidence)	Thank you for your comment. This recommendation has been revised to include the warning on the use of clomethiazole. The GDG found no evidence to support the widely held belief that clomethiazole is any less safe than the other agents.
257.	SH	College of Mental	12	NICE	1.2.1.1	10	Please indicate your recommended dose of	Thank you for your comment. There was

Comment No.	Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
		Health Pharmacists					oral thiamine, usually given as 100mg TDS	no evidence for a specific dose of thiamine however the developers recognise there is variation in prescribing practices across the UK. The recommendation asks clinicians to prescribe 'doses toward the upper end of the British National Formularly range.
258.	SH	Royal Pharmaceutical Society of Great Britain	5	NICE	1.2.1.1	10	Oral thiamine – there is a lot of discussion about dose of oral thiamine, whether it is actually effective, dose limited absorption, whether it should be as plain thiamine or whether it should be as Vitamin B compound strong tablets or whether in fact it is a placebo to make the prescriber feel s/he is doing anything. If any is prescribed, how long after detoxification should it be given for? The NICE guidance is too vague. (Appreciate that the appendix also highlights the lack of research evidence)	Thank you for your comment. These recommendations have now been revised and thiamine should be given for as long as the conditions of the recommendation are met.
259.	SH	The National Treatment Agency for Substance Misuse (NTA)	9	NICE	1.3.1	10	*On the recommendation that considerations for assessment for liver transplant should involve 3 months' abstinence.* '3 month period of abstinence from alcohol' should be a recommendation but not an absolute contraindication to transplant	Thank you for your comment. The three month criterion was recommended to allow the liver time to improve after which transplant may not be required, This recommendation is made to give guidance to those that refer patients to transplant units. Transplant units should not consider patients that have not been abstinent for 3 months for transplantation.
260.	SH	The National Treatment Agency for Substance Misuse (NTA)	10	NICE	1.3.1	10	*On the recommendation that considerations for assessment for liver transplant should involve 3 months' abstinence.* Poly-drug and alcohol misusers clients who are abstinent from alcohol and stable on methadone maintenance should be	Thank you for your comment. Poly-drug use was excluded from the scope of this guideline.

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							considered for liver transplant. i.e. that being stable on methadone maintenance treatment should not act as barrier for liver transplant. The NTA suggests that the guidance emphasises this point	
261.	SH	UK Advocates	2	NICE	1.3.1	10	Given that abstinence is identified as the 'primary goal' (3.1, p.14 NICE draft for consulation) for those presenting at hospital with acute and milder alcohol withdrawal, UK Advocates submit that the same presumption of abstinence should logically be extended and included in Section 1.3 regarding the role of Liver Biopsy in the diagnosis and subsequent treatment of people with a history of harmful or hazardous drinking, who have abnormal liver function tests or with suspected acute alcohol-related hepatitis, from the point of referral by a clinician or GP to specialist diagnosis. We recognise the complexity encountered and identified by the GDG surrounding the exact utility and role of the liver biopsy in the diagnosis and appropriate treatment of suspected alcohol-related liver disease and alcoholism as detailed in the Full draft for consultation, (Section 3.1.6, p.106, lines 17-20). Accordingly, we submit that the current draft guidelines should be amended (see below) to include references that reflect that best practice dictates that patients should be advised to remain abstinent from alcohol during the period between referral from the	Thank you for your comment. The developers We agree that abstinence is important but the clinical question was about the utility of liver biopsy and so we do not think the recommendation should be changed.

