NICE National Institute for Health and Care Excellence

Surveillance proposal consultation document

2018 surveillance of Drug misuse in over 16s: opioid detoxification (NICE guideline CG52)

Proposed surveillance decision

We propose to not update the guideline on drug misuse in over 16s: opioid detoxification.

During surveillance editorial or factual corrections were identified, which will be addressed through editorial amendments.

Reasons for the proposal

No new evidence was identified which suggested NICE guideline CG52 should be updated. Limited ongoing research of relevance was identified, comprising 2 small studies, but these are unlikely to publish in the near future.

Feedback provided from topic experts suggested some areas that need to be reviewed. These areas are: 1) pharmacological treatments 2) treatment of prescription opioid dependence and 3) Psychosocial interventions. Some additional evidence is relevant but does not directly impact on the recommendations and will be addressed through editorial changes. Other suggested changes were not supported by sufficient evidence.

For references of all evidence identified in surveillance, see appendix A below.

Overview of 2018 surveillance methods

NICE's surveillance team checked whether recommendations in drug misuse in over 16s: opioid detoxification (NICE guideline CG52) remain up to date.

The 2018 surveillance followed the static list review process, consisting of:

- Feedback from topic experts via a questionnaire.
- A search for new or updated Cochrane reviews and national policy.
- A search for ongoing research.
- Examining related NICE guidance and quality standards.
- Examining the NICE event tracker for relevant ongoing and published events.
- Consulting on the proposal with stakeholders (this document).

After consultation on the decision we will consider the comments received and make any necessary changes to the decision. We will then publish the final surveillance report containing the decision, the summary of the evidence used to reach the decision, and responses to comments received in consultation.

For further details about the process and the possible update decisions that are available, see ensuring that published guidelines are current and accurate in developing NICE guidelines: the manual.

See appendix A: summary of evidence from surveillance below for references of Cochrane reviews and additional studies considered.

Evidence considered in surveillance

Search and selection strategy

Previous surveillance reviews in 2011 and 2014 did not identify any studies that were considered to have an impact on recommendations.

This 2018 review identified 24 studies of relevance to the guideline. These included systematic reviews, randomised controlled trials and observational studies.

Eleven new Cochrane reviews (2-12), were considered to be consistent with current recommendations.

Topic experts identified a further 24 pieces of evidence, of which 13 were within the scope of the guideline (1, 13-24). These included Department of Health Clinical Guidelines on Drug Misuse and Dependence Update 2017 plus additional studies covering pharmacological interventions and the setting of detoxification. These studies were considered relevant to NICE guideline CG52 but they did not provide enough evidence to suggest a need for the recommendations to be updated.

See appendix A below for references of studies considered.

Ongoing research

We checked for relevant ongoing research; of the ongoing studies identified, 2 small studies were assessed as having potential relevance to the guideline; therefore we plan to check the publication status regularly, and evaluate the impact of the results on current recommendations when they become available. These studies are:

- ISRCTN13232859 Take home naloxone intervention in multicentre emergency settings
- ISRCTN09846981 Breaking free online health and justice outcomes in prisons

Intelligence gathered during surveillance

Views of topic experts

We sent questionnaires to 12 topic experts and received 7 responses; 4 indicated that the guideline should be updated and 3 indicated that it should not.

Topic experts were recruited to the NICE Centre for Guidelines Expert Advisers Panel to represent their specialty.

The main areas highlighted by topic experts for potential updating were:

- The need for inclusion of other components of psychosocial interventions. However, NICE guideline CG52 does cross refer to NICE's guideline on drug misuse in over 16s: psychosocial interventions, which covers approaches other than contingency management. Both guidelines are also covered in the NICE Pathway on drug misuse.
- Significant growth in dependence and misuse of over the counter and prescribed opioids. Detoxification of patients in this group was stated as needing a different approach, since the doses are often lower than those using illicit opioids and the socioeconomic circumstances and contexts in which the individuals in this group live is different to those of a typical illicit opioid user. However, the evidence cited did not meet surveillance study design criteria. Furthermore, since this area will be covered by the planned NICE guideline on safe prescribing and withdrawal management of prescribed drugs, evidence in this area is unlikely to impact on NICE guideline CG52.
- Publication of the updated Department of Health 'Orange Book':

  Clinical Guidelines on Drug Misuse and Dependence Update 2017 Independent Expert Working Group (2017)

