NICE National Institute for Health and Care Excellence

Appendix A2: Summary of evidence from surveillance

2019 surveillance alcohol use disorders: diagnosis, assessment and management of harmful drinking and alcohol dependence (CG115)

Summary of evidence 2019 surveillance

Studies identified in searches are summarised from the information presented in their abstracts. Please note, due to the limited information available in abstracts, particularly in relation to which stage of alcohol misuse interventions were aimed at (mild dependence, alcohol withdrawal, or interventions after successful withdrawal), studies for psychological and pharmacological interventions are discussed under the recommendation deemed most likely relevant to the study, but it is acknowledged that they may also be relevant to other recommendations.

Feedback from topic experts who advised us on the approach to this surveillance review was considered alongside the evidence to reach a view on the need to update each section of the guideline.

Previous surveillance was conducted in 2013 and 2015 but using different methodology which considered the impact of new studies by review question, rather than guideline recommendation. At both of these time points the decision was not to update the guideline. Full details of the previous surveillance are available in full online, so only a brief summary of the impact is included below.

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Recommendation 1.1.1 Building a trusting relationship and providing information		
No studies relevant to this section of the guideline were identified.	A topic expert suggested that the referral pathway between acute hospital trusts and community services is often reported as ineffective, and that frequent feedback from service users that they were not referred by hospital staff or given up to date information on alcohol services. One expert identified a need to check the guideline for stigma terminologies e.g. avoid 'misuse' and 'service user' or caution use as they are apparently seen to be stigmatising by some people.	There was no new published evidence identified at any surveillance time point. A topic expert highlighted that there may be issues with referral pathways but no new evidence was identified on how to address this issue and it is not clear how this issue relates to the recommendations in the guideline. A topic expert highlighted that terms like misuse and service user may be stigmatising to some. However, these are commonly used terms that are easily understood by many people, and other topic experts did not identify this as an issue. Furthermore, there is a risk that changing these terms could cause a lack of clarity and as such no change to the guideline will be made. No new evidence was identified.

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Recommendation section 1.1.2 Working with and supporting families and carers		
No studies relevant to this section of the guideline were identified.	One expert queried whether it would be possible to strengthen statements around facilitating a parent who has problems with alcohol use into treatment.	There was no new published evidence found at any surveillance time point. A topic expert highlighted that there should be a statement around facilitating treatment for parents with alcohol use problems. The guideline already covers support for families and carers and no new evidence was identified to add to this. No new evidence was identified.
Recommendation section 1.2.1 General principles (identification and assessment)		
No studies relevant to this section of the guideline were identified. Studies related to identification of alcohol misuse in adults (including AUDIT) are included in the Alcohol-use disorders: prevention (NICE guideline PH24), decision matrix in relation to recommendation 9.	One expert stated that community alcohol and drug treatment is now funded through Public Health budgets in local authorities so the guidelines should reflect that if they are intended to cover community services. The expert said it would make sense to look at how alcohol-specific interventions can be delivered within that context. An expert also highlighted that many treatment services are joint drug and alcohol services and there are anecdotal reports that clients with alcohol-use disorders are put off seeking	There was no new evidence identified at any surveillance time point that would impact the recommendations in this section. A topic expert highlighted that community alcohol and drug services are now funded through Public Health and have established joint drug and alcohol services. Whilst these changes have led to

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	treatment because they see the service as drug focused, with associated stigmas preventing uptake. One expert expressed concern that offenders with alcohol problems are under treated. This is partly because alcohol concerns are not an issue prisons address, as alcohol is not available in prisons and because of the poor state of the criminal justice system.	considerable changes in localities, it is not anticipated that recommendation 1.2.1 (or the guideline more broadly) would be affected as it outlines principles of practice which should apply in any relevant setting. There was also a concern that offenders with alcohol problems are under treated. No new evidence was identified to address this issue. NICE has produced guidance on the Physical health of people in prison (NICE guideline NG57) and Mental health of adults in contact with the criminal justice system (NICE guideline NG66). No new evidence was identified.
Recommendation section 1.2.2 Assessment in specialist alcohol services		
No studies relevant to this section of the guideline were identified.	One expert stated that it is not clear if recommendations 1.2.2.7 and 1.2.2.8 are in line with NICE guidance on Coexisting severe mental illness and substance misuse: community health and social care services (NICE guideline NG58), which states that patients with coexisting severe mental illness and	There was no new evidence at any surveillance time point that would impact the recommendations in this section. A topic expert highlighted that it was unclear if there was concordance

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	alcohol misuse should be treated primarily by mental health service, whilst recommendation 1.2.2.8 within CG115 suggests abstinence from alcohol for 3-4 weeks before considering referring for treatment for a comorbid mental health problem. The expert also made a point about waiting 3-4 weeks after abstinence from alcohol before referring for specific mental health treatment (see recommendation 1.2.2.8) being unhelpful as it allows Improving Access to Psychological Therapies (IAPT) and other psychological therapy services to not treat those with mental health disorders who have turned to alcohol. One expert queried whether additional tests for cognitive functioning should be considered, including MOCA and 6CIT.	across NICE guidelines on treating people with mental health conditions and alcohol misuse. We have checked the NICE guideline on coexisting severe mental illness and substance misuse: community health and social care services (NG58), and identified that it should not conflict with CG115 as the focus of NG58 is severe mental illness, so the 2 guidelines are more complimentary. CG115 currently advises that people with a significant comorbid mental health condition should be referred to a psychiatrist, which does not conflict with NG58. However, to ensure readers of CG115 are aware of NG58, footnote 17 within CG115 will be updated to also include a cross reference to NG58. Topic expert feedback also highlighted that recommendation 1.2.2.8, which suggests waiting 3-4 weeks to see if alcohol abstinence improves mental health problems before treating for mental health, is unhelpful and leads to delays in treatment for mental illness. At the

2019 surveillance summary	Intelligence gathering	Impact statement
		time of guideline development, the committee noted that treatment for comorbid disorders (in particular depression and anxiety) whilst people are consuming significant levels of alcohol does not appear to be effective. However, the committee did acknowledge that some people with depressive disorders will require immediate treatment and the recommendations were not meant to stand in the way of immediate treatment being provided in such a situation. In reviewing the evidence for comorbid disorders, the committee did not find any treatment strategies or adjustments that should be made because of the comorbid problem and, in view of this, decided to refer to the relevant NICE guidelines. During this surveillance review there was no new evidence found to contradict this. There was no evidence found for MOCA and 6CIT tests in people with alcohol use disorders which might trigger an update to the recommendations, although

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		recommendation 1.2.2.11 does already recommend considering brief measures of cognitive functioning. No new evidence was identified.
Recommendation section 1.3.1 General principles for all interventions		
No studies relevant to this section of the guideline were identified.	One expert stated that recommendations in this section are not clear or specific on the content of intensive structured community based intervention, and that the lack of clarity leads to people thinking that this only refers to a 3-week, post-detox structured intervention. The expert also stated that some service users would need an intensive structured community based intervention that lasts longer than 3-weeks. An expert also highlighted that in recommendation 1.3.1.1 a reference should be included about trained and competent staff. They went on to add that there is a tendency in some community services to use untrained staff to conduct initial assessments, when it is particularly important to have competent, trained staff at this point as it determines what interventions will be offered.	There was no new evidence identified at any surveillance time point that would impact the recommendations in this section. A topic expert highlighted that there is a lack of clarity on what constitutes an intensive structured community based intervention and a recommended duration of the intervention. The section covers general principles, whereas the detail of specific intervention duration is covered in sections 1.3.3 and 1.3.4 of the guideline. In this respect, the information is provided by the guideline. A topic expert also highlighted that it is important that staff are appropriately trained to carry out initial assessments,

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		whereas in practice untrained staff can sometimes be employed in this role. However, the guideline recommends that staff are trained and this is covered in recommendation 1.3.1.5. The reasons for untrained staff being employed to carry out initial assessment is unclear, although it is anticipated this relates to resource constraints, so there is no impact on the guideline. Footnote 5 will be amended to the new standard wording for unlicensed medicines, see Editorial and factual corrections below. No new evidence was identified.
Recommendation section 1.3.2 Coordination and case management		
2019 surveillance No studies relevant to this section of the guideline were identified during the 2019 surveillance. **2015 and 2013 surveillance** Two studies were identified in the previous surveillance which	One expert highlighted that this section does not describe how cases are managed in community treatment. The expert stated that the term 'care coordination' has been used differently in community treatment, and that case management and key work processes have been changing as resources diminish. The expert went on to add that it would be useful to	**2019 surveillance** There was no new evidence identified that would impact the recommendations in this section. A topic expert highlighted that services have changed since the

2019 surveillance summary	Intelligence gathering	Impact statement
may be of relevance here, see the 2015 surveillance review for clinical area 2: evaluating the organisation of care for people who misuse alcohol.	have guidance which clearly specifies the essentials of case management that alcohol-dependent adults should be offered if there is evidence on this. The expert stated that the term 'care coordination' has a specific meaning in psychiatric services which can lead to confusion between addiction services (which are public health services rather than psychiatric ones) - the terms care coordination and case management have little meaning in modern addiction services.	guideline was written and that the terms care coordination and case management have different meanings in different settings. On reviewing this issue, it is apparent that the recommendations in this section describe the nature and the elements of care coordination and case management. Further details are available in the full-guideline. Whilst language and terminology naturally change the core elements for practice are described in the recommendations. Furthermore, no new evidence has been found to inform changes to guideline language and recommendations. No new evidence was identified. **2015 and 2013 surveillance** Previous surveillance concluded that evidence identified at that time point was unlikely to change guideline recommendations as the evidence was in line with the guideline.

