NICE National Institute for Health and Care Excellence

Medicines associated with dependence or withdrawal symptoms: safe prescribing and withdrawal management for adults

Consultation on draft scope
Stakeholder comments table

29/08/19 to 26/09/19

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All-Party Parliamentary Group for Prescribed Drug Dependence	**N/A**		Please also include antipsychotics within the scope of the review. It has been decided not include antipsychotics in the forthcoming NICE review. This clearly contradicts the preference expressed by all groups attending the last stakeholder meeting, where the consensus appeared to be, during feedback, that antipsychotics should be in scope. In addition to the support in the room, we would like to highlight the following research, as we believe it clearly justifies including antipsychotics within the review.	Thank you for your comment. The views of stakeholders at the workshop, and those submitted (including the information you provide in your associated comments) have been carefully considered, however antipsychotics have not been included within the scope of the guideline. These medicines are prescribed for very specific defined conditions by specialists and guidance on their safe prescribing, monitoring and withdrawal is included within the NICE guideline for psychosis and schizophrenia in adults CG178.
All-Party Parliamentary Group for Prescribed Drug Dependence	**N/A**		When an antipsychotic, and the dopamine blockade, are removed, or reduced, the brain is effectively overwhelmed with dopamine, partly because of the abnormal drug-induced sensitivity and number of dopamine receptor cells. This process is likely to apply to the other neurochemical systems that antipsychotics influence. These effects may result in a withdrawal psychosis, which is often mistaken for a return of the 'schizophrenia' that the drugs were intended to treat. This in turn often leads to a reinstatement of the drugs that have, paradoxically, caused the neurotransmitter abnormalities.( ) The first cases of dopamine 'Supersensitivity Psychosis' [SP] were reported 40 years ago. ( ) A 2006 reviewer of the available evidence concluded: There is evidence to suggest that the process of discontinuation of some antipsychotic drugs may precipitate the new onset or relapse of psychotic symptoms. Whereas psychotic	Thank you for your comment and for this information, please see our response to your initial comment on this topic above.

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			deterioration following withdrawal of antipsychotic drugs has traditionally been taken as evidence of the chronicity of the underlying condition, this evidence suggests that some recurrent episodes of psychosis may be iatrogenic [caused by medical treatment]. Clinicians may therefore want to re-evaluate the benefits of long-term treatment in some patients. ( ) There have been two recent, comprehensive reviews of the research literature on what now tends to be called 'antipsychotic-induced Dopamine Supersensitivity Psychosis' or 'Supersensitivity Psychosis' [SP] for short. ( ) ( ) One of the reviewers has designed criteria for two SP-based withdrawal syndromes, differentiated primarily by duration. 20-25% of people withdrawing from a specific antipsychotic, clozapine, experienced Supersensitivity Psychosis (SP) or, as the reviewer prefers to call it 'Rapid Onset Psychosis'. ( ) An early study estimated that between 22% and 43% of 224 outpatients diagnosed with schizophrenia had SP. Two recent studies of atypical antipsychotics have reported SP incidence rates of 65%18 and 72%. ( ) All three studies, however, included cases that occurred due to tolerance (see section 1.8) while the person was still taking the antipsychotics. In the latter study, 42% of the	

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			cases were identified as 'Rebound	
All-Party Parliamentary Group for Prescribed Drug Dependence	**N/A**		Psychosis', which means that overall 30% of the sample, not all of whom had tried to stop their antipsychotics, had experienced withdrawal-induced psychosis. Another study found SP in 26% of people while changing from one antipsychotic to another. ( ) This is, however, a very difficult issue to research because of the fluctuating nature of the underlying psychosis. In a recent international survey of people taking antipsychotics, 'new or increased psychosis' was the second most frequently reported 'other side effect' (after 'akathisia/restlessness'). Thirteen reported new reactions and six reported the exacerbation of previous reactions. It was not known, however, how many of the instances of new or exacerbated psychosis reactions followed withdrawal. ( ) Tardive Dyskinesia Tardive Dyskinesia (TD), is a disabling, often irreversible, antipsychotic-induced neurological disorder involving uncontrollable movements of the face, tongue, arms and legs. It is also associated with cognitive impairment. It is likely, but not proven, to be the result of the over activity of the dopamine system caused by changes such as increased receptor numbers and sensitivity caused by antipsychotics. Some researchers consider TD to be either a component or predictor of SP. ( ) It is considered here as a withdrawal effect because the reactions of TD are often masked by	Thank you for your comment and for this information, please see our response to your initial comment on this topic above.

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			the withdrawal of antipsychotics. When the drugs are stopped, it is thought that dopamine activity increases due to the increased sensitivity of the dopamine system produced by long-term antipsychotic treatment. Increased dopamine activity can produce abnormal movements. Thus, the overt physical reactions (but not necessarily the cognitive reactions) of TD are often either seen for the first time, or are exacerbated, after discontinuation, reduction or switching of antipsychotics. People over 50 are three to five times more likely than younger people to develop TD. ( ) Withdrawing slowly, with support A recent study exploring the personal accounts of individuals discontinuing antipsychotic drugs identified that 'weaving a safety net to safeguard wellbeing' was a pivotal process in drug reduction. This involved taking precautionary steps	
All-Party Parliamentary Group for Prescribed Drug Dependence	N/A		prior to reducing drugs taken to establish interpersonal alliances with family, friends, support groups and mental health professionals that can be activated should problems arise. ( ) In another study, 55% of 105 people who attempted discontinuation of Aps described successfully stopping all APs for varying lengths of time, half reported no current use, and half described having some form of professional, family, friend, and/or service user or peer support for their attempt. Having support was associated with less relapse. Furthermore, withdrawing gradually across more than one month	Thank you for your comment and for this information, please see our response to your initial comment on this topic above.

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			was positively associated with successful withdrawal. ( ) There will, of course, be large variability in how long people need to take to withdraw.	
All-Party Parliamentary Group for Prescribed Drug Dependence	N/A	Additional evidence re point1	According to this widely accepted definition, antidepressants are dependency forming. They clearly elicit withdrawal reactions in around 50% of users, (i) many of such reactions being severe and long-lasting, as the recent position statement on antidepressants by the RCPsych also acknowledges. (ii) While the incidence of antidepressant withdrawal alone qualifies these drugs to be classed as dependency forming, it is also clear that they generate symptoms of tolerance for many users (see section on tolerance below). **World Health Organisation's Definition:** According to the WHO's definition, antidepressants are dependency forming: "Dependence or physical dependence is also used in the psychopharmacological context in a still narrower	Thank you for your comment and for this information. The intention is that this guideline will also look at the withdrawal symptoms associated with antidepressants that you refer to here, and will make recommendations as appropriate.

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			sense, referring solely to the development of withdrawal symptoms on cessation of drug use." (iii) **DSM and ICD Definitions**: *DSM-III's definition* According to DSM-III's definition of dependence, antidepressants can be classed as dependency-forming as the DSM-III criteria for substance dependence 'requires only evidence of tolerance *or* withdrawal.' (iv) *DSM-IV's Definition* With respect to DSM-IV, the definition of dependence becomes more restrictive, specifying that a person must experience 3 or more of the following 7 symptoms to meet criteria for dependence: (v)	
All-Party Parliamentary Group for Prescribed Drug Dependence	N/A	Additional evidence re point1	1. Tolerance, as defined by either of the following: (a) a need for markedly increased amounts of the substance to achieve intoxication or desired effect, or (b) markedly diminished effect with continued use of the same amount of the substance 2. Withdrawal, as manifested by either of the following: (a) the	Thank you for your comment and for this information.

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			characteristic withdrawal syndrome for the substance, or (b) the same (or closely related) substance is taken to relieve or avoid withdrawal symptoms. 3. The substance is often taken in larger amounts or over a longer period than intended. 4. There is a persistent desire or unsuccessful efforts to cut down or control substance use. 5. A great deal of time is spent in activities necessary to obtain the substance, use the substance, or recover from its effects 6. Important social, occupational, or recreational activities are given up or reduced because of substance use 7. The substance use is continued despite knowledge of having a persistent physical or psychological problem that is likely to have been caused or exacerbated by the substance (e.g., current cocaine use despite recognition of cocaine-induced depression, continued drinking despite recognition that an ulcer was made worse by alcohol consumption). (vi) As many AD users clearly meet criteria 2 (they generate withdrawal), 6 (i.e. they cause sexual dysfunction in a large proportion of users), arguably 1 (up to 25% of users experience diminished effects) and arguably 4 (as criterion 4 does not exempt	

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			psychological compulsion), antidepressants may be considered dependency forming according to DSM-IV criteria.	
All-Party Parliamentary Group for Prescribed Drug Dependence	N/A	Additional evidence re point1	*DSM-5's Definition* The same can be said for the most recent criteria for substance dependence, in DSM-5. Two criteria out of the following 10 must be met to warrant the specification of mild dependency: 1. Taking the substance in larger amounts and for longer than intended 2. Wanting to cut down or quit but not being able to do it 3. Spending a lot of time obtaining the substance 4. Craving or a strong desire to use the substance 5. Repeatedly unable to carry out major obligations at work, school, or home due to substance use 6. Continued use despite persistent or recurring social or interpersonal problems caused or made worse by substance use 7. Stopping or reducing important social, occupational, or recreational activities due to substance use 8. Recurrent use of the substance in physically hazardous situations 9. Consistent use of the substance despite acknowledgment of persistent or recurrent physical or psychological difficulties from using the substance	Thank you for your comment and for this information.

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			10. Tolerance as defined by either a need for markedly increased amounts to achieve intoxication or desired effect or markedly diminished effect with continued use of the same amount. 11. Withdrawal manifesting as either characteristic syndrome or the substance is used to avoid withdrawal. As many antidepressants users would meet criteria 11 (the generate withdrawal), 7 (they cause sexual dysfunction in a large proportion of users), arguably 10 (up to 25% of users experience diminished effects), and arguably 4 (as criterion 4 does not exempt psychological compulsion) antidepressants could again be classed as dependency forming. *ICD-10's Definition* ICD-10 claims that a 'definite diagnosis of dependence should usually be made only if three or more of the following have been present together at some time during the previous year'. (vii)	
All-Party Parliamentary Group for Prescribed Drug Dependence	N/A	Additional evidence re point1	1. A strong desire or sense of compulsion to take the substance; 2. Difficulties in controlling substance-taking behaviour in terms of its onset, termination, or levels of use; 3. A physiological withdrawal state when substance use has ceased or have been reduced, as evidenced by: the	Thank you for your comment and for this information. As stated above, please note we have edited the scope to acknowledge that there are varying views on this issue.

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			characteristic withdrawal syndrome for the substance; or use of the same (or closely related) substance with the intention of relieving or avoiding withdrawal symptoms; 4. Evidence of tolerance, such that increased doses of the psychoactive substance are required in order to achieve effects originally produced by lower doses (clear examples of this are found in alcohol- and opiate-dependent individuals who may take daily doses sufficient to incapacitate or kill non-tolerant users); 5. Progressive neglect of alternative pleasures or interests because of psychoactive substance use, increased amount of time necessary to obtain or take the substance or to recover from its effects; 6. Persisting with substance use despite clear evidence of overtly harmful consequences, such as harm to the liver through excessive drinking, depressive mood states consequent to periods of heavy substance use, or drug-related impairment of cognitive functioning; efforts should be made to determine that the user was actually, or could be expected to be, aware of the nature and extent of the harm. As many AD users would meet criteria 3 (withdrawal), 5 (i.e. they	

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			cause sexual dysfunction in a large proportion of users) arguably 4 (up to 25% of users experience diminished effects) and arguably 1 (as criterion 1 does not exempt psychological compulsion), ADs should be classed as dependency forming. According to the above, antidepressants are dependency forming from the standpoint of the definitions offered by PHE and World Health Organisation, DSM-III and, arguably, DSM IV; DSM 5 and ICD 10.	
All-Party Parliamentary Group for Prescribed Drug Dependence	N/A	Additional evidence re point1	**Tolerance** Loss of response to antidepressant treatment over time has attracted different names. The popular term in the user community is AD 'poop out' - an experience referred to in the medical literature as 'tachyphylaxis'. (viii) Another more generic term (deployed by both users and medical professionals) is AD 'tolerance' - a term implying physiological acclimatisation to either the concentration or the actions of the drug over time. There is controversy about whether loss of AD response indicates 'tolerance' or other factors such as worsening depression, the	Thank you for your comment and for this information.

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			effects of a new medicine being instated or a new medical condition arising. (ix) In short, the true incidence of AD tolerance in contrast to other explanations for loss of AD response is not known. (x) Therefore questions as to what causes loss of AD response still remain. One immediate implication is that all statements declaring that 'ADs do not produce tolerance' are *not evidence-based*, and therefore should not be issued. What follows is an overview of evidence indicating that denying AD tolerance is counter to what the evidence allows us to say, and that, additionally, AD tolerance is a viable explanation for much loss of AD response. Firstly, it is clear that loss of AD response is widespread. This was first recognised in people receiving monoamine oxidase inhibitors (MAOIs) where those who lost their initial response to an MAOI responded poorly to subsequent treatment and displayed greater depressive severity after relapse than before the new treatment was initiated. (xi, xii) More recently, Frank et al. reported that 18% of people, initially responding to imipramine in a three-year treatment maintenance study, relapsed during that time period. (xiii) Loss of AD response was also later recognised in people receiving SSRIs, after these drugs were introduced in the United States in the late 1980s. (xiv, xv, xvi) From a meta-analysis of studies published prior to 1993, Byrne and Rothschild calculated the rate of	

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			AD 'tachyphylaxis' or 'tolerance' to be between 9% and 33% of people treated for depression. (xvii)	
All-Party Parliamentary Group for Prescribed Drug Dependence	N/A	Additional evidence re point1	More recently, a 20-year follow up study of 103 MDD patients (i.e. National Institute of Mental Health Collaborative Depressive Study) reported that the rate of AD tachyphylaxis/tolerance was 25%. (xviii) While these rates are high, other studies put them higher, such as a 2011 survey indicating that during treatment of dysthymia in the SSRI group, tolerance/tachyphylaxis was observed in 41.9% of cases. (xix) In short, the rate of AD tolerance is estimated to be approximately 25% of people treated for depression (rising to 41.9% in SSRI treatment of dysthymia). However, as causes other than tolerance may help account for diminishing AD effects, (xx) we must ask if it is possible to disentangle AD tolerance from other explanations for loss of AD response. There is some evidence that this is possible. Firstly, Fava and Offidani state that the phenomena associated with loss of AD response in mood disorder bear strong resemblances with progressive loss of response observed with both antidepressant and antianxiety drugs in anxiety disorders. (xxi) Furthermore, a	Thank you for your comment and for this information.

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			recent meta-analysis of maintenance treatment studies, which showed that people taking antidepressant medications run the risk of relapse progressively increasing from 23% within 1 year to 34% in 2 years and 45% in 3 years, (xxii) provides another strong indicator of tolerance. Furthermore, as Targum notes, (xxiii) several reports and reviews have suggested that AD tachyphylaxis/tolerance may result from increasing drug sensitisation, which causes a pharmacokinetic and/or pharmacodynamic tolerance of the concentration or actions of the drug (xxiv, xxv). 'In this regard', states Targum, 'prolonged antidepressant treatment may induce sensitization changes not unlike the tolerance/dependence issues induced by chronic benzodiazepine exposure'. (xxvi)[1] [1] Data supporting this hypothesis have been found in the following study: after a 12 week open-label treatment with duloxetine (60 mg/day) responders (52%) were randomized to the same dose of duloxetine or to placebo. 21% of subjects in the duloxetine condition relapsed within 26 weeks, and, among these, 38% do not respond to a dose increase (120 mg/day) in the successive 12 weeks (Fava et al., 2006).	

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All-Party Parliamentary Group for Prescribed Drug Dependence	N/A	Additional evidence re point1	Given the aforementioned studies, it is probable that ADs generate tolerance in a proportion of users and therefore satisfy another criterion for being dependency-forming medications. **Many Patients Experience Antidepressants as Addictive.** In addition to fulfilling key criteria for dependency, and eliciting tolerance in many users, there is now growing evidence that high percentages of AD users, when asked directly, report 'that they experience the drugs to be "addictive"'. For instance, a 2014 review of studies of 'Patient-centred perspectives on antidepressant use' found that 'the most frequently mentioned reason for a negative opinion of antidepressants is that they may be addictive'. (xxvii) For example, of 192 people in the Netherlands who had been taking ADs for six months, 30% reported that antidepressants are 'addictive', with 30% also stating that 'a person who starts taking antidepressants can never stop using them'. (xxviii) Of 493 antidepressant users in Denmark, 57% agreed with 'When you have taken antidepressants over a long period of time it is difficult to stop taking them' and 56% agreed with 'Your body can become addicted to antidepressants'. (xxix) Among 87 users in Scotland, 74% reported that 'antidepressants are addictive'. (xxx) The largest direct-to-consumer survey of AD users to date found	Thank you for your comment and for this information. As stated above, please note we have edited the scope to acknowledge that there are varying views on this issue.