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							clinician or GP and a definitive diagnosis by a specialist. At the time of submission, many established pathways for suspected alcohol dependents involve referral to treatment models that include further, or 'controlled' alcohol consumption. We submit that exposing a patient already diagnosed as alcohol dependent, one who is already assessed to be at high risk of developing alcohol withdrawal seizures, delirium tremens, has a history of hazardous drinking or may have abnormal liver function tests, to further alcohol consumption could be construed as colluding with the disorder (as defined by WHO ICD-10) and raise false and unachievable expectations in the patient that they will be able to return to unproblematic drinking behaviour. Until such time as an absence of liver disease can either be established beyond doubt or it is decided cannot be ruled out completely, the patient should be advised to remain entirely abstinent from alcohol. If a patient is unwilling to co-operate with advice to abstain then they should be treated according to relapse management/prevention with minimum intervention. It should be generally understood and recognised that the likely outcome of continued alcohol consumption will be multiple and cyclic admissions to hospital for alcohol withdrawal and other related illnesses. This phenomenon seems	

Comment No.	Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
							to be connected to the 'kindling effect' (Full draft for consultation, Section 2.1.1, p.16, line 30). Further drinking for patients who satisfy the criteria for alcohol dependency set out above cannot be considered to be in the interests of the patient or an achievable option. Abstention should be the foundation of therapy for any person displaying clinical characteristics of alcohol dependency.[1] Reference: Levitsky, Josh, Mailliard, Mark E: Seminars in liver disease, 2004, vol. 24, no˚3, pp.233-247, ISSN 0272-8087, Thieme, New York, United States.	
262.	SH	Nottinghamshire Healthcare NHS Trust	10	NICE	1.2.1.1 And 3.5	10 of 24	It would be useful to have a dose and formulation recommendation for oral thiamine recommendations There is an apparent contradiction between section 1.2.1.1 and section 3.5. As no convincing evidence exists regarding parenteral or oral thiamine, recommendation in section 1.2.1.1 should advise parenteral thiamine in acute alcohol withdrawal.	Thank you for your comment. The thiamine recommendation has been amended and specifies 'doses toward the upper end of the British National Formularly range' as they was no evidence available for a specific dose. We do not agree that there is enough evidence to support intravenous thiamine in this setting. The acute withdrawal may be mild and in primary care and not require admission to hospital.
263.	SH	College of Mental Health Pharmacists	11	NICE	1.1.3.1	8	Are you suggesting here, that it is OK to use a 24hour symptom triggered schedule with	Thank you for your comment. None of the evidence the GDG found to support

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							carbamazepine as stated in 1.1.2.1 – please clarify that this symptom regimen is for the benzodiazepines and clomethiazole only	symptom-triggered regimens used carbamazepine.
264.	SH	Inclusive Health	2	NICE	1.1.1.3	8	Under list for consideration of lower threshold, consider adding inadequate housing or homelessness to the list	Thank you.
265.	SH	College of Mental Health Pharmacists	13	NICE	1.2.1.2	10	Please indicate your recommended dose of parenteral thiamine in treatment and prophylactic use	Thank you for your comment. No evidence was found for a particular dose although the GDG acknowledge there is great variation in current prescribing practices. The recommendation now reads 'Thiamine should be given orally or parenterally, in doses toward the upper end of the British National Formularly range'
266.	SH	Nottinghamshire Healthcare NHS Trust	12	NICE	1.3.2	10	It is likely that - for some geographical areas - a specialist in alcohol related liver disease will not be available to all that would benefit from this. It would be beneficial to state a minimum expected standard for access to such assessment and recommend pathways between alcohol services, other parts of the NHS and specialists in alcohol related liver disease	Thank you for your comment. NICE does not provide guidance on service delivery.
267.	SH	UK Advocates	3	NICE	1.3.1.1	10	We submit the following additions (in italics) to the specific wording: 1.3.1.1 For people with a history of harmful and hazardous drinking, who have abnormal liver function tests, exclude alternative causes of liver disease. *Where it is found that abnormal liver function tests are alcohol-related, the patient should be advised to remain abstinent until the possibility of liver damage*	Thank you for your comment. The developers stand by their original recommendation.