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Recommendation section 1.3.3 Interventions for harmful drinking and mild dependence		
2019 surveillance Psychological interventions One systematic review (1) of patient centred care interventions for the management of alcohol use disorders was identified (40 studies, n=16,020 patients). The review found that single sessions of motivational interviewing showed no clear benefit on alcohol consumption outcomes, with few studies indicating a benefit of patient centred care versus control. The results for multiple sessions of counselling were mixed, but many studies showed a significant benefit of the patient centred care interventions. Pharmacologically supported patient centred care interventions were also found to be generally effective, with most studies reaching statistical significance. One pragmatic RCT (2) of 8 x 1 hour sessions delivered over 12 weeks by clinical psychologists of personalised cognitive behavioural therapy, versus usual targeted treatment, in a public health clinic for alcohol use disorders was identified (n=379 participants). The review found that only 25% of participants completed all 12 sessions, with the average being 4.4 sessions. Compared with usual targeted treatment, cognitive behavioural therapy (CBT) had no significant effect on drinking days or consumption, but there was significant reduction in craving (b = -18.97, 95% CI -31.44 to -6.51) and impulsivity (b = -26.65, 95% CI -42.09 to -11.22) modules. One RCT (3) of 12 outpatient manual-guided sessions of	A topic expert noted that alcohol misuse and behavioural couples therapy may be contra-indicated where domestic abuse is an issue, with respect to recommendation 1.3.3.2. An expert highlighted that the evidence for anti-craving medication is weak. One expert stated that the recommendations covering pharmacotherapy for alcohol dependence are still appropriate, but need to be updated to include a recommendation for nalmefene for the management of heavy drinking (note: this drug was not licensed for use for this indication when the Guideline was published). Another expert expressed a need for guidance on interventions with pregnant alcohol users. One expert highlighted that as resources for delivering alcohol services are decreasing there is an increase of online interventions and that voice over interactive protocol is also being used to increase accessibility. One expert said that there is increasing use of group interventions for alcohol-use and queried whether evidence is available that can be reviewed. The expert also highlighted that there is now a widespread practice in community services of requiring service users to attend pre-detox/stabilisation groups before they can access detox and queried if there was	**2019 surveillance** Psychological interventions Published evidence suggests that single sessions of motivational interviewing showed no clear benefit, multiple counselling sessions have uncertain effects, but pharmacologically supported patient centred care was found to be effective. Targeted treatment was not found to be superior to CBT. Likewise, female-specific CBT was not found to be superior to gender neutral CBT. Group couples' therapy was found to be significantly less effective than individual couples therapy. This broad range of evidence is in line with current recommendations which recommend psychological intervention over multiple sessions, and involving a regular partner if willing to participate. A topic expert highlighted that alcohol dependence can be

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female-specific CBT, versus gender neutral CBT, for alcohol dependant women was identified (n=99 women). The trial found no difference between treatments with women in both groups being satisfied and engaged and reporting significant reductions in drinking. Women in the FS-CBT but not in the gender neutral CBT group reported an increase in percentage of abstainers in their social networks in the year following treatment (0.69% per month, p=0.002). One RCT (4) of group behavioural couples therapy versus standard couples behavioural therapy, plus 12-step-orientated individual behavioural therapy, for people with alcohol use disorders was identified (n=101 patients). The trial found that both alcohol and relationship outcomes were significantly worse with group behavioural couple therapy, compared with standard couple behavioural therapy. One RCT (5) of 12 sessions of conjoint CBT, versus 5 individual CBT sessions plus 7 sessions of blended CBT, for women with alcohol use disorders was identified (n=59 women). The trial found that the percentage of drinking days or percentage of heavy drinking days did not differ in the 12 months following treatment. However, the authors reported a small trend favouring blended CBT, patient preference for individual therapy as part of treatment and that some individual sessions decreased the challenges of scheduling conjoint sessions. One RCT (6) of 12 weeks of network support treatment, compared with packaged CBT, in people with alcohol use disorder was identified (n=193 patients). Compared with packaged CBT, network support treatment had better results	evidence on this. One expert identified that recommendations around psychological therapies, in particular 1.3.3.3 – 1.3.3.5, were generally perceived to be unrealistic and hence undeliverable. The expert went on to say that whilst they might represent the 'council of perfection' they could have the adverse effect if commissioners or providers felt that if they couldn't develop what was recommended they would not provide anything at all.	associated with domestic violence and thus recommendation 1.3.3.2 which suggests couples' therapy should be caveated. Recommendation 1.3.3.2 will be amended to highlight that domestic abuse should be ruled out before offering couples' therapy. The editorial amendment is outlined in the section below on Editorial and factual corrections. A topic expert also highlighted that the provision of psychological services recommended in the guideline were seen as unrealistic due to resource constraints. There was no new evidence found that would inform a revision to recommendations in the context of financial pressures. Whilst budget constraints are a factor that may impact implementation, the guideline is intended to be cost-effective and offer a return on investment. It is acknowledged, however, that the changing budgetary landscape will affect commissioning decisions. New evidence is unlikely to

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in terms of both proportion of days abstinent and drinking consequences, and equivalent improvements in 90-day abstinence, drinks per drinking day and heavy drinking days. The effects of network support treatment were mediated by pre-post changes in abstinence self-efficacy, proportion of non-drinkers in the social network and attendance at Alcoholics Anonymous. Acupuncture One meta-analysis (7) of acupuncture for alcohol use disorders was identified (7 studies, n=243 participants).The analysis found that compared with control, acupuncture had a stronger effect on reducing alcohol-related symptoms and behaviours (g = 0.67). The authors suggested that a larger cohort study is required to confirm results One systematic review (8) of acupuncture to reduce alcohol dependency was identified (15 RCTs, n=1,378 participants). The review found that, compared with control, acupuncture reduced alcohol craving (SMD -1.24, 95% CI -1.96 to -0.51); and alcohol withdrawal symptoms (SMD -0.50, 95% CI -0.83 to -0.17). Secondary analyses showed that acupuncture reduced craving compared with sham acupuncture; reduced craving compared with controls in RCTs conducted in Western countries; and reduced craving compared with controls in RCTs with only male participants. Exercise One systematic review (9) of exercise treatment for alcohol use disorders was identified (21 studies, n=1,204 participants). The review found that exercise did not significantly reduce		change guideline recommendations. Acupuncture Published evidence suggests that acupuncture may have some potential to reduce alcohol craving, however the evidence base is limited and more research is needed. Currently the guideline does not recommend acupuncture. This evidence is not thought to be sufficient to change the guideline recommendations, but this area will be revisited at the next surveillance review to see if the evidence base has expanded and evidence of an effect is clearer. New evidence is unlikely to change guideline recommendations. Exercise Published evidence suggests that exercise has inconsistent effects on alcohol-related outcomes but may improve mood and depressive

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daily alcohol consumption or the AUDIT total scores. However, exercise significantly reduced depressive symptoms versus control (p=0.006) and improved physical fitness (VO_2) (p=0.01). One systematic review (10) of clinical exercise interventions for alcohol use disorders was identified (14 studies). The review found that exercise may have beneficial effects on certain domains of physical functioning but inconsistent effects on anxiety, mood management, craving, and drinking behaviour, although the trend was towards a beneficial effect. Exercise interventions were found to be safe. The authors caveated that results should be interpreted cautiously due to the heterogeneity of the interventions and measures, and methodological flaws. One RCT (11) of exercise (30-45 mins twice weekly running or brisk walking) plus treatment as usual, compared with treatment as usual, in the treatment of alcohol use disorders was identified (n=105 patients). The trial found no significant difference in drinking habits between groups. One RCT (12) of physical activity (group or individual) as an adjunct to outpatient alcohol treatment, versus standard care, in people with alcohol use disorder was identified (n=175 patients). Compared with control, there was no significant difference in excessive drinking in the group exercise group (OR 0.99, p=0.976) or individual exercise group (1.02, p=0.968). Subgroup analyses found that participants with moderate level physical activity had lower odds for excessive drinking than participants with low level physical activity (OR 0.12, p<0.001). The amount of alcohol consumed in the		symptoms. This evidence is not thought to be sufficient to change the guideline recommendation, but this area will be revisited at the next surveillance review to see if the evidence base has expanded and evidence of an effect is clearer. New evidence is unlikely to change guideline recommendations. Drugs for alcohol dependence A network meta-analysis covering naltrexone, acamprosate, baclofen and topiramate came to the conclusion that there was no high grade evidence for drugs used in alcohol use disorders and that the drugs only showed a low to medium efficacy on alcohol-related outcomes, such as total alcohol consumption, with a high risk of bias. It should be noted that it is unclear from the abstract if all of the included studies were in alcohol dependence, but nalmefene, acamprosate and