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			that of 1,521 users in New Zealand who answered a question about addiction 27% reported that they did experience addiction, 23% of whom described the addiction as 'severe'. (xxxi) In the international survey 37% reported being addicted and 36% of those described the addiction as 'severe'. (xxxii) In both the New Zealand and international studies self-reported addiction was strongly correlated with length of time talking the ADs. Furthermore, when the Nordic Cochrane Centre reviewed 45 papers on benzodiazepine addiction and 31 papers on SSRI so-called 'discontinuation syndrome' its concluded: 'Withdrawal reactions to SSRIs appear to be similar to those for benzodiazepines; referring to these reactions as part of a dependence syndrome in the case of benzodiazepines, but not selective serotonin re-uptake inhibitors, does not seem rational'. (xxxiii)	
All-Party Parliamentary Group for Prescribed Drug Dependence	N/A	Additional evidence re point1	The Nordic Cochrane Centre thus concluded that SSRI antidepressants should be considered drugs of dependence like benzodiazepines, given the similarity of the withdrawal reactions. This conclusion is consistent with the World Health Organisation's view of dependence: "When the person needs to take repeated doses of the drug to avoid bad feelings caused by withdrawal reactions, the person is dependent on the drug". (xxxiv)	Thank you for your comment and for this information. Antidepressants have been included within the scope of the guideline so that reviews of the evidence you refer to can be undertaken, including the evidence for the withdrawal symptoms experienced and the support required. Recommendations on these issues will be made as appropriate. Our definition given in the

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			Furthermore, withdrawal charities in the UK are now encountering widespread AD withdrawal in clients. For instance, the Bristol and District Tranquiliser Project reports that more people are now requesting support for AD than for benzodiazepine withdrawal. Ian Singleton of BDTP says: ''Antidepressants seem to cause just as many problems as benzodiazepines... many of the symptoms are the same as benzodiazepine withdrawal... in many cases we have found that the symptoms of antidepressant withdrawal go on for even longer than benzodiazepine withdrawal." (xxxv) ***For all these reasons, it is inconsistent with the evidence base, with accepted definitions of dependency and with much patient experience to define antidepressants as non-dependency forming medicines. We urge you therefore to change your position.***	scope now acknowledges that there are varying views on whether or not antidepressants should be considered as dependence forming.
All-Party Parliamentary Group for Prescribed Drug Dependence	N/A	Supporting evidence re point 10, include antipsychotics in scope.	**The Evidence** The most recent survey found that of 105 people who tried to come off antipsychotics, 65 (62%) experienced unwanted withdrawal effects 'across the full-range of physical, emotional, cognitive, and functional domains'.(xxxvi) As is the case for other central nervous system drugs, such as	Thank you for your comment and for this information. We agree antipsychotics are associated with withdrawal symptoms, however please see our response to your initial comment on this topic above.

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			benzodiazepines and alcohol, the brain can develop a tolerance to antipsychotics. (xxxvii) Antipsychotics, however, are clearly not addictive, if one's definition of addiction involves a craving for the drugs. Despite not being addictive in the strict sense of that word, there are two types of withdrawal syndrome that can make it very difficult to reduce, or come off, these drugs. The first type has much in common with the withdrawal effects of the other central nervous system drugs such as benzodiazepines. The second type is somewhat more specific to psychosis and/or antipsychotics. **Classic withdrawal reactions** A recent review found that antipsychotics share a range of 'classic symptoms of withdrawal' with all central nervous system drugs. (xxxviii) These reactions, which usually emerge within four days of stopping, include: Nausea, Sleep disturbances, anxiety, headache, aggression, tremor, decreased concentration agitation, irritability and depression. The reviewers suggest that these reactions usually last 'up to six weeks' and 'may last more than six weeks and become a post-withdrawal disorder' but the review provides no data to support these suggestions. There are, in fact, relatively few studies of the frequency or duration of classic withdrawal reactions following discontinuation of	

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			antipsychotics. The largest direct-to-user, international survey, of 832 people prescribed/taking antipsychotic medication, found that 65% reported withdrawal effects when trying to stop or reduce, and that half of those people (51%) described those withdrawal effects as 'severe'. (xxxix) It has since been established that the brain's attempted compensation after antipsychotic use also includes an increase in the number, and sensitivity, of dopamine receptor cells, a process that is not unique to antipsychotics.	
All-Party Parliamentary Group for Prescribed Drug Dependence	002	General	Please revise the decision to classify antidepressants (ADs) as non-dependency forming. As to whether antidepressants are considered dependency-forming medications significantly depends on how dependency is defined. According to DSM and ICD criteria, the World Health Organisation's & Public Health England's definition of dependency, it is more reasonable and consistent with the evidence-base to class antidepressants as dependency-forming medications than not to class them as such. As well as causing withdrawal in a large proportion of users, available evidence undermines the claim that ADs do not generate tolerance (tolerance being a key criteria for dependence). Rather, ADs may generate tolerance in a proportion of users (up to 25%), while, additionally, about a third of users report being 'addicted' to ADs, according to their own definition of	Thank you for your comment. We accept that there are differing views on whether antidepressants are dependence forming, and equally that there are a number of definitions for dependency. We have edited the introductory text in the scope to acknowledge this debate.

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			that concept. For all these reasons, and as will be elaborated below, it is inconsistent with the evidence base, with accepted definitions of dependency and with much patient experience to define antidepressants as non-dependency forming medicines. **Definitions of Dependency:** The recent review by Public Health England of prescribed drugs associated dependence and withdrawal, defined dependency in the following way: [As] an adaptation to repeated exposure to some drugs and medicines usually characterised by *tolerance* and *withdrawal*, though *tolerance* may not occur with some. Dependence is an inevitable (and often acceptable) consequence of long-term use of some medicines and is distinguished here from *addiction (p.8)*	
Arden and Greater East Midlands Commissioning Support Unit	004	017	A key emerging issue when managing safe withdrawal is applying the principles of shared decision making with patients who choose not to start withdrawal or continue withdrawal to safer limits. For example, in prescription opioid dependence it is common to find people >120mg Morphine equivalent per day and the goal is to reduce to at least below that, if not further for safety reasons.	Thank you for your comment. Shared decision making is a principle that applies across all NICE guidelines. Shared decision making is covered by published NICE guidelines CG138 (Patient experience in adult NHS services), and by the scope of NICE guideline GID-NG10120 (Shared Decision Making; in development). The guideline will cross-refer to these NICE guidelines

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			However some patients may refuse to reduce or to engage in specialist service help, especially non-drug interventions, in spite of the dangers to their health, leaving the prescriber in the difficult position of being required to continue unsafe prescribing. On some occasions the prescriber has been the subject of a complaint from the patient because they requested that the patient reduce to safer levels. Whilst every effort is made to engage with the patient and help them on their journey, frequently the healthcare professional cannot truly engage in shared decision making with the patient in such situations. It would be useful to know the evidence of shared decision making in this group of drugs and/or this group of patients, where the aim is to avoid patient harm by continued prescribing. The principles we promote in the NHS appear to be largely based on evidence of shared decision making in secondary care and primary care diabetes treatments. For the guideline to be effective, in implementing the recommendations for safe prescribing, health care professionals would find it helpful to have guidance on the principles of shared decision making with opiates and other addictive substances, for people prescribed them as prescription medicines for eg chronic non-cancer pain.	where appropriate.

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Arden and Greater East Midlands Commissioning Support Unit	004	017	It would also be useful to have clear evidence based NHS recommendations on drug reduction, drug substitution and dose tapering regimes, as there are a variety of tools, guidelines and opinions available and it is sometimes difficult to identify a single, evidence based treatment reduction plan. Staff training is needed also, as many pain management centres are based in Trusts when they could be operated in primary care under specialist supervision. It would be useful to know the recommended model for such a system eg with MDT with health and social care staff. Also which staff type is best suited to help manage and support the patient during withdrawal eg GP/specialist nurse/clinical pharmacist Also when to refer to specialists for advice and/or management	Thank you for your comment. Evidence reviews will be undertaken on all of the review questions set out in the scope. The specific interventions or topics included will be agreed by the committee when discussing the protocols for these reviews. The staffing structure for any recommended service is beyond the scope of this guideline however, as is when to refer as this will be dependent on the particular situation and experience of the healthcare professional at the time.
Arden and Greater East Midlands Commissioning Support Unit	004	019	There needs to be greater public awareness about the dangers of eg long term opiates for chronic non-cancer pain, and the benefits of going through a reduction programme Also information to prepare people that as this prescribing is potentially harmful it will be reduced and stopped at some time i.e. it will not be long term	Thank you for your comment. Information required by patients is included within the scope of this guideline.
Arden and	004	022	There are increasing instances where people have purchased	Thank you for your comment. We acknowledge that

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Greater East Midlands Commissioning Support Unit			these medicines through the internet/black market and have become addicted eg dihydrocodeine/codeine. They present to the GP for help and under this exclusion these patients would not be included in recommendations for care	some of these medicines are available to purchase online, and if people present to their GP with related issues, this guidance would be relevant. The scope has been edited to clarify this.
Arden and Greater East Midlands Commissioning Support Unit	007	010	It would be useful to have information on nondrug intervention 'prescribing' strategies. There is variable provision in availability of support services, specialist physiotherapy, CBT, counselling, pain management therapies across the NHS. This group of patients do not feel able to attend the usual drug addiction services and so generally lack access to such support services. In particular, if available, it would be useful to have evidence based recommendations on what non-drug interventions work best for this group of people, to inform commissioners in delivering support. Many patients reduce their opiates and have to learn to live with the pain in order to reduce the risk of side effects. This reduces their quality of life and can lead to depression and poorer mobility. People withdrawing from these treatments need evidence based strategies and support systems for managing their pain and/or insomnia.	Thank you for your comment. The efficacy of the non-pharmacological alternatives for different conditions is covered within the condition specific guidelines which will be cross-referred to by this guideline. Non-pharmacological interventions for the prevention of dependency or to aid withdrawal will be covered in questions 1.2 and 3.1 of this guideline.
Arden and Greater East Midlands Commissionin	007	028	Although desirable, in its basic sense patient satisfaction is not a likely outcome in bringing someone off opioids/benzodiazepines because they will likely continue to suffer pain, and in travelling the journey of withdrawal experience difficulties, especially when	Thank you for your comment. The list of outcomes in the scope are intended as suggested outcomes that will be in the majority of the questions covered. These will be discussed by the guideline committee during

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g Support Unit			suffering from long term pain. Non drug strategies such as CBT/specialist physio input would likely improve patient satisfaction	protocol development. We acknowledge your comment about patient satisfaction and will consider this when refining the outcomes and interpreting the evidence.
Arden and Greater East Midlands Commissionin g Support Unit	007	030	Healthcare resource use needs to include the realistic number of appointments required in primary care in managing withdrawal, especially when managed through MDT which may include several staff with different skills.	Thank you for your comment. The guideline will recommend best approaches for managing withdrawal, and recommendations for monitoring. The resource use required will be taken into account when drafting the recommendations and detailed in the guideline.
Arden and Greater East Midlands Commissionin g Support Unit	008	029	Possibly also include morbidity as well as mortality. Many of these patients have other chronic conditions, or may suffer side effects that reduce health eg CV effects of opioids	Thank you for your comment. The list of outcomes in the scope are intended as suggested outcomes that will be in the majority of the questions covered. These will be discussed by the guideline committee during protocol development and additional outcomes will be added as required. We will consider your comment at this stage, however this guideline will not focus on the adverse effects of the specific drugs or their efficacy as this is covered in the condition specific guidelines.
Bangor University	General	General	There is a need to clarify terminology. At 2:4-6, "dependence" is defined in terms of the physiological effects of tolerance and withdrawal. However, throughout the document, dependence and	Thank you for your comment. We now state clearly in the introduction to the scope that the term dependence is characterised by tolerance and

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			withdrawal are presented as alternatives – "dependence OR withdrawal". What distinguishes "dependence" from "withdrawal"? If it is addiction behaviours – drug-seeking behaviour, dis-controlled and harmful use of a drug, etc. – this should be made clear. However, there are patients, particularly users of opioids for chronic pain, who experience negative consequences of their prescribed drugs without showing addictive behaviours or significant withdrawal effects. This is true of some patients who are adversely affected by benzodiazepines and gabapentinoids.	withdrawal. The terms dependence and withdrawal have been presented as alternatives to encompass medicines which may result in withdrawal symptoms but may not be associated with physiological dependence. We agree that in some cases the symptoms may overlap.
Bangor University	General	General	Management of these conditions differs according to how many features of addiction behaviour are present, which can become a problem with drugs which are not normally regarded as drugs of potential misuse. There is a functional spectrum; there are differences between the management of people who have features in common with addiction and those who have none of these features.	Thank you for your comment. The guideline will cover the management of people across this spectrum. During protocol development, the guideline committee will consider subgroups in which management may differ. We will take your comment into account at this stage.
Bangor University	General	General	Our organisation includes clinicians with experience of pain management; opioid prescribing in primary care; medicines management of psychoactive drugs; and medicines management of dependency-forming drugs in prisons. Current clinical activities include a secondary care clinic for patients prescribed high doses of opioids and other drugs for chronic pain, managing dysfunctional opioid use in primary care, detecting, reducing, and monitoring prescribed dependency forming	Thank you for your comment and for this information.

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			medication use in men admitted to prison; and assessing and treating patients in secondary care pain management service. Current research activities include evaluation of an intervention to reduce high doses of opioids prescribed for chronic pain; evaluation of a programme to eliminate unsafe and medically inappropriate prescribing of dependency-forming medication in prison, investigations of the effects of long-term, high-dose use of prescribed opioids; investigations of high-dose opioid prescribing in primary care; and work towards the development of interventions to control and reduce opioid prescribing in primary care.	
Bangor University	General	General	We recognise that there must be clear limits to the drugs and drug regimes that fall within the scope of this guidelines group. Nonetheless, with respect to the main drugs of concern – benzodiazepines, gabapentinoids, antidepressants, opioids and z-drugs – we believe that it is important that they should not be understood in narrow terms of addiction or withdrawal and that there are a range of other problems which it should be understood are associated with continued use of these drugs over long periods of time.	Thank you for your comment. The adverse events associated with these medicines are detailed in the summary of product characteristics and the BNF and are beyond the remit of this guideline. Other NICE condition-specific guidance may provide more details about their long term use for each condition.
Bangor University	001	020	It is controversial to suggest that antidepressants do not cause dependence. Addiction behaviours with these drugs are uncommon but some would argue that withdrawal and dependence are the same thing.	Thank you for your comment. We are aware that there are differing views on this topic, as well as on the definition of dependence. The scope has been edited to reflect this.
Bangor	001	027	A sentence should be added here which states that some of these	Thank you for your comment. The introduction is

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University			drugs can make the symptoms for which they were originally prescribed worse. This is true for both analgesic and anxiolytic drugs.	intended to briefly set out the background and reason the guideline is being developed. We have not included statements that may be covered within the review topics so as not to pre-judge the evidence and therefore have not added the sentence you suggest.
Bangor University	002	001 - 003	The idea should not be propagated that the reason why people continue to use these drugs is to prevent withdrawal effects; this is not even true of many people who are drug addicts. Many patients have no idea that these drugs have withdrawal effects because they do not withdraw them, they just continue to be prescribed them. Fear of being overwhelmed by the symptoms for which the drugs were originally prescribed is a significant factor in very many cases.	Thank you for your comment. We have taken note of your comment and made this section of the scope clearer.
Bangor University	002	012	Whilst **overall** rates of opioid prescribing appear to be levelling out or falling, numbers of prescriptions for high doses and "strong" opioids (i.e. those most likely to give rise to harm) are continuing to increase.	Thank you for your comment and for this information.
Bangor University	002	016 - 018	There is also an association between levels of social deprivation and the prescribing of these drugs.	Thank you for your comment. We agree, however have not included this as believe it is implied by the text as written.
Bangor University	002	022 - 025	Patients are also reluctant to attend addiction services because they do not see their problems as being ones of dependence; they see them as being related to the control of another problem (e.g. pain, anxiety) and their drug related difficulties as a consequence of	Thank you for your comment and for this information. Question 4.1 on information required by people prescribed these medications, and question 1.2 for optimum prescribing strategies will review evidence