  This document is considered by topic experts to be more comprehensive than NICE guideline CG52. It covers a wider use of opioid substitution therapy and management of clients, not just a focus on detoxification; therefore in clinical practice it has a tendency to be viewed as a preferred resource. A cross reference is proposed to the updated version of Orange Book to address the gaps in NICE guideline CG52.
- Lofexidine is temporarily unavailable due to changing manufacturer. Experts were not aware of the date of future availability or what its cost will be, but it is expected to become available again. Experts highlighted a lack of research and innovation in this area, and that the related research recommendation remains ongoing. There is unlikely to be any impact on recommendation 1.3.1.2 regarding lofexidine.
- The age of opiate users is rising with increasing comorbid physical health problems. An expert highlighted that this is not covered sufficiently by the guideline. No evidence was cited. Recommendation 1.2.2.3 advises that comorbid physical or mental health problems should be treated alongside opioid dependence in line with related NICE guidance, and is likely to remain valid. Cross reference to the Department of Health

'Orange Book' from NICE guideline CG52 will also ensure alignment with national advice relating to older people who are dependent on opioids.

Other sources of information

We considered all other correspondence received since the guideline was published.

- Safety of Methadone

The Medicines and Healthcare products Regulatory Agency (MHRA) highlighted drug-related mortality data from a retrospective administrative data study(19), published since the guideline, relating to the safety of methadone and buprenorphine. The MHRA did not take any regulatory action at the time, partly because of concerns about poor methodology of the study. In addition, there is already awareness of the risks of fatal poisoning with methadone and appropriate warnings are provided in in the product information. The MHRA suggested that the findings of the study may warrant a review of any relevant NICE guidance. The evidence was not considered in the surveillance review but was passed on to the NICE technology appraisals team for consideration in reviewing TA114 Methadone and buprenorphine for the management of opioid dependence. No further new evidence in this area has been highlighted by topic experts or stakeholders, and no impact is anticipated on NICE guideline CG52.

- Mechanism for assessing the benefits of the depot route for buprenorphine

A stakeholder suggested that the surveillance review of NICE guideline CG52 could assess the benefits of the depot route for buprenorphine (FluidCrystal depot injection (CAM2038) for opioid abuse/dependence). Subcutaneous injection of buprenorphine (RBP-6000) for opioid dependence, was also proposed for inclusion by a stakeholder. This has not been included in this surveillance review as the NICE medicines and technology appraisal teams are already reviewing evidence for these formulations of buprenorphine, with an estimated publication date of late January 2019.

Views of stakeholders

Stakeholders are consulted on all surveillance proposals except if the whole guideline will be updated and replaced. Because this surveillance proposal is to not update the guideline, we are consulting on the proposal.

See ensuring that published guidelines are current and accurate in developing NICE guidelines: the manual for more details on our consultation processes.

Equalities

No equalities issues were identified during the surveillance process.

Editorial amendments

During surveillance of the guideline we identified the following points in the guideline that should be amended.

The following amendment should be made to the hyperlink in the final paragraph of the introduction of the short version of the NICE guideline:

Existing hyperlink:

Drug misuse and dependence – guidelines on clinical management: update 2007

To be replaced by:

Drug misuse and dependence - UK guidelines on clinical management: update 2017

The link to the National Treatment Agency for Substance Misuse should be replaced with a link to the government health and social care Drug misuse and dependency topic page.

Overall decision

After considering all evidence and other intelligence and the impact on current recommendations, we propose that no update is necessary for NICE guideline CG52.

Appendix A: Summary of evidence from surveillance

2018 surveillance of CG52 Drug misuse in over 16s: opioid detoxification

The surveillance review followed the static list process, in which the search for published evidence covers Cochrane reviews and studies identified through intelligence gathering, without undertaking a full literature search.

Reference	Recommendation	Impact statement
Independent working group (2017) Clinical Guidelines on Drug Misuse and Dependence Update 2017: UK guidelines on clinical management. Department of Health	All recommendations	This document is considered by topic experts to be more comprehensive than NICE guideline CG52. It covers a wider use of opioid substitution therapy and management of clients, not just a focus on detoxification; therefore in clinical practice it has a tendency to be viewed as a preferred resource. A cross reference is proposed to the updated version of Orange Book to address the gaps in NICE guideline CG52.
Amato L, Davoli M, Minozzi S, Ferroni E, Ali R, Ferri M (2013) Methadone at tapered doses for the management of opioid withdrawal. Cochrane Database of Systematic Reviews (2)	1.3.2.1 and 1.3.2.2 Dosage and duration of detoxification	This evidence is relevant to recommendations 1.3.2.1 and 1.3.2.2 on dosage and duration of detoxification, but this area is covered by the following NICE technology appraisal guidance and therefore no immediate impact is anticipated on NICE guideline CG52: Methadone and buprenorphine for the management of opioid dependence (January 2007) TA114