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intervention groups decreased by 4% (p = 0.015) for each increased exercising day. ### Drugs for alcohol dependence One network meta-analysis (13) of nalmefene, naltrexone, acamprosate, baclofen or topiramate for alcohol dependence or alcohol use disorders was found (32 RCTs, n=6,036 participants). The network analysis found that compared with placebo, nalmefene, baclofen and topiramate showed superiority over placebo on total alcohol consumption. No efficacy was observed for naltrexone or acamprosate compared with placebo. Nalmefene and naltrexone had increased withdrawals due to safety reasons. Indirect comparisons found that topiramate was superior to nalmefene, naltrexone and acamprosate on alcohol consumption outcomes, but with a poor adverse event profile. ### Anticonvulsants One Cochrane review (14) of anticonvulsants for alcohol dependence was identified (25 studies, n=2,641 participants).There was moderate-quality evidence that, compared with placebo, anticonvulsants reduced drinks or drinking days (MD -1.49, 95% CI -2.32 to -0.65) and heavy drinking (SMD -0.35, 95% CI -0.51 to -0.19), and there was no difference in withdrawal for medical reasons, but for specific adverse effects the analyses generally favoured placebo. Compared with naltrexone, anticonvulsants did not have an effect on dropout rates, severe relapse rates, or continuous abstinence rates, but anticonvulsants were associated with fewer heavy drinking days (MD -5.21, 95% CI -8.58 to -1.83),		naltrexone are drugs used in alcohol dependence. This new evidence does not seem sufficient to change current guideline recommendations in section 1.3.3 on interventions for harmful drinking and mild alcohol dependence, as the new evidence does not provide greater clarity on which drugs should be used. The evidence will be revisited at the next surveillance review to see if there is greater clarity on which drugs should be used in alcohol dependence. New evidence is unlikely to change guideline recommendations. ### Anticonvulsants A Cochrane review found that anticonvulsants were superior to placebo, but not to naltrexone, and the authors concluded that the evidence for anticonvulsants for treating alcohol dependence was insufficient. This new evidence does not seem sufficient to change current

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more days to severe relapse (MD 11.88, 95% CI 3.29 to 20.46) and lower withdrawal for medical reasons (RR 0.13, 95% CI 0.03 to 0.58). ### Naltrexone One RCT (15) (16) of naltrexone versus placebo in young adult heavy drinkers aged 18-25 years old (n=118 adolescents) found that there was no significant difference between placebo and naltrexone for percentage of heavy drinking days and percent days abstinent. Compared with placebo, naltrexone significantly reduced the number of drinks per drinking day (p=0.009) and percentage of drinking days with estimated blood alcohol concentrations of 0.08 g/dL or more (p=0.042). There were no serious adverse events, although sleepiness was more common with naltrexone. ### Nalmefene **Related NICE guidance:** • Nalmefene for reducing alcohol consumption in people with alcohol dependence NICE technology appraisal guidance (TA325) In addition there were 10 studies (13,17–25) concerning nalmefene identified during the 2019 surveillance process. ### Antipsychotics One systematic review (26) of antipsychotics for alcohol dependence in patients without schizophrenia or bipolar depression was identified (13 double-blind studies, n=1,593 patients). The review included a range of drugs including		guideline recommendations in this section of the guideline, as the new evidence does not show a clear benefit of anticonvulsants compared with naltrexone, which is currently recommended in the guideline. The evidence will be revisited at the next surveillance review to see if there is greater clarity on the use of anticonvulsants for alcohol dependence. New evidence is unlikely to change guideline recommendations. ### Naltrexone One RCT found that naltrexone was effective in reducing the number of drinking days in young adults aged 18-25 years, but not percent days abstinent or heavy drinking days. This evidence does not conflict with the guideline which currently suggests naltrexone or acamprosate may be used for alcohol dependence. However, footnote 7 will be amended to reflect changes

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aripiprazole, olanzapine, quetiapine and tiapride. The review found that none of the antipsychotics improved abstinence or reduced drinking or craving. One RCT (27) of 12 weeks of 5mg or 2.5mg olanzapine, versus placebo, in the treatment of alcohol dependence was identified (n=129 participants). The trial found that there were reductions in alcohol use and craving and an increase in control over alcohol use across all treatment groups. Dose-response analyses indicated that, compared with placebo, participants in the 5 mg group experienced reduced craving for alcohol and participants in the 2.5 mg group decreased the proportion of drinking days and increased their control over alcohol use. The improved control over alcohol use in the 2.5mg group remained significant 6 months post-treatment. Both the 2.5mg and 5mg doses were equally well tolerated. ### Varenicline One systematic review (28) of varenicline in the treatment of alcohol use disorders in 'heavy drinkers' was identified (8 studies, number of participants not reported). The review found that varenicline reduces alcohol craving as well as reduction of overall alcohol consumption in patients with alcohol use disorders, but not abstinence rates. One RCT (29) of varenicline (titrated to 2mg/day) versus placebo, in combination with a computerised behavioural intervention, for alcohol dependant participants (smokers and non-smokers) was identified (n=200). The trial found that, compared with placebo, the varenicline group had significantly lower weekly percent heavy drinking days, drinks per day,		in naltrexone licensing, see Editorial and factual corrections below. New evidence is unlikely to change guideline recommendations. ### Nalmefene There is a NICE guideline covering nalmefene for reducing alcohol consumption in people with alcohol dependence (TA325). We identified 10 studies relating to nalmefene use and these will be passed to the NICE technology appraisals programme for consideration during review of TA325. However, topic expert feedback highlighted that this section of the guideline should be updated to refer to the NICE guideline TA325 nalmefene. An editorial amendment will be added to recommendation 1.3.3.2 to cross-refer to information on Nalmefene for reducing alcohol consumption in people with alcohol dependence (2014) NICE technology appraisal guidance 325.

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drinks per drinking day, and alcohol craving ($p<0.05$). Adverse events were mild. ### Other drugs One RCT (30) of 600mg once daily benfotiamine (a high potency thiamine analogue), versus placebo, in alcohol dependant participants was identified (n=120 non-treatment seeking participants). The trial found that alcohol consumption reduced significantly for both groups and there were no significant adverse events. Compared with placebo, the reductions in total alcohol consumption over 6 months were significantly greater for benfotiamine treated women ($p=0.02$). One RCT (31) of 30mg/day mirtazapine versus placebo in male high alcohol consumers, sub-grouped by hereditary alcohol use disorder, was identified (n=59 participants). There was no benefit of mirtazapine in the intention-to-treat analysis but participants with heredity for alcohol use disorder showed a benefit in terms of self-reported drinking with mirtazapine compared with placebo. One phase II RCT (32) of samidorphan (1, 2.5, or 10 mg/day) versus placebo in adults with alcohol use disorder was identified (n=406 patients). During weeks 5 to 12 there was no statistical difference between samidorphan and placebo groups on the primary outcome of percentage of people with no heavy drinking days. However, compared with placebo, dose-dependent reductions in cumulative rate of heavy drinking days were observed for samidorphan 10 mg/day (-41%, $p<0.001$) and for samidorphan 2.5 and 1 mg (-30% and -32%, $p<0.05$ for both). Statistical significance was also		An editorial amendment is outlined in the section below on Editorial and factual corrections. New evidence is unlikely to change guideline recommendations. ### Antipsychotics One systematic review found that antipsychotics were not effective in reducing alcohol drinking, abstinence or craving in patients without schizophrenia or bipolar depression, whilst 1 RCT found that olanzapine was effective compared with placebo in reducing alcohol use and craving. This evidence is not deemed sufficient to change the guideline recommendations as it does not provide clear evidence to demonstrate a benefit of antipsychotics in alcohol dependence. The evidence will be revisited at the next surveillance review to see if any new evidence provides support for antipsychotics for alcohol dependence.

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reached for 10mg samidorphan on alcohol craving, and Patient Global Assessment of Response to Therapy (PGART). **2015 and 2013 surveillance** A total of 24 studies were found during previous surveillance conducted in 2013 and 2015 that covered psychological interventions (see clinical area 5: psychological and psychosocial interventions in previous surveillance), and 29 studies focused on pharmacological treatments for alcohol dependence or harmful alcohol use (see clinical area 6: pharmacological interventions in the previous surveillance review). Note that the methods used for previous surveillance did not separate out studies according to recommendations but instead looked at clinical areas.		New evidence is unlikely to change guideline recommendations. Varenicline One systematic review found that varenicline did reduce alcohol craving and alcohol consumption but not abstinence rates. It was unclear if any of the included studies were against an active comparator. Currently the guideline recommends naltrexone or acamprosate for alcohol dependence, and this new evidence does not provide an indication if varenicline is superior to these drugs, as such no impact on the guideline is anticipated. The evidence will be revisited at the next surveillance review to see if a more robust evidence base is available. New evidence is unlikely to change guideline recommendations. Other drugs

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		Limited evidence was available for samidorphan, benfotiamine and mirtazapine, which showed benefits of these drugs, compared with placebo, for some alcohol-use outcomes. Currently the guideline recommends naltrexone or acamprosate for alcohol dependence, and this new evidence does not provide an indication if any of these drugs are superior to naltrexone or acamprosate, as such no impact on the guideline is anticipated. Furthermore, samidorphan is currently not licensed in the UK. The evidence will be revisited at the next surveillance review to see if a more robust evidence base is available. New evidence is unlikely to change guideline recommendations. **2015 and 2013 surveillance** Previous surveillance concluded that cumulative evidence identified at the 2013 and 2015 surveillance time