Comment No.	Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
							can be ruled out.	
268.	SH	Alder Hey Children's NHS Foundation Trust	5	NICE	1.1.1.4		Para 1.1.1.4 re admission of under 16s to essentially adult provision – in light of national advice on this NOT happening this will need to be revised.	Thank you for your comment. This recommendation does not say admit a person under the age of 16 to adult services. They should be admitted under paediatric care.
269.	SH	South Asian Health Foundation	5	NICE	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. We agree that this is sensible but is there evidence for the 3 month threshold? Should there also be a role for non-hepatologists eg. psychiatrists in referral recommendations?	Thank you for your comment. The Veldt et al (2002) study showed improvement in liver function always began within 3 months if it occurred at all. This was then used to recommend a three month threshold. The developers agree that there is a role for non-hepatologist however not until later in the assessment for transplantation process.
270.	SH	South Asian Health Foundation	12	NICE	1.3.3		Treat with corticosteroids11people with severe acute alcohol-related hepatitis and a discriminant function of 32 or more. – we agree but also feel additional RCT evidence is required for treatment agents in this context	Thank you for your comment. We could not agree more. At present, steroids should be the recommendation for this condition, but the evidence is not water tight. We are excited by the prospect of a large RCT that will help with the future versions of this guidance.
271.	SH	Nottinghamshire Healthcare NHS Trust	5	NICE	1.1.1.4	8	Again needs definition of which hospital is being referred to. Should this be to a psychiatric, a general or a specialist inpatient detoxification unit? It would also be useful to indicate what a minimum assessment should be – should this be by a specialist or by the general staff?	Thank you for your comment. All three types of hospital you suggest would be suitable so long as they were under paediatric services. This has not been specified as NICE do not provide guidance on service provision.
272.	SH	The National Treatment Agency for Substance Misuse (NTA)	6	NICE	1.1.5	9	*On treatment for seizures* The NTA recommends that the guidance mentions the risk of adverse interaction	Thank you for your comment. This guidance excludes poly-drug use although all prescription of medication should be done in line with the British National

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							between methadone and carbamazepine – one of the drugs recommended for the management of alcohol-related withdrawal symptoms	Formulary guidance unless specified.
273.	SH	The National Treatment Agency for Substance Misuse (NTA)	7	NICE	1.1.5	9	The NTA also recommends that the guidance is consistent with the findings of the current and ongoing review of alcohol and drug treatments by the British Association for Psychopharmacology (BAP)	Thank you for your comment. NICE develops its guidance according to evidence-based methodology described in the NICE Technical Manual (2009). For this reason its recommendation may differ to those written by other advisory groups.
274.	SH	UK Advocates	4	NICE	1.3.1.2	10	We submit the following additions (in italics) to the specific wording: A clinical diagnosis of alcohol-related hepatitis should be confirmed by a specialist experienced in the management of alcohol-related liver disease. *Where liver damage is confirmed or cannot be ruled out by a liver specialist then long-term abstinence should be recommended as the basis of the patient's treatment plan.*	Thank you for your comment but the developers stand by their original recommendation.
275.	SH	South Asian Health Foundation	6	NICE	1.4.2.1		Refer people with pain from chronic alcohol-related pancreatitis to a specialist centre for multidisciplinary assessment –again, is there an evidence-base for this assessment pathway?	Thank you for your comment. This recommendation was based on consensus expert opinion.
276.	SH	Nottinghamshire Healthcare NHS Trust	7	NICE	1.1.4.2	9	It would be useful to include recommended dosing regimens for the management of alcohol withdrawal delirium	Thank you for your comment. The developers are not able to specify dosages in recommendation unless there is evidence that a drug is often prescribed at the wrong doses or clear evidence about the effectiveness of different dose levels. Neither was the case for this recommendation.
277.	SH	Nottinghamshire	13	NICE	1.3.4	11	Needs to mention refeeding syndrome –	Thank you for your comment. Re-feeding