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			attempts to control that other problem. Whilst there are patients for whom the prescription of these drugs is a route into addiction and who display a need for the intervention of addiction services, there are groups of patients who do not display addiction behaviours but who need to reduce or stop their medication use because it is ineffective or because its negative effects, particularly in terms of functioning and quality of life, clearly outweigh any benefits. The needs of these patients cannot be met by addiction services and are currently neglected. There are very successful prescribed medication withdrawal services, including one in North Wales which we work with, which are often more acceptable to patients than addiction services and which need to be supported.	related to the issues you raise.
Bangor University	003	022 - 024	This should not be just about "bad drugs". There is a wide range of psychoactive drugs which can lead to withdrawal symptoms and associated with addiction behaviours, e.g. steroids, anti-psychotics, L-dopa.	Thank you for your comment. We accept that there are other medicines that are associated with withdrawal symptoms but are outside of the scope of this guideline. Parkinson's disease treatment and antipsychotics have not been included as these medicines are prescribed for specific defined conditions by specialists and guidance on their safe prescribing, monitoring and withdrawal is included within the NICE guideline for Parkinson's disease NG71 and Psychosis and schizophrenia CG178.
Bangor	003	025 - 026	We suggest as a group which requires specific consideration is	Thank you for your comment. It is not thought that

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University			people prescribed long-term, high-dose opioids for chronic pain who show no addiction behaviours; this includes many elderly people.	guidance should differ in terms of the general principles in this group. Therefore they are not listed as a group needing specific consideration. The guideline committee will specify subgroups which need to be considered for each individual question during development of the protocols.
Bangor University	004	002	It is suggested that patients living with cancer and prescribed opioids for pain may similar experiences to other chronic pain patients – decreasing effectiveness, increasing doses and consequent negative effects on functioning and quality of life.	Thank you for your comment. Chronic non-cancer pain is included within the scope, however use of strong opioids for cancer pain is covered in other NICE guidelines and is beyond the scope of this guideline.
Bangor University	004	017 - 018	There are issues around enforced withdrawal when there are safety considerations with patients who do not wish to reduce or withdraw their prescribed drugs, both in prisons and in the community. We hope the guidance will consider the role, if any, of forced withdrawal in the community.	Thank you for your comment. The methods of withdrawal that will be included within the review will be agreed by the committee when the review protocols are refined from the draft questions.
Bangor University	004	024 - 026	It is our view that it is not possible to safely prescribe or effectively manage the withdrawal of opioids prescribed for chronic pain without taking into account that they induce hyperalgesia.	Thank you for your comment. The committee will take your comment into account when considering the evidence for these reviews.
Bangor University	007	010	Whilst there is a well-established role for tapering with benzodiazepines and antidepressants, this is not the case with opioids. Whilst tapering is widely recommended as a strategy for reducing or stopping opioid drugs, there is little systematic evaluation of its use with these drugs. Experience suggests it is a	Thank you for your comment. We agree that we may find it difficult to find evidence in some areas. Where evidence is lacking, the guideline committee will consider making recommendations based on consensus or recommendations fo future research.

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			procedure which is difficult to carry out, particularly with patients on high doses.	
Brighton & Hove CCG – Medicines Management Team	Scope Comment Form Question	Scope Comment Form Question	**Q. Are there any cost saving interventions or examples of innovative approaches that should be considered for inclusion in this guideline?** A. Please find below an example of how primary care reduced high dose opioids. The project was carried out in 2017/18 & had great results. The work has been published on SPS website (WHO Good Practice Repository) and referenced in the Pharmaceutical Journal and the BMJ. I will be also presenting on the project at the SPS conference in London on 23rd October – including patient experience video clips. Please feel free to contact me for any further information. https://www.sps.nhs.uk/repositories/review-of-high-dose-opioids-in-chronic-non-malignant-pain/ WHO Good Practice Repository Review of high dose opioids in chronic non-malignant pain Brighton & Hove CCG · Published 12th April 2019, updated 15th April 2019 Summary of the example	Thank you for your comment and this information. The publications you mention reporting this evidence will be considered by the committee within the relevant review question if they meet the protocol inclusion criteria.

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			• The Faculty of Pain Medicine (Royal College of Anaesthetists) states that the morphine dose for which harms outweigh benefits is 120mg oral morphine or equivalent/24 hours. Above this dose the risk of harm and mortality increases substantially but there is no increased benefit. • Figures from NHS Digital show that the number of prescriptions for opioids has risen dramatically in recent years in England, from 3 million in 1991 to 7.5 million in 2001 and 24 million in 2016. • Patients often confuse sedation/euphoria that is caused by opioids with pain relief Long term use leads to tolerance to the analgesic effects and can increase pain sensitivity (e.g. hyperalgesia and allodynia). • Long term risks of opioids include immunosuppression, hypogonadism and adrenal insufficiency in both men and women, and possible effect on cognitive function. • The MMT Medicines Management Team in Brighton & Hove CCG led baseline reviews to identify patients prescribed in GP practice high dose opioids for chronic non-malignant pain. • These findings were passed to individual GP surgeries to review the identified patients that require intervention with an aim to reduce morphine equivalent dose to <120mg/day. Why we think it's important	

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			The Faculty of Pain Medicine (Royal College of Anaesthetists) states that the morphine dose for which harms outweigh benefits is 120mg oral morphine or equivalent/24hours. Above this dose the risk of harm and mortality increases substantially but there is no increased benefit. We identified 227 patients in Brighton & Hove on high dose opioids (>120mg morphine per day or equiv.) for chronic non-malignant pain (the actual figure is likely to be higher). These patients were escalated to this dose historically due to the belief that chronic pain should follow the WHO analgesic ladder. We now know that opioids largely do not help for chronic pain and have substantial long term risks, as well as reducing patients quality of life (function, mobility, alertness, mood). Reducing these patients doses in primary care has been 'time consuming yet highly rewarding' and has led to a 'very apparent improvement in quality of life of patients' who 'feel more energised, engaged and happier'. Aims and objectives of the work To identify patients in primary care in Brighton & Hove with non-malignant chronic pain who were on >120mg morphine per day (or equivalent) and subsequently for GP surgeries to review with an aim to reduce the high dose opioids patients were taking. Therefore reducing the potential and real harm they are experiencing from	

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			these medications. Methodology This was a domain for the Prescribing Incentive Scheme in Brighton & Hove 2017/18 and as such GP surgeries who completed it (to a satisfactory standard) were awarded money that they could spend on specified items for their patients (see PIS 17/18 document for more details). Medicines Management Team (technicians) granted access to GP surgery records in order to run a search to identify patients on >120mg morphine/day (or equivalent) for chronic non-malignant pain. Technicians calculated each identified patients total daily dose as an equivalence to morphine. The patient list and morphine equivalent dose were passed onto the practice for their review. GP surgery reviewed identified patients that require intervention and if appropriate reduced the dose to <120mg morphine (or equivalent). Wherever possible the clinical pharmacists conducted a pain medication review and agreement of a reduction plan, with option for the community pharmacist to receive a copy of their reduction plan to enable extra support and advice. Regular follow up calls or appointments were provided. The Brighton & Hove CCG Chronic Non-Malignant Pain Prescribing Guidelines were used to support the pain management review in addition to national documents such as Royal College of Anaesthetists: Faculty of Pain	

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			Medicine (Tapering & Stopping of opioids) listed below. 27 out of 36 practices participated during the PIS year, with more surgeries now undertaking the work. Results were measured via the use of a 'summary and data collection form' (see PIS 17/18 document for more details. Key findings • 27/36 practices in Brighton & Hove took part. • 227 patients identified on high dose opioids (>120mg morphine equiv./day). • 123 patients (54%) originally had their dose increased to >120mg morphine equiv./day by primary care; 44 patients [19%] were increased by a specialist; 60 patients [26%] unknown origin). • 210 patients (93%) were reviewed. • 119 patients (52%) were undergoing a dose reduction. • 70 patients (31%) had their dose decreased to <120mg morphine equiv./day • 59 patients (26%) declined a dose reduction at this point. • Remaining 49 patients were not reviewed or commenced on dosage reduction due to awaiting a review by a specialist or GP surgery pharmacist. Overall GP Feedback themes: • 'Opioid reduction is a time consuming yet highly rewarding intervention.'	

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			• 'The results are rewarding and well worth the efforts.' • 'As the topic has been highlighted it has brought a higher level of opiate prescribing awareness amongst our prescribers.' • 'Pharmacist and GPs worked together as a team and discussed patients at the weekly clinical meetings.' 'Patients were contacted by the practice pharmacist – and introduced as the expert in opiates who was able to build a trust relationship with the patient'. • 'I have observed a very apparent improvement in quality of life of patients who have achieved reduction. Feedback from these patients is that they feel more energised, engaged and happier.' • 'Small and gradual reductions have made very little impact on frequency and intensity of pain experienced.' • 'This audit has encouraged us to look further into alternative ways to manage chronic pain and to ensure patients have the correct support to help them engage with their health needs. Documents Strong Opioid Reduction Summary and Data Collection Form Attachments • For WHO Strong Opioid Reduction - Summary and Data Collection Form (https://www.sps.nhs.uk/wp-content/uploads/2019/04/For-WHO-Strong-Opioid-Reduction-	

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			Summary-and-Data-Collection-Form.docx) Links • Brighton & Hove CCG Prescribing Incentive Scheme 2017/18 (domain 5, with submission form in the appendix) (https://www.gp.brightonandhoveccg.nhs.uk/prescribing-quality-improvement-scheme-and-action-plan) • Brighton & Hove CCG Chronic Non-Malignant Pain Prescribing Guidelines (https://www.gp.brightonandhoveccg.nhs.uk/files/bh-ccg-non-malignant-chronic-pain-prescribing-guidelines-finalpdf) • Article in Brighton & Hove City Scripts Dec 17 on Tips for reducing Opioid Usage (https://mailchi.mp/e42efd13f11f/cityscriptsoct-dec17) Background National guidance, data and publications • Royal College of Anaesthetists: Faculty of Pain Medicine (Tapering & Stopping of opioids) • There are various online self-help and information services tailored specifically to chronic pain patients, such as the Pain Toolkit; the Faculty of Pain Management; Living with Chronic pain; and the British Pain Society, Live Well with Pain. • Opioids Aware: A resource for patients and healthcare	

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			professionals to support prescribing of opioid medicines for pain – (produced by UK healthcare professionals and policymakers, funded by Public Health England and hosted by the Faculty of Pain Medicine, Royal College of Anaesthetists) publish a range of information available for both GPs and patients. • BMJ article: Pain specialists call for annual review of long term opioid use	
British Association for Counselling and Psychotherapy	General	General	On behalf of the British Association for Counselling and Psychotherapy (BACP), I would like to add our support to the submission from the All-Party Parliamentary Group for Prescribed Drug Dependence to the consultation on guidance for Safe prescribing and withdrawal management of prescribed drugs associated with dependence and withdrawal. The British Association for Counselling and Psychotherapy (BACP) is the leading professional body for counselling and psychotherapy in the UK, with over 49,000 members. Our members work across the professional disciplines in the fields of counselling and psychotherapy and are based in a range of settings, including the NHS and the third sector, providing therapy to clients with a wide range of presenting issues. Our register of therapists has been independently assessed and	Thank you for your comment. We have responded to the All-Party Parliamentary Group for Prescribed Drug Dependence comments above.

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			approved by the Professional Standards Authority for Health and Social Care (PSA). All BACP members are also bound by the Ethical Framework for the Counselling Professions and within this, the Professional Conduct Procedure.	
British Geriatrics Society	003	015	Particular relevance for people with cognitive impairment acknowledged. Perhaps this should specify dementia specifically. In addition, older people with frailty are more likely to be prescribed medications, resulting in polypharmacy. This, along with physiological changes, leads to a higher risk of adverse drug reactions and a lower probability of drug efficacy. Coupled to this, atypical presentations, such as falls and delirium, lead to a greater risk that adverse effects, including withdrawal reactions, will be missed. Please consider giving extra attention to people with dementia, frailty and those who reside in care homes.	Thank you for your comment. The equality impact assessment details groups that have been raised as important to consider within the guideline, which includes people with cognitive impairment. People with dementia haven't been listed specifically as we believe this should be broader and include any form of cognitive impairment. The section on which groups his guidance will be particularly relevant has been removed from the scope as it was agreed that it should equally apply to all.
British HIV Association	General	General	Does the scope need to include something about when to seek more specialist advice? i.e. where would the GP refer the more complex patients? Are there specialists in managing addiction specifically to prescribed drugs?	Thank you for your comment. This has not been included within the scope of this guideline as the decision to refer will vary depending on the experience of the GP and the specific circumstances, and therefore will be determined by clinical judgement.
British HIV Association	004	001	Do we need to signpost to the HIV Liverpool drug interactions website and highlight it as a useful resource re safe prescribing in people living with HIV	Thank you for your comment. This will be considered if relevant during the development of the guideline.
British HIV Association	004	019	What services can patients access themselves to assist with withdrawal of prescribed drugs? Signposting would be important.	Thank you for your comment. This guidance will intend to recommend the best approaches and

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			Would this be part of the information for patients? (section 3.34). I am not aware of any support services that exist for prescribed drug dependence (current services available seem to be for illegal drug use and those patients addicted to prescribed drugs may not identify/engage with services that deal with illegal drug dependence).	interventions, however how the services themselves are commissioned and delivered is beyond the remit of the guideline.
British HIV Association	007	009	It would be most helpful to include the details of specific recommended regimes for each drug to assist with safe withdrawal. I presume this would be included here.	Thank you for your comment. Draft review question 3.1 is intended to look at a range of withdrawal methods for all of the medicines in the scope of the guideline.
British Orthopaedic Association	006	020 - 026	We are concerned at the number of patients being started on opioid medication for osteoarthritis and chronic deteriorating conditions. We are particularly concerned at the number of CCGs whose commissioning policy includes 'optimal opioid dose' for at least 6 months as part of a pain management strategy. Clearly the biggest risk factor for opioid dependence is taking the first dose. We would urge this committee not to actively avoid this important issue. Arthritis is a chronic relapsing condition with acute flare ups and exacerbations of pain. These exacerbations can be so painful that there may be a role for extremely short term use of opioids, but not for repeat prescriptions. Opioids have no ceiling dose and no proven efficacy in treatment of chronic pain, with psychobiosocial activity based treatments being much more effective. Large joint	Thank you for your comment. The efficacy of the drugs for different conditions and indications for (or against) treatment are covered within the condition specific guidelines which will be cross-referred to by this guideline.

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			arthritis has a surgical option which is efficacious, cost effective and shown by NICE methodology to be exceptionally good value healthcare. It is well known that patients admitted for joint replacement surgery who are taking opioids have a longer length of stay, more complications - particularly respiratory, gastrointestinal and urinary tract infections - and a large percentage are still taking opioids a year later. This is after the painful stimulus has been removed/treated. The BOA and NICE cannot condone policies where opioids are being recommended for use in such open ended indications. **In terms of the scope, we would urge the committee to define conditions or situations where opioids are clearly inappropriate, particularly repeat prescriptions. Given that the project title includes 'safe prescribing', there should be coverage of current areas of unsafe prescribing so that these can be highlighted and addressed.**	
Change, Grow, Live	General	General	The mention of special groups (eg older adults in group 1) is important. However, the principles are the same. On review, I was surprised that experts did not seek to categorise conditions according to the likelihood of symptomatology placing someone more at risk of developing a dependence syndrome (eg depressive illness with prominent anxiety features; painful condition without specific treatable pathology identified).	Thank you for your comment. Draft review question 1.1 is intended to look at risk factors for dependence, including those mentioned in your comment. Furthermore, when protocols are developed, the guideline committee will consider whether there are specific subgroups in which management may differ.

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Change, Grow, Live	002	004	The statement "Dependence is characterised by.." is not in accord with ICD-10, which defines the dependence syndrome as being "a cluster of physiological, behavioural, and cognitive phenomena." Neuroadaptation is not necessary. Much of the intractable nature of the dependence syndrome is linked to cognitive and behavioural aspects.	Thank you for your comment. We are aware that there are a number of differing definitions of dependence. The scope introduction is intended to briefly set out the background to the topic and therefore a concise definition has been provided here. Specific details of the population and condition included in the reviews will be agreed by the committee and included in the protocols.
Change, Grow, Live	003	011	Thus, the focus is overly narrow and risks missing generalisable the cognitive and behavioural issues associated with the dependence syndrome.	Thank you for your comment.
Change, Grow, Live	005	016	Depression in adults: recognition and management (2009) NICE guideline CG90 does not mention the risk of dependence. There is a body of evidence that supports the primary mood improving effects of TCAs, SSRIs and SNRIs relates to anxiolysis rather than a primary antidepressive effect, with some patients experiencing recrudescence if anxiety features (as commonly occurs with benzodiazepines.	Thank you for your comment. Antidepressants have been included within the scope of this guideline to address the issue of safe prescribing and withdrawal of these drugs.
Change, Grow, Live	005	General	None of the guidelines (except perhaps TA77 on "z-drugs") emphasise the distinct possibility of rebound anxiety/panic/insomnia on stopping the range of psychotropic medication used in these conditions unless the stressors (eg work pressures) have remitted and/or there has been effective engagement in appropriate psychological intervention (eg CBT, ACT, EMDR).Failure to engage	Thank you for your comment. We intend to consider these issues within the review questions on the common symptoms associated with withdrawal (2.3) and the methods for safe withdrawal (3.1).