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		points was unlikely to change guideline recommendations.
Recommendation section 1.3.4 Assessment and interventions for assisted alcohol withdrawal		
2019 surveillance Psychosocial interventions One systematic review (33) of psychosocial interventions in inducing or maintaining alcohol abstinence in patients with chronic liver disease was identified (13 studies, n=1,945 participants). The psychosocial interventions included motivational enhancement therapy, CBT, motivational interviewing, supportive therapy, and psycho-education either alone or in combination with another intervention or usual care. All studies of induction of abstinence (10 studies) reported an increase in abstinence among participants in the intervention and control groups. However, an integrated therapy that combined CBT and motivational enhancement therapy with comprehensive medical care, delivered during a period of 2 years, produced a significant increase in abstinence (74% increase in intervention group vs 48% increase in control group, p=0.02). All studies of maintenance of abstinence (3 studies) observed a return to alcohol in the intervention and control groups. However, an integrated therapy that combined medical care with CBT produced a significantly smaller rate of return to alcohol (32.7% in integrated CBT group versus 75% in control group, p=0.03).	One expert identified that in relation to recommendation 1.3.4.2 (which recommends offering an intensive community programme following assisted withdrawal in which the service user may attend a day programme lasting between 4 and 7 days per week over a 3-week period), some service users would need an intensive structured community based intervention that lasts longer than 3 weeks (although not necessarily 7 days per week).	**2019 surveillance** Psychosocial interventions Published evidence suggests that psychosocial interventions may have a role in inducing abstinence if they offer combined CBT and motivational enhancement therapy with comprehensive medical care. This is in line with the guideline which recommends offering outpatient-based community assisted withdrawal programmes should consist of a drug regimen and psychosocial support including motivational interviewing (recommendation 1.3.4.3). However, a topic expert highlighted that recommendation 1.3.4.2 may be misinterpreted as meaning therapy should last for a maximum of 3 weeks which might not be sufficient. Recommendation 1.3.4.2 does state that community based programmes

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Treatment setting One systematic review (34) of community detoxification for alcohol dependence was identified (n=20 studies).The review found that compared to patients undergoing facility based detoxification, those who underwent community detoxification had better drinking outcomes. Community detoxification was also found to be cheaper than facility based detoxification, had good completion rates, and was reported to be safe. One RCT (35) of treatment for alcohol dependence in primary care, compared with outpatient specialist care, was identified (n=288 participants). The trial found that it was not possible to confirm the non-inferiority of primary care compared with outpatient specialist care for the primary outcomes of change in weekly alcohol consumption. Subgroup analysis found that specialist care was superior to primary care only for patients with high severity of dependence. **2015 and 2013 surveillance** A total of 24 studies were found during previous surveillance conducted in 2013 and 2015 that covered psychological interventions (see clinical area 5: psychological and psychosocial interventions in previous surveillance). Note that the methods used for previous surveillance did not separate out studies according to recommendations but instead looked at clinical areas.		should 'vary in intensity according to severity of dependence, available social support and the presence of comorbidities'. Furthermore, 3-weeks was based on the evidence included at the time of guideline development and no new evidence was found to suggest a change in duration for these programmes. As such no change to recommendations is anticipated. New evidence is unlikely to change guideline recommendations. Treatment setting Published evidence suggests that community treatment is more effective for alcohol detox and cheaper than inpatient/facility based detox. Primary care based treatment was found to be non-inferior to outpatient specialist treatment. This is in line with current guideline recommendations which recommends community based detox.

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		New evidence is unlikely to change guideline recommendations. **2015 and 2013 surveillance** Previous surveillance also concluded that cumulative evidence identified at the 2013 and 2015 surveillance time points was unlikely to change guideline recommendations.
Recommendation section 1.3.5 Drug regimens for assisted withdrawal		
2019 surveillance Drug combinations One systematic review (36) of combined pharmacological interventions intended to treat alcohol use disorder was identified (16 studies). The majority of published trials included naltrexone combined with gabapentin, quetiapine, ondansetron, acamprosate, gamma-hydroxybutyrate, sertraline, or escitalopram plus gamma-hydroxybutyrate. There was no significant benefit of combinations over single agents, but the results were limited by low statistical power, and heterogeneity of outcome measures and drug combinations. Drug combination effect sizes were comparable	A topic expert highlighted that there is a need to consider the use of other pharmaceutical interventions than just those covered by the guideline for the management of alcohol withdrawal, A topic expert indicated that recommendation 1.3.5.5, which states 'Prescribe for instalment dispensing, with no more than 2 days' medication supplied at any time' does not reflect common practice, especially in more rural areas, as in most areas there is no payment for true 'instalment dispensing' for these drugs. An expert indicated that there is increasing evidence to support using acamprosate/naltrexone earlier, and not wait until detox is completed.	**2019 surveillance** Drug combinations Published evidence from 1 systematic review suggests that there is no significant benefit of drug combinations over single agents for treating alcohol use disorders, although specific drug combinations may be effective in treating certain symptoms or populations. This new evidence does not seem sufficient to change current guideline

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to those observed in single-agent trials. However, the authors noted that the use of drug combinations may be useful to treat specific symptoms, or subpopulations. Baclofen One systematic review (37) of low (30-60mg/day) and high (>60mg/day) dose baclofen, versus placebo, for alcohol dependence was identified (13 RCTs). Compared to placebo, baclofen significantly increased time to lapse (SMD=0.42; 95% CI 0.19 to 0.64), and patients abstinent at the end point (OR=1.93; 95% CI 1.17 to 3.17), but there was no significant difference in percentage days abstinent. Overall, studies with low dose baclofen showed better efficacy than studies with high dose baclofen, and the tolerability of high dose baclofen was worse. Meta-regression analysis showed that the effects of baclofen were greater with high daily alcohol consumption as a starting point. One meta-analysis (38) of baclofen versus placebo for the treatment of alcohol use disorders (14 RCTs, n=1,522 patients) was identified. The review found a small non-significant difference with baclofen compared with placebo for all primary outcomes (SMD=0.22; 95% CI -0.03 to 0.47). One meta-analysis (39) of baclofen versus placebo for reducing harmful drinking, craving and negative mood was identified (12 RCTs). The trial found that compared with placebo, baclofen had a significant effect on abstinence rates when using intention-to-treat analysis (OR=2.67, 95% 1.03 to 6.93; p=0.04). There was no significant effect on other drinking outcomes such as heavy drinking days (p=0.21), or craving	An expert indicated that there is no evidence to suggest a fixed dose regime is superior to a symptom-triggered dose for treatment in the community and the recommendation could be revised.	recommendations, as the new evidence does not provide greater clarity on which drugs should be used for the treatment of alcohol use disorder. Please note, due to abstract level detail it was unclear if all of the included studies within the systematic review were specifically for alcohol withdrawal. However, if the review does include studies for alcohol dependence or relapse prevention, the interpretation of results would not change and there would not be an anticipated impact on the guideline. The evidence will be revisited at the next surveillance review to see if there is greater clarity on combination drugs for the treatment of alcohol use disorders. New evidence is unlikely to change guideline recommendations. Baclofen New published evidence from 1 systematic review suggests that baclofen may be more effective than placebo, with low dose (30-

2019 surveillance summary	Intelligence gathering	Impact statement
(p=0.24). There was substantial heterogeneity across each analysis. One RCT (40) of baclofen (50mg/day) versus placebo, plus standard psychosocial treatment, for alcohol dependence was identified (n=64 participants). There were no between group differences for the percentages of heavy drinking and abstinent days. Both arms had a significant reduction in levels of distress, depression and craving, but self-efficacy and social support remained unchanged in both groups. There were no adverse events. One RCT (41) of 12 weeks baclofen (30mg/day or 60mg/day) versus placebo, alongside a structured psychosocial therapy called BRENDA, in alcohol dependant patients was identified (n=69). The trial found that heavy drinking days and drinks per drinking day significantly reduced across all 3 groups, and there were no statistically significant advantages to baclofen. A post hoc analysis found an advantage of baclofen 30mg/day and 60mg/day in patients with comorbid anxiety disorder on time to relapse ($p < 0.05$). There were no serious adverse events with either dose of baclofen. One RCT (42) of oral baclofen 30mg/day versus placebo in adults with chronic hepatitis C and alcohol use disorders was identified (n=180 participants). The trial found that compared with placebo, baclofen did not improve the percentage of days abstinent or the percentage of no heavy drinking. There were also no significant differences between baclofen and placebo participants outcomes. One RCT (43) of high dose baclofen (180mg/day) versus		60mg/day) baclofen showing better efficacy and safety than high dose (>60mg/day) baclofen. Meta-regression analysis showed that the effects of baclofen were greater with a starting point of high daily alcohol consumption. Two further meta-analyses and 3 RCTs showed mixed results against placebo. The single trial of baclofen versus an active comparator showed that chlordiazepoxide provided more rapid and more effective control of anxiety and agitation requiring less lorazepam supplementation than baclofen. Given the inconsistent benefits of baclofen compared with placebo, and the fact that chlordiazepoxide provided better outcomes compared with baclofen, the evidence is not deemed sufficient to change current recommendations. The evidence will be revisited at the next surveillance review to see if there is a more robust evidence base. New evidence is unlikely to change guideline

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placebo in alcohol dependant patients was identified (n=320 participants). The trial did not find a statistically significant difference for its primary outcome of the percentage of abstinent patients during 20 consecutive weeks (baclofen: 11.9%; placebo: 10.5%, p=0.618). A reduction in alcohol consumption was observed from month 1 in both groups, but was not statistically significant between groups (p=0.095). In patients with high drinking risk level at baseline, the reduction in alcohol consumption was greater with a difference at month 6 of 15.6 g/day between groups in favour of baclofen (p=0.089). There was a significant reduction in craving assessed with Obsessive-Compulsive Drinking in the baclofen group (p=0.017). There were no major safety concerns. One RCT (44) of 9 days of 30mg baclofen versus 75mg chlordiazepoxide in participants with uncomplicated alcohol withdrawal syndrome was identified (n=60 participants). Lorazepam was used as rescue medication. The trial found that both baclofen and chlordiazepoxide showed a consistent reduction in the total Clinical Institute Withdrawal Assessment for Alcohol-Revised Scale (CIWA-Ar) scores. However, chlordiazepoxide showed a faster and more effective control of anxiety and agitation requiring less lorazepam supplementation. Both drugs were well tolerated with mild self-limiting adverse events. ### Gabapentin One systematic review of gabapentin for alcohol withdrawal and dependence (45) was identified (10 trials). The review found limited data suggesting that gabapentin can provide		recommendations. ### Gabapentin Published evidence suggests that gabapentin may have a benefit in mild alcohol withdrawal and alcohol dependence. Currently gabapentin is not mentioned in the guideline, as the evidence was limited at the time of guideline development. Gabapentin is also currently unlicensed for alcohol withdrawal in the UK. This evidence is not deemed sufficient to change current recommendations. The evidence will be revisited at the next surveillance review to see if there is a more robust evidence base. New evidence is unlikely to change guideline recommendations. ### Sodium oxybate One trial of sodium oxybate versus oxazepam for alcohol-dependent outpatients with uncomplicated alcohol withdrawal found no