Amato L, Minozzi S, Davoli M, Vecchi S (2011) Psychosocial and pharmacological treatments versus pharmacological treatments for opioid detoxification. Cochrane Database of Systematic Reviews (9)	Sections 1.3 Pharmacological interventions (1.3.3.1-1.3.5.1) and 1.5 Contingency management (1.5.1.1-1.5.2.2)	This evidence is relevant to sections 1.3 Pharmacological interventions and 1.5 Contingency management. The results showed that psychosocial treatments offered in addition to pharmacological detoxification treatments are effective in terms of completion of treatment, use of opiate, participants abstinent at follow-up and clinical attendance. This reinforces the recommendations in section 1.5 which advise the use of contingency management to support detoxification. No impact is anticipated.
Gowing L, Ali R, White JM (2017) Opioid antagonists with minimal sedation for opioid withdrawal. Cochrane Database of Systematic Reviews (5)	1.3.3 Ultra-rapid, rapid and accelerated detoxification (1.3.3.1-1.3.3.4)	This evidence is relevant to recommendations 1.3.3.1-1.3.3.4 particularly for accelerated detoxification, but this area is covered by the following NICE technology appraisal guidance and therefore no immediate impact is anticipated on NICE guideline CG52: Naltrexone for the management of opioid dependence (January 2007) TA115
Gowing L, Ali R, White JM, Mbewe D (2017) Buprenorphine for managing opioid withdrawal. Cochrane Database of Systematic Reviews (2)	1.3.1.1 Choice of medication	This evidence is relevant to recommendation 1.3.2.1 for choice of medication of detoxification, but this area is covered by the following NICE technology appraisal guidance and therefore no immediate impact is anticipated on NICE guideline CG52: Methadone and buprenorphine for the management of opioid dependence (January 2007) TA114

Gowing L, Farrell M, Ali R, White JM (2016) Alpha2-adrenergic agonists for the management of opioid withdrawal. Cochrane Database of Systematic Reviews (5)	1.3.1.2 and 1.3.1.3 Choice of medication	This evidence is relevant to recommendations 1.3.1.2 and 1.3.1.3 on clonidine and lofexidine. Results indicated that clonidine and lofexidine are more effective than placebo for the management of withdrawal from heroin or methadone. There was no significant difference in efficacy between treatment regimens based on clonidine or lofexidine and those based on reducing doses of methadone over a period of around 10 days, but methadone was associated with fewer adverse effects than clonidine, and lofexidine has a better safety profile than clonidine. No impact is anticipated as the results are consistent with recommendations 1.3.1.2 and 1.3.1.3.
Minozzi S, Amato L, Bellisario C, Davoli M (2014) Detoxification treatments for opiate dependent adolescents. Cochrane Database of Systematic Reviews (4)	1.3.1.1 choice of medication	This evidence is relevant to recommendation 1.3.1.1 for choice of medication of detoxification, but this area is covered by the following NICE technology appraisal guidance and therefore no immediate impact is anticipated on NICE guideline CG52: Methadone and buprenorphine for the management of opioid dependence (January 2007) TA114
Perry AE, Neilson M, Martyn-St JM, Glanville JM, Woodhouse R, Hewitt C (2015) Interventions for	1.4 Opioid detoxification in community, residential, inpatient and prison settings (1.4.1.1-1.4.1.4)	This evidence is relevant to section 1.4 Opioid detoxification in community, residential, inpatient and prison settings. The results did not provide

female drug-using offenders. Cochrane Database of Systematic Reviews (6)		strong enough evidence to draw definite conclusions on the effectiveness of interventions and as such are unlikely to impact on the guideline.
Rahimi-Movaghar A, Gholami J, Amato L, Hoseinie L, Yousefi-Nooraie R, Amin-Esmaeili M (2018) Pharmacological therapies for management of opium withdrawal. Cochrane Database of Systematic Reviews (6)	Section 1.3 Pharmacological interventions (1.3.3.1-1.3.5.1)	This evidence is relevant to recommendations 1.3.3.1-1.3.5.1 for choice of medication of detoxification, but this area is covered by the following NICE technology appraisal guidance and therefore no immediate impact is anticipated on NICE guideline CG52: Methadone and buprenorphine for the management of opioid dependence (January 2007) TA114
Saulle R, Vecchi S, Gowing L (2017) Supervised dosing with a long-acting opioid medication in the management of opioid dependence. Cochrane Database of Systematic Reviews (4)	1.3.2 Dosage and duration of detoxification (1.3.2.1-1.3.2.2)	This evidence is related to recommendations 1.3.2.1-1.3.2.2 on dosage and duration. The results showed uncertainty about the effects of supervised dosing compared with unsupervised medication due to the low and very low quality of the evidence. Therefore there is unlikely to be an impact on the guideline.
Terplan M, Ramanadhan S, Locke A, Longinaker N, Lui S (2015) Psychosocial interventions for pregnant women in outpatient illicit drug treatment programs compared to other interventions. Cochrane Database of Systematic Reviews (4)	1.2.2.2 special considerations and 1.5 Specific psychosocial interventions (1.5.1.1-1.5.2.2)	This evidence is related to recommendations 1.2.2.2 and section 1.5 on specific psychosocial interventions. Results showed no difference in treatment outcomes to address drug use in pregnant women with use of psychosocial interventions, when taken in the presence of other comprehensive care options. This is consistent with