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			in more definitive (and sustainable) treatments is often a false economy, understandable in terms of its availability and the time commitment involved.	
Change, Grow, Live	006	011	Patient experience in adult NHS services (2012) NICE guideline CG138 does not go far enough to emphasise the inequalities in referral for/access to psychological therapies. This becomes even more important if more emphasis in placed on these therapies as evidence based and sustainable interventions.	Thank you for your comment. The equalities impact of all recommendations will be considered by the committee when drafting recommendations, bearing in mind that no group should be disadvantaged by the recommendations that are made.
Change, Grow, Live	006	020	Key issues and draft questions should include a specific question to patient and prescriber: "what are the barriers to stopping this particular medication, and how can those barriers be overcome in evidence based and sustainable ways?".	Thank you for your comment. Question 4.1 will cover the information that people need at all stages of this guideline, including when stopping medicines, and question 3.1 will include interventions such as support for people withdrawing from the medicines, therefore this topic should be covered across both of those questions.
Change, Grow, Live	007	022	Main outcomes should include changes to burden of care (as a set of indirect costs).	Thank you for your comment. The list of outcomes in the scope is intended as a suggestion of those that will be in the majority of the questions covered. These will be discussed by the guideline committee during protocol development and additional outcomes will be added as required.
Change, Grow Live	010	Flow chart	Should emphasise the whole range of the dependence syndrome (ie physiological, behavioural, and cognitive phenomena). What to include in review should include the key questions "what are the	Thank you for your comment. The flowchart provided in the scope is an outline of the pathway that will be developed. It will be adapted and detail added as the

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			barriers to stopping this particular medication, and how can those barriers be overcome in evidence based and sustainable ways?".	recommendations in the guideline are written.
College of Mental Health Pharmacy	General	General	What is the rationale for including antidepressants in this draft? We feel that including antidepressants will send out an incorrect message to the general public. Patients with a clinical need for antidepressant therapy might be put-off/discouraged from taking it which could put them at risk of relapse or further deterioration. Furthermore, including antidepressants might add to the stigma associated with mental illness and reduce the likelihood of patients seeking treatment in the first place.	Thank you for your comment. For all of the medicines included within the scope there are legitimate uses that can benefit patients if prescribed safely. Antidepressants have been included because there is some concern that there may be withdrawal symptoms experienced when they are not safely withdrawn. This guideline intends to provide recommendations on safe prescribing and withdrawal of all of the included medicines to reduce any risk to patients and to enable their safe use where appropriate.
College of Mental Health Pharmacy	General	General	Committee recruitment – Considering that the focus is on the use of medication, there should be increased pharmacy representation	Thank you for your comment. The committee composition is intended to cover a range of expertise across the topic. If during development the committee require additional expertise, additional committee members can be co-opted or invited as expert witnesses however.
College of Mental Health Pharmacy	001	019 - 021	We accept that antidepressants can cause withdrawal effects, especially if stopped abruptly. These can be addressed in NICE CG90 and CG91. However there are other medications that can also cause withdrawal effects such as beta-blockers, anti-epileptics, antipsychotics, some antihistamines. We are not suggesting that	Thank you for your comment. We accept that there are other medicines that are associated with withdrawal symptoms but are outside of the scope of this guideline. Antidepressants were included in the remit given to NICE by the Department of Health and

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			these should be included in this draft. However, would NICE please re-consider why antidepressants have been isolated.	therefore it has been decided that they will remain within the scope for this guideline.
College of Mental Health Pharmacy	003	021 - 024	Could children/ young people be included?	Thank you for your comment. We acknowledge that there are equally important issues in children and young people. However, many of these medicines are not licensed in people under 18 years old and there are specific considerations in this population which cannot be adequately addressed within a single guideline.
College of Mental Health Pharmacy	004	001 - 003	Have people prescribed opioid substitute treatments such as buprenorphine and methadone to manage dependency not been included? Have people buying/abusing opioids over the counter e.g. codeine not been included?	Thank you for your comment. Medicines such as methadone and buprenorphine will be covered when prescribed for pain or as a withdrawal strategy for withdrawal from prescribed medicines. However, the scope does not cover the use of these medicines to manage withdrawal from illicit drugs. We acknowledge that some of the medicines included in the guideline may be obtained over the counter or via the internet and if these people seek help from relevant services, this guideline would apply. The scope has been edited to reflect this.
College of Mental Health	007	005 - 007	We suggest removing antidepressants from this list because withdrawal symptoms can be highly variable between different	Thank you for your comment. Anti-depressants were included within the remit for the

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Pharmacy			classes of antidepressants and with specific antidepressants. Furthermore, there can be variability in occurrence and severity between individuals.	guideline from the Department of Health and therefore remain in the scope of this guideline. We accept that the review of withdrawal symptoms may be variable between the antidepressant classes and will consider with the committee how the evidence for antidepressants should be grouped when finalising the protocol for this review.
DrugScience	General	General	It is cnclear why the scope has been extended to antidepressants, but then does not include other medication known to be associated with withdrawal symptoms e.g. beta blockers, antipsychotics and sedating antihistamines. Furthermore, including antidepressants may then add to the stigma/impact upon people appropriately seeking treatment for their mental health, which is already a challenge. DrugScience proposes that antidepressants are excluded from scope at this stage.	Thank you for your comment. We acknowledge that there are a number of medicines that are associated with withdrawal symptoms, but have been agreed as not within the scope of this guideline. Antidepressants were included as they were highlighted in the remit given to NICE by the Department of Health as a medicine class that required guidance relating to their safe prescribing and withdrawal.
DrugScience	General	General	Regarding the recruitment of the committee, it is unclear why 2xGPs would be needed, and this is rather medic-heavy. Given the focus is on the use of medication, there should be increased pharmacy representation. Moreover, there is a need to ensure additional representation from third sector/prisons/private, particularly given that many specialist services are now delivered by non-NHS providers.	Thank you for your comment. The committee composition is intended to cover a range of expertise across the topic and does include a pharmacist and applicants from different settings were eligilble to apply. If during development the committee require additional expertise, additional committee members can be co-opted or invited as expert witnesses however.

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DrugScience	General	General	Groups that will not be covered include "People taking opioids prescribed for end of life care". The guidelines do need to ensure that unforeseen problems do not arise with providing such people (and others who really need it) the pain relief they require.	Thank you for your comment. Opioids prescribed for end of life care is covered by the remit of another clinical guideline published by NICE (palliative care for adults: strong opioids for pain relief). For further information on the guideline see https://www.nice.org.uk/guidance/cg140/
DrugScience	003	020 - 026	Is over the counter medication is also being considered- this is not clear? It would be useful if it was, given that in clinical practice people may use solely/top up legally obtained supplies via this mechanism.	Thank you for your comment. We acknowledge that some of the medicines included in the guideline may be obtained over the counter or via the internet and if these people seek help from relevant services, this guideline may apply. The scope has been edited to reflect this.
DrugScience	003	020 - 026	Is opioid substitute treatment also covered? This is unclear. How this fits in to scope? This is important as especially e.g. methadone and buprenorphine may be used to manage withdrawal/dependency.	Thank you for your comment. Medicines such as methadone and buprenorphine will be covered when prescribed for pain or as a withdrawal strategy for withdrawal from prescribed medicines. However, the scope does not cover the use of these medicines to manage withdrawal from illicit drugs.
DrugScience	003	020 - 026	Should children/young people be included in scope? In clinical practice the principles of management are essentially the same.	Thank you for your comment. We acknowledge that there are equally important issues in children and young people. However, many of these medicines are not licensed in people under 18 years old and there

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				are specific considerations in this population which cannot be adequately addressed within a single guideline.
DrugScience	007	001 - 002	This issue is likely to be difficult to determine- because as typically dictated by clinical need and the person's engagement, so it is not clear how helpful this inclusion really is.	Thank you for your comment. We agree that frequency of review is determined by a number of factors and is complex to answer within a systematic review, however it has been identified as an area where guidance is required and the committee will take into account the available evidence as well as their experience when drafting recommendations.
DrugScience	007	005 - 006	Given that the symptoms (especially if antidepressants are included) can be extensive and highly variable both in terms of risk of occurrence and severity, this may be difficult. In this way, if the scope keeps to medicines associated with dependency such as z-drugs, gabapentinoids, opioids, benzodiazepines, this would be more achievable.	Thank you for your comment. We accept that the review question for symptoms associated with withdrawal may be extensive. Antidepressants were however included within the remit given to NICE by the Department of Health however. Futhermore, withdrawal management is a key focus of this guideline and so understanding the symptoms has been agreed as an important question to include for all medicines in the scope.
Faculty of Pain Medicine of the Royal College of Anaesthetists	General	General	This is a highly desirable and long overdue guidance. We in particular appreciate the planned guidance on safe deprescribing. Clinicians and patients need this quite urgently.	Thank you for your comment.

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Faculty of Pain Medicine of the Royal College of Anaesthetists	006	020	Is the prescribed medication assessed to be effective?	Thank you for your comment. The efficacy of the drugs for different conditions is covered within the condition specific guidelines which will be cross-referred to by this guideline.
Faculty of Pain Medicine of the Royal College of Anaesthetists	006	020	What tool / score is used for assessment of efficacy at review?	Thank you for your comment. The efficacy of the drugs for different conditions and tools used to assess efficacy are covered within the condition specific guidelines which will be cross-referred to by this guideline.
Faculty of Pain Medicine of the Royal College of Anaesthetists	006	020	Review needs to assess the combined risk of "Co Prescription" like both Opioids AND Gabapentinoids	Thank you for your comment. The use of more than one of the medicines within the scope will be considered within the guideline. The details of what should be covered within the review will be considered within question 2.2.
G.R Lane Health Products Ltd	007	003	An assessment of clinically proven non-habit-forming alternatives to benzodiazepines should be included in a review of prescribed medicines associated with dependence or withdrawal symptoms e.g. Clinically proven traditional herbal remedy alternatives such as pharmaceutical quality lavender oil taken as an oral capsule as a first line treatment option in sub-threshold anxiety, before the prescription of benzodiazepines. Evidence provided to NICE in a separate document and also available to view here	Thank you for your comment. The efficacy of the alternative treatment options for different conditions is covered within the condition specific guidelines which will be cross-referred to by this guideline.
G.R Lane	007	015	Patients should be provided with informative decision aids to make	Thank you for your comment. The efficacy of the

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Health Products Ltd			them aware of alternative treatment options to prescribed medicines associated with dependence or withdrawal symptoms. E.g. Clinically proven non-habit-forming traditional herbal remedy alternatives to benzodiazepines such as pharmaceutical quality lavender oil taken as an oral capsule as a first line treatment option in sub-threshold anxiety, before the prescription of benzodiazepines. Evidence provided to NICE in a separate document and also available to view here.	alternative treatment options for different conditions is covered within the condition specific guidelines which will be cross-referred to by this guideline.
Grünenthal Ltd	General	General	All 4 groups participating in the guideline scoping workshop proposed extending the scope of the guideline to include antipsychotic medicines as prescribed drugs associated with dependence or withdrawal.	Thank you for your comment. The views of stakeholders at the workshop, and those submitted (including the information you provide in your associated comments) have been carefully considered, however antipsychotics have not been included within the scope of the guideline. These medicines are prescribed for very specific defined conditions by specialists and guidance on their safe prescribing, monitoring and withdrawal is included within the NICE guideline for psychosis and schizophrenia in adults CG178.
Grünenthal Ltd	004	003	It is unclear why people having treatment for epilepsy are not covered by the guideline. Epilepsy is no different to the other chronic, complex and difficult to treat conditions that these medicines are used to treat, therefore the condition should not be specifically excluded from the guideline	Thank you for your comment. The scope has been edited to clarify that it is gabapentinoids prescribed for epilepsy that will not be covered by this guideline, rather than people having treatment for epilepsy. Medicines prescribed for

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				specific diagnoses in specialist settings (e.g. the treatment of epilepsy) is outside the remit of this guideline, due to the requirement for specialist management.
Grünenthal Ltd	006	026	The identification of co-morbid emotional challenges and mental health co-morbidities as risk factors for dependence has been removed from the current practice section of the scope. It is important that they are captured here as key areas that will covered by the guideline.	Thank you for your comment. This information was removed from the introductory section of the scope so as to keep this as a concise background to the topic, however we agree it's an important factor to consider, and risk factors for dependence remain a key area that is considered in the guideline as detailed in section 3.3.
Grünenthal Ltd	007	001	The guideline should also address the additional resource required to undertake the review of prescribed medicines associated with dependence and withdrawal, highlighting the opportunity to involve clinical pharmacists.	Thank you for your comment. The resource impact of all recommendations will be considered by the committee and detailed in the guideline.
Grünenthal Ltd	007	007	Given the burden associated with their use, it would be appropriate to extend guidance on the methods for safe withdrawal to include over the counter (OTC) medicines associated with dependence and withdrawal	Thank you for your comment. We acknowledge that some of the medicines included in the guideline may be obtained over the counter or via the internet and if these people seek help from relevant services, this guideline would apply. The scope has been edited to reflect this.
Grünenthal Ltd	007	013	The recently published PHE evidence review of dependence and withdrawal associated with some prescribed medicines identified the need for support for patients in addition to the provision of	Thank you for your comment. Draft review question 3.1 is intended to look at a broad range of withdrawal methods, including non-pharmacological interventions.

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			information. It would therefore be helpful if this guideline could include recommendations on the support to be provided to prevent and manage patients experiencing dependence or withdrawal. Such support may include non-pharmacological treatment options, social prescribing, telephone helplines, counselling and support groups, individualised plans and include signposting to other services that can help.	The specific interventions considered will be agreed by the guideline committee when agreeing the review protocol. Your comment will be taken into account when we do so.
Grünenthal Ltd	007	013	Given the burden associated with their use, it would be appropriate to extend guidance on what information and support is required for patients taking over the counter (OTC) medicines associated with dependence and withdrawal	Thank you for your comment. We acknowledge that some of the medicines included in the guideline may be obtained over the counter or via the internet and if these people seek help from relevant services, this guideline would apply. The scope has been edited to reflect this.
Grünenthal Ltd	007	021	The PHE review highlighted the lack of evidence with respect to the risk factors for; the harms associated with; and interventions to prevent dependence and withdrawal. The PHE review was based on systematic reviews, randomised controlled trials (RCTs) and non-randomised studies of the various medicines in scope. It would therefore seem appropriate for the literature review conducted to inform the development of this guideline to additionally focus on research findings which define best prescribing practice and holistic patient care from a health service perspective.	Thank you for your comment. We intend to build on the systematic reviews conducted for the PHE report in the development of this guideline.
Health & Social Care	General	General	Need to include guidance on potential need for 'forced withdrawal' if in the patient's best interest	Thank you for your comment. The methods of withdrawal that will be included within the review will

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Board NI			Include reference to other useful resources, e.g. Opioids Aware and Live Well with Pain website resources.	be agreed by the committee when the review protocols are refined from the draft questions.
Health & Social Care Board NI	002	001	However, they may continue to be prescribed when they are no longer useful, ~~solely~~ because of various reasons e.g. stopping could cause unpleasant withdrawal symptoms	Thank you for your comment. We have taken note of your comment and made this section of the scope clearer.
Health & Social Care Board NI	004	015	Review and monitoring arrangements to identify..	Thank you for your comment. The wording has not been edited as we believe this is adequately covered by 'monitoring' as a broad key area.
Health & Social Care Board NI	004	017	Methods for safe withdrawal, including for patients taking combinations, of prescribed medicines	Thank you for your comment The use of multiple concurrent medicines will be considered by the committee in the development of the guideline.
Health & Social Care Board NI	004	019	Patient education and information for people taking…	Thank you for your comment. This wording has not been changed as this is a broad key area heading. The specifics of the draft review questions will be refined by the guideline committee during development however.
Health & Social Care Board NI	006	024	Prior to prescribing consider: - what suitable alternative options are available to avoid prescribing drugs associated with dependence or withdrawal - what is the plan for subsequently stopping these drugs?	Thank you for your comment. Alternative treatment options will be considered in condition specific NICE guidelines, which this guideline will cross-refer to. Withdrawal management strategies are within the scope of this guideline and the evidence will be reviewed.
Health &	006	029	Review and monitoring to....	Thank you for your comment. The wording has not

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Social Care Board NI				been amended as monitoring will encompass review.
Health & Social Care Board NI	007	013	How should patients taking combinations of these medicines be managed particularly in relation to their underlying clinical condition?	Thank you for your comment. People on multiple therapies will be considered by the guideline committee during development.
Health & Social Care Board NI	007	015	Additional point: Prior to prescribing, what information should be provided to people about the risk of dependence or withdrawal.	Thank you for your comment. The information people require prior to starting these medicines will be included under question 4.1.
Midlands Partnership NHS Foundation Trust	001	007 - 028	No comments	Thank you for your comment.
Midlands Partnership NHS Foundation Trust	002	001 - 018	Nothing to add	Thank you for your comment.
Midlands Partnership NHS Foundation	002	019 - 021	A clear outline is needed who will audit and finance this work.	Thank you for your comment. This guidance will intend to recommend the best approaches and interventions, however how the services themselves are commissioned and delivered is beyond the remit