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benefit in managing mild alcohol withdrawal syndrome, with improvements in sleep, mood and anxiety-related outcomes, although there were 5 suspected seizures in the withdrawal studies. Studies evaluating gabapentin for alcohol dependence found dose-dependent benefits for complete abstinence, rates of no heavy drinking and alcohol cravings, and gabapentin was well tolerated with no severe adverse reactions. One RCT (46) of gabapentin (900 or 1800 mg/day) versus placebo for alcohol dependence was identified (n=150 patients). The trial found that gabapentin significantly improved the rate of abstinence with 4% abstinence with placebo versus 11% with 900mg and 17% with 1800mg gabapentin (p=0.04 for linear dose effect). Gabapentin also significantly reduced heavy drinking, with 22.45% heavy drinking rate with placebo versus 29.6% with 900mg, and 44.7% with 1800mg gabapentin (p=0.02). The trial found no serious drug-related adverse events. Sodium oxybate One RCT (47) of 10 days of sodium oxybate versus oxazepam for alcohol-dependent outpatients with uncomplicated alcohol withdrawal was identified (n=126 patients). The RCT found no difference in the mean total CIWA-Ar score between groups, with both groups having significant reductions from baseline. There were no severe side effects reported with either therapy and both were well tolerated. **2015 and 2013 surveillance**		difference in effectiveness. Currently recommendation 1.3.6.14 does not recommend sodium oxybate (or Gamma-hydroxybutyric acid (GHB) as it is known in the guideline) as the committee who developed the guideline felt that the harm due to GHB misuse outweighed the benefits. As such, this new evidence is not deemed sufficient to update the guideline. The evidence will be revisited at the next surveillance review to see if there is a more robust evidence base to warrant an update. New evidence is unlikely to change guideline recommendations. Other issues Topic exerts highlighted that there is no evidence to suggest that fixed dosing is superior to symptom-triggered dosing in the community. However, the guideline committee came to the conclusion that symptom-triggered assisted

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A total of 29 studies focused on pharmacological treatments for alcohol dependence or harmful alcohol use (see clinical area 6: pharmacological interventions in the previous surveillance review). Note that the methods used for previous surveillance did not separate out studies according to recommendations but instead looked at clinical areas.		withdrawal was only practical in those inpatient settings that contained 24-hour medical monitoring and high levels of specially trained staff. No new evidence has been found to contradict this and as such it does not appear warranted to update the guideline. A topic expert suggested that recommendation 1.3.5.5 which advocates only prescribing for instalment dispensing, with no more than 2 days' medication supplied at any time, was not practical in current practice, especially in rural areas. This recommendation is focused on preventing overdose and diversion and it is assumed that rural practices will have policies in place to balance the risks of overdose with dispensing practicalities. Whilst this is an important consideration it is not possible to cover and address all contextual factors within a guideline of this nature. In addition, 4 editorial amendments are required. Recommendation

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		1.3.5.3 will be amended to add: 'Prescribers should be aware of the following legislation and advise patients accordingly: Drugs and driving: blood concentration limits to be set for certain controlled drugs in a new legal offence 2014'. Recommendation 1.3.5.11 will be amended to add: 'Prescribers should also see Addiction to benzodiazepines and codeine July 2011. Footnotes 12 and 13 will be amended with the new standard wording for unlicensed medicines. See Editorial and factual corrections below. **2015 and 2013 surveillance** Previous surveillance also concluded that cumulative evidence identified at the 2013 and 2015 surveillance time points was unlikely to change guideline recommendations.
Recommendation section 1.3.6 Interventions for moderate and severe alcohol dependence after successful withdrawal		
2019 surveillance	One expert stated that there is a need to examine the use of adjunctive medication in preventing relapse,	**2019 surveillance**

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### Disulfiram One meta-analysis (48) of disulfiram for supporting abstinence was identified (22 studies). The analysis found a higher success rate of disulfiram compared to controls. The results were significant across open label studies but when looking at RCTs with blind designs the results were not significant. Disulfiram was also more effective than the control condition when compared to naltrexone and to the no disulfiram group. The authors noted a high degree of heterogeneity across studies. One RCT (49) of 6 months disulfiram versus naltrexone, together with group psycho-education, for relapse prevention in adolescents was identified (n=52 adolescents). The trial found that at the end of the study, relapse occurred at a mean of 93 days with disulfiram compared with 63 days for naltrexone, and 84.61% patients receiving disulfiram remained abstinent compared with 53.85% receiving naltrexone. One RCT (50) of disulfiram versus placebo, with and without adjunctive mailed letters therapy outlining alcohol harms, for the treatment of alcohol dependence was identified (n=109). The trial found no significant differences among treatments in terms of abstinent patients or study dropouts. However, patients with inactive ALDH2 significantly sustained abstinence with the use of disulfiram (p = 0.044). The trial also found that the ratio of abstinence was not related to the severity of alcohol dependence or the degree of alcohol craving. ### Naltrexone	and that gabapentin is being studied for its potential in relapse prevention. However, given concerns in the UK about its misuse and interactions with opioids, a statement about gabapentin use in treating alcohol misuse would be welcome. One expert stated that the use of pharmacotherapy for relapse prevention continues to be a challenge given associated costs, how services are commissioned, increased number of 3rd sector providers and a lack of prescribing in primary care. One expert identified that recommendation 1.3.6 needs updating as there are now several trials of baclofen and it is being used off-label quite widely. One expert highlighted there is little about recovery interventions in the guideline, and that there is a need to strengthen the use of drugs used to maintain abstinence (prevent relapse) to better support GP prescribing. One expert highlighted that there is a need to update information on naltrexone because it's UK marketing authorisation has been updated. An expert reported that pre- and post-detox the guideline should refer to use of vitamins, as this remains a contentious issue nationally, and clinical practice varies widely as a result of a lack of guidance. One expert said there is some new evidence that Acceptance and Commitment Therapy (ACT) has some impact in preventing alcohol relapse.	### Disulfiram Published evidence for disulfiram for relapse prevention showed some benefits compared with naltrexone and controls. However, the effects were uncertain due to heterogeneity across studies and results were more likely to be significant in open label studies than blinded RCTs. This new evidence generally suggests disulfiram may have some benefits in supporting abstinence and is unlikely to change recommendations which cover disulfiram use. **New evidence is unlikely to change guideline recommendations.** ### Naltrexone Published evidence suggests that naltrexone may be effective in reducing quantity of alcoholic drinks and time to relapse, but mixed effects on other outcomes such as drinking frequency. This evidence is in line with current guideline

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One RCT (51) of 6 monthly injections of extended release naltrexone versus placebo in prisoners with HIV and alcohol use disorder who were released early was identified (n=100 participants). The trial found no statistically significant difference in time-to-heavy-drinking day between treatment arms overall. In the subgroup of participants aged 20-29 years there was a longer time to first heavy drinking day with naltrexone compared to placebo (24.1 versus 9.5 days; p<0.001). There were no statistically significant differences for other individual drinking outcomes with naltrexone. One systematic review (52) of oral or injectable naltrexone compared to placebo with or without behavioural intervention in women with alcohol use disorder was identified (7 RCTs, 903 women). The review found a trend towards a reduced quantity of drinks (2 trials) and time to relapse (3 trials), but mixed effects on drinking frequency (4 trials). Acamprosate One systematic review and meta-analysis (53) of acamprosate versus placebo and naltrexone to prevent relapse in participants who are alcohol-dependent was identified (22 RCTs, n=5,236 participants). The review found that the risk of returning to any drinking at 6 months was significantly lower for acamprosate (RR=0.83, 95% CI 0.78 to 0.89), but there was no significant difference in risk of participants discontinuing treatment for any reason or due to adverse events for the acamprosate compared to placebo groups. For the naltrexone group, the risk of individuals returning to any drinking at 3 months was significantly reduced (RR=0.92, 95%		recommendations which state consider offering naltrexone. One expert highlighted that the marketing authorisation for naltrexone has changed. An editorial amendment to footnote 2 within the guideline will be made to update the UK marketing authorisation for naltrexone, see the section below on Editorial and factual corrections. New evidence is unlikely to change guideline recommendations. Acamprosate Published evidence suggests that acamprosate is effective in preventing relapse and maintaining abstinence. This evidence is in line with current guideline recommendations, which state consider offering acamprosate. New evidence is unlikely to change guideline recommendations.