		NICE guideline CG52 which doesn't make specific recommendations for psychosocial interventions for pregnant women.
Law FD, Diaper AM, Melichar JK, Coulton S, Nutt DJ, Myles JS (2017) Buprenorphine/naloxone versus methadone and lofexidine in community stabilisation and detoxification: A randomised controlled trial of low dose short-term opiate-dependent individuals. Journal of psychopharmacology (Oxford, England) 31(8):1046–55	Section 1.3 Pharmacological interventions (1.3.3.1-1.3.5.1)	This evidence is relevant to recommendations 1.3.3.1-1.3.5.1 for choice of medication of detoxification, but this area is covered by the following NICE technology appraisal guidance and therefore no immediate impact is anticipated on NICE guideline CG52: Methadone and buprenorphine for the management of opioid dependence (January 2007) TA114
Wright NMJ, Sheard L, Adams CE, Rushforth BJ, Harrison W, Bound N, et al. (2011) Comparison of methadone and buprenorphine for opiate detoxification (LEEDS trial): a randomised controlled trial. The British journal of general practice : the journal of the Royal College of General Practitioners 61(593):e772	Section 1.3 Pharmacological interventions (1.3.3.1-1.3.5.1)	This evidence is relevant to recommendations 1.3.3.1-1.3.5.1 for choice of medication of detoxification, but this area is covered by the following NICE technology appraisal guidance and therefore no immediate impact is anticipated on NICE guideline CG52: Methadone and buprenorphine for the management of opioid dependence (January 2007) TA114
Sanders NC, Mancino MJ, Gentry WB, Guise JB, Bickel WK, Thostenson J, et al. (2013) Randomized, placebo-controlled pilot trial of gabapentin during an outpatient, buprenorphine-assisted	Section 1.3 Pharmacological interventions (1.3.3.1-1.3.5.1) and 1.3.4.1 Adjunctive medications	This evidence is relevant to recommendations 1.3.3.1-1.3.5.1 for choice of medication of detoxification, and 1.3.4.1 for adjunctive medications. As a small pilot study, the findings would need to be substantiated by further

detoxification procedure. Experimental and clinical psychopharmacology 21(4):294–302		adequately powered and high quality studies of gabapentin adjunctive to buprenorphine versus placebo to establish any potential impact on the guideline.
Tanum L, Solli KK, Latif Z-E-H, Benth JŠ, Opheim A, Sharma-Haase K, et al. (2017) Effectiveness of Injectable Extended-Release Naltrexone vs Daily Buprenorphine-Naloxone for Opioid Dependence: A Randomized Clinical Noninferiority Trial. JAMA psychiatry 74(12):1197–205	1.3.3 Ultra-rapid, rapid and accelerated detoxification (1.3.3.1-1.3.3.4)	This evidence is relevant to recommendations 1.3.3.1-1.3.3.4 particularly for accelerated detoxification, but this area is covered by the following NICE technology appraisal guidance and therefore no immediate impact is anticipated on NICE guideline CG52: Naltrexone for the management of opioid dependence (January 2007) TA115
Gao L, Dimitropoulou P, Robertson JR, McTaggart S, Bennie M, Bird SM Risk-factors for methadone-specific deaths in Scotland's methadone-prescription clients between 2009 and 2013. Drug and alcohol dependence 167:214–23	1.3.1.1 Choice of medication and 1.2.2.3 special considerations	This evidence is relevant to recommendation 1.3.1.1 for suitability of methadone and recommendation 1.2.2.3 on special considerations for people who are opioid dependent and have comorbid health problems. Cross reference to the updated Department of Health 'Orange Book' from NICE guideline CG52 will ensure alignment with national advice relating to older people who are dependent on opioids.
Pierce M, Millar T, Robertson JR, Bird SM (2018) Ageing opioid users' increased risk of methadone-specific death in the UK. The International journal on drug policy 55:121–7	1.3.1.1 Choice of medication and 1.2.2.3 special considerations	This evidence is relevant to recommendation 1.3.1.1 for suitability of methadone and recommendation 1.2.2.3 on special considerations for people who are opioid dependent and have comorbid health problems. Cross reference to the updated Department of Health 'Orange Book' from NICE guideline CG52 will ensure alignment with