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Trust				of the guideline.
Midlands Partnership NHS Foundation Trust	002	022 - 025	Further clarification is needed as currently community drug teams are not funded both in terms of staffing/medication/dispensing cost or commissioned to support patients to withdraw from Prescription only medication. Furthermore patients who are addicted to POM often do not wish to engage with community substance misuse teams hence the need for a separate service.	Thank you for your comment. This guidance will intend to recommend the best approaches and interventions, however how the services themselves are commissioned and delivered is beyond the remit of the guideline.
Midlands Partnership NHS Foundation Trust	002	026	It was felt that this guidance is limited to primary care and excluded patients who misuse prescription only medication i.e. purchased off the internet in order for these guidelines to be effective specialist expertise (not only addictions expertise) and expert patients need to be involved in the process	Thank you for your comment. As detailed in section 2, this guideline is for all healthcare professionals who prescribe and administer these medicines, or who provide care for people taking these medicines as well as commissioners of NHS and local authority services and people using services, their families and carers and the public. It is not intended to be limited to primary care. We acknowledge that some of these medicines may be available to purchase over the counter or via the internet and the guideline may apply to these people if they experience dependency or withdrawal symptoms. The scope has been edited to clarify this.
Midlands Partnership NHS Foundation	002	027 - 030	Research is needed as part of the development of these guidelines to utilise the best available evidence and this then should form part of the discussion of the stake holder group	Thank you for your comment. We will search for and review all the available and relevant clinical and cost effective evidence for the guideline. The guideline committee will consider this evidence when making

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Trust				recommendations. Stakeholders will be invited to comment again on the recommendations during consultation of the guideline at the end of development.
Midlands Partnership NHS Foundation Trust	003	002 - 007	No comment	Thank you for your comment.
Midlands Partnership NHS Foundation Trust	003	008 – 010	No comment	Thank you for your comment.
Midlands Partnership NHS Foundation Trust	003	011 - 014	No comment	Thank you for your comment.
Midlands Partnership NHS Foundation Trust	003	015 - 018	This would benefit from further review and clarification in order to establish how to look at benefits as part of this guidance. BAME people should also be part of the considerations.	Thank you for your comment. The section on which groups his guidance will be particularly relevant has been removed from the scope as it was agreed that it should equally apply to all.

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Midlands Partnership NHS Foundation Trust	003	019 - 021	No comment	Thank you for your comment.
Midlands Partnership NHS Foundation Trust	003	022 - 024	Clarification is needed who is going to be the target group for this guideline i.e. patients who adhere to their pom prescription or those who overuse it. Also specialist services and psychosocial interventions and where these are best provided and by whom need to be given consideration as part of the guideline development.	Thank you for your comment. People who are using medicines not prescribed for them are excluded from the guideline. If they are dependent or withdrawing from a prescribed medicine the guidance will apply. Interventions will be considered within question 3.1 for withdrawal strategies.
Midlands Partnership NHS Foundation Trust	003	025 - 026	The guideline needs to be clear if it will also include patients with co-dependency on illicit opiates +/- Alcohol	Thank you for your comment. We acknowledge that this is a complex area for consideration by the guideline committee during the development of the guideline. The guideline will cover all people with dependence to prescribed medicines and provide recommendations on safe prescribing and withdrawal as appropriate. People who are using both prescribed medicines and illicitly obtained drugs or alcohol are not excluded from the guideline and we acknowledge this is a complex group, however, the guideline will only provide recommendations for withdrawal from prescribed medicines. The guideline

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				will cross refer to other NICE guidance on drug misuse or harmful drinking where necessary.
Midlands Partnership NHS Foundation Trust	004	001 - 003	The guideline needs to be clear if it will also include patients with co-dependency on illicit opiates +/- Alcohol	Thank you for your comment. We acknowledge that this is a complex area for consideration by the guideline committee during the development of the guideline. The guideline will cover all peopledependent on prescribed medicines and provide recommendations on safe prescribing and withdrawal as appropriate. People who are using both prescribed medicines and illicitly obtained drugs are not excluded from the guideline and we acknowledge this is a complex group, however, the guideline will only provide recommendations for withdrawal from prescribed medicines. The guideline will cross refer to other NICE guidance on drug misuse or harmful drinking where necessary.
Midlands Partnership NHS Foundation Trust	004	004 - 007	Clarity needed with regard to which treatments are being covered. Does this include community drug teams,	Thank you for your comment. Community drug teams are included within the settings, as long as they are providing NHS or local authority commissioned care.
Midlands Partnership NHS	004	008 - 011	No comment.	Thank you for your comment.

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Foundation Trust				
Midlands Partnership NHS Foundation Trust	004	012 - 020	Clarification is needed if this guideline is going to cover patients who are misusing prescription medications and also clear references need to be put in place to clarify treatment pathways and interagency working. It needs to be clarified if the guideline will include non-pharmacological treatments and who is going to deliver those treatments as part of the pathway. There should be a clear reference how this guideline is going to be funded.	Thank you for your comment. People who are using medicines not prescribed for them are excluded from the guideline. If they are dependent or withdrawing from a prescribed medicine the guidance will apply. Non-pharmacological interventions for withdrawal are included within the scope, however interventions to manage the specific conditions are beyond the scope of this guideline and are covered in the condition specific guidelines that will be cross-referred to. Commissioning and implementation of the recommendations is beyond the remit of the guideline.
Midlands Partnership NHS Foundation Trust	004	021 - 027	No comment	Thank you for your comment.
Midlands Partnership NHS Foundation Trust	005	001 - 032	No comment	Thank you for your comment.
Midlands	006	001 - 011	No comment to make.	Thank you for your comment.

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Partnership NHS Foundation Trust				
Midlands Partnership NHS Foundation Trust	006	012 - 019	Economic aspect - Is there going to be specific allocated funding to implement this guidance and support these patients perspective of postcode in their treatment. As part of the development of this guideline economic aspects need to be taken into consideration. The stakeholders should give consideration how to finance this guideline but also how to protect funding.	Thank you for your comment. All the review questions in the guideline will consider economic aspects. Areas will be prioritised according to economic trade-off. Recommendations will be made that are cost effective (good value for money). It is then up to the NHS, PHE and the commissioners to decide on funding.
Midlands Partnership NHS Foundation Trust	006	020 - 030	Should the key issues and draft questions not include 'what agencies other than GPs might be involved I supporting these patients and what will this interagency working look like'	Thank you for your comment. This guidance will intend to recommend the best approaches and interventions, however how the services themselves are commissioned and delivered is beyond the remit of the guideline.
Midlands Partnership NHS Foundation Trust	007	001 - 021	No comment	Thank you for your comment.
Midlands Partnership NHS	007	023 - 024	In order to establish effectiveness of this guideline clear outcome measures need to be defined .This will have to include epact or similar data from CCG's in order to establish whether the aim of the	Thank you for your comment. Section 3.6 of the scope refers to the main outcomes that may be considered when searching for and assessing the evidence.

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Foundation Trust			guideline has been achieved.	These are outcomes that are considered likely to apply for the majority of questions but the list will be considered by the guideline committee during development of the protocols and edited as appropriate per question.
Midlands Partnership NHS Foundation Trust	007	025 - 029	No comment	Thank you for your comment.
Midlands Partnership NHS Foundation Trust	007	030 - 031	The guidelines needed to be clear as to which agencies are going to collaborate in evidence used for assessing outcomes. Where are NICE going to search for evidence?	Thank you for your comment. Evidence will be searched for and reviewed in accordance with NICE methods, as described in Developing NICE guidelines: the manual. The search strategies will be discussed during protocol development and published in the final guideline.
Midlands Partnership NHS Foundation Trust	008	001 - 007	No comment	Thank you for your comment.
Midlands Partnership NHS	008	008 - 013	Will the pathway will include referral to specialist addiction services. Guideline needs to be clear around roles and responsibilities in the pathway. Pathway needs to be clear that people who misuse	Thank you for your comment. The pathway provided in the scope is an outline of the pathway that will be developed. It will be adapted and detail added as the

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Foundation Trust			alcohol or drugs will not be included, the pathway needs to include educational tools for patients and health care professionals - there aren't any at present. Pathway needs to include training packages for health care professionals and for all sectors, and patients and their carers to raise awareness about these medications.	recommendations in the guideline are written. The scope of the guideline does not include training however and although educational tools will be included if evidence is identified in the reviews, the remit of the guideline does not include the development of these tools.
Midlands Partnership NHS Foundation Trust	008	014 - 029	No comment	Thank you for your comment.
Midlands Partnership NHS Foundation Trust	009	001 - 019	No comment	Thank you for your comment.
Midlands Partnership NHS Foundation Trust	010	General	Flowcharts – The last box in the flowchart needs to be clear who is expected to deliver these non-pharmacological strategies and how it is going to be funded.	Thank you for your comment. The flowchart provided in the scope is an outline of the pathway that will be developed. It will be adapted and detail added as the recommendations in the guideline are written. Recommendations will be made that are cost effective (good value for money). It is then up to the NHS, PHE and the commissioners to decide on funding.
Mind	General	General	We welcome the development of this guideline. Recognition and	Thank you for your comment. The areas you suggest

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			awareness of withdrawal effects of prescribed drugs has been very much consumer-driven and has taken a long time to reach mainstream clinical practice; it is still far from well established. We know that people can still struggle to get support to come off prescribed drugs. Having a guideline should make a significant difference to people's health and safety when drugs that can cause withdrawal effects are being considered/prescribed and when people taking these drugs wish or need to reduce their dose or come off altogether, and/or when are they are no longer receiving any benefit from the drug.	are all included within the scope of the guideline and will be reviewed to provide recommendations on the best available evidence.
Mind	002	022	People may be reluctant to go to addiction services, but may also reasonably not consider this as a relevant option as the problem relates to a medication being prescribed by a clinician.	Thank you for your comment. This is intended to be addressed within question 4.1 about information needed by people being prescribed these mediations.
Mind	002	022	It is also the case that people want to talk to health professionals but cannot find anyone who will help them, or who is knowledgeable on withdrawal or will take them seriously.	Thank you for your comment. Question 4.1 is intended to cover the information people need about these prescribed medicines.
Mind	002	022	In addition people may not realise they have become dependent on a drug until they try to stop taking it, and even then may not recognise the symptoms as being withdrawal-related. The same may apply to the prescribing clinician.	Thank you for your comment. Question 2.3 is intended to highlight the symptoms associated with withdrawal of these prescribed medicines. Furthermore Question 4.1 is intended to cover the information people need about these prescribed

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				medicines which may include highlighting these issues.
Mind	003	022	We are very concerned at the omission of antipsychotic drugs and mood stabilisers from the list of drugs covered by the scope. While these may not be dependence forming they are certainly associated with withdrawal effects. As stated in the British National Formulary, "There is a high risk of relapse if medication is stopped after 1–2 years. Withdrawal of antipsychotic drugs after long-term therapy should always be gradual and closely monitored **to avoid the risk of acute withdrawal syndromes or rapid relapse**. Patients should be monitored for 2 years after withdrawal of antipsychotic medication for signs and symptoms of relapse." (my bold) Therefore we are strongly of the view that antipsychotics, and also mood stabilisers, should be included in the scope. Further reasons are given below.	Thank you for your comment. Antipsychotics have not been included within the scope of the guideline. These medicines are prescribed for very specific defined conditions by specialists and guidance on their safe prescribing, monitoring and withdrawal is included within the NICE guideline for psychosis and schizophrenia in adults CG178.
Mind	003	022	Inclusion of antipsychotics and mood stabilisers as drugs associated with withdrawal effects should encourage explicit consideration of this impact when initiating prescribing and inform (shared) decision-making.	Thank you for your comment. Antipsychotics have not been included within the scope of the guideline. These medicines are prescribed for very specific defined conditions by specialists and guidance on their safe prescribing, monitoring and withdrawal is included within the NICE guideline for psychosis and schizophrenia in adults CG178.
Mind	003	022	Antipsychotic drugs and mood stabilisers (as well as some of the	Thank you for your comment. Antipsychotics have not

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			drugs in the scope) may be administered against the person's will under the Mental Health Act. This creates an even stronger duty to consider the impact of withdrawal effects when making treatment decisions.	been included within the scope of the guideline. These medicines are prescribed for very specific defined conditions by specialists and guidance on their safe prescribing, monitoring and withdrawal is included within the NICE guideline for psychosis and schizophrenia in adults CG178. We do agree that the impact of withdrawal effects should be considered when making treatment decisions for the medicines included in the scope, and this will be considered within the reviews.
Mind	003	022	One reason why people may not get (or ask for) support to come off antipsychotic medication or mood stabilisers is that the clinician does not agree that they should do so. Inclusion of these drugs in the guideline should support clinicians to work as safely as possible with their patients' choices.	Thank you for your comment. Antipsychotics have not been included within the scope of the guideline. These medicines are prescribed for very specific defined conditions by specialists and guidance on their safe prescribing, monitoring and withdrawal is included within the NICE guideline for psychosis and schizophrenia in adults CG178.
Mind	003	022	Inclusion in the scope would also support recognition and awareness of withdrawal effects of antipsychotics and mood stabilisers.	Thank you for your comment. Antipsychotics have not been included within the scope of the guideline. These medicines are prescribed for very specific defined conditions by specialists and guidance on their safe prescribing, monitoring and withdrawal is included within the NICE guideline for psychosis and schizophrenia in adults CG178.

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Mind	003	022	Omission of antipsychotics and mood stabilisers from the scope may mislead people into thinking that they do not have withdrawal effects. The drugs currently in scope may sit naturally together as a group with features in common, and they have been treated as such in the excellent recent Public Health England report. Antipsychotics and mood stabilisers may not 'fit' with this group, but this would not be a good reason to exclude them from the scope. This is a clinical guideline and drugs that meet the criteria for inclusion (in this case, have withdrawal effects) should be included. If antipsychotics and mood stabilisers are to be omitted, there should be a clear statement to that effect, with reasons, in the scope and NICE should develop separate guidance focused on these drugs.	Thank you for your comment. We accept that there are other medicines associated with withdrawal symptoms that are beyond the scope of this guideline. Antipsychotics have not been included within the scope of the guideline. These medicines are prescribed for very specific defined conditions by specialists and guidance on their safe prescribing, monitoring and withdrawal is included within the NICE guideline for psychosis and schizophrenia in adults CG178. This has not been stated as an excluded area in the scope because the inclusion list clearly states those medicines that are included.
Mind	003	025	We recommend including pregnant women as needing specific consideration. There are specific risks associated with medication in pregnancy, including withdrawal symptoms in the new born baby, and women will need information and advice around treatment decisions.	Thank you for your comment. Pregnant women have been added to the equalities impact form, however the management of withdrawal in new born babies is beyond the scope of this guideline.
Mind	003	025	We recommend including people who are detained under the Mental Health Act as needing specific consideration. In the context of involuntary treatment, it is particularly important that the implications of possible dependence and withdrawal are considered	Thank you for your comment. People with a mental health diagnosis are included within the equalities impact form. However, it is not thought that the overall principles of recommendation will differ for any of the

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			and that the person has the maximum informed say in how they are treated.	listed groups, and therefore they are not listed as requiring special consideration.
Mind	004 006	009 020	Within the key issues and questions, consideration needs to be given to people for whom withdrawal is a protracted process. We hear that many practitioners regard withdrawal as something that persists for weeks, not months and they expect the symptoms to resolve. When this does not happen people can find that the harm they are experiencing is challenged or misdiagnosed and they do not receive appropriate help. NICE's guideline must not reinforce the impression of a standardised experience when it can be so variable.	Thank you for your comment. The guideline is intended to cover people with a range of experiences of withdrawal from prescribed medicines. The population will be further refined by the committee during development of the protocols. We will take your comment into account at this stage.
Mind	004 006	013 024	Within risk factors for dependence, consideration should be given to the length of time on the drug, as a longer time is associated with greater difficulty coming off.	Thank you for your comment. The protocol for the review question will be discussed and refined by the guideline committee, including detailing the risk factors to consider. We will take your comment into account when doing so.
Mind	004 007	017 007	We strongly agree with the inclusion of safe withdrawal methods and information that people will need in the key areas for the guideline. However we think there is a gap in terms of the support people may need in the process. This may be included as an aspect of withdrawal methods, but we recommend it is referenced explicitly.	Thank you for your comment. We have added support as an example to the question for clarity as suggested.