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CI 0.86 to 1.00), as was the risk of individuals relapsing to heavy drinking at 3 months (RR=0.85, 95% CI 0.78 to 0.93). There was no significant difference between naltrexone and placebo for the risk of individuals discontinuing treatment for any reason but there was a significantly greater risk of participants discontinuing treatment due to adverse events for naltrexone compared to placebo (RR=1.72, 95% CI=1.10 to 2.70). One RCT (54) of 24 weeks acamprosate (1,998 mg/d orally) or placebo in maintaining complete abstinence in Japanese patients with alcohol dependence was identified (n=327 participants). The trial found that significantly more patients remained abstinent with acamprosate (47.2%) compared with 36% in the placebo group (p = 0.039). The difference in complete abstinence rates between with acamprosate compared with placebo was 11.3% (95% CI, 0.6%-21.9%). Baclofen One meta-analysis (55) of baclofen versus placebo on the maintenance of abstinence and the decrease of craving in alcohol-dependent patients was identified (number of trials and participants not reported in abstract). The review found that baclofen was associated with a significant increase of 179% in the percentage of abstinent patients at the end of the trials, compared with placebo. There was no significant effect of baclofen compared to placebo for secondary outcomes. One RCT (56) of individually titrated high dose baclofen (30-270mg/day) for the treatment of alcohol dependence was identified (n=93). The trial found that, compared with placebo,		Baclofen New published evidence from 1 meta-analysis and 2 trials suggest that baclofen improves alcohol abstinence compared with placebo, but 1 trial showed no difference compared with placebo. One trial showed that baclofen was superior to benfotiamine (a thiamine supplement). Currently baclofen is not covered in the guideline, and as such it's use is neither recommended nor precluded for moderate and severe alcohol dependence after successful withdrawal. This evidence does not indicate if baclofen is superior or equivalent to drugs already mentioned in this guideline section and therefore evidence is deemed insufficient to change current guideline recommendations. The evidence will be revisited at the next surveillance review to see if there is a more robust evidence base to warrant a statement on the use of baclofen after successful withdrawal. New evidence is unlikely to

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statistically significantly more baclofen patients maintained total abstinence (68.2% versus 23.8%, p=0.014), and had a higher cumulative abstinence duration (mean 67.8 versus 51.8 days, p=0.047). There were no serious drug-related adverse events during the trial. One RCT (57) of 30mg/day baclofen versus benfotiamine (a dietary thiamine supplement), plus brief motivational intervention, to promote abstinence in alcohol-dependent patients was identified (n=122 participants). The trial found that, compared with the benfotiamine group, participants receiving baclofen remained abstinent for significantly more days ($p < 0.05$), had a significantly lower percentage of heavy drinking days ($p = 0.001$), and had significantly lower craving and anxiety scores ($p = 0.001$). The time to first relapse was similar in both groups. One RCT (58) of 10 weeks high dose baclofen (up to 150mg per day), low dose baclofen (30mg per day), or placebo for alcohol dependence was identified (n=151 patients). The primary outcome measure was time to first relapse. The trial found that neither low nor high doses of baclofen were effective in the treatment of alcohol disorder and that adverse events were frequent, although usually mild and temporary. One RCT (59) of 12 weeks baclofen (30mg/day or 75mg/day) versus placebo in alcohol dependant patients with or without liver disease was identified (n=104). The trial found a significant effect of the composite groups of baclofen on time to lapse ($p<0.05$, Cohen's $d=0.56$) and relapse ($p<0.05$, $d=0.52$). There was a significant treatment effect of baclofen for percentage of days abstinent (placebo 43%, baclofen		change guideline recommendations. Topiramate New published evidence generally suggests that topiramate is effective in improving abstinence, drinking days and craving, compared with placebo, although1 trial found no benefit. There were no trials against an active comparator. Currently topiramate is not covered in the guideline, and as such it's use is neither recommended nor precluded for moderate and severe alcohol dependence after successful withdrawal. This evidence does not indicate if topiramate is superior or equivalent to drugs already mentioned in this guideline section and therefore evidence is deemed insufficient to change current guideline recommendations. The evidence will be revisited at the next surveillance review to see if there is a more robust evidence base to warrant a statement on the use of topiramate after successful withdrawal.

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30mg 69%, baclofen 75mg 65%; p<0.05). There was one overdose with 75mg baclofen. Topiramate One meta-analysis (60) of topiramate versus placebo for the treatment of alcohol use disorders was identified (7 RCTs; n=1,125 participants). Compared with placebo, topiramate was identified to improve abstinence (g=0.468, p<0.01), heavy drinking (g=0.406, p<0.01), and craving (g=0.312, p=0.07) outcomes. One RCT (61) of 100mg oral topiramate twice daily, versus placebo, plus rehabilitation twice weekly, for relapse prevention was identified (n=52 patients following detoxification). The trial found that after 6 weeks of treatment patients receiving topiramate had significantly fewer drinking days (p<0.05); less daily alcohol consumption (p<0.05); more days of treatment (p<0.05), compared with placebo. One RCT (62) of 100-300 mg/day topiramate for relapse prevention in alcohol dependant minimal withdrawal patients receiving a residential treatment program was identified (n=106 patients). The trial found that there was no significant difference between topiramate and placebo on the mean percentages of heavy drinking days, time to first day of heavy drinking, or other secondary outcomes. **2015 and 2013 surveillance** A total of 29 studies focused on pharmacological treatments for alcohol dependence or harmful alcohol use (see clinical area 6: pharmacological interventions in the previous		New evidence is unlikely to change guideline recommendations. Other issues One expert stated that there is a need to examine the use of adjunctive medication in preventing relapse. However, no new evidence was found to address this issue. A topic expert said that a statement on gabapentin misuse would be welcomed. This drug is not currently mentioned in the guideline, and no new evidence was identified for relapse prevention, although evidence was identified for withdrawal which is discussed above under recommendation 1.3.5. As the evidence on gabapentin is not deemed sufficient to update the guideline to include gabapentin as a treatment option, a statement on gabapentin misuse might cause confusion. Furthermore, a number of drugs used in alcohol withdrawal and relapse prevention have the potential to be addictive and thus misused.

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surveillance review). Note that the methods used for previous surveillance did not separate out studies according to recommendations but instead looked at clinical areas.		Recommendation 1.3.5.5 does already recommend that, for withdrawal in the community, people should not be given large quantities of medication to prevent overdose and diversion. One expert highlighted that there is little about recovery interventions in the guideline. However, no new evidence was identified that would address this issue. One expert said that the guideline should refer to use of vitamins pre- and post-detox, as clinical practice varies widely as a result of a lack of guidance. However, no new evidence was found to address this issue. One expert said there is new evidence that Acceptance and Commitment Therapy (ACT) has some impact in preventing alcohol relapse. However, no systematic reviews or RCTs of ACT were found that would address this issue. **2015 and 2013 surveillance** Previous surveillance also concluded

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		that evidence identified at those time points was unlikely to change guideline recommendations.
Recommendation section 1.3.7 Special considerations for children and young people who misuse alcohol		
2019 surveillance No evidence identified. Parent-based interventions One systematic review (63) of parent-based alcohol use interventions with adolescents (up to 18 years) (20 studies) found that the average treatment effect size across all drinking outcomes was statistically significant (g = -0.23; 95% CI 0.35 to -0.10). Parent-based interventions seemed to have larger mean effect sizes on adolescent drinking intention rather than binge drinking. The interventions targeting both alcohol-specific and general parenting strategies had larger average effect sizes than those targeting alcohol-specific parenting only. **2015 and 2013 surveillance** No relevant evidence identified.	Some topic experts suggested that there is an overlap between recommendations 6 and 7 in Alcohol-use disorders: prevention (NICE guideline PH24), and recommendations 1.3.7.1 to 1.3.7.4 in NICE guideline CG115. In particular, both guidelines cover initial assessment. However, views were mixed on whether the recommendations in the different guidelines are complementary or at odds, with some experts suggesting that the guidelines did not need amending as there was no overlap, whilst others felt an overlap was an issue that needed addressing.	**2019 surveillance** Parent-based intervention Published evidence indicates that parent-based interventions can be effective in reducing adolescent drinking, in particular drinking intention. The interventions targeting both alcohol-specific and general parenting strategies were most effective. This new evidence is in line with the guideline which recommends a range of interventions involving the parents, including multidimensional family therapy, functional family therapy and brief strategic family therapy. For details of parent strategies in relation to school-based interventions for alcohol misuse, see the scope of the NICE guideline in development on Alcohol: school-

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		based interventions. New evidence is unlikely to change guideline recommendations. Some topic experts also thought that there might be an overlap between recommendations 1.3.7.1 to 1.3.7.4 in CG115 and recommendations 6 and 7 in NICE guideline Alcohol-use disorders: prevention (NICE guideline PH24). However, other experts felt these recommendations were complementary as the focus of PH24 is prevention of alcohol misuse, whilst CG115 focusses on treatment of alcohol misuse. The guidelines have different treatment settings and as such recommendations 1.3.7.1 to 1.3.7.4 in CG115 are deemed complementary to PH24, and no change is deemed necessary in either guideline. Footnote 16 will be amended to the new standard wording for unlicensed medicines, see Editorial and factual