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		Healthcare NHS Trust					risks, prevention and interventions – test and treatments.	syndrome is discussed in the full guideline.
278.	SH	The National Treatment Agency for Substance Misuse (NTA)	11	NICE	1.4.2.1	12	*On the recommendation that people with pain from chronic alcohol-related pancreatitis should be referred to a specialist centre for multidisciplinary assessment.* The NTA recommends that for poly-drug and alcohol misusers on methadone maintenance treatment, the multidisciplinary assessment should involve these clients' specialist drug treatment service or GP	Thank you for your comment. Poly-drug use was excluded from the scope of this guidance.
279.	SH	Nottinghamshire Healthcare NHS Trust	8	NICE	1.1.6.1 1.1.6.2	9	Who should provide assessment immediately on admission to hospital? Most hospitals will lack specialists to provide assessment so this will be a generalist doctor/ nurse role. The minimum training needs of such staff groups should be recommended.	Thank you for your comment. The assessment should be conducted by anyone trained in the management of acute alcohol withdrawal. The recommendation has been revised to make this more clear to the reader.
280.	SH	South Asian Health Foundation	4	NICE	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 –we agree that resources for alcohol-related conditions are very important.	Thank you.
281.	SH	Nottinghamshire Healthcare NHS Trust	14	NICE	3	14	Research is required on the treatment of Alcohol Withdrawal Delirium and Refeeding Syndrome also	Thank you. The GDG can only include 5 recommendations for research in the NICE guidance.
282.	SH	Nottinghamshire Healthcare NHS Trust	15	NICE	3.1	14	Patients presenting at hospital who are at risk of alcohol withdrawal seizures or alcohol withdrawal delirium MAY require admission to hospital.	Thank you for your comments. Those people at high risk of seizures or DTs should be admitted into medical care as both can be fatal. If a person continues to drink then they are not at high risk for

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							It will not always be appropriate or clinically indicated to admit to hospital: for example for patients in A&E who have risk factors for developing seizures or delirium but plan to continue drinking. To recommend that all such patients should be admitted to hospital seems to be in contradiction to National Indicator 39 ' reducing alcohol related hospital admissions' Abstinence is cited as a goal – this may not always be the goal – rather a variety of options may be chosen by the patient. Some may plan permanent abstinence, some may choose temporary abstinence, and some may plan to continue drinking post discharge.	developing either.
283.	SH	Nottinghamshire Healthcare NHS Trust	16	NICE	3.3	15	No mention in this section of carbemazepine; this could also be included in line with recommendations in section 1.1.2.1 This section could also include recommendations for the treatment of alcohol withdrawal delirium	Thank you for your comment
284.	SH	The Alcohol and Drug Service	2	NICE	3.4	16	This suggests a RCT to test the effectiveness of interventions delivered by an ASN in an acute hospital setting. I suggest that this is compared to the same interventions being delivered by an alcohol	Thank you but the developers believe this comment pertains to the public health guidance.

Comment No.	Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
							health worker trained in line with DANOS – as if there is no difference in effectiveness then the AHW is likely to be more cost effective.	
285.	SH	Yorkshire Humberside Improvement Partnership	3	NICE	3.4	16	REFERS TO A COHORT STUDY ON BRIEF INTERVENTIONS IN HOSPITALS & POTENTIAL EFFECTIVENESS BUT NEED FOR FURTHER RCT'S – MAY BE USEFUL TO MENTION OTHER EVIDENCE & ONGOING SIPS TRIALS THAT INDICATE EFFECTIVENESS?	Thank you. Please see response to duplicate comment above.
286.	NICE	NICE Editorial Team	50	NICE	1.4.3.1 and 1.4.3.2	12	Is acute alcohol-related pancreatitis ever moderate or between mild and severe? What should happen then? Or in someone with mild but at risk of developing severe? Would it be useful to include a recommendation about these patients or about monitoring patients with mild who are at risk of developing severe?	Thank you. We didn't end up addressing the relative accuracies of the various scoring systems used to predict severe acute pancreatitis at 48 hours, such as the Glasgow (Imrie) prognostic score, the Ranson score, APACHE-II or CRP. In practice, they are used to discriminate between patients with a predicted severe course (who might get organ failure etc) and those in whom severe acute pancreatitis unlikely (mild acute pancreatitis group). We don't/can't define a moderate acute pancreatitis group and therefore can't make a recommendation about how to identify and monitor them.
287.	SH	Inclusive Health	3	NICE	Footnote 6	9	This implies carbamazepine is acceptable as monotherapy. I understood that this is usually as an adjunct in persons who are particularly prone to seizures	Thank you for your comment. Carbamazepine is acceptable as monotherapy. All the treatments will reduce the risk of seizures if used appropriately.