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Mind	004 007	017 007	Within safe withdrawal methods, consideration needs to be given to the pace of withdrawal; key feedback from people prescribed benzodiazepines is that they are withdrawn too quickly.	Thank you for your comment. Draft review question 3.1 is intended to look at a broad range of withdrawal methods, which is likely to include pace of withdrawal. The details of what will be included in this review will be agreed by the committee when discussing the protocol for this question, your comments will be taken into account when this discussion takes place.
Mind	007	023	When considering the evidence for this guideline, we recommend that weight is given to the collective experiences of people who have come off or are coming off these prescribed drugs, and those of people supporting them. Lived experience is always important, but in an area where much learning and practice development has been consumer-led it is even more crucial to draw from this knowledge. Patient reports submitted to the yellow card scheme, and the useful contacts listed in our information resource on stopping or coming off medication are key sources, as is the resource itself.	Thank you for your comment. We agree these are important to consider and expect to include qualitative evidence as well as quantitative evidence for a number of questions in this guideline including 2.3 on the common symptoms associated with withdrawal and 4.1 on information required by people, their families or carers.
Napp Pharmaceuticals Limited	General	General	This is a complex area of medicine and is not isolated solely to prescribed medicines. Many people with dependence to prescription medicines are also using illicit drugs or cocktails of prescribed medicines (more than one class) and illicitly obtained drugs.	Thank you for your comment. We acknowledge that this is a complex area for consideration by the guideline committee during the development of the guideline. The guideline will cover all people with dependence to prescribed medicines (including

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			What will NICE do to ensure that those people who are currently using **both** prescribed medicines and illicitly obtained drugs (diverted prescription medicines or other drugs obtained from various sources) are able to access treatment for dependency and withdrawal when it may be impossible to state with certainty the cause of the dependency? Many people with dependency issues also use drugs from different medicines classes which have been described in the draft scope. For example they may have been prescribed multi modal treatments for pain including combinations of opioids, gabapentinoids and or antidepressants. NICE may wish to consider how people on multiple therapies should be managed and what safeguards and screening before prescribing are needed before any new treatments are initiated or before any treatments are tapered down or withdrawn. This is particularly pertinent when initiating treatments or titrating treatments for those people with addictive tendencies or who may have a history of alcohol abuse.	people on multiple therapies) and provide recommendations on safe prescribing and withdrawal as appropriate. People who are using both prescribed medicines and illicitly obtained drugs are not excluded from the guideline and we acknowledge this is a complex group, however, the guideline will only provide recommendations for withdrawal from prescribed medicines. Other NICE guidance relating to drug misuse and withdrawal from illicit drugs will be cross-referred to where necessary.
Napp Pharmaceutica	General	General	There is currently much concern about the funding of services for addiction and the supply of "take home" naloxone for those at risk	Thank you for your comment. This guideline will include people dependent on prescribed opioids and

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ls Limited			of overdose. People who are dependent on prescribed opioids may try to access these services for support when trying to reduce or stop using opioids. We suggest that NICE should ensure that this group of people are also considered within the guideline and that the relevant referral processes are highlighted to health care professionals, commissioners, providers and people using the services.	consider the best strategies for preventing dependence or withdrawal symptoms as well as the information required when prescribing these medicines. The guideline is intended to be used by all health care professionals, commissioners and providers and people using the services, as you suggest.
Napp Pharmaceutica ls Limited	007	013	Should also consider information relevant for carers of people prescribed medicines associated with dependence or withdrawal symptoms, especially if the people prescribed have cognitive problems/mental illness. Carers could play a key role here e.g. remembering to attend for monitoring, encouragement and support during tapered withdrawal.	Thank you for your comment. Information for family and carers will also be considered under question 4.1, the wording has been amended to clarify this.
Napp Pharmaceutica ls Limited	007	028	Suggest add carer and/or relative satisfaction, especially for people prescribed with mental illness affecting cognition.	Thank you for your comment. The list of outcomes in the scope are intended as suggested outcomes that will be in the majority of the questions covered. These will be discussed by the guideline committee during protocol development and additional outcomes will be added as required.
NHS England/Impro vement	General	General	In then final page where there are the boxes there is no reference to antidepressants although antidepressant are referenced throughout the scope (H&J)	Thank you for your comment. This has now been added to the pathway.
NHS	General	General	Whilst we don't have any specific comments regarding the	Thank you for your comment.

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England/Improvement			draft scope, we welcome the development of the guideline, which will support AHPs with the management of people to whom the guideline applies, from both an independent prescribing and holistic care. perspective. (SC)	
NHS England/Improvement	003	022 - 023	Need to consider young people in transition. a cohort of adult long term users of these medications commence these medications as children and young people eg antidepressant prescribing in CAMSH and in YOIs (H&J)	Thank you for your comment. We acknowledge that there are equally important issues in young people. However, many of these medicines are not licensed in people under 18 years old and there are specific considerations in this population which cannot be adequately addressed in a single guideline.
NHS England/Improvement	006	General	One of the key questions about withdrawing/reducing from dependence forming medicines is who should undertake or oversee this- that is who should be the lead clinician or specialist. In many cases, the initiating clinician of the medicines is not the GP but arose from a hospital-based episode of care. GPs are often reluctant to tackle a possible dependency and withdrawal plan as they do not feel they have the skills to manage the clinical and psychosocial aspects of managing the patient. Equally other specialists and providers such as substance misuse providers are not commissioned for or have the capacity to manage these patients. The outcome is that the patient is left without any clear options for reducing the medicine.	Thank you for your comment. This guideline is intended to apply to all healthcare professionals in NHS or local authority services delivering NHS commissioned care. We acknowledge that the ongoing management may fall under someone who had not initially prescribed the medication, and the committee will take this into consideration when drafting the recommendations. It is unlikely that evidence based recommendations will be able to be made on who should undertake withdrawal however. The commissioning and implementation of the recommendations is beyond the remit of the guideline.

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			We recommend that the scope revised to include advice about the factors that need to be considered when identifying which lead clinician or which service type should be taking the lead for managing a patient requiring withdrawal from a prescribed medicine. The evidence review may uncover some options about this as well as whether a multidisciplinary approach is best. (H&J)	
NHS England/Improvement	006	027	Consideration of MDT ways of working that ensure alternatives to medications form an integral part of care planning and also the mechanisms that avoid dose escalation and encourage step down (H&J)	Thank you for your comment. Alternatives to medicines are covered in condition specific NICE guidelines, which will be cross-referred to. This guideline will review the evidence for different prescribing strategies, which may include mechanisms to avoid dose escalation and encouraging step down, as you suggest. The details of this review will be discussed and agreed by the committee when setting the review protocol.
NHS England/Improvement	007	030	Would like to see consideration of the relationship between good prescribing practice and offering interventions that are evidenced to address trauma and are trauma informed (H&J)	Thank you for your comment. The guideline will review the evidence for prescribing strategies, and interventions for withdrawal, however efficacy of interventions to treat specific issues is beyond the scope of the guideline.
NHSE Primary Care	006 - 011	General	The draft questions are a good summary of the main concerns for GPs which include identifying patients with prescription drug	Thank you for your comment. We have passed your comments regarding implementation on to the NICE

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			dependency, engaging them in conversation, agreeing together an appropriate withdrawal plan (if indicated) and being able to refer and signpost to support services. The draft algorithm is brief and succinct and includes all the essential steps. From a GP perspective the issues to consider are: 1. Additional capacity required to identify and engage with dependent patients-they may need more frequent medication reviews and longer consultations 2. Hopefully the emergence of PCNs (Primary Care Networks) and introduction of more clinical pharmacists will support and enable this to happen 3. By the very nature of the dependency issue these patients can be vulnerable and often very defensive about their access to medication and withdrawal discussions and implementation is likely to result in an increase in patient complaints 4. In large practices all GPs and prescribers need to be willing to 'sign up' to the same medicine optimisation. Outliers who continue to prescribe large volumes or doses outside good evidence should be prepared to explain their reasoning 5. For patients who agree to engage in medicine optimisation there needs to be adequately resourced and easily accessed psychological support-GPs do not have the capacity to provide this and this will need investment.	implementation support team to inform their support activities for this guideline

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			The current IAPT service would not have capacity for this support- where I am a GP the average waiting time is now 8-9 months to see a psychologist	
Parkinson's UK	General	General	We recommend that throughout the guideline any changes to Parkinson's medications should be made in consultation with Parkinson's specialists as stated in recommendation 1.3.4 of the NICE Parkinson's disease in adults guideline (NG71).	Thank you for your comment and this information. Parkinson's medications have not been included within the scope of this guideline however.
Parkinson's UK	002	015	We recommend that the scope of this guideline is widened to include other medications that may also need safe withdrawal processes and guidance in place for clinicians and commissioners. For instance, the NICE Parkinson's disease in adults guideline (NG71) states in recommendation 1.3.2 that Parkinson's medications should not be withdrawn abruptly and in recommendation 1.3.3 it states that withdrawing people with the condition from their Parkinson's medications can cause neuroleptic malignant syndrome (NMS). Research outlines the situations this can happen in and the impact this can have on people living with the condition (Rajan S, Kaas B, Moukheiber E. Movement disorders emergencies. InSeminars in neurology 2019 Feb, Vol. 39, No. 01, pp. 125-136).	Thank you for your comment. We accept that there are other medicines that are associated with withdrawal symptoms but are outside of the scope of this guideline. Parkinson's disease treatment has not been included as these medicines are prescribed for a specific defined condition by specialists and guidance on their safe prescribing, monitoring and withdrawal is included within the NICE guideline for Parkinson's disease NG71, as you have highlighted.
Parkinson's UK	003	025 - 026	We would dispute this statement, as a small subset of people with Parkinson's may suffer from dopamine agonist withdrawal syndrome (DAWS), which can lead to profound disability. Clinicians should monitor patients closely when tapering these medications.	Thank you for your comment. Medicines used for Parkinson's disease are beyond the scope of this guideline however, so this has not been edited.

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			(Yu XX, Fernandez HH. Dopamine agonist withdrawal syndrome: a comprehensive review. Journal of the neurological sciences. 2017 Mar 15;374:53-5). Also, around 3-4% of the Parkinson's population being seen in specialist centres may experience dopamine dysregulation syndrome (DDS), which is a dysfunction of the bodies reward system. This affects those who have taken dopaminergic medications for a long period of time. These people will need extra monitoring by their GP and clear links into specialist services to ensure effective management. (O'sullivan SS, Evans AH, Lees AJ. Dopamine dysregulation syndrome. CNS drugs. 2009 Feb 1;23(2):157-70) and (Warren N, O'Gorman C, Lehn A, Siskind D. Dopamine dysregulation syndrome in Parkinson's disease: a systematic review of published cases. J Neurol Neurosurg Psychiatry. 2017 Dec 1;88(12):1060-4). We would therefore recommend that this guideline includes Parkinson's and gives people with the condition special consideration. The guideline should also widen its focus from just benzodiazepines, Z-drugs, opioids, gabapentin and pregabalin to include other medications such as those containing levodopa, subcutaneous apomorphine and dopamine agonists.	
Parkinson's	004	012 - 020	We agree with the areas that the guideline will cover but would also	Thank you for your comment.

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UK			recommend the guideline covers the need to consult Parkinson's specialists for advice. This aligns with recommendation 1.3.4 of the NICE Parkinson's disease in adults guideline (NG71).	However medicines for Parkinson's disease are beyond the scope for this guideline.
Parkinson's UK	005	003 - 027	We recommend the Parkinson's NICE guideline (NG71) is included in this list as people with the condition are impacted by NMS, DAWS or DDS.	Thank you for your comment. This has not been included in the list as medicines for Parkinson's disease are excluded from the scope, and this list intends to focus on the guidelines most directly related.
Parkinson's UK	006	025 - 026	We recommend that Parkinson's medications (those containing levodopa, subcutaneous apomorphine and dopamine agonists) are added to this list as people with the condition are impacted by NMS, DAWS or DDS.	Thank you for your comment. We accept that there are other medicines that are associated with withdrawal symptoms but are outside of the scope of this guideline. Parkinson's disease treatment has not been included as these medicines are prescribed for a specific defined condition by specialists and guidance on their safe prescribing, monitoring and withdrawal is included within the NICE guideline for Parkinson's disease NG71.
Parkinson's UK	006	029 - 030	We agree with this question and believe that regular monitoring of people with Parkinson's experiencing DDS is crucial. We would recommend that this monitoring should be done in consultation with specialists – this could be cross-referenced with recommendation 1.3.4 of the NICE Parkinson's disease in adults guideline (NG71).	Thank you for your comment. Medicines for Parkinson's disease are beyond the scope of this guideline however and are covered in NG71 as you highlight.
Parkinson's UK	007	001 - 002	We agree with this question and would suggest the frequency of reviews adopted in recommendation 1.2.5 of the NICE Parkinson's	Thank you for your comment. Medicines for Parkinson's disease are beyond the scope of this

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			disease in adults guideline (NG71) could be considered.	guideline however and are covered in NG71 as you highlight.
Parkinson's UK	007	003 - 004	We agree with this question as it is crucial there is a holistic review of medications a person experiencing DAWS or DDS is taking. However, we recommend that this is conducted in consultation with specialists – this could be cross-referenced with recommendation 1.3.4 of the NICE Parkinson's disease in adults guideline (NG71).	Thank you for your comment. Medicines for Parkinson's disease are beyond the scope of this guideline however and are covered in NG71 as you highlight.
Parkinson's UK	007	013 - 018	We agree with this recommendation as it is crucial that people taking prescribed medicines associated with dependence or withdrawal symptoms have clear oral and written information they can refer to between consultations. It is also crucial that carers and family members are informed so they can support the individual. This could be cross-referenced with recommendations 1.1.3, 1.1.4, 1.3.1 and 1.3.8 of the NICE Parkinson's disease in adults guideline (NG71).	Thank you for your comment. Medicines for Parkinson's disease are beyond the scope of this guideline however and are covered in NG71 as you highlight.
Parkinson's UK	009	010	We recommend the Parkinson's NICE guideline (NG71) is included in this list as people with the condition are impacted by NMS, DAWS or DDS.	Thank you for your comment. This has not been included in the list as medicines for Parkinson's disease are excluded from the scope, and this list intends to focus on the guidelines most directly related.
Pfizer Ltd	General	General	We recognise that the clinical areas identified for focused consideration within this guideline are areas of known unmet need for patients where medicinal products and/or therapies have the potential to significantly impact patients' care and quality of life. We	Thank you for your comment. We acknowledge that some of the medicines included in the guideline may be obtained over the counter or via the internet and if these people seek help from relevant services, this

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			support the development of this guidance using the methods and processes outlined in developing NICE guidelines manual as a way to support save prescribing within the NHS and fully agree that close alignment to related NICE guidance, published or in development, should be maintained. However, non-prescription medication often results in substantial burden to the patient, their family and to the NHS, and as repetitively identified by the workshop groups, inclusion of non-prescription medication may provide a more holistic reflection of the management burden associated with dependence or withdrawal of drugs.	guideline would apply. The scope has been edited to reflect this.
Pfizer Ltd	General	General	The medicines have some common pharmacological features and are categorised in a single group. However we need to consider that they have different properties and different licensed indications. Indeed while recognising that current or past history of substance abuse is an important consideration, the vast majority of patients have a legitimate need of these medications. Please refer to the most recent data from US which highlights the abuse rate of some of the drugs which are in scope of this draft Ref : https://cpdd.org/wp-content/uploads/2019/07/abstracts_2019.pdf(abstract ID: 371)	Thank you for your comment. The medicine classes will be considered separately, and the guideline committee will determine whether recommendations need to differ per class during guideline development. It is expected that principles for safe prescribing will apply irrespective of the indication. It is noted that these medications do have legitimate uses when safely prescribed.
Pfizer Ltd	General	General	Pfizer suggests that the guidance around appropriate use of multiple concurrent medicines within the scope of this draft should also be included in the guideline	Thank you for your comment. The use of multiple concurrent medicines within the scope of the guideline will be considered by the committee in the development of the guideline.