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		corrections below.
Recommendation section 1.3.8 Interventions for conditions comorbid with alcohol misuse		
2019 surveillance Depression One RCT (64) of 12 weeks naltrexone combined with citalopram versus 12 weeks naltrexone alone in patients with co-occurring alcohol dependence and depression was identified (n=138 depressed alcohol-dependent adults who were not required to be abstinent at the commencement of the trial). The trial found improvements in both mood and drinking related outcomes in both groups, with no significant differences between groups. Women were found to have a slightly better response in terms of percent days abstinent. One RCT (65) of 12 weeks citalopram versus placebo, combined with group psychotherapy, in depressed alcohol-dependent individuals was identified (n=265 participants). The trial found that citalopram was not superior to placebo in terms of treatment outcomes, and actually produced poorer results for some outcomes. The participants in the citalopram group had a higher number of heavy drinking days throughout the trial, and had smaller reductions in frequency and amount of alcohol consumption at 12 weeks. Neither treatment group had changes in depression severity. One systematic review (66) of combining CBT and motivational interviewing, versus usual care, to treat comorbid	With reference to recommendation 1.3.8.2, 1 expert suggested that the risk of suicide may be too high to wait for an appointment with a psychiatrist which can takes several weeks. They queried whether there should be a reference to people at high risk of suicide being advised to seek an immediate appointment with the GP or going to A&E if there is a likely to be a wait for an appointment with the psychiatrist. One expert highlighted that there is now evidence on vaping that could be referred to in recommendation 1.3.8.4. One expert said that intramuscular Pabrinex is now offered extensively in the community, the previous restriction to inpatient settings is now lifted, with reference to recommendation 1.3.8.5 which addresses Wernicke-Korsakoff syndrome. The expert also highlighted that addiction services do not have access to budgets to treat Wernicke-Korsakoff syndrome and suggested that recommendations covering Wernicke-Korsakoff syndrome belongs in a NICE dementia guideline. One expert said that there has been a growing recognition that alcohol use disorders are often part of a complex pattern of comorbidities and this could be	**2019 surveillance** Depression Published evidence suggests that citalopram alone was not effective in reducing alcohol consumption in alcohol dependant patients with depression. Naltrexone alone or combined with citalopram was found to improve mood and drinking outcomes in patients with co-occurring alcohol dependence and depression, but the study was small. Combined motivational interviewing and CBT was also found to improve depressive symptoms and alcohol consumption, with digital interventions having higher efficacy than face-to-face interventions. Evidence in studies of people who misuse alcohol and have comorbid depression is unlikely to change current guideline recommendations, which encourages treating alcohol

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alcohol use disorder and major depression was identified (12 studies, n=1,721 patients).The review found that, compared with usual care, CBT/motivational interviewing decreased alcohol consumption (g=0.17, p<0.001) and decrease in depressive symptoms (g=0.27, p<0.001). Subgroup analysis found that digital interventions had a higher effect size for depression than face-to-face interventions (g=0.73 versus g=0.23, p=0.030). Post-traumatic-stress disorder One systematic review (67) of pharmacotherapy and psychotherapy for co-occurring post-traumatic stress disorder (PTSD) and alcohol use disorder was identified (16 studies). The review found that pharmacological interventions were generally effective in reducing drinking outcomes; but only one study using sertraline found that it was superior to placebo in reducing PTSD symptoms. However, psychotherapies were not found to be superior to a comparative treatment in reducing drinking outcomes. The authors noted that the evidence base was limited. One RCT (68) of 12 once-weekly individual sessions of integrated CBT, versus CBT plus supportive counselling, for coexisting PTSD and alcohol use disorders was identified (n=62 participants). The trial found that both groups reduced PTSD symptoms but participants with integrated CBT who had received one or more sessions of exposure therapy had a two-fold greater rate of clinically significant change in clinician administered PTSD scale severity at follow-up than supportive counselling participants (OR 2.31, 95% CI 1.06 to 5.01).	given more detailed consideration here. One expert highlighted that they have seen the development of assertive outreach services, such as Alcohol Concerns “blue light” project and that consideration could be given to the effectiveness of this approach in patients with complex mental and physical health comorbidities.	misuse first, with referral to a psychiatrist if indicated, and use of condition specific guidelines. New evidence is unlikely to change guideline recommendations. Post-traumatic stress disorder Integrated CBT and CBT plus supportive counselling were shown to have beneficial effects in alcohol use disorders with PTSD. However, the study was limited by a small sample size. Naltrexone with or without supportive counselling or prolonged exposure therapy was shown to reduce drinking days and PTSD symptoms but the results diminished by 6 months. This evidence is unlikely to change current guideline recommendations which encourages treating alcohol misuse first, with referral to a psychiatrist if indicated, and use of condition specific guidelines. New evidence is unlikely to

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However, supportive counselling participants had larger reductions in alcohol consumption compared with integrated CBT. One RCT (69) of 100mg/day naltrexone plus prolonged exposure therapy (12 weekly 90-minute sessions followed by 6 biweekly sessions), prolonged exposure therapy plus placebo, supportive counselling plus 100 mg/day naltrexone, or supportive counselling plus placebo in participants with PTSD and comorbid alcohol dependence was identified (n=165 participants). Participants in all 4 treatment groups had large reductions in the percentage of days drinking, and reductions in PTSD symptoms, although the naltrexone groups had lower percentages of days drinking than those who received placebo (p=0.008). Participants in all 4 groups had increases in percentage of days drinking after 6 months but those in the prolonged exposure therapy plus naltrexone group had the smallest increases. One RCT (70) of seeking safety (a type of CBT) plus sertraline, versus seeking safety plus placebo, for co-occurring PTSD and alcohol use disorder was identified (n=69 participants). The trial found that both groups demonstrated significant improvement in PTSD symptoms. The sertraline intervention group had a significantly greater reduction in PTSD symptoms than the placebo group at end of treatment, which was sustained at 12-month follow-up. ### Anxiety One Cochrane review (71) of pharmacotherapies for comorbid alcohol use disorders and anxiety was identified (5 RCTs,		change guideline recommendations. ### Anxiety The published evidence from a Cochrane review for pharmacotherapies for comorbid alcohol use and anxiety was inconclusive. This evidence is unlikely to change current guideline recommendations which encourages treating alcohol misuse first, with referral to a psychiatrist if indicated, and use of condition specific guidelines. New evidence is unlikely to change guideline recommendations. ### Tobacco use The published evidence from a single RCT found varenicline may reduce smoking overall but heavy drinking was only reduced in men, rather than the overall trial population. Given this limited evidence and uncertainty regarding

2019 surveillance summary	Intelligence gathering	Impact statement
n=290 participants). The review found some effects of buspirone in reducing measures of anxiety, there was no effect of sertraline or paroxetine. However, paroxetine was identified to be equally effective as tricyclic antidepressants in reducing the severity of PTSD symptoms. There was no evidence that alcohol use was responsive to medication. Overall the authors concluded that the evidence base was inconclusive and further research is needed. ### Tobacco use One RCT (72) of varenicline 1mg twice daily plus medical management versus placebo for the treatment of co-occurring alcohol use disorder and smoking was identified (131 participants). The trial found that varenicline was associated with decreased heavy drinking among men and increased smoking abstinence in the overall sample. ### Drug misuse One Cochrane review (73) of psychosocial interventions for comorbid problem alcohol and illicit drug use (mainly opiates and stimulants) was identified (4 studies, n=594 participants). The review found no difference in effectiveness between different types of interventions to reduce alcohol consumption in concurrent problem alcohol and illicit drug users. The authors noted the low quality of the included studies and lack of evidence. **2015 and 2013 surveillance** No relevant evidence identified.		whether varenicline can also reduce drinking, no impact on the guideline recommendation is expected. A topic expert also highlighted that there is new evidence on vaping. Recommendation 1.3.8.4 will be updated to cross-refer to Stop smoking services and interventions NICE guideline NG92, which includes advice on e-cigarettes and has replaced NICE guideline PH1. New evidence is unlikely to change guideline recommendations. ### Drug misuse The published evidence from a Cochrane review for psychosocial interventions for comorbid alcohol use and drug misuse was inconclusive. This evidence is unlikely to change current guideline recommendations. New evidence is unlikely to change guideline

2019 surveillance summary	Intelligence gathering	Impact statement
		recommendations. Other issues Topic experts highlighted several issues. One expert said there is an issue around waiting times for psychiatrist appointments if someone is at risk of suicide. The committee did acknowledge that some people with depressive disorders will require immediate treatment (such as those at significant risk of suicide) and the recommendations were not meant to stand in the way of immediate treatment being provided in such a situation. Professionals are anticipated to safe guard individuals and take appropriate action if they are concerned about risk of suicide. Feedback was also received that there has been a growing recognition that alcohol use disorders are often part of a complex pattern of comorbidities and this could be given more detailed consideration. The committee was aware of this at the time of guideline development and in reviewing the

2019 surveillance summary	Intelligence gathering	Impact statement
		evidence for comorbid disorders related to recommendations within section 1.3.8, the committee did not find any treatment strategies or adjustments that should be made because of the comorbid condition and, in view of this, decided to refer to the relevant NICE guidelines. An expert said they have seen the development of assertive outreach services in relation to comorbid mental health conditions, but we did not find any RCT or systematic review level evidence that was available for consideration in this surveillance review. In relation to recommendation 1.3.8.5 which concerns Wernicke-Korsakoff syndrome, 1 expert stated that intramuscular Pabrinex [thiamine containing vitamin product] is now offered extensively in the community. The NICE guideline on alcohol-use disorders: diagnosis and management of physical complications (CG100) is being updated on thiamine, which recommendation 1.3.8.5 cross-refers to.

2019 surveillance summary	Intelligence gathering	Impact statement
		One expert highlighted that addiction services do not have access to budgets for treating Wernicke-Korsakoff syndrome. However, Wernicke-Korsakoff syndrome is such a significant complication of alcohol dependence that recommendations 1.3.8.5 and 1.3.8.6 are considered important to NICE guideline CG115, although it is acknowledged that they may be relevant to a range of service providers, as well as alcohol services. Footnote 17 will be amended to include Antisocial personality disorder: prevention and management (CG77). It will also be amended to say: 'Also see NICE guideline Coexisting severe mental illness and substance misuse: community health and social care services (NG58).' See Editorial and factual corrections below. **2015 and 2013 surveillance** No relevant evidence identified.