		national advice relating to older people who are dependent on opioids.
Marteau D, McDonald R, Patel K (2015) The relative risk of fatal poisoning by methadone or buprenorphine within the wider population of England and Wales. BMJ open 5(5):e007629	1.3.1.1 Choice of medication	This evidence is relevant to recommendation 1.3.1.1 for choice of medication of detoxification, but this area is covered by the following NICE technology appraisal guidance and therefore no immediate impact is anticipated on NICE guideline CG52: Methadone and buprenorphine for the management of opioid dependence (January 2007) TA114
Evans E, Li L, Min J, Huang D, Urada D, Liu L, et al. (2015) Mortality among individuals accessing pharmacological treatment for opioid dependence in California, 2006-10. Addiction (Abingdon, England) 110(6):996–1005	1.3.1.1 Choice of medication	This evidence is relevant to recommendation 1.3.1.1 for choice of medication of detoxification, but this area is covered by the following NICE technology appraisal guidance and therefore no immediate impact is anticipated on NICE guideline CG52: Methadone and buprenorphine for the management of opioid dependence (January 2007) TA114
Sigmon SC, Dunn KE, Saulsgiver K, Patrick ME, Badger GJ, Heil SH, et al. (2013) A randomized, double-blind evaluation of buprenorphine taper duration in primary prescription opioid abusers. JAMA psychiatry 70(12):1347–54	1.3.2.1 and 1.3.2.2 Dosage and duration of detoxification	This evidence is relevant to recommendations 1.3.2.1 and 1.3.2.2 on dosage and duration of detoxification, but this area is covered by the following NICE technology appraisal guidance and therefore no immediate impact is anticipated on NICE guideline CG52:

		Methadone and buprenorphine for the management of opioid dependence (January 2007) TA114
Sullivan M, Bisaga A, Pavlicova M, Choi CJ, Mishlen K, Carpenter KM, et al. Long-Acting Injectable Naltrexone Induction: A Randomized Trial of Outpatient Opioid Detoxification With Naltrexone Versus Buprenorphine. The American journal of psychiatry 174(5):459–67	1.3.3 Ultra-rapid, rapid and accelerated detoxification (1.3.3.1-1.3.3.4)	This evidence is relevant to recommendations 1.3.3.1-1.3.3.4 particularly for accelerated detoxification, but this area is covered by the following NICE technology appraisal guidance and therefore no immediate impact is anticipated on NICE guideline CG52: Naltrexone for the management of opioid dependence (January 2007) TA115
Day E, Strang J (2011) Outpatient versus inpatient opioid detoxification: a randomized controlled trial. Journal of substance abuse treatment 40(1):56–66	1.4.1 The choice of setting (1.4.1.1-1.4.1.4)	This evidence is relevant to section 1.4 Opioid detoxification in community, residential, inpatient and prison settings. The results did not provide strong enough evidence to draw definite conclusions on the effectiveness of interventions and as such are unlikely to impact on the guideline.
Krupitsky E, Nunes E V, Ling W, Illeperuma A, Gastfriend DR, Silverman BL (2011) Injectable extended-release naltrexone for opioid dependence: a double-blind, placebo-controlled, multicentre randomised trial. Lancet (London, England) 377(9776):1506–13	1.3.3 Ultra-rapid, rapid and accelerated detoxification (1.3.3.1-1.3.3.4)	This evidence is relevant to recommendations 1.3.3.1-1.3.3.4 particularly for accelerated detoxification, but this area is covered by the following NICE technology appraisal guidance and therefore no immediate impact is anticipated on NICE guideline CG52: Naltrexone for the management of opioid dependence (January 2007) TA115

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10. Rahimi-Movaghar A, Gholami J, Amato L, Hoseinie L, Yousefi-Nooraie R, Amin-Esmaeili M (2018) Pharmacological therapies for management of opium withdrawal. Cochrane Database of Systematic Reviews (6)

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13. Law FD, Diaper AM, Melichar JK, Coulton S, Nutt DJ, Myles JS (2017) Buprenorphine/naloxone versus methadone and lofexidine in community stabilisation and detoxification: A randomised controlled trial of low dose short-term opiate-dependent individuals. Journal of psychopharmacology (Oxford, England) 31(8):1046–55

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