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Pfizer Ltd	003	022	Pfizer suggests the inclusion of adolescents. The incidence and impact of mental health diseases amongst adolescence is well documented with 20% of adolescents may experience a mental health problem in any given year and 75% of mental health problems are established by age 24 (1,2,3). The need for inclusion of adolescents into the guidance development was also highlighted by the workshop groups.. 1. McGinnity Á, Meltzer H, Ford T, Goodman R. Mental health of children and young people in Great Britain, 2004. 2. Kessler RC, Berglund P, Demler O, Jin R, Merikangas KR, Walters EE. Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. Archives of general psychiatry. 2005 Jun 1;62(6):593-602. NHS Digital; Mental Health of Children and Young People in England, 2017; https://digital.nhs.uk/data-and-information/publications/statistical/mental-health-of-children-and-young-people-in-england/2017/2017; accessed 25th September 2019	Thank you for your comment. We acknowledge that there are equally important issues in children and young people. However, many of these medicines are not licensed in people under 18 years old and there are specific considerations in this population which cannot be adequately addressed within a single guideline.
Pfizer Ltd	003	024	Pfizer suggests the inclusion of antipsychotics and stimulants. This would also adequately reflect the workshop discussions which demonstrated broad consensus that these drug groups are relevant to the guidance topic.	Thank you for your comment. Antipsychotics have not been included within the scope of the guideline. These medicines are prescribed for very specific defined conditions by specialists and guidance on their safe prescribing, monitoring and withdrawal is included

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				within the NICE guideline for psychosis and schizophrenia in adults CG178.
Pfizer Ltd	003	025	Aligned with the workshop discussions, Pfizer suggests that various relevant subgroups should be considered during the guidance development, namely; • Adolescents • Older people • cognitive impaired people and people learning disabilities • people treated for mental health conditions Within the context of the proposed guidance these groups are of particular relevance and which has been partially acknowledged by the NICE Draft Scope in the Equality consideration sub-section on page 3.	Thank you for your comment. We acknowledge that there are equally important issues in children and young people. However, many of these medicines are not licensed in people under 18 years old and there are specific considerations in this population which cannot be adequately addressed in a single guideline. The equality impact assessment details groups that have been raised as important to consider within the guideline, which includes people with cognitive impairment, people with learning difficulties, people with current or past mental health diagnoses and people with multimorbidity and frailty (associated with, but not limited to older adults). However, it is not thought that guidance should differ in terms of the general principles in these groups. Therefore they are not listed as groups needing specific consideration. The guideline committee will specify subgroups which need to be considered for each individual question during development of the protocols.
Pfizer Ltd	005	002	Please include NICE guidance CG137 on Epilepsies: Diagnosis	Thank you for your comment. This has not been listed

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			and management. https://www.nice.org.uk/Guidance/cg137	as a related guideline as gabapentinoids prescribed for epilepsy will not be covered by this guideline,, and this list intends to focus on the guidelines most directly related.
Pfizer Ltd	007	024	AS the scope of the guidance focusses not only on the safe prescribing but also on the withdrawal management associated with dependence and withdrawal, Pfizer considers the following additional outcomes as appropriate; • drug seeking behaviour and withdrawal type behaviour withdrawal associated symptoms, e.g. somnolence, tiredness, confusion, etc	Thank you for your comment. The list of outcomes in the scope are intended as suggested outcomes that will be in the majority of the questions covered. These will be discussed by the guideline committee during protocol development and additional outcomes will be added as required.
Pfizer Ltd	008	015	Please include NICE guidance CG137 on Epilepsies: Diagnosis and management. https://www.nice.org.uk/Guidance/cg137	Thank you for your comment. This has not been listed as a related guideline as gabapentinoids prescribed for epilepsy will not be covered by this guideline, and this list intends to focus on the guidelines most directly related to the scope.
Public Health England	General	General	The National Institute for Health and Care Excellence (NICE) may wish to consider whether it would be more helpful to exclude antidepressant withdrawal from this guideline and instead include them in the upcoming depression guidance where full consideration of the range of issues that apply to antidepressants can be considered. Following that, NICE could update all other guidance where they	Thank you for your comment. Antidepressants were included in the remit given to NICE by the Department of Health and therefore it has been decided that they will remain within the scope for this guideline.

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			recommend antidepressants (anxiety disorders guidance etc where the same problems apply). This will avoid some of the arguments about things like selective serotonin reuptake inhibitors (SSRIs) and make the guideline more straightforward.	
Public Health England	002	006	The data from the National Drug Treatment Monitoring System (NDTMS) is likely to be a significant under representation of the scale of need because addiction treatment services are targeted at illicit drug users. This needs to be acknowledged.	Thank you for your comment, this sentence has been amended to acknowledge this as you suggest.
Public Health England	003	General	Public Health England (PHE) suggests clarifying who the guideline is for by including the following: "healthcare professionals … who provide care for people taking these medicines **or for those coming off them".** This then covers safe management of potential withdrawal symptoms.	Thank you for your comment. This has been added as suggested.
Public Health England	003	General	People with a learning disability may also be a group for whom "the guideline will have particular relevance"	Thank you for your comment. The equality impact assessment details groups that have been raised as important to consider within the guideline, which includes people with learning difficulties. The section on the groups for which this guidance will be particularly relevant has been removed from the scope as it was agreed that it should equally apply to all.
Public Health England	003	General	We note the scope is adults-only. However young people have equally important issues which need some consideration. PHE accepts this is not covered, but this needs attention, perhaps in separate guidance.	Thank you for your comment. We agree that there are equally important issues in children and young people. You may wish to consider suggesting a new topic for a guideline to NICE via the website.

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Public Health England	003	General	We note the guideline will be for adults taking prescribed medicines, not over the counter or prescription medicines taken without prescription such as those obtained from the internet. These are important and interlinked issues which will need to be addressed in some way, as the groups of people obtaining medicines in this way and via prescription are not mutually exclusive.	Thank you for your comment. We acknowledge that some of the medicines included in the guideline may be obtained over the counter or via the internet and if these people seek help from relevant services, this guideline would apply. The scope has been edited to reflect this.
Public Health England	004	General	Settings: as above – private prescribing, including online, is an issue which overlaps and needs to be addressed, or at least referred to. There is risk that people will turn to online or private prescribing as result in changes in primary care practice.	Thank you for your comment. We acknowledge that some of the included medicines may be available to purchase online, or privately. If people who have accessed the included medicines in this way attend NHS or local authority services for support for issues included, this guidance would apply. The committee will be mindful of the current context when making recommendations.
Public Health England	004	General	3.3 Activities, services or aspects of care: Please include "information **and support"** "for people taking or **coming off** medicines …"	Thank you for your comment. This section of the scope has been edited to include information for people coming off these medicines. Support for people coming off these medicines is intended to be covered in draft question 3.1 for methods for withdrawal. This has been added to the draft question to clarify.
Public Health England	007	013	4. Information for people taking prescribed medicines associated with dependence or withdrawal symptoms. As above – PHE	Thank you for your comment. This section of the scope has been edited to include information for

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			suggests the wording is amended to include "information **and support** for people taking **or coming off** medicines …"	people coming off these medicines. Support for people coming off medicines is intended to be covered in draft question 3.1 for methods for withdrawal. This has been added to the draft question to clarify.
Public Health England	007	013	Informed choice or consent needs to be a central focus of the guideline. Provision of improved information for patients needs to serve a purpose, such as supporting informed consent. Other processes apart from the provision of information will have a role, for example shared decision making between practitioners and patients, offering non-medicinal interventions such as talking therapies and social prescribing options. Therefore, the guideline should explore what can enhance informed choice and which information will have a significant role but may not be the only factor. Practitioner skills will also play a role.	Thank you for your comment. Shared decision making is a principle that applies across all NICE guidelines. It is specifically covered by NICE guideline CG138 (Patient experience in adult NHS services), and by the scope of NICE guideline GID-NG10120 (Shared Decision Making; in development). This guideline will cross-refer to these NICE guidelines where appropriate.
Royal College of General Practitioners	General	General	To help GPs, the RCGP has produced a 'top tips' for dependence forming medications. Can the committee considering signposting to this? https://www.rcgp.org.uk/-/media/Files/CIRC/Desktop-guides/Top-Ten-Tips-Dependence-Forming-Medications-April-2019.ashx?la=en	Thank you for your comment. This will be considered by the committee during the development of the guideline.
Royal College of General Practitioners	General	General	The guideline committee should note that the initiation of many of the medications under consideration is not within general practice, but rather within A&E, chronic pain, psychiatry and other services	Thank you for your comment. This guideline will apply in all settings where NHS or local authority care is provided. The guideline will review prescribing

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			within secondary care. The separation between initiator and on-going prescriber/reviewer is essential to recognise within the guidance. It is exceptionally difficult within the community, when good practice of de-prescribing occurs by the reviewer (in primary care), in the best interests of the patient, but for secondary care to reinstate the medication or increase doses again at the patient request, which frequently occurs. Can the committee consider highlighting this, with the aim of ideally preventing the initial prescriptions being given, but also to empower primary care clinicians, if they feel the on-going prescribing is not in the best interests of the patient to request the responsibility is referred back onto the initiator (in secondary care) to continue the prescribing, de prescribing and review processes.	strategies as well as monitoring and these issues will be considered when addressing those topics.
Royal College of General Practitioners	General	General	Can the committee consider adding 1. Prison/ secure setting staff to the list of who this guidance who is useful for. There is a high number of prisoners who use these medications and experience withdrawal an de-prescribing in these settings. 2. Private health care professionals and providers in addition to NHS commissioners. It is essential that this medication, that is often sought from multiple professionals is accounted for and a centralised record of all prescribed	Thank you for your comment. Prisons / secure settings and third sector agencies have not been listed specifically as they are covered within the statement 'all settings within which NHS or local authority commissioned care is provided'. Although we agree that this may be of interest to private health care professionals, this is beyond the remit of NICE guidance to specify.

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			drugs kept within the GP record. 3. Third sector agencies who have programmes for withdrawal programmes including telephone support services	
Royal College of General Practitioners	001	017	Can the committee consider adding more detail to this sentence to fully reflect the PHE review from September 2019? PHE's analysis shows that, in 2017 to 2018, 11.5 million adults in England (26% of the adult population) received, and had dispensed, one or more prescriptions for any of the medicines within the scope of the review https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/829777/PHE_PMR_report.pdf	Thank you for your comment. We have edited this sentence in line with the PHE review.
Royal College of General Practitioners	001	022	Can the committee consider acknowledging that clinicians sometimes prescribe these drugs off licence or out of guidance for the conditions mentioned? F	Thank you for your comment. Section 1 is only intended to be an introduction to the guideline scope. However, the guideline committee will consider that these medicines are sometimes prescribed off licence during guideline development.
Royal College of General Practitioners	003	024	We note that the draft scope currently does not include antipsychotic medication. Can the committee consider including these in this guidance or in future guidance since problems with dependence and withdrawal, particularly associated with antipsychotics with sedative properties e.g. quetiapine and olanzapine, are regularly observed in clinical practice and within secure settings.	Thank you for your comment. Antipsychotics have not been included within the scope of the guideline. These medicines are prescribed for very specific defined conditions by specialists and guidance on their safe prescribing, monitoring and withdrawal is included within the NICE guideline for psychosis and schizophrenia in adults CG178.

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Royal College of General Practitioners	004	012 - 014	Can the committee consider adding clinician decisions prior to prescribing drugs that risk dependency, shared decision making and alternatives to prescribing where safer effective non-pharmacological management options are available.	Thank you for your comment. The alternative non-pharmacological therapies to consider prior to prescribing for specific conditions is outside the remit of this guideline. The guideline will cross-refer to condition specific NICE guidelines for the appropriate alternatives which may be considered prior to prescribing these medicines for the individual indications. Shared decision making is covered by published NICE guidelines CG138 (Patient experience in adult NHS services), and by the scope of NICE guideline GID-NG10120 (Shared Decision Making; in development). The guideline will cross-refer to these NICE guidelines where appropriate.
Royal College of General Practitioners	004	017 - 018	Can the committee consider adding holistic support to point 2 "Methods for safe withdrawal and consideration of patient *holistic support* during withdrawal".	Thank you for your comment. We have added support as an example to the draft question in this area (question 3.1).
Royal College of General Practitioners	004	022	It is important to note that whilst illicit drugs and dependence on and withdrawal from drugs that have not been prescribed are not included in this guidance that they often coexist and are interdependent so cannot be treated in an isolated fashion.	Thank you for your comment. We acknowledge that this is a complex area for consideration by the guideline committee during the development of the guideline. The guideline will cover all people with dependence to prescribed medicines and provide recommendations on safe prescribing and withdrawal as appropriate. People who are using both prescribed

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				medicines and illicitly obtained drugs are not excluded from the guideline and we acknowledge this is a complex group, however, the guideline will only provide recommendations for withdrawal from prescribed medicines. Other NICE guidance relating to drug misuse and withdrawal from illicit drugs will be cross-referred to where necessary.
Royal College of General Practitioners	006	020	Can the committee consider adding a qualitative review question in order to gain greater insight into issues around de-prescribing: What are the barriers and facilitators to healthcare professionals reviewing and potentially stopping medicines associated with dependence and withdrawal?	Thank you for your comment. We accept that this might be an area of uncertainty. The evidence for monitoring, prescribing strategies and withdrawal will all be considered in this guideline and the committee will consider the feasibility of implementing these based on their clinical experience. We therefore expect that barriers and facilitators will be covered within the existing questions. However additional questions may be considered by the committee if deemed essential to the guideline.
Royal College of General Practitioners	006	023 - 028	The draft scope currently asks the question 'what are the optimum prescribing strategies to limit the risk of dependence?' Can the committee consider adding 1. 'What are the considerations prior to prescribing and communication skills/tools required to avoid initiating medicines with potential for dependence unnecessarily?' 'What are the optimum non-prescribing strategies to limit the risk of	Thank you for your comment. Question 1.2 is intended to cover non-pharmacological interventions used alongside prescribing to limit the risk of dependence. Question 4.1 is intended to cover the information people need before taking these medicines. However, the alternative non-pharmacological therapies to consider prior to prescribing for specific conditions is

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			dependence?'	outside the remit of this guideline. The guideline will cross-refer to condition specific NICE guidelines for the appropriate alternatives which may be considered prior to prescribing these medicines for the individual indications.
Royal College of General Practitioners	006	029	Can the committee define which healthcare professionals should be involved in monitoring and how best monitoring information can be shared. Patients may see multiple healthcare professionals and carers who can monitor risk of dependence and withdrawal. Multidisciplinary team discussions and/or clear information sharing processes prior to medicines reviews may lead to earlier identification and better risk management.	Thank you for your comment. The review questions will address how frequent the reviews should be and what should be included within them, however it is unlikely that the committee witll be able to make evidence based recommendations on who should undertake monitoring reviews. The commissioning and implementation of the recommendations is beyond the remit of the guideline.
Royal College of General Practitioners	006 007	023 - 024 009 - 012	When considering safe prescribing and the most clinically cost effective non pharmacological strategies, it is essential to address the communication skills/tools and shared decision making approaches required for 'de-prescribing' and the additional holistic care resources (e.g. counselling and support) patients will need to complete this successfully. If these resources are not available, then there is a high risk of on-going dependency with prescribed medications or by defaulting to non prescribed or illicit drugs.	Thank you for your comment. This question is intended to cover a broad range of strategies, including the support required and interventions such as counselling. Both the clinical and cost effectiveness of all interventions, including the details of what they include will be considered within the clinical and economic reviews of the evidence.
Royal College of General Practitioners	007	001	When considering the frequency of review of prescribed medicines associated with dependence and withdrawal it is essential to consider the impact on the health care services performing these	Thank you for your comment. The feasibility and resource impact of all recommendations will be considered by the committee when drafting

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			focussing on time and economic pressures. Using the wider team, including community pharmacists, or centralising the reviews with the newly appointed clinical pharmacists for Primary Care Networks could be considered, rather than simply increasing the number of GP review appointments which is unsustainable. Collaboration between primary, secondary and third sector agencies is essential during this process to ensure one voice is consistent across all areas and patients do not get conflicting advice.	recommendations and will be detailed in the guideline.
Royal College of Nursing	General	General	The Royal College of Nursing (RCN) welcomes proposals to develop the NICE guideline for Safe prescribing and withdrawal management of prescribed drugs associated with dependence and withdrawal. The RCN invited members who work in this area to review and comment on behalf of the RCN. The comments below reflect the views of our reviewers.	Thank you for your comment.
Royal College of Nursing	001	019 - 020	It might be worth mentioning that although there is limited research on whether anti-depressants are associated with physical / psychological dependence some patients and clinicians have concerns that about this aspect. This is an issue that has not been explored particularly so needs to be investigated.	Thank you for your comment. We are aware there are differing views on this topic, the scope has been edited to reflect this.
Royal College of Nursing	002	006 - 007	This 5% estimate is unlikely to represent the scale of the issue as most people who develop a problem will not access specialist drug treatment. A point made in lines 27-30.	Thank you for your comment. This sentence has been edited to acknowledge the likely underestimation.