2019 surveillance summary	Intelligence gathering	Impact statement
Areas not covered in the guideline		
2019 surveillance Digital based interventions One Cochrane review (74) of digital interventions for reducing hazardous and harmful alcohol consumption in people living in the community (57 studies; n=34,390 participants) was found. Compared with no intervention, 15 studies (16 comparisons, 10,862 participants) found that participants who engaged with digital interventions had less than one drinking day per month fewer, 15 studies (9791 participants) found intervention participants drank one unit per occasion less, and 15 studies (3587 participants) showed about one binge drinking session less per month. Five studies (n=390 participants) compared digital and face-to-face interventions, and they found no difference in alcohol consumption. The authors noted that overall there is moderate-quality evidence that, compared with control, digital interventions may lower alcohol consumption, with an average reduction of up to 3 UK standard drinks per week. However, there was substantial heterogeneity and risk of publication and performance bias, which may mean the reduction was lower. One RCT (75) of computerised CBT plus treatment as usual, computerised CBT plus brief weekly clinical monitoring, or treatment as usual for alcohol use disorders was found (n=68 participants). The trial found significantly higher rates of	A topic expert highlighted that there is growing evidence of digital interventions for alcohol misuse. Experts provided several references which were incorporated in the 2019 surveillance summary as appropriate.	**2019 surveillance** Digital based interventions Published evidence suggests that digital based interventions may have a role in reducing alcohol consumption. However, the evidence included in the Cochrane review was heterogeneous and it is not clear if the interventions are specifically for harmful drinking, or at what stage of alcohol misuse (mild dependence, withdrawal, relapse prevention). Currently the guideline does not cover digital interventions. At present there is limited evidence on digital interventions for harmful alcohol use and no impact on the guideline is anticipated. This will be revisited at the next surveillance review to see if the evidence has progressed. New evidence is unlikely to change guideline

2019 surveillance summary	Intelligence gathering	Impact statement
treatment completion among participants assigned to one of the computerised CBT groups compared to treatment as usual (Wald = 6.86, p<0.01). All 3 treatment groups had significant reductions in alcohol use, with participants assigned to computerised CBT plus treatment as usual demonstrating greater increases in percentage of days abstinent compared to treatment as usual (p<0.01). The estimated costs of all self-reported alcohol-related services accessed by participants were considerably lower for those assigned to computerised CBT groups compared to treatment as usual. One RCT (76) of automated telephone continuing care following CBT for alcohol dependence, versus usual care, was found (n=158 participants). The trial found that drinking days per week increased over time for the usual care group but not for automated telephone continuing care, but there were no significant differences for other alcohol-related outcome measures between groups. The subset of participants abstinent at the end of CBT showed higher rates of continuous abstinence with telephone continuing care. One RCT (77) of a mobile phone intervention, versus a less intense mobile phone intervention, to increase adherence to naltrexone (50mg/day) for alcohol use disorders was found (n=76 participants). The intervention consisted of a medication event monitoring system and a prepaid smartphone, which received a daily text message querying medication side effects, alcohol use, and craving, as well as additional medication reminders and adherence assessment via text message. Those in the control group did not get the additional medication reminders and adherence assessment via text		recommendations **2015 and 2013 surveillance** There were no relevant studies identified.

2019 surveillance summary	Intelligence gathering	Impact statement
message. The trial found no difference in the primary outcome of proportion of participants with adequate adherence, or mean adherence at study midpoint (week 4) was 83% in the intervention group and 77% in the control condition. However, survival analysis found that the intervention group sustained adequate adherence significantly longer than those in the control group during the first month of treatment (19 days versus 3 days, p=0.04). But medication adherence did not predict drinking outcomes. One RCT (78) of optional videoconferencing-based treatment, versus usual care, for alcohol use disorders was found (n=71 participants). The trial found that compared with control, participants in the videoconferencing group had significantly lower drop outs at 6 months (6% versus 31%, p=0.008) and 1 year (25% versus 44%, p=0.02), and significantly more were still attending treatment after 1 year (p=0.03). One RCT (79) of a smartphone based application (A-CHESS) plus usual care, versus usual care, to support recovery from alcoholism after residential treatment was identified (n=349 participants). The A-CHESS group reported significantly fewer risky drinking days than the control group, with a mean of 1.39 vs 2.75 days (p=0.003) at 12 months. **2015 and 2013 surveillance** There were no relevant studies identified.		

Research recommendations

4.1: Is contingency management effective in reducing alcohol consumption in people who misuse alcohol compared with standard care?		
No relevant studies identified at any surveillance time point.	No expert feedback was provided.	No relevant evidence identified. This research recommendation will be considered again at the next surveillance point.
4.2: What methods are most effective for assessing and diagnosing the presence and severity of alcohol misuse in children and young people?		
No relevant studies identified at any surveillance time point.	A topic expert highlighted that Alcohol-use disorders: prevention (NICE guideline PH24) does not recommend using AUDIT in this age group whereas CG115 does.	No relevant evidence identified. This research recommendation will be considered again at the next surveillance point.
4.3: Is acupuncture effective in reducing alcohol consumption compared with usual care?		
2019 surveillance One meta-analysis (7) of acupuncture for alcohol use disorders was identified (7 studies, n=243 participants).The analysis found that compared with control, acupuncture had a stronger effect on reducing alcohol-related symptoms and behaviours (g = 0.67). The authors suggested that a larger cohort study is required to confirm results One systematic review (8) of acupuncture to reduce alcohol dependency was identified (15 RCTs, n=1,378 participants). The review found	No expert feedback was provided.	Published evidence suggests that acupuncture may have some potential to reduce alcohol craving, however the evidence base is limited, and more research is needed. This research recommendation will be considered again at the next surveillance point.

that, compared with control, acupuncture reduced alcohol craving (SMD -1.24, 95% CI -1.96 to -0.51); and alcohol withdrawal symptoms (SMD -0.50, 95% CI -0.83 to -0.17). Secondary analyses showed that acupuncture reduced craving compared with sham acupuncture; reduced craving compared with controls in RCTs conducted in Western countries; and reduced craving compared with controls in RCTs with only male participants. **2015 and 2013 surveillance** There were no relevant studies identified		
4.4: For which service users who are moderately and severely dependent on alcohol is an assertive community treatment model a clinically- and cost-effective intervention compared with standard care?		
No relevant studies identified at any surveillance time point.	No expert feedback was provided.	No relevant evidence identified. This research recommendation will be considered again at the next surveillance point.
4.5: For people with moderate and severe alcohol dependence who have significant comorbid problems, is an intensive residential rehabilitation programme clinically and cost-effective when compared with intensive community based care?		
No relevant studies identified at any surveillance time point.	No relevant studies identified at any surveillance time point.	No relevant studies identified at any surveillance time point.
4.6: For people with alcohol dependence, which medication is most likely to improve concordance and thereby promote abstinence and prevent relapse?		
No relevant studies identified at any surveillance time point.	No expert feedback was provided.	No relevant evidence identified. This research recommendation will be considered again at the next surveillance point.

Editorial and factual corrections

During surveillance we identified the following areas that require editorial amendment:

- Recommendation 1.3.3.2 will be amended to say: ‘Offer behavioural couples therapy for harmful drinkers and people with mild alcohol dependence who have a regular partner who is willing to participate in treatment, unless there are indicators that the person is currently experiencing, or is a current perpetrator of, domestic abuse.’
- Recommendation 1.3.3.2 will be amended to include the following cross-referral: ‘For advice on the use of nalmefene for alcohol dependence see Nalmefene for reducing alcohol consumption in people with alcohol dependence NICE technology appraisal guidance (TA325).’
- Recommendation 1.3.5.3 will be amended to add: ‘Prescribers should be aware of the following legislation and advise patients accordingly: Drugs and driving: blood concentration limits to be set for certain controlled drugs in a new legal offence 2014’.
- Recommendation 1.3.5.11 will be amended to add: ‘Prescribers should also see Addiction to benzodiazepines and codeine July 2011.
- Recommendation 1.3.8.4 will be amended with a cross reference to Stop smoking interventions and services NICE guideline NG92, which has since replaced PH1.
- Footnote 1 will be amended to the new standard wording for unlicensed medicines: ‘The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information.’
- Footnote 2 will be amended to reflect changes in licensing: ‘Oral naltrexone is licensed for alcohol dependence. See SPC https://www.medicines.org.uk/emc/product/6073/smpc Prescribers should follow the safety advice around opioids’.
- Footnote 5 will be amended to the new standard wording for unlicensed medicines: ‘The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information.’
- Footnote 7 will be amended to reflect changes in licensing: ‘Oral naltrexone is licensed for alcohol dependence. See SPC https://www.medicines.org.uk/emc/product/6073/smpc Prescribers should follow the safety advice around opioids’.

- Footnote 12 will be amended to the new standard wording for unlicensed medicines: ‘The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information. Prescribers should check the licensing status of benzodiazepines in this age group.’
- Footnote 13 will be amended to the new standard wording for unlicensed medicines: ‘The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information. Prescribers should check the licensing status of benzodiazepines in this age group.’
- Footnote 16 will be amended to the new standard wording for unlicensed medicines: ‘The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information.’
- Footnote 17 will be amended to include Antisocial personality disorder: prevention and management (CG77). It will also be amended to say: ‘Also see NICE guideline Coexisting severe mental illness and substance misuse: community health and social care services (NG58).’

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