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			In addition these services have faced significant budget cuts which has reduced their capacity.	
Royal College of Nursing	003 007	025 007 - 012	The geographical variation in the prescribing of medicines associated with dependence or withdrawal symptoms is noted. It is also noted that the highest number of prescriptions occur in north east of England. The guideline developers should consider and be mindful of the impact on populations already taking prescribed medicines and provide guidance that will be perceived by that population as safe and supportive and not punitive.	Thank you for your comment. We agree that the included medicines can benefit people when prescribed appropriately and safely for legitimate indications. The committee will be mindful of this when making recommendations.
Royal College of Nursing	006	020	One of the key issues and questions should be about how clinicians and patients can distinguish withdrawal symptoms from those of mental health problems such as depression and anxiety, as there is considerable overlap this at least should be acknowledged and advice offered as to any distinctions that can be made.	Thank you for your comment. We agree that this is an area of uncertainty that may require further research. We will intend to acknowledge it within the guideline but do not think it can be appropriately addressed by a review question.
Royal College of Physicians	General	General	The RCP is grateful for the opportunity to respond to the above consultation. We have liaised with our Patient Safety Committee and Joint Specialty Committee for Clinical Pharmacology and Therapeutics would like to make the following comments.	Thank you for your comment.
Royal College of Physicians	General	General	Overall we welcome the development of NICE guidance on safe prescribing and withdrawal management of prescribed drugs associated with dependence and withdrawal	Thank you for your comment.

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			We strongly support the development of this guidance in an area of increasing harm to patients.	
Royal College of Physicians	General	General	We would make the following recommendation to the draft scope. It will be important to include drugs with associated dependency used for pain management, and anxiety disorders. Where these medicines are used for other therapeutic uses which are life threatening such as Epilepsy, their use in these conditions should be outside the scope of this work. It is important that the recommendations include shared decision making in prescribing, and clarity of monitoring when used for these conditions, as well as guidance on when and how to deprescribe and limit the side effects.	Thank you for your comment. We agree, gabapentinoids prescribed for epilepsy is excluded from the scope of this guideline. The scope has been edited to clarify this, rather than people having treatment for epilepsy The guideline will cover safe prescribing, monitoring and safe withdrawal of these medicines. Shared decision making is a principle that applies across all NICE guidelines. Shared decision making is covered by published NICE guidelines CG138 (Patient experience in adult NHS services), and by the scope of NICE guideline GID-NG10120 (Shared Decision Making; in development). This guideline will cross-refer to these NICE guidelines where appropriate.
Royal College of Physicians	General	General	The scope should have greater emphasis on what people taking prescribed medications associated with dependence/withdrawal can do for themselves to prevent problems with these medications, including:	Thank you for your comment. The specific interventions and approaches covered within the guideline will be agreed by the committee when agreeing the review protocols for the draft questions. These views will be taken into account when these

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			• How to reduce risk of dependence • How to taper or withdraw medications safely • How to access support and advice to facilitate taper or withdrawal • How to access comprehensive advice about alternative strategies for pain relief (vs medications associated with dependence/withdrawal) including the provision and role of pain management clinics.	discussions are held.
Royal College of Physicians	General	General	Following on from the above, there should be a clear expectation on the prescriber and/or expert clinical advisor advising on the use of these medications at the outset that a discussion has been had with the patient (and recorded) in relation to: • The aims of treatment • The reason for selection of the medication and indication that alternative strategies (eg for pain management) not available or failed • The duration of the treatment (is it short term or indefinite - if short term • duration should be stated and duration agreed) • The planned strategy to taper or withdraw the medication - where this is for short term use only and who will be the responsible clinician to oversee implementation	Thank you for your comment. This is intended to be covered within the draft review questions on information for people taking prescribed medicines associated with dependence or withdrawal symptoms, as well as methods for safe withdrawal.

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			This is touched on - on p 7, line 13 - but the scope is largely written from the perspective of the prescriber and greater recognition needs to be given to the fact that use of these medications is as a result of a partnership between the prescriber and the consumer/patient. The consumer/patient needs a greater level of knowledge and responsibility at every stage about the medications being prescribed their advantages/disadvantages and be encouraged to challenge the prescriber to seek alternatives/taper or withdraw at every medication renewal.	
Royal College of Physicians	General	General	Item 1.2 states 'What are the optimum prescribing strategies to limit the risk of dependence?'; Item 3.1 'What are the most clinically and cost effective pharmacological and non-pharmacological strategies, for example tapered withdrawal etc?' - Item 1.2 should mirror Item 3.1 and should also have non-pharmacological strategies to prevent development of dependence at the time of starting the drug (before they become dependent). This is because it may be too late for such strategies in Item 3.1 to fully work when the patient is already dependent and needs to face withdrawal.	Thank you for your comment. We agree that in some cases a non-pharmacological approach, or not prescribing the medicine may be an alternative appropriate option. However, this draft question does not include non-pharmacological strategies as other management options are covered within the condition specific guidelines. The questions in the scope are draft questions and the guideline committee may refine the wording during development and will also agree the protocol specifying in more detail the different strategies that will be included.
Royal College	General	General	The document refers to 'Dependence' as characterised by	Thank you for your comment. We are aware that there

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of Psychiatrists			tolerance and withdrawal symptoms. This could be understood as 'physiological' dependence, with the implication that managing the withdrawal symptoms is all that is required. We believe that the topic demands a full understanding of dependence as described in ICD-10/ICD-11 i.e. a syndrome where physiological features are only one element. In ICD-11 2 of the following 3 areas are required: *1. Impaired control over substance use i.e. onset, level, circumstances or termination of use, often accompanied by a subjective sensation of urge or craving to use the substance* *2. Substance use becomes an increasing priority in life such that its use takes precedence over other interests, daily activities, responsibilities or health or personal care. Substance use often continues despite the occurrence of problems* *3. Physiological features (i.e. neuroadaptation to the substance) as shown by (i) tolerance, (ii) withdrawal symptoms following cessation or reduction in use or (iii) repeated use of the substance to prevent or alleviate withdrawal symptoms* Failure to understand the psychological component of dependence will mean it will be very difficult to manage these cases.	are a number of differing definitions of dependence. The scope introduction is intended to briefly set out the background to the topic and therefore a concise definition has been provided here. Specific details of the population and condition included in the reviews will be agreed by the committee and included in the protocols.
Royal College of Psychiatrists	003	022	Groups covered should include (i) children and adolescents and (ii) those with learning disability	Thank you for your comment. We acknowledge that there are equally important issues in children and young people. However, many of these medicines are

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				not licenced in people under 18 years old and there are specific considerations in this population which cannot be adequately addressed within a single guideline. The equality impact assessment details groups that have been raised as important to consider within the guideline, which includes people with learning difficulties. However, it is not thought that guidance should differ in terms of the general principles in this group. Therefore they are not listed as a group needing specific consideration. The guideline committee will specify subgroups which need to be considered for each individual question during development of the protocols.
Royal College of Psychiatrists	003	024	Should include antipsychotics and ADHD medications	Thank you for your comment. Antipsychotics and ADHD have not been included within the scope of the guideline. These medicines are prescribed for very specific defined conditions by specialists and guidance on their safe prescribing, monitoring and withdrawal is included within the NICE guideline for psychosis and schizophrenia in adults CG178 and Attention deficit hyperactivity disorder: diagnosis and management (NG87).

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Royal College of Psychiatrists	004	015	'Structured medication review' strategies may need to be considered to identify risk-benefit appraisal of continuation of medications (Reference: JAMA Network Open 2018; 1(6):e183750).	Thank you for your comment. This will be considered when the evidence review is undertaken.
Royal College of Psychiatrists	007	009	This section refers to pharmacological *and* non-pharmacological strategies, however the only example given is a pharmacological one i.e. weaning. There is a risk that non-pharmacological strategies are side-lined and so this section should explicitly include holistic assessment, social prescribing and psycho-social support and interventions.	Thank you for your comment. We have added support as an example to the question for clarity as suggested.
Royal College of Psychiatrists	007	022	Given the risk to a multi-morbid population which will include those at risk for cognitive impairment we recommend that consideration is given to the inclusion of measures of cognitive function and functional ability.	Thank you for your comment. The list of outcomes in the scope is intended as a suggestion of those that will be in the majority of the questions covered. These will be discussed by the guideline committee during protocol development and additional outcomes will be added as required.
South Gloucestershire Council- Public Health and Wellbeing	General	General	GPs would love time to review everyone on painkillers, gabapentinoids, z drugs and antidepressants and spend the time [redacted] (a worker involved in a project to identify alternatives to opioid prescriptions) spent exploring and supporting but are pretty flat out mostly firefighting the front line of acute illness. I'm concerned the guidelines may become a burden and allow a finger	Thank you for your comment. We are sympathetic to the workload of GPs and feasibility and impact of recommendations will be taken into account in the development of the guideline.

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			point of blame to be at the GPs door not the patient who takes them. (South Gloucestershire GP)	
South Gloucestershire Council-Public Health and Wellbeing	General	General	So lots to do to get better and avoid us being another USA, we are hopefully not at a similar opioid epidemic quite yet, in general a good thing but hopefully the guidelines will give us a sensible time line to begin to sort opioid problematic use/prescribing.	Thank you for your comment.
South Gloucestershire Council-Public Health and Wellbeing	003	022	We (GP's/prescribers) do need to be more proactive in limiting script duration for pain killers and not just repeating them on request, we do need to review antidepressant prescribing and use a social prescription first line when treating life misery rather than true biological depression.	Thank you for your comment. The draft review questions included in the scope of the guideline intend to cover the issues you have highlighted.
South Gloucestershire Council-Public Health and Wellbeing	003	025	2 cohorts to think about: People already in a mess with whatever drug they now take because withdrawal is too painful, New people who we can warn and control prescribing from the outset. The low hanging fruit are the new people and the tree is quite tall and difficult to climb for the others mostly	Thank you for your comment. These issues will be highlighted to the committee when developing the guideline.
South Gloucestershire Council-Public Health	004	010	So the guidelines may become a burden and allow a finger point of blame to be at the GPs door not the patient who takes them.	Thank you for your comment. The committee will take into account the feasibility and implementation issues when drafting recommendations. The intention is to provide guidance on best recommended approach,

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and Wellbeing				not to apportion blame.
South Gloucestershire Council- Public Health and Wellbeing	007	009	Pharmacological withdrawal in the community will need to be reviewed as a part of these strategies. Consideration of who the client resides with, as well as the length of the tapering of the withdrawal.	Thank you for your comment. Draft review question 3.1 is intended to look at a broad range of withdrawal methods in all settings where the guideline applies (including in the community). The details of what will be included in this review will be agreed by the committee when discussing the protocol for this question, your comments will be taken into account when this discussion takes place.
South Gloucestershire Council- Public Health and Wellbeing	007	010	The non-pharmacological elements of consideration will vary depending on the areas of residence and service availability or will the guidelines list a variety in order for local PH teams to consider commissioning.	Thank you for your comment.
South Gloucestershire Council- Public Health and Wellbeing	007	015	When will this information be issued- at the time of first prescription/on a regular basis (monthly/bi-annually/yearly). If patients are presenting with pain and being prescribed benzo's/Z-Drugs or Opioids, will they worry about addiction at the beginning of their treatment if they are presenting whilst in pain.	Thank you for your comment. The scope and draft review questions cover the time of first prescription (or when considering prescribing these medicines) as well as their ongoing monitoring.The question on information required is intended to cover all stages in the person's treatment.
The Cranstoun Group	General	General	There is no mention of appropriate 'social prescribing' or psychosocial interventions to complement the pharmacological interventions offered.	Thank you for your comment. The guideline will cross-refer to condition specific NICE guidelines for the appropriate non-pharmacological options for treatment of the individual indications. Once the decision has

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				been made to prescribe one of these medicines, question 1.2 of this guideline will cover non-pharmacological strategies to limit the risk of dependence. Question 3.1 will cover non-pharmacological strategies to aid withdrawal. The specific non-pharmacological interventions considered will be agreed by the guideline committee when agreeing the review protocol. Your comment will be taken into account when we do so.
The Cranstoun Group	002	004	ICD classification of dependence specifies a number of criteria of which physical tolerance and withdrawal phenomena is only one, it is therefore possible to be dependent without this	Thank you for your comment. We are aware that there are a number of differing definitions of dependence. The scope introduction is intended to briefly set out the background to the topic and therefore a concise definition has been provided here. Specific details of the population and condition included in the reviews will be agreed by the committee and included in the protocols.
The Cranstoun Group	002	015	Could this be a reflection of the ageing population?	Thank you for your comment. That is a possible rationale, however this section is just intended to set the scene and we have not added our interpretation of the data.
The Cranstoun Group	003	025	In view of the well documented/ publicized ageing population, should the draft scope not include 'older adults' as a specific subgroup needing specific consideration?	Thank you for your comment. The equality impact assessment details groups that have been raised as important to consider within the guideline, which

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				includes people with multimorbidity and frailty (associated with, but not limited to older adults). However, it is not thought that the recommendations should differ in terms of the general principles in this group. Therefore they are not listed as a group needing specific consideration. The guideline committee will specify subgroups which need to be considered for each individual question during development of the protocols.
Turning Point	001	004 - 006	The scope does not include the use of Over-The-Counter (OTC) medication particularly combination opioid formulations such as co-codamol. We feel this should be included in the scope as this is a significant cohort of clients who can often present with significant physical health problems often associated with misuse of the OTC medication and mental health problems which expert opinion suggests may be a contributory factor to misuse of the medication. This should be reflected throughout the document if it was included.	Thank you for your comment. We acknowledge that some of the medicines included in the guideline may be obtained over the counter or via the internet and if these people seek help from relevant services, this guideline would apply. The scope has been edited to reflect this.
Turning Point	002	004 - 006	The definition of dependence is limited. Do NICE want to consider the more comprehensive definition from the ICD-10 which also takes into account the psychological elements of dependence?	Thank you for your comment. We are aware that there are a number of differing definitions of dependence. The scope introduction is intended to briefly set out the background to the topic and therefore a concise definition has been provided here. Specific details of the population and condition included in the reviews

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				will be agreed by the committee and included in the protocols.
Turning Point	002	001 - 003	We feel that a lack of review by a prescriber should be added to this section. Part of the scope is to review the "optimal frequency of review of prescribed medicines" and as this is recognised as an issue with continuation of a prescribed medication NICE should consider highlighting this early in the document.	Thank you for your comment. Monitoring is included as a key area within the scope and the frequency and content of the monitoring reviews will be considered, thereby recognising that review is required.
Turning Point	004	001	Add "People taking OTC medication" if NICE choose not to look at this area of dependence	Thank you for your comment. We acknowledge that some of the medicines included in the guideline may be obtained over the counter or via the internet and if these people seek help from relevant services, this guideline would apply. The scope has been edited to reflect this.
Warwick Clinical Trial Unit, University of Warwick	General	General	1. Are there any cost saving interventions or examples of innovative approaches that should be considered for inclusion in this guideline? We are currently running a large randomised controlled trial (Improving the Wellbeing of Opioid Treated Chronic Pain) the I-WOTCH study. This is a study funded by the National Institute of Health Research, Health Technology Assessment. We are testing the effectiveness and cost effectiveness of a complex intervention aimed at helping people taper of their opioids against best usual care (a self-help booklet and relaxation CD). The intervention	Thank you for your comment. For all the areas listed in the scope, the guideline committee will discuss and refine more detailed review protocols which will be used to search for and review the available evidence. The guideline committee will consider both clinical and cost effectiveness evidence for each question.

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			involves a combination of group and one to one support with trained staff. We have developed a facilitator manual as well as training package for staff. We have also developed a tapering App to generate a tapering plan during the one to one consultations. The intervention draws on a behaviour change and self-management framework with cognitive behavioural approaches, motivational interviewing and opioid and pain education. We will be completing a full health economic costing model. We have recruited 608 people into the trial from the Midlands and North East of England and now in follow up stage (which is due to end in Feb 2020). Results of this study will be available in late 2020. However in developing the intervention we have drawn o current evidence and consulted with lay people (those that have chronic non-malignant pain and experience of opioid use and opioid tapering). Details of the study can be found at: https://warwick.ac.uk/fac/sci/med/research/ctu/trials/iwotch	
Warwick Clinical Trial Unit, University of Warwick	General	General	We would like to raise the point about alternative services and what should be available for people with selected disorders who might otherwise have a first repeat prescription for these medications. Could there be more scope to look at prevention? This might include individual and population initiatives. When we are considering alternative services, we may also need to be mindful of the access to such services.	Thank you for your comment. The guideline will cross-refer to condition specific NICE guidelines for the appropriate alternatives which may be considered prior to prescribing these medicines for the individual indications. Once the decision has been made to consider prescribing one of these medicines, question 1.2 of this guideline will cover safe prescribing strategies to limit the risk of dependence, and

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				question 4.1 will cover the information required with the intention of preventing dependence.
Warwick Clinical Trial Unit, University of Warwick	General	General	It may also be useful to consider what is meant by an appropriate drug trial and more importantly monitoring the response to provide appropriate action.	Thank you for your comment. Question 1.2 is intended to cover prescribing strategies, which may include trials for a short duration. This will be considered by the committee when agreeing the review protocol. Section 2 will also cover monitoring of thee medicines.
Warwick Clinical Trial Unit, University of Warwick	007	013	Information for people – could we broaden this to also include information for family members/carers etc – so beyond just the individual as often the social network is important.	Thank you for your comment. Information for family and carers will also be considered under question 4.1, this has been reworded to clarify.

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